**QUESTION BANK (VETERINARY PHARMACOLOGY)**

**PAPER NO. 21.**

**Autacoids**

**1.Name the following:**

1.A five hydroxyl tryptamine receptor antagonist.-( cisapride)

2.A drug which promote release of serotonin from platelets and neurons.-( para chloro amphetamine(4-chloroamphetamine))

3.Amino acid from which histamine is synthesized –(Histidine)

4.Angiotensin receptor antagonists .—(saralasin)

5.An enzyme which destroy histamine.-( histamine N methyl transferase)

6.An alkaloid with serotonin receptor antagonistic action.—( yohimbine)

7.An alkaloid which deplete 5 HT from serotonergic neuron .-( reserpine)

8.A mushroom alkaloid having serotonin receptor agonistic action.-( psilocin)

9.A drug which inhibits the release of histamine and other autacoids from mast cells. –( cromolyn sodium)

10.A selective 5-HT2 A receptor blocking agent.-( ritanserin)

11. An antagonist of 5-HT 3 receptor .-( ondansetron)

12.NK 3 receptor antagonists ( osanetant and talnetant)

13.One physiological antagonist to histamine.-( sympathomimetic drugs like epinephrine)

14.One kinin synthesis inhibitor .—( aprotinin)

15.One first generation antihistamine from piperdine derivative.-( cyproheptadine)

16.One second generation antihistamine from piperdine derivative.-(Loratadine)

17.One first generation alkylamine antihistamine.-(chlorpheniramine)

18.One kinin receptor antagonist .—( icatiban)

19.Prostaglandin which increase the affinity of the sympathomimetic amine to the adrenergic receptors.-( PG –E1)

20.Prostaglandin which relaxes bronchial muscles in asthma.-( PG-E1 and E2)

21.Prostaglandin which inhibit gastric acid secretion in dogs.-( PG-E1 and A1)

22.Prostaglandin which are effective in inducing abortion.-( PG-E2 and F2)

23.Scientists who noted the smooth muscle stimulant activity of human seminal fluid.-( Goldblat and Von Euler)

24.The first chemically derived fatty acid known to be pharmacology active.-(Prostaglandin)

25.The only monoamine neurotransmitter receptor that is known to function as a ligand gated ion channel.-(5-HT3)

26.The primary prostaglandins.-(PG - E and F)

27.The principal prostaglandin synthesized in mammalian renal medulla.-(E2)

28.The rate limiting enzyme in the synthesis of 5-HT.-( tryptophan hydroxylase)

29.Thromboxane A2 ( TXA 2) receptor antagonist .—( Ramatroban)

30.Two PGF 2 alpha synthetic analogue --(Etiproston,doprostenol)

31.Two peptide autacoids .—( bradykinin and kallidin)

32.Two serotonin receptor modifying drugs.-(cisapride, metoclopramide, cyproheptadine)

33. Two thromboxane synthase inhibitors .—( dazoxiben, pirmagrel)

34.Two inhibitors of eicosanoids receptors .—( montelukast and zafirlukast)

**II.State true or false**

1.Aliskiren and remikiren are rennin inhibitors.—( T)

2.Alpha –methyl histamine is an agonist on H3 receptor .\_(T)

3.Angiotensinogen is an alpha 2 globulin synthesized by the vascular muscles .-(F)

4.Angiotensin II causes release of PGE in to the venous blood from the kidney.-(T)

5.Angiotensin II regulate blood pressure , fluid and electrolyte balance.-(T)

6.Aprotinin is a polypeptide from bovine lung with kinin synthesis inhibitory action.—(T)

7.Approximately 90% of the serotonin in the body is found in the gastro intestinal tract in enterochromaffin cells.-(T)

8.Astemizole is a non sedative antihistamine withdrawn from market in several countries because of its action on H3 receptors.-(T)

9.Azapirone is a partial agonist of 5-HT 1A in brain.-(T)

10.Basophils contain small amounts of histamine.-(T)

11.Betahistine is a strong antagonist for H3 receptors .-(T)

12.Betahistine is a histamine analog used for the treatment of vertigo.-(T)

13.Bradykinin and kallidin are polypeptide that dilate blood vessels.-(T)

14.Bradykinin and kallidin are synthesized from circulating kininogens.-(T)

15.Bradykinin and kallidin produce their biological effect through two types of kinin receptors B1 and B2.-(T)

16.Cetirizine is a second generation H1 antihistamine.-(T)

17.Chlorpromazine is having antagonistic action on 5- HT1 and 5-HT2 receptors, are responsible for the anxiolytic action.-(T)

18.Cromolyn sodium inhibits H1 andH2 receptors.-(F)

19.Cromolyn sodium open the chloride channel to hyperpolarize the cells and inhibits the release of histamine and other autacoids.-(T)

20.Cyproheptadine is a 5 HT , histamine and cholinergic antagonist.-(T)

21.Dazoxiben i

s a selective thromboxane synthase enzyme inhibitor .—(T)

22.D-lysergic acid diethylamide , a potent hallucinogen is a serotonin receptor agonist or partial agonist.-(T)

23.Eicosanoid are found only in animals not in plants.—(F)

24.Eicosanoids include prostaglandins , thromboxanes and leucotrienes.-(T)

25.Epinephrine is a physiological antagonist of histamine.—(T)

26.Ergotamine and methysergide are partial agonists at serotonin receptors.-(T)

27.Five H3 receptors are mainly seen in the peripheral nervous system especially in nociceptive afferent nerves.—(T)

28.Four percent chromolyn sodium eye drops can be recommended to control allergic conjunctivitis.-(T)

29. 4– methyl histamine is an agonist on H4 receptors.-(T)

30.Five hydroxy tryptamine is synthesized from Tryptophan.-(T)

31.Histamine receptors H1 –H4 is G protein coupled.-(T)

32.Histamine can increase the catecholamines from the adrenal medulla and stimulate salivery secretion.-(T)

33.Histamine is stored in mast cells along with heparin and protein in the ratio 1: 3 : 6.--(T)

34.H2 antihistamines inhibit not only hydrochloric acid secretion by histamine but also secretion stimulated by gastrin, acetyl choline (vagus), and food.-(T)

35.Histamine release is a major factor in the stimulation of acid production by both acetyl choline and gastrin.-(T)

36.Histamine content in mast cell is approximately 0.1 to 0.2 P.mol/mast cell.—(T)

37.Histamine is stored along with heparin and protein in mast cells in the ratio 1:3:2.-(F)

38.H4 receptors are highly expressed in bone marrow and white blood cells , it regulate neutrophil release from bone marrow.-(T)

39.H 3 receptors are located mainly presynaptically on neurons in brain and inhibit transmitter release.-(T)

40.H3 and H4 receptors are coupled to G i/o protein .(T)

41.H2 receptors are coupled to Gs protein adenylate cyclase.-(T)

42.In bronchi prostaglandin E2 predominate over prostaglandin F2 alpha.-(T)

43.Irbesartan is an angiotensin II receptor antagonist.—(T)

44.loprost is a synthetic analogue of prostacycline PGI 2.(T)

45.Johnin test is not recommended in animal undergoing antihistaminic treatment.-(T)

46.Ketanserin is a 5HT 2 receptor antagonist.-(T)

47.Kinins are potent vasodilator , 10 times more potent than histamine.-(T)

48.Leukotrienes are so called because they were first found in leucocytes.—(T)

49.Lexipafant a PAF receptor antagonist is useful in acute pancreatitis.-(T)

50.Lungparenchyma is a rich source of prostaglandin F2 alpha .-(T)

51.Leukotrienes are 1000 times more potent than histamine in bronchoconstriction.-(T

52.Leukotrienes B4 serves as algesic agent during inflammation.(T)

53.Losartan is a non-peptide competitive blocker of AT 1 receptor.—(T)

54.Metoclopramide is having serotonin receptor agonistic action.—(T)

55.Metabolism of arachidonic acid by 15-lipoxygenase pathway leads to synthesis of hydroperoxy eicosa tetraenoic acid.-(T)

56.Montelukast and Zafirlukast are LT receptor antagonist .-(T)

57.Only PGE and PGF2 alpha analogs are used therapeutically in veterinary practice.-(T)

58.Parachlorophenylalanine is a synthetic aminoacid act as an inhibitor of tryptophan hydroxylase.-(T)

59.Piboserod is a selective 5-HT 4 receptor antagonist.-(T)

60.Prostaglandins are so called because they are first identified in seminal fluids.—(T)

61.Propranolol is a rennin secretion inhibitor.—(T)

62.Prostaglandin E and F are destroyed by lungs.-(T)

63.Prostaglandin F2 alpha fragilise lysosome.-(T)

64.Prostaglandins E inhibit the release of nor epinephrine from sympathetic nervous system via activation of EP3 receptors.-(T)

65.Prostaglandin E1 mimicks the action of the thyroid stimulating hormone on the thyroid.-(T)

66.Prostaglandin E1 causes nasal vasoconstriction and decrease nasal airway resistance.-(T)

67.Prostaglandin E1 increases the capillary permeability .-(T)

68.Prostaglandin E1 and B1 have regulatory function on epithelial growth and keratinization.-(T)

69.PGE 2 and PGI 2 inhibits histamine release as well as contraction of respiratory smooth muscle .—(T)

70.PGE2 act as a negative regulator of gastric acid secretion as PGE2 activate G i/o coupled EP3 receptors on parietal cells.-(T)

71.Proton pump inhibitors block the H+ K+-ATP ase in the canalicular membrane.-(T)

72.Ramatroban is effective in allergic rhinitis.—(T)

73.Ripatadine blocks H1 and PAF receptors.—(T)

74.Second generation H1 receptors antagonist will not crosses the blood brain barrier.-(T)

75.Serotonin is synthesized from tryptophan and degraded by MAO –(T)

76.Serotonin is also found in venoms of stings .-(T)

77.Terfenadine is metabolized to the active form fexofenadine by intestinal cytochrome P-450.—(T)

78.Thromboxanes are synthesized in thrombocytes.—(T)

79.The respiratory smooth muscle is contracted by TXA2 and PGF2 alpha but relaxed by PGE1 , PGE2 and PGI 2 –(T)

80.Thioperamide is an antagonist of H4 receptors.-(T)

81.Thioperamide and clobenpropit are H3 receptor antagonist.-(T)

82.Thioperamide is an H3 and H4 receptor antagonist.-(T)

83.Trimeprazine is a second generation antihistamine of phenothiazine group.-(F)

84.Two- Methyl histamine is a prototype of H1 receptor agonist.—(T)

**III. Fill up the blanks with most appropriate words:**

1.Metabolism of arachidonic acid by ………………………………pathway leads to the synthesis of prostaglandins, thromboxanes and prostacyclins.-(cyclooxygenase)

2.Metabolism of arachidonic acid by ………………………………pathway leads to the synthesis of leukotrienes.-( 5-lipoxygenase)

3.Montelukast and zafirlukast are indicated for the treatment of ……………….—(asthma)

4.Prostaglandin …………..and …………………reduces the gastro intestinal secretion.-( E and F)

5.Prostaglandin E ………………(action) the longitudinal muscles and …………………… the circular muscles in the GI tract.-( contract , relax)

6.PGE 2 and F2 …………………………..uterine smooth muscles.—( contract)

7.Prostaglandin E and F ……………………the tone of bronchial and tracheal muscle caused by histamine.-( reduces)

8.Serotonin is synthesized mainly in the………………………..cells of the G.I.tract and in the serotonergic neurons of CNS. ---(Enterochromaffin )

9.The broncho constriction by kinins are most prominent in …………………(animal). -(guinea pigs)

10.Zileuton is an inhibitor of …………………………………, the enzyme that generate leukotrienes from arachidonic acid.—(5-lipoxygenase)

11.…………………………is a structural analogue of PG I 2.—(periprost)

12.………………………is a 5 HT2 receptor blocking agent.-( ketanserin)

**IV.Match the following:**

A B

1. H1-agonist thioperamide.—(8)

2. H1- antagonist cimetidine—(4)

3. H2-agonit 2-methyl histamine—(1)

4. H2-antagonist clobenpropit—(6)

5. H3-agonist 4-methyl histamine-(7)

6. H3 –antagonist chlorpheneramine.—(2)

7. H4 agonist betazole—(3)

8 . H4 antagonst immethridine-(5)

**V.Choose the correct answers from the given one**

1.Anaphylactic reactions are produced by the autacoids: a) bradykinin b) 5-HT c) PAF d) histamine .—(d)

2.Cisapride a) agonist for Gs coupled 5-HT 4 receptors b) used in gastric/ intestinal stasis)c) used in reflex esophagitis d) all the above.-( d)

3.Following drugs are angiotensin converting enzyme inhibitor. a) Enalaprilat, b) benazepril, c) lisinopril, d) ramipril e) all the above.-(e)

4.Five hydroxyl tryptamine is a) mostly seen in argentaffin cells b) mast cells c) release in allergic reaction d) all the above .—(d)

5.Following drugs are having serotonin receptor antagonistic action: a) ergot alkaloids b) chlorpromazine c) cyproheptadine d) yohimbine e) all the above.—(e)

6.Following drugs are having serotonin receptor antagonistic action : a) yohimbine b) ketanserin c) ritanserin d) metoclopramide . e) except metoclopramide—(e)

7.Histamine shock is associated with : a)reduced venous return to the heart b) rise in CSF pressure c)engorge large blood vessels d) haemo concentration.-( a)

8. H 1 receptors are coupled to Gq protein phospholipase C and mediate the following effect. a) contraction of smooth muscles and neuronal action due to increase in (Ca++) and activation of protein kinase-C. b) relaxation of vascular smooth muscle involves Ca++ induced formation of nitricoxide. c) contraction of bronchiolar and intestinal smooth muscles, vasodilation of small arteries and vein , increased capillary permeability and pruritus. d) all the above. –(d)

9.Leukotrienes ( LTs) are a) potent vasoconstrictor b) potent broncho constrictor c) stimulate capillary permeability d) stimulate mucous secretion e) all the above.-( e)

10.Metoclopramide a) Gi/o coupled D2 receptor antagonist b) used to treat vomition c) used in reflex oesophagitis and gastric stasis d) all the above.-(e)

11.One of the following is a kinin receptor antagonist a) RMR-7 b) aprotinin c) icatibant .-(c)

12.One of the following is having serotonin reuptake inhibitory action: a) reserpine b) ephedrine c) caffeine d) theobromine .—( a)

13.Prostaglandins are rapidly synthesized in response to stimuli like a) nervine b) burns c) histamine d) trauma e) all the above .-(e)

14.Platelet activating factor ( PAF) a) is a potent vasodilator b) increase vascular permeability c) promote platelet aggregation d) contract GI , uterine and small bronchiolar smooth muscle e) all the above.-(e)

15.Release of histamine from mast cell is depended on a) temperature b) energy c) calcium d) all the above.-(d)

16.Serotonin a) act as a neurotransmitter in the CNS b) involved in inflammatory reaction, allergy, anaphylaxis. c) involved in regulation of peristalsis , nausea, vomition. d) involved in platelet aggregation e) all the above.-(e)

17.The unwanted effect of classical H1 antihistaminics is :-- a) emesis b) sedation c) purgation d) all the above.—(b)

**VI.Choose the correct answer from the given one and give your explanations.**

1.Which of the following is a major effect of angiotensin II A) stimulation of thirst and vasopressin secretion. B) vasodilation C) inhibition of aldosterone secretion D) tachycardia.

The answer is A. angiotensin II stimulates the thirst center in the hypothalamus , and increases vasopressin secretion .Angiotensin II does not cause vasodilation,it is a vasoconstrictor. It increase aldosterone secretion. it could cause bradycardia but not tachycardia, which is attributed to baroreceptor reflex in response to hypertension.

2. which of the following is a function of angiotensin converting enzyme (ACE) A) converts angiotensinogen to angiotensin I. B) converts bradykinin to inactivate metabolites. C) directly promotes aldosterone secretion. D) convert angiotensin II to angiotensin III.

The answer is B. ACE converts bradykinin to biologically inactive products. This is the reason that feline patients on an ACE inhibitor may have broncho constriction as a side effect. ACE converts angiotensin I to angiotensin II, but does not affect the conversion of other angiotensin- related proteins, nor does ACE directly affect aldosterone secretion.

3. which one of the following is the most frequently associated side effect of H1 antihistamines? A) anti-androgenic activity in males. B) sedation C) inhibition of cytochrome P450 enzymes. D) constipation.

The answer is B. most of the first generation H1 antihistamines posses some sedative properties. The newer (second generation) H1 antihistamines tend to have minimal or no sedative properties. Cimetidine , an H2 – antihistamine, is a potent inhibitor of cytochrome P 450 enzymes, which also inhibits testosterone synthesis. Many H1 –antihistamines have antimuscarinic properties, which will decrease GI motility, and they cause constipation occasionally.

4. how does diphenhydramine work to relieve the symptoms of hypersensitivity? A) it competitively antagoniszes the effect of histamine at H1- receptors. B) it stabilizes mast cells to inhibit histamine release. C) it inhibits the binding of allergens to Ig E. D) it promotes the endocytosis of H1- receptors. E) it promotes the shift of active H1- receptors to the inactive state.

The answer is E . In the past , the general concept was that H1 – antihistamines competitively antagonized H1 –receptors. However recent evidence indicates that H1 –antihistamines shift the active H1 –receptors to the inactive state. These drugs do not stabilize mast cells to inhibit histamine release, nor do they evokeH1 –receptor endocytosis.

5. which of the following statements is incorrectly associated with prostacyclin ( PGI 2) .A) PGI 2 is a vasoconstructor. B) PGI2 is formed from platelet endoperoxides. C) PGI2 inhibits platelet aggregation D) PGI2 is spontaneously hydrolyzed into inactive 6-keto-PGF 1alpha.

The answer is A. PGI2 is a vasodilator, but not a vasoconstrictor. PGI2 receptors are coupled to Gs , thereby increasing cAMP synthesis and leading to relaxation of vascular smooth muscles and a decrease in platelet aggregation. PGI2 is synthesized in endothelial cells utilizing platelet endoperoxides, which can be inhibited by NSAIDs, aspirin in particular.

6. which of the following statements regarding H2 antihistamines is correct? A) Nizatidine may cause drug interaction because of its inhibition of the cytochromeP450 enzyme system. B) ranitidine is more potent than cimetidine. C) ranitidine is a potent CNS depressant. D) famotidine has a plasma half life much longer than that of cimetidine.

The answer is B. Ranitidine is more potent than cimitidine as an H2 –antihistamine. Cimetidine , but not nizatidine may cause drug interactions , because of its inhibition on the cytochrome P 450 system. Ranitidine at very high doses may cause CNS disturbances including depression. Famotidine, cimetidine, ranitidine, and nizatidine have similar plasma half –lives of 2-3 hours.

7. which of the drugs listed below inhibits the release of histamine? A) Betazole B) cimetidine C)dimenhydrinate D) cromolyn sodium.

The answer is D. Cromolyn sodium inhibits histamine release. This is due to cell membrane hyperpolarization induced by opening of chloride channels. Dimenhydrinate , betazole, and cimitidine are H1 –antihistamine, H2- agonist, and H2 –antihistamine, respectively.

8. which of the following statements regarding serotonergic receptors is incorrect? A) All serotonergic receptors are G protein- coupled receptors, except 5-HT 3 receptors. B) there are more classes of seotonergic receptors than any other receptors of biogenic amines. C) stimulation of 5-HT 1 receptors increases GI motility. D) stimulation of 5-HT 2 receptors evokes severe vasoconstriction , which accounts for fescue grass toxicity.

The answer is C. Stimulation of 5-HT4 receptors by agonists such as cisapride, but not stimulation of 5-HT1 receptors, increases GI motility. Because 5HT4- receptors are coupled to Gs, which results in an increase in cAMP synthesis and acetylcholine release from the vagus nerve.

9. which one of the following statements is incorrect? A) arachidonic acid is the precursor for the synthesis of the leukootrienes. B) Aspirn inhibits the formation of PGF 2 alpha. C) PGE2 increases body temperature. D) leukotrienes are potent relaxants of bronchiolar smooth muscles.

The answer is D. leukotrienes are potent stimulators of the contraction of bronchiolar smooth muscles. The other statenments are all true.

10.which of the following autacoid inhibitors/ antagonists is a leukotriene (LT) receptor antagonist that blocks LT induced broncho constriction? A) cetrizine B) lisinopril C) montelukast D) zileuton.

The answer is C. Montelukast is a leukotriene (LT) receptor antagonist that block LT induced bronchoconstriction. Because asthma in cats may be attributable to increased autacoids release including histamine and LT. LT receptor antagonist can be used as adjunctive therapy. Cetrizine is a second generation H1 antihistamine, lisinopril is an ACE inhibitor, zileuton is a 5-lipoxygenase inhibitor, which inhibits LT synthesis.

11.why doesn’t fexofenadine cause sedation? A) it is a drug that blocks H2 receptors in the CNS. B) it is not effective blocking cerebral H1 receptors. C) it is an excellent substrate for P-glycoprotein, which pumps drug including fexofenadine out of the CNS efficiently. D)it is ionized at pH 7.4 and does not cross the blood –brain barrier.

The answer is D. The second generation H1 antihistamines including fexofenadine are ionized at physiological pH and the ionized form of the drug does not cross the blood –brain barrier to cause sedation. Fexofenadine can block cerebral H1 – receptor in vitro, but it cannot reach the target site in the CNS in vivo. P-glycoprotein is not the reason that fexofenadine does not cause sedation.

**VII. Answer the following questions:**

1.Classify Autacoids depending on the chemical structure:

A. Biogenic amines- 1) Histamine

2) Serotonin/ 5-hydroxytryptamine (5-HT)

B .Poly Peptide - 1.kinins bradykinin and kallidin

2. Angiotensin

3. Tachykinins-substance –P and neurokinin –A

4. Cytokines

C. Lipid derived autacoids. 1. Eicosanoids-prostaglandins, leukotrienes, thromboxane

2. platelet activating factor.

2.Classify H1 receptor antagonist.:

a. Ethanolamines- eg. Diphenhydramine, dimenhydramine.

b. Ethylenediamines-eg. Mepyramine , tripelennamine.

c. Alkylamines-chlorpheneramine,dexchlorphenamine

d. Piperazines –cyclizine, buclizine

1. Phenothiazines- promethazine, alimemazine
2. Miscellaneous-cyproheptadine, phenindamine.

II.Second generation H1 receptor antagonist .-( non sedative)

1. piperazine –cetirizine, lavocitirizine .

2. piperidine- astemizole, loratadine

3. miscellaneous- azalastine, acrivastine.

3. Classify histamine receptors and brief their action and mechanism of action.

H1 receptors are coupled to Gq protein phospholipase C and mediate the following effect. a) contraction of smooth muscles , neuronal action due to increase in (Ca++)i and activation of protein kinase-C. b) relaxation of vascular smooth muscle involves Ca++ induced formation of nitric oxide. C) contraction of bronchiolar and intestinal smooth muscles, vasodilation of small arteries and vein , increased capillary permeability and pruritus.

H2 receptors coupled to Gs protein-adenyl cyclase stimulate cAMP –primarily mediate gastric acid secretion and vasodilation.

H3 receptors coupled to G i/o protein- inhibition of histamine and other neurotransmitter involved in inhibition of cAMP synthesis-opening of K channels to increase K+ efflux and closure of C++ channels to block Ca++ entry in to nerves block the transmitter release.

H4 coupled to Gi/o protein and activate phospholipase C beta- these are expressed in mast cells, basophils and eosinophils- activation mediate histamine induced mast cell chemotaxis and leukotrienes B4 production. Play a role in early events of inflammation ,edema, and thermal hyperalgesia.

4. What are autacoids? Autacoids are chemical mediators that are synthesized and function in a localized tissue or area and participate in physiologic or patholophysiologic responses to injury. They act on locally so they are also called as local hormones-do not function as the classical hormones –short lived and rapidly degrade . 1)modulate smooth muscle function 2) play a key role in allergy , inflammation, smooth muscle function, pain and certain type of drug reactions.

5. What are Eicosanoids : they are lipid derived autacoids consisting of prostaglandins (PGs), thromboxanes (TXs), leukotrienes (LTs),lipoxins (LXs), hepoxilins. Derived from 20 carbon essential fatty acids, primarily arachidonic acid which is a component of membrane phospholipids –implicated in the control of many physiological and pathological process-important mediators and modulators of the inflammatory reactions.

6. what are the pharmacological effect of H1 antihistamines? a) relaxation of contracted bronchiolar smooth muscles and intestinal smooth muscles b) inhibition of histamine induced vasodilation and increased capillary permeability , block oedema and wheals formation. C) inhibit itch sensation by prevention of stimulation of sensory nerves, H1 antihistamines have potent local anaesthetic action. Other pharmacological action include sedation, antimuscarinic effects, antimotion sickness(antiemetic)

7. What are the therapeutic uses of H1 antihistamines? H1 antihistamines are administered orally ,parenterally or topically for the following condition. Treatment of allergy- urticaria, pruritus-allergic reactions to drugs- anaphylaxis, prevention of motion sickness and sedation induction.

**VIII.Write short notes on**

1. Action of prostanoids on cardio vascular and respiratory system: Cardiovascular system- PGE 2 cause relaxation of vascular smooth muscles leading to vasodilation in most vascular beds. PGI 2 is uniformily vasodilatory and appears to maintain blood flow in vital organs. PGF2 alpha constrictive effect on veins and pulmonary vasculature but can cause vasodilation in some other area. TXA 2 produce vasoconstriction. PGG 2 and PGH 2 are potent vasoconstrictor. PGE2 stimulate heart when blood pressure is down. On respiratory smooth muscle is contracted by TXA 2 and PGF2 alpha, relaxed by PGE1 , E2 and PGI2. PGE 2 and PG I 2 also inhibits histamine release.

2.Action of histamine on cardio vascular system. Dilate arterioles, capillaries and venules- increase cardiac contractility and heart rate by activating both H1 and H2 receptors- decrease in peripheral resistance resulting in hypotension. Activation of sympathetic nervous system –increase in capillary permeability brought about by contracting endothelial cells-fluid and protein pass across the basement membrane to produce oedema.

3.Action of prostanoids on digestive system: PGE2 and PGF 2 alpha causes constriction of longitudinal muscles. PG I 2 and PGF 2 alpha causes constriction of circular muscles and relaxed by PGE2 . PG reduce transit time in the small intestine. E2 and F 2 alpha stimulate the movement of water and electrolytes in to the intestine where as PGI 2 prevent it. E 2 inhibit gastric acid secretion and stimulate gastric mucous secretion.

4.Actions of leukotriens on inflammation and immune response: Leukotrienes play a major role in inflammation and immune response-pro inflammatory with LTB 4 a potent chemoattractant for polymorphs, eosinophils, and monocytes. LTC4 and LTD 4 chemotactic for eosinophils. LTB 4 promote aggregation of polymorphs ,degranulation, generation of superoxide, adhesion and migration. It also stimulate synthesis of cytokins from macrophage and lymphocytes. Leukotriens stimulate T cell clonal expression by stimulating the formation of interleukins one and two as well as the expression of interleukins 2\ receptors.

5. Action of of leukotrienes in the body: It markedly increase the capillary permeability -cause exudation of plasma, -- potent chemotactic agent for polymorphs, eosinophils and monocytes- promote neutrophil adhesion –major role in immune response. contract most smooth muscles- sensitise nociceptive receptors and mediate pain. In inflammation -it is proinflammatory with LTB4, a potent chemoattractant for polymorps. LTB4 promote aggregation of polymorphs, degranulation, generation of superoxide, adhesion and migration. Stimulate the synthesis of cytokins from macrophages and lymphocytes. --stimulate the T cells clonal expression by stimulating the formation of interleukins 1 and 2 and the expression of interleukins 2 receptors.

6.Action of histamine on dermal tissues. 1)Produce triple response ( flush, flare, wheal) A reddening at the site of injection is due to dilation of the small arterioles 2) dilation of arterioles extends beyond injection site(flare) the flare involves an axon reflex , since cutting the cholinergic nerves abolishes the reflex 3) swelling (Wheal) occurs at injection site due to separation of endothelial cells and edema caused by the increased capillary permeability. The intra dermal inj. Of histamine causes pain and itching by stimulation of H1 receptors on sensory nerve endings.

7.Drugs affecting serotonin : Tryptophan is the precursor of serotonin- can crosses the BBB and can act as effective serotonergic agent . Parachlorophenylalanine can act as a selective and irreversible inhibitor of tryptophan hydroxylase.- reduce synthesis of serotonin and reduce its action –act as indirect serotonergic agent. Parachloroamphetamine promote the release of serotonine from platelets and neurons result in profound decline in 5 HT in brain result in neurotoxicity. Selective serotonin reuptake inhibitor cause increase level of serotonin in cleft.( Eg. Fluoxetine and trazodone used as antidepressant) . Reserpine also can cause depletion of serotonin from the serotonergic neurons and it inhibit serotoinin storage in to synaptic vesicle . MAO inhibitors prevent the metaboliam of serotonin also.

8.Histamine: . Is an imidazole derivative biogenic amine distributed widely in animal tissues and certain plants. Synthesised from histidine stored in mast cells and basophil along with heparin and protein –release during physiological, mechanical or chemical stimuli It plays an important role in regulation of gastric secretion , allergy, anaphylaxis, neurotransmission , haemodynamics , immune and inflammatory response. Agents which stimulate cAMP formation inhibit histamine release, some neuropeptides ( eg. Substance –P) and drugs (eg.Morphine) cause histamine release. Act via histamine receptors ( H1 to H4) which are G protein coupled.

9.Histamine blocking drugs: There are three classes of histamine blocking drugs I. Prevent /reduce histamine release from sensitized mast cells. Eg. Sodium chromoglycate, corticosteroids, cetirizine II. Drugs opposes the action of histamine on smooth muscles arteriols and vascular permeability eg.Epinephrine-- useful to antagonize the biological action of endogenous histamine particularly in hypersensitive reaction III. Histamine receptor antagonist-prevent the action of histamine in the body by competitively blocking the histamine receptors - used therapeutically ,termed as antihistamines.

10.H1 receptor antagonists: H1 antagonists do not produce cellular action of their own but they block the action of histamine at H1 receptors in the tissue. Antihistamine blocks the fall in BP by low dose of histamine , block the increased capillary permeability and formation of oedema, block the histamine induced contraction of bronchi and intestinal smooth muscles. Allergic response is blocked. Tripple response , itching, respiratory suppression, lachrymal and other exocrine gland secretion are reduced - abolish histamine induced release of catecholamine, CNS suppression, and sedation. Some of them posses antitussive action.

11.Histamine H2 receptors: H2 receptors are bound to G protein coupled (Gs), present in gastric glands blood vessels, uterus and CNS ,mediate mainly gastric secretion and vasodilatation along with H1 receptors. Associated with inhibition of antibody synthesis, T-cell proliferation and cytokine production. H2 activate adenyl cyclase cAMP system-activate protein kinase –in turn leads to phosphorylation of series of enzymes and produce response.

12.Histamine H3 and H4 receptors: H3 receptors are couple to Gi protein –located presynaptically or neurons in the brain where it mediate histamine release.–reduce cyclic AMP –activate potassium channels and or inhibit Ca influx These receptors are also present in lungs, spleen and skin. In bronchi and ileum causes inhibition of acetylcholine release. In arteries causes vasodilation. H4 receptors are coupled to G proteins –highly expressed in bone marrow and white blood cells-regulate Neutrophil release from bone marrow, also expressed in colon, liver, lung ,small intestine, thymus and spleen.

13. Inhibitors of Eicosanoids receptor: mainly Cysteinyl leukotriene receptor type -1 antagonist,(CYSLT 1) Montelukast – block the action of D4 (primary ligand) and also LTC4 and LTE4(second ligand) ,the effect is significant in bronchi and lung –reduce inflammatory \seasonal allergy. Zafirlukast is another example for CYSLT 1 action similar to montelukast- long acting bronchodilator. Ramatroban- thromboxane A2(TXA2)receptor antagonist-potent TP receptor antagonist- effective against allergic rhinitis-also block PGD2 receptor (which induce migration and degranulation of eosinophils) –suppress the late phase of inflammation, indicated for coronary artery disease and treatment of asthma.

14. Inhibitors of Eicosanoids synthesis : a) Glucocorticoids- inhibit the release of arachidonic acid which in turn inhibit the synthesis of all eicosanoids- this effect is mediated indirectly by stimulation of synthesis of a peptide called lipocortin which blocks phospholipase A2 (the enzyme responsible for the synthesis of arachidonic acid.) b) NSAIDs inhibit cyclooxygenase (COX) and block synthesis of prostanoids. Inhibition of COX in fact increases production of leukotrienes by promoting availability of substrate to the lipoxygenase pathway. c) Zileuton –is an inhibitor of 5-lipoxygenase that generate leukotrienes from arachidonic acid. d) Periprost – structural analogue of PGI 2 –primarily inhibits 5-lipoxygenase enzyme and block the synthesis of leukotrienes. e) Dazoxiben and pirmagrel are selective thromboxane synthase inhibitor –decreases the plasma concentration of thromboxane A and hence platelet aggregation. Ridogrel is a thromboxane synthesis inhibitor and a thromboxane receptor antagonist.

15. Mechanism of action of Histamine: exert its action by combining with specific H receptors (H1-H4). H1 is a G protein coupled- seen in smooth muscles, vascular endothelium heart and CNS- associated with contraction of bronchi, intestinal smooth muscle, vasodilatation of small arteries and vein, capillary permeability and prurites. H1 receptors Coupled to Gq activate phospholipase –C and phosphatidyl inositol (PIP2) signaling pathway. In smaller vessels causes dilation by releasing nitrous oxide by the endothelium.

16. Platelet activating factor: (PAF) is a cell membrane derived autacoids. It is a mediator of many leucocyte function including platelet aggregation, synthesized by phospholipase A2, act via G protein coupled receptor - unmask the fibrinogen binding sites on the surface of platelets. Accumulation of PAF with in cell is associated with the adhesion of neutrophil to the surface of endothelial cells – reduce vascular resistance, vasodilatation- fall in BP , stimulate vascular permeability- promote thrombosis, contraction of respiratoy, GI, uterine smooth muscles- pro inflammatory action.

17. Role of serotonin in the body: Act as a neurotransmitter in the CNS -- involved in a number of brain function- mood disorders and anxiety. Many antidepressant and antianxiety drug mediate their action through serotonergic mechanism --involved in inflammatory reactions ,allergy. Anaphylaxis, not a strong mediator- involved in regulation of peristalsis and local reflexes in gut. (Prokinetic agents like cisapride mediate action through serotonin). Involved in nausea and vomition particularly due to cytotoxic drugs and radiation injury mediate via 5-HT 3 receptors. (Ondansetron an antiemetic drug act via this.) It is involved in haemostasis through platelet aggregation and vasoconstriction. It initiate vasoconstrictor phase of migraine . Hyper secretion (in tumour of enterochromaffin cells) cause bowel hyper motility colic episodes and bronchospasm.

18. Serotonin receptor agonist: Metoclopramide is a non selective drug act both on dopamine and serotonin receptors. It is 5 HT receptor agonist and 5 HT 3 receptor antagonist used in control of nausea and vomition. Lysergic acid diethylamide is a non selective agonist but antagonize 5 HT 2A in the ileum. Psilocin is a mushroom alkaloid structurally similar to serotonin- agonist on many 5HT subtypes. Azapirones a class of antianxiety drug – is a partial agonist of 5 HT1A. Triptans , a group of drug used in the treatment of migraines and cluster headaches-- The antimigrain action is attributed to binding to serotonin receptors in cranial blood vessels. Benzamides -- used as antiemetic and prokinetic agent mediate their action through selective 5 HT 4 receptor

19.Serotonin ( 5-hydroxy tryptamine) is a monoamine neurotransmitter and an autacoids synthesised from 1-Tryptophan . Primarily seen in GI tract, serotonergic neurons. Are concentrated in raphae nucleus of brain stem.-stored in vesicle –released by exocytosis- act on receptors- terminated by reuptake and metabolism. All 5 HT receptors are coupled to G proteins except 5HT3 which is directly linked to ionic channels- have both inhibitory and excitatory actions pre and post synaptic action. It is involved in several aspects of behavior – sleep and wake cycle, temperature control, pain perception, appetite depression, sexual activity, aggressiveness, release of pituitary hormones- also involved in regulation of mood and muscle contraction.

20.Synthesis, storage and release of serotonin: Serotonin is synthesized mainly in the enterochromaffin cells of G.I.tract and serotonergic neurons of CNS from dietary aminoacid I-tryptophan. I tryptophan is hydroxylated by tryptophan 5-hydroxylase to 5- hydroxytryptophan (5-HTP)which is then decarboxylated by l-aromatic acid decarboxylase to 5-hydroxytryptamine or serotonin- often stored in neurons and chromaffin cells together with various peptide hormones such as somatostatins , substance –P, and vasoactive intestinal polypeptide, mostly stored in enterochromaffin cells –after release enter the portal vein and subsequently metabolized mostly in the liver.

21. Tachykins:A family of peptide seen in CNS and peripheral tissues- mainly include substance P, neurokinin A (NKA) and neurokinin B (NKB) -- involved in excitation of neurons, behavioural responses vasodilation and contraction of smooth muscles, Substance P and NKA occur mainly in nerves system particularly in the nociceptive sensory neurons. These tachykins binds to NK1, NK2 and NK 3 receptors respectively. Most types of smooth muscles contracts, blood vessels shows contraction and dilation, neurons shows slow excitatory response. Substance P is involved in transmission of pain impulse, stimulate vomition, activate mast cells and release of histamine. NK 1 antagonists are used as antidepressant and anti emetic and anxiolytic drug. NK2 antagonists are used as antidepressant, anxiolytic. NK3 antagoists are useful to treat schizophrenia and drug addiction.

22.Types of serotonin receptors: (5-HT 1 to 7 and total 14 including subtypes). All of them except 5HT3 are coupled to G proteins-- activate an intracellular second messenger-produce excitatory or inhibitory action. 5 HT 3 is an ionotropic receptor that regulate Na and Ka channels. 5 HT1 inhibit adenylate cyclase 5 HT1A activate receptor operated K channel and inhibits a voltage gated Ca channel. 5HT1D function as an autoreceptor on axon terminals and inhibits 5 HT release, 5HT 2 and subtypes are linked to G2/ G11 protein to phospholipase C with the generation of second messenger diacyl glycerol and inositol triphosphate . 5 HT 3 is the only monoamine neurotransmitter receptor that is known to function as a ligand gated ion channel. 5HT 4 receptor are widely distributed coupled to Gs protein and activate adenyl cyclase leading to a rise in intracellular cyclic AMP.

**IX. Write Essays on :**

What are autacoids? Explain in detail amine autacoids.

Explain the pharmacological actions of prostaglandins on various systems in the body. What are the therapeutic uses?

What are eicosanoids explain the action and use of PG F and E in animal practice.

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