QUESTION BANK (VETERINARY PHARMACOLOGY)

PAPER NO. 19

General pharmacology -2

I. DEFINE / EXPLAIN (1-2 sentences.)

1. Aerosol ---- is a suspension of fine solid or liquid drug packed in a container under pressure in the gaseous form. The drug is released upon activation of an appropriate valve system in the form of a mist or fog. Intended for local application in to nose, mouth lungs or topical application.

2. Agonist ----- (Agonists are chemicals which have affinity and efficacy)

3. Antagonism: ----Antagonism is the interaction between 2 drugs such that the response of one drug (agonist) is reduced in the presence of second drug (antagonist)

4. Antagonist ----Antagonists are chemicals which have only affinity and have no efficacy.

5. Antagonism ---- opposing action of two drugs on the same tissue ,drugs with almost same structure may compete for the same receptor site .eg. morphine x naloxon.

6. Additive effect --- If two drugs with same effect is given together the effect produced is equal to the sum of the effect when the drugs are given individually, 1+ 1= 2

7. Bioavailability ---- Bioavailability is the quantity of active drug available at the target site.

8. Bio equivalence--- drugs are said to be bioequivalent if two related drugs are showing comparable bioavailability and similar time to achieve peak blood concentration. It is also said to exist when the bioavailability of the drug from different formulation is the same.

9. Ceiling dose (effective dose -100) ----it is the minimal dose that produce the maximal (100%) respond. Beyond this dose there will be no increase in response even if the dose is increased many fold no more spare receptors are available to be occupied by drug.

10. Chemotherapy -----It is the use of specific chemical in the treatment of systemic infections/malignancy –that has specific toxicity on the infectious organism/malignant cells with nominal effect on the host cells.

11. Clinical pharmacology ----It is the study of effect of drugs in animals in clinical cases.

12. Clearance of drug ---- Clearance of drug is the theoretical volume of plasma from which the drug is completely removed in unit time.

13. Clysters: ---administration of medicine via rectal cavity (enema) nutrient enema or retention enema.

14.Collutorea ---- are solutions of drug intended for washing the mouth.

15. Cumulative action----- minute quantity of drugs when enter in the body will accumulate in certain tissues and produce toxicity when toxic level is reached. eg. plumbism.

16. Dermojet------ method of administration of medicine in which no needle is used –high pressure is used for s/c injection of a fine jet of microscopic droplets of medicinal solution.

17. Dose------ Dose is the quantity of drugs which must be administered to produce a particular biological response ie. To achieve a specific target plasma drug concentration.

18. Drug dependence----- ability of certain drug to induce a state in which continued presence of drug is essential for the takers well being.

19. Drug----Drug may be a chemical substance (except food) which modifies the function of organism or cells, which is more beneficial to the recipient-more elaborately a substance used in alleviation, prevention, diagnosis and treatment of disease and also that which prevent pregnancy.

20. Ebers papyrus ? It is one of the earliest known record of medical therapy thought to have been written in 1550BC . is a record of invocations to the gods and recipes used in treating disease. Among many agents used at that time there are some which are still employed in medicine include opium, castor oil etc.

21. ED50---The dose which give non fatal response in 50% of the experimental animal is called Median effective dose or ED 50.

22. Efficacy----Efficacy of a drug refers to the maximal response that can be elicited by it eg.morphine produce a degree of analgesia not obtainable with any dose of aspirin

23. First order kinetic----First order kinetic(Exponential) is the rate at which drug is removed from a compartment –it is proportional to the drug concentration in it – A constant fraction of the drug present in the body is eliminated in unit time.

24.First pass metabolism ----metabolism of drugs during the passage from intestine to system. (intestinal wall and liver)

25. Gs protein coupled to adenyl cyclase ----It increase the formation of cyclic AMP activate protein kinase –A. which phosphorylate cellular constituents eg. Glucagon, Beta adrenergic agonist, gonadotropin and thyrotropin.

26. G i/o protein ----couples negatively to adenyl cyclase and decrease the formation of cyclic AMP. In addition G i/o protein can close Ca2++ and open k+ channels. Eg. Alpha adrenergic agonists, M2 and M4 muscarinic agonists , 5HT agonist, GABA B agonists, somatostatin.

27. Graded dose response –-- as the dose administered to a single subject or an isolated tissue is increase the effect will also increase at a particular dose until it reads the maximum.

28. Hyposprey (dermojet)---- administration of medicine with the help of very high pressure-no needle is necessary

29. Hypodermis----administration of medicine below the skin , s.c, i.m.

30. Idiosyncrasy-- Is a qualitatively abnormal reactivity of an individual to a chemical that has no obvious relation to dose or duration of therapy- occur only in a small population of individual drugs like chlorpromazine and clozapine cause frequent reactions rhabdomyolysis and liver toxicity , halothane produce malignant hyperthermia and hepatitis.

31. Insufflations------ is a medicated dusting powder that is blown by an insufflators in to body cavities such as nose , throat, vagina, ears etc. To which it would be difficult to apply the powder directly. In veterinary practice it is mostly used for the flock treatment of birds.

32. Inunctions----administration of medicine through the skin by rubbing.

33. Iontophoresis----process of administration of some poorly absorbed ionizing drugs through the skin by means of electric current of about 50 m.amp. –rarely used in vet. Practice.

34. LD 50--- The dose of drug which is fatal to 50% of the animal is called Median lethal dose or LD50.

35. Levigation -----is reducing the drug to very fine powder by triturating with little water and drying the resulting part.

36. Lethal synthesis (suicidal metabolism)---- process by which a highly toxic compound is synthesised from a non toxic precursor in biological system. Eg.synthesis of Fluorocitrate from Fluoroacetate –Fluorocitrate inhibit aconitase and subsequent chemical reactions for energy production.

37. Ligand----- ligand is a specific substance that is able to bind to and form a complex with biomolecule to serve a biological purpose. The ligand may include a signal triggering molecule such as a hormone, neurotransmitter.

38. Loading dose -----It is relatively large dose of a drug given at the beginning of therapy to get the desired pharmacological effect at the earliest .

39.Margin of safety/ safety index---- is the ratio of toxic dose to 1 % of the population to the dose that is desirably effective to 99 % of the population. LD 1/ED 99

40. Maintenance dose ---- dose given during the course of therapy to maintain desired pharmacological effect produced by the initial dose.

41. Metrology----- is the study of weights and measurers applied to preparation and administration of drugs.

42. Oleo resin-Resin with volatile oils obtained by distillation , semisolid, aromatic smell-eg.Asafoetida.

43. Partial agonist ----- Partial agonist have less degree of efficacy eg.Nalorphine is a partial agonist of Morphine it can be used to block morphine, at the same time if given alone produce same effect as morphine with less degree.(Naloxone is the true antagonist of morphine – has no efficacy.)

44. Parenteral ----- means beyond enteral or intestine , administration of medicine via route other than the intestine, but technically it refer to administration by injections under one or more layers of skin or mucous membrane.(i.v, i.m, s.c, i.p, epidural)

45. Pharmacogenetics----It deals with how genetic factor determine inter individual variability in drug response

46. Pharmacotherapeutic-----It is the study of use of drug in prevention and treatment of disease.

47. Pharmacognosy -----It is the study of source of drug of plant origin.

48. Pharmacodynamics ---- is the study of physiological and biochemical effects and their mechanism of action of drugs in the body , is what the drug does to the body.

49. Pharmacokinetic ----It is the study of absorption distribution biotransformation and excretion of drugs , is what the body does to the drug.

50. Plasma half life (t ½) –of a drug is the time taken for its plasma concentration to be reduced to half of its original volume.

51. Potentiation ---- if a drug lacking an effect of its own increase the effect of a second active drug, (0+ 1=>1) is called potentiation

52. Prodrug--- is an inert drug precursor on biotransformation the compound become pharmacologically active the parent compound is said to be prodrug Eg. Enalapril

53. Potency is a comparative measure---- it is the amount of drug needed to produce a certain response , dose required by a particular drug to get a given effect is less means that is more potent.(right ward shift of dose effect graph indicate lower potency)

54. Prescription-----Prescription is a written order to a pharmacist from a registered physician, Dentist or a veterinarian containing instruction for compounding, dispensing and give the preparation to the client with proper direction.

55. Resins-- Rosin like substance –insoluble in water, soluble in fat solvent-smooth shining refracture- usually quite irritant to mucous membrane-some are cathartic eg.Jalop resin, some are mild antiseptic-eg.Benzoin, they are soluble in alkalies and form resin soaps.

56. Risk –benefit ratio- term indicate a judgement on the estimated harm (adverse effect, cost) versus expected advantages (cure/ relief) . the ratio can not be measured accurately- based on data from a large population and on the clinicians own experience of the drug and patient. A drug should be prescribed only when the benefit overweight the risk.

57. Saponins--saponins are plant glycosides having distinctive property of frothing when shaken with water, can use as an emulsifying agent. A glycon moiety of saponin is sapogenin eg. Glycyrrhizin.

58. Posology---- Posology is the study of dosage of drugs.

59. Pharmacometrics----- it deals with the study of qualitative and quantitative evaluation of activity of drugs.

60. Renal clearance—Renal clearance is the volume of plasma completely cleared of by that substance by the kidney per unit time expressed in ml/min.

61. Receptors-- (Specific chemical groups in the cells which react with the drugs.)

62. Selectivity of a drug--It is the capacity of a drug to affect one receptor or cell population in preference to others . eg. Metoprolol selectively act on B1 adrenergic receptor in heart.

63. Selective action –It means drug have more affinity towards certain organs and act there eg. cardiac glycosides. Non selective –most of the cells require this eg. vitamins.

64. Soporific-- are drugs or other substances that induce drowsiness or sleep.

65.Saporifics: agents having the power to produce the sensation of taste-agents imparting flavor or taste-

66. Spansules--Spansules are hard capsule which contain medicinal agent in the form of granules coated with different substances that will dissolve at specific intervals for release the medicine so that to get longer duration of action with single administration.

67. Spare receptors-- are reserve receptors, which remain unoccupied at therapeutic concentration.

68. Specificity--Specificity is the capacity of a drug to manifest only one kind of action increase or decrease a specific function of a given cell types. Eg. Warfarin is having very specific action in preventing the blood coagulation.

69. Sensitivity --ability of a population (individual, a tissue or a receptor) to respond in a qualitatively normal fashion to a particular drugs. The smaller the dose required for producing an effect the more sensitive is the responding system.

70. Silent receptors-- These are the receptors which do not elicit a pharmacological response even when they are occupied by an agonist. It is suggested that presence of silent receptors or drug acceptors usually prolong the action of drugs in the body, as the receptor bound drugs are slowly released from such receptors and are then available for the active receptors.

71. Sonopreparations----Administration of medicine through the surface of the skin with the help of ultrasonic sound.

72. Synergism ---- occur if two drugs with same effect when given together produce an effect that is greater than the sum total of their separate action, 1+1+>2.

73. Teratogenicity –congenital deformities due to chemicals-In pregnant individual give birth to teratogenic babies. Thalidomide causes babies with phocomelia (seal like limbs) Steroids- causes cleft palate and lips, cardiac defects. Tetracyclins causes discolouration of teeth.

74. T-max ----(time maximum concentration, time of peak concentration) . it is the time required for a drug to reach peak concentration in plasma. The faster the absorption rate the lower is the T-max. It is also useful in assessing the efficacy of drug used to treat acute conditions which can be treated by a single dose. The t max is expressed in hours.

75. Titrated dose-- it is a dose of a potent drug that is arrived at by titrating it with acceptable degree of adverse effect-\ low initial dose and upward titration or high initial dose and downward titration (in critical situation) can be practised.

76. Volatile oils--Volatile oils are otherwise called as essential oils-volatalizes by heat, characteristic aroma, used as flavouring agent, some of them are having carminative action eg.peppermint oil some are irritant eg. oil of wintergreen, stimulate flow of gastric juice eg. Peppermint oil, camphor,

77. Tannins-- Tannins are non nitrogenous plant substances having astringent action on m.m. and are phenolic derivatives of plant acids- with iron salt give blue colour which has been used to make inks . It is insoluble in water and alcohol, form precipitate with heavy metal salts, alkaloids and proteins. Tannic acid is a tannin obtained from nut galls. Eg. Catechu.

78. Types of drug interactions-- 1. Additive effect . 2. Potentiation effect 3. Synergism 4. Antagonism.

79. Types of antagonism-- 1.Chemical antagonism 2. Functional antagonism 3. Dispositional antagonism 4. Receptor antagonism (competitive and non competitive).

80. Xenobiotics-- is a chemical substance that is not nutrient for body but foreign to body and which enters the body through ingestion, inhalation, or dermal exposure. It include drugs industrial chemicals, pesticides, pollutants, plant and animal toxins.

81. Zero order kinetic -- a constant amount of drug present in the body is eliminated in unit time , here the rate of elimination remain constant irrespective of concentration in the body eg. Ethyl alcohol,

II. ANSWER THE FOLLOWING:

1. Enumerate the factors affecting the absorption of drugs:---- 1. Physic-chemical properties of the drugs 2) Nature and type of dosage forms 3) Concentration and volume of drugs 4) Blood flow to site of administration 5) Area of absorbing surface 6) Route of administration 7) Disease status.

2. How drugs are classified? Give eg. ---Different types of classifications are there

I. Chemical nature. a) Organic eg.penicillin b) Inorganic eg. kaolin.

II. Target organ. a) Drugs acting in CNS eg. ethyl ether, b)Cardio vascular eg. digitalis.

III. Source of drugs. a) Natural eg. caffeine b) Synthetic eg. paracetamol.

IV. Mode of action. a) Channel blocker eg . verapamil b) Receptor blocker eg. diphen - hydramine.

V.Therapeutic use. a)Antimicrobials eg.penicillins b) Anticonvulsants eg. phenobarbitone.

VI. physiological system. a) sympathomimetics.eg. ephedrine b)anticoagulants eg. warfarin

VII. Physical effect . a) emollient eg coconut oil b) caustics. Eg. silver nitrate.

3. Drugs that have steep slopes for their concentration response relationship curves is more difficult to use Why? Steep slope indicate that small increase in dose produce toxicity.

4. What is apparent volume of distribution (Vd) ?--- is a proportionately constant relating the plasma drug concentration to the total amount of drug in the body. Vd = Dose/ (A/Alpha + B/Beta)/ Beta

5. What is biological assay ?-- certain drugs can be standardised by chemical means –when its activity can not be estimated quantitatively, the strength of the preparation is estimated by observing the minimum fatal dose of each by administering to a large number of animals or by observing their effect on isolated organs in biological experiment.

6. What is bio availability? ---Bioavailability is a term describes the fraction of drug entering the systemic circulation intact from the site of administration.

7. What is clearance ? -------clearance is the rate of drug removal from the body that is independent of t 1/2.

8. What is drug displacement interaction ?--- this occurs between 2 or more drugs which binds to same plasma protein site .A second drugs with high affinity to the same site of first drug , the first drug is displaced suddenly and the concentration of free drug is increased suddenly and also biological action. Eg. phenyl butazone to patient with warfarin therapy –warfarin is replaced suddenly and produce toxicity.(Warfarin is having high plasma protein binding, 99%)

9. What is enterohepatic recycling ?---Glucuronide form of drug is eliminated via bile-may be hydrolyzed by B-glucuronidase from the gut bacteria and free drug is again formed and reabsorbed in to system is called enterohepatic recycling.

10. What is half life of a drug (t1/2)--- is the time needed for the drug concentration to be reduced by half. Determind during the elimination phase of the drug. t1/2 = In 2/Beta = 0.693/Beta.

11. What is meant by the following ?

Fortis -- (strong)

Ferv --(hot)

Vet --(or)

q.s.- --(sufficient quantity)

mitt. --(send)

mitis. --- (weak)

ad. lib- --(as much as required)

ad.- --(Make up the volume to)

add --(Specified quantity is to be added)

12. What is meant by Area under the curve (AUC) ?-- it indicated the total amount of drug that comes in to systemic circulation after its administration.

13. What is non competitive antagonism?--- It may be due to antagonist binding to a separate site to the receptor or due to covalent binding . eg.phenoxybenzamine blockade of alpha one adrenergic receptor are irreversible due to covalent bonding with receptor protein. Picrotoxine antagonism of GABA receptor is reversible .

14. What is Phase II drug metabolism(synthetic reactions ?---metabolism of drugs by the enzyme systems in microsomes, cytosol, mitochondria - product is more water soluble. Biotransformation is conjugation(glucuronide, glycine, sulphate etc)

15. What is a partial agonist?--- Partial agonist is a drug that provoke response but the maximum response is less than the maximum response to a full agonist –because partial agonist have much higher affinity but less intrinsic activity than full agonist.

16. What is placebo therapy ?---- it is the use of inert harmless substances(like calcium lactate or dextrose) simply to satisfy the owner/ patient. It is mostly used in human medicine for psychological or psychophysiological effect on the patients.

17. What are receptor antagonist?--- Drugs which has an affinity for the receptor site but lacks intrinsic activity . Anagonist block or reduce the effects of an agonist.

18. What are saponins?--- Saponins are plant active principle-glycosides having distinctive property of frothing when shaken with water -- used as an emulsifying agent , a glycon moiety of saponin is sapogenins eg. Glycyrrhizin.

19. What are the source of drugs ? give examples.---

Plants-- products from all parts of the plants, Roots-gentian, Bark-cinchona, flower-pyrithrins, bulb-squil, wood-wood tar, fruits-anisi, Rhizome- ginger, leaves-tea, seeds-coffee.

Minerals-- copper, iron, iodine, mineral oil.

Animals--thyroid extract, insulin .

Syntheic--Sulfonamide, anti histaminic.

20. What is structural activity relationship ?---it is the relationship between the structure of a drug and its pharmacological activity . primarily deals with the study of how chemical alterations to a basic chemical pharmacophore (basic structure which gives a pharmacological effect) could alter the action of a drug.

21. What is total body clearance ?--- (ClB) is the volume of blood that is effectively cleared of a drug in a specified period of time.

22. What is meant by Zero order kinetic / constant rate kinetic?--- it is a pharmacokinetic process whose rate is independent of the concentration of the drug. A fixed amount of drug is processed per unit time eg. ethyl alcohol, phenytoin, salicylates.

Differentiate::

1.Agonist and antagonist-- Agonist is a drug that interact with specific receptors and elicits an observable positive response .It has both affinity and intrinsic activity- can be full or partial agonist. Antagonists are drug that interact with specific receptors or other part of the effectar mechanism to inhibit action of an agonist – devoid of intrinsic activity- does not initiate a biological response upon binding to the receptor but block the agonist

2. Collunaria and collutoria-- Collunaria is a liquid form of medicinal preparation intended for washing the nasal canal mostly for local action. Collutoria is also liquid form of medicinal preparation intended for washing the oral cavity.

3. Creams and Paste-- Cream is a soft semisolid emulsion preparation of drug which usually contain more than 20% water , volatile oils and or less than 50% hydrocarbons (Waxes, polyols as the vehicle). Intended for skin or mucous membrane applied with gentle rubbing eg. Calamin cream. Paste is a semisolid preparation of drugs which contain a large proportion of (20-50%) of finely divided solids dispersed in a fatty vehicle. Generally very thick, stiff and do not melt at ordinary temperature. Provide protective coating on skin or mucous membranes.eg BIPP.

4. Drug action and drug effect --drug action is the biochemical or physiological by which a drug produce a biological response in living organism-drug receptor combination result in a series of biochemical and metabolic changes in the cell. Drug effect is the ultimate observable changes in the biological functions of the cell or tissue as a result of drug action- Eg. Action of digitalis inhibition of Na+ K+ pump- the effect is increase force of heart beat.

5. Drug affinity and efficacy-- Affinity is the ability of the drug to combine with its receptor- high affinity drug binding results from greater intermolecular force between the drug and its receptors low affinity drug binding involves lesser inter molecular force. Efficacy (or intrinsic activity) refers to the relative ability of a drug to evoke a pharmacological response.

6. Decoctions and Infusions-- Decoctions and Infusions are aqueous extract of plant preparation differ in the methods of preparation. For the preparation of decoction the medicinal agent is mixed with water and boil for some time then decant it , the extraction process is more severe. Infusion is prepared by pouring boiling water over the powdered medicine and decant it – the extraction process is mild..

7. Effective dose -50--(ED-50) and Lethal dose -50 (LD-50):Effective dose -50 or median effective dose (MED)is the dose that produce the maximal response in 50 % of the population . LD -50 (MLD)

is the dose that is lethal to 50% of the population exposed to a given chemical under defined condition.

8. Elixier and Linctus-- Elixier is a liquid preparations containing alcohol,, syrups and aromatic substances –mainly used as flavouring agent may containing active drugs – mostly used as vehicle for cough remedies. Linctus is a viscous and sweet preparation of drugs having demulcent action on the mucosa of throat . it contain a high proportion of syrup and some time glycerine . it is mainly used in the treatment of irritating cough.

9. Full agonist and partial agonist --a full agonist activates a receptor to elicit the greatest response in the tissue (If the intrinsic activity of full agonist is considered as one) eg. Isoprenalin on beta adrenergic receptors. partial agonist act on the same receptor but it can not elicit response as full agonist(less than one) partial agonist have affinity but have only less intrinsic activity. In the presence of full agonist partial agonist will act as an antagonist. Eg. nalorphine is a partial agonist of morphine.

10. Induction and inhibition of drug metabolising enzymes-- Several agents have this ability-these agents interact with DNA and cause proliferation of smooth endoplasmic reticulum in liver-enhance synthesis of microsomal enzymes (Cytochrome-P-450 and glucuronyl transferase results in enhanced metabolism of endogenous substrate and drugs metabolised by this. Some drugs like carbamazepin and rifampicin may stimulate their own metabolism called as auto-induction. Phenobarbitone affect the metabolism of a large number of drugs. Several agents reduce the hepatic microsomal enzymes by hepatic damage due to carbon tetrachloride, carbondisulphide, reduce enzyme synthesis by puromycin, dactinomycin. Nutritional deficiency or hormonal imbalance , undesirable drug interaction may also inhibits microsomal enzymes

11.Liniments and Lotions ----Liniment is a liquid or semisolid preparation of drugs in oil, alcohol or soaps –intended for external application on intact skin by innunction (rubbing) . Meant for counter irritant action. Lotions are also liquid preparation of drugs in water meant for external application over skin without innunction. Applied for local soothing, cooling, protective purpose.eg. calamine lotion

12. Local action and systemic action --- Local action is limited to only a specific area eg.Local anaesthetics. Systemic means drug is absorbed in to system and action in whole body. Primary action eg. Adrenaline cause a rise in B.P.primarily due to direct action on artery at the peak there is a fall in B.P. due to reflex vagal stimulation which is the secondary effect.

13. Pills and tablets----pill is a spherical or ovoid preparation- usually sugar coated- preparation is intended to be swallowed without being chewed -contain one dose of medicine- now pill is less used. Tablets is a small disc shaped preparation usually made by moulding or compressing the granulated or powdered drug –vary in size and shape- not necessarily a single dose of medicine.

14. Resin and oleoresin---- Resins are viscous secretions of many plants (particularly coniferous tree) collected by incising the bark of the plants- is complex chemicals – exist in amorphous and brittle form insoluble in water , soluble in organic solvents. Soluble in alkali forming non-detergent resin soaps. Eg.Jalop, podophyllum. Oleoresins are semisolid mixtures of resin with volatile oils- natural secretions of plants - vary considerably in their composition.

15. Risk benefit ratio ---- risk benefit ratio is used to described the adverse effect of a drug in relation to its beneficial effects. In therapeutics the beneficial effects should out weight the adverse effects -can not be measured accurately- based on the data collected from use of drug in large population and on the clinicians experience of the drug and the patient.

16.Suppositories and pessaries--- Suppositories are conical preparations of medicinal agent for introduction in to the rectal cavity. Pessaries are also conical preparation of medicine intended for introduction in to the vaginal cavity.

17. Tachyphylaxis and Tolerance ----Tachyphylaxis is a phenomenon in which a rapid appearance of progressive decrease in tissue response following repetitive administration of a drug over a short period of time .increasing the dose of the drug will not increase the pharmacological response. Tolerance is used to describe a gradual decrease in responsiveness (de sensitization to a drug) taking days or weeks to develop. An increase dose may elicit a maximal response.

18. Up regulation and down regulation of receptors--- Up regulation of receptor is the process by which body increase the number of receptors in a tissue- usually seen when receptors in a tissue are continuously deprived of their ligand for a prolonged period. Down regulation is a process by which a cells decreases the quantity of receptor or protein in response to an external variable- causing diminished drug effect. Down regulation occurs when the tissue are continuously exposed to an agonist causing their over activation.

III. WRITE SHORT NOTES ON:

1.Absorption of drugs in to the biological system---- Drugs are absorbed mainly by four different methods. 1) Passive diffusion through the cell membranes –depend on the lipid solubility and molecular size regulate their filtration through pores. Weak base and weak acid vary in their absorption from GI tract of different animals 2) Filtration –some low molecular weight chemicals eg. water , urea enter through membrane pores, glomerular filtration of chemicals. 3) Facilitated diffusion- transfer across the membranes involves attachment to a carrier. No cellular energy is required- does not operate against a concentration gradient eg. reabsorption of glucose by the kidney, vit.B12 absorption from intestine. 4) active transport- require cellular energy- operate against concentration gradient- eg. Penicillin, thiazides diuretics, by active transport in the kidney tubule. 5) Pinocytosis- mostly the absorption of some polypeptide , bacterial toxins, antigen and food protein by the gut.

2. Active transport of drugs --- It is an energy depended transport system in which the solute take the help of a carrier cross the lipid bilayer. Carrier is usually a membrane protein that binds reversibly with the solute molecule on the exterior membrane –transport across the membrane to the other side to discharge the solute molecule. Carrier returns to the original place and energise for the next transport. Transport of solute is against concentration gradient. Generally large hydrophyllic, polar electrolyte substances , drugs having structural similarity to endogenous substances are transported via this.

3. Acute toxicity testing--- acute toxicity study revelas the type and extend of adverse effect by compounds when administered as a single high dose or multiple dose during a 24 hour periods. This

study provide the median lethal dose (LD 50) and also help to determin the therapeutic index. acute toxicity is mainly carried out at least in two mammalian species. Rodents such as mouse, rat, hamster etc,. are commonly used (equal number of males and females). One rodent species may be replaced by the species for which the medicine is intended. At least 2 different routes must be taken , one must be identical to that is going to be used in target species.

4. Additive effect of drug interaction---- when two or more drugs are used together the effect will be the sum of the effect of each drug given alone the drug interaction is called addition, effect produced is called additive effect. The additive effect is produced mainly when two drugs are administered together, have same/similar mechanism of action. Combination of sulphonamides , sulphadiazine + sulphamerazine+ sulphamerazine produce additive antibacterial effect (1+1= 2).

5. Adenylcyclase cAMP system---- One of the most important effector system. Which has a wide variety of receptor population and produce diverse effect. The effector protein is a membrane bound adenylate cyclise which is activated or inhibited by Alpha GTP complex. Activation of adenyl cyclise by stimulation of G- protein increase the synthesis of second messenger c AMP from ATP. Which activate cAMP dependent protein kinase which phosphorylate and alter the function of many enzymes, ion channels, carrier molecules and structural proteins to manifest various pharmacological effect like glycosylation, lipolysis, inhibition of secretion / mediator releasae increase contractility in heart and modulation of hormone synthesis.

6. Advantages of rectal route of administration --- can be used in the unconscious animals and animals which are vomiting. Absorption is slow compared to the intramuscular route. Some drugs which have erratic oral absorption (eg. Diazepam and phenytoin) can have better absorption rectally. Influence of first pass effect is reduced because rectal veins bypass the portal circulation and goes to the caudal venacava.

7. Advantages and disadvantages of fixed dose combination--- In a fixed dose combination products of 2 or more active drugs in a fixed dose ratio available in a single dosage form. They are useful only when developed based on sound pharmacokinetic and pharmacodynamic criteria. Advantages- more convenient to administer as a single dose, increase the therapeutic efficacy when combination have synergistic effect and additive effect, reduce administration cost as there is single pack, reduce chances of development of drug resistance, reduce chances of adverse effect , side effect of one may be masked by others (furosemide and spironolactone). Disadvantages- Not useful when animal requires action of only one drug- (cost and side effect may increase), not successful when different drugs have different pharmacokinetic value, if adverse effect is seen it is difficult to ascertain the responsible agent in the combination.

8. Adverse effect of drugs --- Unwanted or unintended effects of a drug that is harmful to the patients- may cause even with therapeutic dose –intensity of effect vary from inconvenience - organ function-death. In veterinary practice it may occur by use of inappropriate drug-inappropriate dosage-inappropriate species. Different types are there . Type A (mostly pharmacological) - exagerated desirable effect : mostly observed in overdosage or prolonged use of drugs. Side effect: unavoidable , unwanted effect occur even with therapeutic dose. Secondary: indirect consequences of a primary action eg. diarrhoea following antibiotic therapy. Drug interaction: one drug affect the activity of another drug. Type B (mostly non pharmacological effect) Hyper sensitivity, idiosyncrasy,

photosensitivity, intolerance. Type C Drug dependence. Type D delayed effect- carcinogenicity, mutagenicity. Type E end of treatment effect Iatrogenic disease.

9. Aerosole therapy---- administration of drugs in the form of aerosols directly to the resp.tract. because the drugs are deposited locally in the airway . It allows lower dosage, provide rapid action, minimize side effects and systemic toxicity. The drugs commonly employed by this technique include bronchodilator and anti-inflammatory agents used for obstructive air way disease such as asthma and chronic obstructive pulmonary disease. Commonly used in human medicine , some application in animal practice also devices used are nebulizer, metered dose inhalers and dry powder inhalers

10.Antagonism---- when the combined effect of 2 drug is lesser in magnitude than the sum of the effects of each drug given alone or when one drug is having no effect of its own decreases or inhibits the pharmacological effect of other drug the interaction is called antagonism and the effect produced is called antagonistic effect. Antagonist mainly seen when partial agonist is combined with a full agonist or when an antagonist and an agonist are combined together. Eg. morphine and naloxon

11. Alkaloids--- Alkaloids are basic nitrogenous substances widely distributed in many plants-leaves, roots, seeds. One of the most important plant active principles. It represent a waste product of plant metabolism-seen as precursors which convert to alkaloids in favourable condition- the same alkaloid may seen in several species of plants –same plants may contain many alkaloid. They posses basic properties contain amino group –viewed as ammonia derivative .Which do not contain oxygen are liquid in nature (eg.nicotine). insoluble in water, form salt with acids which are more soluble. When this salt come in contact with alkaline substance salt release free alkaloid . It form precipitate with tannic acid, salt with heavy metals (form coloured compound)The names of alkaloids end in “ine”, solutions of many alkaloids are bitter to taste. Some are highly toxic many with high medicinal value .

12. Area under the curve---- it is the total integrated area under plasma drug concentration curve and expressed the total amount of drug that comes in to the systemic circulation after administration of drug. An important parameters in evaluating the bioavailability of a drug –used to calculate several other pharmacokinetic parameters. AUC is expressed as the product of concentration of drug and time) Microgram/ml. X hour) For one compartment model AUC = B/Beta and for a two compartment model AUC=A/alpha+ B/Beta. An alternate method to find AUC is trapezoidal method- using non compartmental analysis.

13. Bioavailability--- Bioavailability is the percentage or fraction of administered drug that reaches systemic circulation in chemically unchanged form. The bioavailability of any drug after i/v administration is 100 %, and in general it is assumed to be close to 100% by i/m or s/c route. After oral administration it from 10-100% depending on the extent of absorption and first pass effect. It is determined by measuring the area under plasma drug concentration verses time curve vary (AUC) after oral or other non vascular routes and comparing this with AUC measured after i/v of the same drug. Bio availability (oral) AUC oral x100/AUC i.v.

14. Biotransformation of drugs---- It is the biochemical changes taking place to the drugs. Many are detoxified before excretion. It include Oxidation, reduction and conjugation. Conjugation depend on the availability of endogenous co-substrate-enhancing the availability of co substrate speed up

conjugation and useful in the treatment of poisoning.eg. paracetamol induced liver toxicity can be prevented by making available sufficient glutathione by administering N-acetyl cystein. Cyanide detoxification by conversion to thiocyanate can be accelerated by administering sodium thiosulphate. Some inactive drugs are biotransformed to active metabolites ,eg.prontosil to sulphanilamide, phenacetin to paracetamol.

15. Blind design in clinical studies of drugs---- It is a clinical trial in which the investigator does not know which are the control and treated groups. The drug and vehicle both look alike and are coded and the animals are numbered . The investigator is unaware of the type of treatment and has recordings are not due to any bias. In human experiment the term single and double blind studies are used .In single blind study either the patient or the investigator does not know which treatment is being used . In double blind study both investigator and patients does not know the treatment until the final analysis is done.

16. Blood Brain Barrier--- The capillary endothelial cells in brain have tight junction and lack pores or gaps. Surrounding the tight overlapping endothelial layer is a continuous basement membrane. The basement membrane is enveloped by peri-vascular foot process formed by astrocytes, which cover 85% of surface area of brain capillaries-together these layers are called Blood Brain Barrier (BBB) It allow drugs having high / moderate lipid solubility to diffuse passively to CNS. Polar drugs will not penetrate . In Chemoreceptor trigger zone and posterior lobe of hypothalamus BBB is not seen.

17. Chelation----chelation is a process in which an organic compound combines with or binds with another substance usually a metallic ion. Such chelates are not very susceptible to dissociation and there fore the metallic ion is effectively removed from the biological medium. Metallic ion functions as catalysts or prosthetic agents for vital chemical process. It can produce profound effect in the body. Eg. chelation of Mg+ by tetracyclins, lead and calcium with EDTA salt. Some chelator binds with heavy metal ions render them biologically inactive and excreted by the kidney. Used in poisoning due to arsenic, mercury, lead, copper, iron etc. agents include dimercaprol, succimer, penicillamine, calcium disodium edentate, deferoxamine, deforiprone, etc.

18. Competitive antagonism (reversible antagonism)---- In competitive antagonism agonist and antagonist compete with each other for occupying the same binding site (active site) on the receptor. The interaction between the drug and receptor is due to formation of weak bonds. So the effects of one drug can be easily overcome by increasing the concentration of the second drug. Both agonist and antagonist have affinity for the same receptors but drug with high concentration occupies the receptors. Antagonist may posses almost similar structure or not . In the dose response relationship the competitive antagonist causes a parallel shift of the log dose response curve to the right . eg. atropine and acetyl choline on muscarinic receptor, Naloxone and morphine on opioid receptor.

19. Compartmental models for pharmacokinetic studies----- Drug movement within the body is a complex process . In order to describe the complex and overlapping pharmacokinetic process, certain assumptions have been made regarding the movement of drug and some pharmacokinetic models were developed to compute meaningful pharmacokinetic parameters . presently three types of models are used and compartmental model is one among this. Compartmental model – body is considered to be composed of several compartments. Each organ tissue or body fluid can form separate compartments. Generally one, two and three compartment- models are used to

describe kinetics of most drugs. These compartments are called open model because there is no restriction to the movement of drugs between compartments. In one compartment model whole body is considered as a single compartment. In two compartment models the central compartment is highly perfused organs (blood, liver, kidney, lungs, heart and brain) The peripheral compartment comprise of less perfused tissues like skin, muscles, bone, cartilage etc. In three compartment models one central and two peripheral compartments.

20. Glucuronide conjugation of drugs --- Glucuronide conjugation is the major proportion of metabolite of many drugs that contain a phenol ,alcohol or carboxylate group. Glucuronides hydrolyzed enzymatically in the intestine following excretion and subsequently reabsorbed prolong the action of the drug. Glucuronide-acetaminophen, Acetylation-Isoniazide, Glycine- Salicylic acid, Sulphate-steroids.

21. Cytochrome C-450---- The most important component of mixed function oxidase is the cytochrome P-450. –a microsomal superfamily of isoenzymes. The wide distribution of cytochrome P-450 containing mixed function oxidase CYP-450 can be induced or inhibited by many drugs and substances causing several drug interactions. It is normal on the basis of their cellular location and their absorption of wave length of light near 450 n.m. when the heme iron is reduced. seen primarilty in liver also found in intestine, lungs, kidney, brain etc.-consist of a number of isoenzymes.

22. Cytosolic tyrosin kinase --–activation leads to phosphorylation of janus kinase (JAK) (a form of tyrosin kinase present in the cytosol). Activation of JAK inturn phosphorylate signal transduction and activation of transcription (STAT) protein- phosphorylated STAT form diamers and move in to nucleus where they act as transcription factors.eg. growth hormone, prolactin, leptons and cytokins.

23. Darting (Remote injection)--- It is a special technique by which drug is administered with the help of a gun or arrow to non domesticated animals the advantage is i/m injection can be given from a distance without handling or restraining . The injection is made generally in to the rump or back of hind leg of the animals. For larger species the neck or shoulder muscles may also be used . The animals may get hurt either due to the excessive impact force or the dart, hitting the dart at a wrong site of animals.

24. Dialysis—-Dialysis may be described as the movement of an agent across a semi-permeable membrane. Haemodialysis, peritoneal dialysis and haemoperfusion are the important types. Haemo dialysis involves passage of blood from artery through dialysis membrane which is then returned to body via vein. In peritoneal dialysis an isotonic solution is introduced in to the peritoneal cavity and later withdrawn -- peritoneum itself serves as the dialysis membrane. Haemoperfusion involves passage through charcoal or some other chambers . Dialysis is useful when patient is in a comatose condition or in cases of renal failure, anurea, hypotension, hepatic failure, fluid and electrolyte imbalance, drug over dose, poisoning etc.

25. Disadvantages of oral route of administration- --a) Acidic environment of the stomach and digestive enzymes may destroy the drug . b) In ruminents the bacterial enzymes may inactivate the drug c) some drugs may irritate the GI mucosa d) the presence of food may adversely affect absorption e)may get first pass effect extensive metabolism by GI mucosa and the liver before

they reach the systemic circulation .f) Antimicrobials may alter the digestive process in ruminants and other the curve

26. Disadvantages of parenteral routes--- Asepsis is necessary, causes pain, may penetrate a blood vessel during i/m injection. The speed and onset is so rapid with i.v administration so that cardio vascular response may occur to drugs. In food animals discolouration of the meat or abscess formation may occur to i.m. injection.

27. Dose response relationship ---It is the relationship between dose and effect- as the dose change effect also change . when this is plotted on a graph two types of curves will be obtained 1) Graded 2) Quantel. In graded type- response increase with increase in dose and reduce with decrease in dose. Most drugs falls in the category –mostly seen in individuals- eg. contraction or relaxation of smooth muscles, change in blood pressure –Dose / response when plotted on an ordinary graph paper curve will be parabolic and on a log paper it become sigmoid in shape . In quantel relationship involve all or none response. Increasing the dose of a drug response is either produced or not.eg. in blood coagulation, death etc. this type of response is seen in a population- if plotted a sigmoid curve will be obtained. A linear curve will be obtained when log dose probit response is ploted.

28.Down regulation of receptors---- Process of decreasing the quantity of receptors or protein in response to an external variable, result in diminished drug effect , usually seen when exposed continuously to an agonist causing their over activation. In such situation drug receptor complex on the surface of the cell undergoes endocytosis and subsequent metabolism. When this process occur faster than synthesis of the receptor the total number of cell surface receptor is reduced – refractoriness to drug is developed – an example for locally acting negative feed back mechanism . Down regulation is particularly exhibited by the tyrosin protein kinase receptors. . continuous exposure to hormone insulin , adrenergic Alpha and Beta receptors also shows down regulation.

29. Drug affinity and efficacy--- Affinity is the ability of the drug to combine with its receptor- high affinity drug binding results from greater intermolecular force between the drug and its receptors low affinity drug binding involves lesser inter molecular force. Efficacy (or intrinsic activity) molecular or receptor site occupied by the drug refers to the relative ability of a drug to evoke a pharmacological response. On combining with receptors high affinity drug produce maximal response while occupying a relatively low proportion of the receptors in that system. Low affinity drug may not be able to produce the same maximal response even when they occupy entire receptors.

30. Drugs and Cosmetic rules 1945--- The important schedule applicable to vet. are- Schedule D- substances not intended for medicinal use. E- Poisonous substances must have a label “Poi son” . F-Provision applicable to the production of vaccine , toxins, antisera etc. G-Labeled with the word “caution” it is dangerous to take the preparation except under medical supervision. H-not sold in retail except on prescription of a registered medical practitioner. L-specific substances contained in the preparation- shall not sold by retail except on prescription. M& T – requirement of factory premises. N- Minimum equipment for efficient running of pharmacy. P- Life period of drugs. Q- List of coal tar colour permitted to be used in cosmetics. R- Standards for medicinal contraceptives. S- Standards for cosmetics.

31. Drug dependence--- Is a state produced by repeated use of a drug. The use may be necessary for psychological or physical well being of the individual –mainly seen in human beings who continuously use mood or behaviour altering drug.(ethanol, cigar) for non –medical or recreational purpose. Certain therapeutic agents also(eg. analgesic, antihypertensive, hypnotics.)which are continuously taken for longer period . in psychological dependence individuals believe that his well being is achieved only through the action of a drug although the drug is not essentially required by the body. Withdrawal symptoms include anxiety, anorexia, insomnia and depression but no abstinence syndrome eg. cannabis, LSD, mescaline. Physical dependence is a physiological state in which individual is depended upon drug for normal physiological syndrome. Eg. opium it can be reduced by slow withdrawal of drug for a long period.

32. Drug standards and regulation---The preparation and sale of medicine is regulated by special laws which are intended to establish and maintain standards of purity, quality, uniformity etc. It is enforced by Food and Drug Administration (USA). Drugs and cosmetic acts are there . The standards and regulations are recommended by a number of professionals of Medicine, Veterinary, Dentistry, Pharmacy etc. These standards are found in United State Pharmacopoeia (USP), National formulary (NF), British Pharmacopoeia (BP), Indian Pharmacopoeia (IP), British Veterinary codex(B.VET.C)now BP.Vet, French codex(FC) etc. National formulary by pharmacist , for new drugs which are produced in preceding 10 years American medical association for drug evaluation gives the details.

33. Drug schedules--- Controlled drugs (which may be abused) are classified in to different groups coming under different schedules.

Schedule I. Drugs having high abuse potential-eg. Heroin, LSD, Marihuana etc. not easily available obtained only for research.

Schedule II. High abuse potential, produce severe psychic and physiological dependence eg. Opium, Morphine, Codeine, Cocaine.

Schedule III. Less abuse, less physiological dependence, high psychological dependence, Preparations containing limited amount of of opium , morphine, codeine etc.

Schedule IV. Less abuse- Diazepam, Phenobarbital etc.

Schedule V.Less abuse- other narcotics.

34. Drug receptor theory of drug action---- They concept of drug receptor theory credited to Paul Ehrlich and John Newport Langley. This theory explained the specific action of a drug with a single receptor using a Lock and Key analogy. The structure of the drug (key) is related to the correlative structure of the receptor (lock) . Only correctly sized key can fit in to one lock so also one drug is specific for one receptor type .Large smaller or incorrect teeth on key (incorrect drug or sized drug molecule) do not fit in to key hole (active site)of the lock (receptor)and can not open the lock (initiate action)

35. Drug interactions---- Is a process of affecting the activity of a drug by another agent interaction may occur between two drugs, between drug and food, between drug and herb. In practice this

term is used for interaction between two or more drugs in quick succession. It affect the outcome of therapy –mostly occur out of accidental misuse of drug or due to lack of knowledge of pharmacological action of ingredients. The mechanism of drug interaction is either pharmacokinetic or pharmacodynamic of one or both drug because of the presence of other drugs. Four types of interactions are there Addition, Potentiation, Synergism, and Antagonism. When the combined effect of two drugs is equal to the sum total of the effect of each drug given alone is called addition. When one drug having no effect of its own increase the effect of another drug is called potentiation. When combined effect of two drug is greater in magnitude than the sum of the effect of each drug given alone the interaction is called synergism. When combined effect of two drug is less in magnitude than sum of the effect of each drug given alone or when one drug having no effect of its own decrease or inhibits the pharmacological effect of other drug it is called antagonism.

36. Drug transport--- Drug are transported by diffusion, filtration, active transport, facilitated diffusion and pinocytosis. A) Diffusion- is most important –means of drug passage across biological membranes. The drug present in aqueous medium at one side of the biological membrane dissolves in lipid phase of the membrane and finally leave it by dissolving in aqueous medium at the other side of the membrane. Simple diffusion is meant for lipid soluble substance . The un ionised drug also penetrate biological membrane by diffusion -the driving force is the concentration gradient across a biological membrane. B) Filtration- simple passage of drug through pores or channels in the membranes. Many small polar / non polar substances can pass by this- the driving force is hydrostatic pressure. Bulk fluid movement carrier or drugs solute molecule through this process in the moving direction. Large molecule can not pass via this. C) Active transport; is energy depended transport system. Solute take the help of carrier to cross the barrier- Carrier is a membrane protein binds reversibly with solute. Transport occur against a concentration gradient hence require energy. D) Facilitated diffusion ; carrier mediated transport operated along the concentration gradient. No energy is required. E) Pinocytosos : a minor mechanism- engulfing extracellular drug droplets with in a segment of the cell membrane to form vesicles or saccules- pinched off and transported across cell membrane and release the engulfed substance.

37. Ebers papyrus---- Famous ancient Egyptian document written about 1550 BC. It is found in a tomb of a mummy in Thebes and is now preserved at the university of Leipzig Germany- contain information about a number of diseases and some 700 formulations and remedies. Included chapters on diagnosis of pregnancy, contraception, and other gynaecological matters, intestinal diseases, Parasites, skin and eye problems, dentistry, surgical treatment, bone setting , burns .various prescriptions including those of castor oil, opium, colchicum and some other drugs mentioned are still in use.

38. Elimination half life (t ½) ----half life is the time taken for the concentration of the drug in plasma to decline by one-half or 50 % of its initial value (time required for the body to eliminate half of the drug) this is determind during the elimination phase of a drug therefore it is also called elimination half life. T1/2 is inversely related to the elimination rate constant Beta. It can readily obtained from the Beta – slope of the plasma drug concentration –time profile . the elimination half life can also be obtained from clearance (Cl).

39. First pass effect/ first pass metabolism/ pre-systemic metabolism--- Is the loss of drugs through biotransformation before it enter systemic circulation-occur while passing through intestinal or liver

for the first time after oral administration. Intestinal first pass effect, metabolism take place in the G.I tract by enzymes present in gut mucosa or lumen before they absorb –microbs in G.I tract also can inactivate some drugs. In hepatic first pass effect metabolised in liver before enters in the circulation.eg. lidocaine, nitroglycerine, propranolol. These drugs are not suitable for oral administration.

40. Factors related to drug which modify the action of drug--- A) nature and type of dosage forms-liquid forms are fastly acting than tab.form or powder. B) type of salt form- various salt form vary in their absorption and bioavailability eg,novobiocin sodium salt is 2.5 times more bioavailable than its calcium salt. C) Formulation and vehicle effect- different formulations of same drug vary in their action. Including of excipient greately influence the action – macromolecular gums reduce the absorption of drug. D) Physico-chemical property of drugs like solubility and dissolution rate , degree of ionization, particle size affect absorption.

41. Factors related to subject which affect drug action ---A) species-eg. rabbits can tolerate large dose of atropine. B) Breeds- Grey hounds are more susceptible to thio barbiturates. C) strain-different strains of white mice vary in barbiturate metabolism. D) sex – females rats are more susceptible to red squill. E) age- young ones and very old patients are more susceptible to toxic action of drugs. F) pregnancy- enhance the metabolic rate of many drugs. G) lactation-some drugs are excreted with milk. H) hormonal status- increase thyroxin stimulate cytochrome P-450. I) body weight- dose is depended on body weight. J) genetic factors- glucose 6 phosphate dehydrogenase deficiency cause more susceptible to the haemolytic effect of drugs. Other factors include nutritional status, Emotional status, Tolerence, Individual variation, disease etc.

42. Factors affecting drug disposition in topical application --- A) thickness of the stratum corneum. Drug movement is difficult when the stratum corneum become thicker , enhanced by application in areas where the epidermis is thinner like axial, inguinal region, and abdominal region B) Intergrity of the stratum corneum -damage like aberrations ,will reduce the effectiveness of the barrier function and increase the drug absorption. C)Alterations in physiological behavior- Desqumation is an important factor in epithelial turnover. Inflammatory diseases ,metabolic disorders, and familial conditions such as familial seborrhea, may alter the desquamation of keratinocytes. Which will alter the disposition of drugs. D) Temperature-- increase temperature of the skin will allow for enhanced absorption of most drugs by increasing the solubility of the drug and increasing vascular flow to the area.

43. First order kinetic (linear kinetic)--- It is a pharmacokinetic process whose rate is directly proportional to the concentration of drug ie greater the concentration faster the process. A fixed fraction of drug is eliminated per unit time. First order process is said to follow linear kinetic ie log-plasma concentration time curve is linear. Most drugs follow first order kinetic in absorption, distribution , metabolism and excretion.

44. Functional antagonism (physiological antagonism)--- occurs when two drugs counterbalance (neutralise) each other by producing opposite effects on the same physiological system. Here two drugs are active on two different systems or receptors and produce pharmacological response in opposite directions. Eg. Acetyl choline act on muscarinic receptors and reduce heart rate . epinephrine act on adrenergic receptors on heart to produce increase heart rate. If give together neutralise the effect.

45. Flavanoids ---- Vitamin –P),vitamin for permeability, A veriety of naturally occurring substances possess vit. P activity. Later identified chemically as derivatives of flavones. Members of this group together is called flavonoids . Three of the compounds rutin, quercetin and hesperidin are insoluble yellow pigment that are widely distributed in the fruits and green leaves of plants . Flavonoids directly constrict the capillaries and decrease the permeability and the fragility of the vessels. It form an oxidation reduction system. Block the metabolism of epinephrine. Anti oxidant in action, anti cancer action.

46. GABA receptors ---GABA receptors are ionotropic receptors and ligand gated ion channels. Endogenous ligand is Gama amino butyric acid –major inhibitory neurotransmitter in the CNS. GAB A receptors are blocked by picrotoxin and bicucullin and direct activation of ion channels binding to receptors triggers opening of a chloride ion selective pore . increased chloride conductance drives the membrane potential towards the reversal (-75 mv)inhibiting firing of neuron and action potential. Flumazenil is the antagonist. GABA B receptors are metabotropic transmembrane receptors for GABA that are linked via G protein to potassium channels-the changing potassium concentration hyperpolarise the cell at the end of action potential. One of the agonist is Baclofen-

47. Gastric lavage ---- is washing the stomach with water or a solution. it is a rapid and useful way of removing the poison from stomach –performed when emesis is not possible . A tube equivalent to the distance from the tip of nose to the last rib is inserted in to stomach. After insertion the head is lowered to a 30 degree angle and the fluid is first flushed in to stomach at the rate of 10 ml/kg and removed by gravity flow or application of suction pressure. Repeated several times until the fluid is clear. It is useful in small animals up to 4-6 hours after ingestion of a poison. Tepid water, isotonic sod. Chloride, p.p . lotion (1:2000) weak iodine solution 1: 250 of 5 %, tannic acid solution, sodium bicarbonate etc. can be used.

48. Gene therapy --- Is a genetic engineering technique in which a DNA is used as a drug to supplement or alter defective genes responsible for disease development .Two important types are there. Somatic gene therapy and germ-line gene therapy. In somatic gene therapy the therapeutic gene are transferred in the somatic cells or body of patients. The modification in the genes and therapeutic effects are restricted to the individual patient only and not inherited to the later generation. In germ line gene therapy the germ cell is sperm or eggs are modified by the introduction of functional gene which are integrated in to their genomes . This allow the therapy to heritable and passed on to later generations. Somatic gene therapy currently applied in three categories Ex-vivo, in situ, in vivo. In ex- vivo – cells are removed from the body incubated with a vector and then gene – engineered cells are returned to body – usually done with blood cells- used to treat sickle cell anaemia. In in situ vector is directly placed in to the affected tissue used for infusion of adenoviral vector into trachea and bronchi of cystic fibrosis patients, muscular dystrophy patients. In vivo gene therapy vector is directly injected in to the blood stream.

49. Graded dose response relationship. Graded dose response relationship is measured in individual animal or tissues increased with increase in dose and decrease with reduction in dose. Most drug response fall in this category. Eg. contraction and relaxation of smooth muscles. The effect is proportional to the fraction of molecular or receptor site occupied by the drug. When a graded dose response is ploted on a simple graph paper-dose response curve assume a shape of parabolic with its origin at zero on both axis. when plotted on a semi log paper the curve become

sigmoid . From the curve some parameters like threshold dose ceiling dose, ED-50 etc. can be obtained..

50. Gums ---Amorphous transparent substances- polysaccharide dissolved in water to form thick mucilaginous colloid solution- sticky in nature, pharmacologically inert. In solution it can be used as emulsifying agent, as a protective and suspending agent for solids- do not hydrolyse and absorbed orally – take some water and helps in evacuation of gastro intestinal content.

51. Glycosides--- Glycosides are Plant active principles-are combination of sugar with other organic substances of plant origin, may or may not contain nitrogen-acids do not form salt with this but hydrolyzed in to sugar (glycon) and non sugar (aglycon or genin) . Aglycon is the active ingredient and glycon helps to penetrate in to the cell eg.Digitalis glycoside. They are neutral in reaction, soluble in alcohol- less soluble in water. Some glycosides , following enzymatic hydrolysis produce HCN (Cyanogenic glycosides) which is highly toxic.eg. amygdalin in tapioca leaves. Glycosides having specific action on heart is known as cardiac glycoside eg.Digitalis.

52. Gq proteins ---Gq proteins coupled to phospholipase C beta ,which increases the formation of inositol 1,4,5 –triphosphate (IP3) and diacylglycerol (DAG), IP3 elevate intracellular ca++ concentration by increasing Ca+release from the endoplasmic reticulum and Ca2+ influx through store – operated calcium (SOC) channels. DAG activate protein kinase C which phosphorylate cellular constituents.Eg. oxytocin , muscarinic M1 andM3 agonist, Alpha 1 adrenergic agonist, bradykinin.

53. G i/o protein ---G i/o protein couples negatively to adenylcyclase thereby decreasing the formation of cyclic AMP. In addition Gi/o protein can close Ca2+ and open potassium channels Eg. Alpha-2 adrenergic agonist, M2 and M4 muscarinic agonist , D2, D3,D4 dopaminergic agonist , GABA agonist, somatostatin etc.

54. Guanylyl cyclase ----protein kinase G- Guanylyl cyclase catalyzes cyclic GMP formation from GTP. The plasma membrane receptors of atrial natriuretic peptide (ANP) and guanylin have guanylyl cyclase activity . In addition nitric oxide (NO) can activate cytosolic guanylyl cyclase . cGMP activate protein kinase G, which mediates many effects including closure of sodium and calcium channels, opening of potassium channels.

55. Gs proteins ---Gs protein receptors: G protein may couple stimulatory response as well as inhibitory response. Each cell may have more than one G protein types. In general there are three G proteins Gs, Gi/o,Gq. Gs –protein couples to adenyl cyclase which increase the formation of cyclic AMP. C AMP activate protein kinase A, which phosphorylates cellular constituents. eg. Glucagon, glucagon like peptide, D1, D2 dopaminergic agonist, 5 HT agonist, gonadotropin, thyroxin, ACTH, Beta adrenergic agonist.

56.Habituation and addiction --- Habituation is a condition produced due to repeated consumption of a drug where there is a desire but no compulsion to continue taking the drug or increasing the dose. No abstinence syndrome in case of habituation. Addiction is a pathological or socio-behavioural abnormality condition where there is a strong carving and compulsion to continuous taking the drug despite its dangerous effect on the body. Drug dependence not necessarily leads to addiction. Antidepressants , antihypertensive , antihistaminics all produce physical dependence

with withdrawal syndrome but there is no strong motivation to continue the use of these drugs. Addiction can also occur without appreciable physical dependence eg. Cocaine. Habituation is primarily detrimental to the individual but addiction is to the individual and to the society. Opium produce strong addiction.

57.Henderson –Hasselbalch equation-----most drugs are weak acid or weak base and exist in physiological solution in both ionised and un ionised form . Both forms depend on pH of the fluid in which it dissolve and pka of the drug. (negative log of dissociation constant).when pH of the fluid is same as pka value of the drug the ratio of unionised to ionised form is 1:1 (Pka is numerically equal to the pH at which drug is ionised 50%) The degree of its ionisation depends primarily on the pH of the medium. It depend on H and H equation- For weak acidic drugs: Pka-pH=Log con.of unionised drug/ionised drug.(% ionised drug =100/1+ antilog (pka-pH) . For weak basic drug : PH –pka + log con. of unionised drug/con. Ionised drug(% ionised drug = 100/1+ antilog (pH-pka). There are exceptions for H and H equations.

58.Hydrolysis of drugs --- is the cleavage of drug taken up by water molecule eg. Ester and water to form acid and alcohol – cholinesterase. Ester such as procaine are hydrolyzed by a variety of non specific esters in liver, plasma, G I tract and other tissues. Hydrolysis of amides such as lidocaine can occur in blood vessels, liver , proteases and peptidases in plasma , RBC and many other tissues for hydrolysis of poly peptide.

59. Hypersensitivity /allergic reactions --- Immunologically mediated untoward drug effects which are unrelated to the pharmacodynamic profile of drugs- not dose related – severe manifestations even for minute amount of drug. Drugs can act as incomplete antigen or haptens –become complete antigen in combination with body protein. First exposure leads to sensitisation to the drug and subsequent exposure result in allergic reactions (a latent period of 1-2 weeks is required after the first exposure) . Chemically related drug often show cross-sensitivity . target organ for drug allergy are skin, respiratory tract, G.I. tract, blood . Allergic reactions are reversible if not very sivere.

60.Idiosyncrasy----- Qualitatively abnormal reactivity of an individual to a chemical, that has no obvious relationship to either dose or duration of therapy- unrelated to pharmacological profile of drug- occurs only in a small population of individual. Some evidence suggests that the reactions have metabolic basis involving drug metabolism. Studies showed that during therapy the tissue become peculiarly susceptible to adverse effect leading to idiosyncratic reactions- which are harmful and some time fatal even with low dose. Occur more frequently with exposure to new drug as they have not fully tested for their side effects. Many drugs precipitate idiosyncratic reactions. Eg. chlorpromazine causes rhabdomyolysis (breakdown of striated muscles) and liver toxicity in humans. Halothane produce malignant hyperthermia and hepatitis, sulphonamide produce haemolytic anaemia in some individuals.

61. Iatrogenic disease (physician induced disease) ---are drug induced-- happen occasionally during the course of therapy or after the termination . generally occur due to alteration in the concentration of some endogenous substances (hormone, neurotransmitters) persist even after the withdrawal of the drugs. It may include various nosocomial disease.(acquired in hospital) and those induced by medical negligence, medical error or misjudgement. Use of drugs without observing contraindications eg. Parkinson syndrome due to prolonged use of phenothiazine, gastric ulcer by NSAIDs , fluoroquinolone produced cartilage destruction in young ones.

62.Intracellular receptors ----Steroid hormones (including vitamin-D),thyroxin (T3)binds to these receptor proteins. Corticosteroid receptors are in cytosol and the receptor for other steroid hormones and T3 are in nucleus. Activated receptor proteins form diamer and move to the promoter region of the DNA altering transcription process.

63. Intrinsic activity / efficacy --- is the relative ability of a drug to evoke a pharmacological response on combining with the receptor .High efficacy drug can produce maximal response even by occupying low proportion of the receptor . While low efficacy drugs will not produce the same maximal response even by occupying all the receptors

64. Inverse agonist ---- Inverse agonist is a drug that interact with the same receptors as the agonist but it produces response opposite to that of the agonist. Inverse agonist has affinity but possess intrinsic activity with a minus signs. Eg. Dimethoxy ethyl carbomethoxy B-carbolin produce stimulation , increase muscle tone and anxiety acting via $GABA_A$ receptors, the stimulation of the same receptor by diazepam produce muscle relaxation, sedation and anxiolysis.

65. IP3 as a second messenger ----- I P3 – DAG system is an important intracellular second messenger in which the effector protein is a membrane bound phospholipase –C . Activation of this hydrolyse membrane phospholipase phosphatidyl inositol 4,5 biphosphate to generate 2 second messengers . Inositol 1,4,5 triphosphate (IP3) and diacyl glycerol (DAG)- IP3 migrate to cytosol and causes Imobilisation of calcium (3^{rd} messenger). Increase free calcium ion intra-cellularly produce a range of cellular responses including modulation of ion channels, enzymes and contractile protein. DAG is another second messenger facilitate translocation of protein kinase from the cytosol to the plasma membrane and its activation which in turn control many cellular functions by phosphorylation of a variety of intracellular protein.

66. Ion channels ---- An ion channel is a space or pathway through the cell membrane which allows free movement of a specific ion like sodium, potassium, calcium or chloride. Two types are there voltage gated and ligand gated channels. Voltage gated ion channels include sodium channels, calcium channels and potassium channels. Some of the examples for inhibitors of voltage gated sodium channels are local anaesthetics, anti arrhythmics and anti epileptics. Voltage gated calcium channels are seen in skeletal muscles, osteoblasts, ventricular myocytes etc. Voltage gated potassium channels associated with sulphonyl ureas , glibenclamide . The action of ionotropic receptors is similar to that of voltage gated ion channels, but they open and close in response to a ligand and not to the membrane potential. eg. GABA, Glycine receptors . NMDA receptors.

67. Ion trapping --- the principle of ion trapping is that ionized compounds do not readily travers cell membrane and not distributed to target site and subsequently not reabsorbed by the renal tubule. It is more useful for enhancing excretion of poison and then altering their distribution. Alteration of urine pH is a useful method of preventing renal re absorption of poison which undergoes glomerular filtration and passive tubular re absorption. The ion trapping is carried out with the help of an appropriate urinary acidifier or alkaliniser and is clinically useful for enhancing the excretion of many weakly acidic or basic compounds from body. Eg. Acidic agents like aspirin, paracetamol, and barbiturate more effectively ionised and excreted in alkaline urine conversely basic agents like amphetamine and most alkaloids are more effectively ionised and excreted in acidic urine

68. Kinase linked receptors--- (Receptor with tyrosine kinase activity) Some hormones ,insulin (reserve receptors)and certain growth factors have tyrosin kinase as a part of plasma membrane receptors. Insulin receptors is used as an example to explain how the tyrosine kinase receptor works. The activated insulin receptor (tyrosin kinase) phosphorylate its substrate (insulin receptor substrate),(IRS-1-4)Activated IRs is thought to phosphorylate a number of cellular constituents including phosphor inositol 3 kinase. (PIB Kinase) which can activate other cellular proteins including glucose transporter -4 (GLUT 4)in the skeletal muscle cells and adipocyte, leading to increased glucose transport in to these cells.

69. Ligand gated ion-channels (ionotropic receptors)---- are cell surface receptors –enclose ion selective channels (Na,K,Ca, CI) which are opened or closed in response to the binding of a chemical messenger do not involve any second messenger . The action of ionotropic receptors is similar to that of voltage gated ion channels which opened and close in response to ligand and not to the membrane potential. The direct link between ligand binding and opening or closing of the ion channel is also in contrast with the indirect function of metabotropic receptors which use some intermediary substance such as G-protein or second messenger to open the channel. The ionotropic receptors are located primarily in nerve synapse. Eg of ionotropic receptors nicotinic cholinergic receptors, glycine receptors, GABA a receptors, NMDA receptors.

70.Liposomes ---- minute vesicles consisting of one or more encapsulated compartment formed by one or more phospholipid bilayers. The water soluble drug molecules are incorporated in the aqueous compartment of liposomes and the amphiphilic and lipophilic molecules are solubilised with in the phospholipid bilayer according to their affinity towards and the phospholipids. Liposomes are available in different sizes . (25-5000 n.m) and are administered by parenteral routes. Liposome carrier system take the drug across cell membranes to the target site or areas not normally accessible to the free form of the drug. Liposomes themselves are biodegradable ,non-toxic and immunologically inert .major application of liposomes is in the application of antineoplastic agent.

71. Microsomal enzymes----- a veriety of enzymes located within the lipophylic membranes of the smooth endoplasmic reticulum of liver and other tissues. The endoplasmic reticular enzymes are called microsomal enzymes. When endoplasmic reticulum is isolated and centrifuged SER membrane reformed in to minute vesicles called microsomes . All enzymes present in microsome is microsomal enzymes-catalyze glucuronide conjugation, most oxidative reactions, some reductive and hydrolytic reactions. The monooxygenase and glucuronyl transferase are important microsomal enzymes can be induced by drugs, diets and other factors.

72. Nano shells and bucky balls---- Nano shells are spherical nano particles consisting of a dielectric core which is covered by a thin metallic shell (usually Gold) –called gold shelled nano particle with silica and or liposome cores- used in cancer therapy and bio imaging . Nano particles have binding sites on them to attach to cancer cells. These are shuttled in to tumors by the use phagocytosis- after this it is shuttled in to a cell . Once the nano shells are at the necrotic centre- near infrared illumination is used to destroy the tumour associated macrophages. Another example for nano shell plasmonics in cancer treatment involve placing drugs inside of the nanoparticle and using this as a vehicle to deliver toxic drugs to cancer sites only. this is accomplished by coating the outside of a nanoparticle with iron oxide (allowing for easy tracking with an MRI mechine) once the area of the

tumour is coated with the drug –filled nanoparticlle this can be activated using resonant light wave to release the drug. Bucky balls: also called as fullerenes –one of the first nanoparticle discovered-composed of a carbon atoms linked to other carbon atoms by covalent bonding. It has a cage like fused ring structure that resembles a soccer ball (foot ball)–in a molecule of carbon in the form of a hollow sphere ellipsoid tube and many other shapes. Resembles foot ball. cylindrical fullerenes are also called carbon nanotubes.

73. Non-competitive antagonist (NCA)/ irreversible antagonism ---the antagonist forms strong bonds (co-valent) with its receptors and irreversibly blocks it. Therefore antagonist can not be displaced by the agonist even when its higher concentration is used . The NCA generally binds to a distinctly separate binding site (allosteric site) from the agonist and may prevent the conformational changes in the receptor required for receptor activation after the agonist with reduced efficacy. Eg. phenoxy benzamine and epinephrine at alpha adrenoceptors. The affinity of the agonist is thus unaltered but its efficacy is reduced. The log dose response relationship shows flatter curves

74. Orphan receptors---- these receptors have similar structures to other identified receptors but for them the endogenous ligand has not yet been identified or synthesised. These types of receptors are generally synthesized by cloning of a conserved segment of DNA molecule (that encode for receptors) and are utilized for search of a new endogenous ligand or drugs. If a ligand for an orphan receptor is later discovered the receptor is referred to as an adopted orphan receptor Orphan receptors are found in the G. Protein- coupled receptor and nuclear receptor super families.

75. Orphan drugs---- are pharmaceutical agents which have been designed specifically to treat rare medical condition. These are not developed in to usable medicine because the cost involved in their manufacturing is very high and is not likely to be recovered by the developer due to limited number of patients. Several countries are giving tax incentives to companies for the development of such drugs in the interest of the patients.

76. Oxidative metabolism of drugs---- Oxidation is the addition of oxygen or negatively charged radical or removal of hydrogen or positively charged particle . include-hydroxylation, oxidative deamination, oxygenation at C , N , S atoms, N or O dealkylation. It can take place in liver involving cytochrom P-450, haemoprotein, NADPH and oxygen. Several P-450 differ in affinity to different drug s like barbiturates, paracetamol and theophylline. Sulfoxidation- chlorpromazine, R-oxidation-guanethidine. N or O dealkylation- desipramine, Aliphatic and aromatic hydroxylation-phenobarbitone to phenytoin.

77. Parenteral nutrition(parenteral alimentation)---- feeding other than enteral route-method of getting nutrition in to body intra venously by-passing the usual process of eating and digestion. Digested nutrients are administered from a bag attached to a needle or catheter – given through superior venacava. Digested protein, carbohydrate, fat vitamins and minerals all are included. It is indicated in inadequate absorption resulting from short bowel syndrome, gastro-intestinal fistula, bowel obstruction, prolonged bowel rest, severe malnutrition, significant weight loss, hypoproteinaemia when enteral therapy is not possible.

Pharmacopoeias---- These are official book on drugs.-explain physical, chemical properties, test for their identification, potency of selected list of drugs and medicinal preparations-published under the authority of a recognised body. Generally constituted by law to ensure uniformity in composition

and strength of medicine. Drugs included in pharmacopoeia are called official drugs-others are called non official drugs. Many countries have their own pharmacopoeia. United state pharmacopoeia, Indian pharmacopoeia, British pharmacopoeia, European pharmacopoeia etc.

78. Phase –I drug metabolism----Non synthetic or non conjugative phase include reactions which catalyse oxidation, reduction and hydrolysis of drugs. Small polar groups like OH, NH2, SH ,COOH etc. are either added or unmasked . The resulting products undergoes phase II reactions / directly excreted. Phase I reactions result in activation / no change in activity Oxidative reactions are the most important one. –enhance hydrophilicity of drugs by introducing polar functional groups such as OH- enzymes involved are microsomal mixed functional oxidase (cytochrome P-450)or monooxygenase, non microsomal enzymes are also involved. Reduction reactions can also happen to drugs-opposite of oxidative reaction-usually convert inactive metabolite in to active drug- mostly seen in liver, kidney, intestine and plasma. Liver is the most important organ for biotransformation of drugs.

A.Oxidation. I. Microsomal oxidation a) side chain and aromatic hydroxylation eg.pentobarbitone. O –dealkylation eg.morphine, N-oxydation eg. acetaminophen, S-oxidation eg phenothiazine , Deamination or N-dealkylation eg. Lidocaine. Desulfuration eg.thiopental.

II. Non microsomal oxidation ;some chemicals are oxidized by cytosol or mitochondrial enzymes eg.Ethanol by alcohol dehydrogenase, Epinephrine by monoamine oxidase, theophylline by xanthine oxidase

B. Reduction. Enzymes are microsomal or non microsomal. Reduction of chloramphenicol and naloxone.

C. Hydrolysis. Reaction occur with either ester or amide linkage . Esters are found in plasma, liver, eg. Acetyl choline,procaine. Amides-non microsomal primarily in the liver- eg acetazolamide , lidocaine.

79. Phase II drug biotransformation ---Phase II. biotransformation (conjugation) may occur to a phase I metabolite or to a parent drug/ chemical. This involves the coupling of an endogenous chemical (glucuronic acid, acetate, glutathione , glycine, sulfate, or methyl group to the drug) Enzyme systems are present in the microsomes, cytosol, and in the mitochondria- species variation is seen. In cats often have a longer plasma t1/2 for drug undergoing glucuronidation. In dogs acetylation of aromatic –NH2 group is less affect metabolism of sulfonamides. Glucuronide metabolites may be eliminated via the bile, can be hydrolyzed by intestinal bacterial beta glucuronidase, releasing free drug(entero hepatic cycling) give long action.

80. Phase II controlled clinical evaluation of drugs ---Phase II trial are carried out in relatively large number (several hundred) of target animal spread over a period of several months to 2 years. Trials are extension of phase one but it is strictly controlled, closely monitored and mainly animal to ascertain safety and efficacy of the new drugs. In target species in disease condition . Toxicity and therapeutic usefulnes are carefully recorded and evaluated.

81. Placebo studies ---- Placebo is a pseudo drug identical in appearance with the drug being tested but is pharmacologically inert – widely used in experimental research. It can be used for

blind trial to minimise changes of bias. In human medicine use of placebo constitute a positive means to psychological therapy to satisfy the patients demand for medicine. Many chronic disease of humans which have a substantial psychogenetic element respond favourable to the placebo

82. Plasma protein binding of drugs ---- drugs will bound to plasma protein that is called bound form of drugs-this will act as a reservoir which supplies free drug whenever required. Bound form is reversible. Generally drugs bound to albumin, lipoprotein, glycoprotein and globulin. Acidic and neutral drugs generally bound to albumin, basic drugs bound to globulin. Protein bound drugs are non diffusible and so pharmacologically inactive.

83. Potentiation effect of drug interaction ---- When one drug is having no effect of its own increase the pharmacological effect of another drug, the interaction is called potentiation and the effect produced is called potentiative effect (1+0 = >1) the inactive drug may increases the concentration of other drugs at its site of action either by increasing its absorption or by reduce its elimination eg. carbidopa (dopa decarboxylase inhibitors) no action of its own enhances the central effect of levodopa by reducing its peripheral metabolism, probenacid enhances effect of penicillins by decreasing their renal excretion.

84. Pour –on and spot-on preparations ---- Pour-on is the application of a drug solution particularly an ectoparasiticide solution along the animals dorsal mid line behind the shoulders to the hipbones. In some case it is applied to the top of head and around the base or horns. Some preparation absorbed percutaneously and produce systemic action. Commonly used for the control of horn flies, lice and other arthropods of cattle and sheep. Spot-on application is similar to pour-on , but in this method the specified amount of drug solution is applied to a small area on the head or back. Spot-on treatment are commonly used for application of ectoparasiticides .

85. Primary and secondary active transport --- In primary active transport only one solute is taken by the carrier -energy is necessary .In secondary active transport two solute share a common carrier out of which one is driving solute (Na+, K+, Ca++) and the other is a substrate that is transport against concentration gradient . cell energy is utilized for the transport. The free energy of driving solute is thus utilized to transport the substrate when the substance move in the same direction of the driving solute the process is called co-transport or symport(eg. sodium co-transport glucose) and amino acid in the intestinal epithelial cells. When the substrate moves in the opposite direction of the driving solute it is called counter transport or anti port eg. sodium counter transport H+.

86. Principles of drug action ----1. Stimulation-enhance the activity of specialized cells –epinephrine stimulate the effecter cells innervated by adrenergic nerves. 2. Depression – Depressed the activity of specialized cells eg.Barbiturates. 3. Irritation- mild irritation may be used as a stimulant. 4.Demulcent-protective. 5. Osmotic effect- inj. of hypertonic solution, lymph lavage. 6.Replacement- tissue extracts in deficiency. 7. Chemotherapy- specifically toxic to invading pathogen.

87. Protective index (PI) ----- Protective index may be defined as the ratio between the toxic dose 50 (TD-50) and the effective dose -50 (ED-50) . PI= TD 50/ED 50). PI is similar to therapeutic index but concerns toxicity (TD-50) rather than lethality(LD50). Thus PI is a smaller ratio. The PI is useful in clinical condition where a side effect or an adverse effect is taken in to consideration and not the

lethality. Similar to T I a high PI is preferable than a lower value. A drug should be used if the P I is sufficiently greater (at least more than one) indicating that the benefit out weight the risk.

88. Proprietary name (brand name, trade name)--- brand name is a name given to a drug by the pharmaceutical firm which sells the drug ,need not be the manufacturer of that drug, .same drug can have different trade name by different firm. Non proprietary name is a short name given to a drug that is not subjected to trade mark rights-easy to speak and spell .

89.Quantal dose response relationship (All or none dose response) ----- is one involving all or none response –on increasing the dose of a drug the response is either or not-the effect can not be graded. Eg. death , blood coagulation . This type of DRR is seen in a population. The dose response curve is sigmoid in character. The curve is linear position between 16-84 % a small portion of the population at left and right side of the curve respond to low and high dose (hypo or hyper reactivity)To make the relationship linear the responses are converted in to probits (probability units) the curve can be used to calculate LD-50, ED-50, Toxic dose 50 etc.

90. Rate theory of a drug action ---- introduced by WDM Paton. The theory postulates that occupation of receptor alone is of not importance to the action of drug instead it is the rate of drug –receptor complex formation and rate of complex break down that determine the intrinsic activity of drugs. The greater the number of drug receptor complex formation in unit time, greater is the stimulus to the cells. However, for the sustenance of a response the complex formed has to be broken and remade. The more rapid the complex dissociation the more rapidly can new association take place. According to this hypothesis the agonist have high rate of association and dissociation. Antagonists make complex rapidly but dissociate very slowly.

91. Reduction of drugs---- reduction is removal of oxygen or negatively charged radical or addition of hydrogen or positively charged radical . Eg. Convertion of chloral hydrate to trichloro ethanol. Enzymes in the endoplasmic reticulam and cytosol of liver and other tissues can catalyse the reduction removal of nitro group-chloramphenicol. Cleavage and reduction of an azo linkage-prontosil.

92. Receptor occupancy theory --- describes the concept of agonist and competitive antagonist. The magnitude of response produced by a drug is directly proportional to the number of receptors occupied and the maximum response is elicited once all receptors are occupied at equilibrium. The theory was based on the presumption that drug exert an all or none action on each receptors . and that each occupied receptors deliver a constant unit response. This theory does not explain the action of partial agonist which are unable to elicit maximal response even after occupying all receptors . Modified form of this theory states that different drugs have different efficacies. A drug with high efficacy elicit a maximal response after occupying only a small proportion of receptors. Where as drug with lower efficacy has to occupy a greater proportion of receptor to elicit an equal response . partial agonist fails to produce maximal response even after occupying all receptors because of low efficacy. Efficacy is zero for antagonist.

93. Reverse tolerance ----reversal / suppression of the side effects of a drug or reduction of insensitivity caused after drug tolerance has been established . This occur after the use of an additional drug or abstinence from a drug for a period of time- seen with drugs like amphetamine.

As a result of this regular administration of some drug produce a quick decrease of side effects without loss of desirable properties.

94. Role of P-glycoprotein in drug excretion --- P glycoprotein is a transmembrane efflux pump which has a role in first pass clearance of some oral drugs found in biliary and renal tubular epithelia and play a role in the secretion of some drugs in to gut and renal tubule . This is found also in BBB and helps to expel the drugs from the CNS . Substrate for G-glycoprotein include azole antifungal agents, corticosteroids, opioids, digoxin, macrolide antibiotics, quinidine , cyclosporine etc.

95. Spare receptors (reserve receptors)--- are receptors which remain unoccupied (free) during elicitation of the pharmacological response by an agonist. Highly active drugs (eg.epinephrine) require only a small fraction of receptors to produce their maximum response. In such situation a large number of receptors remain unoccupied at therapeutic concentration.

96. Specialised drug delivery system----- Several specialised drug delivery system /devices have been developed to deliver the drug specifically to site of action. Targeted delivery to avoid flactuation in plasma drug level (controlled release) to achieve greater efficacy, to overcome cellular barrier and enzymatic degradation or to minimize toxic effect. Various specialized drug system or formulations are available for application on skin (transdermal delivery system) parenteral injection. Eg.needle free injection and administration by oral route (eg. sustained release capsule and enteric coated tablets) some other drug delivery systems such as liposomes microparticles and nanoparticles are highly selective in the releaseof drug to the target site.

97. Species variation of drug action---- The action of various drugs vary with species. a) Xylazine is a potent sedative in cattle than other species, more sensitive to alpha 2 agonist because ruminants have alpha 2D receptors and non ruminants have alpha 2 A receptors. Ruminants are highly sensitive to the depolarizing muscle relaxant succinyl choline but horses are not because the esterase level is low in ruminants. b) Morphine is more potent in cats than in dogs –higher dose in cats may produce excitation mediated by central dopamine receptors, Cats have a low level of glucuronyl transferase hence drugs which require conjugation for elimination may have longer duration of action and toxicity. c) Greatdane and Irish Setter breeds of dogs are more sensitive to bloat following xylazine administration due to aerophagia. d) Ivermectin can cause CNS depression in Collies at normal dose because of defective P-glycoprotein transporter. Ivermectin is toxic in tortoise and crocodiles.

98. Species variation in drug metabolism--- Cattle and horse have generally have shorter t ½ value than dogs and cats because cattle and horse oxidizes drugs more effectively. In ruminants the cholinesterase level is lower than human or horse . The t ½ value for human is generally longer than animals (except cats) which have longer ½ life . The oxidation of drug by C 450 in domestic animal is faster than human beings –exceptions(,eg. Methyl xanthenes in horse and phenyl butazone in cattle). Between closely related species also difference is there. Trimethoprim and sulphamethazone have shorter half life in goats than sheeps. Between different species of birds also significant variation is there.

99. Synergism ----- when the combined effect of two drug is greater in magnitude than sum of the effect of each drugs given alone. The interaction is called synergism and the effect produced is

called synergistic effect.(1+1 is >2.) The synergistic effect is produced mainly when two drugs used together have same or similar effect and they increase each othe's action At the site of action. Eg. both carbon tetrachloride and ethanol are hepatotoxic. Together they produce much more injury to the liver than expected from the mathematical sum of their individual effect. Sulphamethoxazole and trimethoprim are bacteriostatic but their combination produce synergistic bactericidal effect.

100. Synthetic reactions --- It involves a) conjugation of drugs Glucuronide conjugation – chloramphenicol, aspirin, morphine steroid hormones. b) Acetylation amino or hydrazine residue are conjugated with the help of acetyl co-enzymes- eg. Sulfonamide, isoniazid, PAS. c) Methylation- amino and phenols can be methylated. d) Sulphate conjugation – phenolic compounds and steroids. e) Glycine conjugation- salicylate f) Glutathion conjugation. g) Ribonucleoside synthesis- for activation of many purine and pyramidine, anti metabolite in cancer therapy.

101. Standard margin of safety ---It is (LD 1/ED 99-1) x100 shows the percentage by which the ED 99 (the dose active in 99% of the population) must be increased in order to cause toxic effect in 1% of the population. For eg.100 mg cause toxicity in 1% of the population and 10 mg is effective in 99% of the population. Then the margin of safety is 100/10-1 x 100 =900, ie the dose that is effective in 99% must be increased to 900% (9 times) in order to be toxic to 1% of the population.

102. Standard safety margin ---more conservational measure of a drug safety than the therapeutic index and is used to relate the therapeutic effect in all animals without the risk of producing hazardous effect. The standard safety margin is the percent by which the ED99 must be increased before an LD is reached. Standard safety margin (LD1- ED99/ ED99) x 100.

103. Tachyphylaxis and Tolerance ---Tachyphylaxis is a phenomenon in which a rapid appearance of progressive decrease in tissue response following repetitive administration of a drug over a short period of time .increasing the dose of the drug will not increase the pharmacological response. Eg. repeated dose of Ephedrine causes tachyphylaxis. It is an indirectly acting sympathomimetic amine causes the release of NA from the nerve terminals producing the action- repeated dose cause a depletion of NA in the terminals to release resulting in decreasing the action-body has to synthesise fresh NA to show action which will take days.

104. Tannins --- Tannins are complex non nitrogenous phenolic compound which have an astringent action on the mucous membranes. Widely distributed in many species of plants –role is to protection from predation and growth regulation. Occurs mainly in leaves, root, bark and can cause precipitation of protein and exert an astringent action on mucous membrane possess irritant and bitter taste. Soluble in water – react with iron compounds to yield purple violet or black colour. Also precipitate metallic salt and alkaloids. Mainly 2 types pyrogallol tannins and pyrocatechol tannins.

105. Teratogenicity --- (dysmorphogenicity) It is the capacity of a drug to cause foetal malformation to pregnant animals. It may happen as a result of physiological and biochemical alterations in the formation of cells, tissues and organs resulting in abnormal development of organ system . Embryo development can be affected at any time during the whole period . exposure during organogenesis phase of gestation is most vulnerable period for foetal malformation. Should be avoided during the first trimester of pregnancy . eg. alkylating agent, antithyroid drugs, coumarins etc.

106. Therapeutic ratio -- (TR) It is defined as the ratio between the lethal dose 25 (LD-25) and the effective dose-75 (ED-75) , TR= LD 25/ ED 75. LD 25 is the dose that is lethal to 25% of the population ED-75 is the dose that is effective for 75 % of the population . TR is considered as a better index of safety of a drug as it includes slope of curve also. Shallow dose response curve usually have low therapeutic ratio. A flat curve is considered more toxic because the hyper sensitive groups are at much more risk than the hypo sensitive or normal group.

107.Tolerance ---is a gradual decrease in responsiveness to a drug , taking days or weeks to develop , cannot be demonstrated invitro experimentally. Reversible if the drug is discontinued for a period-multiple mechanisms are involved. Inductuion of microsomal enzymes(barbiturates)- activation of homeostatic mechanisms (vasodilator , antihypertensive) down regulation of receptors (opioid analgesic)

108. Trans dermal drug delivery systems --- Comprises medicated adhesive patch that delivers the contaminated drug at a predetermined and controlled rate in to systemic circulation via stratum corneum . Trans dermal drug application alter the drug kinetic and dynamic s with graded and continued absorption enhanced bio availability - longer duration of action and minimal side effects. TDDS by-passes the first pass effect. In veterinary Practice transdermal patches are used primarily in dogs and cats to deliver drugs like opioids.

109. Therapeutic index --- It is the ratio between lethal dose 50 (LD-50) and the effective dose 50 (LD-50) (TI=LD50/ED50.) LD 50 is the dose that is lethal to 50% of the population and ED 50 is the dose that is effective for 50 % of the population. TI is used widely for evaluating the safety and usefulness of drug. TI is The higher safer the drug. It is a valid comparison only if the ED50 curve and LD50 curves are parallel. If the dose response curve is shallower than therapeutic curve there will be decreasing safety at lower dose and thus hyper sensitive group will be at higher risk. Here the TI is misleading and in such case therapeutic ration is considered.

110. Tolerance is used to describe a gradual decrease in responsiveness (de sensitization to a drug) taking days or weeks to develop. An increase dose may elicit a maximal response.Multiple mechanism is responsible for the development of tolerance -eg. induction of microsomal enzymes by barbiturates develops tolerance to it, activation of compensatory mechanism for vasodilator drugs as anti hypertensive agents causes the development of tolerance to it

111. Volatile oils --- Volatile oils are also called as essential oils, aromatic oils, flavouring oils. They are diverse group of aromatic chemical compounds such as terpenes, alcohols, aldehydes, ketones ,esters and phenols. Produced by plants usually responsible for the odour of a plant and can be separated by steam distillation.-used for various medicinal purpose- mostly colourless liquid (Turpentine, eucalyptus) some are crystalline solids (Camphor, Menthol) Some of them sublimes on heating- less soluble in water- highly soluble many organic solvent. Evaporate on exposure to atmosphere.

112. Zero order kinetic ---(constant rate kinetic) defined as a pharmacokinetic process whose rate is independent of the concentration of the drug. The rate of pharmacokinetic process remain constant and cannot be increased further by increasing the concentration of drug. A fixed quantity of drug is processed per unit time. Eg. alcohol, phenytoin, salicylates. The half life of drug undergoing zero order elimination is not constant but is proporional to the concentration of drug in the plasma. Therefore the zero order half life rises with increase in drug concentration and decline with

decrease in concentration. Administration of drug by a constant rate i/v infusion or by controlled delivery system (eg. implants) also tends to follow zero order kinetic.

IV. WRITE ESSAYS ON:

1.Adverse effect of drugs.

2. Application of nanotechnology in modern drug development and delivery.

3. Biotransformation of drugs.

4. Explain the various mechanisms involved in Phase II biotransformation of drugs.

5. Classify receptor subtypes and illustrate the mechanism of signal transduction in any one of them.

6. Compartmental models for study of pharmacokinetics.

7. Describe the factors modifying drug action.

8. Drug interactions

9.Explain the plant active principles.

10. Explain in details the factors affecting the action of drugs –give appropriate examples

11. G-protein coupled receptors

12. Intracellular receptors and regulation of gene expression.

13. Kinase linked receptors.

14. Nanotechnology in targeted drug delivery.

15. Physico chemical factors that affects the transfer of drug across biologic membranes.

16. Receptor concept of drug action.

17. Signalling mechanisms in drug action.

18. Structural activity relationship and synthesis of new drugs.

19. Signal transduction in cells

20. Species variation in drug action.

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