।पशुधनं नित्यं सर्वलोकोपकारकम्।

XXIII Annual Conference of

Indian Society of Veterinary Pharmacology and Toxicology

and

National Symposia on

"Integrated Animal Health Care System: Opportunities and Challenges"

and

"Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective"

November 02–04, 2023

COMPENDIUM

INVITED PAPERS AND ABSTRACTS

Organized by

Department of Veterinary Pharmacology and Toxicology

College of Veterinary and Animal Science, Bikaner

Rajasthan University of Veterinary and Animal Sciences, Bikaner, Rajasthan

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ISVPT-2023

XXIII Annual Conference of
Indian Society of Veterinary Pharmacology and Toxicology
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Department of Veterinary Pharmacology and Toxicology
College of Veterinary and Animal Science, Bikaner
Rajasthan University of Veterinary and Animal Sciences
Bikaner, Rajasthan

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Title	:	**Compendium of Invited Papers and Abstracts of XXIII Annual Conference of ISVPT and National Symposia on "Integrated Animal Health Care Systems- Opportunities and Challenges" and "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective".**
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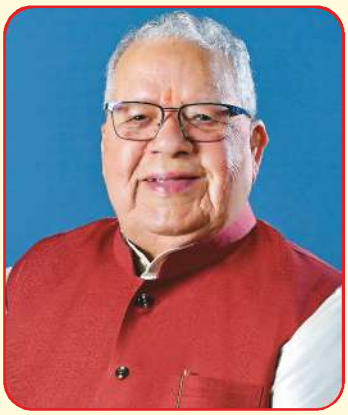

कलराज मिश्र
राज्यपाल, राजस्थान

सत्यमेव जयते

कलराज मिश्र
राज्यपाल, राजस्थान

सन्देश

मुझे यह जानकर प्रसन्नता हुई है कि राजस्थान पशु चिकित्सा एवं पशु विज्ञान विश्वविद्यालय, बीकानेर द्वारा 'इण्डियन सोसायटी ऑफ वेटरनरी फारमोकोलॉजी एण्ड टोक्सिकोलॉजी के 23वें राष्ट्रीय सम्मेलन' पर स्मारिका का प्रकाशन किया जा रहा है।

पशु चिकित्सा एवं पशु स्वास्थ्य विज्ञान के साथ आधुनिक दृष्टि से पशुधन संरक्षण के आलोक में यह राष्ट्रीय सम्मेलन विमर्श की नई राहें खोलेगा, ऐसा विश्वास है। मैं चाहता हूं इसमे भाग लेने वाले पशु चिकित्सा एवं विज्ञान से जुड़े विशेषज्ञ भारतीय संदर्भों में पशु चिकित्सा एवं स्वास्थ्य के गहन मंथन से वेटरनरी क्षेत्र में भविष्य की विकास से जुड़ी दृष्टि का सृजन करें।

आपके इस सम्मेलन में देशभर से आने वाले पशु चिकित्सकों, वैज्ञानिकों का राजस्थान में अभिनंदन और स्वागत है।

मेरी इस सम्मेलन की सफलता के लिए हार्दिक शुभकामनाएं हैं।

कलराज मिश्र

(कलराज मिश्र)

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सत्यमेव जयते

मुख्य मंत्री
राजस्थान

मुम./सन्देश/ओएसडीएफ/2023
जयपुर, 09 अक्टूबर, 2023

सन्देश

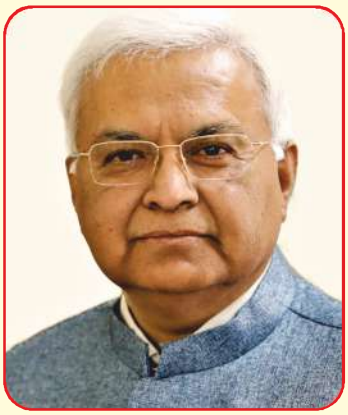
मुझे यह जानकर प्रसन्नता है कि राजस्थान पशुचिकित्सा और पशु विज्ञान विश्वविद्यालय, बीकानेर और इंडियन सोसायटी ऑफ वेटरनरी फारमोकोलॉजी एंड टोक्सिकोलॉजी के संयुक्त तत्वावधान में सोसायटी के 23वें वार्षिक सम्मेलन का 2 से 4 नवम्बर, 2023 तक आयोजन और इस अवसर पर स्मारिका का प्रकाशन किया जा रहा है।

''एकीकृत पशु स्वास्थ्य देखभाल प्रणाली, अवसर, चुनातियां और रोजगार'' के परिप्रेक्ष्य में फारमोकोलॉजी और टोक्सिकोलॉजी के क्षेत्र में नवीनतम ज्ञान, अनुभव और तकनीकों पर विचार–विमर्श के लिए ऐसे सम्मेलन अपने आप में महत्वपूर्ण हैं। इससे पशु चिकित्सा के क्षेत्र में सेवारत नई पीढ़ी को सही दिशाबोध होता है।

आशा है इस सम्मेलन में विषय विशेषज्ञों के विचार और निष्कर्ष पशुचिकित्सा और पशु विज्ञान की नई पीढ़ी का ज्ञानवर्द्धन करने की दृष्टि से सार्थक सिद्ध होंगे।

मैं सम्मेलन में शामिल सभी विषय विशेषज्ञों का स्वागत करते हुए इस आयोजन और स्मारिका के प्रकाशन की सफलता के लिए अपनी हार्दिक शुभकामनाएं प्रेषित करता हूं।

(अशोक गहलोत)



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MESSAGE

I am pleased to learn that Rajasthan University of Veterinary and Animal Sciences, Bikaner, will host the 23rd Annual Conference of the Indian Society of Veterinary Pharmacology and Toxicology from November 2-4, 2023, along with symposia on "Integrated Animal Health Systems - Opportunities and Challenges" and "New Directions for Pharmacologists and Toxicologists from an Employability Perspective." The theme of the conference seems very apt considering the use of synthetic drugs in the treatment of human and animal health and the adverse effects associated with them.

I am sure that the scientific deliberations during the conference and symposia will be very fruitful in advancing and promoting the application of the health-care management system not only in the treatment of human diseases, but also in animal diseases. The theme of the second symposium, which focused on student employability, seems to be in line with the goals of the National Education Policy 2020, which states that educators should design their education system to make scholars more professionally qualified and competent to pursue new avenues of employability by starting their own businesses or entering the private sector. I am certain that the recommendations of the conference and symposia will pave the way for necessary action the government and higher education levels.

I wish the conference a grand success.

(Sanjay Kumar)

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Prof. (Dr.) A.K. Srivastava
Vice-Chencellor

U.P. Pandit Deen Dayal Upadhyaya Pashu Chikitsa Vigyan Vishwavidyalaya Evam Go Anusandhan Sansthan (DUVASU), Mathura-281001 (U.P.)

MESSAGE

It gives me immense pleasure to know that Department of Veterinary Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner (Rajasthan) is organizing the XXIII Annual Conference of "Indian Society of Veterinary Pharmacology and Toxicology (ISVPT)" and National Symposia on "Integrated Animal Health Care System: Opportunities and Challenges" and "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective" from 02-04 November, 2023.

In India over 70 million households are directly dependent on Dairying for their livelihood. Among them 75% are small and marginal producers. Indian dairy sector is not only a contributor to National GDP (4.1-5%) and also 26-30% in agricultural GDP, but also has dignified the socio-economic status of farmers and establishing them as one of the bench marks in the progress of India. In India a loss of Rs. 1.5 Lakh Crore per year is due to animal health associated diseases, which must be checked so as to boost the economy of animal production. For this, there is an urgent need of wide coverage of vaccination for which adequate facilities need to be developed for vaccine production, storage and effective distribution. Further, lack of health integration across human, animal, plant, and environment shifts the health services to create a community based "One Health" approach. Therefore, now it has become imperative that to achieve the holistic development in the plethora of "One Health", integrated approach in biomedical sciences and judicious use of drugs, agrochemicals and feed additives are advocated on priority.

I am sure that this conference will provide a forum to students, academicians, researchers and industrialists to interact and involve in discussion for newer Research and Innovation. Such academic events immensely benefit the students, teachers and researchers to widen the horizons of their knowledge and to understand the newer field of research.

I give my best wishes to all delegates and organizing committee to make this event a grand success.

Srivastava.

(A.K. Srivastava)

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MESSAGE

It gives me immense pleasure that this year the Department of Veterinary Pharmacology and Toxicology, College of Veterinary and Animal Science, Rajasthan University of Veterinary and Animal Sciences, Bikaner, is organizing XXIII Annual Conference of Indian Society of Veterinary Pharmacology and Toxicology (ISVPT) and National symposia on "Integrated Animal Health Care System: Opportunities and Challenges" and "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective" during 2-4 November, 2023.

As one of the members and office bearers of ISVPT, I have personally attended many conferences. In the year 2017, Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar, organized its XVII annual conference.

Both the topics of the National Symposia are pertinent and right to be addressed in today's context. I hope that good recommendations shall come out of presentations, discussions, and conclusions drawn by an august gathering of academicians, researchers, and industry persons.

The technical sessions have been partitioned keeping in view the present thrust areas of research in the discipline.

We are all aware of the recently adopted revolutionary education policy in India named 'The National Education Policy-2020', which is a significant step towards transforming the Indian education system. The policy aims to make education more inclusive, equitable, and holistic. It focuses on the development of 21st-century skills such as critical thinking, creativity, and problem-solving. The objective is to give equal emphasis on all subjects-science, social sciences, art, languages, sports, mathematics - with integration of vocational and academic streams.

All the above issues require imperative solutions and I am sure that the symposia will address the skill gaps by bringing together experts from academia, industry, and government and discuss the skills and knowledge required for employability in the field of pharmacology and toxicology. This will certainly help in identifying such areas where training and education need to be improved to meet the demands of the job.

I congratulate the organizers and wish XXIII Annual Conference of ISVPT and National Symposia a grand success.

Prof. (Dr.) Vinod Kumar Verma

Prof. (Dr.) Satish K. Garg
Vice-Chancellor

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MESSAGE

I am delighted that Department of Veterinary Pharmacology and Toxicology, College of Veterinary and Animal Sciences, Rajasthan University of Veterinary and Animal Sciences, Bikaner and Indian Society of Veterinary Pharmacology and Toxicology (ISVPT) are jointly organizing the 23rd Annual Conference of ISVPT along with national symposia on National Symposia on "Integrated Animal Health Care System: Opportunities and Challenges" and "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective" on November 2-4, 2023.

Theme of the National Symposium on "Integrated Animal Health Care System: Opportunities and Challenges" seems very apt in view of the increasing concerns of human, animal and environmental health and emerging challenges due to antimicrobial resistance. UN Human Rights Council has declared access to a "clean, healthy and sustainable environment" a human right. Therefore, importance and necessity for immediate and effective measures for "One Health Mission" have increased many folds. Quality assurance of food of animal origin which is free from residues of drugs and agrochemicals is a very big challenge. Therefore, scientists should take up joint research projects on evaluating the efficacy and safety of not only allopathic drugs but also herbal and homeopathic drugs in treatment of animal diseases and make efforts to encourage and promote use of such drugs in veterinary clinical medicine.

The Indian Pharmaceutical industry is valued at around $50 billion and is expected to grow at a CAGR of 10.7% by 2030. The pharmaceutical market in India is expected to reach $65 billion by 2024 and $130 billion by 2030," while Indian CRO Market Size will be of worth USD 979.8 Million by 2030 with 7.50% CAGR. Therefore, I am very optimistic that the National symposium on "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective" will open new vistas for budding pharmacologists and toxicologists from their employability perspective in view of such potential and promising sectors. We should make efforts to customise our course curricula as per need of the industry.

I will be eager to see the recommendations emerging from the presentations of distinguished invited speakers and delegates and deliberations held during the scientific sessions. I welcome all the delegates who are attending this conference and wish you all a comfortable and memorable stay in "Chhoti-Kashi-Bikaner". I also convey my best wishes to the organizers for grand success of the 23rd Annual Conference of ISVPT.

Prof. (Dr.) Satish K. Garg

Dr. A. M. Thaker
President

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MESSAGE

It is pleasing to know that Department of Veterinary Pharmacology and Toxicology, College of Veterinary and Animal Science, RAJUVAS, Bikaner is organizing XXIII Annual Conference of Indian Society of Veterinary Pharmacology and Toxicology (ISVPT). Besides this National Symposia on "Integrated Animal Health Care System: Opportunities and Challenges" and "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective" are also arranged to commemorate the celebration of Platinum Jubilee Year of CVAS, Bikaner. It gives me immense pleasure to welcome all the distinguished guests and fellow delegates to historic city of Bikaner.

The society has crossed two decades and since establishment it is well engaged in providing a common platform to scientific communities and students along with industry personnel to discuss, deliberate and review the latest national and global advances in the pertinent subject of Veterinary Pharmacology and Toxicology (VPT). With the existence of 23 years, the society has 825+ life members, representing various streams of VPT and various disciplines of Veterinary Science. The society tries to fulfil its goals and mandates by organizing annual conference and national/international symposia and many times preconference workshops. The society regularly publishes its mouth piece 'Journal of Veterinary Pharmacology and Toxicology (JVPT)' along with post conference proceedings for dissemination of research findings for scientific community. To encourage/recognize young researchers the society has instituted various awards, honours and fellowships.

The topics selected by organizers for symposia are befitting in the present-day context as freshly graduating post graduates and doctorate candidates in our discipline today face tough time in getting suitable placement and hence condition like 'brain drain loss' impacts national productivity; a great loss to nation. The symposia will provide some solution or will bring awareness about newer areas to venture for livelihood and may bring up newer startups in our field. Looking to this, the organizers of this conference deserve big applaud and compliments.

I congratulate Dr. (Mrs.) Pratishtha Sharma and her team under visionary guidance of Prof. Satish K. Garg, Hon. Vice Chancellor of RAJUVAS for untiring efforts to make this conference scientifically fruitful and socially memorable.

Lastly my warm greetings to all and best wishes for grand success of the conference.

(Aswin M. Thaker)

Desk of Organizing Secretary.....

Dr. (Mrs.) Pratishtha Sharma
Organizing Secretary, ISVPT–2023
Department of Veterinary Pharmacology & Toxicology
CVAS, RAJUVAS, Bikaner

With the blessings of God Almighty who is most kind and merciful, the Department of Veterinary Pharmacology and Toxicology, College of Veterinary and Animal Science (CVAS), Rajasthan University of Veterinary and Animal Sciences (RAJUVAS), Bikaner, is organizing the 23rd Annual Conference of Indian Society of Veterinary Pharmacology and Toxicology during 2–4 November 2023.

It is a pleasant coincidence that the historical CVAS Bikaner is also observing its Platinum Jubilee Year. I am honoured to extend a very warm welcome to all the esteemed delegates from all over the country who have gathered here to keep abreast with the latest developments in the discipline.

Organizing a national conference, is always a big achievement and recognition for any Department. My sincere regards are due to Prof. (Dr.) Satish K. Garg, Hon'ble Vice-Chancellor, RAJUVAS, who believed in me and my department. He has been ever available since sending the proposal to ISVPT headquarters, guiding me to apply for grant-in-aid from funding organizations, and sharing his experience with me in every step I have taken. Few words shall not be sufficient to express my gratitude.

I am thankful to the Dean and Chairman Faculty, the University and college authorities for boosting our morale and supporting us. Special thanks to the president and office bearers of ISVPT headquarters for awarding us with the conference and providing necessary documents, guidance and support.

I am thankful to all the colleges and institutes under the umbrella of RAJUVAS for their wholehearted support and cooperation.

The financial assistance from all our sponsors under Govt. of India like, ICAR, SERB, NABARD, Union Bank of India, and our campus bank ICICI, is duly acknowledged and appreciated.

I express my sincere thanks to all the conveners and members of the local organizing committee, the departmental faculty, staff and students for their untiring support in making this event happen.

Last but not least, I wish to take this opportunity to thank those unsung heroes who diligently and sincerely worked behind the curtain to make this event a success.

(Pratishtha Sharma)

XXIII Annual Conference of
Indian Society of Veterinary Pharmacology and Toxicology

Dr. Pratishtha Sharma
Chief Editor

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ABOUT THE UNIVERSITY

The Rajasthan University of Veterinary and Animal Sciences (RAJUVAS), Bikaner came into existence on May 13th, 2010 to foster, cater and promote services in teaching, research and extension activities in the fields of Veterinary and Animal Sciences. The University has its expansion in most of the districts in Rajasthan with the vision to impart quality education to the students, to conduct need based research, generating new and suitable technology and further transferring to the stakeholders and ultimately to enhance the income of livestock owners and farmers through animal husbandry. The long term goal of the University is to train and produce skilled and competent human resources and to provide vital linkages with the concerned allied departments (eg animal husbandry, fisheries and dairy sector etc) on the national level.

The University is located in the royal heritage buildings of the erstwhile 'The Ganga Avenue' near Lalgarh Palace, spreading over in 200 acres of land in 1954. The main building 'The Bijey Bhavan Palace', a magnificent red sandstone architecture designed by Sir Swinton Jacob and built by Maharaja Ganga Singh as the residence of his son Prince Bijey Singh in 1927. Two other royal buildings, the 'State Museum' now known as 'Sadul Sadan' and the 'State Library' were built contemporarily over the years.

The University is having three running constituent Veterinary Colleges at Bikaner, Navania (Udaipur), and Jaipur. Keeping in view the major contribution of livestock sector in state economy, especially in the rural areas, during the last three financial years, the Government of Rajasthan sanctioned eight more new constituent Veterinary Colleges in the state which are coming up at Jodhpur, Nawan (Nagaur), Bharatpur, Kotputli, Bassi (Jaipur), Sirohi, Malsisar (Jhunjhunu), and Lalsot (Dausa). In 2021-22, the Government of Rajasthan also sanctioned College of Dairy Science and Technology, Bikaner, and College of Dairy and Food Technology, Bassi (Jaipur), thus the University has changed its functionality from single-stream to multi-disciplinary sectors.

The University has sixteen state government funded Pashu Vigyan Kendras (PVKs) spread over seventeen different districts of the state and one ICAR-funded Krishi Vigyan Kendra situated at Nohar (Hanumangarh). Through these PVKs and KVK, University has its outreach to majority of farmers and livestock owners of the state for extension activities and capacity building in the agriculture and animal husbandry sectors. University is maintaining the "Heritage Gene Bank" of six native cattle breeds and two native breeds of goats through its nine "Livestock Research Stations". It has seven constituent Animal Husbandry Diploma Programme (AHDP) Institutes, four affiliated Govt. AHDP Institutes, eight affiliated Private Veterinary Colleges and hundred private affiliated AHDP Institutes in its jurisdiction to achieve different mandate of the University.

ABOUT THE COLLEGE

College of Veterinary and Animal Science, Bikaner

The College of Veterinary & Animal Science was started in 1954 at Bikaner, the heart of the Great Thar Desert, keeping in view the importance of livestock in the rural economy of Rajasthan state. This year, it is observing the Platinum-Jubilee Year of establishment. It was started as a government college and named as the 'Rajasthan Veterinary College'. Over years, College of veterinary and animal science, Bikaner came into existence as a separate entity under Rajasthan University of Veterinary and Animal Sciences (RAJUVAS), Bikaner in May 2010, under subsection (3) of section 1 of the Rajasthan University of Veterinary and Animal Sciences Act, 2010.

The college campus is housed in the lush greenery, which spreads in an area of about 200 acres under erstwhile 'Ganga Avenue' consisting the main building 'Bijey Bhawan'. It has 17 well established departments with well-equipped laboratories having basic as well as sophisticated state-of-art facilities. Moreover, every department is equipped with smart classroom to facilitate improved and quality teaching. The Library of the college is having more than 30,000 books, journals to cater updated knowledge to the students. Along with that, the college has examination halls with ample sitting arrangement for the students, a Veterinary Clinical Complex building with indoors, outdoors and outpatient treatment facility, an apex centre for diagnosing monitoring and for surveillance of the disease. Major clinical departments with richest clinical facilities like CT scan, ultra sonography, laparoscopy, dentistry, laser surgery etc are its asset. The college also has animal biotechnology laboratory, a radioisotope laboratory, computer facilities, LAN server, central instrumentation facility, animal house, canine welfare society, placement cell, internet facility and 24x7 days a week clinical and hospital facility, diagnostic laboratory, NCC (R&V) squadron unit, numerous research projects. Much emphasis is being given to the practical training to the students to prevent and treat the diseases.

The facilities for students are excellent in terms of boys' hostels, girls' hostels, spacious canteen and an elegant auditorium. The college is having ample student and faculty amenities. Ample space for playgrounds like football, hockey, basketball, tennis, volleyball, kabaddi, badminton, TT is there within the campus. Moreover, a branch of ICICI bank is also located within the college and a post-office nearby to the campus. The college is offering postgraduate and doctoral programmes in almost all disciplines thus ensuring higher education as well. Different schemes and research projects are also running in various disciplines of veterinary and animal health sector. The Directorate of Research (Veterinary and Animal Science), Extension education is also located within the campus.

The college is as of now offering four academic programmes namely Bachelor of Veterinary Science and Animal Husbandry (B.V.Sc. & A.H.), Master of Veterinary Science (M.V.Sc.), Doctor of Philosophy (Ph.D) and Animal Husbandry Diploma Programme (AHDP).

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XXIII Annual Conference of Indian Society of Veterinary Pharmacology and Toxicology and National Symposia on "Integrated Animal Health Care System: Opportunities and Challenges" and "Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective"

(November 02–04, 2023)

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XXIII Annual Conference of "Indian Society of Veterinary Pharmacology and Toxicology"
and
National Symposia on
"Integrated Animal Health Care Systems- Opportunities and Challenges"
and
"Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective"

November 02-04, 2023

Programme

Day 1 (02.11.2023)

Venue: Auditorium CVAS, Bikaner

Time	Events
8:30-9:30 AM	Breakfast (Faculty House) and registration (Auditorium)
9:30-11:45 AM	Inauguration
11:45- 12:00 AM	High Tea
12:00 - 12:45 PM	**Chellappa Memorial Oration :** Dr. Jyoti Misri, Former Principal Scientist, ICAR, New Delhi Chairperson: Prof. A.K. Srivastava, Mathura Co-Chairperson: Dr. M. J. Raja, Orathanadu Rapporteur: Dr. R. D. Varia, Navsari
12:45 - 1:30 PM	**Dr. M. Sabir Oration :** Prof. Prakas h V. Diwan, Former President, Indian Pharmacological Society, Belgaum Chairperson: Prof. Satish K. Garg, Bikaner Co-Chairperson: Prof. S.P.S. Saini, Ludhiana Rapporteur: Dr. V.N. Sarvaiya, Anand
1:30 -2:30 PM	Lunch (Faculty House)
2:30-4:45 PM	**Symposium Session I** **Integrated Animal Health Care Systems- Opportunities and Challenges** **Key note lecture:** 1. Dr. Debabrata Chanda, CIMAP-Lucknow 2. Dr. Anup Kalra, Ayurvet - Ghaziabad 3. Dr. D.U.Bawankule, CIMAP-Lucknow Chairperson: Prof. Vinod Kumar, Hisar Co-Chairperson: Dr. Vina y Kant, Hisar Rapporteur: Dr. Meemansha Sharma, Izatnagar, Bareilly

4:45 -5:15 PM	**Symposium Session II** **Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective** **Key note lecture** : Prof. Vyas M. Shingatgeri, Dean, School of Biosciences, APEEJAY Stya University, Gurugram Chairperson: Prof. A.M. Thaker, Anand Co-Chairperson: Dr. Vijeyta Tiwari, Hisar Rapporteur: Dr. H. B. Patel, Junagarh
Venue: Faculty House, CVAS, Bikaner	
5:15-6:15 PM	**Technical Session: Animal Welfare and Regulatory Pharmacology/Toxicology** **Lead Paper:** Prof. Vinod Kumar, VC, LUVAS, Hisar Chairperson: Dr. Anup Kalra, Ghaziabad Co-Chairperson: Dr. Soumen Choudhury, Mathura Rappoorteur: Dr. Aneesha V.A., Izatnagar, Bareilly
6:15-7:30 PM	General Body Meeting
7:30-8:30 PM	Cultural Evening (Auditorium)
8:30 PM onwards	Dinner (Front Lawn)

Day 2 (03.11.2023)

Time	Events
8:00-9:00 AM	Breakfast (Faculty House)
9:00-10:00 AM (Auditorium)	**Award session** **Dr. A. M. Thaker Young Scientist Award for Woman** Chairperson: Dr. Debabrata Chanda, Lucknow Co-Chairperson: Dr. G. K. Choudhary, Patna Rapporteur: Dr. Gaurav Gupta, Hisar
10:00- 10:40 AM (Auditorium)	**Award session** **Prof. V.V. Ranade Young Scientist Award** Chairperson: Prof. A.H. Ahmad, Pantnagar Co-Chairperson: Dr. Atul Prakash, Mathura Rapporteur: Dr. R. K. Yadav, Mathura
10:40 - 11:20 AM (Auditorium)	**Award session** **Dr. R. Natarajan Award** Chairperson: Prof. Usha Rani M, Rajendranagar Co-Chairperson: Dr. P. Mekala, Udumalpet Rapporteur: Dr. Vikrama Chakravarthi P, Udumalpet
11:20 -12:15 PM (Auditorium)	**Award session** **Dr. J. V. Anjaria Award** Chairperson: Prof. S. P. Singh, Pantnagar Co-Chairperson: Dr. Pallavi Bhardwaj, Palampur Rapporteur: Dr. R. Yogeswari, Namamkkal

Time	Events
12:15- 12:40 PM (Auditorium)	**Award session** **Intas Pharma Young Scientist Award** Chairperson: Prof. K. P. Mini, Puducherry Co-Chairperson: Dr. R. K. Nirala, Patna Rapporteur: Dr. Rishi Kant, Ayodhya
9:00-11:00 AM Surgery Department Seminar Hall, First Floor	**Technical Session: Ethnopharmacology** Chairperson: Prof. C. C. Barua, Guwahati Co-Chairperson: Dr. Nirbhay Kumar, Patna Rapporteur: Dr. P. S. Daundkar, Palampur
11:00 -12:00 PM Surgery Department Seminar Hall, First Floor	**Technical Session: Molecular and Neuropharmacology** **Lead Paper:** 1. Dr. T. U. Singh, Sr. Scientist, ICAR-IVRI, Izatnagar, Bareilly 2. Dr. Soumen Choudhury, AP, DUVASU,Mathura Chairperson: Dr. Dinesh Kumar, Noida Co-Chairperson: Dr. R. D. Singh, S.K. Nagar Rapporteur: Dr. Sakthi Priya M, Namakkal
9:00-10:30 AM (Faculty house)	**Technical Session: Toxicology of Xenobiotics** **Lead Paper:** 1. Prof. A. H. Ahmad, GBPUA&T, Pantnagar 2. Dr. Varun Ahuja, Head-Toxicology, Syngene International Ltd. Biocon Park, Bangalore Chairperson: Prof. S. K. Bhavsar, Anand Co-Chairperson: Dr. K. A. Sadariya, Anand Rapporteur: Dr. Sunil Hajare, Akola
10:30 -12:00 PM (Faculty house)	**Technical Session: Nutritional Pharmacology and Nutraceuticals** **Lead Paper:** Prof. A.K. Srivastava, VC, DUVASU, Mathura Chairperson: Dr. R. D. Rana, Sikar Co-Chairperson: Dr. K. Kanagarajadurai, Madurai Rapporteur: Dr. B. Rajendar, Rajendranagar
12:00- 1:30 PM (Department of Microbiology)	**POSTER SESSION**
1:30-2:30 PM	Lunch (Faculty House)
3:30PM	Visit to Raisar Village

Day 3 (04.11.2023)

Time	Events
8:00-9:00 AM	Breakfast (Faculty House)
9:00-10:00 AM (Auditorium)	**Technical Session: Pharmacokinetics/Toxicokinetics** **Lead Paper:** Prof. S. P. Singh, Dean, CVASc, GBPUA&T, Pantnagar Chairperson: Prof. N. K. Pankaj, Jammu Co-Chairperson: Dr. M. K. Lonare, Ludhiana Rapporteur: Dr. K. V. Venkata Rao, Rajendranagar
9:00-10:00 AM (Faculty house)	**Technical Session:Clinical Pharmacology and Toxicology** **Lead Paper:** Prof. S.P.S. Saini, GADVASU, Ludhiana Chairperson: Prof. D.U. Bawankule, Lucknow Co-Chairperson: Dr. C. M. Modi, S.K. Nagar Rapporteur: Dr. Anshuk Sharma, Izatnagar, Bareilly
10:00-11:00 AM (Auditorium)	**Technical Session: Antimicrobials and Antimicrobial Resistance** **Lead Paper:** 1. Prof. Rajesh Katoch , SKUAST-JAMMU 2. Dr. Nitin Bhatia, Excutive Director, Intas Animal Health, Ahmedabad Chairperson: Prof. S.P.S. Saini, Ludhiana Co-Chairperson: Dr. R. Aruna Devi, Chennai Rapporteur: Dr. B. Anilkumar, Rajendranagar
11:00-12:30 PM (Auditorium)	**Valedictory Function**
12:30 PM onwards	**Lunch (Faculty House)**

CONTENTS

।पशुधनं नित्यं सर्वलोकोपकारकम्।

ISVPT-2023

Chellappa Memorial Oration

Dr. Jyoti Misri

Former Principal Scientist, ICAR

AMR and Zoonoses Specialist

FAO, United Nations, New Delhi

Chairperson	:	**Prof. A. K. Srivastava**
Co-Chairperson	:	**Dr. M. J. Raja**
Rapporteur	:	**Dr. R. D. Varia**

CMO-01

ANTIMICROBIAL RESISTANCE IN LIVESTOCK SECTOR-AN INTEGRATED APPROACH FOR MITIGATION

Dr. Jyoti Misri
Former Principal Scientist, ICAR
AMR and Zoonoses Specialist
FAO, United Nations, New Delhi
Email : misrijyoti026@gmail.com

Antimicrobial resistance (AMR) is considered as one of the biggest threats to modern civilization which can jeopardize global health, economy, and human development. Life-threatening infections that were previously manageable are poised to be untreatable because of AMR. Without action, by 2050 the global economy may lose more than USD 6 trillion dollars annually because of AMR – nearly 4% of Gross Domestic Product (GDP). By 2030, 24 million more people may be forced into extreme poverty because of AMR. Consequences of AMR are more felt in low-income countries as the burden of infectious diseases makes these countries more vulnerable to hardships. This puts the achievement of Sustainable Development Goals in peril. Resistant bacteria cross borders: AMR is a global problem that requires a global 'One Health' solution and changes in agricultural production practices to help keep antimicrobials working.

Resistance is driven by a variety of factors that are complex, diverse, and cross-sectoral in nature. In addition to sharing the same habitat, humans and animals also share several infectious diseases that may have started in animals at some point during their evolution into humans. There are several ways in which resistant bacteria can spread across international borders, either through direct exposure or through the food chain and environmental transmission. The occurrence of AMR organisms and antimicrobial resistance genes (ARGs) are regularly reported from a variety of sources, including people, animals, food, plants, and the surrounding environment. Strengthening AMR and Antimicrobial usage (AMU) policies is just one of the many fronts that we need to address to proactively tackle AMR.

Significant changes in food intake because of increased population density may have been one of the driving forces behind the resistance. This is in addition to the global sanitation and water pollution concerns posed by sewage, manure runoff, and waste generated by pharmaceutical manufacturing and hospitals. Addressing the rising threat of AMR requires a holistic and multisectoral integrated (One Health) approach because antimicrobials used to treat various infectious diseases in animals may be the same or be like those used in humans.

The Food and Agriculture Organization (FAO), the World Organization for Animal Health (OIE), and the World Health Organization (WHO), the Tripartite partnership, take collective action to minimize the emergence and spread of AMR. A Global Action Plan (GAP) on AMR has been supported with a strategic action plan on AMR. The 'Tripartite partnership' has been leading the global campaign on AMR and initiated country self-assessments on AMR to monitor progress with implementing their National Action Plan (NAP) on AMR (WHO, 2017), and it encourages a multi-sectoral involvement. The United Nations General Assembly (UNGA) has recognized AMR as a global priority health issue. It is an unprecedented move, as AMR became just the fourth global health issue that the UNGA formally addressed.

The FAO is at the forefront of the campaign to mitigate AMR, especially in the food and agriculture sectors. It is leading in assisting member countries in the development of their National Action Plans (NAPs) and implementing innovative public awareness and surveillance approaches in livestock production, aquaculture, and crop farming. One of the key focus areas of the FAO action plan on AMR is strengthening governance related to antimicrobial use and AMR in food and agriculture. There are challenges in addressing AMR through government policies because of limited political commitment, low awareness, and weak engagement among stakeholders. Often institutions have limited capacity to implement policies because of limited technical capacity and constraints in financial resources. If ignored, the AMR would cost the worldwide market USD100 trillion within the equivalent time frame. As a result of drug resistance, antibiotics and other antimicrobial agents become ineffective and infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness and death. FAO has an on-the-ground network in more than 150 countries. The Organization also has wide expertise in a variety of disciplines, including aquatic and terrestrial animal health, welfare, and production; food and feed safety; crop production and protection; water and land stewardship; legal affairs, communication, and behavior change; surveillance and more. In accordance with its mandate, FAO plays an essential role in supporting governments, producers, and other stakeholder groups to use antimicrobials responsibly to keep antimicrobials working and to protect food and agriculture sectors from the harms of AMR.

FAO is working in towards the goal of building resilience in the food and agriculture sectors by limiting the emergence and spread of AMR depends on controlling AMR effectively as a shared responsibility among livestock and aquaculture farmers, prescribers and policymakers in food and agriculture – as well as other sectors. Preventive action will provide an economic benefit, especially when compared to the considerable percent of GDP expected to be lost if AMR is permitted to develop into a global emergency through the widespread failure of medicines as it impacts many sustainable development goals (SDG's).

The availability and use of effective antimicrobials is essential for the health and welfare of terrestrial and aquatic animals' production. So, the miracle therapy of antimicrobials should mandatorily be used judiciously. The rise of drug-resistant pathogens threatens to undo more than a century's work of health progress and undermine the very foundation of modern medicine. For example, bacterial infections resistant to antibiotics could make vital medical procedures like organ transplants, joint replacements, cancer care, and care of preterm infants too dangerous to perform. AMR can affect anyone, of any age, in any country.

Antimicrobial resistance also affects and is affected by animals and the environment. The use of antimicrobials in animal health is driven by the large and growing burden of animal diseases, the increasing scale of animal production, and underinvestment in veterinary services and animal health. Reducing the inappropriate use of antimicrobials in animals must first address these underlying issues.

In 2015, countries adopted a Global Action Plan. Its first objective is improving awareness and understanding of AMR through effective communication, education, and training. Organizing a global annual awareness campaign was identified as an activity to contribute to this objective. Thus, an annual campaign was established to raise global awareness and understanding on AMR, while serving as an important example of One Health collaboration. This campaign was known as World Antimicrobial Awareness Week (WAAW). WAAW is celebrated from 18 to 24 November every year.

The overuse and misuse of antimicrobials in animal and aquatic animals are influenced by an interplay of factors. These serve as targets for action to address challenges ranging from: i) treatment failures driving

production losses and food insecurity; to ii) the impacts on human health. Once individuals become carriers of antimicrobial-resistant microorganisms, they can easily spread AMR among communities and across borders. AMR can also reach the general population by spilling over into agriculture products and the environment, contaminating waterways, wildlife, and soil. Given the global interconnected web of transmission, a multisectoral and multidisciplinary approach is critical to the success of NAPs for delivering on the Global Action Plan on AMR and FAOs own AMR Action Plan 2021-25 with an understanding that Globally we are only as protected as our most vulnerable members because resistant microbes cross borders.

Initiatives Taken in Animal and Fisheries Sector

FAO and its experts actively took part in shaping the NAP on AMR. India's NAP on AMR is a robust one which kept no stone unturned to make a sincere effort to resolve the problem which has already gripped the developing countries like ours. Surveillance and monitoring of AMR resistance form an integral part of the NAP, as does the antimicrobial usage.

The NAP warrants an evidence-based database on both AMU and the dynamics of AMR emerging in all the three sectors - human, agriculture, and environment; so that appropriate remedial measure may be taken in advance to extenuate the problem before it moves into a complete slugfest. The crux of the problem is gaining useful denominator data, particularly, in the livestock sector where a large section still relies on local quacks, pharmacists or unorganized veterinary practitioners. Although it is relatively easy to get data on AMU from the veterinary hospitals/ polyclinics where such records are being maintained on daily basis, it will be hard to get accurate information from unorganized sector particularly, at the local level. As the resistance rate of the common pathogens varies frequently over short distance or period, a nationwide surveillance programme is required - that too, using uniform Standard Operating Procedure (SOP) and sampling frame, to get meaningful data. Taking such consideration into account, ICAR with the support of FAO has started a network programme on AMR surveillance in food animals and aquaculture, the first of this kind in the world. In a FAO-ICAR collaborative meeting on establishment of a national network of veterinary laboratories for AMR held in Kolkata, India from 7-8 March 2017, this programme came into existence with the name INFAAR (Indian Network for Fishery and Animals Antimicrobial Resistance) with an aim to explore the resistance pattern of the indicator and pathogenic bacteria isolated from food animals and fishes. The operational mechanism for INFAAR was finalized on 14th July 2017, in Mumbai. Hence, there is an urgent need for systematic surveillance of AMR in fisheries, poultry and livestock sector with awareness campaign and incorporation of effective antimicrobial stewardship activities.

Scientific knowledge and science-based evidence are needed to identify and manage AMR risks before they become large-scale emergencies. India will benefit from surveillance and research to design programmes to minimize and contain AMR and monitor their effectiveness, as has been developed as INFAAR.

Stakeholders need to be enabled, empowered, and incentivized to transform awareness of AMR risks into action. Opportunities should be to boost profitability through more effective agriculture practices will also help to reduce the burden of infections and emergence of AMR. Training stakeholders through better guidance on responsible practices such as biosecurity and biosafety will help to prevent diseases, reducing the need for antimicrobials in animals and antimicrobial pesticides in plants. Equal access to expert advice, prescriptions, and appropriate antimicrobials, as well as AMR-relevant policies and legislation, will help tackle the challenge of antimicrobial misuse while also boosting production.

Support is needed for research and innovations in antimicrobials, alternatives, diagnostics, and production. The economic case for public and private investments can support resource mobilization to deliver effective national plans to curb AMR. Mainstreaming AMR into programmes for achieving the SDGs will help accelerate progress and boost resilience to health crises for global prosperity.

A One Health integrated response to AMR will help save millions of lives, preserve antimicrobials for generations, and secure the future from drug-resistant pathogens.

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ISVPT-2023

Prof. M. Sabir Oration

Prof. Prakash V Diwan

Expert Member, FSSAI

Former President

Indian Pharmacological society

Chairperson	:	**Prof. S. K. Garg**
Co-Chairperson	:	**Prof. S. P. S. Saini**
Rapporteur	:	**Dr. V. N. Sarvaiya**

MSO-01

EMBRACE PROFESSIONALISM: ADOPT TO CONQUER EMPLOYABILITY

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"Education is a manifestation of perfection already in man"- Swami Vivekanand.

A person willing to play the game with every intention to win and willing to accept defeat is Professional:" – Chinmai Swamy. According to Harward Business school: Your technical skills contribute only 15% to your success and soft skills contribute 85% towards your success.

You need 4C's in 21st century professional skills!!! A Critical thinking, Creativity, Collaboration and Communication skills are required to be successful as professional. Employability skills required are listening, communication, leadership, team work, problem solving, literacy, creativity, presentation, positive attitude and independence. Importance of focussing on studies, focus on follow one course, until successful.

Employability depends more on attitudes and "approaches" more than key skills, and on a central self-awareness and growth process as well as possessed "assets. If your employer can increase their reverence and profits using your skills & knowledge.

The concept of veterinary professionalism and how it relates to veterinary ethics is receiving increasing focus within educational and practice contexts. The veterinary profession aligns to the expectations of a classic profession: its members have a set of unique knowledge and skills and retain the privilege of self-regulation around codes of conduct.

The professionalism is one of the biggest factors in your career success. It might sound dramatic, but it's true! This trait affects every aspect of how you do your job. A lack of professionalism can cost you a job or promotion, and it can even put you first in line for a layoff.

Signs of professionalism are appropriate attire, strong communication skills, ethical actions, calm under stress, time management, digital literacy, initiative, time management, digital literacy, initiative. Academic low achievers need not necessarily end up being the same in a career. What is important is to identify/ignite passion towards a profession/career option, guide and support them towards learning the necessary skills, adapting and moulding their behaviour to become successful.

Veterinary professionals need to maintain currency with the rapidly expanding knowledge, techniques, and diagnostic skills available to the profession, while also accommodating the developing needs and expectations of clients and other veterinary stakeholders. Today, societal influence and expectations impose a heavy demand on veterinary practitioners, making it essential for tertiary veterinary education to equip veterinary graduates with the skills necessary to face these challenges and flourish in their profession. Veterinary professionalism remains in constant flux as societal influence and expectations have influenced the role of the veterinary practitioner. This has resulted in a continuous evolution of the skills required by practicing veterinarians to flourish in the profession. Health is wealth. To adopt professionalism, you must have sound health and be away from illegal drugs.

The value of sweet professionalism;

- Ice factory in head……. Keep cool even you are angry!
- Sugar factory in tongue…..Appreciate others, speak well.
- Knowledge factory in your brain…Share with others.
- The 4th Factory is Satisfactory!

Our satisfaction is measured by our own soul, mind & heart.

Learning and embracing professional behaviour is crucial to excelling in the workplace. Professionalism is the ability to be dependable, hardworking and respectful in a working environment. The characteristics of professionalism often include dressing appropriately, being respectful and staying positive.

Key Characteristics of Professionalism

"Your level of professionalism can make or break your career" Walker says. "Without it, you will never be taken seriously and you may even be looked over when it comes time to be considered for a promotion."

It's a sign of loyalty, dependability and responsibility lack of professionalism suggests a lack ofrespect towards an employer.

Do you have what employers are looking for?

Here are some attributes and habits you can use to develop professionalism in yourself: Modesty, Reliability Etiquette, Consideration, Neatness Work ethics Accountability, Organisation, Expertise and Integrity.

The demand and supply gap in talent

With the increasing gap between demand and supply, it is necessary that industry and academia work in tandem, just like in any other business – they form a "demand – supply – demand" chain or cycle. Also, creating awareness around career opportunities and options means to assess an individual's interests, educating them on the importance of setting goals and finally providing them an environment to pursue them. . This will reduce the excessive demand for typical unproductive university degrees and create talent pool that's passionate, skilled and productive. Also, the reasons for underperformance are multitude. I believe that there's no quick fix for this problem.

Technology is the key to bring about large scale changes. Young people are adept in using technology so we need to use it this tool to influence, educate, and create the necessary competitive spirit and fun filled environment to overcome these issues

We as a veterinary profession and as individual veterinarians within the profession must embrace the social, technological, and environmental disruption occurring in the world around us.

Veterinary professionals need to maintain currency with the rapidly expanding knowledge, techniques, and diagnostic skills available to the profession, while also accommodating the developing needs and expectations of clients and other veterinary stakeholders. Today, societal influence and expectations impose a heavy demand on veterinary practitioners, making it essential for tertiary veterinary education to equip veterinary graduates with the skills necessary to face these challenges and flourish in their profession. This paper explores four challenges faced by veterinary education in the development, maintenance, and upkeep of professional skills training: the divarication between employer expectations and veterinary education, the impact of demographic changes on the profession, the influence of institutional structures on the teaching of professionalism, and the risks associated with outdated models of professionalism training. The teaching of professionalism in veterinary education must continually evolve. One issue that may hinder this process is a divergence between the

expectations of employers and tertiary institutions regarding the employability skills required by veterinary graduates. Veterinary professionalism education must also consider changing demographics within the profession and within society to provide all new graduates with the skills and tools necessary to succeed in the workplace, establish a sustainable work–life balance, combat burnout in new graduates, and be equipped to serve the general public. Failure to do this could result in professionalism teaching becoming complicit in a socialization process that perpetuates gender and cultural inequalities. This paper outlines some ofthe changes that have occurred in the veterinary profession and their implications on veterinary professionalism education. The article champions the necessity for veterinary professionalism education to evolve in concert with the constant changes in the profession.

The identity of a veterinary professional is characterized by the need and the capacity to balance the components of the rapidly changing environment of medical knowledge, animal welfare, client and colleague communication, business finesse, and statutory obligations. Veterinary professionals must, therefore, maintain currency with the rapidly expanding knowledge, techniques, and diagnostic skills available to the profession and must also be able to manage these in the face of the developing needs and expectations of clients and other veterinary stakeholders. The ability to balance competing core values has come to lie at the very heart of contemporary healthcare professionalism such that it is now no longer sufficient for veterinary students to simply acquire the knowledge and technical skills necessary for practicing veterinary medicine. Nor is it sufficient for students to simply replicate the professional behaviors that will be expected of them as practitioners. Rather, professionalism education must ensure that students fully internalize its precepts into their own system of core values, attitudes, and tendencies and that these dictate their professional and ethical behavior

Furthermore, it is suggested that women veterinarians are at greater risk for the development of stress, anxiety, depression, compassion fatigue, and burnout than their male counterparts. These findings must, however, be interpreted with caution, as the risk factor may be related as much to age rather than to gender, with younger veterinarians more at risk for stress and burnout than older veterinarians. Veterinary professionalism remains in constant flux as societal influence and expectations have influenced the role of the veterinary practitioner. This has resulted in a continuous evolution of the skills required by practicing veterinarians to flourish in the profession. Clearly, veterinary professionalism education must evolve in concert with these constant changes in the profession.

Here are 12 ways you can develop and practice professionalism:

- Be productive.
- Use your time productively at work. Focus on your job responsibilities and avoid getting pulled into social media, web browsing and phone activity while on the clock.
- Develop a professional image.
- Project a professional presence and dress appropriately for your industry and organization. A good rule of thumb is to dress in the position you aspire to have.
- Take the initiative.
- Ask for more projects to be given to you or think of assignments that will meet your organization's goals. You don't want to be under-utilized.
- Maintain effective work habits.
- Prioritize, plan and manage your assignments and projects. Follow up and follow through with your supervisor and team members.

- Manage your time efficiently.
- Establish priorities, set goals and create action plans to meet deadlines.
- Demonstrate integrity.
- Be accountable for your work and actions while behaving ethically at all times.
- Provide excellence.
- Produce work and results that reflect a sense of pride and professionalism, often exceeding expectations.
- Be a problem-solver.
- When you run into problems and obstacles take the time to brainstorm a few solutions and alternatives before you meet with your supervisor.
- Be resilient.
- Develop coping skills to manage setbacks and challenges with a positive and constructive attitude.
- Communicate effectively.
- Practice professional on-line, in person and interpersonal communication skills.
- Develop self-awareness.
- Learn to manage your emotions and gain awareness of your emotional triggers so you can manage your reactions positively and productively. Accept and reflect on feedback to assist as you learn and grow.
- Build relationships.
- Network with colleagues, customers and clients to build professional cordial relationships, work on teams and collaborate effectively.

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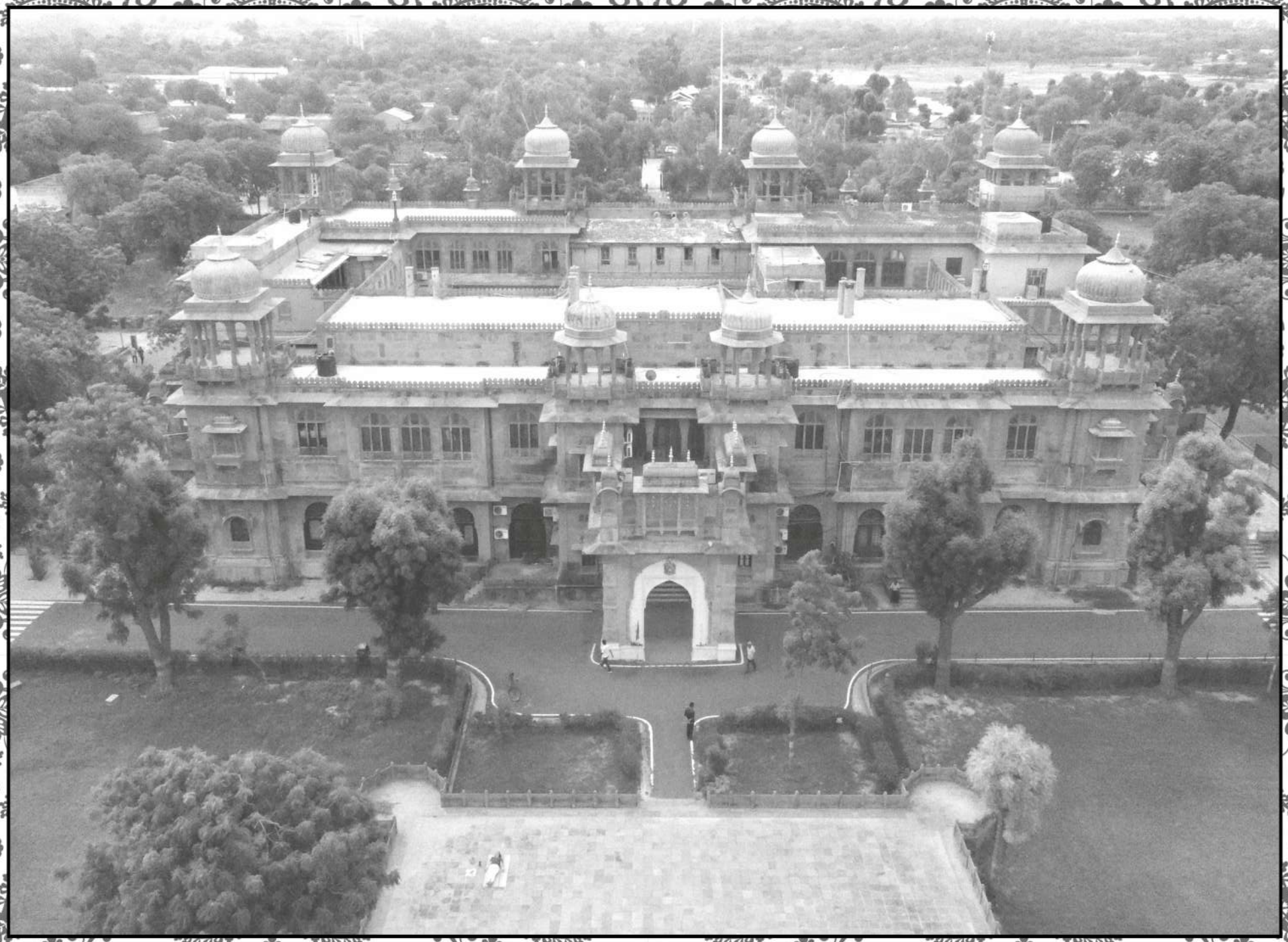
ISVPT-2023

SYMPOSIUM SESSION-I

National Symposia on
"Integrated Animal Health Care System : Opportunities and Challenges"

Chairperson	**:**	**Prof. Vinod Kumar**
Co-Chairperson	**:**	**Dr. Vinay Kant**
Rapporteur	**:**	**Dr. Meemansha Sharma**



KNL-01

APPLICATION OF INDUCIBLE PLURIPOTENT STEM CELLS (IPSC) TECHNOLOGY IN DRUG DISCOVERY AND DEVELOPMENT: A CASE STUDY WITH ACTIVATION AND DIFFERENTIATION OF IPSC INTO CARDIOMYOCYTES AND ITS POSSIBLE APPLICATION IN *IN-VITRO* AND *IN-VIVO* STUDIES

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Induced pluripotent stem cells (iPSCs) are a kind of stem cells generated from directly from regular somatic cells. Japanese workers Shinya Yamanaka and Kazutoshi Takahashi from Kyoto pioneered the science of iPSCs. They demonstrated in 2006 that introduction of four specific genes (namely Myc, Oct3/4, Sox2 and Klf4), collectively known as Yamanaka factors could convert somatic cells into pluripotent stem cells. This path breaking and landmark discovery earned Shinya Yamanaka Nobel Prize in 2012 along with Sir John Gurdon for the discovery of reprogramming matured cells into pluripotent stem cells. iPSC technique hold a great promise in regenerative medicine and drug discovery and development. iPSCs can be differentiated into more than 200 cell types including neurons, heart, pancreatic, liver cells etc. Experimentally they have been observed as a single source of cells that could be used to replace cells which were lost or damaged in a disease process. Before the immergence of iPSCs, embryonic stem cells were the most well known pluripotent stem cells explored for various therapeutic applications. However, ethical issues concerning destruction or manipulation of pre-implantation embryo drew many many controversy. On the contrary, iPSCs can be derived directly from adult tissues; thus bypassing the need for embryos, but can also be made in an immunologically patient-matched manner. iPSCs technology made it possible atleast experimentally for each individual having their own pluripotent stem cell line which can have therapeutic application for vast array of diseases ranging from cancer, CVDs, perkinsons and other neurological disorders where replacing the diseased or damaged cells/tissues can be planned using patient specific iPSCs. An attempt was made to differentiate iPSCs into beating cardiomyocytes using cardiomyocyte specific differentiation medium in view of its important role in drug discovery in cell based assay as well as its application as cell based therapy in MI and heart failure.

KNL-02

AYURVEDA AND ANIMAL HEALTH AND BETTER PRODUCTIVITY

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Ayurveda

Ayurveda (The Science of healthy living), a centuries old traditional Indian system of health care, is an evidence based science and one of the oldest medical discipline. A 5000 year old science, Ayurveda is a complete system which emphasizes living in harmony with the environment. Ayurveda is the synthesis of Ayur- meaning 'life' and Veda meaning – 'knowledge'. Ayurveda, the Science of Life , based on strong pillar of positive health, is a holistic approach to total healthcare by means of preventive & curative medicine to maintain complete internal-milieu (dhatusamaya), 'Homeo-stasis' or equilibrium of the various dhatus. It insists on the pro-host approach: "Strengthening the body defense system to fight infection". Ayurveda emphasizes mainly on prevention of illnesses and maintenance of health. Any deviation from dynamic state of internal milieu or homeostasis is disease. This term 'disease' includes sickness, illness, ill health, and malady.

Potential Role of Ayurveda & herbal nutraceuticals in Improving Livestock Health

Ayurvedic preparations incorporate ingredients derived from plant origin. The plant materials have been scientifically evaluated to testify the ancient wisdom blended with modern scientific precision & technology validating their usage for animal & human health care to achieve health, wellness & maximum productivity from livestock. Emergence of the resistant pathogenic strains against antibiotics & deadly chemicals coupled with ever-growing concerns of toxicity & environmental contamination has led to scientific & technological advancement in last few decades, reviving the interest of modern scientist & health care practitioners in herbals. Relevance of science of Ayurveda, as applied to animal health, can be traced back to *Mahabharata*.

Animal Nutrition plays very important role in our day to day lives for our health. The same is true for Livestock. Rather it is more important since it directly linked with efficient reproduction & milk production. Any deviation in digestive, reproductive or udder health directly affects the production of animals.

Scientific feeding is aimed towards fulfilling the physiological needs of animals and that is where balanced cattle feeding and compounded feeds play a significant role. The Herbaceuticals have been documented for improving the health & milk production when used along with proper feed. Ayurveda, the precious gift from Mother Nature is playing a significant role and likely to play greater role in future along with right nutrition. This would help in improving the overall health and welfare of the humanity.

Bioactive molecules derived from nature and referred to as botanicals, herbs, or phytogenic, which have a history of medicinal use, and animal feed applications. In recent years, the ban of in-feed antibiotics, which was implemented in Europe in January 2006, has driven research activities regarding the potential of plant extracts and essential oils as alternatives to antibiotic growth promoters. The potential benefits such as increased feed intake, stimulation of digestion and improved feed efficiency among others have therefore raised the

interest among animal nutritionists. However, it is not only in recent years that there were ideas around phytogenic in animal feed. In 1993, Ayurvet Limited took the steps of developing phytogenic/herbal feed additives for animals. Now, 30 years later and backed up by more than 750 research papers and trials, herbal feed additives are approaching a point where they are a standard ingredient or supplement in modern livestock ruminant and non-ruminant diets. Here we focus upon role of herbal feed additives in animal & poultry nutrition.

Role of Phytogenic and herbal feed additives

Feed additives depending on the specificity of function of additive improve the health, digestibility, productivity, product quality and immunity. It is scientifically established that inclusion of herbal feed additives to ration improves overall growth, performance and productivity of animals, enhances nutrient utilization and feed efficiency, possess immunopotentiating and antioxidant effect, improves gut microflora and also have antimicrobial activity.

Improves gut function. Improvement in gut function is mainly attributed to the possible stimulatory effect of phytogenic substances on digestive secretions, such as digestive enzymes, bile, and mucus. Phytogenic substances from certain herbs *viz. Aegle marmelos, Plantago ovata, Acacia catechu, Corriandrum sativum,* many more herbs and their extracts have also been shown to improve gut microflora and to exert pharmacologic actions within the digestive tract, as evidenced by their gut function-modulating efficacy (Satyavati and Gupta, 1987). Pathogenic bacteria are always present in the gut, but the balance between pathogenic and beneficial bacteria determines whether disease will occur or otherwise. Maintaining a healthy balance between all microfloras within the gut is known as eubiosis and can be influenced by bacteria endemic to the microflora (Kolte *et al.,* 2009). In the intestine, bacteria considered beneficial to the gut, including lactic acid forming bacteria like *Lactobacillus* spp, prevent proliferation of pathogens, such as *Salmonella* spp., through competitive exclusion for nutrients and for receptor sites on the gut wall. Beneficial bacteria can also produce an adverse environment for pathogenic bacteria to colonise and grow. For example, by the production of short-chain fatty acids, which lower the pH and prevent growth of pH sensitive pathogenic bacteria (Kolte *et al.,* 2009). The microflora also have functions in the development of the digestive and immune tissue in the host animal, can produce nutrients that can be used by the host as a nutrient source and also can neutralize some feed toxins and promote an environment in the gut where anti-nutritional factors and toxins are minimised. In the past, manipulation of the microflora to create eubiosis has been achieved by the use of antibiotic feed additives. However, with the severe restriction of antibiotic feed additive use in the EU and increasing consumer concern, alternatives to antibiotic feed additives have been investigated and found to significantly influence this balance also.

Increase feed intake: The stimulatory effect of herbal feed additives on feed intake is due to the claimed improvement in palatability of the diet resulting from the enhanced flavor and odor. The addition of certain herbs *viz. Woodfordia fruticosa, Zingiber officinale, Allium sativum, Trigonella foenum graecum etc.* to poultry and pig ration is also known to improve feed efficiency (Satyavati and Gupta, 1987). Increased palatability of the diets associated with the addition of phytogenics also may be due to their anti-oxidative effects, which might contribute to preserving the desired organoleptic qualities of the diet.

Digestive tonic and growth promoter: Digestion is critical and plays important role in nutrient utilization in monogastric and fermentation process in ruminants to produce volatile fatty acids and microbial proteins by the action of ruminal microflora. Role of ruminal microflora in digestion of nutrients is vital, so interactions of

the normal microbial flora with the host can be manipulated to improve the efficiency of nutrient utilization (Waghmare *et al.,* 2009). Supplementation of certain herbs that have property to modulate the rumen function may be supplemented to animals for efficient cellulose breakdown and digestion, maintenance of normal ruminoreticular function, intestinal movement, optimum utilization and absorption of nutrients, thus improving feed conversion ratio, productivity and body weight gain in animals. *Ruchamax*® is a potent herbal formulation, which contains 28 different herbs and some minerals. The ingredients of *Ruchamax*® include *Allium sativum*, *Azadirachta indica, Calotrophis orocera, Centratherum anthelmenticum, Commiphora mukul, Eclipta elba, Embelica ribes, Picorrhiza kurora, Zinziber officinale* and *Piper longum* etc. It is used as an appetizer, restorative, stomachic, digestive tonic & growth promoter product (Bhatt *et al.,* 2009 and Kolte *et al.,* 2009).

Hepatic Efficiency Enhancers: Supplementation of certain liver tonic preparations also help to increase the secretion and flow of bile for better digestion and to treat anorexia by maintaining the liver parenchyma in healthy state and regulating liver functions like detoxification of metabolic products, toxic drugs and chemicals, and treatment of hepatic dysfunction. The herbal ingredients such as *Andrographis paniculata, Eclipta alba, Picrorhiza kurroa, Phyllanthus niruri, Tephrosia purpurea, Tinospora cardifolia* and *Boerhavia diffusa* (Superliv® concentrate premix & Liquid) have been proved to improve feed conversion efficiency, body weight gain and reduce mortality in poultry and swine; owing to their Hepato-protective, Hepato-stimulants and growth promoting properties (Dwivedi et al., 1986).

Another example of polyherbal liver tonic & growth promoter product for cattle is Yakrifit®, comprising of herbs namely, *Andrographis paniculata, Eclipta alba, Picrorhiza kurroa, Phyllanthus niruri, Tephrosia purpurea, Tinospora cordifolia* and *Boerhaavia diffusa*, each with documented hepato-protective and hepato-stimulant properties. Yakrifit® has earlier been found to counteract hepatopathy and restore liver functions in bovines (Pradhan and Dey, 1996). Polyherbal liver tonic formulations also protect the hepatic parenchyma from various parasitic and liverfluke infestations such as visceral larvae migrans.

Anti-oxidant, Immunomodulator and antistress effect: Various stressors such as high ambient temperature and relative humidity influence the performance of animals and birds by reducing feed intake, feed efficiency, nutrient utilization and feed conversion ratio (Sahin et al., 2003). Various kinds of stressors such as physical, performance, environmental, disease or many more.

Ayurvedic formulas that treat stress contain herbs with adaptogenic (antistress) effects. Herbs with high antistress and antioxidant activity like amla (*Emblica officinalis*), ashwagandha (*Withania somnifera)*, tulsi (*Ocimum sanctum*), Shilajit and many more have proved to be potent oxygen free radical scavenger *in vitro* and *in vivo* models. Medicinal plants or herbs owing immunopotentiating properties can provide an alternative to conventional therapy for a variety of diseases, especially when the host's defense mechanism has to be activated under conditions of impaired immune response (Atal *et al.,* 1996).

Herbs namely *Mangifera indica, Echinacea purpurea, Phyllanthus emblica, Uncaria tomentosa, Withania somnifera, Ocimum sanctum, Tinospora cordifolia, Asparagus racemosus* and many more are scientifically validated to possess antistressor, immunostimulant or immunomodulator and adaptogenic properties. Mangiferin, active constituent of herb *Mangifera indica,* is a strong inducer of *in-vivo* and *in-vitro* activation of peritoneal macrophages. Induction of interferon release from macrophages by *Mangifera* has a potent lymphoproliferative effect on macrophage activation, thus establishing the therapeutic potential of *Mangifera* as a immunomodulator. Another herb; *Echinacea purpurea* is known to stimulate macrophages, but does not increase resistance to a wide variety of stressors (e.g., physiological stress). However, *Uncaria tomentosa* has

been shown to stimulate interleukin-1 and interleukin–6 in macrophages, stimulate endothelial cells to produce a lymphocyte proliferating regulating factor, and enhance recovery of leukopenia induced by doxorubicin. Similarly, *Withania somnifera* is well established to augment endogenous antioxidants, maintenance of myocardial antioxidant status, significant restoration of most haematobiochemical and oxidative stress marker parameters by its free radical scavenging activity in addition to potentiating agglutinin antibody titres and complement fixing antibodies (Ziauddin *et al,* 1996). The antioxidant potential of Methanolic extracts of *Ocimum sanctum* as studied by HPLC based hypoxanthine/xanthine oxidative assay indicated their prime role in free radical elimination, thus combating immunosuppression. It can be interpreted that the characteristic dysregulation of stress hormones and neurotransmitters, and the immunosupression thereby can be successfully ameliorated by the botanical adaptogenic remedies including either single herb or polyherbal formulation (Manoharan *et al.,* 2004). An example of such a polyherbal immunomodulator, adaptogenic & antistressor formualation is Stresroak®, scientifically validated in amelioration of various kind of stressors e.g. production, vaccination, overcrowding, water deprieviation, lead toxicity, cadmium toxicity and to potentiate immune response during different disease conditions eg. Infectious Bursal Disease, and New Castles Disease in poultry (Pradhan, 1995; Sujatha *et al.,* 2010).

Antimicrobial effect: The medicinal or antimicrobial properties of plant-derived substances have been well known for centuries. This property is mainly attributed to the essential oils of these plants namely *Trichyspermum ammi, Cinamonum camphora, Mentha piperita* & many more. *Oregano* and *thyme* are among those which have received a great deal of interest. These plants contain the monoterpenes carvacrol and thymol, respectively, and have demonstrated high efficacy *in-vitro* against several pathogens found in the intestinal tract. This suggests that phytogenic feed additives may be suitable replacements for in-feed antibiotics to improve health and growth performance, particularly during the first few weeks post weaning.

Toxin Binder: Aflatoxins have been found to reduce growth and feed efficiency, suppress immune system, reduce antibody titre and cause mortality and morbidity leading to severe economic losses to poultry farmers (Sakhare *et al.,* 2007). Synergistic action of herbal toxin binders (Toxiroak®) alongwith liver tonic formulations are scientifically well proven to improve growth, reduce mortality in broiler chickens by better protein and energy utilization by limiting the adverse effects of aflatoxins (Kalorey *et al.,* 2009). In addition to it, other polyherbal toxin binders namely Vilocym® and Vilocym Z® are popular in poultry industry, among farmers and veterinarians for control of mycotoxicosis.

Natural Methionine: Poultry feeding is one of the most important areas, since feed alone accounts for about 65-70 % cost of the total poultry enterprise. Protein synthesis in chicken is required at a very rapid pace for fast growing broilers and prolific layers and it is necessary that all essential amino acids are available through diet in right proportions. From the nutrition point of view, the amino acids that make up the protein are more important rather than the protein molecule itself. Methionine is required in free as well as conjugated form to perform various metabolic functions. It assists in the breakdown of fats and thereby prevents the build-up of fat in liver and arteries, as well as assisting the digestive system and removing heavy metals from the body since it can be converted to cysteine, which is a precursor to glutathione, which is of prime importance in detoxifying the liver. Its deficiency may manifest in symptoms like fatty liver, retarded growth, reduced feed efficiency, weakness, edema, skin lesions, poor feather condition, decreased egg production, small egg size, immuno-suppression, low carcass yield and disturbances in various metabolic pathways (Ramarao *et al.,* 2003). Improper conversion of methionine can lead to atherosclerosis. Most plants contain very little amounts of Methionine; however, some have significant amounts. High levels of methionine are found in fish, meats,

and some other plant seeds. Almost all feed ingredients of plant origin used for compounding poultry ration are deficient in methionine and hence DL-methionine is commonly added as supplement in poultry feeds. In the past, the requirement of amino acids of chickens used to be met from more than one sources of protein from plant and animal origin.

However, due to increase in prices of quality fish meal and availability of comparatively cheaper soybean meal, use of all soya feed started with addition of methionine as soybean meal is deficient in methionine which again is a costly supplement. In poultry ration, just like protein, the vitamins and minerals have equally important role in development of musculature. In the list of vitamins, choline (growth promoter) is playing vital role by acting as lipotropic agent, thereby preventing abnormal fatty infiltration in liver, thus ensuring proper metabolism of the body and effective utilization of nutrients (Kanchi *et al.,* 2009). Moreover, it helps in formation of an excitatory neurotransmitter acetylcholine, which is responsible for proper functioning of nervous system and maintains harmony. There is no consistency in the choline content in the natural feed stuffs and also their bioavailability is not predictable. Therefore, in broilers as well layers, choline in combination with chloride (CC) is added as an important feed ingredient.

However, herbal or natural products, which have proven results in various areas of poultry production, can be combined as a mixture and apremix can be prepared, which may be used in feed formulations. Supplementation of polyherbal formulations containing ingredient herbs that mimic methionine, choline and biotin like activity, namely Methiorep® & Repchol®, have scientifically well proven to prevent fatty liver syndrome and to improve overall carcass quality, yield and egg production in broilers (Kalbande *et al.,* 2009). These herbal amino acid supplements have an added advantage over harmful effects of synthetics, the use of which is totally prohibited in organic poultry production (Moritz *et al.,* 2005).

Conclusion:

The traditional system of medicines has stood the test of tie for over 4000 years and should not be considered as an alternate to the modern medicine; rather they complement and enhance the production of livestock. Since ancient times, herbs and their products are constantly used for curing illness. However, herbal additives have aroused much scientific interest over the past few years to explore their role as performance enhancers in livestock production. The cited instances in this text are just glimpses from the vast and virgin world of Ayurveda through the clear eye of modern science. It is upto our scientist and industry how best they use this precious gift from Mother Nature for health and welfare of livestock and in turn, humanity.

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KNL-03

ESSENTIAL OILS FOR HEALTHCARE: OPPORTUNITIES AND CHALLENGES

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Essential oils extracted from aromatic crops are concentrated lipophilic liquids containing aroma chemicals used in aromatherapy, pharmaceuticals, personal care products, and feed additives in poultry & ruminant nutrition apart from the flavour and fragrance agents. In general, aroma chemicals are natural or synthetic compounds that are used to enhance the smell of products. Aromatherapy is a complementary therapy that uses essential oils and other aroma chemicals to improve physical and emotional well-being. In pharmaceuticals, aroma chemicals can be used as flavouring agents or to mask unpleasant odours. In personal care products, aroma chemicals can be used to enhance the scent of soaps, lotions, and other products. In veterinary health care, essential oils/ aroma chemicals can be used as feed additives to enhance the growth of livestock/improve the gut immunity as well as it can be applied topically on the skin to alleviate skin diseases. As per the market analysis report, the global aroma chemicals market size was valued at USD 5.35 billion in 2021 and is expected to expand at a compound annual growth rate (CAGR) of 4.1% from 2022 to 2030. Aroma chemicals are witnessing an increase in demand owing to the growing application scope in key end-use industries such as dairy, poultry, human health and cosmetics are the major factors driving the growth of the aroma industry.

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ISVPT-2023

SYMPOSIUM SESSION-II

National Symposia on
"Exploring New Avenues for Pharmacologists and Toxicologists from Employability Perspective"

Chairperson	**:**	**Prof. A. M. Thaker**
Co-Chairperson	**:**	**Dr. Vijeyta Tiwari**
Rapporteur	**:**	**Dr. H. B. Patel**


संविधान पार्क

KNL-01

EXPLORING CAREER PROSPECTS IN VETERINARY PHARMACOLOGY AND TOXICOLOGY- UNLOCKING EMPLOYABLE PERSPECTIVES

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Veterinary pharmacology and toxicology are being increasingly recognized as important disciplines and have been rapidly changing and evolving being the translational sciences. Pharmacology translates fundamental insights into drug action and fate into clinical therapy. Toxicology translates science, transferring knowledge from fundamental science into practical applications to safeguard animal health, human health, and the environment. Those who completes their master's degree in this subject are considered to be having a greater insight in translational sciences that uses basic and clinical science to address the multiple issues that arise during drug discovery and development, development of agrochemicals and materials (medical devices). Veterinary Pharmacology and toxicology are contributing to a great extent in reducing the risk at animal-human ecosystem interface. Thus, a Master's in Veterinary Pharmacology and Toxicology offers a diverse skill set that extends far beyond the traditional boundaries of veterinary practice. Graduates of this program are poised to explore a multitude of emerging opportunities that align with their expertise in Pharmacodynamics and Pharmacokinetics, drug interactions, animal health, and safety. Therefore, the scope and employability prospects for these graduates is wide and diverse and hence their expertise is invaluable in Pharmaceutical Industry, Clinical Research, Contract Research Organizations (CROs), Pharmacovigilance, Regulatory Affairs, Marketing, Business development, Academia and Research & are well equipped to start on their own. While undergoing their curriculum if they delve in learning and acquiring the necessary skillset in crafting disease models, developing personalized avatar models, and integrating artificial intelligence (AI) will certainly pave the way for an array of employable opportunities. In a rapidly evolving world where holistic health, precision medicine, and AI-driven advancements are paramount, graduates in Veterinary Pharmacology and Toxicology emerge as versatile professionals primed for dynamic and rewarding careers.

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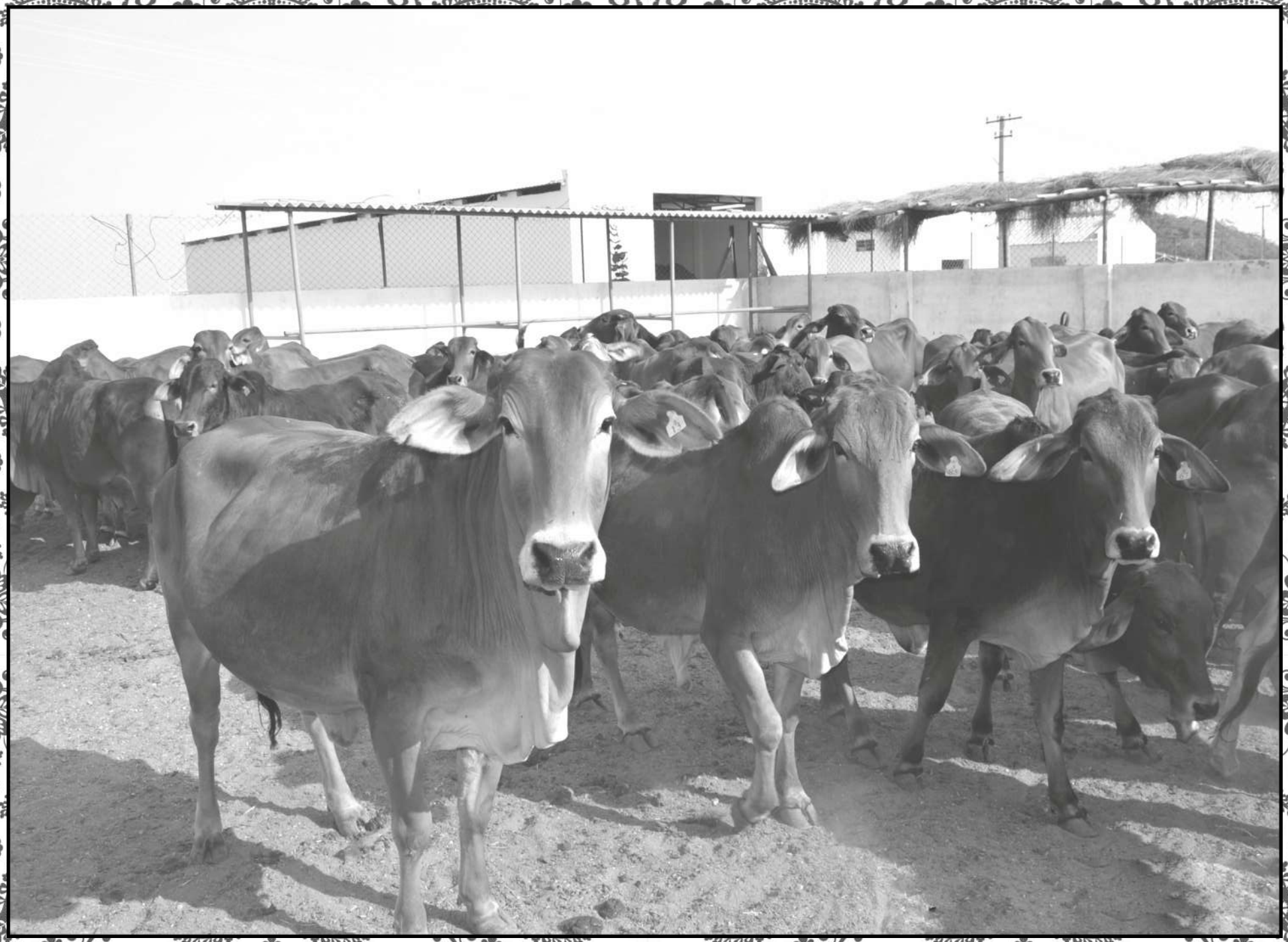
ISVPT-2023

TECHNICAL SESSION-I

Dr. A.M. Thaker Young Scientist Award for Women

Chairperson	**:**	**Dr. Debabrata Chanda**
Co-Chairperson	**:**	**Dr. G. K. Choudhary**
Rapporteur	**:**	**Dr. Gaurav Gupta**



AMT-01

PRE-084, A SIGMA-1 RECEPTOR AGONIST REDUCED ACQUISITION OF PROFIBROTIC CHANGES IN THE KIDNEY OF ADENINE FED RATS

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Chronic kidney disease (CKD) is one of the most common and serious health problems worldwide. Irrespective of initial cause all kinds of kidney injury if left unchecked will develop into the similar endpoint, CKD and fibrosis. CKD associated fibrosis is indicated by a loss of typical renal epithelial cells and accumulation of extracellular matrix (ECM) in the interstitium. The present study was carried out with the objective to investigate the effects of 2-(4- morpholinoethyl)-1phenylcyclohexane-1-carboxylate hydrochloride (PRE-084), a sigma 1 receptor agonist in adenine-induced renal fibrosis in rats which is yet unexplored. Male rats were exposed to adenine by oral gavage (150 mg/kg) for 28 days and treated with PRE-084 from day 22 to 28 (10 mg/kg) via intraperitoneal route. Adenine administration in rats caused renal damage as shown by increased serum creatinine along with urinary excretion of high molecular weight proteins. Further, profibrotic changes were observed in the kidney of adenine administered rats as reflected by reduced cytokeratin expression and increased expression of alpha-smooth muscle actin (α-SMA), fibroblast specific protein-1 (FSP-1), and matrix metalloproteinase-2 (MMP-2) activity leading to over ECM deposition. However, the treatment of these rats with PRE-084 led to slight restoration of cytokeratin along with significantly reduced expression of α-SMA, FSP-1, MMP-2 activity and lesser ECM deposition. These findings reveal the convincing anti-fibrotic potential of PRE-084 in the injured kidney.

AMT-02

AMELIORATIVE EFFECT OF HYDROETHANOLIC EXTRACT OF *AMARANTHUS HYPOCHONDRIACUS* ON DIABETES INDUCED REPRODUCTIVE TOXICITY IN MALE RATS

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Diabetes mellitus is a chronic metabolic endocrine disorder associated with various systemic complications including male infertility. Oxidative stress has been suggested as one of the main mechanisms involved in testicular toxicity and reproductive dysfunction. *Amaranthus spp.* has seen resurgence of interest in recent decades attributable to nutritional, medicinal and economic importance. Therefore, taking into consideration the antioxidant and antidiabetic activity of *Amaranthus*, this study aimed to evaluate the effect of *Amaranthus*

hypochondriacus on reproductive and oxidative parameters in streptozotocin (STZ) induced diabetes in rats. 30 male Wistar albino rats weighing 200-250 gm were divided into five groups: group I served as control. In group II-V, diabetes was induced by injecting STZ intraperitoneally @ 50 mg/kg b wt once, with group II serving as diabetic control, group III treated with glibenclamide @ 1 mg/ kg b wt p.o., group IV and V administered with hydroethanolic seed (HESAH) and leaf extract of *Amaranthus hypochondriacus* (HELAH) @ 250 mg/kg b wt, p.o. for 30 days, respectively. A significant ($P<0.05$) increase in total sperm count, motility, viability, catalase, superoxide dismutase alongwith significant ($P<0.05$) decrease in % abnormal sperm and lipid peroxidation was observed in HESAH and HELAH-treated diabetic rats as compared to diabetic control group II, which upon histopathological and scanning electron microscopic examination revealed an improvement in degenerative and inflammatory changes in testes, with HELAH showing higher protective efficacy. Thus, it can be concluded that administration of HESAH and HELAH ameliorated the reproductive dysfunction, oxidative stress and testicular damage in STZ-induced diabetic rats.

AMT-03

IN VITRO CYTOTOXIC POTENTIAL OF DIFFERENT EXTRACTS OF *CYCLEA PELTATA* IN HEPG2 CELL LINES

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Cyclea peltata also known as Padal belonging to the family Menispermaceae, is a slender twining climbing shrub, found in eastern and southern India particularly western ghats used largely for its antipyretic, diuretic, antidandruff, antioxidant, anti-inflammatory, anti-cancer and snake venom neutralising properties. The present study was conducted to assess the cytotoxicity of aqueous, methanolic extracts and different fractions of methanolic extract of whole plant of *C. peltata* in Human hepatocellular carcinoma (HepG2) cell lines. The cytotoxic potential of *C. peltata* extracts was analyzed using 3-(4, 5-dimethyl thazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay in HepG2 cell lines and its apoptotic nature was evaluated using acridine orange/ethidium bromide (AO/EB) and 5, 5', 6, 6' -tetrachloro-1, 1', 3, 3'-tetra-ethyl benzimidazol-carbocyanine iodide (JC-1) staining. The n-hexane fraction of methanolic extract showed a potent cytotoxic activity in HepG2 cell lines. The vital dye staining also demonstrated that HepG2 cells were significantly more sensitive to the cytotoxic effects of the n-hexane fraction of *C. peltata* than other extracts and fractions, as determined by the loss of MMP (Mitochondrial membrane potential), nuclear condensation, and apoptosis. The plant extracts of *C. peltata* especially n-hexane fraction was indicating a vital cytotoxicity through intrinsic pathway of apoptotic cell death and may be further analysed for the presence of detailed bioactive anti-cancer compounds and its potency.

AMT-04

TOXIC EFFECTS OF SILVER NITRATE ON OVARIES OF ADULT ZEBRAFISH

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Silver nitrate is a toxic substance widespread in freshwater that causes adverse effects. Its harmful effect on zebrafish has been little investigated, so we used zebrafish in this study to fill in the knowledge gap. The present study was carried out to investigate the toxicological effect of silver nitrate ($AgNO_3$) on the ovaries of adult zebrafish in different groups at different concentrations of 8.75, 17.5, and 35 µg/L for 28 days. After exposure to silver nitrate, behavioural alterations, oxidative stress markers, mRNA expression of antioxidant genes (*sod, cat,* and *nrf2)*, and histological alterations in the ovary were evaluated. Following a 28-day exposure to $AgNO_3$, adult female zebrafish showed behavioural changes such as anxiety-like behavior, hypo-locomotor activity at high doses, and less social interaction compared to the control group. Rapid freezing and circling swimming with left-over feed were observed at high doses. Oxidative stress-related alterations like decreased SOD and CAT activity, reduced GSH levels, and increased MDA levels have been observed in the ovary of zebrafish following $AgNO_3$ exposure for 28 days at medium and high doses. The suppression of mRNA expression of the *sod*, *cat*, and *nrf2* (nuclear factor erythroid 2-related factor 2) genes at medium and highest exposure levels supports the oxidative stress-related alterations. The various histopathological changes observed in the ovary at 17.5 µg/L were mild depletion of yolk granules in mature oocytes, and at 35 µg/L there was severe depletion of yolk granules, detachment of vitelline membrane, thickening of granulosa cell layer, and proliferation of interstitial connective tissue. The findings elucidated that silver nitrate damages the ovary due to oxidative stress through down-regulation of the *sod*, *cat*, and *nrf2* genes.

AMT-05

EFFECT OF LEMON PEEL EXTRACT GOLD NANOPARTICLES ON REPRODUCTIVE TOXICITY INDUCED BY ARSENIC AND LEAD IN MALE WISTAR RATS

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The present study was carried out to evaluate the molecular mechanism Lemon peel extract gold Nanoparticals (LPGNP) on As and Pb induced reproductive toxicity in rats. The gold nanoparticles synthesized with $HAuCl_4$ and lemon peel extract were characterized by UV-Vis spectra analysis, Fourier Transform Infra-Red spectrometry analysis, X-Ray Diffraction analysis, Zeta potential measurement, Nanoparticle Tracking Analysis and Field

Emission Scanning Electron Microscopy. The solution from pale yellow to dark purple indicates the formation of the nanoparticles. The peak absorbance at 557 nm conform the synthesis of GNP with the SPR band appears in the range of 535-580 nm. The size of LPGNP ranges from 20 nm to 100 nm and the concentration was found to be 2.5 X 10^9 particles/ml. The potential for As and Pb related changes on oxidative and reproductive parameters were evaluated in male rats given dosing of Sodium Arsenate and Lead acetate @ 13.8mg/kg and @ 116.4 mg/kg, respectively for 14 days. Our study showed that supplementation with LPGNP @ 10mg/kg and 20mg/kg significantly prevented reproductive toxicity as indicated by lesser alterations in biomarkers oxidative stress–related parameters SOD, CAT and GR. The serum testosterone concentration, sperm motility, total sperm count, sperm abnormalities and sperm viability in As and Pb or their combination toxic groups decreased significantly whereas LPGNP caused significant improvement. In histopathology of testis, As and Pb caused degenerative changes of seminiferous tubules, and sloughing of spermatogenic cells. These changes found minimal in LPGNP treated rats. Thus, LPGNP supplementation caused significant protection against As and Pb or their combination induced deleterious effects on reproductive and antioxidant system.

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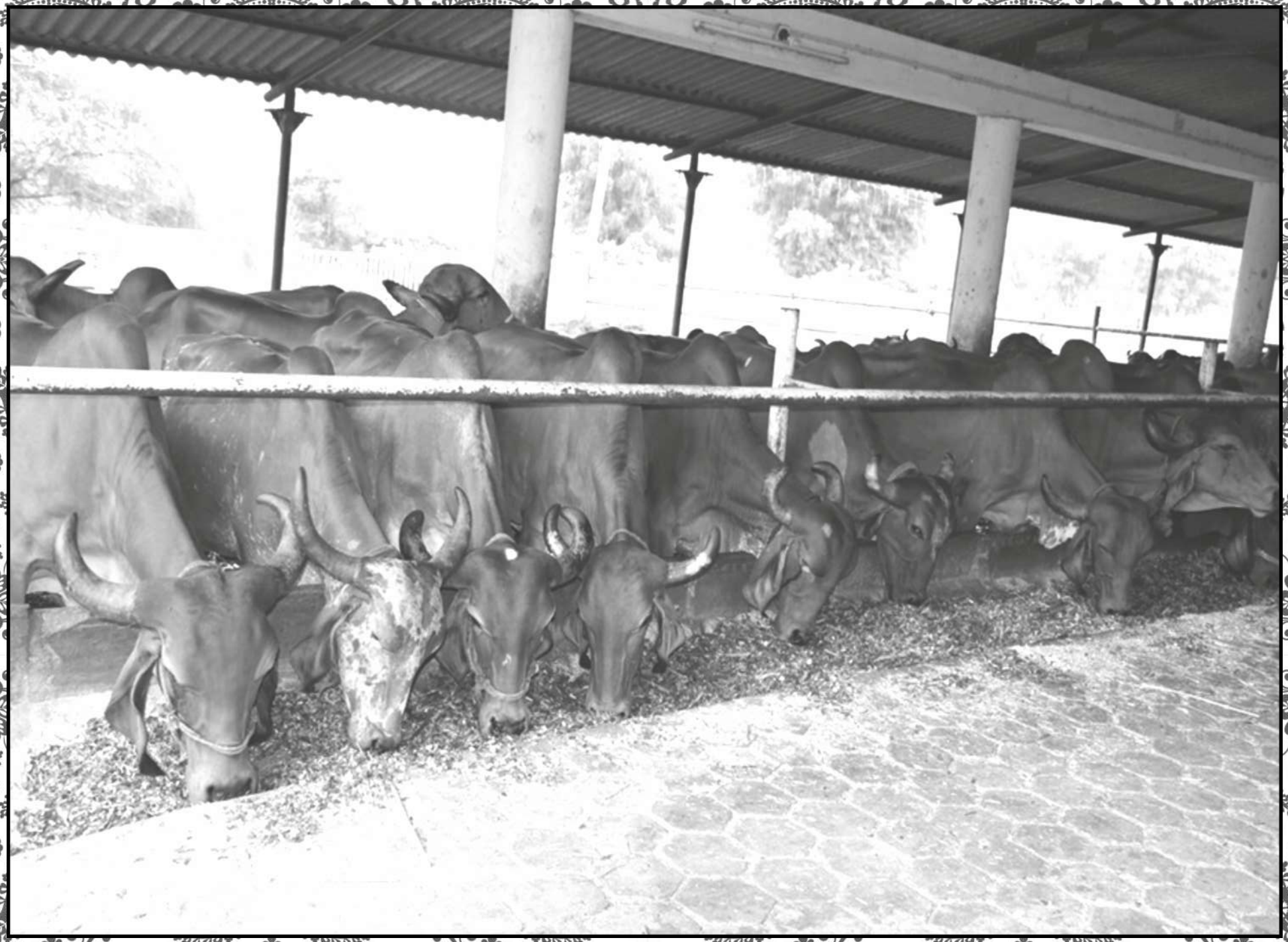
TECHNICAL SESSION-II

Prof. V.V. Ranade Young Scientist Award

Chairperson	**:**	**Prof. A.H. Ahmad**
Co-Chairperson	**:**	**Dr. Atul Prakash**
Rapporteur	**:**	**Dr. R. K. Yadav**

Dr. R. Natarajan Award

Chairperson	**:**	**Prof. Usha Rani M**
Co-Chairperson	**:**	**Dr. P. Mekala**
Rapporteur	**:**	**Dr. Vikrama Chakravarthi P**



VVR-01

DOSAGE DERIVATION OF MARBOFLOXACIN IN LACTIC ACID PRE-TREATED BROILER CHICKENS BASED ON PHARMACOKINETIC-PHARMACODYNAMIC INTEGRATION

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Investigation was carried out to study the disposition kinetics of marbofloxacin at the dose rate of 5.0 mg/kg b.wt. after a single oral administration in lactic acid pre-treated broiler chickens and an appropriate dosage regimen was calculated. Plasma concentrations of marbofloxacin were measured by Ultra High Performance Liquid Chromatography (UHPLC) method. The PK parameters were calculated from plasma concentrations versus time data by non-compartmental analysis. Following oral administration of marbofloxacin in broiler chickens (pre-treated with lactic acid), the mean peak plasma drug concentration (C_{max}) of 0.96 ± 0.08 µg/mL was achieved at 2 h. The value of half-life ($t_{½\beta}$) was 2.81 h. The respective values of AUC and AUMC were 6.16 µg·h/mL and 36.28 µg·h^2/mL. The values of $V_{d(area)}$ and Cl_B were 3.50 L/kg and 1.03 L/h/kg, respectively. In lactic acid pre-treated broiler chickens, the drug absorption from gastro intestinal tract was delayed, but plasma concentration was maintained above therapeutic level for up to 12 hours. Based on the values of PK-PD integrated indices, it is suggested that while treating susceptible bacterial infections caused by bacteria having MIC e" 0.1 µg/mL a higher dose of marbofloxacin is required to increase the value of C_{max}/MIC equal to or more than 10 (e"10). It indicated lower exposure of birds to marbofloxacin in pre-treated broilers chickens and this needs a dosage of marbofloxacin to be optimized in pre-treated birds.

VVR-02

ASSESSMENT OF ACRYLAMIDE INDUCED RESPIRATORY TOXICITY IN ADULT MALE ZEBRAFISH: OXIDATIVE STRESS, GENE EXPRESSION AND HISTOLOGICAL IMPAIRMENT IN GILLS

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Acrylamide (ACR) is a water-soluble alkene substance used in the production of polyacrylamides which poses a health threat to both human and aquatic animals. Hence, a present study was carried out to investigate the toxicological effects of ACR on gills of adult male zebrafish at two different concentrations (8.5 mg/L and 17 mg/L) following 28 days. The endpoints evaluated include: oxidative stress parameters (SOD and CAT

activities, GSH and MDA levels), mRNA expression of antioxidant genes (*sod*, *cat* and *nrf2*) and histopathological changes. ACR exposure at 17 mg/L has shown to produce significantly decreased superoxide oxide dismutase (SOD) activity, decreased reduced glutathione (GSH) levels and significantly increased malondialdehyde (MDA) levels in gills as compared to control group. The exposure of ACR for 28 days has shown significant decrease in *sod* and *nrf2* mRNA expression levels and non-significant decrease in *cat* mRNA level in gills of zebrafish of treatment groups as compared to control group. ACR exposure at 8.5 mg/L showed normal architecture of gills of adult male zebrafish; however exposure at 17 mg/L showed histopathological changes viz. congestion in primary lamellae along with fusion/clubbing of secondary lamellae, epithelial hyperplasia at the end of secondary lamellae and vacuolization formation in secondary lamellae in gills of adult male zebrafish. In conclusion, ACR exposure for 28 days showed oxidative stress mediated damage (enzymatic and non-enzymatic antioxidant defense system) in gills of zebrafish. The noticeable histopathological changes in gills of zebrafish of 17 mg/L indicate toxic effects of ACR in adult male zebrafish.

VVR-03

EXPLORING THE POTENTIAL EFFECTS OF BIO-ANTIOXIDANTS AGAINST ARSENIC INDUCED TOXICITY ON ADIPOSE-DERIVED MESENCHYMAL STEM CELLS OF BUFFALO (*BUBALUS BUBALIS*)

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The current study was conducted with the aim of investigating the use of the bio-antioxidants resveratrol (RES) and DL-catechin (CT) to attenuate the toxic effects of sodium arsenite (SA) on mesenchymal stem cells (MSCs) of buffalo. The cells were first isolated from adipose tissue by enzymatic digestion and then characterized for stem cell markers. The cells were positive for CD105, CD73, CD90 and CD44 and negative for CD34 and CD45 by RT-PCR. Osteogenic, adipogenic and chondrogenic differentiation were induced and confirmed by differential staining and molecular markers such as osteopontin (OST), fatty acid binding protein-4 (FABP4) and aggrecan (ACAN), respectively. The cytotoxic and genotoxic effects of SA were also studied, finding that the half-maximal inhibitory concentration of SA was 67.28 µM for 24 hours and 10.89 µM for 48 hours. The dose of antioxidants supporting maximal cell proliferation was also calculated and was 1.56 µM for RES and 100 µM for CT. Three different concentrations of SA, namely 25 µM (high), 12.5 µM (moderate) and 6.25 µM (low), were then selected for co-culture with a dose of antioxidants that support cell proliferation to prevent various cytotoxic and to investigate genotoxic effects. It was observed that exposure to arsenic resulted in a significant ($P<0.05$) reduction in cell viability and an increase in cytotoxicity markers such as lactate dehydrogenase (LDH), alkaline phosphatase (ALP), and creatinine kinase (CK). The SA-exposed cells also showed significant ($P<0.05$) reduction in glutathione peroxidase (GPx), total protein content (TPC), catalase (CAT), superoxide dismutase (SOD), and reduced glutathione (GSH) levels. On the other hand, oxidative stress indicators, namely lipid peroxidation level (LPO) and reactive oxygen species (ROS) levels, were found to increase significantly with SA treatment ($P< 0.05$). Parameters indicative of genotoxicity were found to increase significantly with SA treatment ($P<0.05$). The harmful effects induced by SA were found to be attenuated by treatment with RES and CT, indicating the beneficial effect of preconditioning MSCs with bio-antioxidants.

RNA-01

MECHANISTIC INSIGHTS INTO THE POTENTIAL OF ORLISTAT IN ATTENUATING ISOPRENALINE-INDUCED CARDIAC HYPERTROPHY AND FIBROSIS IN MOUSE MODEL

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The aim of the current study was to investigate the effect of the anti-obesity drug, orlistat on the morphometric, lipid profile, fibrotic markers, and histopathological alterations in isoprenaline-induced cardiac fibrosis in the mouse model. Isoprenaline was administered at 20 mg/kg body weight through a subcutaneous route for 14 days in mice to induce cardiac fibrosis. Administration of the orlistat was done at the 30 mg/kg body weight through the intraperitoneal route for 14 days in the mice of the isoprenaline co-administered group. After 24 hours of the last isoprenaline administration, mice of all groups were anesthetized to scarify. Body weight, heart weight, and tibial lengths of all groups of mice were measured to assess the effect of orlistat on the various morphometric parameters, including change in body weight (day zero to day 15th), absolute heart weight, relative heart weights viz., heart weight to body weight (HW/BW) and heart weight to tibial length (HW/TL) ratios. Furthermore, blood and heart tissues were collected to evaluate the serum lipid profile, tissue fibrotic markers, and histopathological alterations. Administration of isoprenaline significantly increased the absolute heart weight as well as relative heart weights (HW/BW and HW/TL ratios) in comparison to the control groups. However, a significant reduction in morphometric parameters was observed in the orlistat co-administered isoprenaline group mice in comparison to the isoprenaline alone group mice. Moreover, isoprenaline significantly enhanced the levels of serum lipid profile parameters such as cholesterol, triglycerides, and low-density lipoproteins (LDL) along with a reduction in high-density lipoproteins (HDL) and the ratio of HDL to LDL in comparison to the control group. Nevertheless, orlistat improved the lipid profile in the isoprenaline co-administered group in comparison to the isoprenaline alone group. Furthermore, orlistat also significantly reduced the level of fibrotic markers, such as hydroxyproline, and glucosamine in the heart tissue of the isoprenaline co-administered group in comparison to the mice of the isoprenaline alone group. Histopathological evaluation of heart showed the significant inflammatory and fibrotic lesions in the isoprenaline-alone group, which were attenuated in the orlistat co-administered group mice. In conclusion, orlistat (@ 30 mg/kg body weight) showed improvement in morphometric, lipid profile, fibrotic markers, and histopathological alterations in the isoprenaline-induced cardiac injury mice.

RNA-02

THERAPEUTIC EFFICACY OF *GLYCYRRHIZA GLABRA* AND *CURCUMA LONGA* BI-HERBAL EXTRACTS ON CHRONIC KIDNEY DISEASE RAT MODEL

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The present study was planned to evaluate the therapeutic efficacy of aqueous and alcoholic bi-herbal extracts of *Glycyrrhiza glabra* (GG) and *Curcuma longa* (CL) powder on adenine-induced chronic kidney disease (CKD) using 36 male Sprague-Dawley rats. The rats were randomly divided into six different groups, each group contains six rats. CKD was induced in the group II, III, IV, V and VI by adenine @ 200 mg/kg daily once through the intragastric route for 28 days. Group I served as control and was given standard pelleted diet. Group II served as adenine control and was given adenine (200 mg/kg, orally) for 28 days. Groups III, IV, V and VI were therapeutic groups, received adenine @ 200 mg/kg orally once daily for 28 days to induce CKD, after that rats were given bi-herbal aqueous and alcoholic extracts of GG and CL orally for another 42 days. In groups III and IV, received bi-herbal aqueous extract of CS and MK @ 250 and 500 mg/kg, respectively. In groups V and VI, received bi-herbal alcoholic extracts of CS and MK @ 250 and 500 mg/kg, respectively. Blood samples were collected twice during the experiment on the day 28th and 70th. Haematology, serum biochemistry, urine analysis, renal ultrasonography and histopathology were carried out. After Induction of CKD, treatment with aqueous and alcoholic bi-herbal extracts of GG and CL, significantly restored body weight and feed consumption in a dose-dependent manner as compared to adenine control group. Adenine administration for 28 days resulted in significant decrease in haemoglobin, total erythrocyte count and lymphocyte, while significant increase in TLC and granulocyte, however treatment with bi-herbal aqueous and alcoholic extracts significantly ameliorated haematological alterations. Adenine induced CKD resulted in elevated serum creatinine, uric acid, BUN, ALT and Phosphorus while significantly reduced levels of serum uromodulin, albumin, total protein, and calcium. Conversely, treatment with aqueous and alcoholic bi-herbal extract significantly improved biochemical changes as compared to adenine control rats. Notably, the therapeutic efficacy was most pronounced in rats treated with bi-herbal alcoholic extracts at the dose rate of 500 mg/kg body weight, as they exhibited a restoration of all hemato-biochemical alterations. In addition, significant increased levels of urine calcium and total protein, with decreased levels of urine creatinine, phosphorus and urine pH were observed in adenine control group as compared to normal control group. These changes were significantly reverted with treatment of aqueous and alcoholic bi-herbal extracts for 42 days. Moreover, the treatment showed dose-dependent therapeutic efficacy with regard to restoration of urine parameters. Following CKD induction, treatment with aqueous and alcoholic extracts of GG and CL attenuated ultrasonographic changes and improved histopathological damage in the kidney. Results showed that the bi-herbal alcoholic extracts of *Glycyrrhiza glabra* and *Curcuma longa* in the ratio of 1.5:1 given at the dose rate of 500 mg/kg body weight orally for 42 days after induction of CKD is more efficacious in the treatment of CKD in rats.

RNA-03

IMPROVED VASCULAR REACTIVITY & ENDOTHELIAL FUNCTION FOLLOWING T-AUCB TREATMENT CONTRIBUTE TO SURVIVAL BENEFIT IN POLYMICROBIAL SEPSIS

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Sepsis is a life-threatening condition contributing to high mortality globally. Vascular dysfunction is pivotal to sepsis pathology and a leading cause of tissue hypoperfusion leading to multiple organ failure. In the present study we evaluated the effect of sepsis on vascular oxylipins and their modulation in therapeutic outcome in special reference to soluble epoxide hydrolase (sEH). Sepsis was induced by caecal ligation and puncture (CLP) in mice. Sepsis significantly ($p < 0.01$) reduced the survival time (19.11 ± 1.14 h, N=22) in mice as compared to SO mice (N=20) while treatment with t-AUCB, a sEH inhibitor (EET stabilizer), either alone or in combination with imipenem significantly ($p < 0.05$) improved the survival time in septic mice to 26.51 ± 2.48 h (N=10) and 32.56 ± 1.13 h (N=18), respectively, despite being the notion that sepsis significantly ($p < 0.05$) downregulated mRNA expression of the metabolic enzyme of EET (i.e., sEH) in aorta, mesenteric artery, and kidney of septic mice. This survival benefit was further accompanied by reduced sepsis score, decrease in systemic and peritoneal bacterial load in septic mice. Further, a significant improvement in vascular reactivity to nor-adrenaline (NA) and acetylcholine (ACh) was also observed in combined treatment group. In addition, reduction in the degenerative and inflammatory changes in the vital organs (lungs, heart, kidney etc.) with lesser infiltration of inflammatory cells was observed following combined therapy. Thus, stabilization of vascular EET by t-AUCB is a potential target for the treatment of sepsis.

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ISVPT-2023

TECHNICAL SESSION-III

Dr. J. V. Anjaria Award

Chairperson	**:**	**Prof. S. P. Singh**
Co-Chairperson	**:**	**Dr. Pallavi Bhardwaj**
Rapporteur	**:**	**Dr. R. Yogeswari**

INTAS Pharma Young Scientist Award

Chairperson	**:**	**Prof. K. P. Mini**
Co-Chairperson	**:**	**Dr. R. K. Nirala**
Rapporteur	**:**	**Dr. Rishi Kant**

JVA-01

GROWTH PROMOTING EFFECTS OF *CURCUMA LONGA*, *OCIMUM SANCTUM* AND *PIPER NIGRUM* POWDERS ALONE AND IN COMBINATIONS IN BROILER

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The present research was planned to evaluate growth promoting effects of *Curcuma longa*, *Ocimum sanctum* and *Piper nigrum* powder alone and their combinations in broiler. A total of 240 chicks were divided randomly into 10 groups with 4 replicates of 6 birds in each. Group I served as control and was given basal diet without any treatment. Group II served as standard control and was given avilamycin antibiotic at the dose rate of 15 mg/kg feed as standard growth promoter. Chicks of group III and IV were given basal diet plus *Curcuma longa* (2.5 and 5.0 g/kg feed), group V and VI were given basal diet plus *Ocimum sanctum* (2.5 and 5.0 g/kg feed), group VII and VIII were given basal diet plus *Piper nigrum* powder (5.0 and 10.0 g/kg feed), group IX and X were given basal diet plus *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powder at the lower and higher doses (2.5, 2.5 and 5.0 g/kg feed and 5.0, 5.0 and 10.0 g/kg feed, respectively). The study was conducted for 42 days. All the birds of different experimental groups were observed for parameters like weekly body weight, weekly and overall body weight gain (BWG), weekly and total feed consumption, feed conversion ratio (FCR), livability and carcass characteristics. At the end of experiment return over feed cost was calculated. At the end of experiment, body weight and BWG of birds supplemented with all three powders alone and their combinations, were significantly higher as compared to control birds. Feed consumption remained unchanged in the all three powders alone and their combination supplemented broiler indicated no adverse effect on feed consumption of broiler. FCR has improved significantly in birds supplemented with all three powders alone and their combinations as compared to control birds. *Ocimum sanctum* at 5.0 g/kg feed had improved FCR as compared to standard drug avilamycin supplements. The dressing and giblet percentage remained unchanged while abdominal fat percentage was significantly decreased in *Curcuma longa* (5.0 g/kg feed) and *Ocimum sanctum* (5.0 g/kg feed) supplemented broiler. *Ocimum sanctum* (5.0 g/kg feed) supplemented birds showed the highest return over feed cost (Rs. 80.88/kg chicken) than birds given avilamycin (Rs. 76.53/kg chicken). *Curcuma longa, Ocimum sanctum* and *Piper nigrum* in combination at lower dose (2.5, 2.5 and 5.0 g/Kg feed) has comparable return over feed cost (Rs. 72.60/kg chicken) than birds given standard antibiotic avilamycin (Rs. 76.53/kg chicken). The results revealed that the combination of *Curcuma* longa (2.5 g/Kg feed), *Ocimum sanctum* (2.5 g/Kg feed) and *Piper nigrum* (5.0 g/Kg feed) has potential to be used as alternative to conventional growth promoters in broiler.

JVA-02

PROTECTIVE AND IMMUNOMODULATORY EFFECT OF POLYHERBAL FORMULATION ON *ESCHERICHIA COLI* CHALLANGED BROILER BIRDS

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Total of 120, day old broiler chicks were procured and randomly assigned to 4 groups consisting of 6 replicates with 5 birds per replicate. Environment control group was fed on standard ration without supplementation whereas, polyherbal formulation was supplemented from 0 day till end of experimental period in test group and antibiotic was given to standard drug control group from 9th to 14th day post infection. All groups other than environment control were given *E. coli* infection on 7th day. For confirmation of *E. coli* infection, samples were collected five days post infection and streaked on EMB agar. Other than environmental control group, all three groups showed metallic sheen colony on agar confirmed infection. Weekly bodyweight gain, feed consumption and FCR and on 21st and 42nd day, blood and serum parameters were measured. Feed intake data revealed no major difference among all treatment groups. Birds treated with standard antibiotic gained highest weight. Moreover, no mortalities were documented in all three groups except infection control group. Haematology on 21st and 42nd day showed all key parameters improved in polyherbal and standard drug control group. H/L ratio is one of the markers for stress indicator was found normal in all groups except increased in infection control group at 42nd day of experiment. In addition, uric acid, ALT and AST were found significantly improved in polyherbal treated group. Gross and histopathological examination of liver and intestine from environment control group revealed apparently normal structure. Mild changes were found in polyherbal and standard antibiotic treated group whereas, marked pathological changes observed in infection control group. Polyherbal formulation can effectively act as immunostimulant as highest antibody titre was found against NDV and IBDV antigens. In conclusion, polyherbal formulation containing *Allium sativum*, *Cinnamomum zeylanicum*, *Coriander sativum*, *Cuminum cyminum*, *Mentha piperita*, *Syzygium aromaticum* and *Withania somnifera* found effective in amelioration of *Escherichia coli* infection in broiler birds.

JVA-03

COW GHEE-BASED *SHOREA ROBUSTA* GAERTN F. RESIN POWDER PREPARATION ENHANCED RE EPITHELIALIZATION, DEPOSITION OF THICK COLLAGEN FIBRES, AND NRF2 EXPRESSION IN CUTANEOUS WOUND BED ON TOPICAL APPLICATION

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Traditional use of *Shorea robusta* Gaertn f. resin and cow ghee by indigenous tribes for medicinal purposes has been well-documented. In this study, we evaluated the healing potential of cow ghee-based *Shorea robusta* resin powder (SRP) preparation after creating excisional wounds (400 mm2 area) in 12 adult male Wistar rats. Cow ghee was applied topically twice daily for 14 days in vehicle control group (n=6) while the treatment group received cow ghee based-SRP preparation (0.625% w/w). The animals were sacrificed on day 14 for healing tissue collection. The per cent wound closures on days 7, 9, 11, and 14 were significantly higher in the treatment group, as compare to cow ghee control. Hydroxyproline and glucosamine levels improved significantly in the treatment group which indicated better extracellular matrix deposition. The immunohistochemical (IHC) expression of thick collagen-I fibers was evidently higher in healing tissue sections of treatment group. However, the expression of thin collagen-III fibers did not differ significantly among both the groups. Histological studies after H&E and Masson's trichrome staining revealed markedly better collagen fiber deposition, fiber orientation, re-epithelialization and hair follicle formation in treatment group sections. SRP treatment also increased the IHC expression of Nrf2, a master regulator of redox homeostasis, to counter oxidative stress in the wound bed. Enzymatic and non-enzymatic anti-oxidants were found to be markedly elevated in the treatment group. Conclusively, cow ghee-based SRP ointment may serve as a cost-effective wound healing modality.

JVA-04

TERMINALIA CHEBULA FRUIT EXTRACT ATTENUATES INFLAMMATORY RESPONSE AND OXIDATIVE STRESS IN LPS-INDUCED ACUTE LUNG INJURY IN MICE

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Acute lung injury (ALI) is the manifestation of an inflammatory response of lung resulting from severe sepsis, bacterial or viral pneumonia, trauma, and burns in animals. Pneumonia is the second major cause of morbidity and mortality among calves and may account for 50% of mortality. In this study, we explored the protective effects of an ethanolic *Terminalia chebula* fruit (TCE) extract against LPS-induced ALI in mice. Mice were

divided into five groups: control, LPS, TCE alone (200 mg/kg bwt), LPS+TCE (100 mg/kg bwt), and LPS+TCE (200 mg/kg bwt). TCE was given orally as a pretreatment for 7 days in TCE alone and in both LPS+TCE groups @ 100 & 200 mg/kg bwt, respectively. After last dose of extract, LPS was administered through intranasal route @ 40 mg/kg bwt under ketamine and xylazine anaesthesia to induce acute lung injury in mice. Further, 24 hr of LPS administration mice were sacrificed and samples were collected for experimental study. TCE administration improved the ratio of wet to dry lung weight and markedly decreased the levels of increased inflammatory markers such as MPO, total protein, and matrix metalloproteinases-9. The antioxidant enzymes reduced glutathione and catalase were significantly raised by TCE administration @200 mg/kg bwt, nevertheless MDA, tissue ferritin, and D-dimer levels were decreased significantly. Furthermore, Treatment with TCE showed improvement in histopathology findings as evident by decreased neutrophilic infiltration and lung inflammation. In conclusion, TCE exhibited protective effects against LPS induced ALI by inhibiting inflammatory response and oxidative stress.

INTAS-01

BIOENHANCER ACTIVITY OF PUNGANUR COW URINE DISTILLATE (PCUD) ON DISPOSITION KINETICS OF ENROFLOXACIN IN CHICKEN

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Antimicrobial resistance has become an imminent threat for both humans and livestock. Enrofloxacin is a second-generation antimicrobial quinolone used exclusively in veterinary practice, which has been used in livestock as well as poultry indiscriminately in the recent past. Use of antibiotics and natural compounds together has been identified as one of the strategies to combat antimicrobial resistance. Urine distillate from indigenous cows is found to be an activity enhancer of antimicrobial, antifungal, and anticancer drugs in addition to enhancer of their bioavailability. Therefore, the present study was hypothesised with an objective to determine the bioenhancer activity of PCUD on enrofloxacin after oral administration in chicken. 30 birds were randomly assigned to 3 groups. Group-I served as enrofloxacin control, Group-II coadministration of PCUD along with enrofloxacin and Group-III pretreated with PCUD for 10 days continuously prior to enrofloxacin administration. Blood samples were collected until 72h of post administration of enrofloxacin at predetermined time intervals and plasma was separated and analysed immediately for enrofloxacin by reverse (C_{18}) HPLC method. The pharmacokinetic parameters were calculated from plasma concentration *versus* time data by non-compartmental analysis using 'PK Solver version.2.0' software. Following oral administration of enrofloxacin at the dose rate of 10mg/kg bodyweight, mean values of C_{max} and AUC_{0-t} were $2.187\pm0.032 \mu g.ml^{-1}$ and 38.065 ± 1.471 $\mu g.h.ml^{-1}$, which were significantly ($p\leq0.05$) enhanced $2.734\pm0.0728 \mu g.ml^{-1}$ and $49.008\pm0.9112 \mu g.h.ml^{-1}$, respectively in the presence of PCUD (Group-II). There was no significant ($p\geq0.05$) difference in other pharmacokinetic parameters like elimination rate constant (β) and T_{max} in all the three groups. Enhancement of AUC and C_{max} values of enrofloxacin will be increasing surrogate markers of AUC/MIC and C_{max}/MIC that reveal positive outcome on antimicrobial activity of enrofloxacin and helps in combating antimicrobial resistance in poultry.

INTAS-02

IMPACT OF ALPHA-1-MONOLAURIN PRE-TREATMENT ON THE ORAL PHARMACOKINETICS OF MARBOFLOXACIN IN POULTRY

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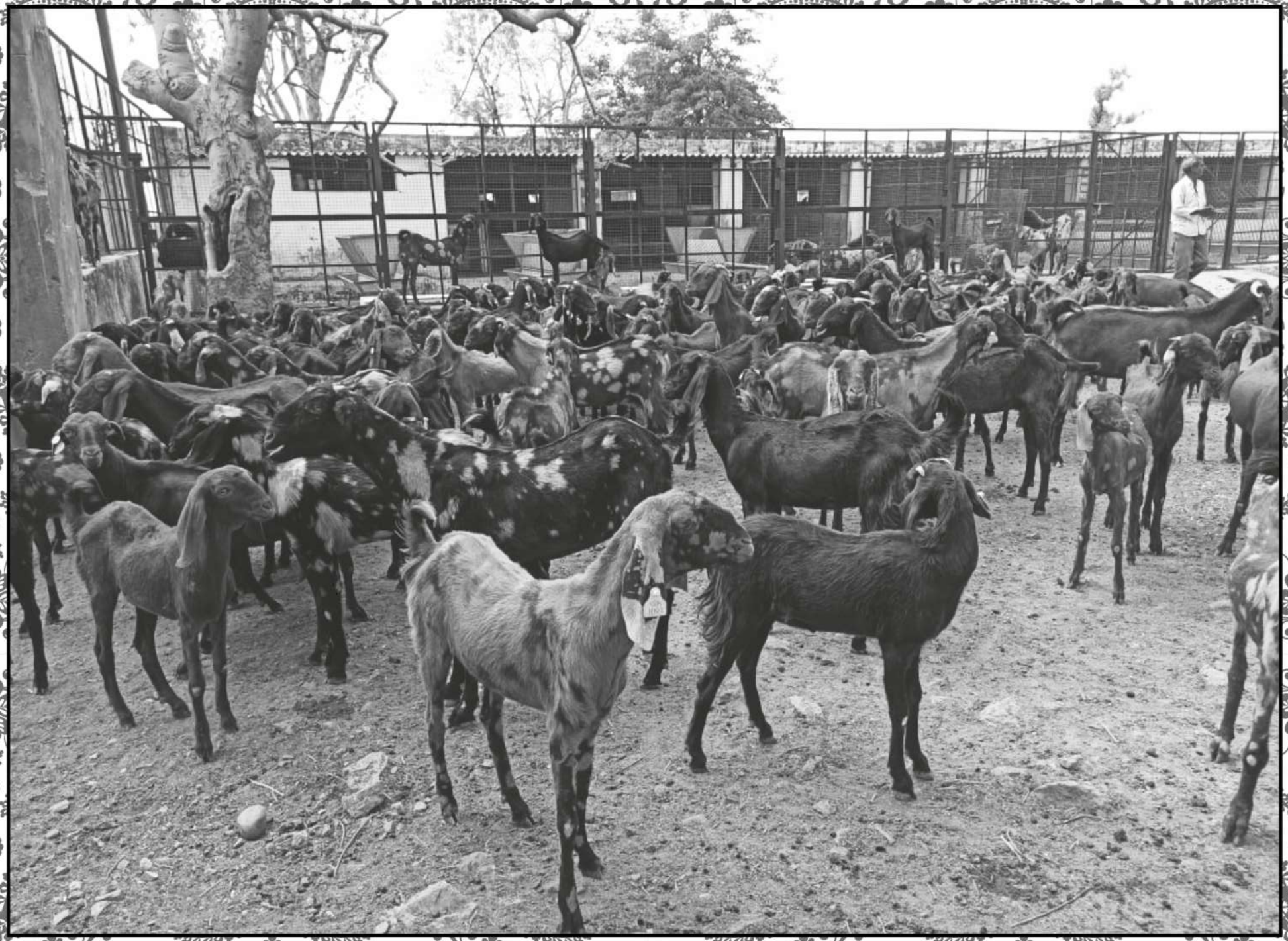
The current study explored the effect of alpha-1-monolaurin pre-treatment on the oral pharmacokinetic profile of marbofloxacin in healthy male broiler birds. A total of sixteen birds were divided into two groups: control birds and pre-treated birds, each group containing eight birds. Control birds were administered a single dose of marbofloxacin (5 mg/kg BW), whereas in the pre-treated group, after a 10-day regimen of alpha-1-monolaurin (4g/kg feed), the birds were orally administered marbofloxacin at the same dose rate. Blood samples were collected at specified intervals to assess marbofloxacin levels in the plasma using ultra-high performance liquid chromatography (UHPLC). Pharmacokinetic parameters were computed using the 'PK solver 2.0' software, and statistical analysis was conducted on plasma marbofloxacin concentrations using a t-test. The broiler birds subjected to alpha-1-monolaurin pre-treatment exhibited a higher mean peak plasma concentration (C_{max}: 2.43 g/ml) achieved earlier (T_{max}: 1.38 h). The plasma concentrations of marbofloxacin remained notably elevated, surpassing 0.10 and 0.18 µg/ml for up to 24 hours. Key pharmacokinetic parameters like the area under the curve and total body clearance displayed substantial differences. Remarkably, the average relative oral bioavailability in birds was found to be 119.61% higher. These findings affirm that pre-treatment of broiler chickens with alpha-1-monolaurin significantly enhances the oral pharmacokinetic profile of marbofloxacin in a favourable manner.



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ISVPT-2023

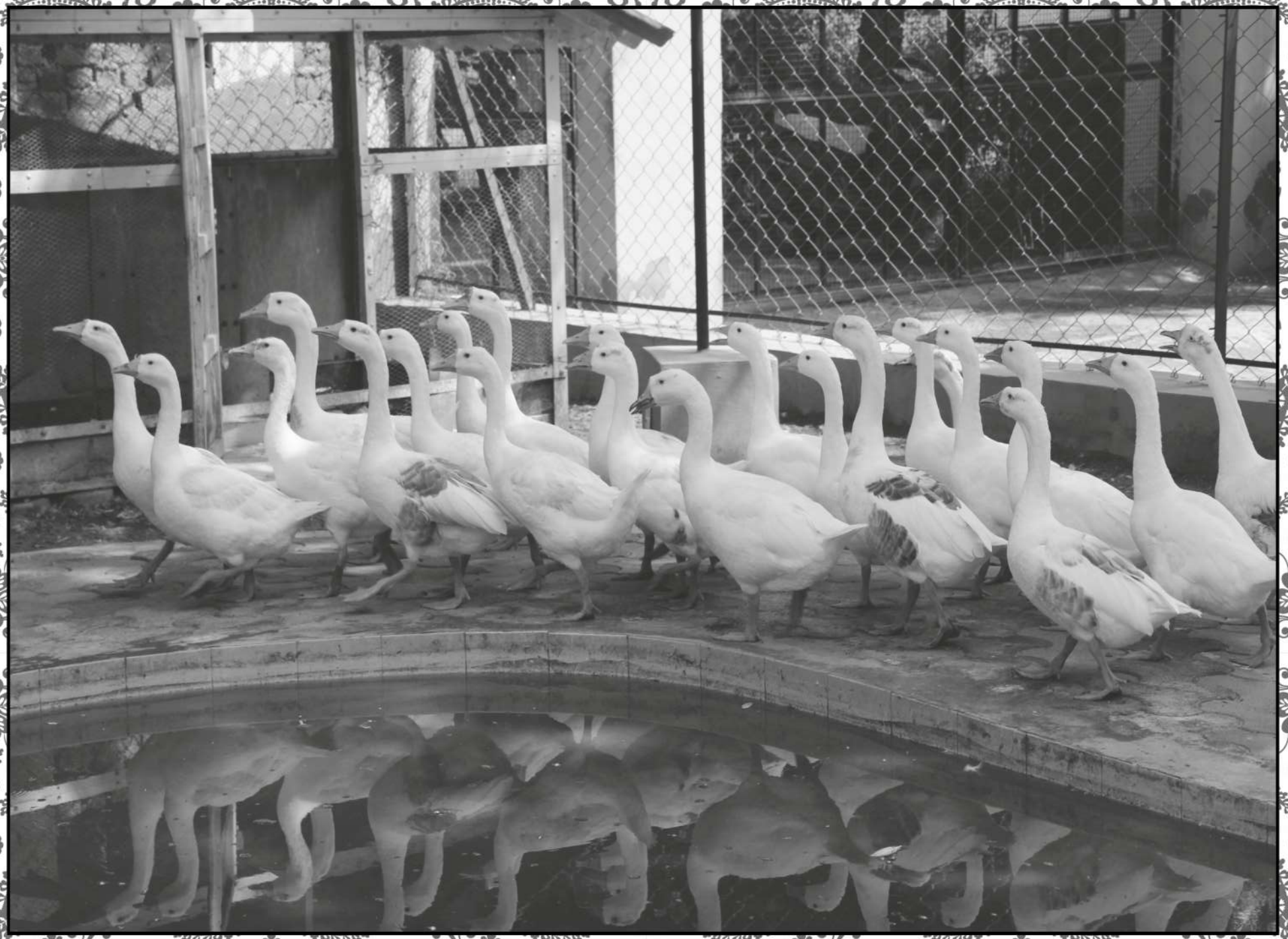
TECHNICAL SESSION-IV

Ethnopharmacology

Chairperson : **Prof. C. C. Barua**

Co-Chairperson : **Dr. Nirbhay Kumar**

Rapporteur : **Dr. P. S. Daundkar**



EP-OP-01

QUALITATIVE AND QUANTITATIVE PHYTOCHEMICAL ANALYSIS OF AN ORAL POLYHERBAL FORMULATION FOR IMMUNOMODULATION

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In recent days there is much-growing interest in the use of medicinal plants as modulators of the complex immune system. Numerous therapeutic consequences of plant extracts have been recommended, because of their extensive assortment of immunomodulatory effects and persuade on the immune system. The objective of this study is to formulate and analyze the phytochemicals of the oral polyherbal formulation having immunomodulatory action. Selection of medicinal plants including *Asparagus racemosus, Withania somnifera, Andrographis paniculata, Ocimum sanctum* and *Piper nigrum* was made based on the traditional uses and scientific reports. Crude extracts of the selected plants were prepared and used for qualitative and quantitative studies. The equal ratio of selected plants was utilized for the development of a polyherbal formulation using decoction method. Qualitative preliminary phytochemical screening showed the presence of major phytoconstituents like alkaloids, flavonoids, saponins, tannins, terpenoids etc., in the crude extracts. The quantitative analysis was carried out by using HPTLC fingerprinting analysis and the results showed the appreciable quantity of immunomodulatory phytochemicals such as shatavarin, withaferin A, andrographolide, eugenol and piperine in the polyherbal oral formulation. The qualitative and quantitative results of this study revealed the enriched immunomodulatory phyto-components of the herbs selected and further may become an alternative oral source for immunomodulation in animals.

EP-OP-02

PHYTOCHEMICAL SCREENING AND ANTIOXIDANT ACTIVITIES OF SELECTED MEDICINAL PLANTS

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The objective of the present study was to analyse phytochemical constituents and antioxidant properties of aqua-methanaloic extracts obtained from the leaves of *Mangifera indica, Azadirachta indica*, *Ocimum sanctum* and *Psidium guajava.* In present work, The leaves of selected medicinal plants *i.e. Mangifera indica, Azadirachta indica*, *Ocimum sanctum* and *Psidium guajava* were processed for preparation of aqua-methanolic extracts. Phytochemical analysis for the important chemical constituents and antioxidant activity of different extracts were also carried out. The phytochemicals such as phenols, flavonoids, tannin and non- tannin were determined

quantitatively. The antioxidant property of the extracts was evaluated using *in vitro* assays i.e. 2, 2'-Azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS. +) and 2,2-diphenyl-1-picrylhydrazyl (DPPH). The total phenolic, total flavonoids and tannin contents were maximum in extract of leaves of *Mangifera indica.* The IC_{50} values was determined and revealed that *Psidium guajava* extract was better scavengers of ABTS and DPPH radicals as compare to other extracts showing its potent antioxidant activity.

EP-OP-03

ASSESSMENT OF OXIDATIVE STRESS AND LIVER FUNCTION PARAMETERS IN SWISS ALBINO MICE PRE-TREATED WITH *WITHANIA SOMNIFERA* AND COW URINE AGAINST ACETAMINOPHEN INDUCED LIVER DAMAGE

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The present study was undertaken to investigate hepatoprotective activity of *W. somnifera* root extract, cow urine and their combination against acetaminophen induced hepatotoxicity in mice. Adult male swiss albino mice (n=30) were divided into six equal groups. Group I was control group which received 2% gum acacia suspension for 14 days orally. Group II, III, IV, V and VI were received 2% gum acacia, silymarin (@25 mg/kg b.wt.), *W. somnifera* root extract (@100 mg/kg b.wt.), cow urine (@7.8 ml/kg b.wt.) and their combined treatment ie*: W. somnifera* root extract (@100 mg/kg b.wt.) and cow urine (@7.8 ml/kg b.wt.) both orally for 14 days respectively and on day 14, APAP (@300 mg/kg b.wt.) intraperitoneally was administered after 30 min of treatment in all the groups. On day 15th blood samples were collected to separate plasma to study the various liver marker enzymes activities *ie:* Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), lactate dehydrogenase (LDH). Total bilirubin level was also estimated in plasma. Lipid peroxidation and antioxidant status (Superoxide dismutase and Reduced glutathione content) were estimated in liver and kidney tissue homogenate. Acetaminophen induced hepatotoxicity was evident by significant increase in a in plasma AST, ALT, ALP, GGT, LDH activity, total bilirubin level and lipid peroxidation where as there is simultaneous reduction of reduced glutathione and SOD content in liver and kidney. Pre-treatment of *W. somnifera* root extract (100 mg/ kg b.wt.) and cow urine (7.8 ml/ kg b.wt.) notably reversed all these changes towards normal values in APAP treated group as compared to control group. However the results of co-treatment group were more pronounced as compared to individual treatment groups. So we can conclude that treatment with *W. somnifera* root extract and cow urine curtailed the toxic effect of APAP, however, co-administration of both potentiated the hepatoprotective effect.

EP-OP-04

EVALUATION OF *IN VITRO* ANTIOXIDANT POTENTIAL OF *CORIANDRUM SATIVUM* LEAVES ESSENTIAL OIL

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Oxidative stress induced free radicals is an important event in cell that cause ageing and degenerative diseases including cancer, heart diseases, parkinson's disease, autoimmune diseases and senile dementia. Antioxidants are essential for prevention and treatment of free radical-mediated disorders. The usefulness of artificial antioxidants are under scrutiny due their suspected role in carcinogenesis. Thus, there is an urgent need of natural antioxidants, having an important role in preventing a variety of stress-related diseases. The essential oils, apart from their use as aroma additives, have many medicinal properties. *Coriandrum sativum* is a well-known herb widely used as spice, in folk medicine and food industries. Hence in this study the *in vitro* antioxidant potential was evaluated in the essential oil of *Coriandrum sativum* leaves. The coriander plants were purchased from the local market, washed, ground and the essential oil was extracted using Clevenger's apparatus. The yield of the essential oil was 750 µl/100 g of the leaves. The percentage radical scavenging activity of the essential oil and the positive control, Butylated Hydroxytoluene (BHT) at the concentrations 1.25, 2.5, 5, 10, 20, 40 and 80 µl/ml was estimated by 2,2-Diphenyl-1-Picrylhydrazyl (DPPH) assay at 575 nm and Hydrogen Peroxide (H_2O_2) assay at 230 nm in UV Visible Double beam Spectrophotometer. The percentage of radical scavenging activity was dose dependant in both essential oil and control by both methods. The EC50 values of the essential oil and BHT by DPPH assay was 10.32 and 10.05 µl/ml and by H_2O_2 assay was 5.148 and 2.508 µl/ml.

EP-OP-05

TOXICITY STUDY OF TIKSHNA SHODHAN DRAVYA- SNUHI (*Euphorbia neriifolia*) LATEX IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Euphorbia neriifolia commonly known as *Snuhi* is considered a poisonous plant and classified under *Upvisha* (less virulent poison). *Snuhi Ksheer* (latex of *Euphorbia neriifolia*) is indicated in *Prameha/ Madhumeha*. Because it is a poison, so, it should be used very carefully. It is indicated in many diseases but its scientific toxicological effects are still unknown. Hence, the present study was conducted to evaluate the toxicity of *Tikshna Shodhan Dravya- Snuhi (Euphorbia neriifolia)* latex in streptozotocin induced diabetic male Wistar rats that were used as experimental model for the study. Biochemical parameters like aspartate transaminase (AST) and alanine transaminase (ALT) levels were highly increased and nodules were found in liver in *Shodhit*

Snuhi Ksheer (SSK) control rats. However, AST and ALT levels were not increased in diabetic control group as well as SSK treated diabetic rats, and no nodule was found in these groups. Maximum ameliorating effect was seen at higher dose (1850 mg/ kg) compared to lower dose (925 mg/ kg). Hence, it can be concluded that *Snuhi (Euphorbia neriifolia)* latex is hepatotoxic in normal rats but non-toxic in diabetic rats which justifies the Ayurvedic recommendation for usage of this medicine in treatment of diabetes.

EP-OP-06

ANTIDIABETIC AND ANTIOXIDANT POTENTIAL OF HYDROETHANOLIC EXTRACT OF *PIPER BETLE* LINN. IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Piper betle (Piperaceae) commonly known as betle possess several bioactivities and are used in traditional medicinal systems. The present study was conducted to investigate the antidiabetic and antioxidant activity of *Piper betle* leaves in Streptozotocin (STZ) induced diabetic rats. Diabetes was induced by single intraperitoneal injection of STZ @ 60 mg/kg body weight. A total of 36 male Wistar rats were divided into six groups consisting of six animals in each group. Group I consisted of normal control. Animal of group II were given *P. betle* hydromethanolic Extract (PBHM) @ 400 mg/kg b.wt. to serve as extract positive control. Animals of Group III to VI were made diabetic by administration of Streptozotocin (STZ) @ 60 mg/ kg b.wt. intraperitoneally. Animals of Group III served as diabetes control in which no treatment was given, Group IV received PBHM @ 200 mg/kg b.w) and rats of Group V received PBHM @ 400 mg/kg b.wt. Rats of Group VI was given standard antidiabetic drug, glibenclamide @ 10 mg/kg b.wt. daily for 30 days. The haematological and biochemical profile of the animals in diabetes control group indicated a significant deterioration in all the blood parameters compared to normal control, but in PBHM treatment groups, these parameters improved as compared to diabetes control. The improved status of the serum biochemical parameters in the PBHM treated groups (Group IV, PBHM @200 mg/kg and Group V, PBHM@400 mg/kg) substantiates the ability of PBHM extract in counteracting diabetogen induced stress. In antioxidative studies, there was decline in elevated levels of lipid peroxidation in PBHM treated groups which can be considered as an indication of the antioxidative property, which can in turn lead to inhibition in the progression of diabetes. Overall, PBHM extract @ 400 mg/kg b.wt. recorded maximum antidiabetic and antioxidant activity which was comparable to the standard antidiabetic drug Glibenclamide. It can be concluded that the hydromethanolic extract of *Piper betle* exert inhibitory effects on STZ-induced diabetes mellitus which may be attributed to their phytochemicals with antidiabetic and antioxidant properties.

EP-OP-07

EFFICACY OF POLYHERBAL FORMULATIONS IN LUMPY SKIN DISEASE IN CATTLE

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The proposed study was carried out on adult cross cattle showing classic clinical signs of Lumpy skin disease in the Bikaner district. This was verified by a clinical examination and PCR for the experiment. The 16 cattle were selected for this experiment, which underwent clinical examinations and had their hematology, serum biochemistry, oxidative stress marker, inflammatory marker, and immunological marker evaluated. Cattle were randomly divided into 2 groups, Group-II was treated with polyherbal preparation A and Group-III was treated with polyherbal preparation B and Eight healthy adult cattle were retained as the control group (Group-I). In LSD affected cattle, Major clinical manifestations were pyrexia, lacrimation, lethargy, lymph node enlargement, skin nodules and oedema. Clinical vital parameters revealed significantly ($p<.05$) higher values of rectal temperature, heart rate and respiration rate while significantly ($p<.05$) decreased rumen motility, where haematological results show significantly reduced ($p<0.01$) in mean values of Hb, PCV, TEC, TLC and platelet count were compared to healthy cattle. There was significant neutrophilia and lymphopenia, in affected cattle. Pre-treatment hypoproteinemia, hypoalbuminemia, hyperglobulinemia, and increased concentration of total bilirubin, creatinine, AST, ALT and ALP and increased level of blood urea nitrogen (BUN) showed by LSD affected cattle. In the oxidative stress, immunoglobulins and inflammatory biomarker there was significantly decrease ($p<0.01$) in mean values of GSH-Px, while mean values of MDA, IgG, IgM IL-4, TNF-α and IFN-γ was significantly increased in LSD affected cattle. Therapeutic effect of polyherbal formulations was observed in the LSD affected cattle and all therapeutic groups showed significant results of G-III found better in various clinical signs, haemato-biochemical parameters, serum level of oxidative stress, immunological and inflammatory biomarkers.

EP-OP-08

PHYTOCHEMICAL ANALYSIS AND ANTIMICROBIAL ACTIVITY OF DIFFERENT PLANT EXTRACTS AGAINST *KLEBSIELLA PNEUMONI*

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Klebsiella pneumoniae is a gram negative, non-motile, encapsulated, lactose fermenting facultative anaerobe, belonging to the Enterobacteriaceae family. Leaves of *Moringa* species have been traditionally been reported to possess various biological activities, including antitumoral, antioxidant, anti-inflammatory, diuretic, hepatoprotective properties, hypotensive, hypocholesterolemic and hypoglycemic actions. Extractability percentage of aqueous, methanolic and chloroform extract of *Moringa oleifera* and *Murraya koenigii* plant were 8.36, 10.05, 7.67, 8.51, 9.27 and 4.17 respectively. The MIC for methnolic extract of *M. oleifera* against ATCC strain of *K. pneumoniae* 100 mg/ ml, while for NRCC strain of *K. pneumoniae*, it was 25 mg/ ml. The MIC for chloroform extract of *M. oleifera* against ATCC strain of *K. pneumoniae* 6.25 mg/ ml. However, the MIC for chloroform extract of *M. oleifera* against NRCC strain of *K. pneumoniae* was 25 mg/ml. The MIC for

methanolic extract of *M. koenigii* against ATCC strain of *K. pneumoniae* was 50 mg/ ml, while it was 25 mg/ ml against NRCC strain of *K. pneumoniae*. The MIC for chloroform extract against NRCC strain of *K. pneumoniae* was 25 mg/ ml, while for ATCC strain of *K. pneumoniae*, it was 50 mg/ ml. Alkaloid was present in methanolic and chloroform extract of both plants.

EP-OP-09

EVALUATION OF IMMUNOMODULATORY AND ANTIOXIDANT ACTIVITIES OF *DAUCUS CAROTA* L. ROOTS ON CYCLOPHOSPHAMIDE-INDUCED IMMUNOSUPPRESSED RATS

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The present study was carried out to evaluate the antioxidant and immunomodulatory activities of *Daucus carota* L. polysaccharide (DCP) on cyclophosphamide-induced immunosuppression in rats. In this study, forty-two male SD rats were divided into seven different groups. i.e., control group (C1), vehicle control group (C2), toxic control group (C3), standard treatment group (ST), and three treatment groups (treated with DCP at the dose rate of 50, 100 and 150 mg/kg, PO, daily) for 21 days. Various parameters like haematology, biochemistry, organ indices, delayed-type hypersensitivity, antibody titre, levels of TNF-α and IL-10, and splenocyte proliferation were evaluated. Histopathological examinations were also carried out for the spleen, kidney and liver. Cyclophosphamide-induced alteration of hemoglobin, packed cell volume, platelet count, total erythrocyte count and total leukocyte count were improved in animals in all treatment groups. The levels of total protein, albumin and globulin in all treatment groups were significantly higher as compared to the toxic control group. All DCP treatments significantly stimulated splenic T-B lymphocyte-mediated proliferation as compared to the toxic control group. Neutrophil adhesion (%) was modified at a higher dose of DCP as compared to the toxic control group. DCP treatment (T1, T2 and T3) significantly improved the HA titre, which is an indication of antibody production. The treatments also significantly improved the cell-mediated immunity as compared to that of the toxic control group. In cyclophosphamide-treated rats, the DCP restored the levels of TNF-α and IL-10 in a dose-dependent manner. The DCP treatment (T1, T2 and T3) significantly enhanced the antioxidant activity in toxic control rats, as shown by the evaluation of SOD, CAT and GSH activities, as well as MDA levels in the liver, kidney, and spleen. Moreover, hepatic CAT, SOD, GST and GPx mRNA expression of genes for the antioxidant enzymes was down-regulated by CYP treatment, which was reversed by DCP. Histopathological findings revealed alterations in different organs (liver, kidney, and spleen) of the toxic control group, which were markedly improved by treatment with DCP in a dose-dependent manner. The FI-IR fingerprint of the polysaccharide extract of *Daucus carota* L. shown presence of functional groups like O-H, C-H, C=O and C-O. These results suggest that *Daucus carota* L. polysaccharide (DCP) can be considered a good herbal drug candidate for immunomodulatory formulation.

EP-OP-10

UNRAVELLING THE ANTIBACTERIAL POTENTIAL OF HYDROETHANOLIC BARK EXTRACT FROM *MELIA AZEDARACH*: *IN VITRO* AND *IN SILICO* INVESTIGATION

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Finding new and effective antimicrobial drugs is a prerequisite to reducing the rising number of drug-resistant microbes. *In vitro* analysis was used to evaluate antibacterial activity of hydroethanolic bark extract of *Melia azedarach* against *Escherichia coli* and *Staphylococcus aureus*. An in-silico screening was performed to find potential components of the chosen plant extract that could be employed in the development of new medications against *E. coli* and *S. aureus*. The minimum inhibitory concentration (MIC) of the bark extract against *E. coli* and *S. aureus* was found to be 8 mg/ml and 1 mg/ml respectively. The hydroethanolic extract of bark of *M. azedarach* exhibited remarkable antibacterial ability. GC-MS analysis was conducted to elucidate distinctive phytochemical constituent; *M. azedarach* bioactive constituents were identified as glycerin, hexadecanoic acid, methyl ester., methyl stearate, glycidyl palmitate etc. Furthermore, binding interactions were explored through molecular docking to identify bioactive components against *E. coli* and *S. aureus*. Molecular docking study of compounds was performed against protein of *E. coli* (PDB ID 1IEM) and *S. aureus* (PDB ID 2ZCO). The identified compounds viz. CID 535221, CID 5363099 and CID 500095 had binding energy of -9.9 kcal/mol, -8.4 kcal/mol and -7.4 kcal/mol respectively against PDBID 2ZCO. Compounds viz. CID 535221 and CID 500095 had binding energy of -9.2 kcal/mol and -7.4 kcal/mol respectively against *E. coli*. The current study suggests that bark extract from *M. azedarach* holds promise as a potential alternative for development of bioactive antibacterial agents to combat antibiotic resistant bacteria.

EP-OP-11

GYMNEMA SYLVESTRE LEAF EXTRACT RESTORES NORMOGLYCEMIA, IMPROVES ECG INDICES AND MODULATES GLUT-4 ACTIVITY IN STREPTOZOTOCIN-INDUCED HYPERGLYCEMIC WISTAR RATS

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The objective of the present study was to explore the therapeutic potential of *Gymnema sylvestre* and ITK formulation against obese streptozotocin-induced diabetes and diabetic cardiomyopathy in male Wistar rats. Forty two obese male Wistar rats were divided into seven groups viz. group I (Normal control), group II (Obese control), group III (Obese diabetic), group IV (Obese diabetic + Metformin), group V (Obese diabetic + *Gymnema sylvestre*), group VI (Obese diabetic + ITK) and group VII (Obese diabetic + *Gymnema sylvestre* + ITK) consisting six animals in each, were experimentally-induced-diabetes with streptozotocin @ 35 mg/kg body weight, i.p. *Gymnema sylvestre* extract, ITK formulation and metformin were given @ 400 mg/kg, @

445 mg/kg and @ 50 mg/kg body weight by oral gavage continuously for 60 days. Extracts alone and combination lowered blood glucose and percent HbA1C. Dyslipidemia, increase in CK-MB and cardiac troponin-I, significant increase in Mean arterial pressure and altered ECG was observed in diabetic rats. Both extracts alone and in combination significantly restored the above alterations and also the ECG indices (QRS interval, R-amplitude and ST-height) were shifted towards normal control values. A significant increase in expression of cardiac tissue glucose transporter-4 (GLUT-4) was observed in both extracts alone and combination of extracts compared to obese diabetic group revealing their protective action against hyperglycemia induced cardiac injury. Thus, it can be concluded that, ITK formulation was emerged as a potent hypoglycaemic formulation and was comparable to metformin.

EP-OP-12

IN VIVO IMMUNOMODULATORY AND ANTIOXIDANT ACTIVITIES OF COMBINATIONS OF *CURCUMA LONGA, OCIMUM SANCTUM* AND *PIPER NIGRUM* POWDERS IN BROILER

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The present research was planned to evaluate *in-vivo* immunomodulatory and antioxidant activities of *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powders combinations at different dose in broiler. A total of 48 chicks were divided randomly into 4 groups each of 12 chicks. Group I served as control and was given basal diet without any treatment compound. Group II served as standard control and was given vitamin E and selenium containing product in water. Chicks of group III and IV were given basal diet plus *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powder at the lower and higher doses (2.5, 2.5 and 5.0 g/kg feed and 5.0, 5.0 and 10.0 g/kg feed, respectively). The duration of study was 35 days. Cutaneous basophil hypersensitivity (CBH) response at two different doses (100 µg and 200 µg) of phytohemagglutinin-P was carried out to assess the cell mediated immunity on 14th day of age. Blood was collected on 7th, 21st and 35th day of age and serum was separated to estimate antibody titer against ND vaccine by haemagglutination inhibition (HI) test and biochemical parameters like serum total protein, serum albumin, serum globulin and A/G ratio. On 35th day, antioxidant enzymes such as superoxide dismutase, catalase and malondialdehyde were measured from the serum. On 35th day, thin blood smears were prepared and stained with field's stain to determine differential leucocyte counts (DLC) microscopically and H/L ratio was calculated. At the end of experiment, birds of all groups were slaughtered and tissues like bursa of Fabricius, thymus and spleen were collected for histopathological examinations. *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powders in combination, had significantly ($p<0.05$) higher CBH response and HI antibody titer in broiler. The effect was similar to that produced by vitamin E and selenium supplementation. It evinced that dietary inclusion of all three powder in combination stimulated cell mediated and humoral immune response in broiler. Dietary inclusion of all three powders in combination, significantly improved the serum total protein, serum globulin and significantly ($p<0.05$) decreased the albumin to globulin ratio. The combinations of all three powders had better effect than Vit. E and selenium as standard supplement. Dietary inclusion of all three powders in combination decreased H/L ratio. *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powders at higher dose (2.5, 2.5, 5.0 g/kg feed)

combination showed lower H/L ratio as compared to standard supplements of Vit. E and selenium. Histopathological examination did not reveal any alteration in normal architecture among all experimental groups. Superoxide dismutase and catalase were significantly increased whereas malondialdehyde significantly ($p<0.05$) reduced in birds supplemented with all three powders combination at lower and higher doses as compared to birds of control group. Results indicates that *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powders combination has immunostimulants and antioxidant activities in broiler.

EP-OP-13

SCREENING OF SOME PLANT LEAVES EXTRACTS FOR *IN VITRO* ANTIBACTERIAL EFFECTS AGAINST VAP A AND VAP C POSITIVE *RHODOCOCCUS EQUI*

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The study was conducted to evaluate *in vitro* antibacterial activity of ethanolic, chloroformic and Sequentially Extracted Water Extract (SEWE) leaves extracts of leaves of *Zizyphus nummularia*, *Bougainvillea*, *Tamarix articulata*, *Leptadenia pyrotechnica*, *Crotalaria burhia* and *Tecomella undulata* against Vap A and Vap C positive *Rhodococcus equi.* In initial screening ethanolic leaves extract of these plants, only *Tecomella undulata* showed good *in vitro* antibacterial activity with 20 mm zone of inhibition at concentrate 134.75 mg/ml by disc diffusion method against *Rhodococcus equi*. Chloroformic leaves extracts of *Tecomella undulata* did not showed in vitro antibacterial activity, while SEWE showed good *in vitro* antibacterial activity with 15 mm zone of inhibition at concentrate 162 mg/ml by agar well diffusion method against *Rhodococcus equi*. Further, solvent based fractionation, Ethanol Soluble Fraction (ESF), Methanol Soluble Fraction (MSF) and Water Soluble Fraction (WSF) of polar compounds of SEWE did not showed *in vitro* antibacterial activity against *Rhodococcus equi*. On comparison with currently used antibiotics (azithromycin and rifampicin), required concentration of the leaves extract of *Tecomella undulata* was too high for their possibilities of *in vivo* use, so abundant availability of *Tecomella undulata* leaves and their activity against *Rhodococcus equi* suggests their potential for use as disinfectant against *Rhodococcus equi.*

EP-OP-14

ANTIDIABETIC AND HEPATO-RENAL EFFICACY OF *AMARANTHUS HYPOCHONDRIACUS* IN STREPTOZOTOCIN INDUCED DIABETIC MODEL IN RATS

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This study aimed to evaluate the antidiabetic and hepato-renal efficacy of *Amaranthus hypochondriacus*. For this, 30 male Wistar albino rats weighing 200-250 gm b wt were randomly and equally divided into five groups. Group I served as normal control group. Diabetes was induced in group II to V rats by single

intraperitoneal injection of streptozotocin (prepared in citrate buffer, pH 4.5) @ 50 mg/kg b wt in rats. Group II represented diabetic control group, group III received glibenclamide @ 1mg/kg b wt, group IV and V received hydroethanolic extract of *Amaranthus hypochondriacus* seeds (AHSE) and hydroethanolic extract of *Amaranthus hypochondriacus* leaves (AHLE) @ 250 mg/kg b wt for 30 days, respectively. The presence of apparent clinical signs such as polydipsia, polyuria and weight loss were observed in group II rats throughout the experiment which following treatment with AHSE and AHLE in group IV and V were reverted in a time dependent manner. The treatment with AHSE and AHLE significantly ($P<0.05$) reduced elevated fasting blood glucose, glycosylated Hb, impaired glucose tolerance, ALT, AST, ALP, BUN, creatinine, lipid peroxidation and caused significant ($P<0.05$) increase in total protein, albumin, reduced glutathione, superoxide dismutase and catalase in group IV and V, respectively. The histopathological and electron microscopic examination of tissues of pancreas, liver and kidney showed mild to moderate degree pathological lesions in group IV and V indicating the ameliorative effect of AHSE and AHLE, suggesting antidiabetic and hepato-renal efficacy of *Amaranthus hypochondriacus* against streptozotocin induced diabetes in rats.

EP-OP-15

COMBINED SUBACUTE TOXICITY OF MALATHION AND CHLORPYRIFOS IN MALE RATS AND ITS AMELIORATION BY *WITHANIA SOMNIFERA* AND RESVERATROL

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Present study was undertaken to ascertain the effects of combined subacute exposure of chlorpyrifos and malathion in 14 days trial and its amelioration by *Withania somnifera* and resveratrol in male Wistar rats. Adult male Wistar rats were randomly divided into six groups with seven rats in each group. Group I, served as the naïve control. Group II, III and IV rats were given combined exposure of chlorpyrifos at 19 mg/kg bwt. and malathion at 90 mg/kg bwt. Additionally, group III and IV rats were also given *Withania somnifera* at 12.5 mg/kg bwt., and resveratrol at 5 mg/kg bwt., respectively. Group V and VI rats were given *Withania somnifera* at 12.5 mg/kg bwt. and resveratrol at 5 mg/kg bwt., respectively. Combined exposure of chlorpyrifos and malathion significantly altered the levels of malonaldehyde, myeloperoxidase, nitric oxide, reduced glutathione, glutathione peroxidase, protein carbonyl, tissue protein in liver, kidney and brain which were significantly attenuated by *Withania somnifera* and resveratrol treatment. Similarly, combined exposure of chlorpyrifos and malathion significantly increased the plasma levels of liver and kidney function biomarkers like ALT, AST, GGT, BUN and creatinine but these levels were significantly decreased by *Withania somnifera* and resveratrol treatment. Combined exposure of chlorpyrifos and malathion produced histopathological alterations like congestion and sinusoidal dilatation in liver and hypercellularity in glomeruli of kidney, which were attenuated by *Withania somnifera* and resveratrol treatment. Results conclude that combined exposure of chlorpyrifos and malathion produced toxic effects on liver, kidney and brain of male Wistar rats. *Withania somnifera* and resveratrol possesses potential to ameliorate the toxicity produced by combined exposure of chlorpyrifos and malathion.

EP-OP-16

COMPUTATIONAL APPROACHES TO UNVEIL THE EFFECT OF MEDICINAL PLANTS AGAINST BOVINE PAPILLOMA VIRUS

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Bovine cutaneous papillomatosis (warts) is an infectious and proliferative, benign neoplasm caused by Bovine Papilloma Virus (BPV), a group of DNA viruses of the family Papillomaviridae which is characterized by small to medium sized growths on skin or mucous membranes. In India, bovine cutaneous warts were reported to be BPV type 1 and type 2 (Singh *et al.,* 2009). Though various treatment protocols are available either alone or in combination, due to their unsatisfactory results and possibilities of recurrence, along with high cost of drugs and long duration of therapy, current trend is leading to focus on herbal therapy. Nowadays, there is an increasing awareness and acceptability on the usage of herbal drugs, since they are safe, effective, and cheaper as well as shows more promising results on healing. In India, few herbal plants reported to have the antiviral and anti-wart effects. Hence, the present study has been designed to explore the best possible molecular interaction between selected active phytochemicals and target protein E2 in BPV1 through *in silico* studies to give guidance to formulate a polyherbal formulation against the bovine cutaneous papillomatosis. A few medicinal plants such as *Curcuma longa, Azadirachta indica, Acalypha indica, Andrographis paniculata* and *Mukia maderaspatana* are selected based on the literature report. The active principle of the selected medicinal plants is surveyed for their antiviral activity and selected based on the literature report and Lipinski's Rule. The three-dimensional structure of all these compounds and its target E_2 protein of bovine papilloma virus 1 were retrieved from PubChem and RCSB-PDB database, respectively. A ligand binding pocket is predicted based on the HPV11 E2 protein. Molecular docking was performed by screening all the ligand molecules against BPV1-E2 protein employing autodock algorithm. Docking study revealed that few compounds from the selected medicinal plants shows good interaction with BPV1-E2. A few hot-spot residues were found to have hydrogen bond and hydrophobic interaction with the ligand molecules. Based on scoring, top scored molecules were selected and reported to have effect against Bovine cutaneous papillomatosis. Hence, the study throws lights on predicting important molecules or the selected plants, which may be used in polyherbal formulation against Bovine cutaneous papillomatosis. However, further studies are warranted through *in vitro* and *in vivo* studies to understand their mechanism of action, effect and toxicity.

EP-OP-17

DRUG DEVELOPMENT FROM BIOACTIVE ETHNOVETERINARY COMPOUND THROUGH *IN-SILICO* AND *IN-VITRO* APPROACH

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Bovine mastitis, a pervasive issue in our country, significantly undermines the national economy by causing a substantial loss through decrease in milk production. *Staphylococcus aureus* and *Escherichia coli* play pivotal roles in causing bovine mastitis. While antibiotics undeniably are the first-choice of treatment, their widespread and indiscriminate usage has fostered the emergence of anti-microbial resistant pathogens. Thus, aim of this study was designed as to explore the antibacterial potential of Aegle marmelos through an *in-silico* and *in-vitro* analysis against *S. aureus* and *E. coli.* A GC-MS analysis of A. marmelos revealed that this plant contains many bioactive components such as fatty acids, methyl esters, etc. and molecular docking of these bioactive compounds was performed against *S. aureus* protein 2FNP and *E. coli* protein 1IEM which declared astonishing results. Compounds with PubChem CID 534400, 12858404, and 120099 from A. marmelos had shown binding energy of -8.6, -6.7, and -6.7 for *E. coli* protein 1IEM and -8.2, -6.1 and -6.2 for *S. aureus* protein 2FNP, respectively. In an *in-vitro* analysis of hydro-ethanolic extract of leaves of A. marmelos minimum inhibitory concentration (MIC) was determined for *S. aureus* and *E. coli.* The results were appreciating with MIC value of 8mg/ml and 32mg/ml for *S. aureus* and *E. coli,* respectively. Study suggests that bioactive compounds from A. marmelos can be good candidates for development of new drug to curb the antibacterial resistant pathogens responsible for mastitis.

EP-OP-18

IN VITRO EVALUATION OF ACARICIDAL EFFECT OF THE ETHANOLIC LEAF EXTRACTS OF *LEUCAS ASPERA* AND *VITEX NEGUNDO* AGAINST THE BROWN DOG TICKS *RHIPICEPHALUS SANGUINESIS*

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Tick infestation has significant health impact in dogs. They are the major causative factor for tick paralysis, tick injury, tick pyaemia and also transmit different causative pathogens to the host. *Rhipicephalus sanguinesis,* brown dog tick is most prevalent species in Indian subcontinent and serves as a vector for the protozoal infections such as Ehrlichiosis, Babesiosis, etc. Prevention of ticks is one of the fundamental preventive measures to control tick borne protozoal, bacterial and viral infections. The problem of toxicity and development of resistance to conventional insecticides necessitates the need for newer herbal drugs for the control and management of ticks. Many plants were reported were used by the traditional healers for the control of insects in livestock and whose scientific merit was not validated. This study was aimed at investigating the acaricidal

potential of the *Leucas aspera* and *Vitex negundo* against Rhipicephalus sanguinesis. The ethanolic extracts of these plants were evaluated for acaricidal efficacy by Larval Packet Test at different concentrations ranging from 50mg/ml -150mg/ml. The ethanolic extract of *Vitex negundo* exhibited efficacy against larvae of *Rhipicephalus sanguinesis* with 80-90% mortality compare to *Leucas aspera*. The findings of this study provide valuable insights into the development of natural alternatives for acaricidal control in veterinary practices. Further investigations are warranted to elucidate the underlying mechanism and assess the extracts potential for practical application in tick management strategies.

EP-OP-19

EVALUATION OF HEPATOPROTECTIVE ACTIVITY OF *PICRORHIZA KURROA* RHIZOME EXTRACT AGAINST COPPER SULPHATE INDUCED TOXICITY IN *ALBINO* RATS

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The present investigation was conducted to investigate the hepatoprotective activity of *Picrorhiza kurroa* against copper sulphate induced toxicity in albino rats. In the present experiment 30 albino rats were divided into five groups each consisting 6 animals i.e., I, II, III, IV and V. The control group received saline water and the experimental groups received oral copper sulphate in dose of 100 mg/kg body weight and *Picrorhiza kurroa* in dose of 400 mg/kg body weight respectively. The evaluation of biochemical and hematological parameters was done on 0, 14th and on 28th day. All the animals were sacrificed on 28th day of experiment and liver tissues were collected for histo-pathological evaluation. The mean values of AST in control group I, were 107.15±3.32 IU/L, 116.43±3.11 IU/L, 127.58±2.85 IU/L and the mean values of copper treated group were 108.96±12.17 IU/L, 135.33±16.92 IU/L, 242.40±10.80 IU/L on 0, 14th and 28th day, respectively. The mean AST values were significant reduced as 109.83±5.89IU/L, 125.20±5.60IU/L, 182.58±2.43IU/L, respectively on *P. kurroa* treatment. The mean values of ALT, ALP, bilirubin, total protein and albumin were increased on copper sulphate treated group. However, the increased values were reduced on *P. kurroa* treatment. Microscopic lesion of liver section of copper sulphate treated rats revealed severe cellular swelling and hepatocyte degeneration However, treatment given with *P. kurroa* revealed minimal to mild congestion with normal hepatocytes. The present study is concluded that the *P. kurroa* showed the amelioration in hepatic toxicity caused by copper sulphate.

EP-OP-20

EVALUTAION OF ANTIOXIDANTS POTENTIAL OF *EMBLICA OFFICINALIS* IN *WISTAR* RAT

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Traditional medicine plays a critical role in the treatment of various types of diseases. Nowadays, the use of complementary medicine and natural products has been increasing rapidly worldwide because they are effective and inexpensive and have fewer side effects. The therapeutic value of Indian medicinal plants is well recognized and acknowledged all over the world. *Emblica officinalis* commonly known as Indian gooseberry or *Amla*, is perhaps the one of the important medicinal plant possesses pharmacotherapeutic activity. Present study was conducted for evaluation of antioxidant potential of Methanolic extracts of *Emblica officinalis* in Wistar rat at the dose rate of 200 mg.kg^{-1} following oral gavage administration and measures oxidative profiles in wistar rats *Emblica officinalis* extracts caused an apparent decreases of Super Oxide Dismutase (0.595± 0.07), as compared to antigen control (0.664± 0.06) and normal saline control. *Emblica officinalis* showed significant variation in Serum Total protein was found (6.87± 0.225) higher value in *Emblica officinalis* as compared to Antigen(SRBC) and saline control group. Lipid per Oxidation and Glutathione peroxidase was also decreases (0.156± 0.007), (0.731± 0.021) as control group(0.177± 0.009), (0.780± 0.02) respectively. It was found significant variation with saline and antigen control group. The above finding showed Antioxidant potentials of *Emblica officinalis* extracts and reduces oxidative stress.

EP-OP-21

EFFICACY EVALUATION OF *PHYLLANTHUS AMARUS* AS AN ANTIVIRAL AGENT AGAINST NEWCSATLE DISEASE VIRUS *IN-OVO*

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The present study was undertaken to investigate the effect of ethanolic extract of *Phyllanthus amarus* using an *in ovo* assay. Nine days old embryonated eggs were divided into six groups (n=6) and received various treatments. Five groups were inoculated with the field strain of New Castle disease virus isolated and propagated in chicken embryo allantoic fluid at Poultry Disease Diagnosis and Surveillance Laboratory, Namakkal. The remaining three groups were treated with different concentrations of the extract with DMSO as the solvent. The uninoculated and the inoculated groups were left as the negative control and the positive control respectively. Embryo survival was observed daily. Allantoic fluid was harvested from the treated eggs for haemagglutination (HA) test to detect NDV in the eggs. Results showed that the extracts significantly reduced the virus titres ($P< 0.05$) with no detectable virus in the plant extract treated groups suggesting that the herb was capable of

destroying the NDV before stimulating the developing chick's immunity. Phytochemical analysis of the extract revealed the presence of alkaloids, flavonoids, saponins, tannins, terpenoids and carbohydrates which has been regarded as novel antiviral agents. Thus the current findings have clearly demonstrated that the ethanolic extract have strong antiviral activity against NDV *in ovo* and can act as a substitute for conventionally used synthetic drugs thereby assuring safety and quality of poultry meat against drug resistance and residues. However, *in vivo* trials are needed to validate the use of this herb in controlling New castle disease in chickens.

EP-OP-22

ACCELERATION OF HEALING OF WOUND IN DIABETIC RATS DUE TO ANTIOXIDANT POTENTIAL OF *SHOREA ROBUSTA* RESIN

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Increased oxidative stress at wound site is markedly responsible for impairment in the wound healing in diabetics. Previous studies have shown various biological activities of *Shorea robusta* resin including antioxidant action. The time-dependent and concentration-dependent effects of alcoholic extract of *Shorea robusta* resin (SRE) were evaluated on cutaneous wound healing in diabetic rats. Diabetes was induced in male Wistar rats by streptozotocin. Open excision wounds of 2x2 cm^2 were experimentally created on dorsal region of the diabetic rats. SRE ointment (3, 10 and 30%) was applied topically on the wound area twice daily for 19 days. Six animals from each group were sacrificed on days 3, 7, 14 and 19 to collect the granulation tissue which was used for the estimation of antioxidant enzyme activity and lipid peroxidation by spectrophotometer. Topical application of SRE markedly decreased the wound size, as compared to that of control group on day 3, 7, 14 and 19 post-wounding. The levels of GSH and activities of SOD and catalase were markedly higher in SRE treated group with concomitant decrease in MDA and NO level on day 3, 7, 14 and 19 as compared to control. The results of this study revealed that SRE treatment caused faster as well as better organized healing of cutaneous wounds in diabetic rats. The quality of the healed tissue was much better than the diabetic control rats. Thus, the SRE has shown great potential in treating wounds in diabetic rats.

EP-OP-23

PROSOPIS JULIFLORA LEAVES EXTRACT ALTERS BACTERIAL ULTRASTRUCTURE TO EXERTS ITS ACTION AGAINST *E. COLI* ISOLATED FROM CLINICAL CASES OF ENDOMETRITIS

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Endometritis is the leading cause of reproductive inefficiency, infertility and reduced milk yield in high yielding cattle and buffaloes. Indiscriminate use of synthetic antimicrobials results in emergence of resistance whereas phytoconstituents are considered to be an effective alternative to combat the bacterial resistance. In the present study we reported the mechanism of antibacterial action of *Prosopis juliflora* leaeves (PJ) extract against *E. coli.* isolated from clinical cases of endometritis. The bacterial isolates were charactrized by their cultural, morphological, biochemical characteristic and genetic analysis. Ethanolic PJ extract exhibited a marked *in vitro* antibacterial action against S4 clinical isolate and reference strain (ATCC 25922) as evidenced by agar well diffusion test with MIC value of 0.39 mg/ml owing to the presence of large quantity of total phenolic acid and flavonoid contents. This antibacterial action of PJ extract was shown to initiate at 6 h post-exposure while the complete bactericidal action was achieved at 12 h post-exposure. Mechanistically, the test extract produced damage to the bacterial cell wall and caused loss of cell membrane integrity leading to release of the intra-cytoplasmic contents and formation of vacuole as evidenced by examining the bacterial ultrastructure following electron and fluorescent microscopy studies. Based on the above findings it may be inferred that *Prosopis juliflora* leaves extract possesses promising therapeutic potential against bacterial endometritis.

EP-PP-01

PHYTOCHEMICAL ANALYSIS AND ANTIMICROBIAL EVALUATION OF *OCIMUM SANCTUM* LEAVES EXTRACTS AGAINST *E. COLI*

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Ocimum sanctum Linn also known as Tulsi or Holybasil is an aromatic plant. It belongs to the family Lamiaceae. It is widely used in Ayurveda and Siddha system of medicine to cure various ailments. This plant is known to possess antiseptic, analgesic, anti-inflammatory, antimicrobial, antistress, Immunomodulatory, hypoglycemic, hypotensive and antioxidant properties. There are many chemical constituent present in *ocimum sanctum* such as, oleanolic acid, rosmarinic acid, ursolic acid eugenol, linalool, carvacrol, β-elemene, β-caryophyllene, germacrene. *Escherichia coli (E. coli)* is a Gram negative lactose fermenting bacteria belonging to family Enterobacteriaceae. Extractability percentage of methanolic, chloroform and aqueous extract of *Ocimum sanctum* were 8.82, 4.68 and 9.42 respectively. Aqueous extract of *Ocimum sanctum* leaves showed no

antibacterial activity against *E. coli.* The MIC for methanolic extract of *Ocimum sanctum* against *E.coli* was 12.5 mg/ ml, while for NRCC strain of *E. coli*, it was 25 mg/ ml. Likewise MIC for chloroform extract of *Ocimum sanctum* against ATCC and NRCC strain of *E. coli* was 12.5 mg/ ml. Methanolic extract of tulsi contain alkaloid, reducing sugar, phenol and tannin phytochemical.

EP-PP-02

PROPHYLACTIC EFFECT OF *CORIANDRUM SATIVUM* AND *MURRAYA KOENIGII* BI-HERBAL EXTRACTS ON ADENINE INDUCED CHRONIC KIDNEY DISEASE IN RATS

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The present study was carried out to evaluate the prophylactic efficacy of *Coriandrum sativum* (CS) and *Murraya koenigii* (MK) on adenine-induced chronic kidney disease in rats using 36 male Sprague-Dawley rats. For evaluation of prophylactic efficacy of bi-herbal aqueous and alcoholic extracts *Coriandrum sativum* (CS) and *Murraya koenigii* (MK), were mixed in a 1:1.5 ratio after determined by *in-vitro* nucleation assay. The rats were randomly divided into six different groups, each group contains six rats. Chronic kidney disease (CKD) was induced in the group II, III, IV, V and VI by adenine @ 200 mg/kg daily once through the intragastric route for 28 days. Group I served as control and was given standard pelleted diet. Group II served as adenine control and was given adenine (200 mg/kg, orally) for 28 days. Groups III and IV received bi-herbal aqueous extracts of CS and MK @ 250 and 500 mg/kg for 28 days respectively. Groups V and VI received bi-herbal alcoholic extracts @ 250 and 500 mg/kg for 28 days respectively. The blood was collected on 28th day of experiment to analyse the haemato-biochemical parameters. Urine samples were collected by using metabolic cages on 28th day and analyzed for different qualitative and biochemical parameters. The experimental rats were studied for ultrasonographic, gross and histopathological changes in kidneys of different groups. Bi-herbal aqueous and alcoholic extracts treated rats (groups III, IV, V and VI) produced significant improvement in mean body weight and feed consumption as compared to adenine control rats (group-II). The administration of bi-herbal aqueous and alcoholic extracts of CS and MK leaves, along with adenine in prophylactic groups revealed significant improvement on haemato-biochemical and urine parameters. Results of ultrasonographic and histopathological examination of kidney tissues in prophylactic groups was well supported and prevent alterations in kidney associated changes in adenine-induced CKD in rats. Result of the present study showed that the bi-herbal aqueous extracts of CS and MK leaves at dosage of 250 mg/kg, while bi-herbal alcoholic extracts at dosage of 500 mg/kg showed greater efficacy among all prophylactic study groups. Results showed that aqueous and alcoholic bi-herbal extracts of *Coriandrum sativum* and *Murraya koenigii* leaves revealed prophylactic efficacy against adenine induced CKD in rats.

EP-PP-03

EFFECTS OF GANDH PAALASHI (*HEDYCHIUM SPICATUM*) ON THE EXPRESSION OF HEPATIC GENES ASSOCIATED WITH BIOTRANSFORMATION, ANTIOXIDANT AND IMMUNE SYSTEMS IN WLH COCKERELS FED INDOXACARB

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The ameliorative efficacy of *Hedychium spicatum* root powder (HSRP) on gene expression in Indoxacarb intoxicated in WLH cockerels was investigated. Forty-nine White leghorn Cockerels of 6 to 8 weeks age, weighing about 300 to 400 gm were divided randomly into seven groups with each group consisted of 7 birds. Group I served as Control and given normal feed and water, Group II was fed with Indoxacarb @ 250ppm in feed, Group-III Silymarin@250ppm in feed, Group IV Indoxacarb @ 250 ppm+ Silymarin@250ppm in feed, Group V (*Hedychium spicatum* Rhizome powder (HSRP) @ 4000ppm), Group VI Indoxacarb @ 250 ppm+ *Hedychium spicatum* Rhizome Powder (HSRP) @ 2000ppm in feed, Group VII Indoxacarb @ 250 ppm+ *Hedychium spicatum* Rhizome Powder (HSRP) @ 4000ppm in feed, respectively. After 16 weeks of treatment all birds from different groups were sacrificed humanly and the liver sample was collected in DNA latter for expression study by RT- PCR to evaluate fold changes in the expression of genes involved in antioxidant function [catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione S-transferase (GST)], biotransformation [epoxide hydrolase (EH), cytochrome P450 1A1 and 2H1 (CYP1A1)] and the immune system [interleukins 6 (IL-6)]. Changes in gene expression were determined using the quantitative real-time PCR technique. There was significant ($P<0.05$) upregulation of IL-6, CYP1A1 and GPx genes in indoxacarb treated groups in comparison to control. The significant ($P<0.05$) down regulation of CAT and SOD genes in indoxacarb treated groups in comparison to control was observed. Simultaneous treatment with HSRP resulted in ameliorative effect and restores the gene activities at par with control. The present study demonstrated protective effects of *Hedychium spicatum* root powder (HSRP) on changes in expression of antioxidant, biotransformation, and immune system gene in cockerels fed indoxacarb.

EP-PP-04

PHYTOCHEMICAL CHARACTERIZATION OF *ANNONA SQUAMOSA* BY HIGH PERFORMANCE THIN LAYER CHROMATOGRAPHY

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Leaves of *Annona squamosa* (Custard apple) are rich in secondary metabolites such as flavonoids, alkyl ketones, sesquiterpenes, essential oil etc. and the plant is reported to possess various medicinal properties. HPTLC is an invaluable quality assessment tool for the evaluation of botanical materials. The present investigation was undertaken to screen the physicochemical and phytochemical characteristic of *Annona*

squamosa leaves via High Performance Thin Layer Chromatography that contributes to various biological activities. Preparation of ethanolic extract by soxhlet method using ethanol and per cent extractability was calculated. Ethanolic extract of *Annona squamosa* was screened for presence of phyto-constituents like alkaloids, tannins, glycosides, flavonoids, saponins etc. using standard test procedures. The quantification of Rutin was done by HPTLC using a standard solution of rutin (50 µg/ml) and mobile phase consisting of toluene : ethyl acetate : methanol : formic acid (3:1.5:1.3:0.4). According to the observational record of our present research work, it was found that preliminary study of ethanolic extract of *Annona squamosa* leaves showed the presence of many phytochemicals where rutin (flavonoid compound) was responsible for the analgesic activity of *Annona squamosa*. On HPTLC analysis, the concentration of Rutin in *Annona squamosa* was found to be 0.06 per cent.

EP-PP-05

EFFECT OF *TERMINALIA CHEBULA* FRUIT EXTRACT ON INFLAMMATORY LUNG INJURY MARKERS AND MORPHOMETRIC PARAMETERS IN LPS-INDUCED ACUTE LUNG INJURY

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Acute lung injury (ALI) is a prominent clinical condition characterized by rapid hypoxia, respiratory dysfunction and inflammatory pulmonary edema due to various etiologies. Fruit extract from *Terminalia chebula* (TCE) has been shown to have anti-inflammatory properties, although its potential as therapy for ALI is still unexplored. Hence, we investigated the effects of an ethanolic *Terminalia chebula* fruit (TCE) extract against ALI mice. Five groups of mice were created: control, LPS, TCE alone (200 mg/kg bwt), LPS+TCE (100 mg/kg bwt), and LPS+TCE (200 mg/kg bwt). TCE was administered orally as a pretreatment for 7 days in the LPS+TCE groups of 100 mg/kg and 200 mg/kg, respectively, and in the TCE alone group (200 mg/kg bwt). To induce acute lung injury in mice after the final dosage of extract, intranasal LPS @ 40 mg/kg bwt was given under ketamine and xylazine anesthesia. Further, mice were sacrificed after receiving LPS for 24 hours, and samples were obtained for experimental research. In LPS induced injury mice, body weight and lung weight were altered, however, TCE extract administration were not improved them. Treatment with TCE extract decreased the elevated levels of tissue inflammatory cytokine IL-6 and serum C-RP, respectively. Further, the level of TNF-alfa and matrix metalloproteinases was estimated in lung tissue homogenates which was not influenced with the treatment with TCE fruit extract. In conclusion, the present study suggested that TCE administration showed improvement in LPS-induced acute lung injury by improving the level of serum C-RP and IL-6 inflammatory cytokine.

EP-PP-06

IN-VITRO INVESTIGATION OF PLANT-DERIVED DRUG AGAINST DRUG-RESISTANT *STAPHYLOCOCCUS AUREUS*

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The study was planted to assess the *In Vitro* antibacterial properties of ethanolic and aqueous extracts of Turmeric (*Curcuma longa*), Pudina (*Mentha arvensis)*, Garlic (*Allium sativum*), Tulsi (*Ocimum sanctum*), and Curry leaves (*Murraya koenigii*), against Multi Drug Resistant strains of *S. aureus* sourced from bubaline mastitis. Concentrations of 2.5, 5.0, and 10mg/100µL were tested using agar well diffusion, while Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were determined via broth dilution and MSA plates respectively. Ciprofloxacin served as the standard antibiotic, showing an 18.2±0.66mm zone of inhibition. Ethanolic extracts from all plants, except Garlic, exhibited superior activity compared to Ciprofloxacin and aqueous extracts. Ethanolic extract of Turmeric showed the highest activity with a 26.4±2.42mm zone of inhibition. Pudina, Curry leaves, and Tulsi had moderate activity with 22±2.09, 22.2±1.82, and 22.8±2.26mm zones of inhibition at a 10mg/100ml concentration. Ethanolic extract of garlic had lower activity, with a 12±0.83mm zone of inhibition at the same concentration. Aqueous extracts were less effective than ethanolic ones at all concentrations with statistically significant differences ($P<0.01$). Pudina, Curry leaves, Tulsi, and Turmeric had similar MIC and MBC values (1.562 mg/ml) against all resistant strains, lower than other extracts. Both ethanolic and aqueous Garlic extracts shared similar MIC and MBC values (6.250 mg/ml). This study suggests the potential use of these plants in treating diseases caused by MDR *S. aureus*. Further research is needed to identify the active phytochemicals responsible for their antibacterial activity.

EP-PP-07

COMPARATIVE STUDY ON *MADHUCA LONGIFOLIA* (SEED) OIL POTENTIAL IN CANINE MANGE

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The study was designed to observe the effect of *Madhuca longifolia* oil in mange infested dogs. Seed oil was extracted with a yield of 33%. 30 dogs were divided into five groups. First group was treated with standard drug i.e. Benzyl benzoate (25%), II group 100% oil was used, III group 80% oil with 20% DMSO, group IV 50% oil with 50% DMSO and in group V 20% oil with 80% DMSO was used topically. Various clinical findings, hematological and biochemical parameters were recorded after 0, 14, 28 and 42 days of treatment. On zero day in total score of clinical signs and lesions in mange infested dogs varied from (20.44 ± 0.12 to 22.36 ± 0.15). After treatment with various concentrations most significant results were appeared in group III

followed by group I. Significant changes were found in Hb, PCV, TEC, TLC and DLC. Highest increase in Hb and PCV was observed in group III followed by group I then group II, IV and V at 14, 28 and 42 days post treatment. Biochemical profile was also recorded. At zero days SGOT level was higher than normal level in all groups. At 14 days the SGOT level was start reducing. Maximum reduction in SGOT level was found in I, followed by III and II where as in group IV and group V little increase in SGOT level. At 28 days SGOT level was continue to decrease and highest reduction was found in group III followed by group I, II and group IV. In group V SGOT level was continue to rise. After 14 days of treatment SGPT level was reduced in all the groups. Highest reduction was observed in group I where standard drug was used followed by group III, group II and group IV where as in group V slight increase in SGPT level was observed. On 28 days maximum response was observed in group I followed by III, II, IV and group V. On 42 days SGPT level was continued to decrease in the same pattern as it was on 28 days. Present study suggests that *Madhuca longifolia* seed oil has moderate protective action on haematological and biochemical parameters altered by mange infestation in dogs.

EP-PP-08

ANGIOGENIC AND MMPS MODULATORY EFFECTS OF *SHOREA ROBUSTA* RESIN IMPROVED CUTANEOUS WOUND HEALING IN DIABETIC RATS

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Alcoholic extract of *Shorea robusta* resin (SRE) has shown cutaneous wound healing potential in some preliminary studies. We hypothesize that SRE facilitate wound healing in diabetic rats by modulating important healing factors in concentration and time-dependent manner. Diabetes was induced in male Wistar rats by streptozotocin. Open excision wounds of 2x2 cm^2 were experimentally created on dorsal region of the diabetic rats. SRE ointment (3, 10 and 30%) was applied topically on the wound area twice daily for 19 days. Wound closure measurement and tissue collection were done on days 3, 7, 14, and 19 post-wounding. SRE significantly accelerated wound closure, as compared to control. Western blots revealed upregulation of IL-10 and downregulation of TNF-α. Increased expression of CD-31 showed abundance of micro vessels in healing tissues after treatment. The MMP-2 and MMP-9 activities were reduced in SRE treated groups. Masson's trichrome staining revealed relatively better completion of re-epithelisation as well as increased deposition of well organised collagen fibres in the healing tissues compared to control. Topical application of SRE might be of great use in cutaneous wound healing in diabetic patients.

EP-PP-09

PROTECTIVE EFFECTS OF MORIN ON KIDNEY AGAINST CADMIUM CHLORIDE INDUCED OXIDATIVE DAMAGE

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Oxidative damage occurs due to imbalance between free radicals generated and antioxidant defence mechanisms. Excess of free radical generation leads to oxidative stress and produces deleterious effects on the kidney which is the major organ of excretion. Heavy metals like cadmium produces nephrotoxicity due to their oxidative damage and interaction with proteins. In the present study cadmium chloride @ 10,30,100 µM solution were used to induce the oxidative stress in kidney tissues collected in chilled Krebs-Henseleit buffer (PH: 7.5). Tissue homogenate was prepared using 10% potassium chloride. Antioxidant activity of morin was determined using phosphomolybdenum assay keeping ascorbic acid as reference. Markers of oxidative stress viz., SOD, GSH, TBARS and total protein were estimated in the tissue homogenate as per the standard protocols. Ascorbic acid and morin were used to revert back the oxidative damage produced by the cadmium chloride by incubating the tissues with ascorbic acid and morin. Treatment with ascorbic acid and morin normalized the altered levels of SOD, GSH, TBARS and total protein in the kidney tissue due to their free radical scavenging ability.

EP-PP-10

CARDIOPROTECTIVE EFFECT OF *FICUS RELIGIOSA* ON ISOPRENALINE INDUCED MYOCARDIAL INFARCTION IN WISTAR RATS

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Ficus religiosa (FR) (Moraceae family) possess numerous therapeutic properties in folk medicine, reported to be used as ethnomedicine to treat heart problems, which lead to further elucidate its cardioprotective properties. To evaluate the cardioprotective effect of leaves of FR in animal model of isoprenaline (ISO) induced myocardial infarction, thirty male wistar rats were selected and divided into five groups, group I (control), group II (ISO 150 mg/kg BW on 27th and 28th day at 24 h interval), group III (FR 200 mg/kg BW), group IV (FR 100 mg/kg BW + ISO 150 mg/kg BW on 27th and 28th day at 24 h interval) and group V (FR 200 mg/kg BW + ISO 150 mg/kg BW on 27th and 28th day at 24 h interval). ECG was conducted on anaesthetized rats. HW/BW ratio, percentage infarcted area, heamatological parameters, lipid profile, biochemical parameters, myocardial enzymes, lipid peroxidation, histopathological observations were carried out at the end of experimental trial. Administration of ISO in rats results in increase in heart rate, QT interval, ST segment and decrease in QRS complex. FR treated animals showed dose dependent significant ($p<0.05$) improvement in percentage infarcted area, HW/BW ratio, lipid profile, heamatological and biochemical parameters, myocardial enzymes, lipid

peroxidation and histopathological alterations in heart tissue when compared to ISO alone treated rats. In conclusion the hydroethanolic extract of leaves of *Ficus religiosa* @ 200 mg/kg BW showed remarkable cardioprotective effect in isoprenaline induced myocardial infarction. Thus, present findings may qualify the FR as a potential cardioprotective agent.

EP-PP-11

EFFICACY OF *ACTINIDIA DELICIOSA* EXTRACT AGAINST COMPLETE FREUND'S ADJUVANT INDUCED ARTHRITIS IN RATS

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The study was conducted at the Department of Pharmacology and Toxicology, Krantisinh Nana Patil College of Veterinary Science, Shirwal, District Satara, to determine the efficacy of *Actinidia deliciosa* extract against CFA-induced arthritis in rats. In this study, a total of thirty male Wistar rats were divided into three groups, each consisting of ten rats. CFA was administered intraarticularly in the right knee joint of animals to groups B and C whereas group A was kept as control. Group C was administered with indomethacin at a 2 mg/kg BW; 14 days after CFA injection. while group B was given ethanolic extract of *Actinidia deliciosa* at a dose of 250 mg/kg BW. The extract considerably significantly improved parameters such as hemoglobin, erythrocyte, and leukocyte count in the treatment group compared to the arthritic control group. Compared to the arthritic control, treatment with extract reduced BUN, serum creatinine, total protein, and albumin. According to radiological findings, the standard drug indomethacin, as well as extract, has significant efficacy in reducing tissue swelling and restoring reduced joint spaces to normal. Ethanolic extract of *A. deliciosa* appears to be extremely promising due to its antiarthritic effect as per the present findings. To completely understand the precise mechanisms of action of this herb, further extensive detailed clinical and preclinical research is required.

EP-PP-12

EVALUATION OF ANTIHELMINTIC ACTIVITY OF CARICA PAPAYA IN CAPRINES

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The present study was carried out to investigate the anthelmintic activity of *Carica papaya* in caprines. The helmintic infected 30 goats of either sex selected and were divided into 03 groups consisting of 10 goats in each group .Group A served as untreated, Group B received fenbendazole @ 5 mg/kg b.wt once dosed orally at day 0. Group C received only ethanolic extract of *C. papaya* seed separately at dose of 100 mg/kg b.wt dosed orally for first five consecutive days and booster at 16th day. The experimental parameters recorded for fecal examination, changes in body weight, hematological, biochemical alterations and phytochemical analysis. The qualitative phytochemical analysis showed that ethanolic extract of *C. papaya* seed for the presence of alkaloids, reducing sugar, tannins, and flavonoids. The results of the study indicated that group B fenbendazole

showed significant (ps0.01) anthelmintic effect by reducing EPG counts (84 2% at 15 day and 87.4% at 28 day). Group C showed significant (pd"0.01) anthelmintic effect by reducing EPG counts (60.2% at 15 day and 73.2% at 28 day). Both groups showed non-significant (ps0.05) increase in body weight on 28th day in GIN infected goats. Treatment groups (B and C) showed significant (ps0.01) increase in Hb, TEC, PCV and significant decrease (p50.01) in TLC of treated group (B and C) on 15 day and 28 day. On the basis of biochemical examination treatment groups (B and C) showed non-significant (pd"0.05) increase in TP and non-significantly (ps0.05) decrease in AST, ALP on 15th and 28". The mean value of ALT in groups B and C non-significantly (ps0.05) decreased on 15 day and significantly (pd"0.05) decreased on 28th day. To conclude ethanolic extract of *C. papaya* seed having anthelmintic efficacy at a dose 100 mg/kg b.wt orally for first five consecutive days and booster on 16" day.

EP-PP-13

EFFECT OF DESERT HERB (*LEPTADENIA PYROTECHNICA*) ON *IN VITRO* EXPRESSION OF TGF β1, VEGF IN VERO CELLS

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The present study was carried out to investigate the effect of extracts of desert herb (*Leptadenia pyrotechnica*) on TGF-β1 and VEGF expression *in-vitro* in the Vero cells. Renal epithelial cells (Vero) were maintained in DMEM culture medium supplemented with 10 per cent FBS in a humidified incubator at 37°C and 5 per cent CO_2 level. Methanolic and aqueous extracts of these herbs were obtained by a series of treatments like soaking of the herbal extract powder for 48 hours, sonication and rotatory evaporation. Resazurin dye assay was used for evaluating the non-cytotoxic concentration of methanolic and aqueous extracts of these herb. Non-cytotoxic concentration of methanolic and aqueous extracts of these herbs were added (Treatment group) to the Vero cells culture for 72 hour and then expression of TGF-β1 and VEGF were evaluated by qPCR in treatment and control (no addition of herbal extracts) groups. Expression of TGF-β1 and VEGF were found significantly increase in methanolic extract treated group of cells than control solvent cells. Aqueous extract of *L.pyrotechnica* showed non-significant increase in expression of TGF-β1 and VEGF. Results of the present study indicated that methanolic and aqueous extract of *Leptadenia pyrotechnica* have potential to treat wound, proud flesh, tumors and other inflammatory diseases.

।पशुधनं नित्यं सर्वलोकोपकारकम्।

ISVPT-2023

TECHNICAL SESSION-V

Toxicology of Xenobiotics

Chairperson : **Prof. S. K. Bhavsar**

Co-Chairperson : **Dr. K. A. Sadariya**

Rapporteur : **Dr. Sunil Hajare**


युवा वह है-
• जो अनीति से लड़ता है।
• जो दुर्गुणों से दूर रहता है।
• जो काल की चाल को बदल देता है।
• जिसमें जोश के साथ होश भी है।
• जिसमें राष्ट्र के लिए बलिदान की आस्था है।
• जो समस्याओं का समाधान निकालता है।
• जो नेक इतिहास रचता है।
• जो बातों का बादशाह नहीं बल्कि करके दिखाता है।
स्वामी विवेकानन्द
स्वामी विवेकानन्द

TOX-LP-01

MICROPLASTICS AS AN ENVIRONMENTAL POLLUTANT

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There is increasing scientific and societal concern about the effects of microplastics (MPs) in our environment. MPs commonly defined as plastic particles with sizes below 5 mm. Plastic products are made up of mixtures of polymers, fillers, and multiple additives to improve its usability. However, most of these chemicals are not covalently bound to the polymer, so they can be released at all stages of the plastics' life cycle via migration to liquids or solids or via volatilization. It is likely that unbound monomers resulting from these scenarios would leach into the environment, resulting in extremely small concentrations in drinking-water sources.

Microplastics can be classified as primary or secondary, depending on the manner in which they are produced.

Primary microplastics: Microplastic particles intentionally produced for direct use *e.g.* in cosmetics and abrasives, or as raw materials for production of larger plastic items;

Secondary microplastics: Microplastic particles originating from the fragmentation of larger plastic items by use, waste management or in the environment.

Primary microplastics are released into the environment in their final form, while secondary microplastics, are formed by unintentional degradation and weathering of larger plastics such as plastic bags, boxes, ropes, and nets into smaller particles directly in the environment by ultraviolet radiation from the sun and by mechanical influences, such as waves.

The release of secondary microplastics into the environment happens by three mechanisms:

• Natural disintegration of microplastics by weathering and microbial activity

• Decomposition of macroplastics into microplastics by direct activity of organisms

• Resuspension of past microplastic contamination in soil or sediment.

BisphenolA (BPA) is one of the chemicals with highest volume of production in the world. It is widely used in the manufacturing of plasticwares and also for the coating of thermal papers. BPA is even used to line the inner walls of food and beverage cans to preserve edible substances. BPA leaches out from plastic containers and food and beverage cans when they are exposed to high temperatures, acidic pH, or if cleansed or scrubbed using harsh detergents. The leaching of BPA is reported to be higher from old worn plastic wares as compared to newer ones. Plastic wares are used enormously by people across the world. One of the common uses of plastic is in the form of infant feeding bottles.

Microplastics in Environment

Microplastics enter freshwater environments in a number of ways: primarily from surface run-off and wastewater effluent (both treated and untreated), but also from combined sewer overflows, industrial effluent, degraded plastic waste and atmospheric deposition. Evidence indicates that some microplastics found in drinking-water

may come from treatment and distribution systems for tap water and/or bottling of bottled water.The polymers most frequently detected are polyethylene terephthalate and polypropylene. Land-based sources of microplastics into the aquatic environment, including fresh water, can originate from a variety of activities, infrastructure and land use practices. The road surface run-off from the breakdown of road-marking paints and tyre wear debris is suggested to be a significant input. Another important land-based source of microplastics is microplastic fibres that are released from textiles due to wear-and-tear and washing. "City dust", which is used to describe a number of sources related to abrasion of objects, such as synthetic soles of footwear and artificial turfs, can collectively be significant. Agricultural run-off has been identified as a potential source of microplastics in freshwater environments, particularly where sewage sludge has been applied to the land or where agricultural plastics, such as those used for mulching, have been used. Wastewater effluent is another widely recognized source of microplastic pollution in fresh water. Combined sewer overflows designed to cope with storm events and heavy rainfall can also be direct sources of microplastics in fresh waters. Once macroplastic debris has reached the aquatic environment, UV radiation and high temperatures can cause chemical changes, making plastics brittle and thus more susceptible to fragmentation and degradation. Atmospheric deposition is identified as an additional potential contributor to microplastics in freshwater environments through wet and dry deposition, precipitation and run-off. Some treatment-plant components and distribution networks are made from plastic and their erosion or degradation may contribute to microplastics in drinking-water. A potentially important source of fine microplastic particulates to the atmosphere could be associated with tyre and road-wear particles. Sea salt aerosol formation, wind-driven release of wastewater sludge, degradation of plastic sheeting and other construction materials, clothes drying, and wear and tear of textiles are all possible sources of airborne microplastics. Two of the main inputs of microplastics into fresh water are surface run-off and wastewater effluent.

Entry of Microplastics in Food Chain

The ingestion may be by oral route which involves consumption of contaminated water, food products (honey and beverages), through use of personal care products (toothpaste, face wash, scrubs, soap; also dermal route), marine product (food chain), plant (food chain), contact (dermal) from soil, water or fallout of airborne MPs, from particulate fallout from air during open meal and inhalation. The food chain exposure process is based on human consuming MPs contaminated aquatic organisms, animals or plants, which in turn may have consumed the plastic through MP loaded water or the feeding from other organisms. Another aspect of food chain exposure is by consuming contaminated plants. Dermal exposure occurs when humans interact with water or soil contaminated with MPs or from contact with particulate MPs through skin pores penetration. Exposure by this means is based on individual susceptibility as human skin pores vary by individual. Humans may also be exposed to MPs through inhalation. This is only possible when the MPs become airborne. For MPs to be inhalable, it must have a size that can allow it reaches the respiratory system.

Once microplastics enter the marine food web, there is a strong possibility that it will contaminate the human food chain as well, through a process called bioaccumulation, where chemicals from the plastics enter into the body of the animal when it is feeding on the plastic. Then, it is consumed by the prey and the chemicals pass to the predator—making their way up the food web that includes humans, leading to the development of multiple diseases for wildlife and humans. The main BPA exposure source in animals and humans is through intake of food and beverages that have been in contact with materials manufactured with this compound, which detaches from its matrix and is ingested orally. Oral consumption of contaminated food and dermal absorption from personal care products are considered the main exposure routes for phthalates. Humans may be the most exposed organism because they are at the peak of the food chain.

Microplastics can also be found in canned products, such as sardines and sprats. The occurrence of microplastics has been recorded in bottled water. Besides the contamination of air and water, soil contamination is another possible source of microplastics in the food chain. Soil microplastic contamination occurs via several routes. These include landfills, soil treatment, use of sewage sludge for soil fertilization, irrigation with wastewater, use of compost and organic fertilizers, remnants of mulching foils, tire wear, and atmospheric gradient. In the animal eco-system, the food chain is a relatively important way to deliver and reserve nutrient substances. However, the food cycle can also be a means to transfer plastics and substances attached to them. Although trophic transfer of MPs has been verified in both aquatic and terrestrial ecosystem, more attention is focused on aquatic food chain. Bioaccumulation may be the crucial way for introduction of microplastics into these animals. Therefore, plastic particles are likely to be ingested by various animals due to their pony-size characteristics, which ultimately poses a risk to humans.

Pathological changes induced by microplastics in biological system

Humans and animals are exposed to MPs via trophic transfer or by direct ingestion, contact and inhalation. MPs can also be ingested indirectly through personal care products such as toothpaste, face wash, scrubs and soaps. Results from a recent study showed that 50 % of the face wash products and 67 % of the facial scrubs studied mainly contained microbeads. These microbeads can cause skin aging and dark spots on the skin by letting in bacteria through the tiny rips formed. Microbeads can also injure the cornea when it gets stuck in under the eyelid from face washing. MPs in toothpaste can lead to gingivitis and bleeding with prolonged exposure when trapped between gum. The plausible effects include lung inflammation and genotoxicity may occur.

Two broad classes of plastic-related chemicals are of critical concern for human health—bisphenols and phthalates. Bisphenol A (BPA) is an endocrine-disruptor compound (EDC) with estrogenic activity. The endocrine modulating activity of BPA and its effects on reproductive health has been widely studied. BPA also has effects on the immune system. Phthalates are also EDCs used as plasticizers in a wide array of daily-use products. These compounds exert several cell effects through modulating different endocrine pathways, such as estrogen, androgen, peroxisome proliferator-activated receptor gamma, and arylhydrocarbon receptor pathways. BPA is classified as an EDC with estrogenic characteristic since it can bind to nuclear ERα and ERβ and trigger signaling pathways, even when its affinity is lower. Oral consumption of contaminated food and dermal absorption from personal care products are considered the main exposure routes for phthalates. The exposure of bisphenols and phthalates at critical periods of the development on the immune system and the development of certain types of cancer was described.

The ingestion of MP particles by animals can cause many adverse effects. As a peculiar pollutant, MP particles could cause a variety of physiological harms. The common health risks including inflammation response, metabolism disruption, and intestinal barrier dysfunction, so animal growth and reproduction rate decreased eventually. From the cellular perspective, animals ingested MPs had higher nuclear abnormality rates and morphological changes of erythrocytes, which suggested the mutagenic and cytotoxic damages, respectively. The alteration of intestinal flora has been the major hazard caused by foreign substances since the flora is involved in the defence of the intestines. Exposure to MPs alters the composition of gut microbiota causing gut dysbiosis, leading to various diseases.

MPs may build up in the gastrointestinal system after consumption, producing obstructions across the digestive tract and limiting feeding owing to appetite. Intake of MPs could also induce anatomical and functional changes

in the digestive tracts, causing dietary and development issues in fish. Oxidative stress, decreased mobility, gene expression disruption and damage of reproductive organs are the most common effects of MPs. The presence of MPs in seafood poses a major hazard to human health. Endocytosis and persorption are two of the most common methods for MPs to enter the human body. Seafood is an essential part of the human diet. MPs contamination of the intestinal system poses a serious risk of spreading to other regions of the body. Swelling and blockage are caused due to the buildup of MPs and nano plastics in tissues. As a result, the animals are exposed to MPs for an extended period, potentially leading to chronic discomfort, swelling, cell growth, and death, as well as immune cell impairment. Inflammatory bowel disease was significantly higher in patients with MPs than the healthy people. Oxidative stress, consequent inflammatory, and cytotoxic impacts were thought to be the main effects for MPs toxicity in inhalation exposure experiments. MPs can induce oxidative stress by producing oxidizing substances adsorbing to their surface, as well as reactive oxygen radicals created by the host during the inflammation. Due to the polymerization and processing, MPs include reactive oxygen species. MPs aging also resulted in the formation of free radicals, which oxidized the target tissues. MPs were found to be cytotoxic as an effect of oxidative damage and inflammation.

MPs can either directly influence metabolism by altering metabolic enzymes or circuitously by upsetting the energy equilibrium. MPs were reported to cause systemic or local immune responses after exposure, based on their dispersion and human reaction. Environmental exposure to MPs, on the other hand, was enough to impair immune systems in biologically vulnerable individuals, resulting in autoimmune disorders or immunosuppression.

MPs have been shown to have an effect on neuronal function and behaviour *in vivo*. Exposure to MPs elevated AChE activity in the brain and altered serum neurotransmitters. These events could be the result of direct interaction with teleported particles or the effects of circulating pro-inflammatory cytokines that result in long-term neuronal injury. Oxidative stress and persistent irritation generated by nano plastics revealed evidence of pro-inflammatory agents, which stimulated vasculature, leading to the creation and development of cancers. MPs worked as vectors, delivering germs to target tissues, protecting them from the immune structure, causing proinflammatory replies, and potentially facilitating infections. When MPs came into touch with bacteria and chemicals, their large surface area made them vulnerable to becoming vectors.

Nanoplastics pose a higher risk because their size allows them to cross the placenta and the blood-brain barrier, as well as transport across M-cells in Peyer's patches in the small intestine to the blood and lymphatic system, from where they can contaminate the liver and gallbladder.

Microplastic intake can upset energy balance, metabolism, and the immune system. Another risk associated with the consumption of microplastics in food is microbial association with their surface. The presence of various pathogenic species has been confirmed on the surface of microplastics, and the consumption of seafood increases human exposure to these microorganisms. Harmful chemicals such as bisphenol A, PCBs, PAHs, chlorinated pesticides, BFRs, and antibiotics can be released from microplastics into food, which can subsequently have carcinogenic and mutagenic effects and act as endocrine disruptors. Microplastics with a biofilm can be involved in horizontal gene transfer (HGT) between different bacteria, thus promoting the transfer of antibiotic resistance. Therefore, microplastics are a hot spot for organic micropollutants, mobile genetic elements, and microorganisms. Microplastics can adversely affect human health with potential carcinogenic, teratogenic and mutagenic effects. However, many species either by selective targeting of plastic items, or accidental ingestion by filtration or predation are exposed directly to MPs.

Bisphenol A is a 'substance of serious concern' for its hormonal disrupting properties on the human body. It has been confirmed in several studies to be associated with obesity, cardiovascular disease, reproductive disorder, and breast cancer. BPA is utilized as an antioxidant and a stabilizer that has the potential to damage the endocrine system. It can move out of polycarbonates and adhere to consumable food, allowing it to be consumed by humans. BPA may potentially have a role in the development of overweight by disrupting alpha and beta receptors in fat tissues, changing fat tissue hormone levels, and interacting with the action of lipoprotein lipase, aromatase, and lipogenesis regulators. It has the potential to cause breast and prostate cancer in mammalian species, as well as cancer in humans. The plastic bottles leach out endocrine disruptors and affects bodily functions in terms of biochemical alterations like increased blood urea, raised creatine-kinase–MB levels, and altered lipid profile in infants exposed to bottle feeding.

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TOX-LP-02

CURRENT DEVELOPMENTS IN REGULATORY TOXICITY TESTING OF XENOBIOTICS

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1. Introduction to Regulatory Toxicology: Regulatory toxicology applies the knowledge of toxicology to evaluate the safety of chemicals and help to ensure that society benefits from their use without unacceptable risk to human and animal health and the environment. Regulatory toxicology in industry or government is an excellent career option for biomedical scientists who prefer applied problem solving over basic research. Many regulatory toxicologists work in industries such as pharmaceuticals, pesticides, food, cosmetics, and chemicals that must provide transparent and reliable evidence about the potential effects of their products. Regulatory toxicologists also work for governmental agencies that evaluate industry data and assessments and make a final decision on the registrable uses of a product. Specialist consulting firms also employ regulatory toxicologists. Furthermore, Regulatory Toxicology supports the development of standard protocols and new testing methods to continuously improve the scientific basis for decision-making processes (Malvezzi et al, 2019; Schwenk et al, 2002).

The following methods are characteristic elements in regulatory toxicology:

- conducting animal and *in vitro* experiments to examine acute and chronic toxicity, skin irritation, eye irritation, sensitisation, mutagenicity and carcinogenicity, as well as studies on fertility and teratogenicity. These studies apply standard protocols (experimental toxicology)
- examining and evaluating physical-chemical properties of chemical substances and their behaviour in human and animal bodies (toxicokinetics)
- developing methodologies to examine modes and mechanisms of action (toxicodynamics)
- conducting specific evaluations using mathematical and statistical models
- examining available data regarding their comprehensiveness, quality, and value (data assessment)
- determining the type, extent, and duration of human exposure
- applying adjustment and uncertainty factors to extrapolate appropriate data to the human situation (data evaluation)
- assessing and quantifying risk, its consequences, and uncertainties in the estimates
- providing proposals for risk management (*e.g.* restrictions for use or exposure; classification and labelling) with adequate reasoning
- making recommendations for the generation, application and monitoring of rules, directives, and laws.

2. Regulatory Guidelines:

OECD Guidelines: The Organisation for Economic Co-operation and Development (OECD) publishes guidelines for the assessment of chemical effects on human health and the environment. The OECD Guidelines is a collection of the most relevant internationally agreed testing methods used by government, industry, and

independent laboratories to identify and characterise potential hazards of chemicals. They are a set of tools for professionals, used primarily in regulatory safety testing and subsequent chemical and chemical product notification, chemical registration and in chemical evaluation. They can also be used for the selection and ranking of candidate chemicals during the development of new chemicals and products and in toxicology research. These guidelines describe *in chemico*, *in vitro*, *ex vivo* and in vivo methods that are accepted by regulatory agencies for the testing of various types of chemicals.

Under the mutual acceptance of data (MAD) agreement among the 38 OECD member countries, which aims to reduce duplicate testing, ". data generated in the testing of chemicals in an OECD member country in accordance with OECD Test Guidelines (TG) and OECD Principles of Good Laboratory Practice (GLP), shall be accepted in other member countries". Presently, there are 86 guidelines which describe various methods for testing effects on health under Section 4 (https://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788). Below is a list of some of the relevant OECD test guidelines.

Table 1. OECD Test guidelines (TGs) for commonly used *in vivo* toxicity and genotoxicity tests

S. No.	TG No.	Guideline
1.	410	Acute Oral Toxicity https://www.oecd-ilibrary.org/environment/test-no-401-acute-oral-toxicity_9789264040113-en
2.	402	Acute Dermal Toxicity https://www.oecd-ilibrary.org/environment/test-no-402-acute-dermal-toxicity_9789264070585-en
3.	404	Acute Dermal Irritation/ Corrosion https://www.oecd-ilibrary.org/environment/test-no-404-acute-dermal-irritation-corrosion_9789264242678-en
4.	407	Repeated Dose 28-Day Oral Toxicity Study in Rodents https://www.oecd-ilibrary.org/environment/test-no-407-repeated-dose-28-day-oral-toxicity-study-in-rodents_9789264070684-en
5.	410	Repeated Dose Dermal Toxicity: 21/28-day Study https://www.oecd-ilibrary.org/environment/test-no-410-repeated-dose-dermal-toxicity-21-28-day-study_9789264070745-en
6.	417	Toxicokinetics https://www.oecd-ilibrary.org/environment/test-no-417-toxicokinetics_9789264070882-en
7.	425	Acute Oral Toxicity – Up-and-Down Procedure https://www.oecd-ilibrary.org/environment/test-no-425-acute-oral-toxicity-up-and-down-procedure_9789264071049-en
8.	474	Mammalian Erythrocyte Micronucleus Test https://www.oecd-ilibrary.org/environment/test-no-474-mammalian-erythrocyte-micronucleus-test_9789264264762-en
9.	475	Mammalian Bone Marrow Chromosomal Aberration Test https://www.oecd-ilibrary.org/environment/test-no-475-mammalian-bone-marrow-chromosomal-aberration-test_9789264264786-en

3. New Approach Methodologies (NAMs): Data from traditional animal toxicity test methods have been used for many years to inform human health hazard identification and risk assessment. However, studies relying on animals to characterize effects of chemicals can be of questionable or limited biological relevance to human effects. New approach methodologies (NAMs) are increasingly being used for regulatory decision making by agencies worldwide because of their potential to reliably and efficiently produce information that is fit for purpose while reducing animal use. NAMs are defined as any technology, methodology, approach, or combination that can provide information on chemical hazard and risk assessment without the use of animals, including *in silico, in chemico, in vitro,* and *ex vivo* approaches.

Table 2: Few of the NAMs accepted by regulatory agencies

S. No.	TG No.	Guideline
1.	432	*in vitro* 3T3 NRU Phototoxicity Test https://www.oecd-ilibrary.org/environment/test-no-432-in-vitro-3t3-nru-phototoxicity-test_9789264071162-en
2.	442E	*in vitro* Skin Sensitisation: (h-CLAT) https://www.oecd.org/fr/publications/test-no-442e-in-vitro-skin-sensitisation-9789264264359-en.htm
3.	442D	*in vitro* Skin Sensitization, ARE-Nrf2 Luciferase Test Method https://www.oecd-ilibrary.org/environment/test-no-442d-in-vitro-skin-sensitisation_9789264229822-en
4.	471	Bacterial Reverse Mutation Test – Ames https://www.oecd-ilibrary.org/environment/test-no-471-bacterial-reverse-mutation-test_9789264071247-en
5.	473	*in vitro* Mammalian Chromosomal Aberration Test https://www.oecd-ilibrary.org/environment/test-no-473-in-vitro-mammalian-chromosomal-aberration-test_9789264264649-en
6.	476	*in vitro* Mammalian Cell Gene Mutation Tests using the Hprt and xprt genes https://www.oecd-ilibrary.org/environment/test-no-476-in-vitro-mammalian-cell-gene-mutation-tests-using-the-hprt-and-xprt-genes_9789264264809-en
7.	490	*in vitro* Mammalian Cell Gene Mutation Test using the Thymidine Kinase Gene https://www.oecd-ilibrary.org/environment/test-no-490-in-vitro-mammalian-cell-gene-mutation-tests-using-the-thymidine-kinase-gene_9789264264908-en

3.1 *In-silico* toxicology: *In silico* screening is typically a low cost high-throughput process, which can provide a fast indication of potential hazards for pharmaceuticals and chemicals. Depending upon the toxicology endpoint to be studied, some of the available *in silico* tools are recognised by regulatory agencies. While the European Union and other countries have been very passive in introducing QSARs, they are now actively investing in the development and expansion of QSARs programs with the introduction of the REACH system (Registration, Evaluation, Authorisation and Restriction of Chemicals) that declares 'No Data, No Market' for all chemicals. In addition, institutional support has been established to require that non-testing methods, such as QSARs, be identified first, before conducting a new toxicity test for REACH registration (ECHA, 2008). Table below lists few of the commercial and free *in silico* models:

Table 3: *In silico* systems for toxicity prediction

Categories	Systems	Type
Expert Rule based	Derek Nexus https://www.lhasalimited.org/products/derek-nexus.htm	Commercial
	VEGA https://www.vegahub.eu/portfolio-item/vega-qsar/	Free
	EPA T.E.S.T https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test	Free
	Danish QSAR database https://qsardb.food.dtu.dk/db/index.html	Free
Statistical	Sarah Nexus https://www.lhasalimited.org/products/sarah-nexus.htm	Commercial
	LAZAR https://lazar.in-silico.ch/predict	Free
	TEST https://www.epa.gov/chemical-research/toxicity-estimation-software-tool-test	Free
Hybrid	CASE Ultra https://www.multicase.com/case-ultra	Commercial
	Toxtree http://toxtree.sourceforge.net/download.html	Free
	OECD QSAR Toolbox https://qsartoolbox.org/	Free

3.1.1 Regulatory acceptance of *in silico* assessment:

3.1.1.1 Genotoxicity assessment: Significant amount of work has been done for validation of *in silico* tools for genotoxicity, thus making genotoxicity most studied endpoint for *in silico* analysis (Barber et al. 2017, Hasselgren et al 2019, Benigni et al. 2020). ICH M7 guideline provides specific recommendations for assessing drug impurities, including the use of two complementary computational toxicology methodologies (i.e., statistical-based and expert rule-based models) to predict bacterial mutagenicity (ICH M7-R1, 2017).

3.1.1.2 Risk Assessment of chemicals with limited toxicity data: When chemicals with limited toxicity data are required to be classified and labelled for shipping or other purposes, *in silico* toxicology provides an alternative method for quickly filling the data gaps in the toxicity/safety information, such as predictions of acute toxicity to support assignment to the Globally Harmonized System of Classification and Labelling category (ECHA, 2015). Joint Research Centre report from Europe describes a framework for assessing *in silico* toxicity predictions for pesticides (JRC, 2011a). It mentions use of various *in silico* systems such as Derek, CAESAR, ToxBoxes, Lazar, TOPKAT, HazardExpert, ToxTree.

The REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) regulation in Europe specifically promotes the use of *in silico* prediction (*e.g.* QSAR and read-across methods) as alternatives to animal testing, providing that the results are derived from a QSAR model for which scientific validity has been established; the substance falls within the applicability domain of the QSAR model; the results are adequate for purpose (*e.g.* classification or labelling); and adequate and reliable documentation of the applied

method is provided. ECHA's 4th Report on the Use of Alternatives to Testing on Animals for the REACH Regulation confirms that results from alternative methods continue to be used over and above new animal tests in dossiers submitted for REACH (ECHA, 2020).

3.1.1.3 Dietary Risk Assessment: European food safety authority (EFSA) accepts the use of *in silico* tools for dietary risk assessment of pesticides present as residues in food products (EFSA, 2016). EFSA document mentions use of Derek, OECD toolbox and VEGA tools for genotoxicity assessment. A report from Joint Research Commission from Europe describes the use of computational methods in toxicological assessment of chemicals in food (JRC 2011b). A EFSA report describes *in silico* toxicity prediction of proteins in diet (Palazzolo et al. 2020).

4. Adverse Outcome Pathways (AOPs): Adverse outcome pathways (AOPs) are descriptions of the causal relationships between key events observed at different levels of biological organization that induce an adverse health or ecotoxicological event. A molecular initiating event induces a chain of key events causing toxicity at a higher level, going from molecular level to organelle, cellular, tissue, organ levels, and finally up to organism and population levels. Clear definition of the toxicological question needed to be answered and adaptation of emerging methods to solve questions relevant to regulatory toxicology are key. Not necessarily all new technologies provide better answers compared to methods already in use, but clearly new technologies have great potential. AOP knowledge base (https://aopkb.oecd.org/) can help in further understanding on this.

5. Integrated Approaches to Testing and Assessment (IATA): IATA combine multiple sources of information to conclude on the toxicity of chemicals. IATAs may include existing information from the scientific literature or other resources, along with newly generated data resulting from new or traditional toxicity testing methods to fill data gaps. IATAs can include a combination of methods [(Q)SAR, read-across, *in chemico*, *in vitro*, *ex vivo*, *in vivo*] or omic technologies (e.g. toxicogenomics), the results of which are integrated. These approaches are developed to address a specific regulatory scenario or decision context. Though an AOP can help develop an IATA, interpret results, and identify information gaps, an AOP is not required to develop an IATA.

OECD Guidance document 203 on an Integrated Approach on Testing and Assessment (IATA) for Skin Corrosion and Irritation (https://one.oecd.org/document/ENV/JM/MONO(2014)19/en/pdf) can be referred for this.

6. Career in Regulatory Toxicology: There are several different career paths to becoming a regulatory toxicologist, reflecting its interdisciplinary nature. Most experts in the field begin with a basic education in a relevant scientific area, such as chemistry, biochemistry, biology, pharmacy, or veterinary medicine, with later specialization in toxicology. Higher education (master's or doctorate) in toxicology is usually beneficial since extensive knowledge of the relevant study guidelines and the regulatory environment in different countries is predominantly learned on the job, as is attaining the knowledge and confidence to exercise expert judgment in the evaluation of toxicity results and in the definition of the toxicity profile of a molecule or product. Expert judgment is not only confined to strict scientific assessment; it also includes balancing societal needs for effective chemicals against the risks that their use poses. Judging what risks are acceptable to society is a matter for government policy expressed in regulations. Regulatory toxicologists in industry may need to use their judgment to decide whether a product use is likely to be acceptable to regulators, and in the application and justification of their scientific judgment, ethical conduct and transparency in data evaluation and reporting are essential. These applied aspects of toxicology are generally not the focus of academic programs that tend to orient students toward basic research careers.

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TOX-OP-01

EFFECTS OF FLUBENDIAMIDE AND LEAD EXPOSURE ON CIRCULATING THYROID HORMONE LEVELS IN BUFFALO CALVES (*BUBALUS BUBALIS*)

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The present study aimed to evaluate effects of flubendiamide and lead exposure on changes in thyroid hormone levels in blood of buffalo calves. Male buffalo calves were given lead acetate orally at the rate of 9.2 mg/kg bw/day and flubendiamide at the rate of 0.024 mg/kg bw/day, either alone or in combination for 90 days. Flubendiamide as well as Lead exposure alone resulted into decline in T_3 and T_4 levels. The decline in T_3 and T_4 levels in animals given both lead and flubendiamide were lower than those receiving lead and flubendiamide alone. TSH activity increased significantly in lead alone and combined lead and flubendiamide exposed animals; but changes were inconsistent in animals receiving only flubendiamide. The results of the present study indicated thyrotoxic potential of flubendiamide and lead in buffalo calves. However, further study is required to elucidate the mechanism of thyrotoxic potential of flubendiamide and interactive effects of these two thyrotoxic agents.

TOX-OP-02

PROTECTIVE ROLE OF PLUMBAGIN IN FOLIC ACID-INDUCED OXIDATIVE STRESS IN *SWISS ALBINO* MICE POSSIBLY *VIA* MODULATION OF THE ACTIVITY OF NF-kB, IL-10 AND TGF-β PATHWAY

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An experimental study was conducted to evaluate the pharmacological activity of plumbagin against folic acid-induced acute kidney injury/renal fibrosis. A total of 30 male *swiss albino* mice were assigned to five groups of 6 animals each. Group 1 (control group) was administered normal saline. Group 2 was given folic acid @ 250 mg/kg IP given on 1st day of the experiment, Group 3 was kept as plumbagin *per se* group (10 mg/kg IP). Groups 4 and 5 were kept as treatment groups with plumbagin @ 5 mg/kg IP and 10 mg/kg IP, respectively, daily, along with folic acid on 1st day of the experiment. The experiment was conducted for 14 days. Blood samples were collected to analyse and estimate serum BUN, creatinine, albumin, total protein and uric acid. Subsequently, the mice were sacrificed, and kidneys were collected to analyse anti-oxidant parameters, cytokine profiles, fibrotic markers, and histopathological and immunohistochemical analysis. The present study revealed a significant alteration in serum parameters, cytokines (TNF-α, IL-1β, IL-10, KIM-1and NF-κB), anti-oxidant profile, fibrotic markers, transforming growth factor (TGF- β) of mice treated with folic acid (group 2) when

compared to sham (group 1). There was a significant amelioration of all the parameters in groups 4 and 5 as compared to group 2. In conclusion, high-dose plumbagin was found to possess the ameliorating action against folic acid-induced acute kidney injury/ renal fibrosis *via* modulation of the NF-B, IL-10 and TGF-β pathway activity. Hence, plumbagin can be a protective strategy for acute kidney injury/renal fibrosis.

TOX-OP-03

ANTI-INFLAMMATORY AND ANTI-OXIDANT POTENTIAL OF ABIETIC ACID IN METHOTREXATE INDUCED HEPATIC TOXICITY THROUGH MODULATING NF-kB PATHWAY

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Methotrexate (MTX) is a therapeutically used drug in the treatment of various cancer and inflammatory disorders, and its clinical use is limited due to associated toxicity. The present study investigates the protective effect of Abietic Acid (AA) against MTX induced hepatotoxicity. Treatment with MTX at 10 mg/kg/day, IP for consecutive 3 days on 7, 8 and 9th days of the experiment impaired anti-oxidant mechanisms caused substantial increase in the serum levels of liver injury markers. Pretreatment with AA (20 and 40 mg/kg/day, p.o. for 10 days) inhibited MTX-induced hepatic injury and oxidative stress by decreasing lipid peroxidation and nitrate level, increasing cellular glutathione content and maintaining the levels of anti-oxidant enzymes compared to MTX treated mice. In addition, AA considerably ($P<0.05$) decreased the activity of the pro-inflammatory (TNF-α, IL-1β) and anti-inflammatory cytokines (IL-10) and also decreased the level of expression of TNF-α, NFκB in the AA treatment. These results are well supported by histopathology of liver and serum biomarkers of liver. Furthermore, there was significant ($P<0.05$) improvement in the AA treated groups by alleviating all the parameters compared to the MTX group. However, more significant improvement was noticed in the high dose of AA treated group. Based on the above results, this study concluded that using Abietic acid might exhibit anti-inflammatory and anti-oxidant action by modulating the NF-kB pathway and ameliorating against methotrexate-induced toxicity.

TOX-OP-04

ASSESSMENT OF COMMONLY USED PESTICIDES RESIDUE USING GAS CHROMATOGRAPHY IN POULTRY LIVER AND MUSCLE SAMPLES RANDOMLY COLLECTED FROM HISAR (HARYANA)

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The level of commonly used pesticides residue was investigated using Gas Chromatography technique in twenty five poultry liver and muscle samples each randomly collected from Hisar (Haryana). Nine

organophosphate pesticides were investigated namely dichlorovos, chlorpyrifos methyl, fenitrothion, pirimiphos methyl, malathion, chlorpyriphos, quinalphos, ethion and edifenphos. Likewise, eight organochlorine pesticides were investigated namely α-HCH, β-HCH, γ-HCH, δ-HCH, aldrin, α-endosulfan, β-endosulfan and dicofol and five synthetic pyrethroids pesticides were investigated namely λ-cyhalothrin, cypermethrin, fenvelrate, T-fluvalinate and deltamethrin. . In poultry liver and muscle samples highest percent proportionate pesticide load was of deltamethrin (i.e. 22.06 %) and β-endosulfan (i.e. 20.18 %), respectively. Two poultry liver samples each for chlorpyrifos, γ-HCH, deltamethrin and one poultry muscle sample for chlorpyrifos were found containing pesticide level exceeding MRL as per the Codex Alimentarius Commission (2006). Total pesticide load in poultry liver and muscle samples was 23.84 ppb and 12.87 ppb, respectively. These results indicate that pesticides residue contamination is a food safety issue for poultry meat consumed in India.

TOX-OP-05

CHROMATOGRAPHIC ASSESSMENT OF COMMONLY USED PESTICIDES RESIDUE IN BOVINE MILK SAMPLES RANDOMLY COLLECTED FROM HISAR (HARYANA)

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The level of commonly used pesticides residue was investigated using Gas Chromatography technique in forty seven bovine milk samples randomly collected from Hisar (Haryana). Nine organophosphate pesticides were investigated namely dichlorovos, chlorpyrifos methyl, fenitrothion, pirimiphos methyl, malathion, chlorpyriphos, quinalphos, ethion and edifenphos. Likewise, eight organochlorine pesticides were investigated namely α-HCH, β-HCH, γ-HCH, δ-HCH, aldrin, α-endosulfan, β-endosulfan and dicofol and five synthetic pyrethroids pesticides were investigated namely λ-cyhalothrin, cypermethrin, fenvelrate, T- fluvalinate and deltamethrin. Pesticide load of organophosphate pesticides residue and combined organochlorines and synthetic pyrethroid pesticides residue load was estimated as 2.58 ppb and 7.10 ppb, respectively. In four samples β-endosulfan and in two samples chlorpyrifos was found more than the maximum residue limit (MRL) as per the Codex Alimentarius Commission (2006). β-endosulfan has the highest mean concentration (i.e. 2.45 ± 7.24 ppb) of residues in the tested bovine milk samples. These results indicate that pesticides residue contamination is a food safety issue for bovine milk consumed in India. Therefore, there is a need of national level monitoring programme for pesticides residue in bovine milk.

TOX-OP-06

ACRYLAMIDE INDUCED TESTICULAR TOXICITY IN AQUATIC ANIMAL MODEL: ALTERATIONS IN OXIDATIVE STRESS PARAMETERS, GENE EXPRESSION AND HISTOLOGICAL STRUCTURE

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Aquatic organisms are continuously being exposed and prone to xenobiotic induced toxicity. Acrylamide (ACR) is classified as neo-formed contaminants (NFCs)/pollutants. In present study, we investigatedthe effects of ACR exposure on oxidative stress parameters, mRNA expression of antioxidant genes and histopathological changes in testes of zebrafish. Adult zebra fish (n=270) were randomly divided in three groups (90 fish in each group). The zebrafish of control group were maintained under normal water condition. The zebrafish of T_1 and T_2 groups were exposed to ACR at 8.5 and 17 mg/L, respectively for 28 days. The catalase (CAT) and superoxide dismutase (SOD) activities were significantly ($p < 0.05$) decreased in testes of zebrafish of both toxicity groups as compared to the control group. The levels of reduced glutathione (GSH) and malondialdehyde (MDA) were significantly ($p < 0.05$) decreased and increased, respectively in testes of zebrafish of T_1 and T_2 groups as compared to the control group. The *sod*, *cat* and nuclear factor-erythroid 2 related factor 2 *(nrf2)* mRNA expression levels were significantly ($p < 0.05$) down-regulated in testes of zebrafish exposed to both levels of ACR. Upon histological examination, the testes of zebrafish of T_1 group showed mild congestion and reduction in the quantity of mature spermatozoa. In T_2 group, the testes of zebrafish of showed clumping of spermatocyte, reduction in the quantity of spermatozoa, atrophy of seminiferous tubule, congestion and increase in interstitial space. Findings of antioxidant parameters, gene expression and histopathological changes suggested that long-term ACR exposure had induced dose-dependent testicular damage in adult zebrafish.

TOX-OP-07

ANTI-INFLAMMATORY PROPERTIES OF HINOKITIOL VIA MODULATION OF NRF-2 AND NF-κB PATHWAYS IN THE CONTEXT OF LIPOPOLYSACCHARIDE (LPS)-INDUCED LUNG INJURY IN MICE

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The beneficial effect of Hinokitiol was investigated in an experimental LPS-induced lung injury in mice. 30 male C57BL6 were randomly divided into 5 groups with 6 animals. Group 1 as Normal control, group 2 was kept as disease control and was given LPS (10 µg/kg BW) by the oropharyngeal route on the 6th day of the

experiment, groups 4 and 5 were kept as HLD & HHD treatment @ 50 mg/kg BW and 100 mg/kg BW, (i.p. route) respectively daily, while group 3 treated HPS (100 mg/kg BW, i.p. route) daily for 7 days. Body weights were recorded, and blood samples were taken for haematological and bronchoalveolar lavage fluid to assess inflammatory cells. Antioxidant markers, cytokine profiles, histopathology, and immunohistochemical assays were all performed in the lung tissue samples. The current study found a significant ($P<0.05$) alteration in absolute and relative lung weights, haematology, BALF parameters, inflammatory cytokines (IL-6, TNF-α, IL-1β and IL-10), antioxidant profile (nitrite assay, MDA, SOD, GSH and catalase), immunohistochemistry of (Nrf-2, TNF-α, NF-κB & COX-2) and histopathology of lungs of mice in group 2 when compared to group 1. These alterations were reversed in the Hinokitiol treatment groups observed. Finally, Hinokitiol was revealed to have potent antioxidant and anti-inflammatory properties. The Hinokitiol high-dose group exhibited considerable improvement by lowering pro-inflammatory cytokines and increasing antioxidant enzymes, blocking the NF-kB signalling pathway and positively regulating Nrf-2. Therefore, based on the results, the present study concluded that Hinokitiol might be helpful for the therapeutic management of acute lung injury.

TOX-OP-08

IN VITRO EXPOSURE OF LEAD AFFECTS MOTILITY, VITALITY, MEMBRANE INTEGRITY, MTP, ACROSOME INTACTNESS AND MORPHOLOGY OF SPERM CELLS

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Present study was undertaken to evaluate the adverse effects of lead on motility, livability, functional membrane integrity, acrosome intactness, MTP and on ultra-structures of bucks spermatozoa. Six healthy adult Barbari bucks of similar body weight were selected for collection of semen samples. Each semen ejaculate was diluted using PBS (pH 7.4) with 0.5 % glucose to obtain the final concentration of 40×10^6 sperm cells per ml and the exposure time allowed for different concentrations of lead acetate (2.5, 5, 10, 20 and 50 ppm) was 15 min and 3 h. Compared to the control, significant decrease in live percentage count was observed in semen samples exposed to lead acetate. After 3 hour, significant decrease in total motility was observed in the lead acetate-treated group compared to the corresponding value at 3 h in control group. Lead at lower concentrations did not significantly reduce the HOS response of sperm cells following exposure for 15 min and 3 h. FITC-PSA staining revealed that lead acetate produced concentration-and time-dependent negative effect on acrosome integrity of treated spermatozoa. Following exposure to lead acetate (0.5-20 ppm) after 3h, significant decrease in number of spermatozoa showing high MTP was observed. Further, analysis of SEM images of the spermatozoa showed that lead (5 and 20 ppm) produced more deleterious effects (swollen acrosome and wavy middle piece) on sperm cells after 3 h compared to its effects after 15 min of exposure. From the result of the present study, it can be concluded that lead produced deleterious effects on sperm cells.

TOX-OP-09

AMELIORATIVE POTENTIAL OF GINGER (*ZINGIBER OFFICINALE*) FOLLOWING CO-EXPOSURE WITH FLUORIDE AND DIMETHOATE IN BLOOD OF WISTAR RATS

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Concurrent exposure to environmental contaminants such as fluoride (F^-) and dimethoate (DM) is a serious public health concern. In vivo experiment was conducted on 54 adults healthy Wistar rats of either sex weighing 180-200 gm obtained from Indian Institute of Integrative Medicine (CSIR Lab), Jammu. After acclimatization, rats were randomly allocated into 9 groups with 6 animals in each group. The animals were exposed with orally DM ($1/10^{th}$ LD_{50}), daily alone and along with F (4.5 ppm) in drinking water continuously for 28 days and effectiveness of ginger vis a vis quercetin was assessed in combating the oxidative stress mediated combined toxic effects on blood and erythrocytes. Significant ($P<0.05$) reductions in the levels of total antioxidant status (TAS), blood glutathione (GSH), total thiols (TTH), and erythrocyte activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), Glutathione Reductase (GR), aryl esterase (AE), acetylcholinesterase (AChE) whereas significant elevations ($P<0.05$) in advanced oxidation protein products (AOPP) and malondialdehyde (MDA) were recorded in blood of co-exposed rats. Supplementation of ginger and quercetin could significantly ($P<0.05$) ameliorate the combined F and DM induced hemotoxicity as well as erythrocytic oxidative injury. Observations of the present study indicated that supplementation of ginger ameliorate the fluoride and dimetoate induced hemotoxicity.

TOX-OP-10

SUBACUTE ORAL MANCOZEB EXPOSURE AND ITS DETRIMENTAL IMPACT ON MALE REPRODUCTIVE HEALTH IN *WISTAR* RATS

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Mancozeb is a commonly used fungicide in agriculture, and its impact on reproductive health remains a subject of concern due to its widespread use. In the pursuit of understanding the potential hazards associated with pesticide exposure, the present study was undertaken to investigate the deleterious effects of subacute oral exposure to Mancozeb on the reproductive system of male Wistar rats. This research involved a controlled experiment, utilizing a cohort of healthy Wistar rats, with the aim of shedding light on the consequences of Mancozeb exposure. To assess these effects, a comprehensive evaluation was conducted, encompassing various reproductive parameters. A total of 12 healthy Wistar rats were procured and divided into two groups: Group I (Control) and Group II (Treatment), each consisting of six animals. In Group II, Mancozeb was orally administered at a dose of 500 $mg.kg^{-1}$ body weight for 28 consecutive days, while the control group provided with adlib feed and water without any treatment. Repeated exposure to Mancozeb resulted in alteration in

various reproductive health parameters. The exposure produced mild to moderate signs of toxicity and a significant ($p<0.05$) increase in the absolute organ weight of the testes as well as epididymis. Reproductive parameters were notably affected, with a decrease in the count of live sperm and total sperm, along with an increase in the count of dead and abnormal sperm due to Mancozeb exposure. Consequently, the outcomes of this study suggest that Mancozeb fungicide, when administered at the tested dose, imposes a substantial toxicological burden on the reproductive health of exposed animals and may have detrimental implications for both human and animal reproductive health.

TOX-OP-11

EVALUATION OF POSTNATAL REPRODUCTIVE TOXICITY OF GESTATIONAL EXPOSURE OF ETHION IN RATS

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The present study was conducted to evaluate the postnatal reproductive effects of gestational exposure to ethion in rats. Based on the acute toxicity studies, different doses of ethion were orally administered to pregnant rats from gestational day (GD) 6-19, at doses of 0.86 (1/40 LD_{50}), 1.7 (1/20 LD_{50}), 3.43 (1/10 LD_{50}) and 6.9 mg/kg (1/5 LD_{50}) (LD_{50} = 34.28 mg/kg) in groundnut oil (n=6). Control group were given groundnut oil. Female and male animals were sacrificed on postnatal day (PND) 60, and 75, respectively. Male reproductive parameters assessed are day of testis descent, pubertal onset (preputial separation), oxidative stress in testes, semen evaluation, and histopathology of reproductive organs. Female reproductive parameters assessed are pubertal onset (vaginal opening), oestrus cycle duration, oxidative stress in uterus, and ovary, and histopathology of reproductive organs. Ethion advanced the testis descent and delayed pubertal onset in males. It also reduced sperm count, motility, intact acrosome percentage and increased sperm abnormalities. Ethion caused severe testicular degeneration with necrosis of spermatogonia cells and formation of giant cells. In females, all the ethion exposed groups showed delay in vaginal opening and increased oestrus cycle duration. Malondialdehyde levels were elevated in uterus, ovary, and testis. The uterus of ethion groups showed marked papillary projections and severe myometrial degeneration. The ovary showed disrupted architecture of ovarian stroma and lesser number of developing and matured follicles in the ethion groups. The results indicate that ethion caused significant postnatal reproductive toxicity in F1 offsprings.

TOX-OP-12

THERAPEUTIC EFFICACY OF LACTOFERRIN AGAINST HIGH FAT DIET AND CCL4 IN C57BL/6 MICE

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An experimental study was conducted to evaluate the pharmacological activity of lactoferrin against high fat diet (HFD) + CCl_4 *via* intraperitoneal route for 6 weeks, $_{induced}$ non-alcoholic fatty liver disease (NAFLD). A total of 36 male C57BL/6 mice were randomly divided into 6 groups of six animals each after acclimatization. Group 1 served as control; Group 2 kept as disease Control (HFD + CCl_4); Group 3 treated with lactoferrin *per se* (300 mg/Kg mixed in water) via oral route, Group 4 treated with lactoferrin (300 mg/kg) + HFD + CCl_4, Group 5 treated with Lactoferrin (100 mg/kg) + HFD + CCl_4 and Group 6 treated with simvastatin (10 mg/kg) + HFD + CCl_4. Blood was collected on 2nd, 4th and 6th week for the estimation of cholesterol, triglycerides, AST and ALT levels. The present study revealed significant elevations in Antioxidants profile, HDL, cholesterol, triglycerides, ALT and AST in the NAFLD mice model. These results were also comparable to the findings from simvastatin treated group. Histopathological studies of liver in group 2 revealed degenerative changes, loss of architecture, vacuolization, moderate to severe congestion in liver. These changes were reversed in BLF & simvastatin treated groups. Similarly, immunohistochemical analysis of group 2 liver revealed an intense immunopositivity for Bcl-2, while treatment groups 4, 5 and 6 exhibited mild to very mild immunoreactivity for Bcl2. Therefore, Lactoferrin can be further evaluated for clinical management of hepatic diseases such as NAFLD.

TOX-OP-13

ADVERSE EFFECTS OF CHEMOTHERAPY FOR CANINE TRANSMISSIBLE VENEREAL TUMOUR USING DOXORUBICIN AND VINCRISTINE

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Canine transmissible venereal tumour (CTVT) is a contagious neoplasm that is physically transmitted through direct contact with injured skin or mucous. The aim of this study is to investigate the adverse effects of chemotherapy for canine transmissible venereal tumour using doxorubicin and vincristine. Twelve clinical cases irrespective of age, breed, sex affected with canine transmissible venereal tumour (CTVT) were selected which has been received for examination at the department of veterinary surgery and radiology, CVAS, Bikaner (RAJUVAS). All animals showed genital vaginal and penile ulcerative neoplastic masses with bleeding. Affected dogs were divided equally into two groups on the basis of treatment with chemotherapeutic drugs *viz.* vincristine

therapy (Group I) and doxorubicin therapy (Group II). Vomition, diarrhoea, alopecia, allergic nodules and stomatitis were adverse effects of chemotherapy in TVT affected dogs. More adverse effects of chemotherapy were recorded with vincristine therapy (Group I) followed by less adverse effects with doxorubicin therapy (Group II). Single agent vincristine is considered as the treatment of choice for transmissible venereal tumour and results in a durable complete remission in over 90% of cases but doxorubicin is also a good alternative with less adverse effects.

TOX-PP-01

PRENATAL EXPOSURE OF ETHION INDUCES OXIDATIVE STRESS, LIVER, AND KIDNEY TOXICITY IN F1 MALE OFFSPRINGS

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In the present study, four doses (0.86, 1.7, 3.43, and 6.9 mg/kg) of ethion were orally administered to pregnant rats from gestational day 6 to 19. Control animals were given groundnut oil. The male offspring born were raised up to postnatal day 75. Before sacrifice, blood was collected to estimate the oxidant-antioxidant levels, liver function tests, and kidney function tests in the serum. The relative organ weights, and histopathology of organs like liver, kidney, and lungs were also assessed. Malondialdehyde levels were increased in all the ethion-exposed groups. GSH and SOD levels were increased in all dose groups. Catalase activities were found to be reduced in all ethion-exposed groups. Activities of SGPT, SGOT, and ALP, and total bilirubin levels increased in the ethion-exposed groups. The serum levels of urea, uric acid, and creatinine were also increased. The relative weights of liver, kidney, and lungs were reduced in all the ethion-exposed groups. Liver sections of the exposed group showed moderate to severe degeneration and necrosis of hepatocytes, with cytoplasmic vacuolations compared to the normal hepatic architecture in the control group. Mild to severe degeneration and necrosis of kidney tubular epithelial cells were noticed in higher ethion dose groups. The lungs of higher ethion dose groups revealed mildly engorged pulmonary vessels with oedema. The results indicate that prenatal exposure of ethion in rats caused toxicity in the male offspring of the F1 generation.

TOX-PP-02

SCLAREOL MITIGATES CISPLATIN-INDUCED ACUTE RENAL INJURY: EXPERIMENTAL STUDY IN SWISS ALBINO MICE

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An experimental study was conducted to evaluate the pharmacological activity of *sclareol* against cisplatin-induced acute renal injury. A total of 30 male *Swiss albino* mice were procured and were randomly assigned to

five groups of 6 animals each. Group 1 was sham control, group 2 given Cisplatin @ 20mg/kg BW IP on the 7th day of the experiment, and Group 3 kept as *sclareol per se* group. Groups 4 & 5 were treated with *sclareol* @ 5 & 10mg/kg IP, respectively throughout the experimental period. The experiment was conducted for 10 days. Body weights were recorded on 10th day. Blood samples were collected for hematological analysis, serum BUN and creatinine were estimated on the 11th day. Subsequently, the mice were sacrificed, and kidneys were collected for further analysis. The present study revealed a significant alteration in absolute and relative kidney weights, hematology (Hb, TLC, TEC and PCV), cytokines (TNF-α, IL-1β, IL-10 and KIM-1), anti-oxidant profile (nitrite assay, TBARS, SOD, GSH and Catalase), immunohistochemistry (NF-κB, TNF-α, COX-2 and Nrf-2) and histopathology of mice treated with Cisplatin (group 2) when compared to group 1. There was a significant amelioration in all the parameters in treatment groups 4 and 5 compared to disease control group 2. In conclusion, *sclareol* exhibited the capability to reduce pro-inflammatory cytokine levels and restore antioxidant enzyme levels, potentially through modulation of the activity of NF-κB and Nrf-2 pathways. Therefore, *sclareol* could be considered a protective strategy against acute renal injury.

TOX-PP-03

THE COMBINED INFLUENCE OF IMIDACLOPRID AND CARBENDAZIM ON BIOCHEMICAL PARAMETERS, OXIDATIVE STRESS, AND NEUROTOXICITY IN MALE MICE

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The assessment of the toxicological interplay between carbendazim (CBZ) and imidacloprid (IMI) was conducted using a mice-based experimental model. Mice were administered individual doses of IMI and CBZ, as well as a combination of both substances. Various toxicity endpoints were assessed, including biochemical markers, oxidative stress levels, antioxidant activity, and neurotoxic effects. An interactive index was computed. A reduction in both food and water consumption, along with a noticeable loss of body weight, was observed in the groups treated solely with CBZ and IMI. Additionally, significant alterations in cytotoxic biochemical indicators were noted in the groups that received only IMI and CBZ. No significant alterations (pe”0.05) were observed in the oxidative stress biomarkers and antioxidants within the groups that received combined treatment. However, both plasma and brain AChE activity exhibited significant changes ($p<0.05$) in the group subjected to combined treatment. Motor activity, represented by FLA and SLA, exhibited a significant decrease ($p<0.05$) in groups treated with IMI and CBZ. Furthermore, the response to pain significantly increased ($p<0.05$) in the groups treated with IMI and CBZ individually. These changes followed a dose-dependent pattern in the individual treatments. The group treated with IMI-L and CBZ-L did not exhibit significantly greater changes. The interactive index calculated for these parameters suggests that the majority ofthe effects were antagonistic in nature. The current study indicates that exposure to IMI and CBZ through the dietary medium results in a dose-dependent toxic effect when administered individually. However, when these substances are present together, their combined presence does not appear to influence the overall toxicity in animals.

TOX-PP-04

EVALUATION OF MATERNAL AND FOETAL TOXICITY OF GESTATIONAL EXPOSURE TO ETHION IN RATS

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The main objective of this study was to evaluate the maternal and foetal toxicity of ethion in rats. Acute toxicity studies were conducted to determine the LD_{50} of ethion in adult female rats. Pregnant female rats were divided into 5 groups. Group I served as control (groundnut oil). Group II, III, IV, and V were orally administered with 1/40, 1/20, 1/10, and 1/5 LD_{50}s of ethion respectively, from gestational day (GD) 6 to 19. Dams were sacrificed on GD 20. Maternal toxicity was assessed by body weight gain, foetal resorptions, oxidative stress, liver and kidney function tests, and histopathology. Foetal toxicity was assessed by physical status, gross, teratological and histopathological examination. LD_{50} of ethion was determined as 34.28 mg/kg. Ethion caused dose-dependent reduction in maternal body weight gain, increased resorptions, and reduced gravid uterine weights. Malondialdehyde levels in uterus, ovary, placenta, and serum was significantly elevated in ethion groups. SGOT, SGPT, total bilirubin, urea, uric acid, and creatinine were elevated in ethion groups indicating liver and kidney toxicity. Histopathology revealed myometrial degeneration and mucosal gland atrophy in uterus of pregnant dams and degenerative changes in placenta. Ethion caused reduction in the foetal body weights and placental weights, and degenerative changes in the foetal liver and kidney. Gross evaluation of foetuses showed subcutaneous hematoma. Skeletal evaluation showed partial ossification of skull bones, costal separation, and agenesis of tail vertebrae, sternebrae, metacarpals and metatarsals. The findings show that the gestational exposure of ethion caused maternal and foetal toxicity in rats.

TOX-PP-05

ASSESSMENT OF DEVELOPMENTAL TOXICITY IN ZEBRAFISH EMBRYO FOLLOWING SINGLE AND COMBINE EXPOSURE OF CADMIUM, LEAD AND ARSENIC

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The present study was carried out to investigate the effects of single and combined exposures to Cd, Pb and As in zebrafish embryo. Zebrafish (*Danio rerio*) embryos were maintained in E_3 medium containing Cd, Pb, As, Cd+Pb, Pb+As, Cd+As and Cd+Pb+As at concentrations of 25, 40, 40, 25+40, 40+40, 25+40, and 25+40+40 µg/L for 120 hpf, respectively. The control group of embryos was maintained in E_3 medium. The toxic endpoints evaluated include: embryo/larvae viability, hatchability, as well as heart rate, body length, eye size, cranium size, yolk sac size and developmental anomalies during organogenesis. Cd, Pb and Pb + As exposure caused

100 % mortality 96 h of the exposure. Exposure with Pb, Cd + Pb and Pb + As up to 96 h showed higher toxic effect on hatching rate of zebrafish embryo. Heart rate of zebrafish larvae was significantly reduced in Cd, As, Cd + Pb and Cd + Pb + As whereas, body length, eye size, cranium size of larvae were significantly reduced while, the exposure of Cd and Pb significantly increase yolk sac size in the larvae as compared to the control group. The exposure produced a significant number of developmental anomalies to the zebrafish that included spinal deformity, tail deformity, pericardial edema, yolk sac edema, hemorrhage and hypertrophy of yolk sac. Overall, following single and combine exposure of Cd, Pb & As in zebrafish embryo, early stages of zebrafish embryo life greatly affected their hatching rates which cause mortality, developmental deformities, reduction in heart rate and alteration of the size measurement.

TOX-PP-06

EFFECT OF LEMON PEEL EXTRACT GOLD NANOPARTICLES ON NEPHROTOXICITY INDUCED BY LEAD AND ARSENIC

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Considering remarkable biological activities of nanoparticles, the present study was undertaken to evaluate green synthesized lemon peel extract gold nanoparticles (LPGNP) on As and Pb induced subacute renal toxicity in wistar rats. Sixty male wistar rats were divided and treated as, Group I control, Group II ,V and VI received Sodium Arsenite @ 13.8mg/kg b.wt. p.o for 14 days, Group III,VII and VIII given Lead acetate @ 116.4 mg/kg body weight p.o for 14 days, Group IV,IX and X received Sodium Arsenite 13.8mg/kg body weight + Lead acetate @116 mg/kg body weight for 14 days, Group V,VII and IX received LPGNPs @ 10mg/kg for 4 weeks, Group VI,VIII and X received LPGNPs @ 20mg/kg for 4 weeks. In the result of the study, LPGNPs observed in the range of 20-100 nm. In acute oral toxicity study LD50 of LPGNPs is beyond 2000mg/kg. The Hb decreased and TEC increased in As and Pb or As+Pb toxic control groups whereas improvement observed in LPGNPs treatment groups. As and Pb or As+Pb significantly ($p<0.05$) increased AST, ALT, ALP, serum proteins, BUN and creatinine and in the treatment group receiving LPGNPs restorative effect was observed. The highest LPO level in serum was recorded in As and Pb or As+Pb toxic groups. The LPGNPs at 10 and 20mg/kg caused significant revival in MDA values in LPGNPs received groups. In histopathology of kidney, toxic control group revealed tubular degenerative changes, atrophy of glomerular, coagulative necrosis in renal tubules and glomerular filtration whereas animals receiving LPGNPs showed minimal histological alterations. In conclusion treatment with LPGNP resulted in significant protection in As and Pb or As+Pb induced deleterious effect on renal toxicity in wistar rats.

TOX-PP-07

EVALUATION OF THERAPEUTIC POTENTIAL OF URSODEOXYCHOLIC ACID (UDCA) IN LANTANA INDUCED CHOLESTASIS IN GUINEA PIGS

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The present study is designed to evaluate the therapeutic potential of UDCA in lantana induced cholestasis in guinea pigs. Lantadenes were extracted from red flower variety of lantana leaves. Animals were divided into 4 groups (n=4). Group I (control) were given empty gelatin capsules, Group-II, III, and IV were given lantadene extract (500mg/kg), UDCA (50mg/kg) and lantadene extract + UDCA, respectively, in gelatin capsules. Total bilirubin, ALT, AST, ALP, histopathology of liver, and gall bladder, mRNA expression of BSEP were done. Cholestasis was confirmed by the elevation of serum bilirubin, ALT, and AST levels in group-II compared to control and levels of the same were attenuated in group-IV. ALP has shown no significant changes in group-II. In group II, liver showed periportal necrosis and severe fatty degeneration of hepatocytes with congestion in the sinusoids, central, and portal veins with marked perivascular proliferation of fibrocytes and infiltration of mononuclear cells. In group-IV, there was partial attenuation of the above changes. In group II, gall bladder showed severe congestion of submucosal blood vessels and infiltration of neutrophils, which was ameliorated by UDCA administration in group-IV. The BSEP mRNA expression was significantly downregulated in group-II when compared to control, while UDCA treatment upregulated it in group-IV. In group I and III, there was no significant alterations of the above parameters maintaining the normal liver and gall bladder architecture. The amelioration of biochemical, histological and mRNA expression changes by UDCA in lantana induced cholestasis suggest the potential use of UDCA in treating lantana poisoning.

TOX-PP-08

PHARMACOLOGICAL EVALUATION OF *HINOKITIOL* AGAINST IMIQUIMOD-INDUCED PSORIASIS-LIKE SKIN INFLAMMATION IN C57BL/6 MICE

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A study evaluated the protective effect of *Hinokitiol* against Imiquimod-induced psoriasis-like skin inflammation in C57BL/6 mice. A total of 36 male mice were randomly divided into 6 groups, with 6 mice in each group, and the experiment was carried out for 7 days. *Hinokitiol* was treated with 2 doses of 30,60 mg/kg for 7 days and sacrificed for collection of skin and spleen. The results of imiquimod-treated mice revealed a significant

($P<0.05$) increase in spleen weights, PASI scoring and alteration in the antioxidant profile (nitrite assay and TBARS, SOD, GSH, GPx and catalase) than control mice. Similarly, significantly increased proinflammatory cytokines IL-1β, IL-6, and TNF-α with reduced levels of IL-10, and also increased expression of NF-κB, TNF-α and COX-2 and decreased expression of Nrf-2 in imiquimod-treated mice than normal control mice. All the parameters were significantly improved in *Hinokitiol*-treated groups. The results showed more significant amelioration in high dose of *Hinokitiol* and revealed similar results with the standard treatment group with dexamethasone. Further, these results were substantiated with alterations in the histopathology of skin. Based on the above result, this study concluded that administration of *Hinokitiol* could ameliorate imiquimod-induced psoriasis through upregulation of Nrf-2 and downregulation of NF-κB pathways; therefore, it can be used for the prophylactic use for the management of psoriasis like skin inflammation.

TOX-PP-09

CARTAP INDUCED TESTICULAR INSULT AND ITS AMELIORATION BY ALPHA-TOCOPHEROL IN MALE RATS

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The present work was undertaken to understand the toxicity of cartap following sub-acute (28 days) exposure and ameliorative potential of α- tocopherol (100 mg/kg) in male wistar rats. Forty-two healthy adult male rats were grouped into seven groups of six animals each. Group I, II served as control, vehicle control respectively, while animals of groups (III-VII) received orally α-tocopherol (100 mg/kg), cartap (16.25 mg/kg), cartap (32.5 mg/kg), cartap (16.25 mg/kg) + α-tocopherol and cartap (32.5 mg/kg) + α-tocopherol respectively. At term, impact of the exposure was assessed by evaluating Oxidative stress, Testicular injury biomarkers, expression of HSP-70 gene in testes and level of testosterone in plasma. MDA levels were found to be increased significantly in cartap alone groups compared to the control group indicating lipid peroxidation (LPO). Activities of antioxidant enzymes like CAT, SOD, and GST were reduced significantly in testes of cartap alone group V compared to the control group. Perusal of data revealed that α-tocopherol was unable to produce any significant change in SOD, GSH, and GST levels in treated groups. Significant elevation was found in the activity of testicular injury biomarker like ACP, LDH and GGT in cartap alone group V. Significant up-regulation of HSP-70 gene was observed in the cartap alone treatment groups. Plasma testosterone levels were observed to be significantly reduced in both cartap alone treatment group and α- tocopherol was unable to produce any significant amelioration. The Results suggest that α-tocopherol possesses moderate ameliorative potential against Cartap induced testicular toxicity.

TOX-PP-10

STANDARDIZATION AND VALIDATION OF A HIGH-PERFORMANCE THIN LAYER CHROMATOGRAPHY METHOD FOR THE QUANTIFICATION OF AFLATOXIN B1 IN FEED INGREDIENT MAIZE

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Aflatoxin (AFB1) among mycotoxin contamination is an alarming problem in feed products. It has been identified as a potential carcinogen and the regulatory bodies like European Union Directive 2002/32/EC has set the maximum permissible level of aflatoxin B1 at 20 µg/kg in all feed materials and 10 µg/kg in complete feeds and the Bureau of Indian Standards (BIS) has set at 20 µg/kg in all animal feeds. These stringent regulations necessitate quick, inexpensive, sensitive and validated method for the determination of mycotoxins in feed and feed ingredients. In this study, a High Performance Thin Layer Chromatography (HPTLC) method was standardized and validated with respect to linearity, specificity, sensitivity, precision and accuracy for the quantification of AFB1. Two different maize samples were processed as per Modified Romer's method and the samples and the AFB1 standard (5 µg/mL) were detected using TLC scanner in absorbance mode at a wavelength of 366 nm. HPTLC method was standardized using AFB1 and the Rf value was found to be 0.54 ± 0.04 for the standard and the samples tested. The Limit of detection (LOD) and the Limit of quantification (LOQ) were found to be 0.59 µg/kg and 1.78 µg/kg. The linear regression analysis of AFB1 showed good linearity over 10-50 ng/spot with a regression value of 0.99. Thus the proposed method is simple, rapid and specific and can be successfully employed for quality and quantity monitoring of aflatoxins in maize and other feed ingredients.

TOX-PP-11

AMELIORATIVE EFFECTS OF QUERCETIN NANOPARTICLES ON IMIDACLOPRID INDUCED INFLAMMATION AND OXIDATIVE STRESS IN SWISS MICE

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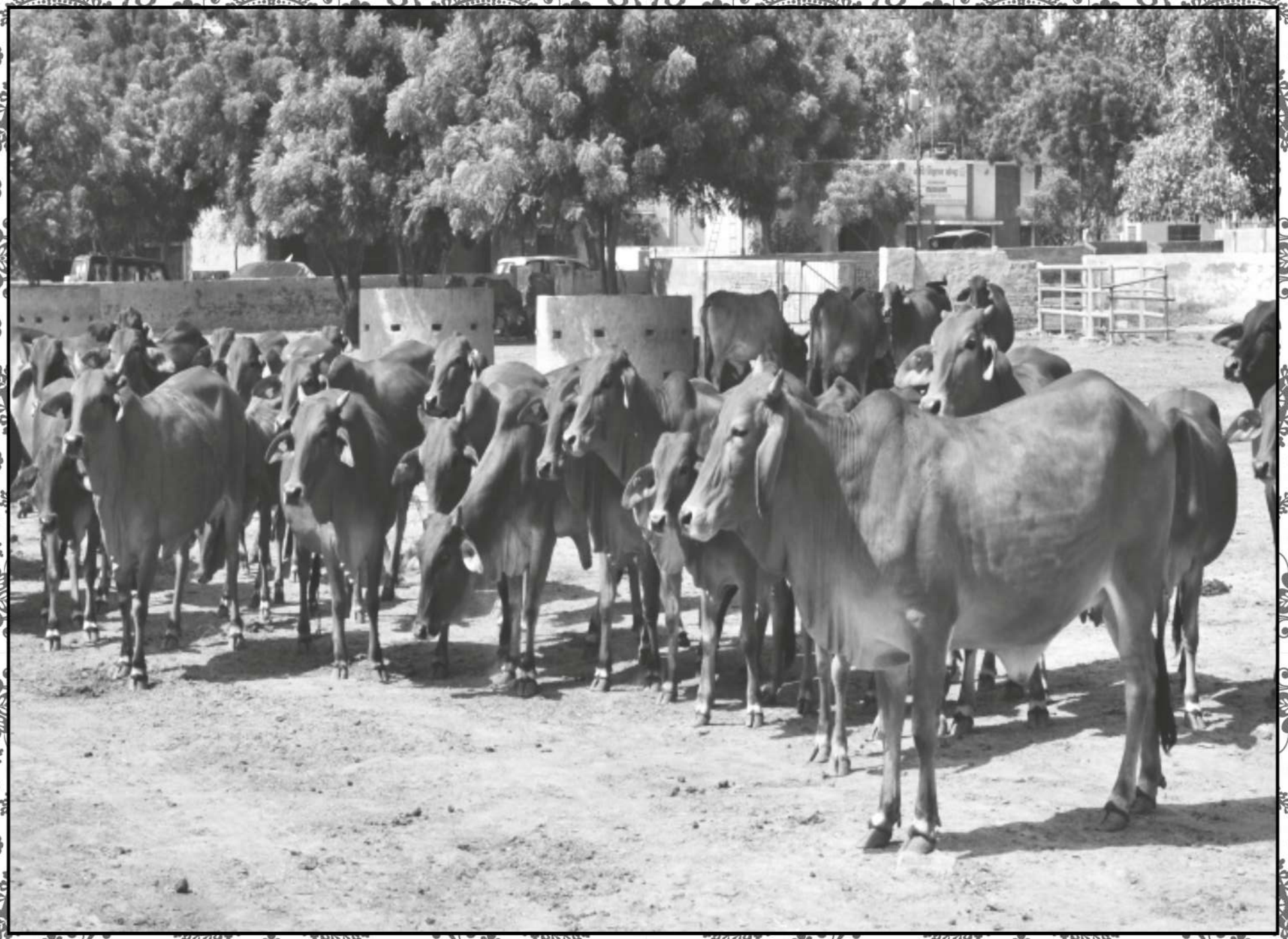
Quercetin is a bioflavonoid which is very well known for its various pharmacological activities like antimicrobial, anti-inflammatory, antioxidative, anti-diabetic, anti-carcinogenic and hepato-protective but these are of limited use due to low bioavailability of quercetin. Imidacloprid is a neonicotinoid which used as termiticide in agriculture mainly via acting on nAChs receptors of insect. The present study investigated the protective potential of quercetin and quercetin nanoparticles against imidacloprid-induced toxicity in Swiss albino mice by using carrageenan induced paw edema test and oxidative stress parameters in brain and liver. For enhancing the bioavailability of quercetin, nanoparticles were prepared and characterized. Total 48 mice were taken and divided into eight groups with six animals in each group. Group 1, 2, 3 and 4 received 3% gum

acacia, 22 mg/kg b.wt. imidacloprid (IMI), 25 mg/kg b.wt. quercetin (Que) and 25 mg/kg b.wt. quercetin nanoparticles, respectively. Group 5, 6, 7 and 8 received 22 mg/kg b.wt. imidacloprid + 25 mg/kg b.wt. quercetin, 22 mg/kg b.wt. imidaclopid + 25 mg/kg b.wt. quercetin nanoparticles, 22 mg/kg b.wt. imidacloprid + 12.5 mg/kg b.wt. quercetin nanoparticle and 22 mg/kg b.wt. imidacloprid + 6.25 mg/kg b.wt. quercetin nanoparticles, respectively. In results, we found that imidacloprid group had a significant rise in paw edema size and percentage inflammation as compared to the control group, while quercetin nanoparticles greatly reduced these. Oxidative stress parameters results revealed increased lipid peroxidation and superoxide anion level and reduced glutathione concentration in brain and liver in imidacloprid group whereas ameliorative effect was seen in both quercetin and quercetin nanoparticle group.



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ISVPT-2023

TECHNICAL SESSION-VI

Animal Welfare and Regulatory Pharmacology/Toxicology

Chairperson : **Dr. Anup Kalra**

Co-Chairperson : **Dr. Soumen Choudhury**

Rapporteur : **Dr. Aneesha V. A.**

AWRP-LP-01

ANIMAL WELFARE AND REGULATORY PHARMACOLOGY AND TOXICOLOGY

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Introduction

The Office International des Epizooties (OIE), commonly known as World Organization for Animal Health, defines animals' welfare to be good if the animal is healthy, comfortable, well nourished, safe, able to express innate behaviour and not suffering from unpleasant states such as pain, fear of distress (OIE, 2010). In other words, animal welfare refers to the quality of life experienced by an animal and encompasses how well the animal is coping with his or her current situation and surroundings.

Animal welfare is now debated in a global context, with local considerations and applications as a legitimate subject of ethical concern and scientific investigation. Standards of care for treating animals humanely are correspondingly complex, involving overlapping laws, regulations, guidelines, and professional codes influenced by a diverse body of philosophy, science, ethics, and law. Global trade and collaborations, and international acceptance of safety data, have required attention to harmonization, but awareness of local history and cultural influences remains crucial to successfully addressing laboratory animal welfare concerns now and into the future. While most regulations share a similar basis in law, utilitarian ethics, and community standards, even these basic pillars are under constant challenge and review.

History

The first organized and mainstream activities to promote the humane treatment of animals began to emerge, generally with a focus on the treatment of horses, as reflected by the founding of the British Society for the Protection of Animals (1824) and its American equivalent (1866). Subsequently, the American Humane Association (1874) and many other humane societies were also created. Several new societies arose with joint interests in animal welfare and the animal sciences (PRIMR [Public Responsibility in Medicine and Research], 1974; NABR [National Association for Biomedical Research], 1979). The founder of one of these, Charles Hume of the Uni-versities Federation for Animal Welfare (1926), initiated the creation of the first systematic approach toward promoting the welfare of animals in the laboratory. The American Association for Laboratory Animal Science was founded in 1950, and laboratory ani-mal medicine was recognized as a speciality of veterinary medicine with the founding of the American College of Laboratory Animal Medicine (1958). The "Three Rs" (Russell and Burch, 1959) proposed that wherever possible the use of animals should be replaced, refined, and reduced. The Three Rs made little impact at the time, but have gradually grown to become an inter-national core doctrine in protecting animals' welfare as it applies to animals in the laboratory.

In 1965, the establishment of the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) by a group of veterinarians and researchers took place as a part of professional desire for better conditions for laboratory animals and an interest in public assurance. The first federal law regulating animal

research was the Laboratory Animal Welfare Act came in existence in 1966. This law covered the transport, sale, and handling of animals and provided for licensing of animal dealers to prevent pet theft and their sale to research facilities. Other organizations *viz.* Americans for Medi-cal Progress (1992) or critique groups such as the Humane Society of the United States (Bayne and Turner, 2013), led to increasingly high pro-file debates over how the use of animals in research, agri-culture, and other areas should be understood, opposed or endorsed, or regulated.

Major domains of animal welfare

The American Veterinary Medical Association states that animal welfare is a human responsibility that encom-passes all aspects of animal well-being, from proper housing and nutrition to preventative care, treatment of disease, and when necessary, humane euthanasia. On the basis of this, animal welfare includes five major domains i.e. nutrition, environment, health, behaviour and mental state.

Rationale

The science of animal welfare provides knowledge and understanding to form the basis from which we make ethical choices regarding animals. There is a role for ethics when look-ing at the concept of animal welfare. Animal welfare becomes essential because of the fact that there are so many animals around the world suffering from being used for various human activities like entertainment, food, medicine, fashion, scientific advancement, and as exotic pets. Every animal deserves to have a good life where they enjoy the benefits of the five domains.

Regulations and guidelines related to laboratory animals

Regulation of animal welfare for the purpose of research, teaching, and testing has a long history. There are country-specific or regional regulations evolved from the scientific, ethical, and cultural values of their respective societies. In most countries, systems of overlapping laws, regulations, and policies create the regulatory framework assuring ani-mal welfare and include consideration of the Three 'R's (replacement, reduction, refinement), minimization of pain and distress, provision of daily care, appropriate training for the individuals providing care, and access to veterinary care.

The use of laboratory animals is governed by an interrelated, dynamic system of regulations, policies, guidelines, and procedures (Institute for Laboratory Animal Resources (ILAR), 2011). The regulations are developed by the United States Department of Agricul-ture (USDA), which is responsible for the enforcement of the Animal Welfare Act (AWA). The principal policy is the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy), to which insti-tutions must adhere in order to obtain funding from the PHS. In addition, the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International) has established position state-ments for institutions that choose to obtain and maintain accreditation.

In Canada the federal government does not have the jurisdiction to regulate the care and use of animals in research. Jurisdiction is at the provincial level, and 7 of the 10 provinces have enacted regulations that involve the care and use of animals acquired and used for research, teaching, and testing purposes. A key component of the Canadian system is the Insti-tutional Animal Care Committee (ACC). These com-mittees are established by the institutions and are set up according to the Canadian Council on Animal Care (CCAC) policy statement on terms of reference for animal care committees. The ACCs are responsible for overseeing all aspects of animal care and use.

European animal welfare regulations have been adopted by the 27-member European Union. In 1986 the European Union passed *Directive 86/609/EEC on the Protection of Animals Used for Experimental and Other*

Sci-entific Purposes with the intent of harmonizing the leg-islation on the use of laboratory animals in European states (Directive 86/609/EEC, 1986). The Directive was updated and made effective on September 22, 2010, as Directive 2010/63/EU (Directive 2010/63/EU, 2010).

In 1960, India enacted the Prevention of Cruelty to Animals Act with the main purpose to "prevent unnec-essary pain or suffering on animals and for that purpose to amend the law relating to the prevention of cruelty to animals". Chapter IV of the Act contained information about experimentation on animals for the advance-ment of physiological knowledge, for knowledge to prolong life, to alleviate suffering, and to combat disease in humans, animals, or plants. The Animal Welfare Board of India was also set up as a product of this section of the Act. The functions of the board are multiple and include advising the government of India on rules to enact to prevent unnecessary pain and suffering. In 1998, the Act was amended (S.O., 1974) to require registration of animal breeders and research institutions. In addition, details of animal experiments and their purpose must be maintained. In this amendment research institutions required to establish Institutional Animal Ethics Committees (IAEC).

Under the Act of 1960, the government initiated the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) whose member-ship includes a member of the Animal Welfare Board, among others. The purpose of this committee is to pro-mote humane care of animals and develop appropriate guidelines. One example is the Standard Operating Pro-cedures (SOP) for IAEC (CPCSEA, 2010). This document defines the function of the IAEC that includes the control and supervision of experiments on research animals. The IAEC reviews and approves animal use proposals in a fashion similar to IACUCs in the United States. The SOP defines the membership of the committee, review pro-cedures, decision-making process, record keeping, and reporting requirements. Another example is the CPC-SEA Guidelines for Laboratory Animal Facility (CPC-SEA, 2003). This is an all-encompassing document that discusses veterinary care, animal procurement, quaran-tine, disease surveillance, physical plant issues, animal husbandry, and training.

Global Animal Welfare Guidance

Organization for Economic Co-operation and Development (OECD)

It was formed in Europe after World War II and has a mission to promote policies that will improve the economic and social well-being of people around the world. The organization is located in Paris, France, and the membership includes 34 countries from around the world, with cooperative agreements with another 70 countries. One of the accepted remits of the OECD is the protection of animals used in experimental work. The work of the OECD led to the creation of guidelines for chemical testing that heavily emphasize Russell and Burch's Three Rs and the seeking of alterna-tive testing strategies. The Mutual Acceptance of Data Council was formed to reduce duplicative testing and to reduce the number of animals used in testing by way of discovering, developing and validating alternative testing systems for chemical testing. The OECD has pub-lished on alternatives to toxicological testing strategies to include Test Guidelines 420, 423, and 425 on acute toxicity testing, Local Lymph Node Assay (Test Guide-line 429), and Test Guideline 428 on "Skin Absorption: *In Vitro* Method" *etc.* Other alternative methodologies have been published and are available for review.

Council for International Organizations of Medical Sciences (CIOMS)

It is an international organization that repre-sents the major contributors in the biomedical research community. It is a non-profit group that was formed in 1949 jointly with the World Health Organization (WHO) and the United Nations Educational, Scientific and Cul-tural Organization (UNESCO). Fifty-five nations are members and represent many of the biomedical dis-ciplines to include national academies of sciences and medical research councils. It promotes interna-tional scientific activities and serves the interests of the biomedical

research community. The long-term programs for CIOMS include Bioethics, Health Policy, Ethics and Human Values, Drug Development and Use, and International Nomen-clature of Diseases. CIOMS, in collaboration with the International Council for Laboratory Animal Sciences, has provided guidance in human and animal bioethics guidelines entitled "International Guiding Principles for Biomedical Research Involving Animals" and "Biomedical Research Ethics: Updating International Guidelines – A Consultation". These guiding documents have served as a resource for guiding global animal bioethics.

International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)

It functions as a platform for regulatory agencies and pharmaceutical industries from Europe, Japan, and the United States to discuss the sci-ence and technical aspects of drug registration. ICH's mission is "to achieve greater harmonization to ensure that safe, effective, and high quality medicines are devel-oped and registered in the most resource-efficient manner". Through the mission of regulatory harmonization ICH aims to decrease duplication of clinical trials in humans and minimize the use of animals while main-taining high standards for safety and efficacy assess-ment of new medicines. The objective is to streamline drug development, reduce the resources necessary for drug development, and shorten the development time. The ICH has produced a set of safety guidelines for drug safety testing that consider such risks as reproductive toxicology, carcinogenicity, and genotoxicity in animals.

World Organisation for Animal Health (OIE)

It is an international intergovernmental organization responsible for improving animal health worldwide. One hundred and seventy-eight delegates represent member countries and territories. The primary objectives for the OIE include: ensuring transparency in global animal disease situations; collection, analysis, and dissemina-tion of veterinary scientific information; facilitation of international solidarity in the control of animal diseases; ensuring sanitary safety for international trade; improve-ment of the legal frameworks and resources of national veterinary services; and promotion of food safety and animal welfare through a science-based approach.

The OIE has published a Terrestrial Animal Health Code that provides recommendations for standards for animal health. Initial work regarding animal welfare began in 2004 and was published in the OIE Guiding Principles on Animal Welfare. The 2011 Terrestrial Animal Health Code includes recommendations for the use of animals in research and education, for the purpose of assistance and advice for OIE members when formulating regulatory requirements or other forms of oversight of live animals used in research and teaching (OIE, 2011).

Animal welfare in relation to regulatory pharmacology and toxicology

Interdependence exists between toxicology and regulatory development. Many government programs use the results of toxicology studies to support regulation of chemicals and other toxic substances. Some government programs impose regulations on the conduct of toxicology studies, while other programs have more informal methods of encouraging and promoting high-quality toxicology studies. This interplay between regulation and toxicology defines the construct of regulatory toxicology. For chemical regulation, the potential for human hazard from exposure, the magnitude of risk, the cost and consequence of regulation may be taken into account. It describes the way these regulations are implemented through guidelines, and how preclinical drug development toxicology is conducted today in response to the guidelines. Regulatory Toxicology encompasses the collection, processing and evaluation of epidemiological as well as toxicological experimental data to permit toxicologically based decisions directed towards the protection of health against harmful effects of

chemical substances. Furthermore, Regulatory Toxicology supports the development of standard protocols and new testing methods in order to continuously improve the scientific basis for decision-making processes. Animal models have long served as a basis for scientific experimentation, biomedical research, drug development and testing, disease modelling and toxicity studies, as they are widely thought to provide meaningful, human-relevant predictions. Current regulatory guidelines usually require safety and tolerability data from two species, a rodent (rat or mouse) and a non-rodent (dog, guinea pig or non-human primate), before administration of potential new medicines to humans in the first clinical trials The animal welfare rules apply to all regulated parties within the biomedical community who conduct nonclinical safety assessment studies. The primary divisions of the biomedical community include industry, academia, and government.

- **Role of government in animal welfare in relation to Regulatory Pharmacology and Toxicology -** Development of animal welfare policies and standards and raises awareness among industry to facilitate compliance with animal welfare legislation.
- Role of academia in animal welfare in relation to Regulatory Pharmacology and Toxicology- Both animal science and veterinary students need to teach about behavior information of animals used in testing in their curriculum
- Role of industry in animal welfare in relation to Regulatory Pharmacology and Toxicology- The Three Rs (3Rs) are guiding principles for more ethical use of animals should be follow in product testing and scientific research. They were first described by W. M. S. Russell and R. L. Burch in 1959. The 3Rs are:
    1. **Replacement**: methods which avoid or replace the use of animals in research
    2. **Reduction**: use of methods that enable researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals.
    3. **Refinement**: use of methods that alleviate or minimize potential pain, suffering or distress, and enhance animal welfare for the animals used.

The 3Rs have a broader scope than simply encouraging alternatives to animal testing, but aim to improve animal welfare and scientific quality where the use of animals cannot be avoided. In many countries, these 3Rs are now explicit in legislation governing animal use.

The methods describe below can be used to help reduce number off animals in regulatory toxicities studies.

I. Development of New *in vitro* Approaches

The development of new *in-vitro* approaches to replace animal bioassay testing for assessing potential human toxicity of compounds in drug development has the potential to greatly reduce the need for animal testing The following models discuss the multiple drivers for developing *in vitro* approaches including scientific and technology advances, and legislative changes.

a. Mechanism-based Models- There is a challenge regarding the lack regulatory acceptance of *in vitro* methods. There are two general classes of biological

methods used in the discovery and development of new products. holistic bioassays and methods that evaluate specific biological mechanism

in vitro and in vivo. The regulatory validation process of in vitro methods to replace an in vivo bioassay test that adequately mimics the performance of the drug when using an in-vivo method.

b. Predicative Toxicology- Currently, the high failure rate of candidate drugs after the decision to begin regulatory toxicology testing represents the largest opportunity to

reduce overall animal use. According to one study "nine out of ten candidates beginning clinical phase-I will not achieve marketing approval. However, much of regulatory animal testing is front-loaded and must be completed before clinical trials may proceed. Therefore, as candidates fail in clinical development, the animal testing associated with those failures could have been avoided".

The use of predictive *in vitro* techniques will attribute to better decisions in the drug design which will lead to improvement of the quality of

candidate drugs, decrease drug candidate attrition rates due to deleterious incompatibility and ultimately reduce the number of animals used. Also, it is important to note, that *in vitro* studies can be used to improve the predictive value of *in vivo* toxicology studies by supporting the selection of appropriate animal species by ensuring that testing is not conducted in species that lack human relevance

II. Ensuring Appropriate Statistical Analysis- This section provides opportunities to improve efficiency in safety pharmacology studies by ensuring appropriate statistical analysis and science are incorporated into practices.

a. Combining Studies- This approach is common among biologics and anti-cancer therapeutics however many drug companies shy away from the combination of toxicology studies because of the fear of regulatory disapproval. Animal use may be reduced by replacing standalone safety pharmacology studies with integrated toxicology studies. When studies are combined, animal use may be reduced by 20-40%".

b. Improve Data- Investigators sometimes fail to incorporate measurement error and statistical power into study designs and interpretation, which leads to repeat experiments. According to the OECD, "information that will help in the focus of the study design on the test substance includes, the identity, chemical structure, and physic-chemical properties of the test substance, this will allow you to more efficiently test for chronic toxicity potential and minimize animal usage" (OECD, 2008 p.2). Likewise, increasing animal use is not necessary to increase statistical power. By employing more sensitive measurement techniques, such as chronic or jacketed telemetry raw measurement error can be reduced". This improvement in statistical power reduces the number of observations necessary to establish given data.

Animal use for biomedical research has a long history and is routinely performed in new drug discovery and development processes. Animal experiments are an integral part of the curriculum for students in the life sciences, including pharmacy, to learn how to conduct animal experiments. These experiments may cause pain and distress to the animals. Laws and regulations have been enacted to make it illegal to cause undue pain or suffering to animals. These guidelines provide that due and full consideration should be given to alternative technologies not involving animal testing. Despite the movement to minimize animal use in research, pieces of evidence show that there has been a continuous increase in the worldwide use of laboratory animals over 10 years, from 115.2 animals to 192.1 million. The lack of suitable animal-alternative technologies and unavailability of required infrastructures are some of the reasons for animal use. (Girme, A. and Pawar, A., 2021)

Future perspectives

Improving animal welfare for the purpose of reducing suffering, respecting the animal's rights and fulfilling the duty to appropriately consider the care of other living species is ingrained with Hindu religious beliefs particularly in India and whole world in general. The notion of Ahimsa, non-violence, in Hinduism includes all life, and appropriate treatment of animals is tied to the tenet of Karma, where causing ill to another will result in ill to oneself. Inherently tied to rebirth, Hindus believe they may be reborn as an animal, and an animal may be reborn as a human, the specifications of which depend on their state of karma. Lastly, the Vedas

describe the code of sarva–bhuta–hita (devotion to the good of all creatures). Likewise other ethical arguments exist for addressing animal welfare, including it being 'the right thing to do' for the animals themselves; however, these arguments may not be compelling to all important parties engaged in this sector. Apart from the obvious benefits to the animals themselves, the espoused benefits for improving animal welfare vary on the basis of different perspectives.

Future of animal welfare lies in the principle of 3Rs: Replacement, Reduction and Refinement, formulated by William Russell and Rex Burch, have become synonymous with the measures to improve the welfare of animals used in research and are now used as an ethical framework for improving laboratory animal welfare throughout the world. The goal of the 3Rs is to find alternatives to animal testing (replacement), to optimise the amount of information obtained from fewer animals (reduction), and to adopt methods that alleviate distress (refinement). The researcher community should look for other replacements like cell culture models, *In silico* modelling and other mathematics based computational models. The studies involving animal use should be contemplated judiciously and number of animals used should be reduced as much as possible. All the research methods should be framed/designed in such a way that they cause minimum distress to the animals. Other than this, research journals should support the development, validation and novel application of alternate (to animal use) approach methodologies and should encourage submissions relating to recent developments in these areas. Additionally, the scientific fraternity should advocate for changes in global animal use policies with the aim to reduce animal suffering and promoting animal welfare.

By applying these approaches and creating education and awareness initiatives in line with benefits, it is likely that an increased engagement with animal welfare initiatives will be seen.

With perpetual increase in the presence of pesticides, food and feed additives in our food chain the role of Regulatory Pharmacology and Toxicology is going to rise in the posterity. In the times ahead, world require stricter guidelines from the Regulatory Pharmacology and Toxicology fraternity from the food safety and health point of view. Research studies are required that involve the generation, evaluation, and interpretation of **experimental animal and human data** that are of direct importance and relevance for regulatory authorities with respect to pharmacological and toxicological regulations in society. More studies should be undertaken that address legal and/or regulatory decisions with respect to risk assessment and management of pharmacological and toxicological compounds on a scientific basis. Journals should encourage and support research studies which addresses to the international readership of scientists, risk assessors and managers, and other professionals active in the field of regulatory pharmacology and toxicology.

Conclusion

At present, important regulatory and advisory stan-dards are provided by federal and state agencies, non--governmental organizations, inspecting regulatory agencies, funding agencies, journal requirements for publication, and others. Scientist involved in using animals for research will typically need to comply with multiple overlapping compulsory and voluntary guidelines, and also take into account the perspectives and expectations of their local community. There is a general pattern of increasing regulation, a high level of public discourse and lobby-ing, and a need for wide harmonization and collabora-tion and high standards of care in support of ongoing animal-based activities. Global animal welfare laws and regulations vary greatly based on culture, societal views, govern-ments and history. This review creates a foundation of the ani-mal welfare laws and regulations in the United States, Canada, Europe, Australia, New Zealand and India. Other world organizations such as the OECD, CIOMS, ICH, and the OIE are key play-ers in shaping the ethics and standards for animal welfare.

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AWRP-OP-01

TOXICITY PROFILE OF HARITKADI YOGA: A CLASSICAL AYURVEDIC FORMULATION

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Haritkadi yoga is an Ayurvedic medicine used classically for rejuvenation therapy. The objective of this study was to determine acute oral toxicity and 90 days repeated dose oral toxicity study in wistar rats. The limit dose of 2000mg/kg body weight was tested for acute toxicity study and 250,500 and 1000mg/ kg body weight were used for 90 days repeated dose oral toxicity study. The studies were conducted as per OECD425 and OECD 408 guidelines. Acute treatment of female wistar albino rats with Haritkadi Yoga at 2000 mg/kg body weight, showed no changes in the autonomic or behavioural responses. No mortality and no severe body weight changes were observed. In 90 days repeated oral toxicity study, animals were observed for mortality, clinical signs, feed intake body weight, haematological, biochemical parameter along with organ weight and histopathology at the end of the study. Haritkadi Yoga did not show any signs of toxicity upon repeated administration of the drug for 90 days orally. There was no significant difference in haematological parameters and biochemical parameters between control and treated groups. Histologically, no comparable difference was observed. Hence, it was concluded that Haritkadi Yoga drug is safe up to 1000 mg /kg bw. on repeated oral administration.

AWRP-OP-02

METHOD VALIDATION FOR DETERMINATION OF PTEROSIN B IN COW'S MILK BY HPLC-UV

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Bracken fern (*Pteridium spp.*) found in the hilly areas of Himachal Pradesh, a north-western Himalayan state of India, is associated with causing enzootic bovine haematuria and urinary bladder tumors in cattle. It contains the toxic principle Ptaquiloside (PTA) which is a potent carcinogen. PTA can be secreted in the milk of cattle grazing on bracken ferns and thus may pose significant health risk to consumers. The quantitative analysis of PTA is challenging because of its unstable nature. PTA is converted to ptaquilosin in aqueous solutions and further to pterosin B (PTB), which is relatively stable in laboratory conditions. The objective of the present study is to develop a rapid and sensitive method for the quantitative analysis of PTB in milk. using the QuEChERS method and. The analytical standard was suspended in an organic solvent to make working standard solutions in the range of 0.05 ppm to 50 ppm. PTB was extracted from milk by QuEChERS method according

to Association of Official Analytical Chemist (AOAC) guidelines. After extraction, the sample was detected using a HPLC-UV system equiped with C18 column (5µm). The chromatographic separation was achieved using acetonitrile:methanol:acidified water as the mobile phase. The 20 µl of aliquots were injected and isocratically evaluated at the flow rate of 1.0 ml/min. The eluted fractions were detected at the wavelength of 230 nm and calibration curve was constructed for further analysis of chromatographic data. The method was found to be suitable, accurate and reliable conforming to European commission guidelines for method validation and quality control.

AWRP-OP-03

MODULATION IN METABOLITES OF *MAGRA* SHEEP EXPOSED TO SUPERIMPOSED STRESSORS

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An exploration was led to assess various metabolites in plasma samples of *Magra* sheep exposed to superimposed stressors. Superimposed stressors were comprised of extreme ambiences and transportation (Set I) and extreme ambiences, transportation and regrouping (Set II). Regrouping is a type of psychological stress experienced by animal due to unfamiliar surroundings. Blood samples were collected in morning hours. The assessment was done by measuring following metabolites in plasma viz. glucose, total proteins, urea, and cholesterol. Account of alterations owing to physiological states included 3-7 months, 7-11 months, 11-15 months and 15-19 months age group in two sets of stressors. The overall mean values for plasma glucose (P_{Glu},m mol L^{-1}) for set I of superimposed stressor were 3.87±0.073, 3.96±0.060 and 3.74±0.072 during dry hot , Humid-hot and Extreme Cold ambience with respect to control value of 3.68±0.85. The overall mean values for set II of superimposed stressors were 4.06±0.060, 4.14±0.148 and 4.04±0.478, respectively for the ambiences mentioned above.The overall mean values for plasma total protein (TP, g L^{-1}) for set I of superimposed stressor were76.92±0.02, 75.83±0.009 and 77.83±0.01 during dry hot, Humid-hot and Extreme Cold ambience with respect to control value of 79.32±0.02. The overall mean values for set II of superimposed stressors were 74.91±0.02, 73.83 ±0.009 and 75.83 ±0.01, respectively for the ambiences mentioned above.The overall mean values for plasma urea (P_{Urea}, m mol L^{-1}) for set I of superimposed stressor were 12.71±0.0675, 13.71±0.062 and 11.65±0.064 during dry hot, Humid-hot and Extreme Cold ambience with respect to control value of 7.62±0.051. The overall mean values for set II of superimposed stressors were 13.47±0.112,14.68±0.067and 12.91±0.073, respectively for the ambience mentioned above.The overall mean values for plasma cholesterol (m molL^{-1}) for set I of superimposed stressor were 4.23±0.003,4.57±0.004 and 4.92±0.003 during dry hot, Humid-hot and Extreme Cold ambience with respect to control value of 3.82±0.003. The overall mean values for set II of superimposed stressors were 4.96±0.002, 5.61±0.002and 6.12±0.002, respectively for the ambience mentioned above. The overall mean values of plasma metabolites except protein were significantly (pd"0.05) higher during dry-hot, humid-hot and extreme cold ambience as compared to respective moderate mean overall value in both the sets of superimposed stressors. The magnitude of increase was more in set II of superimposed stressors.

AWRP-OP-04

COMPARISON OF HPLC AND ELISA METHODS FOR THE DETECTION OF OXYTETRACYCLINE RESIDUES IN CHICKEN MEAT

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The present study was carried out to identify and quantify the level of residues of oxytetracycline (OTC) in chicken meat. For the detection of oxytetracycline residues in chicken meat samples, a simple isocratic HPLC method was standardized. For comparison, a commercial ELISA kit for the detection of oxytetracycline residues was also used. A total of 187 samples of chicken meat collected from ten districts representing the four regions of Tamil Nadu were tested for OTC residues. The HPLC method was a simple isocratic method using a C18 column with a sensitivity of 0.05 µg / Kg. All the samples tested using HPLC tested negative for OTC. Among these, 72 samples were also tested using an ELISA based test kit for oxytetracycline residues. Out of 72 samples tested, 22 samples (30.5% of samples) were found to be positive for OTC residues, with a range of 2.277 to 19.296 µg / Kg., and a mean value of 9.009 µg / Kg. But none of the samples that were positive exceeded the MRL for OTC in chicken, which is 200 µg / kg (as per Codex Alimentarius) and were thus safe for human consumption. The higher positive results of residues by ELISA could be attributed to better sensitivity of ELISA or due to cross-reactivity (lesser specificity) within the tetracycline group of antibiotics.

AWRP-PP-01

TOXIC BEHAVIOUR OF CADMIUM OVER GOAT PULMONARY ARTERY *IN VITRO*, AND THE ASSESSMENT OF AMELIORATIVE POTENTIAL SHOWN BY NARINGIN

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The *in-vitro* effect of Cadmium (Cd) and its amelioration by Naringin (NAR) on the pulmonary arterial rings of goats were studied. NAR is a flavanones-7-O-glycoside with a wide spectrum of pharmacological actions including a significant vasorelaxant effect on smooth muscles. The untreated and Cd acetate-treated pulmonary arterial rings of goats were exposed to the contractile (5-HT and phenylephrine) and relaxing (acetylcholine and sodium nitroprusside) agents both in the absence and presence of NAR in cumulative doses. Mean EC_{50} values for the contractile response of 5-HT and phenylephrine (PE) in the absence of Cd were 7.359×10^{-6} M and 5.953×10^{-6} M, respectively while in presence of Cd the same decreased to 5.080×10^{-7} M and 4.914×10^{-6} M, respectively with a significant left shift of the dose-response curve (DRC). Mean IC_{50} values for relaxant responses of acetylcholine (ACh) and sodium nitroprusside (SNP) were 2.445×10^{-8} M and 8.329×10^{-7} M, respectively. In the presence of Cd increase in the mean IC_{50} values of ACh and SNP to 1.081×10^{-6} M and 1.337×10^{-6} M, respectively was observed with a right shift in DRC. In the presence of NAR, the mean EC_{50} values of 5-HT and PE were increased to 6.983×10^{-5} M and 1.267×10^{-5} M, respectively with a right shift in

DRC. Similarly, IC_{50} values were decreased to 4.401×10^{-8} M and 9.993×10^{-7} M, respectively for ACh and SNP with a left shift in the DRC. Results suggest an ameliorative effect of NAR by vasorelaxation over the toxic effect of Cd on the pulmonary artery of goats.

AWRP-PP-02

FIPRONIL INDUCED SUB-ACUTE TOXICITY AND IT'S AMELIORATION BY *BRASSICA JUNCEA* EXTRACT IN WISTAR RATS

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Fipronil is a broad-spectrum N-phenylpyrazole insecticide and widely used in veterinary products for controlling agricultural pests and ectoparasites in domestic animals. Short-term exposure of fipronil can lead to serious effects on animals. The present study was conducted to evaluate fipronil induced sub-acute toxicity and it's amelioration by *Brassica juncea* extract in Wistar rats. Rats of 100-250g were divided in four groups of six animals each; Group I served as control and received only corn oil. In Group II fipronil @ 10 mg/kg body weight was administered and in group III fipronil along with methanolic extract of *Brassica juncea* seeds @ 300/kg body weight were administered for 28 days. In Group IV *Brassica juncea* seeds methanolic extract @ 300 mg per kg body weight was administered. Sub-acute intoxication resulted in clinical signs as anorexia, dizziness, abnormal gait, lethargy, weakness and aggressive behavior. Lipid peroxidation, reduced glutathione, superoxide dismutase, catalase and glutathione reductase levels were estimated. Lipid peroxidation was significantly increased while reduced glutathione, superoxide dismutase, catalase and glutathione reductase levels were significantly decreased in group II and III compared to control and group IV. There was significant decrease in lipid peroxidation level and increase in levels of reduced glutathione, superoxide dismutase, catalase and glutathione reductase in group III compared to group II. The observed antioxidant effects of *Brassica juncea* seeds could be related to presence of different chemically defined compounds such as phenolic content and flavonoids in their extracts. The study suggested that sub-acute exposure of Fipronil in rats causes general toxicity and oxidative stress which can be ameliorated with administration of *Brassica juncea* extract @ 300mg/kg body weight orally.

।पशुधनं नित्यं सर्वलोकोपकारकम्।

ISVPT-2023

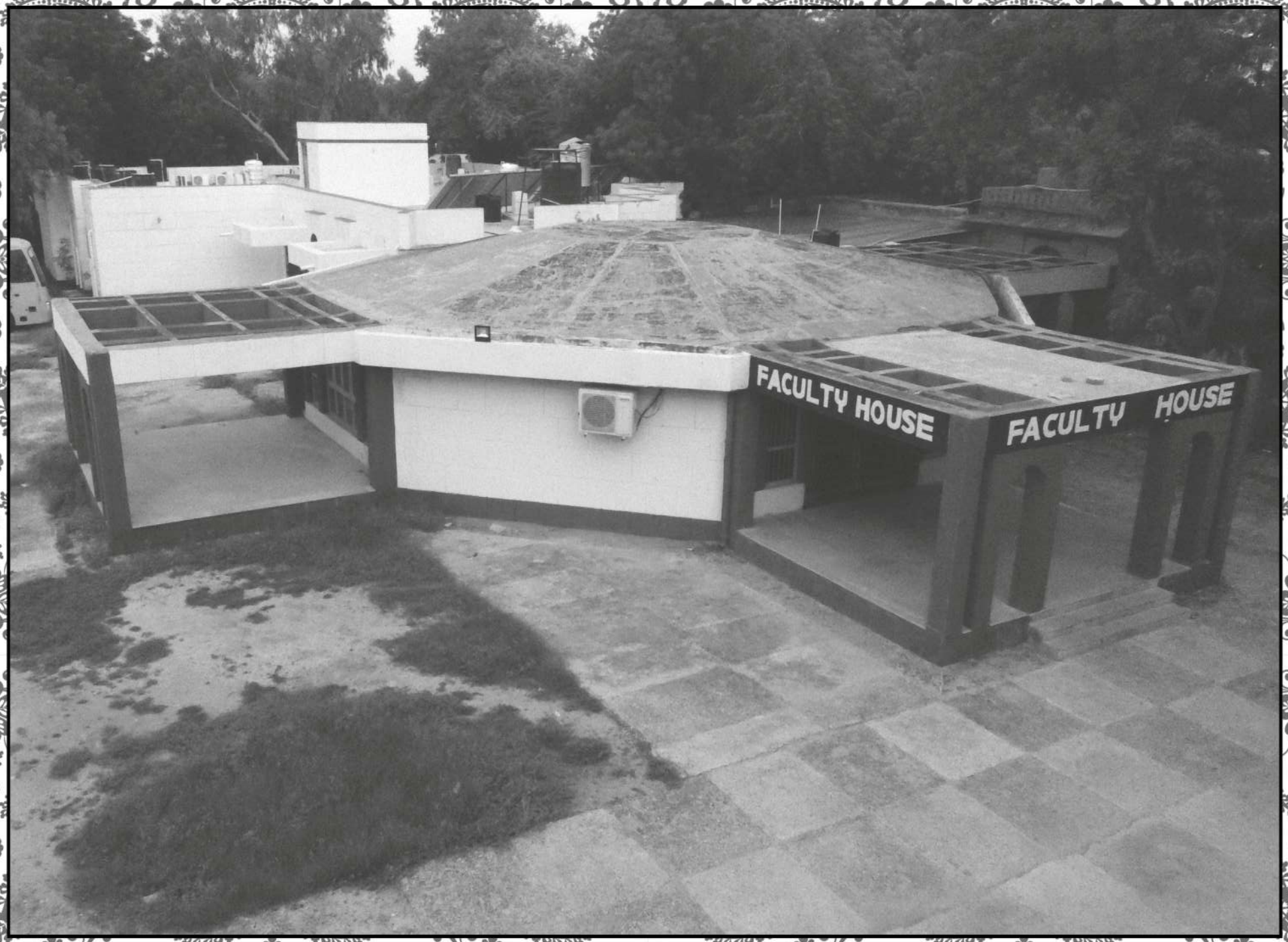
TECHNICAL SESSION-VII

Molecular and Neuropharmacology

Chairperson : **Dr. Dinesh Kumar**

Co-Chairperson : **Dr. R. D. Singh**

Rapporteur : **Dr. Sakthi Priya M**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MNP-LP-01

EXPLORING FUNCTIONAL AND MOLECULAR APPROACHES FOR TARGET DISCOVERY AND THERAPEUTICS IN SEPSIS MANAGEMENT

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Sepsis is a multifactorial disease state caused by a dysregulated systemic inflammatory response of the host's immune system towards infection. Sepsis and septic shock rank among the leading causes of mortality in critically ill or intensive care patients. In sepsis, the uncontrolled systemic production of the inflammatory mediators viz., cytokine storm leads to the systemic inflammatory response syndrome, which progresses to extensive and irreversible cell damage, impaired microvascular, and multiple organ dysfunction resulting in death. Developing effective therapies for sepsis is a critical area of research, and understanding the functional and molecular aspects of this condition is essential for identifying new drug targets.

Functional and molecular approaches

Vascular dysfunctions are frequently occurring clinical manifestations in sepsis. Therefore, exploring the functional aspect of a variety of signaling in the vascular system will be beneficial to unravel the pathophysiology of sepsis as well as newer therapeutic targets for its management. The isolated tissue preparation in the organ bath is a classical pharmacological technique that helps in the identification of receptors and their subtypes, signaling pathways, and therapeutic molecules by using activators, mediators, and inhibitors. Myograph is another important approach that mimics the physiological state and helps to explore the modulation of sepsis signaling in small-size vessels. Molecular techniques *viz.*, western blotting, immunohistochemistry, ELISA, and real-time polymerase chain reactions are used to assess the alteration of various proteins, cytokines, and mRNA expression patterns in sepsis conditions. These functional and molecular techniques help in the identification of the pathophysiological pathways, specific proteins, receptors, cytokines, genes, and other mediators involved in sepsis. Therefore, based on these approaches newer targets can be identified, and novel therapies can be developed by modulating the pathways, cytokines, enzymes, receptors, etc. Furthermore, genetic studies and molecular profiling also help in developing personalized sepsis therapy for an individual. Molecular approaches-based development of the early diagnostic biomarkers for sepsis and better exploring the interaction between host and pathogens also open a window for early diagnosis as well as the identification of novel drugs and therapeutic targets. Drug repurposing is another crucial approach to identifying and unraveling the therapeutic potential of existing drugs that generally have anti-inflammatory, immunomodulatory, or antimicrobial properties in sepsis and could be repurposed for the management of sepsis.

In our laboratory, a number of the molecules were explored for effect on the vascular dysfunctions and lung injury in sepsis. Nitric oxide (NO) and endothelium-dependent hyperpolarisation factors are crucial mediators of endothelium-dependent vasodilation, and sepsis impairs the endothelium-dependent vasodilation. By pre-treating with a statin, specifically atorvastatin, this sepsis-related impaired endothelium-dependent vasodilation has been restored (Subramani *et al.,* 2009). Additionally, atorvastatin has also been shown to reduce excessive

NO production and improve α_{1D}-adrenoceptor mRNA expression in the aorta of septic mice, preventing hyporeactivity to vasoconstrictor noradrenaline, indicating its beneficial role in enhancing hemodynamic functions in sepsis (Kandasamy *et al.,* 2011). Moreover, the combination of atorvastatin and imipenem therapy (Choudhury *et al.,* 2015) has been reported to improve vascular functions and increase survival in septic mice by maintaining the expression of α_{1D}-adrenoceptor mRNA or protein, reversing GRK2/Gβγ pathway-mediated desensitization of α_{1D}-adrenoceptor, and restoring endothelium-dependent acetylcholine relaxation. Rungsung and co-workers (2022) have demonstrated that luteolin which is a flavonoid, reversed the sepsis-induced endothelium dysfunctions and vasoplegia to the nor-adrenaline by modulating the eNOS and NO-producing pathways and iNOS pathways, respectively. Further, acute lung injury caused by sepsis is likewise characterized by enhanced permeability, polymorphonuclear cell infiltration, and edematous lung conditions. Intercellular adhesion molecules-1 (ICAM-1), reactive oxygen species-mediated oxidative stress, cytokine pathways, nuclear factor-kappa B, and inducible nitric oxide synthase pathways are among the crucial pathways that have been implicated in acute lung injury mediated by sepsis. By reducing the bacterial load and exerting anti-inflammatory activity, pre-treating the septic mice with daidzein extended their survival duration and protected them from lung injury (Parida *et al.,* 2015). Furthermore, combining atorvastatin with imipenem has been reported to decrease the bacterial load and attenuate the inflammatory response, suggesting the novel therapeutic potential of combined therapy for the lung injury caused by sepsis. Additionally, the flavonoid luteolin has been suggested to reduce acute lung injury caused by sepsis by inhibiting the ICAM-1, NF-kappa B, oxidative stress, and partially the iNOS pathways (Rungsung*et al.,* 2018). Rabha and co-workers (2018) have reported the beneficial potential of another flavonoid kaempferol in sepsis-induced lung injury by modulating the ICAM-1, iNOS, and oxidative stress pathways.

In conclusion, a multidisciplinary strategy that combines functional and molecular research with cutting-edge technology holds the key to identifying novel pharmacological targets and developing effective therapies for sepsis management. For better sepsis care, clinicians, researchers, and industry must work together to overcome obstacles and advance the area.

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MNP-LP-02

MOLECULAR INSIGHT INTO SEPSIS-INDUCED VASOPLEGIA: A LEARNING EXPERIENCE ON RECEPTOR DYNAMICS

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Sepsis, a systemic inflammatory response syndrome against microbial infection, is a leading cause of death in intensive care units (Hattori *et al.,* 2017). It is a multifactorial disease with uncontrolled systemic production of inflammatory mediators ('cytokine storm') following microbial infection (Bosmann and Ward, 2013). If not recognized in the initial stages with its proper management, it can lead to septic shock, multiple organ failure, and death. It is characterized by vascular hypo-responsiveness, tissue hypo-perfusion, tachypnoea, hyperthermia, systemic hypotension, and multi organs failure despite antibiotic therapy, adequate fluid resuscitation and administration of vasopressors (Dellinger, 2008). Assessment of organ dysfunction is done either by 2 points or more of the Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score, which directly correlates with prognosis (Singer *et al.,* 2016). Despite the progress in clinical and basic research, prognosis in septic patients still remains extremely poor and mortality rate varies from 15 to 40% (Singer *et al.,* 2016; Lelubre *et al.,* 2018). Around 48.9 million cases of sepsis have been reported globally, with almost 85.0% of sepsis cases and sepsis-related deaths occurring in low- and middle-income countries (Rudd *et al.,* 2020). Between 2000 and 2018, among all hospital-treated sepsis cases, 23.6% were of healthcare-associated, with a pooled hospital incidence of 15.4 cases per 1000 patients of all sepsis (Markwart *et al.,* 2020) which leads to around 42% mortality in intensive care patients treated for sepsis (World Health Organization, 2020). Dysregulated host immune responses to infection in an immuno-compromised state coupled with vascular dysfunctions are the predominant cause of death in sepsis (Vincent and Backer, 2005; Perl *et al.,* 2006). Since sepsis continues to be a substantial burden on healthcare, proper understanding of its complex pathophysiology needs to be explored to identify novel therapeutic targets and effective treatment strategy to combat this fatal condition.

Pathophysiology of sepsis

Disruption of equilibrium between the inflammatory and anti-inflammatory pathways leads to the development of sepsis. Interaction and subsequent recognition of pathogen-derived molecular patterns (PAMPs, e.g., endo- and exotoxins, lipids, or DNA sequences) or endogenous host-derived danger signals (damage-associated molecular patterns; DAMPs) with the specific sensing cells of the body forms the foremost step in the development of sepsis. On interaction, these molecules activate toll-like receptors (TLR) on the surface of antigen-presenting cells (APCs) and monocytes, followed by transcription of genes involved in inflammation, cell metabolism, and adaptive immunity (Rubio *et al.,* 2019). This triggers the production of various pro-inflammatory interleukins (IL), e.g., IL-1, IL-12, IL-18, tumor necrosis factor alpha (TNF-α), and interferons (IFNs) via NF-κB pathway. Subsequent to this, activation of other cytokines (e.g., IFN-γ, IL-6, IL-8), complement

and coagulation pathways, and, by suppression of components of the adaptive immune system favours further progression of sepsis (Hotchkiss *et al.,* 2016). All these events include activation of both pro-inflammatory and anti-inflammatory pathways, ultimately causing progressive tissue damage & multi-organ dysfunction. Interaction of proinflammatory cytokines with the endothelium further aggravates the inflammation with release of proinflammatory substances, recruiting additional inflammatory cells and favouring procoagulant activity, and hyperpermeability leading to failure of microcirculation (van Hinsbergh, 2012).

Vascular hyporeactivity in sepsis

The vascular endothelium comes first into contact with circulating bacterial molecules (Peters *et al.,* 2003). Endothelial cells contain structures that recognize various bacterial molecules and subsequently initiate the expression of inflammatory mediators (Henneke and Golenbock, 2002). It is well established that during sepsis, uncontrolled release of pro-inflammatory mediators in blood and tissues (Hotchkiss *et al.,* 2016) like tumor necrosis factor (TNFα), interleukin-1, interleukin-6, chemokines, prostaglandins, leukotrienes, proteases, platelet-activating factor (PAF), histamine and nitric oxide occurs and is directly or indirectly involved in mediating endothelial dysfunctions and alteration in microcirculation (Russel *et al.,* 2011). Circulatory failure in sepsis is characterized by refractory hypotension and vascular hyporeactivity to clinically used vasoconstrictors like nor-adrenaline leading to multi-organ dysfunction. vascular hyporeactivity to vasoconstrictors being one of the clinical manifestations of sepsis is well reported and various factors lead to vascular hyporeactivity. Different mechanisms like *viz.* i) Overproduction of inducible nitric oxide synthase (iNOS)-derived nitric oxide (NO) along with down-regulation and desensitization of α1D-adrenoceptor expression in mouse aorta (Choudhury *et al.,* 2015). Reduced gene and protein expression of α_{1D} adrenoceptor and enhanced desensitization of this receptor are attributed to augmented GRK-2 expression in mouse model of polymicrobial sepsis (Choudhury *et al.,* 2015). ii) Increased aortic expression of cannabinoid type-1 receptor (CB1R) in mouse aorta was found to be responsible for vascular hyporeactivity to noradrenaline in sepsis (Singh *et al.,* 2018). In addition to this, down-regulation of AT1 receptor and P2Y6 receptor (Jagadeesh *et al.,* 2023) and attenuation of aortic Notch1 and Notch 3 receptor with corresponding decrease in myosin light chain kinase expression (MLCK) expression was also found to be responsible for vasoplegia in sepsis (Singh *et al.,* 2022). Thus, unlike macrophages where activation of Notch signalling and its downstream mediators are thought to be responsible for inflammation and cytokine production, inhibition of notch signalling in vascular smooth muscle cells is responsible for vascular hyporeactivity in sepsis. Thus, a complex interaction of immune system and cardiovascular system plays a novel role in sepsis which need to be explored in future to strategically design effective therapy against this most challenging condition in health care system. Excessive activation of the vascular ion channels was also recognised as the major cause of hypotension and vascular hypo-responsiveness to catecholamines in septic shock (Buckley *et al.,* 2006). Further, sepsis-induced myocardial depression was linked to reduced expression of β_1 adrenergic receptor at both gene and protein level along with attenuated cAMP response (Thangamalai *et al.,* 2014).

Taken together, the mechanism of vascular dysfunction is a complex phenomenon that involves a myriad of cellular signalling mechanism. More importantly, the immune system and cardiovascular events may act differentially during the progression of sepsis. Thus, organ-specific and time-dependent therapeutic measures proved to be more beneficial to target this complex phenomenon.

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MNP-OP-01

LEPTIN DECREASES THE TRANSCRIPTION OF BK_{CA} CHANNELS AND Gs TO Gi PROTEIN-RATIO IN LATE PREGNANT RAT UTERUS

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Obesity can have a significant impact on pregnancy outcomes by compromising the ability of the uterus to relax, which increases the likelihood of conditions such as preterm labor. One of the key pathways responsible for uterine relaxation is the β-adrenergic signaling pathway, and it is well-documented that obesity, often linked to a high-fat diet, can disrupt this pathway within the uterine environment. Hyperleptinemia is a significant feature of pregnancy as well as obesity. However, the effect of leptin on β-adrenergic signaling pathway has not been studied. In the present study, we studied the effects of leptin on transcriptions of the major proteins defining the β-adrenergic signaling pathway in pregnant rat uterus. Leptin treatment at a supraphysiological concentration to pregnant rat uterine strips increased the mRNA and protein expressions of Gs protein but not the mRNA of β_2- and β_3-adrenoceptors. It also enhanced the expression of Gi-protein but not the Gq protein. The ratio of Gs to Gi protein mRNA was decreased significantly. Similarly, leptin reduced the transcription of $BK_{Ca\alpha}$ and $BK_{Ca\beta}$ channel subunits. In leptin-stimulated tissues, leptin receptor and JAK-2 expression also increased. In conclusion, leptin decreases the ratio of Gs to Gi proteins and $BK_{Ca\alpha}$ and $BK_{Ca\beta}$ channel subunits suggesting hyperleptinemia is a likely factor inducing uterine relaxant dysfunction in obesity.

MNP-OP-02

STUDIES ON AMELIORATIVE POTENTIALS OF QUERCETIN NANOPARTICLES AGAINST IMIDACLOPRID INDUCED SUB-ACUTE GENOTOXICITY IN SWISS ALBINO MICE

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Worldwide indiscriminate use of pesticides by agricultural industry for controlling pest poses a great threat to non-target animals and even to humans via subsequent residues. Here, using histopathology of testes and bone marrow and genotoxicity assays such as the micronucleus test (MNT), comet assay, and sperm head abnormality assay (SHA), we investigate the protective potential of quercetin and quercetin nanoparticles against imidacloprid-induced genotoxicity in Swiss albino mice. For experimental purpose, total 48 mice were taken and divided into eight groups with six animals in each group. Group 1, 2, 3 and 4 received 3% gum acacia, 22 mg/kg b.wt. imidacloprid (IMI), 25 mg/kg b.wt. quercetin (Que) and 25 mg/kg b.wt. quercetin nanoparticles, respectively. Group 5, 6, 7 and 8 received 22 mg/kg b.wt. imidacloprid + 25 mg/kg b.wt. quercetin, 22 mg/kg

b.wt. imidaclopid + 25 mg/kg b.wt. quercetin nanoparticles, 22 mg/kg b.wt. imidacloprid + 12.5 mg/kg b.wt. quercetin nanoparticle and 22 mg/kg b.wt. imidacloprid + 6.25 mg/kg b.wt. quercetin nanoparticles, respectively. The obtained result demonstrated that imidacloprid causes genotoxicity in bone marrow cells by increasing the frequency of micronuclei and the comet tail length. Additionally, imidacloprid is mutagenic to germ cells in SHA. Both quercetin and quercetin nanoparticles lessen the genotoxicity that imidacloprid induces when administered together or separately. Histopathological findings also revealed degenerative changes in bone marrow and testes in imidacloprid administered group as compared to control. Quercetin and quercetin nanoparticles showed marked ameliorative effect by restoring the degenerative changes produced by imidacloprid.

MNP-OP-03

PROTECTIVE EFFECTS OF ORLISTAT AGAINST ISOPRENALINE-INDUCED OXIDATIVE STRESS-MEDIATED CARDIAC INJURY IN A MOUSE MODEL

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The present study was undertaken to unravel the effect of the lipase inhibitor, orlistat in isoprenaline-induced cardiac injury in the mouse model. The cardiac injury was induced by the subcutaneous administration of a β-adrenoceptor agonist *viz*., isoprenaline (ISP) @ 20 mg/kg body weight for 14 days in mice. Orlistat was co-administrated at 30 mg/kg body weight through an intraperitoneal route for 14 days. Mice were sacrificed under anesthesia after 24 hours of the last dose of isoprenaline (day 15th) administration. Blood and heart tissue were collected to evaluate the effect of orlistat on various parameters, including serum cardiac injury markers, tissue anti-oxidant and lipid peroxidation, and expression of Nrf-2 protein in the heart. Orlistat significantly decreased the level of both CK-MB and LDH in the serum of isoprenaline co-administered mice in comparison to the isoprenaline-alone group. Both enzymatic (SOD and catalase) and non-enzymatic (reduced glutathione) antioxidant levels were significantly reduced in the isoprenaline-administered group in comparison to the control group. Moreover, a significantly enhanced level of MDA was observed in the heart tissue of the isoprenaline-alone group. However, orlistat treatment significantly increased the enzymatic (catalase) and non-enzymatic antioxidant levels along with a significant reduction in MDA level in the isoprenaline co-administration group in comparison to the isoprenaline alone group. Furthermore, orlistat improved the Nrf2 expression in the heart of isoprenaline co-administered mice. In conclusion, co-administration of the lipase inhibitor *viz*., orlistat improved the cardiac injury markers, anti-oxidant parameters, lipid peroxidation, and Nrf-2 expression in isoprenaline-induced cardiac injury in the mouse model.

MNP-OP-04

PREDICTION OF IMMUNE ACTIVE PEPTIDE EPITOPES FOR LUMPY SKIN DISEASE VIRUS (LSDV) USING IMMUNOINFORMATIC APPROACH

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The year of 2022 witnessed the worst hit by the animal disease caused by Lumpy Skin Disease virus (LSDV) and took a toll of 2.4 million cattle. The virus comes under Genus Capripoxvirus. The protein sequences from pathogens were subjected to bio-informatics analysis, to predict the prophylactic immune active peptides for LSDV, protein sequences of 156 putative genes were retrieved from the NCBI and screened for Antigenicity and allergenicity by VaxiJen v.2.0 and AllerTOP v. 2.0 respectively. Then subjected to physiochemical properties analysis by using Protparam tool. The selected fifty-one protein sequence screened for epitopes B-cell and T-cell (MHC-I and MHC-II) using IEDB server. The predicted epitopes also subjected for Antigenicity and allergenicity analysis. It was found that 52 B-cell epitopes and 299 T-cell epitopes were found to be antigenic and non-allergen. Toxicity analysis was done using ToxinPred tool. Water solubility was determined using peptide property calculator PepCalc.com. MHC I and II immunogenicity was determined using IEDB. Around 139 T-cell epitopes were found to be immunogenic. Prediction of IFN- γ cytokine secretion by immunogenic epitope was done using IFNepitope webserver to identify IFN-gamma inducing MHC class II binding peptides. Eventually, 89 T-cell and 47 B-cell predicted epitopes were clustered based on sequence identity.

MNP-OP-05

WEEKLY ADMINISTRATION OF BETULINIC ACID AMELIORATED OXIDATIVE KIDNEY DAMAGE IN MOUSE MODEL OF AKI-CKD TRANSITION

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Acute kidney injury to chronic kidney disease (AKI-CKD) transition refers to the progression of CKD after AKI. Limiting the shift from AKI to CKD is critical for lowering the social and economic cost of CKD. Betulinic acid (BA) has been shown to exhibit various pharmacological activities and it has shown the protective effect on AKI and CKD; however no reports are available on its effect on AKI-CKD transition. In the present work, the effects of BA in folic acid (FA)-induced AKI-CKD transition was explored under two treatment regimen. Mice were injected with a single dose of FA (i/p) for inducing AKI-CKD condition on day 1 in injury group (I). Further, excess of these mice received BA at 30 mg/kg dose for 3 days (on days 1,2,3) (IT3) in one group and for 7 days (on days 1,2,3,7,14,21,28) in another group (IT7). All mice were sacrificed on day 28. Mice in injury group (I) showed elevated serum creatinine levels along with lesser creatinine excretion in

urine. Oxidative stress markers such as tissue lipid peroxidation (MDA), urine nitrite and tissue nitrotyrosine expression were also increased in injury group (I). Treatment with BA (IT7) reduced serum creatinine concentration, urine nitrite, kidney MDA levels and expression kidney nitrotyrosine together with elevation of urine creatinine excretion in comparison to injury group (I). These findings indicate the mitigative potential of BA on oxidative damage in the kidney of mice induced with AKI-CKD transition.

MNP-PP-01

PROPHYLACTIC EFFECT OF SCLAREOL AGAINST CERULEIN-INDUCED ACUTE PANCREATITIS BY MODULATING NF-κB DEPENDENT SIGNALING PATHWAY

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Sclareol is a natural fragrance compound used widely in the food and cosmetic industries with promising anti-oxidant and anti-inflammatory potential. Acute pancreatitis (AP) is one of the leading acute disease condition which leads to hospitalization due to unavailability of a specific therapy. This study examined the ameliorative effect of Sclareol against cerulein induced AP. Mice were pretreated with sclareol intraperitoneally (i.p.) for 7 days (10 and 20 mg/kg, b.wt), (SLD and SHD) and on the final day of the study, cerulein (50 µg/kg, b. wt, i.p.) injected six times with an interval of an hour (DC). On last day, mice were sacrificed and the pancreas were collected for studying effects of sclareol on various inflammatory cytokines, pancreatic injury and expression of inflammatory transcription factor (NF-κB) by Enzyme Linked Immunosorbant Assay (ELISA), Immunohistochemistry (IHC) and Western Blot (WB) assay respectively. Sclareol treatment significantly ($P<0.001$) reduced the pancreas injury in the mice with cerulein induced AP. ELISA analysis revealed that pretreatment with sclareol significantly ($P<0.001$) reduced the cerulein elevated levels of pro-inflammatory cytokines interlukin-6 (IL-6), interlukin-1β (IL-1 β), tumor necrosis factor-alpha (TNF-α) and increased the levels of anti-inflammatory cytokine interleukin-10 (IL-10). The immunohistochemical expression of nuclear factor kappa light chain enhancer of activated B cells (NF-κB) were significantly ($P<0.001$) decreased by sclareol in cerulein treated mice. On western blotting assay, sclareol treatment has significantly ($P<0.001$) reduced the expression of NF-κB. In conclusion, the results of the present study demonstrate that sclareol has significant immunomodulatory potential by modulation of NF-κB pathway to prevent cerulein-induced AP.

MNP-PP-02

IMMUNOMODULATORY AND ANTIOXIDANT ACTIVITIES OF *CURCUMA LONGA, OCIMUM SANCTUM* AND *PIPER NIGRUM* POWDER IN BROILER

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The present research was planned to evaluate *in-vivo* immunomodulatory and antioxidant activities of *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powder alone at different dose in broiler. A total of 96 chicks were

divided randomly into 8 groups each of 12 chicks. Group I served as control and was given basal diet without any treatment. Group II served as standard control and was given vitamin E and selenium containing product in water. Chicks of group III and IV were given basal diet plus *Curcuma longa* (2.5 and 5.0 g/kg feed), group V and VI were given basal diet plus *Ocimum sanctum* (2.5 and 5.0 g/kg feed) and group VII and VIII were given basal diet plus *Piper nigrum* powder (5.0 and 10.0 g/kg feed) respectively). The duration of study was 35 days. Cutaneous basophil hypersensitivity (CBH) response at two different doses (100 µg and 200 µg) of phytohemagglutinin-P was carried out to assess the cell mediated immunity on 14th day of age. Blood was collected on 7th, 21st and 35th day of age and serum was separated to estimate antibody titre against ND vaccine by haemagglutination inhibition (HI) test and biochemical parameters like serum total protein, serum albumin, serum globulin and A/G ratio. On 35th day, antioxidant enzymes such as superoxide dismutase, catalase and malondialdehyde were measured from the serum. On 35th day, thin blood smears were prepared and stained with field's stain to determine differential leucocyte counts (DLC) microscopically and H/L ratio was calculated. At the end of experiment, birds of all groups were slaughtered and tissues like bursa of Fabricius, thymus and spleen were collected for histopathological examinations. *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powders alone had significantly ($p<0.05$) higher CBH response and HI antibody titer in broiler. The effect was similar to that produced by vitamin E and selenium supplementation. The results evinced that dietary inclusion of all three powder alone stimulated cell mediated as well as humoral immune response in broiler. Dietary inclusion of all three powders alone, significantly improved the serum total protein, serum globulin and significantly ($p<0.05$) decreased the albumin to globulin ratio. Dietary inclusion of all three powders alone decreased H/L ratio. *Ocimum sanctum* (5.0 g/kg feed) showed lower H/L ratio as compared to standard supplements of Vit. E and selenium. Histopathological examination of bursa of Fabricius, spleen and thymus did not reveal any alteration in normal architecture among all experimental groups. Superoxide dismutase and catalase were significantly increased whereas malondialdehyde significantly ($p<0.05$) reduced in birds supplemented with all three powder alone at lower and higher doses as compared to birds of control group. Results indicate that *Curcuma longa, Ocimum sanctum* and *Piper nigrum* powder has immunostimulants and antioxidant activities in broiler.

MNP-PP-03

EVALUATION OF QUERCETIN NANOPARTICLES AS A POTENTIAL THERAPY FOR IMIDACLOPRID-INDUCED SUB-ACUTE NEUROTOXICITY IN SWISS ALBINO MICE

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Imidacloprid (IMI), a neonicotinoid which is extensively used against termites rapidly metabolized in mammals and contributes to neurotoxicity via the blocking of nicotinic acetylcholine receptors, as in insects. It also affects non target species including humans. Quercetin nanoparticles are prepared to increase bioavailability of quercetin which is well known antioxidant. Here, using histopathology of brain, various neurobehavioral parameters and brain acetylcholinesterase assay, we investigate the protective potential of quercetin and quercetin nanoparticles against imidacloprid-induced neurotoxicity in Swiss albino mice. Quercetin nanoparticles were synthesized by ionic gelation method. Total 48 mice were taken and divided into eight groups with six animals in each group. Group 1, 2, 3 and 4 received 3% gum acacia, 22 mg/kg b.wt. imidacloprid (IMI), 25 mg/kg

b.wt. quercetin (Que) and 25 mg/kg b.wt. quercetin nanoparticles high dose, respectively. Group 5, 6, 7 and 8 received 22 mg/kg b.wt. imidacloprid + 25 mg/kg b.wt. quercetin, 22 mg/kg b.wt. imidaclopid + 25 mg/kg b.wt. quercetin nanoparticles, 22 mg/kg b.wt. imidacloprid + 12.5 mg/kg b.wt. quercetin nanoparticle and 22 mg/kg b.wt. imidacloprid + 6.25 mg/kg b.wt. quercetin nanoparticles, respectively. Histopathological findings revealed degenerative changes in cerebrum and cerebellum in imidacloprid administered group as compared to control. Quercetin and quercetin nanoparticles showed marked ameliorative effect by restoring the degenerative changes produced by imidacloprid. In heat induced algesia there was significant increase in reaction time in imidacloprid group as compared to control and both quercetin and quercetin nanoparticles significantly reduced reaction time as compared to imidacloprid group. There was no significant change in acetylcholinesterase activity noticed in any group compared to control.

MNP-PP-04

SYNTHESIS, CHARACTERIZATION, MOLECULAR DOCKING AND *IN VIVO* WOUND HEALING EVALUATION OF HEMIN AND BILIRUBIN NANOPARTICLES IN DIABETIC RATS

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Diabetes is one of the major chronic metabolic disorders. Approximately 25 percent of diabetes mellitus patients suffer from impaired wound healing. Hemin and bilirubin have wound healing potential but high hydrophobicity hinders their potential. Therefore, novel hemin and bilirubin nanoparticles were synthesized and characterized. Haemolytic and MTT assay were done to check biocompatibility and cellular uptake was analyzed. Molecular docking was carried out. Nanoparticles were found to be biocompatible and *in-silico* analysis showed good binding energy with different proteins involved in diabetic wound healing. In wound healing study, diabetes was induced in rats using streptozotocin at dose rate of 45mg/kg BW. A 400mm^2 excisional wound was created on back of rats. Pluronic F-127 (PF-127) (control), bulk hemin (bulk H) (0.5%), bulk bilirubin (bulk B) (0.3%), hemin nanoparticles (HNP) (0.02%, 0.1% & 0.5%) and bilirubin nanoparticles (BNP) (0.03%, 0.1% & 0.3%) were applied topically to the wound for 19 days and rats were sacrificed on day 19. HNP and BNP treated groups showed significant increase in rate of wound contraction, hydroxyproline and glucosamine as compared to control group. ELISA revealed higher IL-10 and lower TNF-α level in nanoparticles treated group. Western blot showed significant expression of αSMA, TGFβ1, CD-31, Nrf2 in HNP and BNP treated groups. Reduced expression of MMP-2 and MMP-9 was found in the nanoparticles treated groups. Histopathology revealed mature epidermis and dense collagen in HNP and BNP treated groups. Present findings indicate that HNP and BNP have the potential to accelerate healing in diabetic wounds.

MNP-PP-05

NOVEL BIOACTIVE HYDROXAMATE INDANONES AS VASORELAXANT AGENT IN RODENT CONDUIT AND RESISTANCE ARTERIES

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Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure (WHO). It is also the most important contributor to cardiovascular disease. Patients with hypertension present with obvious changes in vascular tone, which result in changes in SVR and thus hypertension. Because of this, most hypertension drugs target vascular smooth muscles to lower blood pressure, such as angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), β-blockers, and calcium channel blockers (CCBs), and these drugs are used singly or in combination. However, with the long-time use of drugs by patients, the side effects of hypertension drugs have gradually become manifest. Traditional medicine is used by 80% of the world's population, as reported by WHO. Indanone is one of the privileged structures in medicinal chemistry and is commonly associated with various pharmacologically active compounds. Indanones have demonstrated a broad spectrum of biological activity. Because of the biological importance of the indanone core, past several years researchers have produced library of pharmacologically active indanones. Inspired by the success of donepezil several academic and industrial laboratories commenced the active research to develop novel indone analogs as therapeutic agents.

MNP-PP-06

IN SILICO STRUCTURAL ELUCIDATION OF THE RNA POLYMERASE 30 (LSDV036) TOWARD THE IDENTIFICATION OF POTENTIAL LUMPY SKIN DISEASE VIRAL INHIBITOR DRUGS

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The lumpy skin disease virus is a dsDNA virus which causes characteristic nodules on the skin among cattle. When symptoms become evident, the outcome is typically fatal, and thus far, post-exposure prophylaxis is the sole remedy, effective only if administered immediately after exposure. RNA polymerase 30 plays a significant role in viral replication and transcription and can be potential drug target. Herein we generated an energy-minimized homology model of Rpo30 and used it for virtual screening against 748 antiviral compound libraries. The best five ligand-Rpo30 complexes were picked for further energy minimization via molecular dynamics (MDs), where the complex with drug showing a minimum score characterized with stable hydrogen bonds and hydrophobic interactions with the catalytic site residues was selected. Our study identified an important ligand for development of remedial approach for treatment of lumpy skin disease infection.

MNP-PP-07

BETULINIC ACID PREVENTS CKD CHANGES AFTER AKI IN THE MOUSE AKI-CKD TRANSITION MODEL

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Acute kidney injury (AKI) is an influencing element in the development and progression of chronic kidney disease (CKD). The incomplete repair of tubular injury during the course of AKI could lead to the development of CKD. A pentacyclic triterpenoid, betulinic acid (BA) has been shown to exhibit a variety of biological and medicinal properties and it has shown the protective effect on AKI and CKD. This study aimed at investigating the effects of BA on AKI-CKD transition in mice which is yet unknown. The study was conducted in two phases. AKI to CKD model was produced by single dose (250 mg/kg BW) intraperitoneal administration of folic acid in mice on first day and left for 28 days period (I). In these mice, BA was administered at dose rate of 30 mg/kg BW for 3 days (on days 1, 2, 3) in one group (IT3) and for 7 days (on days 1, 2, 3, 7, 14, 21, 28) in another group (IT7) and all mice were sacrificed on Day 28. Mice in injury group (I) showed elevated fibrotic markers such as α–SMA and MMP-2 activity but they had attenuated levels of tissue reparative cytokines such as IL-4 and IL-13. Excess of fibroblasts and extracellular matrix in the interstitial and periglomerular area especially, increased birefringence of collagen in microscopy further support these findings. 7 days BA treatment regimen (IT7) significantly improved reparative cytokines and inhibited maladaptive matrix deposition by reducing fibroblast infiltration and MMP-2 activity. Findings of this study indicate the potential BA to prevent development of CKD changes in the kidney injury model of AKI-CKD transition.


CENTRE FOR ETHNO VETERINARY PRACTICES
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TECHNICAL SESSION-VIII

Clinical Pharmacology and Toxicology

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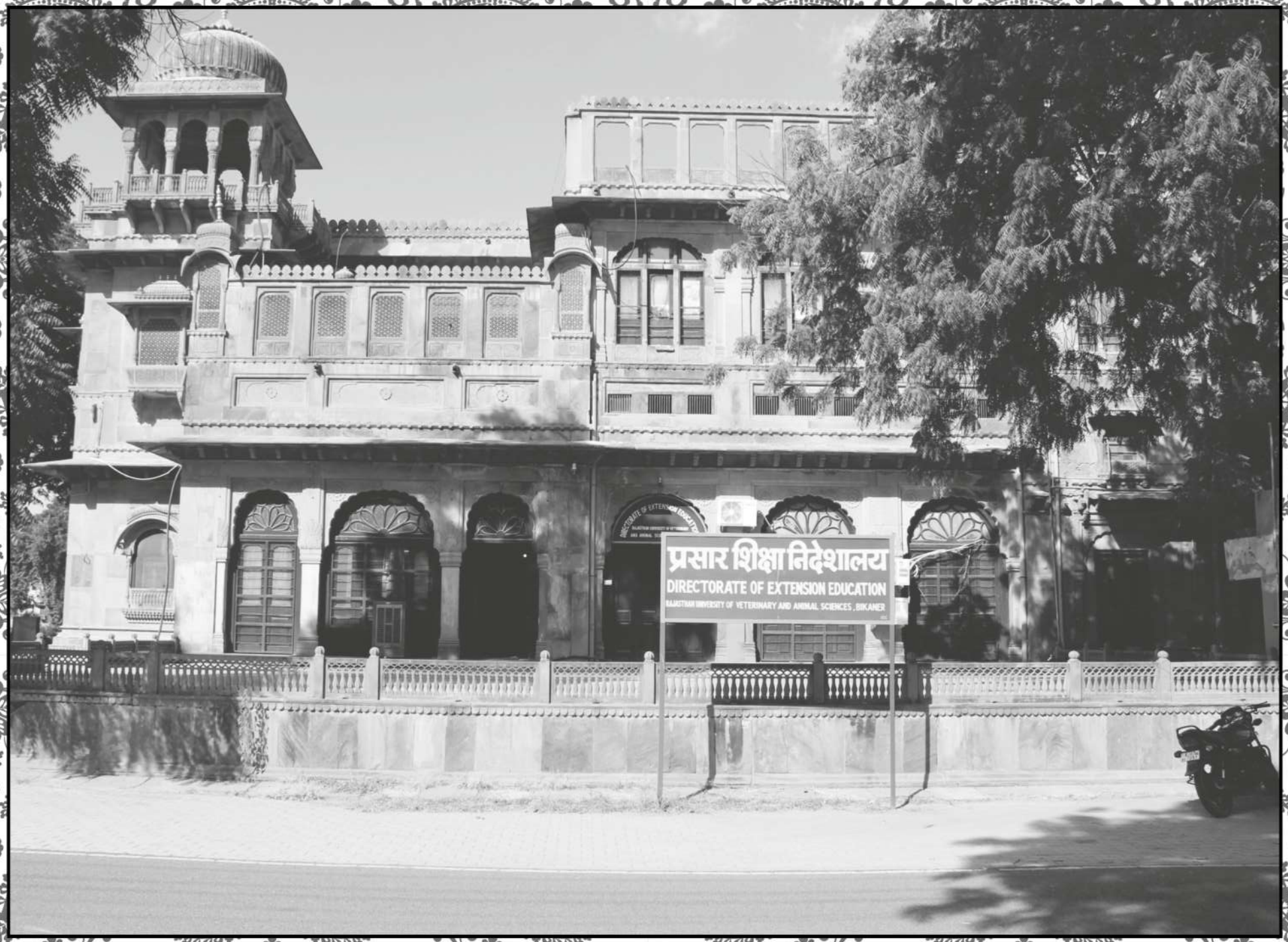
Rapporteur : **Dr. Anshuk Sharma**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CPT-LP-01

MANAGING AGGRESSIVE ANIMALS: THE CHILL PROTOCOL

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Aggression is the most common and serious behaviour problem in small animals, as also in horses. It's also the number-one reason why owners seek help from trainers.

What Is Aggression?

The term "aggression" refers to a wide variety of behaviours that occur for a multitude of reasons in various circumstances. Virtually all animals are aggressive when guarding their territories, defending their offspring and protecting themselves. Species that live in groups, including people, also use the threat of aggression to keep the peace and to negotiate social interactions. To say that an animal is "aggressive" can mean a whole host of things. Aggression encompasses a range of behaviours that usually begins with warnings and can culminate in an attack.

Managing Aggression

Aggressive behaviour in pet dogs is a serious problem across the globe, with bite injuries representing a serious risk to both people and other dogs. There are different types of aggressive behaviours in dogs detailed as follows:

Fear Aggression – from fear of being trapped, especially in exam rooms / OPDs.

Territorial Aggression - attacking an intruder, whether friend or foe.

Protective Aggression- aggressive behaviour when a family member is in peril.

Possessive Aggression - tendency to guard their possessions.

Defensive Aggression – when the animal decides offense is the best defence.

Social Aggression – By an animal who perceives self as high in status.

Frustration-Elicited Aggression- By an animal who's excited or aroused by something but is held back from approaching it.

Redirected Aggression- Aggression towards a person who interferes.

Pain-Elicited Aggression- A friendly animal becoming aggressive when in pain.

Sex-Related Aggression-by Intact males who vie for the attention of females.

Predatory Aggression- a classic behavior, including chasing and grabbing fast-moving things.

Age- Aggression - due to a decline in functioning of body systems with age, especially the brain (Cognitive Dysfunction), summarized with the acronym CRASH, which stands for: Confusion/disorientation, Responsiveness decrease, Activity changes, Sleep disturbances, as House training lapses.

Treatment Options - This will depend on the specific type of aggression and its triggers. It can be drug therapy, behaviour therapy or making changes in dog's environment with the guidance of a Certified Applied Animal Behaviourist (CAAB), Keeping a dog away from whatever triggers his fears or phobias, may be the best option in many cases. However, many drug therapies are available and the Chill Protocol is one of the best options. **It provides adequate and safe management of a dog with fear-induced aggression without**

significant side effects. The Chill Protocol is a relaxation protocol to be prescribed to healthy patients known to be aggressive, fearful, and anxious during hospital visits. The protocol consists of **at-home administration of gabapentin, melatonin, and acepromazine** prior to a medical appointment. Gabapentin and melatonin can be given with a small amount of food, and acepromazine should be administered oral transmucosally (OTM) via syringe.

Gabapentin is a ligand of the $\alpha_2\delta$ subunit of high voltage-dependent Ca^{2+} channels (L-type, N-type). It disrupts the regulatory function of $\alpha_2\delta$, prevents delivery of the Ca^{2+} channels to the cell membrane, thus reducing the activation of the channels and neurotransmitter release. Gabapentin has anxiolytic, sedative, analgesic, and anticonvulsive properties. Oral gabapentin has been used to decrease anxiolysis in humans.

Melatonin is a naturally occurring hormone produced by the pineal gland and has been shown to reduce pre- and postoperative anxiety in humans, and its calming effects plus safety benefits dogs with fear-aggression. Acepromazine elicits tranquilization in animals, and has synergistic taming effects with other sedatives. The primary behavioral effects are due to its potent antagonism of post-synaptic D_2 receptors, and to a lesser degree the other D_2-like receptors. 75% of Collie breed dogs carry the mutated *ABCB1* gene, as do 50% of Australian Shepherds, and thus these breeds have an increased sensitivity to acepromazine.

Chill Protocol Treatment at a Glance :

- Gabapentin (20-25 mg/kg PO) should be administered the evening before the scheduled appointment.
- A combination of gabapentin (20-25 mg/kg PO) and melatonin (small dogs, 0.5-1 mg PO; medium dogs, 1-3 mg PO; large dogs, 5 mg PO) should be administered at least 1 to 2 hours before the scheduled appointment.
- Acepromazine (0.025-0.05 mg/kg OTM) should be administered 30 minutes before the scheduled appointment.

Take home Messages:

- The Chill Protocol aids in reducing aggression to facilitate less stressful handling during physical examinations, blood draws, and non-invasive diagnostic procedures like radiography.
- **It is important that medications take effect prior to the stimulation (caused by the trip to the hospital), so the timing of the chill protocol is most essential.**
- The duration of action is usually 4 to 6 hours, but can last up to 24 hours.
- Additional drugs (opioids, α_2 agonists etc) may be required to provide adequate analgesia and sedation for more invasive procedures.

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CPT-OP-01

STUDY ON SEDATIVE EFFECTS OF DEXMEDETOMIDINE IN CAMELS (*CAMELUS DROMEDARIUS*)

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In present study, the sedative effect of dexmedetomidine alone in groups Dex1 (2.5 µgm kg^{-1}) and Dex2 (4 µgm kg^{-1}) were evaluated. The experimental trials were conducted in group of 6 camels in a randomized crossover design with a wash out period of 14 days. The onsets of sedation recorded as 6.10?0.44 min in Dex2 group was non-significantly lower than 6.85? 0.45 min in Dex1 group. The duration of sedation and recovery time respectively 40.05 ? 1.47 and 64.32± 1.72 min recorded in Dex2 group was significantly higher ($P<0.01$) than the 25.85 ?0.97 and 43.81 ±1.19 min. in Dex1 group. Significantly higher ($P<0.01$) and dose dependent sedative response score and degree of analgesia was observed in Dex2 group compared to Dex1 group. The rectal temperature, respiration rate, heart rate and Pulse rate showed decreased values at different time intervals whereas, systolic and diastolic blood pressure showed increased values at different time intervals in group Dex1and Dex2. However, heart rate and Pulse rate decreased significantly ($P<0.05$) in Dex2 group. The haemato- biochemical parameters showed non-significant variations during the period of study within the group and between two groups at different time intervals. However, the values remained within the normal clinical range in both the studied groups *viz* Dex1, Dex2. In conclusion, Dexmedetomidine is a clinically useful and safe to be employed as sedative drug in camels.

CPT-OP-02

CLINICAL EFFICACY OF NEBULIZED MARBOFLOXACIN IN CAPRINE

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Clinical efficiency of nebulized and intramuscular marbofloxacin (MBX) were compared in goats naturally suffering from pneumonia of bacterial origin. The study was undertaken for period of six months on goats presented at Department of Medicine, Veterinary clinical complex, College of Veterinary Science and Animal Husbandry, KU, Gujrat, Teaching Veterinary Clinical Complex (TVCC, Deesa) and those been survey at nearby Dantiwada village. The overall incidence of pneumonia in studied goats was recorded as 42.85% (90/ 210). Amongst 90, a total of 20 goats confirmed to be suffering from bacterial pneumonia were randomly grouped into two different treatment groups. Prominent physical examination findings recorded in bacterial pneumonia in goats in the present study are dyspnoea followed by tachypnea, tachycardia and moist rales (crackles) at cranioventral lung on auscultation. MBX was administered through an ultrasonic nebulizer (@ 2 mg/kg b.wt. with dilution ratio of 1:3 in normal saline for 3 days, n = 10) and by intramuscular route/injection (@ 2mg/ kg. b.wt., IM. for 3 days, n = 10) in the affected goats. Supportive therapy provided was common for both the treatment groups. Criteria for evaluating the clinical efficacy of the therapy provided was improvement

in clinical signs evidenced through changes in cumulative clinical scoring system (CSS) and improvement in haemato-biochemical parameters at '0' and '5' days post treatment in comparison with the apparently healthy group. Marbofloxacin @ 2 mg/kg b.wt × 3 days via nebulization found superior to intramuscular treatment group in the management of pneumonia caused by bacteria in goats. Noticed improvement in cumulative clinical score on day '2' of treatment for nebulized marbofloxacin and normalization of altered haemato-biochemical parameters formed the basis of this postulated conclusion.

CPT-OP-03

EVALUATION OF *IN VITRO* ANTIBACTERIAL ACTIVITY OF THREE DESERT PLANT AGAINST *STAPHYLOCOCCUS AUREUS* ISOLATED FROM SKIN LESIONS OF AFFECTED HORSES

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Present study is conducted to isolate and identify *Staphylococcus aureus* from skin lesions of horses and to evaluated *in-vitro* antibacterial activity of aqueous, methanolic, ethanolic, chloroform and petroleum ether extract of leaves *Capparis decidua*, *Leptadenia pyrotechnica* and *Eucalyptus camladulensis*. Agar well difusion and broth dilution methods were used to determine the antibacterial activity of seven locally available plants against *S.aureus*. The bunches of grapes like cocci in stained smears prepared from culture and results of various biochemical test and result of Polymerase chain reaction confirm the presence of *S. aureus*. Antibacterial screening revealed that all the extract of *E. camaldulensis* used in this study showed highest antibacterial activity against *S. aureus* with zone of inhibition in range of 15 mm to 21 mm and MIC in range of 1.562 to 3.125 mg/ml. While, none of the extract of *C. decidua* and *L. pyrotechnica* showed antibacterial activity against this bacterium. The results of this study support that *E. camaldulensis* have antibacterial activity against skin pathogen so can be used/ added in topical antibacterial preparations to fight the problem of drug resistance.

CPT-OP-04

EFFICACY OF 0.5% POVIDONE IODINE SOLUTION AS AN ORAL ANTISEPTIC IN DOGS WITH PERIODONTAL DISEASES

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The study was carried out in 14 dogs showing periodontal disease. Clinical findings were halitosis, gingivitis, dental calculus, excessive salivation, gingival bleeding and receding of gums also. Dental scaling was performed in these cases. These 14 dogs divided in two groups and each group had 7 animals. In Group-I, after dental scaling (supra and subgingival), post-operatively, the oral cavity of the dogs was cleaned on a regular basis with 0.5 per cent povidone iodine and the teeth were brushed with a fine bristle toothbrush. Broad spectrum

antibiotics and analgesics (NSAIDs) were also given for 5 to 7 days. Within 20 days, halitosis was disappeared in these cases. Gingivitis also effectively reduced and the colour of the gingival mucous membrane became pale roseate after 7 days of treatment. There was no recurrence of calculus or periodontal disease up to 3 months follow-up. In Group II animals after dental scaling, post-operatively, the oral cavity was cleaned on a regular basis with normal saline and the teeth were brushed with a fine bristle toothbrush. Broad spectrum antibiotics and analgesics (NSAIDs) were also given for 5 to 7 days. Within 20 days, halitosis was disappeared in 4 cases. Gingivitis also effectively reduced and the colour of the gingival mucous membrane became pale roseate after 7 days of treatment. There was recurrence of calculus or periodontal disease in 3 cases again within 3 months follow-up. In conclusion, povidone iodine is potentially beneficial in the management of periodontal diseases and it dominantly prevents reoccurrence of periodontal disease.

CPT-OP-05

AMELIORATIVE EFFECT OF ATROPINE AGAINST CHOLINESTERASE INHIBITORS TOXICITY IN GOAT

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The present study was conducted to evaluate ameliorative effect of atropine in case of cholinesterase (ChE) inhibitors toxicity in goats. Atropine used as an antidote for the treatment of cholinesterase (ChE) inhibitors toxicity such as organophosphate in animals by blocking the muscarinic receptors. In present study 6 goats were brought to VCC, CVAS, Navania, Udaipur with the complaint of licking of insecticide (Chlorpyrifos) from other animal's hair coat after topical application of the insecticide by the owner. Clinical signs observed were profuse salivation, congested mucous membrane, dyspnoea, protrusion of tongue, bradycardia, anorexia, miosis, bloat, muscle fasciculation, ataxia and lateral recumbency. Goats of 3 year age were divided into two groups of 6 animals in each. Total 6 goats which were affected with toxicity kept in one group (group I). Another group of 6 goats of similar age group were taken as a group II (control). In control group, All physical & clinical parameters along with cholinesterase (ChE) activity in blood/plasma were estimated which were in normal range. In group I affected with toxicity, haemato-biochemical examination showed reduction of cholinesterase (ChE) activity in plasma/blood & other physical and clinical parameter were also altered. In group I inj. Atropine sulphate @.5mg/kg b.wt. (1/3rd IV & 2/3rd SC) was administered, along with liquid activated charcoal (orally) supportive, symptomatic and fluid therapy. Liquid Bloatosil was also given intra ruminally. There was a significant improvement in clinical condition. After one hour of treatment with atropine, the animals were able to sit, and started drinking water, there was cessation of profuse salivation. Heart rate, respiration rate & temperature became normal. In group I after treatment cholinesterase activity (ChE) in blood/plasma significantly increased to normal range. After 4 days of successive therapy,the animals were having their normal diet.The study suggested that exposure of insecticide in goats caused cholinergic overstimulation resulting in muscarinic & nicotinic response which can be reversed the use of atropine sulphate.

CPT-OP-06

DIAGNOSIS AND THERAPEUTIC MANAGEMENT OF HYPOTHYROIDISM IN DOG

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Hypothyroidism is one of the most common endocrine diseases encountered in dogs. This indicated that hypothyroidism could be underlying problem in certain obesity, cardiac problem, otitis, pododermatitis and rat tail appearance. In the present study cases presented to VCC, CVAS, Bikaner with the history of dullness, lethargy, increased body weight, skin lesion and exercise intolerance in past six months were taken. A total of 20 cases were presented showing clinical symptoms of alopecia, rat tail appearance and pyoderma, hypothermia, bradycardia. The dogs were diagnosed as hypothyroidism on the basis of history, clinical examination, and blood T_3, T_4 and TSH, values. T_3 levels varied between 0.36 and 0.5 ng/dl compared to the normal range of 0.5 to 2.0 ng/dl, whereas T_4 values varied between 16.58 and 6.68 pmol/l compared to normal values of 16 to 30 pmol/l. Age wise occurrence showed 15 (75%) of cases were between the age of 3-7 years. Skin lesions that were the initial signs of a widespread dermatological condition were observed in 13 (65%) of these 20 cases. The principal involvement in the remaining 35% instances was not a broad dermatological condition, but rather, obesity (100%), heart problems (15%), otitis (10%), pododermatitis (5%) and rat tail appearance (5%). This suggested that certain heart issues, otitis, pododermatitis, and rat tail appearance may all be caused by hypothyroidism. all the dogs were treated with levothyroxine sodium @ 0.1 mg /lb (0.022mg/kg) and continued for approximately 6 month. After continuous treatment dogs showed marked improvement in terms of healing. All the dogs recovered clinically after 2 months of treatment.

CPT-OP-07

INTRATHECAL ANAESTHESIA COMPARISON OF 2% LIGNOCAINE HCL ALONE AND IN COMBINATION WITH BUTORPHANOL TARTRATE IN OPEN METHOD CASTRATION IN BUCKS

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Intrathecal anaesthetic comparison in open method castration surgery in bucks was made between two groups of animals, having 06 animals in each group (group-L and group-LB). In group-L, 2% Lignocaine HCl (4 mg/kg b.wt.) and in group-LB, 2% Lignocaine HCl (4 mg/kg b.wt.) along with Butorphanol (0.04 mg/kg b.wt.) was administered as intrathecal anaesthesia. Observation of physiological parameters and anaesthetic indices were taken before anaesthetic administration and at regular subsequent intervals up to 120 minutes. Haemato-biochemical estimation was done before anaesthetic administration (T_0), at T_{30} and T_{60} minutes. Values of all physiological and haemato-biochemical parameters except rectal temperature, total erythrocyte count, blood glucose and serum cortisol did not vary significantly in post-anaesthetic period, both within and between the groups. Onset of complete analgesia at surgical site (inguinal region) was around at 2 minutes and within 5

minutes at most other hind body regions in both the groups. Motor incoordination with severe ataxia of hindlimbs during anaesthetic induction occurred at around 2 minutes in both the groups and the animals remain recumbent till the first limb movement for around 100 minutes in both groups without any significant difference between them. Time to standing was longer in group-LB (169.1±17.9), as compared to group-L (125.5±13.2) but the difference was non-significant. No sedative effect and any untoward reaction were observed in both the anaesthetic treatment groups.

CPT-OP-08

THERAPEUTIC EFFICACY OF *CORIANDRUM SATIVUM* AND *MURRAYA KOENIGII* BI-HERBAL EXTRACTS ON CHRONIC KIDNEY DISEASE RATS

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The present study was planned to evaluate the therapeutic efficacy of *Coriandrum sativum* (CS) and *Murraya koenigii* (MK) on adenine-induced chronic kidney disease in rats. The experiment was conducted on 36 male Sprague-Dawley rats. In order to assess the therapeutic efficacy of bi-herbal aqueous and alcoholic extracts CS and MK, were mixed in a 1:1:5 ratio after determined by *in-vitro* nucleation assay. The rats were randomly divided into six different groups, each group contains six rats. Chronic kidney disease (CKD) was induced in the group II, III, IV, V and VI by adenine @ 200 mg/kg daily once through the intragastric route for 28 days. Group I served as control and was given standard pelleted diet. Group II served as adenine control and was given adenine (200 mg/kg, orally) for 28 days. Groups III, IV, V and VI were therapeutic groups, received adenine @ 200 mg/kg orally once daily for 28 days to induce CKD, after that rats were given bi-herbal aqueous and alcoholic extracts of CS and MK leaves orally for another 42 days. In groups III and IV, received bi-herbal aqueous extract @ 250 and 500 mg/kg, respectively. In groups V and VI, received bi-herbal alcoholic extracts of CS and MK given @ 250 and 500mg/kg, respectively. Blood samples were collected twice during the experiment on the day 28th (CKD induction) and 70th. Haematology, serum biochemistry, urine analysis and renal ultrasonography were done on the 28th day to confirm chronic kidney disease. On day 28th after inducing CKD in rats and on day 70th after given treatment of bi-herbal extracts urine samples were collected by using metabolic cages and analyzed for different qualitative and biochemical parameters. The experimental rats were studied for ultrasonographic, gross and histopathological changes in kidneys of different groups. Result showed that the bi-herbal aqueous and alcoholic extracts treated rats (groups III, IV, V and VI) produced significant improvement in mean body weight and feed consumption as compared to adenine control rats (group-II). The administration of aqueous and alcoholic bi-herbal extracts of CS and MK leaves, along with adenine in therapeutic groups revealed significant improvement on haemato-biochemical and urine parameters. Results of ultrasonographic and histopathological examination of kidney tissues in therapeutic groups was well supported and prevent alterations in kidney associated changes in adenine-induced CKD in rats. Result of the present study showed that the bi-herbal aqueous extracts of CS and MK leaves at dosage of 250 mg/kg, while bi-herbal alcoholic extracts at dosage of 500 mg/kg showed greater efficacy among all therapeutic study groups. Results of the present study showed that aqueous as well as alcoholic bi-herbal extracts of *Coriandrum sativum* and *Murraya koenigii* leaves revealed therapeutic efficacy against adenine induced CKD in rats.

CPT-PP-01

PROPHYLACTIC EFFECT OF *GLYCYRRHIZA GLABRA* AND *CURCUMA LONGA* BI-HERBAL EXTRACTS ON CHRONIC KIDNEY DISEASE IN RATS

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The present study was carried out to evaluate the prophylactic effects of *Glycyrrhiza glabra* (GG) and *Curcuma longa* (CL) on adenine induced chronic kidney disease (CKD) in rats. The experiment was conducted on 60 male Sprague-Dawley rats with age range from 8-10 weeks. The rats were randomly divided into 10 different groups, each group contains 6 rats. Group I served as control and was given standard pelleted diet. CKD was induced in the group II, III, IV, V and VI by adenine at dose rate of 200 mg/kg body weight daily through the intragastric route for 28 days. Group II served as adenine control and was given adenine (200 mg/kg body weight) for 28 days. In group III and IV, bi-herbal aqueous extract of GG and CL was given at the dose rate of 250 and 500 mg/kg body weight, respectively for 28 days. Group V and VI received bi-herbal alcoholic extract at dose rate of 250 and 500 mg/kg body weight for 28 days, respectively. Various parameters were studied like feed consumption, body weight, haemato-biochemical estimation, urine assessment, ultrasonographic examination and histopathological changes in kidney of different groups at 28 day in rats. Result showed that the administration of aqueous and alcoholic bi-herbal extracts of GG and CL, along with adenine, showed significantly less body weight loss and restored feed consumption compared to adenine control rats. The administration of aqueous and alcoholic bi-herbal extracts of GG and CL, along with adenine, significantly increased haemoglobin, total erythrocyte count, and lymphocyte, while significantly decreased total leukocyte count and granulocyte as compared to adenine control group. Among the prophylactic groups, the bi-herbal alcoholic extract at a dosage of 500 mg/kg body weight exhibited the highest efficacy in preventing haematological changes associated with adenine-induced chronic kidney disease. The marked rise in serum creatinine, uric acid, BUN, ALT, and phosphorus, as well as significant reduction in serum uromodulin and calcium of adenine control rats were significantly protected by co-treatment with aqueous and alcoholic bi-herbal extracts (250 and 500 mg/kg). Additionally, the results indicated that the alcoholic bi-herbal extracts had greater efficacy in preventing serum biochemical changes as compared to the aqueous extract. In addition, aqueous and alcoholic bi-herbal extracts significantly improved elevated level of urine total protein and lower level of urine creatinine as compared to adenine control rats. The administration of aqueous and alcoholic bi-herbal extracts, along with adenine, also prevented ultrasonographic and histopathological alteration in kidney as compared to adenine control rats. Among all prophylactic study groups, aqueous and alcoholic bi-herbal extracts of *Glycyrrhiza glabra* and *Curcuma longa* at the dose rate of 500 mg/kg body weight showed greater efficacy than 250 mg/kg body weight dose. The alcoholic bi-herbal extracts exhibited greater effectiveness in comparison to the aqueous extracts.

CPT-PP-02

A CLINICO-PATHOLOGICAL STUDY OF VINCRISTINE SULPHATE ON TRANSMISSIBLE VENEREAL TUMOR AFFECTED NON-DESCRIPT BITCHES

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Canine transmissible venereal tumor (CTVT) is an important contagious neoplasm that commonly occurs in the genital tract in dogs which is normally transmitted during coitus by viable tumor cells through injured mucosa. CTVT is usually transmitted by coitus and results in the appearance of neoplasms most often in the external genitalia of male and female dogs or by social behaviour (sniffing and licking). Five cases of Non-descript female dogs having clinical signs like anorexia, severe fresh vaginal bleeding and protrusion of tumorous growth (sized around 6cm) at dorsal wall of vagina were presented at Gynaecology section of Veterinary Clinical Complex, CVAS, Bikaner. All the cases were diagnosed as TVT on the basis of history, clinical signs, per-vaginal examination and vaginal cytology. Intravenous administration of Vincristine Sulphate (@0.025mg/kg b.wt) in normal saline was done by repetition of four doses at weekly interval as chemotherapeutic agent. Parenteral administration of fluid therapy, non-steroidal anti-inflammatory and hemostatic drugs were given as a supportive therapy. Oral administrations of multivitamins and hematinic preparations were also suggested for better response and recovery of bitches. A complete disappearance of tumor was observed responsive to Vincristine after four weeks of treatment in four bitches while one was referred for the surgical ablation of the tumor. Few side effects like vomiting, mild depression, anorexia were observed due to Vincristine administrations which were disappeared after complete regression of tumor.

CPT-PP-03

PREDICTION OF PEPTIDE-BASED PROPHYLACTIC DRUG FOR TREATMENT OF CANINE PARVOVIRUS-2 BY IMMUNOINFORMATIC APPROACH

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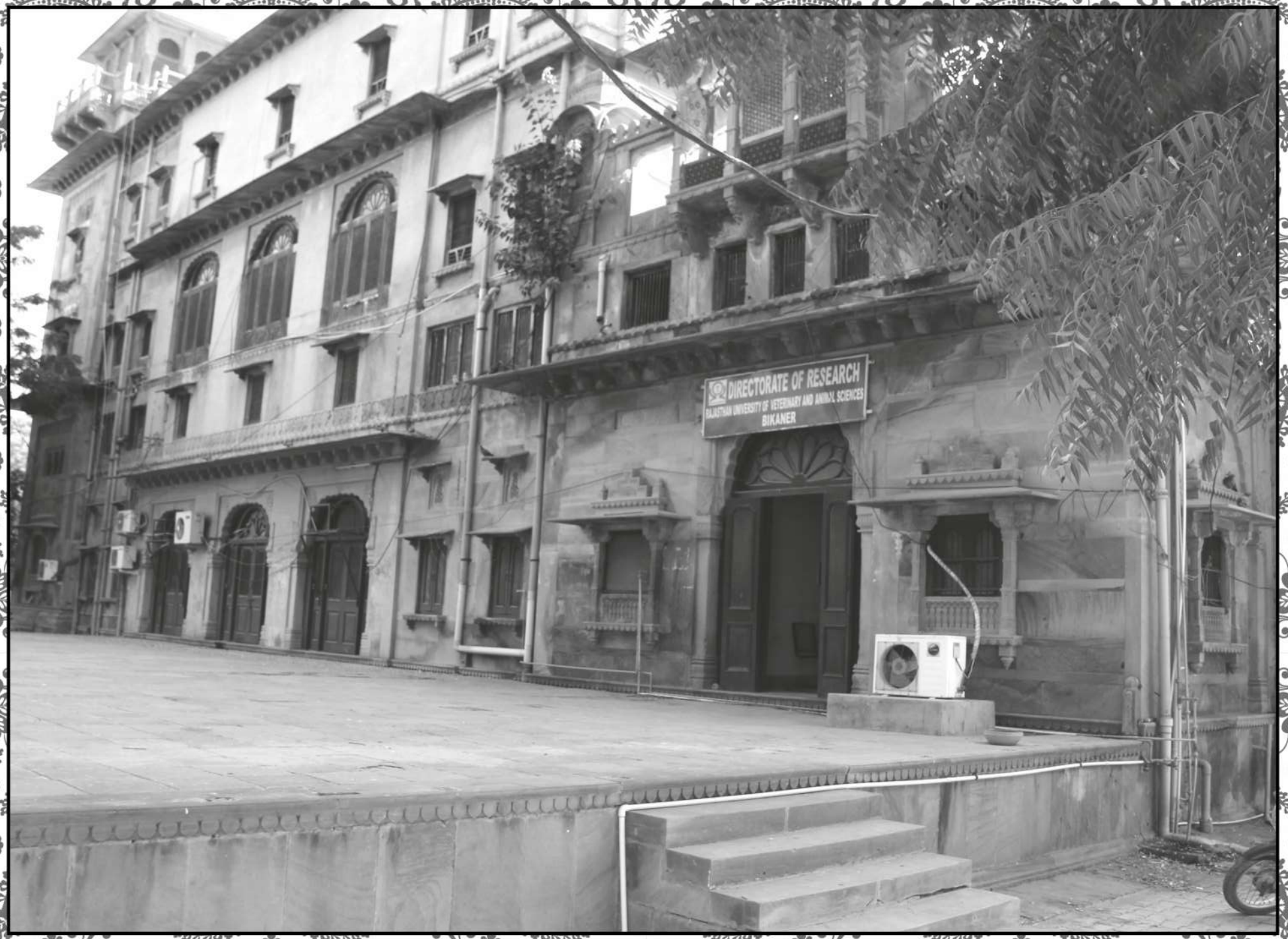
Canine parvovirus (CPV-2) is lethal & hemorrhagic enteritis with high morbidity of 100 % & mortality rate of 10 %. The virus has two open reading frames (ORFs) in the genome. ORF-1 encodes NS1 and NS2, whereas, ORF-2 encodes for VP1 and VP2. Among these VP2 being primary component of viral envelope. In order to predict the prophylactic drugs for CPV-2, protein sequences were retrieved from the NCBI and screened for epitopes binding to B-cell and T-cell (MHC-I and MHC-II) using IEDB server. VaxiJen v.2.0 was used to find potent antigenic epitopes. Allergenicity of the epitopes were assessed by using AllergenFP v.1.0 tool. It was found that nine B-cell epitopes and sixty-nine T-cell epitopes were antigenic and non-allergen. Toxicity analysis was done using ToxinPred tool. Water solubility was determined using peptide property calculator PepCalc.com. Four B-cell epitopes and thirty T-cell epitopes were non-toxic and were speculated to have good water solubility. MHC-I and II immunogenicity was determined using IEDB. Six T-cell epitopes were found to be immunogenic. Prediction of IFN-γ cytokine secretion by immunogenic epitope was done using IFNepitope webserver to identify *IFN*-γ inducing MHC-II binding peptides. Eventually, the 4 T-cell epitopes were selected. All the predicted epitopes were clustered using IEDB tool.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ISVPT-2023

TECHNICAL SESSION-IX

Antimicrobials and Antimicrobial Resistance

Chairperson : **Prof. S. P. S. Saini**

Co-Chairperson : **Dr. R. Aruna Devi**

Rapporteur : **Dr. B. Anilkumar**


राजस्थान पशु चिकित्सा और पशु विज्ञान विश्वविद्यालय (राजुवास)
RAJASTHAN UNIVERSITY OF VETERNARY & ANIMAL SCIENCES (RAJUVAS)

AMR-LP-01

STATUS OF ACARICIDE RESISTANCE IN TICKS WITH SPECIAL REFERENCE TO JAMMU AND KASHMIR

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Introduction

Ticks and tick-borne diseases (TTBDs) cause huge economic losses to livestock industry. The severity of TTBDs depends upon region, species involved, agents, host population, socioeconomic and technological advances in control measures. Ticks rank first as arthropod vectors of protozoa, rickettsiae, bacteria and viruses, causing diseases in nonhuman vertebrates. In an agricultural country like India, majority of livestock holders are poor and marginal farmers and loss of 14% of the lactation would pose a serious threat to sustainable livestock dependent system. The cost of management of TTBDs in livestock of India is as high as US$ 498.7 million per annum (Minjauw and McLeod, 2003). Tick worry is therefore considered as a major constraint by farmers which is addressed by hand removal of ticks or repeated application of acaricides every 21–30 days (Ghosh *et al.*, 2006).

Currently employed strategies for tick control in Indian markets consist of chemical acaricides such as synthetic pyrethroids (SPs), organophosphates (OPs), formamidine (Am) and macrocyclic lactones (MLs) with different application methods and various formulations, tick-resistant animals, and rotations between livestock and crops. Among these, the chemical acaricides form the center of control and eradication efforts because they offer relatively quick and cost-effective suppression of tick populations. However, long-term use of these chemical acaricides is often accompanied by serious drawbacks, including the development of acaricide resistance, environmental contamination, and contamination of milk and meat products (Godara *et al.*, 2019).

Development of resistance

Resistance is defined as the capacity acquired by individuals of a parasite population that allows them to survive doses of chemicals which are generally lethal to a normal population. There is an exponential growth pattern between the discovery of new insecticides and the development of strains resistant to these new products, for DDT resistance appeared 6.3 years after entering the market, for lindane after 5 years, for OPs after 4 years, for carbamates after 2.5 years and for SPs resistance appeared after only 2 years. Resistance is not universal, and is most widespread and diverse in the one-host cattle tick, *R.* (*B.*) *microplus*. It has developed much slowly in the two- and three-host ticks (e.g. *Hyalomma* and *Ixodes*), where longer generation times, less acaricidal exposure of the immature tick stages and the presence of alternative hosts might have helped to reduce selection pressure. The resistance of ticks to acaricides is an inherited phenomenon and occurs due to continuous selection pressure. It results from the exposure of populations of ticks to chemical acaricides and subsequent survival and further propagation of ticks that are less affected by the acaricide. The speed with which resistance develops in a population depends mainly on the initial frequency of resistance genes, selection intensity, the degree of dominance of the gene and the relative ability of the genotype. In general, the frequency of resistance genes is very low in populations that have been under selection pressure. The rate of natural or spontaneous mutation to other genes is low (1/100,000 to 1/1,000,000).

Diagnosis of acaricide resistance

Resistance is usually first recognized as a failure of treatment to eliminate tick burdens from cattle. The tests for the diagnosis of acaricide resistance include-

Larval Packet Test (LPT): This test is adopted by the FAO as the main diagnostic test for resistance in ticks.

Larval Immersion Test (LIT): This test is applied to larval ticks.

Adult Immersion Test (AIT): This test is applied to engorged, female ticks.

Biochemical testing: The correct use of biochemical methods for resistance detection at a mechanistic level can provide a powerful tool for analyzing field and laboratory populations with the aim of improving resistance detection and management.

Molecular tests: PCR assay and PCR- RFLP are used to determine resistance by detecting alteration in sequence of genes encoding the site of action of acaricides in ticks.

Scenario in Jammu and Kashmir

Prevalence of ticks in Jammu and Kashmir

Tick infestation is common in summer and autumn in plain and low altitude areas (May to October), and in autumn and early winter in higher altitudes (October to December). The high-altitude areas have a short active tick season, as environmental conditions of the area are unfavorable for propagation and development of pre-parasitic free-living stages of ticks due to extremely cold weather. The severity of tick infestation is comparatively more in cross-bred animals in comparison to indigenous breed of animals which are mainly maintained for draft purposes. A study showed 40.18% prevalence of *R.* (*B.*) *microplus* in dairy cattle in Jammu region (Godara *et al.*, 2018b), with higher prevalence rate in plain and low altitude areas as compared to high altitudes. Another study reported 42.18% prevalence of *R.* (*B.*) *microplus* in bovines (Khajuria *et al.*, 2015). The *Hyalomma anatolicum* has also been observed from low-lying areas of Kandi belt, Jammu (Godara *et al.*, 2015).

Animal husbandry practices and control of ticks

Mainly unorganised dairy farming is in practice throughout the region having small number of dairy animals (10-20) in plain and low altitude areas while the farmers of high-altitude areas rear only 2 to 3 animals. Among various tick control practices, hand picking is reported as one of the most commonly used methods, particularly at higher altitudes where farmers rear only two to three animals. However, natural control by birds and crows is also seen at higher altitudes where animals are let loose for grazing in the open fields (Ahanger *et al.*, 2015). In the region, synthetic pyrethroids (SPs) (deltamethrin @ 25 ppm and cypermethrin @ 200 ppm), formamidines (Am) (amitraz @ 250 ppm) and macrocyclic lactones (MLs) (ivermectin @ 0.2 mg) are commonly used for tick control (Godara *et al.*, 2019; Nazim *et al.*, 2022). The frequency of acaricide application is comparatively less in areas belonging to higher altitudes as compared to semi-hills or plain areas. The farmers belonging to higher altitude areas are reported to have less access to chemical acaricides and mostly using old-age practices such as grooming, use of natural products like tobacco, turmeric or rubbing of locally available medicinal plants on the body of animals for tick control (Nazim *et al.*, 2022). There is no strategic treatment policy and the farmers are using acaricides only when they see ticks on their animals. In plain and low altitude areas, 10-20 applications of acaricides are being used during active tick season as it offers relatively quick and cost-effective suppression of tick populations.

Resistance status in Jammu and Kashmir

Ticks were collected from cattle sheds of 10 districts (Jammu, Samba, Rajouri, Poonch, Kathua, Udhampur, Doda, Kishtwar, Kulgam and Anantnag) of UT of Jammu and Kashmir and subjected to different tests (AIT,

LPT, LIT) for detection of acaricide resistance. The presence of widespread resistance (mild to severe) has been detected in *R.* (*B.*) *microplus* field populations against SPs (Table 1). Recently, a study conducted to know the status of SPs against *R.* (*B.*) *microplus* collected from eight districts of Jammu region (Godara *et al.*, 2019) revealed moderate to severe resistance against deltamethrin (RFs = 0.94-50.71) and mild to moderate resistance against cypermethrin (RFs = 0.32-13.8). Quantitative analysis of general esterase activity (measured by production of metabolite naphthol) revealed a range of 2.466±0.29 and 8.908±1.68 µmol/min/mg protein for á and â-esterase activity, respectively in field isolates (Godara *et al.*, 2022). Molecular analysis of partial carboxyl esterase gene revealed absence of point mutations in the field isolates of *R. (B.) microplus* (Godara, 2019). The problem is more severe in plain to lower hilly areas (Jammu, Samba, Kathua and Anantnag) of the UT where intensive agricultural and animal husbandry activities, including regular application of acaricides are practiced and pyrethroid compounds are being supplied by the government to local veterinary hospitals. After introduction of SPs in the market, the farmers got attracted towards these products due to their immediate results and pleasant odour which resulted in to indiscriminate and extended use of these insecticides.

Table 1. Status of acaricide resistance in *R.* (*B.*) *microplus* of Jammu and Kashmir

District	Acaricide						
	Deltamethrin	Cypermethrin	Fenvalerate	Malathion	Diazinon	Amitraz	Ivermectin
Jammu	Level IV	Level II	Level I	Level I	Level II	Level I	Level II
Samba	Level IV	Level II	Level I	Susceptible	Level II	Level I	Level I
Rajouri	Level II	Level I	-	Susceptible	-	Susceptible	Level II
Poonch	Level II	Level II	Level I	-	Level II	-	-
Kathua	Level II	Level I	Level I	-	Level II	-	Level II
Udhampur	Level II	Level I	-	Level I	-	Level I	Level II
Doda	Susceptible	Susceptible	Susceptible	-	Susceptible	-	Level I
Kishtwar	Level I	Susceptible	-	-	-	-	Level I
Kulgam	Level I	Susceptible	-	-	-	-	Susceptible
Anantnag	Level IV	-	-	-	-	-	-

In these areas, pyrethroids are the most commonly available drugs since last 12 to 15 years and 10 to 20 applications are been applied per active tick season (as reported by farmers in questionnaire) which could be responsible for development of resistance (Khajuria *et al.,* 2014; Ahanger *et al.,* 2015; Godara *et al.,* 2019, 2022; Nisa *et al.*, 2021). The resistance levels to pyrethroids from high altitude areas (Doda and Kishtwar) are not alarming. The less availability of drugs in the high-altitude areas together with use of age-old practices of hand-picking ticks from tick infested animals (only 2-3 animals reared per family), pasture burning and using locally available herbal preparations with minimum use of chemical acaricides are responsible for low level of resistance. Simultaneously, in these areas susceptible tick populations are conserved because of low selection pressure due to lesser and non-uniform usage of pyrethroids, leading to existence of refugia population. Due to failure of SPs, OPs and Am compounds, dairy farmers attracted towards MLs compounds and their use has increased many folds which resulted into the development of resistant against ivermectin in *R.* (*B.*) *microplus* ticks (Nazim *et al.*, 2022).

Alternative control strategies

In our laboratory, the extracts of some locally available medicinal plants have been prepared and trials were conducted against adults and larvae of economically important tick species with promising results.

Table 2. Mortality and LC_{50} values of different plant extracts against ixodid ticks

Plant	Type of extract (% concentration)	Tick species	Mortality (%)	LC_{50} (%)
Artemisia absinthium	Ethanolic (20%) Ethanolic (20%) Chloroform (20%)	*R. (B.) microplus* *H. anatolicum* *R. sanguineus*	66.7 86.7 93.3	11.22 6.51 8.79
Ageratum conyzoides	Ethanolic (20%)	*R. (B.) microplus*	40.0	34.36
Calendula officinalis	Aqueous (10%) Ethanolic (10%)	*R. (B.) microplus*	20.0 60.0	12.87 9.85
Alstonia scholaris	Aqueous (10%) Ethanolic (10%)	*R. (B.) microplus*	8.3 12.3	173.2 417.2
Glycyrrhiza glabra	Aqueous (10%)	*R. (B.) microplus*	54.2	11.64
Terminalia chebula	Methanolic (10%)	*R. (B.) microplus*	45.8	23.96
Atropa belladonna	Methanolic (20%)	*R. (B.) microplus*	100	6.88
Piper longum	Methanolic (5%)	*R. (B.) microplus*	87.5	2.13
Piper nigrum	Methanolic (1.1%)	*R. (B.) microplus*	95.8	0.48
Sida cordifolia	Methanolic (2%)	*R. (B.) microplus*	100	0.42
Juglans regia	Ethanolic (7.5%)	*R. (B.) microplus*	100	1.43

The ethanolic and methanolic extracts of *Artemisia absinthium, Ageratum conyzoides, Calendula officinalis, Atropa belladonna, Alstonia scholaris, Glycyrrhiza glabra, Terminalia chebula, Sida cordifolia, Juglans regia, Piper nigrum and P. longum* have shown promising efficacy against *R. (B.) microplus* (Godara *et al.*, 2014b, 2015a, 2018a, 2020; Praveen *et al.*, 2014; Bhutyal, 2015; Nazim *et al.*, 2021a, b), *Hyalomma anatolicum* (Godara *et al.*, 2015b) and *Rhipicephalus sanguineus* (Godara *et al.*, 2014a) ticks (Table 2). However, *in vivo* applications are required to determine the true potential of these phytoacaricides as an effective herbal formulation for the control of tick infestation on animals.

Resistance management

Acaricide resistance has usually been managed after emergence, by the use of new products. At present, very effective and long-acting acaricides are available, besides new labour-saving techniques for acaricide application (pour-on, injection, boluses and tags) are also available. However, the main objective of resistance management lies in trying to reduce the number of applications throughout the year by using resistant zebu breeds or 'indigenous' cattle. Where acaricides are required (in cross breeds or 'improved' cattle), careful (i.e. strategic) timing of treatments can reduce the number of treatments. Treatments should be continued and should end only when tick numbers decline to low levels, to prevent large numbers of ticks being exposed to sub-optimal acaricide concentrations. Some basic management and biosecurity principles can be used to reduce the chances of development of acaricide resistance such as:

- ❖ Always use the recommended strength in dips as printed on the chemical label by the manufacturer.
- ❖ If using a plunge dip, always re-dip your stirrer cattle.

- ❖ Never under-dose animals during treatment with pour-on or injectable applications. Treat the mob at the rate of the heaviest animal, reducing the chance of under-dosing.
- ❖ Import only tick-free livestock on to your farm. If this is unavoidable, treat livestock on arrival and only turn out tick-free cattle on to the paddock.
- ❖ If you suspect poor tick kill, notify your nearest concerned authority for investigation and testing.

Conclusion

Alarming acaricidal resistance reveals indiscriminate use of acaricides will soon render us short of acaricides. To overcome problem of acaricide resistance, over reliance and multiple applications of acaricides should be replaced with biological tick predators (rearing of backyard poultry), burning of semi-Pakka floor of animal sheds including manger (burn dry grass), filling of cracks and crevices in animal shed, exploring natural resistance of indigenous cattle and the use of herbal acaricides. Besides, awareness about breeding places should be given to farmers, so that the life cycle of ticks can be broken. It will provide a long-term relief from tick infestation besides minimum use of the acaricides which prolongs the life span of drugs.

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AMR-LP-02

ANTI-MICROBIAL USAGE AND ITS RELEVANCE TO INDIA- THE ANIMAL HEALTHCARE PERSPECTIVE

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As per FAO estimates, the global human population is expected to reach 9.7 billion by 2050 and to suffice the consumption requirements, the world food production has to double in the next 40 years and 70% of the food must come from efficiency improving technologies. It is also postulated that the growing urban population (70% in cities) with increasing income (2.8 times the current income) will focus on higher protein sources and consumption is likely to double. The livestock sector currently contributes 40% of the global value of agricultural output and supports the livelihood and food security for the growing population. Animal source foods would be a major growth drivers for increased consumption of growing population and emerging middle class globally and *esp* in India where both the population and middle class is expanding.

On a worldwide basis, cereals supply more than 50% of human requirements for energy and nearly 50% of the protein. Animal products *viz* meat, milk, eggs and animal fat supply 17% of the energy and 32% of the protein. As per estimates, livestock and its products are estimated to make up over half of the total value of agricultural gross output in the industrialized countries and about a third of the total in developing countries. India's livestock sector is one of the largest in the world with a holding of 11.6% of world livestock population. India is home to 56.7 percent of the world's buffaloes, 12.5 percent of the world's cattle, 20.4 percent of world's small ruminant population, 1.5 percent of pigs and 3.1 percent of poultry. Animal husbandry is an integral component of Indian agriculture supporting livelihoods' for more than two-third of the rural population. The animal husbandry sector in India provides employment to about 8.8% of Indian population. Economically, livestock alone contributes 25.6 percent of the agricultural output of India, contributes 11.87% to the farming household income and 4.11% of total GDP. Animal source foods are best sources of Vitamin A, Vitamin B_{12}, Riboflavin, Calcium, Iron, Zinc and proteins.

Bacterial infections make up a significant proportion of animal illnesses. To mitigate farmer's losses resulting from diseases outbreaks, the Veterinarians take all possible steps to treat the infections and ensure effective treatment and prevention of these infections. Antibiotics are in use in farm animals for decades for the same reason they are used in people to treat or prevent diseases that cause inflammation and suffering. Antibiotics are often the best choice to treat sick animals or prevent animals from getting sick. The scientific deliberations highlighted that antibiotics are an essential part of therapeutic management of infectious diseases in both farm and companion animals, ensuring better animal health and life. In fact, antimicrobials used in the management of bacterial infections assure healthy food from the animal sources.

The '**2nd National Action Plan on Antimicrobial Resistance (NAP-AMR)**' from Ministry of Health & Family Welfare focuses on AMR in humans and raised the concerns of growing resistance to antimicrobial resistance in humans. We feel the core solution to this problem remains with the practices of human healthcare and

usage of antibiotics in their sector. Only a small correlation exists with the animal healthcare of the country and transfer of resistance from animals to human *via* animal sources. As an industry, we duly own the responsibility of judiciously advocating antibiotics in animals and its prudent use for our ailing animals.

The availability of use of antibiotics has transformed the practice of human and animal healthcare. Antibiotics are indispensable tools for effective animal health and welfare. Antibiotics as human healthcare assist the management of tough bacterial infections and diseases improving animal welfare and food security and safety. Antibiotics have a role to play in sustainable livestock production by reducing waste and inefficiencies caused by disease, and help provide a safe supply of food from healthy animals.

As we all are aware Antimicrobial Resistance (AMR) is a global issue and many organizations across the globe are working forward for solutions from different sectors that affect human healthcare. There is significant evidence to prove that the main cause of AMR is over and inappropriate use in humans. The same has been stated in several reports, like that from the European Medicines Agency (EMA), or the UK-Department of Health, which stated that: "…clinical issues with antimicrobial resistance that we face in human medicine are primarily the result of antibiotic use in people, rather than the use of antibiotics in animals." It is also worth stating that the recent report from US-CDC confirmed that out of the 18 species of antibiotic resistant bacteria that pose the greatest threat to human health, only two have their potential source in agriculture. In September 2013, US-CDC released a report called 'Antibiotic Resistance Threats in the United States' According to the report, 50 percent of all the antibiotics prescribed for use in people are not needed or not optimally effective. During the release of the report, then US-CDC Director Thomas Frieden, MD said, "Right now the most acute problems is in hospitals and the most resistant organisms in hospital are emerging in those settings, because of poor antimicrobial stewardship amongst humans"

As per 2016 report entitled '**Antibiotic Use and Resistance in Food Animals- Current Policy and Recommendations**' from Center for Diseases Dynamics, Economics & Policy (CDDEP), (Washington, DC), India currently accounts for 3% of the global livestock antimicrobial consumption and harbor's more than 11% of the world food animal population. By 2030, this consumption would be 4% considering the animal population and antibiotics. Now considering that the country is blessed with a significant proportion of global livestock population (more than 11%) is it not mandatory that we take care of them as they are our food providers. 3-4% of worlds antibiotic consumption is a must for the healthy and secure life of these animals and ourselves; whilst the need is to strike a balance between the benefits and risk of using antibiotics in the food supply chain. While on the contrary, the human antibiotic usage data articulates that India harbors 17% of the world human population and advocates 22% of the world antibiotic medication. As per available scientific data, considering the dosage of antibiotics in kilograms or pounds, human physicians advocate 10 times the amount of antibiotic to humans compared to the same used in food animal production.

Antibiotic use in livestock farming is considered as an added cost to the animal husbandry practices while at times its use in inevitable for effective control of diseases. Considering the low margins associated with animal production, deliberate use of antibiotics makes no economic sense.

A lot of debate is on regarding transfer of resistance from animals to human. In fact, science fully documents that resistance in different species is quite different. Majority of bacteria adapt to live on a particular host species. Reports suggest after genomic sequencing that *Salmonella typhimurium* bacterium and its resistance genes are largely maintained within animal and human population separately and there is limited transmission considering all sources

It is said that drugs used in farm animals reach humans *via* milk, meat and other animal health products. The fact is animals are treated with antibiotics when required to cure them of infections. Not all animals are given antibiotics and not all animal products have drugs and their metabolites. Above all subsequent to treatment worldwide there is a valid concept of withdrawal period and MRLs in place, adherence to the same is a necessity for safe, healthy and nutritious food. The animal health drugs and antibiotics comply with all standard outlined in D & C Act, approved by Drug Controller General of India (DCGI, CDSCO). In fact, all products have a notified withdrawal period on all packs as per Gazette Notification 899 (E) dated 27th December' 2011 and amendment to D & C Act, 1945. Above all the antibiotics used for Veterinary are notified under schedule H or H_1 category and sold on prescriptions.

Further, it would also be worthwhile to note that the annual per capita consumptions of animal food products in India, is much lower than the developed countries. In India, considering the annual per capita consumptions of animal food products is 4.5kg of meat, 68.7 liters of milk and 2.4kg of eggs which is 5.22, 28.44 and 22.85 percent of European annual per capita consumption and 3.63, 27.0 and 17.26 percent of United States in terms of meat, milk and eggs respectively.

Considering our bio-diversity in climate conditions, production systems, emerging disease scenario, availability of resources, we need to adopt and follow our own tailored regulation rather than following the practices of developed countries. It may be unrealistic to opt for any reform by simply adopting the regulations outlined in countries. It is also important to note that in developed countries the major concern is food safety whereas for India food security has to go in hand with food safety.

We fully acknowledge the concerns for responsible and prudent use of antibiotics for animal welfare and protection as well as management of infectious diseases ensuring that the foods from our animals are safe and healthy for humans. **Meanwhile in order to do so we require basic diagnostic and surveillance facilities in Veterinary infrastructure at least at the level of Veterinary polyclinics and hospitals aiding better diagnosis and effective management of ailments.** There is also a need to educate the farmers on drug withdrawal periods and ensure its effective implementation for milk, meat and eggs.

AMR-OP-01

GREEN SYNTHESIS OF SILVER NANOPARTICLES OF *ALOE BARBADENSIS MILLER* AND *CYMBOPOGON CITRATUS* AND EVALUATION OF THEIR SYNERGISTIC ANTIBACTERIAL ACTIVITY

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The present study was taken up to explore the synergistic antibacterial potential of silver nanoparticles synthesized using *Aloe barbadensis miller* and *Cymbopogon citratus* extracts. Aqueous extracts from the plants were prepared and subjected to phytochemical analysis. Silver nanoparticles (AgNPs) were prepared from the extracts separately and characterized by UV spectrophotometry, scanning electron microscopy (SEM), particle size analyser, and inverted microscopy. Antibacterial efficacy of the synthesized nanoparticles was evaluated at 1:1 combination ratio against common field isolates of *Staphylococcus aureus, Klebsiella pneumoniae* and *Escherichia coli* at three different concentrations of 0.5, 1.0 and 1.5 %. Phytochemical analysis revealed the presence of bioactive compounds such as saponins, tannins, phenols, flavonoids, proteins, glycosides, and essential oils. Visible observation of colour changes and UV-visible spectra exhibited plasmon peaks at 409 nm and 410 nm for *Aloe barbadensis miller* and *Cymbopogon citratus*, respectively and new peak emerged for 1:1 combination at 418 nm confirming the formation of AgNPs. The SEM analysis revealed the presence of spherical AgNPs with a smooth surface and uniform distribution. Particle size analysis revealed an average size of 50 nm for the synthesized AgNPs. Observation through inverted microscopy revealed ring structures of the nanoparticles. ABST using disc diffusion (Bauer-Kirby) method revealed substantial zones of inhibition against above mentioned bacterial isolates surpassing few standard antibiotics. Based on the findings, it can be suggested that green nanoparticles prepared using extracts of the plants could be a promising alternative for combating bacterial infections in animals upon confirming its efficacy on different clinical cases.

AMR-OP-02

CINNAMON POWDER AS ALTERNATIVE TO CONVENTIONAL GROWTH PROMOTER IN BROILER

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The present research was planned to evaluate growth promoting effect of cinnamon *(Cinnamomum zeylanicum)* powder in broiler. A total of 120 chicks were divided randomly into 5 groups with 4 replicates of 6 birds in each. Group I served as control and was given basal diet without any treatment compound. Group II served as standard control and was given avilamycin antibiotic at the dose rate of 15 mg/kg feed as standard growth promoter. Chicks of group III, IV and V were given basal diet plus cinnamon powder at the dose rate of 2.5, 5.0

and 10 g/kg feed, respectively. This study was conducted for 42 days. All the birds of different experimental groups were observed for parameters like weekly body weight, weekly and overall body weight gain, weekly and total feed consumption, feed conversion ratio, livability and carcass characteristics. At the end of experiment return over feed cost was calculated. At the end of experiment, body weight and body weight gain of birds supplemented with cinnamon powder were significantly higher as compared to control birds. Feed consumption remained unchanged in the cinnamon powder supplemented broiler indicated no adverse effect of cinnamon powder on feed consumption of broiler. Feed conversion ratio has improved significantly in birds supplemented with cinnamon powder as compared to control birds. Cinnamon powder at 2.5, 5.0 and 10 g/kg feed had similar FCR to standard drug avilamycin supplements. The dressing percentage was significantly increased in cinnamon powder supplemented birds. The birds supplemented with cinnamon powder at 2.5, 5 and 10 g/kg feed had a higher return over feed cost as compared to birds of the control group. Furthermore, the return over feed cost was rupees 64.56, 64.63 and 67.32 per kg chicken from birds supplemented with cinnamon powder at 5, 10 g/kg feed and standard avilamycin growth promoter, respectively. The results revealed that the cinnamon powder can be used as a promising alternative to conventional growth promoters in broiler.

AMR-OP-03

STATUS OF OXYTETRACYCLINE RESIDUE IN MILK AND PANEER SAMPLES FOR HUMAN CONSUMPTION IN JAMMU REGION OF J&K (UT), INDIA

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Oxytetracycline (OTC) is most commonly used antimicrobial in food producing animals in Jammu, J&K (UT). The present study was conceded on presence of antimicrobial residues above MRL in milk and paneer samples and its effect on public health, as it can lead to microbial resistance and allergic reactions in humans. A total of 114 samples of milk and 34 samples of paneer were collected from local vendors in and around Jammu to evaluate the current status of OTC residues. The RP HPLC UV (365nm) was employed for the quantitative determination of OTC residues. The mobile phase was 0.01M oxaloacetic acid: acetonitrile: methanol (450:350:200) of pH 4. The chromatographic separation was achieved by isocratic mobile phase flow at 1ml/min, r^2=0.9974, peak Rt at 5.137 minutes. Out of the gathered milk samples, 42 samples (37%) of milk were positive and beyond the permissible level of MRL. Paneer samples (64.5%) had OTC residue were positive. Regular antibiotic residue monitoring is required to be considered by policy planners essentially. Presence of antimicrobial residues above MRL in milk and their products is an issue of public health importance. Their residues not only expose the humans to allergic reactions, some-time fatal, but also results in the microbial resistance.

AMR-OP-04

PRESENCE OF ENROFLOXACIN AND CIPROFLOXACIN RESIDUE IN MEAT SAMPLES FOR HUMAN CONSUMPTION IN JAMMU REGION

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Owing to the common uses of quinolones among livestock, the study was planned to screen Enrofloxacin and Ciprofloxacin residue status in goat tissues in Jammu, J&K. Tissue samples from Jammu region, gathered and analysed for Enrofloxacin and Ciprofloxacin residues using RP-HPLC-FD. Mobile phase constituted 0.05M, 870 ml orthophosphoric acid (pH 3.4) and 130 ml acetonitrile (87:13 v/v), at 1ml/minute flow rate, $r^2 = 0.999$, peak Rt: 3.42 minutes for Enrofloxacin and 3.76 minutes for ciprofloxacin at Ex 350nm and Em 450nm. The phosphate buffer (pH 7.4) was used during the sample preparation and clean-up. The LOD and LOQ for Enrofloxacin were 1.29 ng/gm and 3.91 ng/ gm respectively. The LOD and LOQ for Ciprofloxacin were 0.6ng/gm and 2ng/gm respectively. Recoveries of Enrofloxacin from kidney, liver and muscle of goat spiked at 200ng/gm, 300ng/gm and 100ng/gm were 86.508± 2.770, 88.260 ± 2.636, and 85.303± 2.414 % respectively. Recoveries of Ciprofloxacin from kidney, liver and muscle of goat spiked at 200ng/gm, 300ng/gm and 100ng/gm were 83.606 ± 2.053, 85.836 ± 2.798, and 83.107± 2.870 % respectively. Out of the samples collected, 67% of the liver, 63% of kidney and 25% of the muscles from Jammu region were positive and 6% of the liver, 12.5% of the kidney and 17% of the muscle had residue beyond established MRL for the enrofloxacin and ciprofloxacin. This may not sound alarming, but may yield microbial resistance, therefore these antibiotics needs to be monitored for the sake of animal health and society.

AMR-OP-05

EVALUATION OF *IN VITRO* ANTIBACTERIAL EFFECT OF LINALOOL COMBINED WITH ENROFLOXACIN, GENTAMICIN AND CEFTRIAXONE

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Present study was planned to evaluate in vitro antibacterial effect of linalool (terpinol a phytochemical), enrofloxacin, ceftriaxone and gentamicin individually as well as interaction of linalool with other three antibacterial drugs. Minimum inhibitory concentrations (MICs) were determined for different gram positive and gram negative organisms like Staphylococcus aureus (ATCC25923), Streptococcus pyogenus (ATCC8668), Bacillus subtillis (ATCC9372), Escherichia coli (ATCC25922), Salmonella typhimurium (ATCC23564), Pseudomonas aerugonosa (ATCC27853) and Proteus mirabilis (NCIM2241) by using microbroth dilution technique in 96 well microtiter plates. Interaction effect of linalool with enrofloxacin, ceftriaxone and gentamicin were determined against above said organisms using microbroth dilution chequerboard assay by evaluating Fractional Inhibitory Concentration Index (FICI). Results showed very promising effect. Linalool (19.53 µg/ml) and ceftriaxone (0.03 µg/ml) has synergistic action against E. coli, linalool (625 µg/ml) and ceftriaxone

(0.002 µg/ml) has synergistic action against P. mirabilis, linalool (625 µg/ml) and ceftriaxone (0.004 µg/ml) has synergistic action against B. subtilis. Similarly, linalool (625 µg/ml) and gentamicin (0.98 µg/ml) has synergistic action against E. coli, linalool (625 µg/ml) and gentamicin (0.49 µg/ml) has synergistic action against P. mirabilis, linalool (312.5 µg/ml) and gentamicin (1.95 µg/ml) has synergistic action against B. subtilis, linalool (78.13 µg/ml) and gentamicin (1.95 µg/ml) has synergistic action against S. typhimurium. Linalool (625 µg/ml) has synergistic action with enrofloxacin (0.002 µg/ml) against P. mirabilis and S. aureus, linalool (625 µg/ml) has synergistic action with enrofloxacin (0.02 µg/ml) against B. subtilis, linalool (1250 µg/ml) has synergistic action with enrofloxacin (0.002 µg/ml) against E. coli. In conclusion, linalool and other such phytochemicals can be used alone or in combinations with conventional antibacterials to combat situations viz. new and re-emerging infectious diseases as well as development of antibiotic resistance. Looking to prosperity of therapeutic use, injectable preparations of phytochemicals may be prepared for better efficacy and fast action which is the need of era particularly in Veterinary practices.

AMR-OP-06

PREVALENCE AND ANTIBIOTIC RESISTANCE PATTERN OF *STAPHYLOCOCCUS AUREUS* IN RAW CHEVON SAMPLES SOLD IN BIKANER CITY

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In this research work prevalence and antibiotic sensitivity pattern of *Staphylococcus aureus* (*S. aureus*) in raw chevon samples sold in Bikaner city (Rajasthan) were studied. A total of 50 chevon samples were collected from various meat shops of Bikaner city, out of which 46 (92%) samples were found to be contaminated with average counts of *S. aureus* 4.347 log 10 cfu/g. Half of the observed values to be in the potentially hazardous category. Among these 46 *S. aureus* isolates, 21 (45.65%) were coagulase positive. The antibiotic sensitivity tests results revealed that all *S. aureus* isolates (100%) were sensitive to ciprofloxacin and doxycycline. In contrast, all isolates of *S. aureus* (100%) were resistant to ampicillin and cloxacillin. Moreover, *S. aureus* isolates were highly sensitive to gentamycin while most of the isolates were highly resistant to tetracycline and ofloxacin. Multidrug resistance was also found in most of the isolates. This study revealed high prevalence of *S. aureus* in raw chevon meat samples sold in Bikaner city. *S. aureus* isolates showed varying antibiotic resistance pattern against different antibiotics. Ciprofloxacin and doxycycline can be used effectively against the organism.

AMR-OP-07

Casting Light on the Antimicrobial Potential of *Melia azedarach* Leaf Extract: Insights from GC-MS Analysis, *in-vitro* Study and Molecular Docking

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The escalating menace posed by drug-resistant microbes has prompted a critical quest for innovative and potent antimicrobial solutions. In this comprehensive study, a multifaceted approach to investigate the antibacterial properties of a hydroethanolic leaf extract sourced from *Melia azedarach* was undertaken. A combination of in-vitro analysis, *in-silico* screening, and GC-MS analysis, were done to illuminate the extract's potential in combating *Escherichia Coli* and *Staphylococcus aureus* infections. The minimum inhibitory concentration (MIC) of the M. azedarach leaf extract was found to be 32 mg/ml against *E. Coli* and 8 mg/ml against *S. aureus*, in the 24-hour study through the microdilution method underscoring its antibacterial efficacy. The GC-MS analysis was conducted for the identification of specific phytochemical compounds within the extract, revealing a rich diversity of bioactive constituents like Methyl stearate, Eicosanoic acid, methyl ester, Glycidyl palmitate etc. Molecular docking studies were done by structures obtained from GC-MS study against proteins of *E. coli* with PDB ID-1HNJ and *S. aureus with* PDB ID- 4CJN. Compound CID 548879, CID 536340, and CID 5283468 showed binding energies -7.58 kcal/mol, -7.399 kcal/mol, and -7.002 kcal/mol respectively against PDB ID 1HNJ. Compound CID 5363760, CID 548879, and CID 5282772 showed binding energies of -7.44 kcal/mol, -7.796 kcal/mol, and -5.8 kcal/mol against PDBID 4CJN respectively. In culmination, findings from the *M. azedarach* leaf extract can serve as a promising natural resource for the development of new drugs to combat antibiotic-resistant bacteria. This research sheds light on its potential and underscores the significance of harnessing its bioactive compounds in the ongoing battle against drug-resistant pathogens.

AMR-OP-08

ANTIBIOGRAM OF BACTERIA ISOLATED FROM SUBCLINICAL MASTITIS COWS IN BIKANER

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The goal of this study was to investigate pathogen types found in milk samples from cows affected with subclinical mastitis in Bikaner, as well as the antibiogram of isolated bacteria to different antibiotics. The study was carried out on 57 milk samples from 24 animals collected from dairy cows with subclinical mastitis. Microbiological isolation and identification were performed to identify bacteria. Antibiogram was done for bacteria isolated from these samples. In the present study from 57 milk samples total of 66 isolates were detected by culture, in which 36 isolates were of *Staphylococcus aureus*, 17 isolates of *Streptococcus agalactia*,

8 isolates of *Klebsiella pneumonia* and 5 isolates of *E.coli. In vitro* antibiotic sensitivity was carried out to determine the sensitivity pattern of different isolates from sub- clinical mastitis against 10 commonly used antimicrobial agents were done. The over all in-vitro sensitivity of various antibiotics in all isolated bacteria were 100 per cent for Marbofloxacin, 92.42 per cent for Cefoperazone, 90.91 per cent for Enrofloxacin, 89.39 per cent for Ceftizoxime, 80.30 per cent for Ampicillin+Sulbactum, 78.79 per cent for Amoxicillin + Clavulanic acid, 77.27 per cent for Gentamicin, 75.76 per cent for Tetracycline, 72.73 per cent for Ceftriaxone and 24.24 per cent for Penicillin-G. The least effective were Penicillin G and the results show resistance has developed against gentamicin, ceftriaxone and tetracyclin by many isolates. The resistance of certain bacterial isolates to a particular antibiotic may be due to indiscriminate use of antibiotic therapy and involvement of large number of pathogenic bacteria.

AMR-OP-09

DETECTION OF FOOD BORNE PATHOGENS & THEIR ANTIMICROBIAL PROFILING

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Foodborne diseases are a major cause of morbidity and mortality and have become a serious public health concern due to the rise in antibiotic resistance over the years. The main cause of foodborne diseases are pathogenic microorganisms including bacteria, viruses, fungi, parasites, and chemicals. Salmonella and *E. coli* are the most important organisms which affects humans through the use of contaminated raw meat. Present study was conducted on 50 freshly cut Chicken meat samples which were collected from different butcher shops located in Jabalpur city. Food borne pathogens mainly *E. coli* & salmonella were isolated and identified by culture methods and biochemical characteristics. The antimicrobial resistance profiling against Cefepime, Cefoperazone, Ceftriaxone, chloramphenicol, Cefoxitin, Imipenem, ticarcillin, ampicillin, gentamicin, ciprofloxacin, tetracycline, amoxycillin were conducted. Further they were subjected for biofilm formation assay by two different methods *viz.* tissue culture plate method and tube adherence method. Amongst 50 samples, twenty *E. coli* and five *Salmonella* were isolated. Out of 20 isolates, 17 (85%) isolates of *E. coli* were found to be resistant for tetracycline and ticarcillin, 13 (65%) for ampicillin and ciprofloxacin, 7 for cefoxitin and 8 for ceftriaxone respectively. Out of five *Salmonella* all showed resistance to ticarcillin (100%) and 3 (60%) isolates were resistant to cefoxitin. Strong biofilm forming ability was shown by all salmonella and ten *E. coli* isolates. *E. coli* and *Salmonella* are highly adaptable microorganisms that have evolved sophisticated means of antibiotic resistance. However, study needs to investigate the interplay of resistance at genetic levels in order to improve the control of foodborne diseases.

AMR-PP-01

IN-VITRO EFFICACY OF CEFTRIAXONE AGAINST MULTI-DRUG RESISTANT *SALMONELLA* SPP. OF POULTRY ORIGIN

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The present study reports the presence of multi-drug resistance *Salmonella* spp. isolated from poultry farms in north Gujarat, PCR confirmation of the isolates, antibiogram and the *in-vitro* efficacy of ceftriaxone. Based on the results of antibiogram using six antimicrobial drug classes, a total of 12 isolates were identified as multi-drug resistant (MDR) isolates and ceftriaxone was found to be one of the most susceptible drugs. Therefore, for *in-vitro* efficacy of ceftriaxone, the minimum inhibitory concentration (MIC) of 12 MDR isolates of *Salmonella* spp. were determined using Epsilometer test (e-test). Out of 12 isolates, six, three, two and one isolate showed MIC of 0.128, 0.064, 0.016 and 0.512 µg/ml, respectively. The MIC for all isolates were ranged from 0.016 to 0.512 µg/ml, showing promising use to ceftriaxone to treat poultry salmonellosis.

AMR-PP-02

EVALUATING THE POTENTIAL OF CHITOSAN NANOPARTICLES FOR ENHANCED DRUG DELIVERY THROUGH PREPARATION AND CHARACTERIZATION

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Ceftiofur sodium (CEF) is a potent third-generation cephalosporin antibiotic known for its bactericidal effects against various microorganisms. To enhance antibiotic penetration and antibacterial efficacy, nanotechnology presents a promising approach. This study presents an innovative method for synthesizing chitosan nanoparticles loaded with ceftiofur sodium through ionic gelation. The resulting nanoparticles underwent characterization using transmission electron microscopy (TEM) and dynamic light scattering (DLS). The TEM analysis revealed spherical nanoparticles with smooth surfaces. DLS measurements indicated an average diameter of 188.63±0.66nm, a polydispersity index (PDI) of 0.478±0.001, and a zeta potential of 26.53±0.38mV. Moreover, the encapsulation efficiency (EE) was found to be 64.37±0.85%, with a 36.96% drug release observed at 24 hours. The drug release kinetics followed the Korsmeyer-Peppas model with a fickian type of diffusion. *In-vitro* safety assessments were conducted using the MDBK cell line, revealing an IC50 value exceeding 10mg/ml. Genotoxicity (COMET assay) and cytotoxicity studies at 2mg/ml and 10mg/ml doses confirmed the non-toxic nature of the nanoparticles. Subsequently, *in-vivo* safety studies were performed

using female Wistar rats, with a therapeutic dose of 2mg/kg. The rats were divided into five groups, including a control group, single-dose CEF and CEF-CHI NPs groups, and 10-day multiple-dose CEF and CEF-CHI NPs groups. Throughout the 10-day study period, there were no signs of toxicity or mortality among any of the treatment groups. Blood samples collected on days 0 and 10 were analysed for various antioxidant and biochemical parameters, further confirming the absence of adverse effects. In conclusion, ceftiofur-loaded chitosan nanoparticles, whether administered as a single dose or as multiple injections over 10 days, demonstrated no toxicity or mortality in the tested animals. These findings support the potential of ceftiofur-loaded nanoparticles as a safe and effective option.

AMR-PP-03

IN VITRO ANTIBACTERIAL ACTIVITY AND MIC OF CLOVE BUD POWDER EXTRACTS AGAINST BACTERIA

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The study was planned to determine the *in vitro* antibacterial activity and MIC of ethanolic and aqueous extracts of clove (*Syzygium aromaticum*) powder against *Staphylococcus aureus*, *Streptococcus agalactiae*, *Bacillus cereus*, *Listeria monocytogenes*, *Escherichia coli and Pseudomonas aeruginosa.* The antibacterial activity of clove powder ethanolic and aqueous extracts at different concentrations (50%, 25%, 12.5%, 6.25% and 3.12%) and standard antibiotics (gentamicin, tetracycline, cefpirome and ampicillin) against all six bacteria were evaluated by disk diffusion method. The minimum inhibitory concentration (MIC) was determined by the micro broth dilution technique against all six bacteria. The study was carried out to determine MIC of clove bud powder ethanolic & aqueous extract at 250, 125, 62.50, 31.2, 15.6, 7.8, 3.9, 1.9, 0.96, 0.48, 0.24, 0.12, 0.06, 0.03, 0.015, 0.0075, 0.0038 and 0.0019 mg/ml concentration with two fold serial dilution in six different gram positive and gram negative organisms in triplicate manner. Results of antibacterial sensitivity test revealed that ethanolic extract of clove bud powder showed antibacterial activities against *Staphylococcus aureus*, *Streptococcus agalactiae, Bacillus cereus*, *Listeria monocytogenes* and *Escherichia coli* except *Pseudomonas aeruginosa.* While aqueous extract of clove bud powder showed antibacterial activities against *Staphylococcus aureus*, *Bacillus cereus*, *Listeria monocytogenes* and *Pseudomonas aeruginosa* except *Streptococcus agalactiae* and *Escherichia coli.* The results revealed that ethanolic extract of clove bud powder showed lower MIC against *Staphylococcus aureus, Streptococcus agalactiae, Bacillus cereus, Listeria monocytogenes* and *Escherichia coli* as compared to aqueous extract of clove bud powder.

AMR-PP-04

ANTIBIOFILM ACTIVITY OF GARLIC OIL ON *S. AUREUS* ISOLATED FROM MASTITIS MILK OF CATTLE

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The rise of multidrug-resistant (MDR) bacteria is associated with selective pressure instigated by the unselective use of antibiotics, which lessens therapeutic possibilities. *Staphylococcus aureus* is recognised as most common bacteria responsible for mastitis in dairy animals has shown a great ability to build surface-associated bacterial communities, called biofilm, being one of the most determinant factors for the development of chronic infections, and it is the major cause of treatment failure. Present study was undertaken on 164 bovine milk samples (cow = 113 and Buffalo = 51) collected from various dairy farms in and around Rewa (M.P.), only 24 samples were found to be mastitis positive when screened through CMT and 140 samples were negative in CMT screening. The prevalence of Subclinical Mastitis in cattle was 21% as determined by California Mastitis Test (CMT). All the 17 isolates were phenotypically characterized by standard biochemical test and susceptibility to novobiocin (5µg disk), resistance to polymyxin B (300µg disk). Positive isolates were observed for biofilm formation ability (n=17) by Congo Red Agar (CRA), Microtiter plate (using crystal violet) and light microscopy method, 90% sensitivity was seen through micro titre plate method. Antibiofilm activity of Garlic oil was observed on positive isolates in 3%,2% and 1% concentration along with positive and negative control in every micro titre plate assay. Maximum inhibition was observed at 3% concentration with O.D values ranging from 0.021±0.007 to 0.291 ± 0.005 in all the samples with per cent inhibition (50 to 60%). The multi-drug resistance profile of isolates showed 100 % sensitivity to cefoxitin and tetracycline, Sulfonamides and Ciprofloxacin 70.59 % and 52.94 %, Erythromycin, Clindamycin, Novobiocin and Polymixin B. less than 50%.

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ISVPT-2023

TECHNICAL SESSION-X

Nutritional Pharmacology and Nutraceuticals

Chairperson : **Prof. R. D. Rana**

Co-Chairperson : **Dr. K. Kanagarajadurai**

Rapporteur : **Dr. B. Rajendar**

NP-LP-01

NUTRITIONAL QUALITY OF MILK: THERE IS NO ALTERNATIVE

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Milk is considered as the single most complete food of the nature and basic component of human food. It is the most diversified food in terms of its composition as it provides body building proteins, bone forming minerals, health giving vitamins and energy giving lactose and fat. Milk is also prime source of important trace elements i.e., copper, zinc, manganese and iron, which play vital role in many physiological functions in human as well as animal body. (Górska-Warsewicz et al., 2019). Milk for human nutrition produced worldwide mainly comes from cows (about 85%), followed by buffalo (11%), goat (2.3%), sheep (1.4%), and camel (0.2%), while milk from other dairy species such as horse, donkey, and yak, accounts for less than 0.1%. Milk composition and production varies from species to species, reflecting its diversified benefits on health. Factors influencing the milk composition are divided in genetic factors, e.g., the species and breed of animals, and in environmental factors, such as type of dietary regimen, seasonal modifications and milking systems. The quality of milk products is also reliant on milk composition that varies with stage of lactation, milking methods, environment, season, diet, feeding system, breed and species (Kittivachra et al., 2007). Milk plays a vital role in building a healthy society and can be used as an important vehicle for rural nutritional security and development. Nevertheless, milk provides an excellent source of all the nutrients; its nutritive value has been most studied and has long been recognized. Milk is also important for many other nutritional and physiological needs since milk and its products are reservoirs of helpful bacteria called probiotics and food for probiotics *i.e.* Prebiotics, which contribute to gut health (Aljutaily et al., 2022)

Macro-components of Milk

Lactose: Lactose, or 0-4-D-galactopyranosyl-(1,4)-glucopyranose, is the major carbohydrate of milk. This sugar has been found in the milk of nearly all mammals and is unique to milk. Its concentration varies slightly in milk of different species (4.5 to 5.2 g / 100 g), as contrary to the concentration of fat, that of lactose cannot be easily modified by feeding and breeds of animals. Compared to milk from other mammals, human milk is considered unique in its high sugar content. Lactose primarily provides energy (17 kJ per gram of lactose), but it also has another function i.e. giving a sweetish flavor to milk. Lactose is the least cariogenic amongst all fermentable sugars and possesses a low glycemic index (Romero-Velarde et al., 2019). It increases the levels of gastrointestinal antimicrobial peptides by colonization of Bifidobacteria thus protecting the neonatal gut against infection (Costa et al., 2013). Lactose also has a number of special applications in the food and pharmaceutical industry like agglomerating agent, flavor enhancer of some foods, to improve the functionality of shortenings, as a diluent for pigments, enzymes, and tablet excipient etc. Lactose is also the preferred carbohydrate in infant and young child formulae; however, the use of lactose-reduced or lactose-free formulae in several countries is increasing. The main driver for this is the often-false coupling of symptoms of intestinal discomfort to (perceived) lactose intolerance.

Lipids: Milk lipids are present as emulsified droplets in globules coated with a membrane called "Milk Fat Globule Membrane". It is the most variable of all the milk components. Among the milk lipids, the major component is triacylglycerol which represents 97-98% of the total lipids in the milk of most species, while

phospholipids represent less than 1 % of the total lipids. Milk fat is not only a source of bioactive lipid components, but it also serves as an important delivery medium for many nutrients, including all fat-soluble vitamins. In milk, fat is the main source of energy, however, there is a low tendency of milk fat in the formation of adipose as the short-chain fatty acids in milk are hydrolyzed and absorbed from the intestine to the portal circulation without resynthesis of triacylglycerides (German and Dillard, 2006). Hassig et al. (1997) suggested the role of butyric acid as an anti-tumor agent by inhibiting growth and promoting differentiation and apoptosis. The anti-colon cancer properties of butyric acid are attributed to its ability to induce apoptosis in colon cancer cells (Avivi-Green et al., 2002). Caprylic and capric acids present in milk have antiviral activities, while monocaprin is reported to have antiviral activity against HIV (Neyts et al., 2000). Bovine milk is the main dietary source of conjugated linoleic acid (CLA) which is reported to have anti-carciongenic, antiatherogenic, fat regulating and immune modulating properties (German and Dillard, 2006). Milk fat is easily and very well digestible, however, long-chain saturated fatty acids especially stearic acid, as liberated from the fat in the small intestine, may not be completely absorbed in the presence of calcium.

Proteins: Milk protein is an important food for the human body because it contains all 9 essential amino acids. Milk protein consists of approximately 82 parts casein and 18 parts whey protein. Protein Digestibility Corrected Amino Acid Score (PDCAAS) for both whey and casein are 1.00 and biological value for whey and casein are 100 and 80 respectively. Casein besides being a complete protein also contains and carries minerals like calcium and phosphorus. Casomorphin peptides present in milk reduce the production of prostate cancer cells (Patel et al., 2020) while casoxins have been reported to have opioid antagonists properties (Severin and Wenshui, 2005). Casein and β-casein by virtue of having several Immuno-modulating peptides can protect the newborn against a large number of bacteria (Van, 2002). Proteins present in milk also contain peptides that exhibit antithrombotic activity by inhibiting fibrinogen binding on platelets (Brody, 2000). Whey proteins in milk, also called serum proteins, provide an excellent balance of essential amino acids. They also play a very significant role in controlling several biologically significant body functions. The ingestion of whey protein is reported to stimulate protein synthesis by 68% (Hoffman and Falvo, 2004). The cysteine and methionine (high content of sulfur-containing amino acids) present in whey protein are the precursors of glutathione, which can fight the cancer and stimulate the immune response. It also helps in removing the toxins from the body. Lysozyme enzyme protein in milk together with lactoferrin, lactoperoxidase and immunoglobulins form the important antimicrobial system of bovine lacteal secretions (Benkerroum, 2008). Milk proteins are densely comprised of branched-chain amino acids such as isoleucine, leucine, and valine and in fact, these amino acids are very high in milk proteins than in any other food. Leucine of milk helps in minimizing muscle wasting due to increased protein breakdown (Davoodi et al., 2016)

Micro-components of Milk: Milk is a valuable source of essential micronutrients that are crucial for human health. The mineral content of milk and dairy products is composed of macroelements (calcium, phosphorus, magnesium, sodium, potassium, and chloride) and numerous microelements present in trace quantities. Both are concentrated in the ash, the inorganic part of the milk nutrients, present in various forms associated with different structural components. Conversely, vitamins are biologically active substances and together with other nutrients are the organic part of the milk nutrients, consisting of lipophilic vitamins (A, D, E, and K) and hydrophilic vitamins (B-complex vitamin and vitamin C). Milk is particularly known for its high calcium content, which supports strong bones and teeth, as well as muscle and nerve function. Additionally, milk contains vital vitamins such as vitamin D, which aids in calcium absorption, and vitamin B12, necessary for red blood cell production and neurological health. Calcium, which is an essential mineral for bone health and various other physiological functions, is highly bioavailable in milk. It is worth noting that the calcium content

can vary between different types of milk, with cow's milk typically containing more calcium than human or donkey milk, while sheep's and goat's milk have higher concentrations. Phosphorus, another crucial mineral in milk, exists in various forms within the milk matrix, both organic and inorganic. This mineral is essential for various cellular processes. Various other micronutrients, including vitamin A, riboflavin, niacin, phosphorus, and magnesium, contribute to overall well-being, from maintaining healthy vision and skin to supporting energy production and metabolic processes. While not present in large quantities, minerals like potassium, zinc, selenium, copper, and iodine also play important roles in immune function, cellular protection, and thyroid hormone production. Incorporating milk and dairy products into one's diet can help ensure a balanced intake of these essential micronutrients, promoting overall health and vitality. Furthermore, the composition of milk in terms of minerals and vitamins differs between various animal species. Selenium, found in milk and dairy products, is primarily bound to casein and whey proteins and exists in inorganic and organic forms. Selenium contributes to numerous biochemical processes in the body. While the mineral composition in milk is generally stable, it can fluctuate based on factors such as the animal's lactation stage, its nutritional status, and overall health. This variability underscores the importance of understanding and monitoring the mineral content in milk to ensure its role as a valuable source of essential micronutrients in human nutrition. Buffalo milk had the highest Ca (204.23 ± 7.98 mg/100 g), P (117.45 ± 5.26 mg/100 g) and Mg (23.53 ± 1.33 mg/100 g) and the lowest Na (42.39 ± 0.82 mg/100 g) as contents compared to goat and cow milk. The mineral content of goat milk varies from 0.70 to 0.85%. Compared to human and cow milk, the goat milk contains more calcium, phosphorous and potassium. Goat milk contains the highest level of K (174.85 ± 4.85 mg/100 g) as compared to milk of other species. Camel milk possesses proteins (2.55%, w/w), fat (2.72%, w/w), minerals (0.87%, w/w), vitamins such as A (0.1 mg L^{-1}), E (0.56 mg L^{-1}), and C (37.4 mg L^{-1}), and lower content of β-casein and β-lactoglobulin free (Galali and Al-Dmoor, 2019).

Vitamins are crucial micronutrients that play vital roles in numerous enzymatic reactions and physiological functions of the body. Milk and its products serve as valuable sources of both water-soluble and fat-soluble vitamins. Water-soluble vitamins, such as those from the B-complex and vitamin C are abundant in milk's watery phase, making them prevalent also in skim milk and other reduced-fat dairy options. On the other hand, fat-soluble vitamins, *i.e.* vitamins A, D, E, and K, are concentrated in the lipid phase of milk and found in whole milk, cream, and cheese due to their higher milk fat content. The vitamin content in milk can also vary among species, with ruminant animals generally containing more vitamin B1 and B2 than non-ruminant species. Vitamin K levels are relatively low in regular milk but significantly more in fermented dairy products like yogurt and Dahi. The human milk stands out for its higher levels of vitamins A and E, which are essential for immune function and antioxidant activity. In this way, milk and dairy products serve as important contributors to a balanced and nutritious diet, offering a wide array of vitamins that are integral to various body functions.

Summary: Milk is a versatile and essential food source with a complex nutrient profile that benefits individuals from infancy through adulthood. The health-promoting effects of milk also arise from the interactions of a wide range of nutrients and compounds that it contains. Different types of milk may also offer customized health benefits, catering to specific dietary preferences and needs. The composition of milk can vary depending on factors like the source, diet, and processing methods, influencing its overall quality and nutrient content. In India with limited access to diverse diets, milk can be a valuable tool in addressing the macro and micro nutrient deficiencies due to its richness in essential vitamins and minerals. Overall, milk contributes to the health and nutrition of individuals, supporting bone health, and muscle growth, and providing a source of energy while being adaptable to various dietary considerations.

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NP-OP-01

SUBACUTE TOXICITY OF IMIDACLOPRID IN 42 DAYS TRIAL IN MALE RATS AND ITS AMELIORATION BY RESVERATROL

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Imidacloprid is one of the most important neonicotinoid insecticide known to target nicotinic acetylcholine receptors in insects and possibly in mammals. Present study was undertaken to ascertain the effects of subacute toxicity of imidacloprid in 42 days trial and its possible amelioration by resveratrol in male Wistar rats. Rats were randomly allocated into six groups with six rats each. Group I, served as the naïve control group, group II rats were given resveratrol at 2 mg/kg b.wt., group III and IV rats were given imidacloprid at 185 mg/kg b.wt. (MTD/10) and 92.5 mg/kg b.wt. (MTD/20), respectively. Rats in group V and VI, were administered resveratrol co-treatment at 2 mg/kg b.wt. along with imidacloprid at 185 mg/kg b.wt. (MTD/10) and 92.5 mg/kg b.wt. (MTD/20), respectively. Imidacloprid and resveratrol were given orally once daily for 28 days. Imidacloprid at 185 mg/kg b.wt. significantly increased malonaldehye levels in liver, testes, brain and plasma which were reversed by resveratrol co-treatment. Imidacloprid at both 185 and 92.5 mg/kg b.wt. significantly increased protein carbonyl levels in liver and testes which were reversed by resveratrol co-treatment. Imidacloprid at both 185 and 92.5 mg/kg b.wt. significantly increased myeloperoxidase and catalase levels in liver. Histopathological findings indicated that imidacloprid exposure resulted in gliosis in brain, congestion in liver and shrinkage of spermatic vesicles.in testes which were attenuated by resveratrol co-treatment. Results conclude that oral exposure of imidacloprid produced toxic effects on liver, brain and testes of male Wistar rats. Resveratrol possesses potential to ameliorate the toxicity produced by imidacloprid.

NP-OP-02

EVALUATION OF GROWTH PROMOTING EFFECTS OF CLOVE POWDER IN BROILER

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The present research was planned to evaluate growth promoting effects of clove (*Syzygium aromaticum*) powder in broiler. A total of 120 chicks were divided randomly into 5 groups with 4 replicates of 6 birds in each. Group I served as control and was given basal feed without any treatment compound. Group II served as standard control and was given avilamycin antibiotic at the dose rate of 15 mg/kg feed as standard growth promoter. Chicks of group III, IV and V were given basal feed plus clove powder at the dose rate of 2.5, 5.0 and 10 g/kg feed, respectively. This study was conducted for 42 days. All the birds of different experimental groups were observed for parameters like weekly body weight, weekly and overall body weight gain, weekly and total feed consumption, feed conversion ratio, livability, carcass characteristics and return over feed cost.

At the end of experiment, body weight and body weight gain of birds supplemented with clove powder, were significantly higher as compared to control birds. Feed consumption remained unchanged in the clove powder supplemented broiler indicated it has no adverse effect on feed consumption of broiler. Feed conversion ratio has improved significantly in birds supplemented with clove powder as compared to control birds. Clove powder at 5 and 10 g/kg feed had improved FCR as compared to standard drug avilamycin supplements. The dressing percentage was significantly increased in clove powder (2.5, 5 and10 g/kg feed) supplemented broiler as compared to birds of control group. The birds supplemented with clove powder at 2.5, 5 and 10 g/kg feed found higher net profit as compared to birds of the control group. Furthermore, the return over feed cost was rupees 61.92 and 67.32 per kg chicken in birds supplemented with clove powder at 5 g/kg and standard antibiotic avilamycin, respectively. The results revealed that the clove powder can be used as altemative to conventional growth promoter in broiler.

NP-OP-03

EVALUATION OF GROWTH PROMOTING POTENTIAL OF COMMON SPICES AND ITS EFFECT ON ANTIOXIDANT AND BIOCHEMICAL STATUS IN BROILER CHICKENS

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Natural herbs have been found to possess great potential as growth promoter in animals. Use of natural growth promoter as feed additive could become safe alternative to antibiotics. The present study was designed to investigate the effects of commonly used spices as growth promoters in broilers. Total hundred broiler chickens were randomly divided into four groups of 25 birds in each group. Turmeric (*Curcuma longa*), garlic (*Allium sativum*), and ginger (*Gingiber officinale*) powders were supplemented @ 0.5 percent of basal diet to treatment groups up to six weeks of age. There were significant increase in body weight in birds treated with turmeric and garlic powder as compared to control group. The activities of antioxidants like Superoxide Dismutase (SOD), Catalase and Glutathione-S-transferase (GST) in 10% hemolysate in treatment groups were in concurrence with control. Similarly, values of enzymes like Blood Urea Nitrogen (BUN), Creatinine and Total bilirubin were similar to those found in control birds. Significant increase in the levels of Aspartate transaminase (AST) and Alkaline Phosphatase (ALP) in the group supplemented with turmeric than control birds may be due to enhanced intestinal isoenzyme activities and skeletal growth respectively. This indicates that supplementation of turmeric, garlic and ginger powder as natural growth promoters do not adversely affect the health status of broiler birds as assessed by antioxidant and biochemical parameters. In conclusion the potential use of these natural growth promoters @ 0.5 percent in broiler feed seems to be an alternative to antibiotics.

NP-OP-04

PROTECTIVE POTENTIAL OF RESVERATROL AGAINST LEAD INDUCED REPRODUCTIVE TOXICITY IN MALE WISTAR RATS

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Lead exposure can produce multi-organ damage in humans and animals throughout the world. Resveratrol, bioflavonoid antioxidant, has showed ameliorative actions against different toxicities. Thus, the present study was designed to study the protective outcome of resveratrol against lead induced reproductive toxicity in male rats. Thirty six rats were divided into six groups. Group 1 received 3% gum acacia. Group 2 and 3 received lead at low dose @ 46.65 mg (kg b.wt.)$^{-1}$ and high dose @ 93.30 mg (kg b.wt.)$^{-1}$, respectively. Co-treatment of resveratrol @ 2 mg (kg b.wt.)$^{-1}$ along with low dose and high dose of lead was given to Group 4 and 5, respectively. Group 6 received resveratrol only. Total fourteen doses of each treatment were given once a day with a gap period of 48 hrs to respective group. In lead alone treated rats, testes and epididymis showed showed elevated levels of superoxide anion radical and MDA, however levels of SOD were found decreased. There was decrease in sperm motility and viability, and increased sperm abnormalities in lead alone treated group. Histopathological examination revealed dose dependent marked deleterious changes in the structures of testes and epididymis of the rats treated with lead alone. Resveratrol co-treatment with lead at both doses partially or completely prevented these lead induced deleterious changes. The resveratrol co-treatment also prevented the increase in plasma lead levels, as compared to lead alone treatments. So, it could be concluded that resveratrol co-treatment produced significant ameliorative effect against lead induced reproductive toxicity in male rats.

NP-OP-05

ANTIOXIDANT POTENTIAL OF ZINC OXIDE AND QUERCETIN NANOPARTICLES: *IN VITRO* CONCENTRATION DEPENDENT STUDY

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A lot of disorders are linked to oxidative stress in living organisms. Highly reactive free radicals, such as superoxide anion (O2-), as well as non-radical species like hydrogen peroxide and reactive nitrogen species, cause damage to cellular macromolecules like protein, lipid, and DNA. Numbers of antioxidants are available, which can counter these radicals. But, many of the existing antioxidants are also associated with some limitations which restricts their full potentials. Thus, there is continuous demand to develop some better alternative antioxidants. In the present study, the antioxidant potential of zinc oxide and quercetin nanoparticles alone and in combinations was evaluated by DPPH and ABTS assay. ZnO nanoparticles were synthesized by chemical precipitation, and quercetin was loaded in chitosan nanoparticles by ionic gelation method. The characterization

studies revealed nano size of particles with net negative charge. Synthesized ZnO and quercetin nanoparticles showed pencil and spherical shape, respectively. The nanoparticles alone and in combination showed the DPPH and ABTS scavenging activity, which increased with the increase in concentration. The combination of ZnO nanoparticles + quercetin nanoparticles at 60 µg/ml of each nanoparticle, showed the highest scavenging activity and the lowest IC_{50} value against the DPPH and ABTS radicals. In conclusion, the combination of ZnO nanoparticles + quercetin nanoparticles may be used as an alternative antioxidant in future.

NP-OP-06

EFFECT OF BOVINE LACTOFERRIN IN CCL_4 AND HIGH FAT DIET INDUCED NON-ALCOHOLIC FATTY LIVER DISEASE IN C57BL/6 MICE

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The study was conducted to know the therapeutic efficacy of bovine lactoferrin on Body weights, Lipid profile and Hepatic markers in the non-alcoholic fatty liver disease (NAFLD) model of male C57BL/6 mice induced by administration of high fat diet (HFD) + CCl_4 (0.5 mg/kg, mixed in olive oil) via intraperitoneal route for 6 weeks. Thirty six mice were divided into 6 groups of six animals each. Group 1 served as untreated control; Group 2 kept as disease Control (HFD + CCl_4); Group 3 treated with bovine lactoferrin *per se* (300 mg/Kg mixed in water) via oral route, Group 4 treated with bovine lactoferrin (300 mg/kg) + HFD + CCl_4, Group 5 treated with bovine lactoferrin (100 mg/kg) + HFD + CCl_4 and Group 6 treated with simvastatin (10 mg/kg) + HFD + CCl_4. Individual body weights of mice were recorded on 0^{th}, 1^{st}, 2^{nd}, 3^{rd}, 4^{th}, 5^{th} and 6^{th} week of experiment. Blood was collected on 2^{nd}, 4^{th} and 6^{th} week for the estimation of Lipid profile and Hepatic markers in liver. The study revealed that bovine lactoferrin dose dependently supressed body weight gain and prevented elevations in Lipid profile and Hepatic markers in the NAFLD mice model. These results were also comparable to the findings from simvastatin treated group. Therefore, bovine lactoferrin can be further evaluated for clinical management of hepatic diseases such as NAFLD.

NP-OP-07

EXPLORATION OF ANTIGOUT ACTIVITY OF P. NIRURI HERB IN GOUT INDUCED BROILER CHICKEN

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Gout is commonly observed in birds as they are uricotelic in nature due to lack of uricase enzyme. The condition is usually treated by the xanthine oxidase inhibitor allopurinol but the adverse effects of the drug limit its use. In the search for alternate herbal remedy, Phyllanthus niruri was selected for the present study,

based on literature. The preliminary qualitative phytochemical analysis on P. niruri leaves revealed the presence of alkaloids, carbohydrates, flavonoids, phenols, terpenoids and saponin and GC-MS analysis revealed 30 phytocompounds. In the biological experiment, a total of forty birds were divided into five treatment groups of 8 birds each and the groups were normal control (T_1), gout induced group (T_2), Allopurinol treated (T_3), P. niruri @ 10 g/kg (T_4) & P. niruri @ 12.5 g/kg (T_5). Gout induction model was induced by using sodium bicarbonate @ 20 g/litre of drinking water from 11th day to 14th day of age (four days) in broiler chicken. The herbal dosing was started on 3rd day and discontinued on 20th day. The serum biochemical parameters viz., uric acid, creatinine, ALT, AST and the clinical signs, mortality rate of gout induced chicken, gross pathology and histopathology of all treatment groups were studied. Also the xanthine oxidase inhibitory activity in liver was measured. Better prophylactic efficacy in gout induced broiler chicken was observed in allopurinol treated group followed by P. niruri @ 10 g/kg, since significant differences were not observed among P. niruri treatment groups on serum uric acid, creatinine and xanthine oxidase inhibitory activity. Based on the results, it was concluded that P. niruri herb supplemented @ 10 g/kg in feed might prevent the development of gout disease in broiler chicken.

NP-OP-08

ROLE OF *SARDINELLA LONGICEPS* FISH EXTRACT AND QUERCETIN ON CCL_4 INDUCED ALTERATIONS IN HEMATOLOGY OF WISTAR RATS

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This study aimed to determine alterations in the hematological profile of rats treated with *Sardinella longiceps* extract (SLFE) and quercetin against CCl_4-induced toxicity. Male Wistar rats weighing 150-200 G, were randomly distributed to five groups, the first served as control and received 1% DMSO orally for 3 weeks and olive oil i.p. twice a week in the 2nd and 3rd week while groups II, III, IV, and V rats received CCl_4 @ 1ml/kg in olive oil (1:1) i.p. twice a week in the 2nd and 3rd week. Groups III & IV were supplemented with SLFE @ 300mg/kg and quercetin @ 30mg/Kg orally daily for 3 weeks respectively. Group V rats were coadministered SLFE @ 300mg/Kg and quercetin @ 30mg/Kg orally daily for 3 weeks. By the end of the experimental protocol, blood was collected from retrobulbar puncture, and hematological parameters were estimated using an auto hematology analyzer. Results were expressed as mean ± SEM for six independent rats per group. One-way analysis of variance followed by Duncan's multiple range test was used for statistical analysis. Exposure to CCl_4 resulted in a highly significant decrease ($p < 0.01$) in hemoglobin and a significant decrease ($p< 0.05$) in RBC, HCT, PLT, and PCT in CCl_4 treated group compared to the control group. However, SLFE and quercetin supplementation individually in CCl_4-treated animals prevented the hematological alterations and their combination offered a better protective effect compared to individual treatments. This study concluded that fish extract and quercetin have the ability to ameliorate the deleterious effect caused by CCl_4 on hematological parameters.

NP-OP-09

AMELIORATION OF PERFORMANCE IN POULTRY BY DIETARY SUPPLEMENTATION OF FLAVONOIDS

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Oxidative stress is refers to a disruption in the pro-oxidant–antioxidant balance that can result a potential damage. Furthermore, poultry having a poor immune system is susceptible to infection by pathogenic microorganisms including bacteria and viruses, which can decrease productivity. Alternatives to antibiotics include natural herbal plants commonly known as *Flavonoids* which have the antioxidants, anti-inflammatory, antitumor, diuretic, antipyretic, antiulcer, antihypertensive, antispasmodic, antidiabetic, antimicrobial, antibacterial properties such as *Tinospora cordifolia*, *Thymus vulgaris*, *Rosmarinus officinalis*, *Moringa oleifera* and *Opuntia ficusindica.* Flavonoids are chemicals with antioxidant activity that have been found in fruits, vegetables, and other plant foods which are associated with stimulation of the immune system and develop the gastrointestinal tract to enhance the productivity in poultry. They are also responsible for osmotic adjustment, activation of enzymes, growth hormones and other organic molecules that increase growth, function and maintenance of life process. Contents of these plants are cheap, easily available and unconventional source of energy. Use of these Flavonoids in poultry may be alternative of antibiotics to promote the growth and therapeutic uses.

NP-PP-01

ASSESSMENT OF ANTIOXIDANT STATUS AND ANTISTRESS EFFECT OF *MORINGA OLEIFERA* LEAF MEAL ON MADGYAL LAMB

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The present work was conducted on eighteen Madgyal lamb divided in three groups with 6 lambs in each for 90 days for the "assessment of antioxidant status and anti-stress effect of *Moringa oleifera* leaf meal on Madgyal lamb". The feeding schedule was stall feeding with dry and green fodder + concentrate mixture (T_0 - Control), T_1 - 15% concentrates mixture replaced by MOLM (T_1) and T_2 - 25% concentrates mixture replaced by MOLM (T_2). Average fortnightly weight gain and ADG values of T_0, T_1 & T_2 groups were 19.35, 19.56, 19.85 (Kg) & 131.21, 136.99, 142.87 gm/head/day, respectively. The TDMI values were 773.71, 778.76 and 788.40 (g/day) in T_0, T_1 and T_2 groups, respectively. Blood samples were collected on monthly interval for evaluation of hematological (Haemoglobin, PCV, TLC, TEC), biochemical (ALT and AST) and antioxidant (SOD and GPx) effect of MOLM. MOLM has significantly ($P < 0.05$) ameliorated the level of SOD and GPx, as well as hematological and biochemical parameters. On day 0^{th} and day 90^{th} of experiment the antistress (serum cortisol) effect were evaluated in the serum by the commercially available ELISA kit and found

significantly ($P < 0.05$) ameliorated in treatment groups. Feeding cost/kg weight gain was recorded as 57.09, 53.80 and 51.54 in T_0, T_1, and T_2 groups respectively. The study indicates that concentrate mixture can be economically replaced by MOLM at 15% and 25% which will be economical for raising the lambs without any adverse effects.

NP-PP-02

PROPHYLACTIC EFFICACY OF *AEGLE MARMELOS* AND *ANNONA SQUAMOSA* BI-HERBAL EXTRACTS ON ADENINE INDUCED CHRONIC KIDNEY DISEASE IN RATS

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The present study was planned to evaluate the prophylactic efficacy of bi-herbal aqueous and alcoholic extracts of *Aegle marmelos* (AM) and *Annona squamosa* (AS) on adenine induced chronic kidney disease (CKD) in rats. Aqueous and alcoholic extracts of AM and AS were mixed in a 0.5:1 and 1:0.5 ratio respectively, after determined by *in-vitro* nucleation assay. Thirty-six male Sprague Dawley rats were divided into six groups; each group comprises six rats. Control group I was untreated group do not receive adenine or plant extracts. Group II was administered by adenine @ 200 mg/kg once day orally for 28 days and was considered as adenine control group. Chronic kidney disease was induced in the groups II, III, IV, V and VI by daily 200 mg/kg dose of adenine through the intra-gastric route for 28 days to produce rat model of adenine-induced CKD. Groups III and IV received bi-herbal aqueous extracts of AM and AS (ratio 0.5:1) orally @ 250 and 500 mg/kg, respectively daily once for 28 days. Groups V and VI received bi-herbal alcoholic extracts of AM and AS (ratio 1:0.5) orally @ 250 and 500 mg/kg, respectively daily once for 28 days. Various parameters were studied like feed consumption, body weight, haemato-biochemical estimation, urine assessment, ultrasonographic examination and histopathological findings in rats. The adenine control group showed a significant decrease in mean haemoglobin, TEC, lymphocyte, serum uromodulin, total protein, albumin, calcium as well as urine pH, urine creatinine and urine phosphorus values along with a significant increase in TLC, granulocyte, serum creatinine, BUN, ALT, uric acid, phosphorus, urine total protein and urine calcium as compared to normal control rats. These findings showed significant changes in the haemato-biochemical parameters, urine parameters in response to adenine treatment. The administration of aqueous and alcoholic bi-herbal extracts of AM and AS leaves for 28 days along with adenine in prophylactic groups revealed significant improvement on haemato-biochemical and urine parameters. Results of ultrasonographic and histopathological examination of kidney tissues in prophylactic groups was well supported and prevent alterations in kidney associated changes in adenine-induced CKD in rats. Result of the present study revealed that aqueous as well as alcoholic bi-herbal extracts of *Aegle marmelos* and *Annona squamosa* leaves at 250 and 500 mg/kg revealed prophylactic efficacy against adenine induced CKD in rats. Furthermore, bi-herbal alcoholic extracts were more effective as compared to bi-herbal aqueous extracts.

NP-PP-03

HEPATOPROTECTIVE EFFECT OF *STOLEPHORUS COMMERSONNII* FISH EXTRACT AND FLAVONOID RUTIN IN RATS

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Marine fish *Stolephorus commersonnii* is rich in essential amino acids and omega-3 PUFAs. Flavonol rutin, found in vegetables and fruits has antioxidant activity and inhibits ROS generation and lipid peroxidation. This study investigated the hepatoprotective effect of *S. commersonnii* fish extract (chloroform: methanol) (SCFE) and rutin, given separately and concomitantly against CCl_4-induced toxicity in Wistar rats. Group I received 1% DMSO orally for 3 weeks and olive oil @ 1ml/Kg b.wt. IP twice a week in 2nd and 3rd week. Group II (toxic group) was administered CCl_4 @ 1ml/Kg b.wt in olive oil (1:1) IP twice a week in 2nd and 3rd week. Group III received SCFE orally @ 300 mg/Kg b.wt. in 1% DMSO for three weeks, along with CCl_4 as in Group II. Group IV was treated with rutin @ 20mg/Kg b.wt. in 1% DMSO orally for 3 weeks, along with CCl_4 as in Group II. Finally, Group V received CCl_4, SCFE and rutin as above. Twenty-four hours post last treatment; all animals were sacrificed after blood collection. Hepatotoxicity in toxic group was evident by decreased weight gain, increased serum ALT, AST, ALP, bilirubin, BUN and creatinine, decreased plasma total protein and albumin, decreased antioxidant (*viz.*, SOD, CAT, GPx, and GSH) and increased lipid peroxidation (TBARS) markers with histopathological changes on liver. Treatment with SCFE and rutin separately or in combination significantly improved weight gain and ameliorated biochemical and histopathological alterations. Though both fish extract and rutin individually exhibited significant hepatoprotective effect, their combination produced better protective effect.

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ISVPT-2023

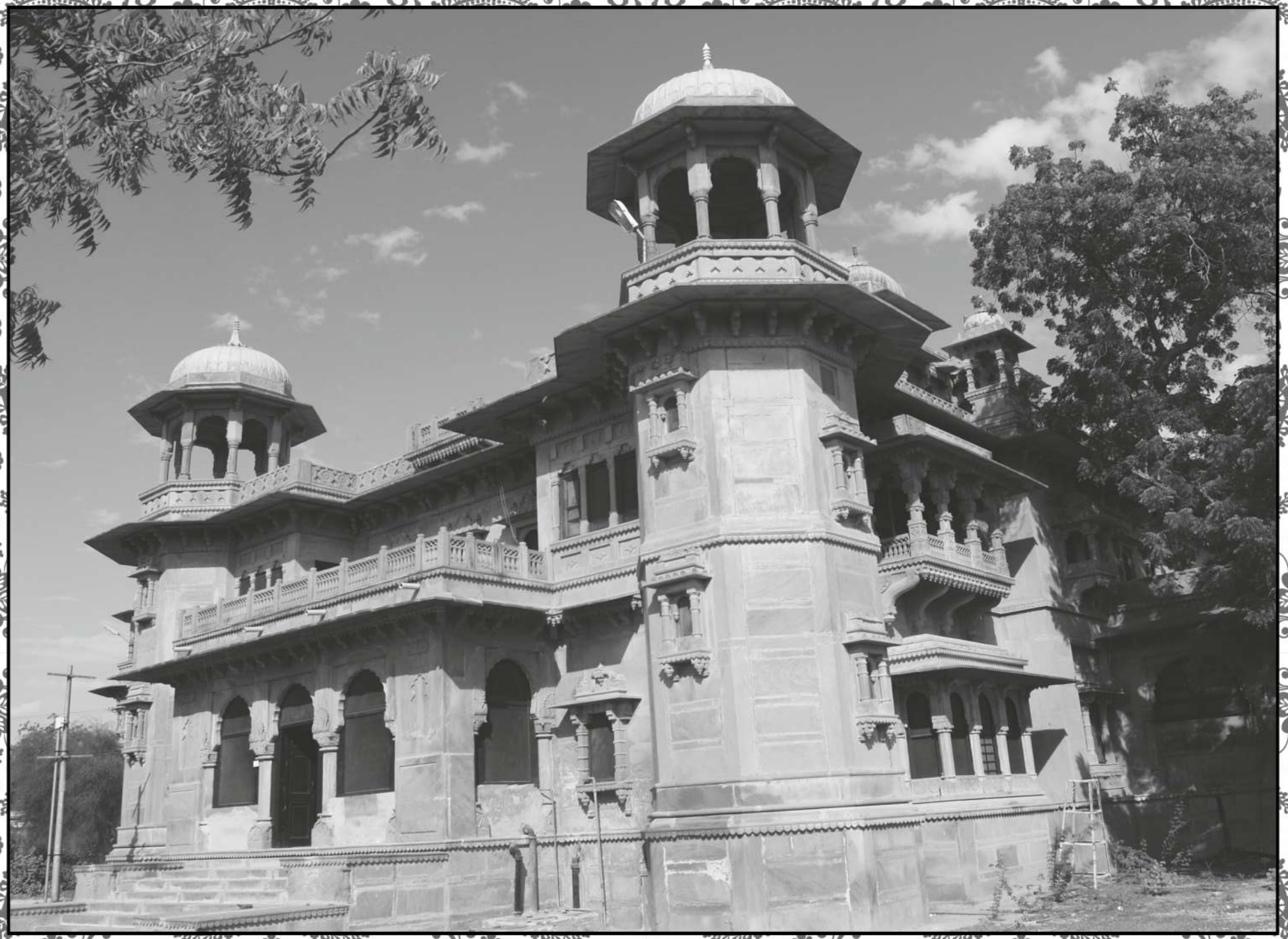
TECHNICAL SESSION-XI

Pharmacokinetics/Toxicokinetics

Chairperson : Prof. N. K. Pankaj

Co-Chairperson : Dr. M. K. Lonare

Rapporteur : Dr. K. V. Venkata Rao



PK-LP-01

TOXICOGENOMICS: APPLICATIONS IN TOXICOKINETICS AND TOXICODYNAMICS

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Toxicogenomics is an interdisciplinary science interlinking the fields of molecular toxicology, functional genomics and pathology that involves elucidation of molecular mechanisms responsible for toxicity and aims to derive molecular pathway including molecular biomarkers associated with toxicity and genetic susceptibility to it. Toxicogenomics means impact of xenobiotics on genomic function and is defined as the application of genomic technologies such as genome sequence analysis, gene expression profiling, metabolomics, proteomics and related approaches to study the adverse effects of environmental and pharmaceutical chemicals on human health and the environment. In 1999, toxicogenomics was first described as the application of omics technologies i.e., transcriptomics, proteomics, metabolomics and genomics to the study of toxicology, taking into account "toxicology" and "genomic" approaches, combining "omics" technologies to field the toxicology, to better understand the response of cells or organisms to xenobiotics and pharmaceutical compounds in the environment and their toxicological evaluation. Toxicogenomics integrates multiple data derived from genomic technologies including transcriptomics, proteomics, and metabolomics with traditional toxicological and histopathological evaluation, and aids in understanding the relationship between toxicological outcomes and molecular genetics. Molecular profiling methods including various bioinformatics and omics techniques permit simultaneous analysis of multitude of gene variants in an organism exposed to toxicant and search for genes susceptible to damage, detect pattern and mechanisms of toxicity, and identify specific gene expression profiles that can provide biomarkers of exposure and risk.

APPLICATION IN TOXICOKINETICS

In human beings, approximately 0.1% of the 3 billion DNA base pairs that make up their genome varies between individuals. This small variation can have profound effects on biology, resulting in serious disease in some cases and often premature death occurs. However, the biggest part of variability of the genome is due to "single nucleotide polymorphisms" (SNPs), which can affect biological function in many ways. These polymorphisms can involve single gene or large segments of the genome, producing deletions, conversions, and duplications of genes. The polymorphisms that induce changes in the translational reading frames lead to synthesis of proteins with alterations in the amino acid sequence, which, with the production of different proteins, undoubtedly leads to the loss of protein activity. The polymorphisms in promoter regions can change the regulation and the level of expression of a protein, while polymorphisms localized close to the intron-exon interface may cause alterations in the processing of mRNA. When polymorphisms exist in the genes implicated in biological and metabolic processes like absorption, metabolism and excretion of pharmaceuticals and xenobiotics from the environment, the reparation of the DNA, in cell cycle control, and in membrane signalling, it imparts some sort of genetic susceptibility in certain individuals. Genetic diversity is an important factor governing the individual response following exposure to xenobiotics and various chemicals.

The presence of variations in the activity or expression of the metabolizing enzymes results in an alteration in the metabolization of the xenobiotic. The metabolization of xenobiotics is carried out by phase I and phase II enzymes. The majority of the genes that code for these enzymes are structural and functionally polymorphic, especially those of the cytochrome P450 (CYP450) superfamily, an enzyme that metabolizes around 56% of existing chemical products. The genetic polymorphisms of these enzymes cause frequent interindividual variation in the ability to metabolize pharmaceuticals and chemical products, either in the process of activation or deactivation, differing markedly in the relative distribution of the variant alleles between ethnic groups. The sequence variation within the genes encoding for a variety of proteins involved in drug disposition accounts for individual differences in response to many xenobiotics and the common drugs of abuse. These variations are probably very important factors in determination of the clinical efficacy and safety of a variety of pharmaceuticals and in the appearance of possible adverse effects on health resulting from the environmental or occupational exposure to diverse chemical substances.

APPLICATION IN TOXICODYNAMICS

It can be used to study the mode of action of chemicals, predict toxicological effects, and characterize and understand species relevance. Toxicogenomics simultaneously measures effects on a wide range of biological pathways via elucidating the interactions between genes, proteins, and metabolites within a resulting phenotype. It aims to obtain and understand gene expression data and the associated protein activity within an organism in response to toxic substances. It identifies common targets between species and determine common molecular processes associated with altering these targets. Comparisons among species are eased by omic technologies. The purpose of toxicogenomics is to derive toxicological mechanisms and identify adverse outcome pathways (AOPs). AOPs can be compared between species to identify specific and shared mechanism of toxicity. AOPs are useful for distinguishing initial (central) events from toxic effects and indubitable adverse effects that affect the health of human beings, and ecosystems. It helps in providing a clear mechanistic representation of critical toxicological effects that extend across different levels of biological organization, from the initial interaction between chemicals and their molecular targets to adverse effect and deleterious outcomes at individual or population level. It analyzes species differences in toxicity and explain the molecular basis, including molecular expression patterns responsible for differences and helps in anticipating the translation of animal observations into estimates of potential human risk. By providing the molecular level comparisons between humans and other species, toxicogenomics assists in identifying the animal species and strains that are most relevant for specific assays. Toxicogenomics can be used to predict adverse detrimental effects of toxic compounds on biological system and help in determination of genetic variants responsible for increasing individual susceptibility. This generally involves application of "-omics" techniques like single nucleotide polymorphism analysis of genetic variations of an individual, DNA microarray, protein microarray, etc.

ROLE OF TOXICOGENOMICS IN PREDICTIVE MECHANISM

The toxicogenomic approach aims to identify and study changes in gene expression "signatures or fingerprints" (based on biomarker genes) for a group of known prototype compounds (factors of oxidative stress, polycyclic aromatic hydrocarbons, etc) with the goal of learning to manage, and even induce, a particular toxic response that later could be used to better understand the mechanism of action of unknown compounds. The intention behind using these signatures is, on the one hand, to better understand the biology that underlies toxic response, thereby determining potential toxicity on the basis of profiles of gene expression. It provides a new paradigm in drug development and risk assessment by providing an insight into the molecular mechanisms leading

to drug toxicity and efficacy, and DNA polymorphisms responsible for individual susceptibility to toxicity. It correlates biological changes occurring in cells, tissues, or organs following exposure to toxic chemicals with changes in global gene expression and enables detection of toxic changes at levels below the limits of detection of traditional measures of toxicity thereby anticipating toxicity potential much earlier. Microarray technology platforms DNA chips, or microarrays, allow quantitative comparisons of the expression levels of potentially thousands of individual genes between different biological samples.

Application of toxicogenomics to mechanistic and predictive toxicology enables the identification of more effective biomarkers associated with adverse health effects, thus highlighting toxicity earlier in a compound's development, and potentially enhancing the announcing prediction using *in vitro* models. Application of genomics to toxicology may also yield a number of substantial dividends, including assisting predevelopment toxicology by facilitating more rapid screens for compound toxicity; allowing compound selection decisions to be based on safety as well as efficacy; a more detailed appreciation of molecular mechanisms of toxicity; the provision of novel idea and new research leads; and an enhanced ability to extrapolate accurately between experimental animals and humans in the context of risk assessment. Toxicogenomic technologies provide new and potentially useful indicators for toxicity screening and is useful in *in vivo* predictive toxicology. The application of omics technologies in particular, helps in understanding toxicity and therefore assist in screening chemicals that causes gene expression changes associated with adverse developmental effects.

CONCLUSION

Toxicogenomics plays principal and crucial role in the identification of important safety biomarkers useful in early prediction of several types of toxicity, such as cardiac toxicity, nephrotoxicity, hepatotoxicity as well as carcinogenicity, and enhances understanding of molecular pathway responsible for toxicoses and helps in correlating the concurrent phenotypic outcome with genotype, both at individual and population level. The toxicogenomic approach facilitates investigations of the molecular mode of action of toxic substances and enhances the accuracy of predictions of the susceptibility of an individual based on the toxic response and the impact of modifying factors.

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PK-OP-01

EFFICACY PREDICTION OF PROPIONIC ACID PRE-TREATMENT ON ORAL ADMINISTRATION OF MARBOFLOXACIN IN BROILER CHICKENS

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Propionic acid, a commonly used broiler chicken feed additives in organic acid category, also serves as an acidifying agent. Its utilization can impact the oral pharmacokinetics of marbofloxacin, a veterinary-exclusive antimicrobial drug used to treat bacterial infections in poultry. The present research work was undertaken to study the influence of propionic acid pre-treatment (4 g/L in drinking water for 10 days) on the oral pharmacokinetics of marbofloxacin after its single oral dose administration (5 mg/kg body weight) in broiler chickens and to know if any alterations in efficacy predictors based on PK-PD integration. Marbofloxacin was administered to experimental birds in two groups: one without propionic acid pre-treatment (Group-I) and the other with propionic acid pre-treatment (Group-II). Blood samples were periodically collected from both groups, and plasma marbofloxacin concentrations were determined using ultra-high-performance liquid chromatography equipped with UV detection. Pharmacokinetic parameters were calculated using non-compartment modeling with the 'PK Solver 2.0' software. An independent sample t-test was used to compare mean differences between the two groups. Statistically significant differences were observed in marbofloxacin concentrations obtained for both groups at time points of 0.0833 hours (5 minutes) and 4 hours (p d" 0.01). Group I exhibited a lower maximum plasma drug concentration (C_{max}) compared to Group II. The mean elimination half-life of marbofloxacin was also longer in Group II than in Group I. However, no statistically significant differences in pharmacokinetic parameters were observed between the two groups. There were also no alterations in efficacious range of values of PK-PD integration indices indicating that dosage adjustment for marbofloxacin is not required when used in broiler chicken flocks receiving propionic acid as a growth promoter.

PK-OP-02

FORECASTING CIPROFLOXACIN EFFICACY AGAINST POULTRY SALMONELLOSIS THROUGH PK-PD INTEGRATION

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Ciprofloxacin finds extensive use in treating various bacterial infections, notably Enterobacteriaceae infections in poultry. Addressing the growing challenge of antimicrobial resistance necessitates a re-evaluation of pharmacokinetic-pharmacodynamic (PK-PD) integration of ciprofloxacin, especially concerning poultry salmonellosis. This study encompassed the collection of blood samples from eight broiler chickens following

the administration of a single dose of ciprofloxacin at 10 mg/kg body weight, both intravenously and orally in cross-over manner (n=8). We measured plasma drug concentrations at various time intervals utilizing UHPLC with UV detector and calculated pharmacokinetic parameters using 'PK solver 2.0'. HiComb™ e-test method was used to determine the minimum inhibitory concentration (MIC) for ciprofloxacin against isolates of *Salmonella* spp. recovered from poultry faecal samples. For *Salmonella*, the MIC breakpoint higher than 1 µg/ml was considered resistance. Most of the isolates showed resistance to ciprofloxacin. For susceptible isolates, a high MIC_{50} breakpoint of 0.50 µg/ml, was observed against the *Salmonella* spp. of poultry origin. The study yielded discouraging PK-PD indices, *viz.* AUC_{0-24}/MIC and C_{max}/MIC (< 20 and < 4, respectively), which predicts failure of ciprofloxacin therapy against poultry salmonellosis even at the high dose of ciprofloxacin (10 mg/kg body weight) used in the study.

PK-OP-03

INFLUENCE OF FLUNIXIN MEGLUMINE ADMINISTRATION ON DISPOSITION KINETICS OF CEFPIROME IN SHEEP

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Fourth generation cephalosporin compounds include cefpirome which has well-balanced antibacterial spectrum, including Gram-negative bacteria and Gram-positive cocci including methicillin-susceptible *Staphylococcus aureus* as compared to third generation cephalosporins. Flunixin meglumine (FM) is used as adjunctive therapy in the treatment of sepsis and various inflammatory conditions in different ruminant species. Synergistic interaction between non-steroidal anti-inflammatory drug (NSAID) and antibiotic can increase antibacterial efficacy and provide broader-spectrum antibacterial activity than antibiotic monotherapy. Looking to this point, the study was conducted to evaluate the effect of intramuscularly administered FM (1.1 mg/kg) on pharmacokinetics of cefpirome following intravenous (IV) and intramuscular (IM) administrations (10 mg/kg) in sheep. Cefpirome was assayed in plasma by high performance liquid chromatography (HPLC). Following IV and IM administrations of cefpirome in healthy sheep, the plasma drug concentration was detected up to 12 h, while plasma drug concentration was detected up to 18 h in FM treated sheep. The plasma drug concentrations were consistently higher in FM treated group as compared to normal sheep. The present study revealed that effect of FM administration altered pharmacokinetic profile of cefpirome following IV and IM administrations in sheep. Therefore, concomitant use of cefpirome with FM requires therapeutic monitoring for potential pharmacokinetic drug interactions.

PK-OP-04

INTERACTION KINETICS OF ENROFLOXACIN WITH TOXIN BINDERS AFTER MULTIPLE ORAL DOSING

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Interaction kinetics of enrofloxacin with commonly used toxin binders viz. Hydrated sodium calcium aluminosilicate (HSCAS) and activated charcoal (AC) was studied in 36 broiler chicken divided into 3 groups of 12 each. Enrofloxacin was administered @ 10mg/kg for 5 days via drinking water as pulse dosing and the binders either HSCAS or AC was supplemented @ 0.5% in feed throughout the study. Blood samples were collected at predetermined time intervals, enrofloxacin concentration in plasma was analysed by HPLC method, and PK parameters were calculated and compared after administration of first and last dose. Enrofloxacin alone administered group revealed highly significant increase in AUC (23.92 vs. 17.34µg.h.ml^{-1}), C_{max} (1.63 *vs.* 1.42µg.mL^{-1}), $\overline{C_F}$ (0.80 *vs.* 0.62µg.mL^{-1}) and F (73.11 *vs.* 53.01%) after last dose when compared to first dose. The group supplemented with HSCAS and administered enrofloxacin revealed significant ($p<0.05$) increase in C_{max} (1.10 *vs.* 1.00µg.mL^{-1}) and (0.62 *vs.* 0.55µg.mL^{-1}) whereas MRT (13.57 *vs.* 17.43h), MAT (4.71 *vs.* 8.57h) and t_{max} (4.33 *vs.* 5.67h) decreased significantly after last dose when compared to first dose. The group supplemented with AC showed a significant decrease in MRT (13.26 *vs.* 17.35h), MAT (4.67 *vs.* 8.49h) and t_{max} (5.67 *vs.* 7.67h) after the last dose. The groups supplemented with binders did not show any significant change in bioavailability after multiple dose administration of enrofloxacin which clearly indicates their interaction with enrofloxacin. Hence it is suggested to withdraw the use of toxin binders containing either HSCAS or AC while administering enrofloxacin to broiler chicken.

PK-PP-01

COMPARATIVE PHARMACOKINETICS OF THE COMBINATION OF PIPERACILLIN AND TAZOBACTAM IN HORSES DURING DIFFERENT ANAESTHETIC PROTOCOLS

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Piperacillin injected at the dose of 88.8 mg.kg^{-1}in combination with tazobactam (11.1mg.kg^{-1}) after intravenous administration in unanaesthetised horses (group A) and horses undergoing maintenance anaesthesia with protocol B (dexmedetomidine, ketamine, midazolam combination), protocol C (xylazine, ketamine, midazolam combination) and protocol D (isoflurane) followed a two-compartment open model. The concentration of piperacillin could be detected in plasma of group A horses up to 2 h, group B up to 12 h, group C up to 24 h and group D up to 4 h. AUC was significantly higher in group A (169.7 ± 3.64 µg.ml^{-1}.h) followed by group B, C and D (91.6± 40.9, 82.3± 17.7 and 33.7± 1.36 µg.ml^{-1}.h, respectively). $Vd_{(area)}$ of group B and C (9.59± 4.00

and 10.6± 3.24 L.kg^{-1}, respectively) were significantly higher than group A (0.567 ± 0.012 L.kg^{-1}), whereas Vd$_{(area)}$ of group D (3.53± 0.19 L.kg^{-1}) was non significantly higher than group A. Elimination half-life was significantly longer in group C (4.87± 0.53 h) followed by groups B (3.16± 0.47h), D (0.82± 0.07 h) and A (0.662 ± 0.11h). Plasma creatinine concentrations significantly increased after 24 hrs of antibiosis in groups B and C. Upon integration of PK-PD data, piperacillin-tazobactam is recommended to be given at the dose of 80 mg.kg^{-1} b.wt at 12 h interval in group B, at the dose of 50 mg.kg^{-1} b.wt at 12 h interval in group C and at the dose of 100 mg.kg^{-1} b.wt at 6 h interval in group D.

PK-PP-02

EFFECT OF TOTAL INTRAVENOUS ANESTHESIA (TIVA) ON DISPOSITION OF AMPICILLIN-CLOXACILLIN COMBINATION IN HORSES

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Ampicillin-cloxacillin combination is commonly used by equine practitioners as a primary prophylactic measure, owing to its broad spectrum of activity, low toxicity, and low cost. However, during anesthesia there is decrease in renal and portal blood flow due to diminished cardiac output as well as compensatory increase in blood supply to vital tissues like brain which can alter the disposition of drugs administered. The present study was aimed to determine the influence of total intravenous anesthesia (TIVA) on disposition kinetics of Ampicillin-Cloxacillin combination in horses. Animals were categorized into 2 groups (n=6 for each group); group-I was unanesthetized horses, group-II comprised horses undergoing total intravenous anesthesia (TIVA) with xylazine, ketamine and midazolam. In all the groups, ampicillin-cloxacillin was administered intravenously at the dose rate of 10 mg.kg^{-1} (in group II, ampicillin-cloxacillin was administered when the animal had attained proper anesthetic depth *i.e.* in plane II of stage 3 of maintenance anesthesia). Blood samples were collected at different time intervals after antibiotic administration, and plasma concentrations of both the drugs were quantified by simultaneous detection method in HPLC. Pharmacokinetic parameters were derived by non-compartmental analysis using Win Nonlin software. Mean (±SE) pharmacokinetic parameters for ampicillin and cloxacillin under TIVA were area under plasma drug concentration time curve (AUC) (27±2.84 µg.hr.ml^{-1} and 42.171±3.86 µg.hr.ml^{-1}), mean residence time (MRT) (1.639±0.09 hrs. and 1.725±0.05 hrs.) respectively, which were significantly (P<0.01) greater and clearance rates (0.3858±0.04 litre.h^{-1}kg^{-1}and 0.2464±0.02 L.h^{-1} kg^{-1})respectively, were significantly(P<0.01) lower when compared to unanesthetized horses. Upon PK-PD integration, it is recommended that in horses undergoing total intravenous anesthesia by isoflurane, ampicillin-cloxacillin combination should be repeated, every 12 h interval to maintain %T>MIC value above 60-70% for bacteria with MICd" 0.4 µg.ml^{-1}.

PK-PP-03

PHARMACOKINETIC SUTDY OF CEPHALEXIN IN BROILER POULTRY

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The present study was undertaken to determine the pharmacokinetic activity of cephalexin following single dose and multiple (5) dose oral administration of cephalexin formulation @40mg/kg b.wt. in broiler chicken. Plasma concentration was analyzed by HPLC. The peak concentration observed following single dose and multiple (5) dose administration was 3.714 and 3.347 $\mu g.mL^{-1}$, respectively at 1 hr. The $C_{max.}$, $T_{max.}$, elimination half life($t_{1/2\beta}$) , distribituon half -life (t1/ α2), mean area under curve (AUC), clearance (CL/F) and volume of distribution (V/F) following single dose were observed as 3.167 $\mu g.mL^{-1}$,1.472 h, 1.095 h, 1.111h ,12.728 $\mu g.mL^{-1}.h$,3.15L.kg^{-1}. h^{-1}, and 5.029L. kg^{-1}, respectively. The pharmacokinetic finding $C_{max.}$,$T_{max.}$, elimination half life($t_{1/2\beta}$) ,distribution half -life (t1/α2), mean area under curve (AUC), clearance (CL/F) and volume of distribution (V/F) finding of the first dose of multiple(5) dose of drug administration were 3.255 $\mu g.mL^{-1}$,1.164 h, 1.139h, 1.147h, 13.067 $\mu g.mL^{-1}.h$,3.073L.kg^{-1}. h^{-1} and 5.06 L. kg^{-1} ,respectively. Whereas, after the administration of last dose of multiple (5) dose study the $C_{max.}$,$T_{max.}$, elimination half life($t_{1/2\beta}$) , distribution half -life (t1/ α2), mean area under curve (AUC), clearance (CL/F) and volume of distribution (V/F) were 2.93 $\mu g.mL^{-1}$, 1.372h,2.164h,0.886 h,13.159 $\mu g.mL^{-1}.h$, 3.07 L.kg^{-1}. h^{-1} and 6.11 L. kg^{-1}, respectively .The study shows effective therapeutic concentration (MIC) of cephalexin (0.25 $\mu g.mL^{-1}$)was maintained upto 6h following single and multiple (5) dose oral administration. Based on the above study, a dose of 11.5$mg.kg^{-1}$ is recommended .

PK-PP-04

TISSUE RESIDUE CONCENTRATION OF CEPHALEXIN IN BROILERS

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The present study was conducted to estimate tissue residue concentration of cephalexin ($\mu g.g^{-1}$) in various tissues following single dose (40$mg.kg^{-1}$ b.w.) and multiple (5) dose (40$mg.kg^{-1}$ b.w.) oral administration in broiler poultry. For tissue residue analysis, liver, lung, kidney, muscles, spleen, heart, and fat samples were collected from broiler birds. The tissue samples were analyzed for residual concentration of cephalexin by HPLC. In the present study, 3 birds each were sacrificed at 24 h, 48 h, and 72h for both single and multiple (5) dose oral administration. Following single dose (40$mg.kg^{-1}$ b.w.) oral administration of cephalexin, the highest tissue residue concentration was observed in kidney (0.355$\mu g.g^{-1}$) and lowest in heart (0.023 $\mu g.g^{-1}$) at 24 h. After 48 h of administration of cephalexin, the residues were only detected in liver (0.023 $\mu g.g^{-1}$) and kidney (0.058 $\mu g.g^{-1}$). No residues were detected at 72 h following administration of cephalexin. The highest

concentration of cephalexin was detected in kidney (2.293 $\mu g.g^{-1}$) and lowest in lungs (0.070 $\mu g.g^{-1}$) following multiple (five) oral dose (40mg.kg^{-1} b.w.) administration. At 48 h, highest and lowest concentrations were detected in kidney (0.644 $\mu g.g^{-1}$) and spleen (0.057 $\mu g.g^{-1}$), respectively. After 72 h post administration residues were detected in kidney (0.062µg.g-1) and liver (0.029$\mu g.g^{-1}$). However, no residues were detected in heart, muscle, spleen, lung, and fat. A withdrawal period of 3 days and 4 days is recommended following single and multiple (5) oral dose (40mg.kg^{-1} b.w.) administration respectively, in broiler poultry.

PK-PP-05

DISPOSITION KINETICS OF MARBOFLOXACIN AND ITS PHARMACOKINETIC INTERACTION WITH MELOXICAM IN GOAT

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Marbofloxacin is a third-generation quinolone developed exclusively for veterinary use. Non-steroidal anti-inflammatory drugs (NSAIDs) such as meloxicam are frequently prescribed with antibacterial agents for the treatment of various infectious diseases. The present research was aimed to investigate the disposition kinetic profile of marbofloxacin at the dose level of 8 mg/kg body weight following a single intravenous administration and its pharmacokinetic interaction with meloxicam when the later was co-administered intravenously at the dose rate of 1 mg/kg body weight in goat. The concentrations of marbofloxacin in plasma samples at various time intervals were determined by microbiological assay method using type culture of *Escherichia coli* (MTCC 443; equivalent of ATCC 25922). Following intravenous administration of marbofloxacin alone, the drug concentration in plasma reached 18.40 ± 0.17 µg/ml at 0.04 h. The AUC, AUMC, MRT, Vd_{arca}, and Cl_B values were 31.77 ± 0.45 µg/ml*h, 78.82 ± 1.41 µg/ml*h^2, 2.48 ± 0.01 h, 0.69 ± 0.01 L/kg and 0.25 ± 0.00 L/kg/h, respectively. Co-administration of meloxicam significantly increased plasma concentrations of marbofloxacin at different time intervals after its intravenous administration in goats. Co-administration also increased certain pharmacokinetic parameters of marbofloxacin like C^0, AUC, AUMC, and MRT when compared to respective pharmacokinetic parameters in goats administered with marbofloxacin alone. However, a significant decrease in mean values of Vd_{area}, V_C, Vd_{ss}, Vd_B, and Cl_B in meloxicam co-administered goats was observed. It was concluded that co-administration of meloxicam significantly alters the pharmacokinetic parameters of marbofloxacin in goats. A daily intravenous dose of marbofloxacin in goat @ 8 mg/kg body weight, along with meloxicam, can combat infections with inflammatory conditions due to susceptible bacteria having MIC values of 0.25 µg/ml or less.

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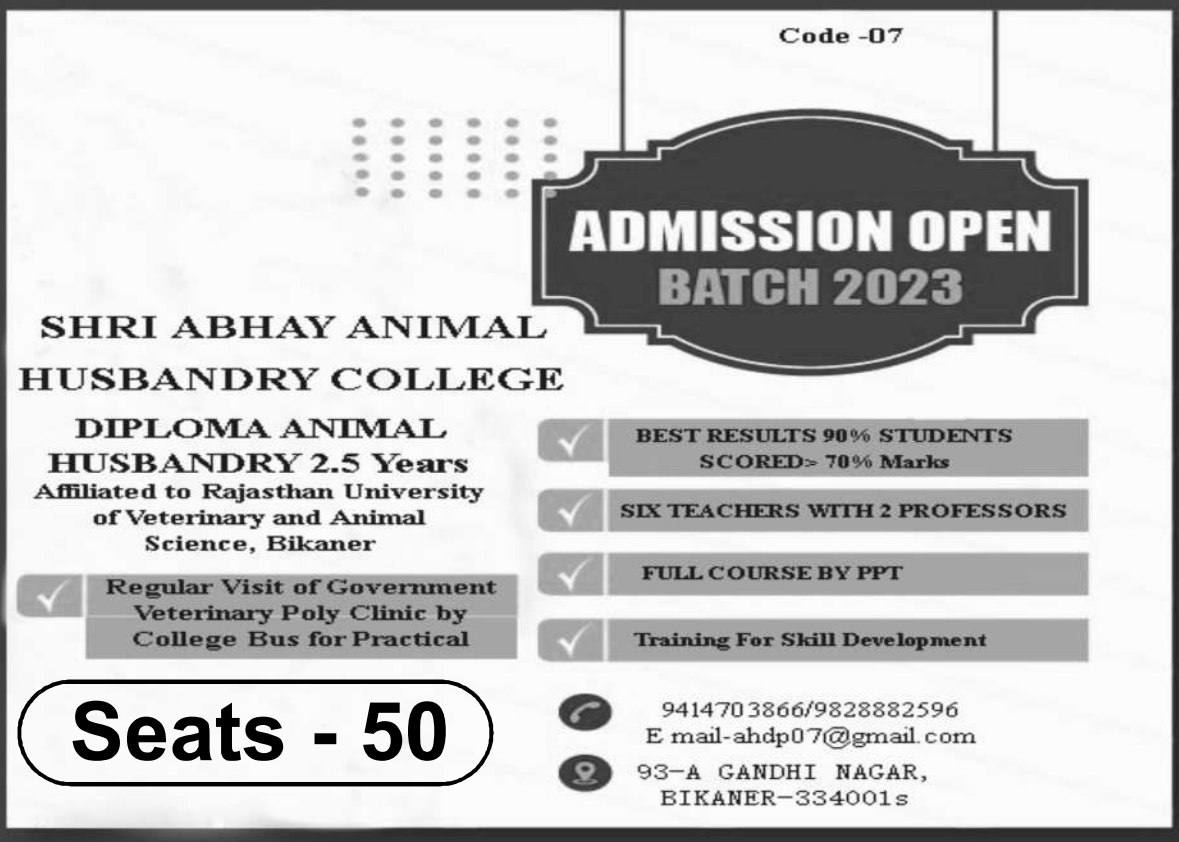

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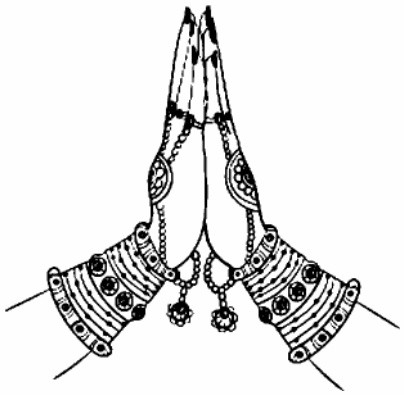

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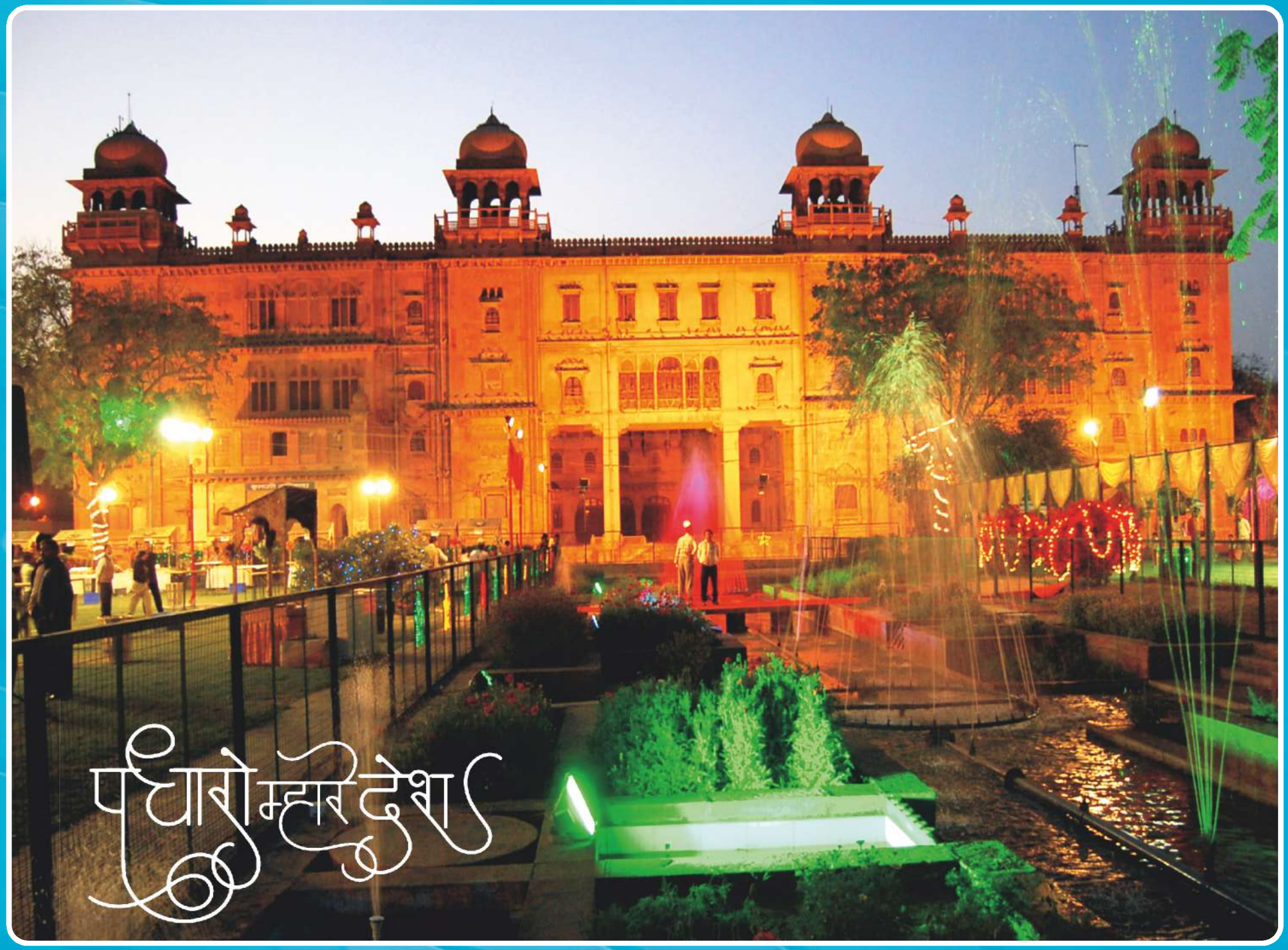
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