Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 1

Name of topic/lesson – General considerations

Subtopic: Structure of biological membrane

Objective: To study the structure and function of Biological membrane.

Topic Outcomes: At the end of topic you should be

1. Able to draw the structure of Biological membrane.
2. Different functions of Biological membrane

A biological membrane or biomembrane is an enclosing or separating membrane that acts as a selectively permeable barrier within living things. Biological membranes, in the form of eukaryotic cell membranes, consist of a phospholipid bilayer with embedded, integral and peripheral proteins used in communication and transportation of chemicals and ions. The bulk of lipid in a cell membrane provides a fluid matrix for proteins to rotate and laterally diffuse for physiological functioning. Proteins are adapted to high membrane fluidity environment of lipid bilayer with the presence of an annular lipid shell, consisting of lipid molecules bound tightly to surface of integral membrane proteins. The cell membranes are different from the isolating tissues formed by layers of cells, such as mucous membranes, basement membranes, and serous

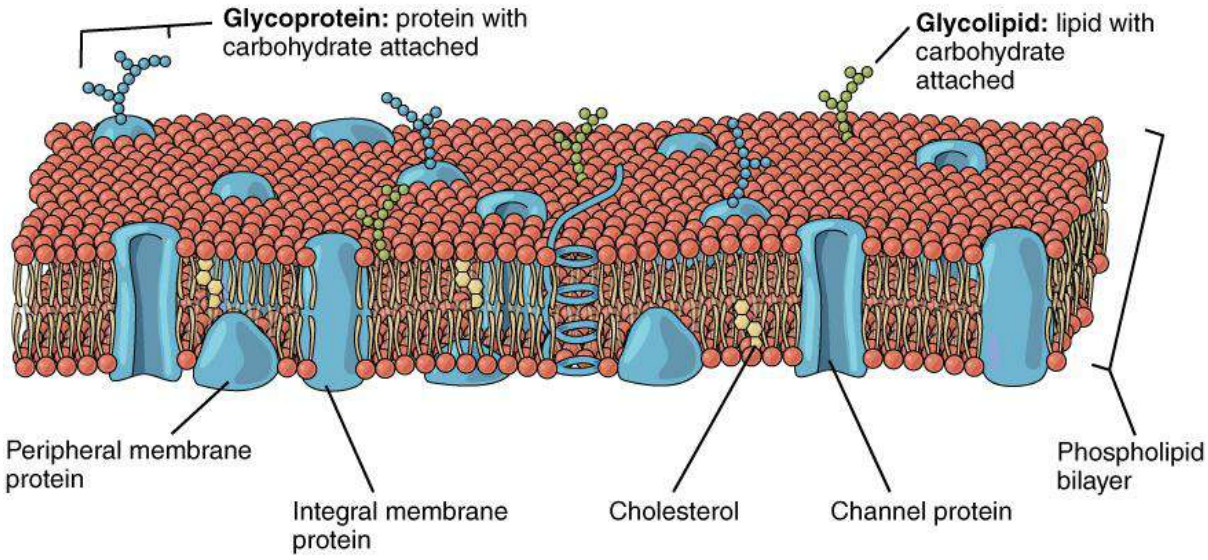

Fig. Structure of biological membrane

References

1. Principles of Chromatography by KR Mahadik, K G Bothara, 1st edition, Nirali Prakashan.

2. Introduction to Chromatography (Theory and Practice) by VK Srivastav and KK Shrivastava

Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 2

Name of topic/lesson – General considerations

Subtopic: physicochemical properties affecting drug action

Objective: To study the physicochemical properties affecting drug action.

Topic Outcomes: At the end of topic you should be

1. Able to study physicochemical properties affecting drug action.

2. Different study different properties affecting drug action.

To the influence of various physical and chemical (physicochemical) properties of the chemical .The ability of a chemical compound to elicit a pharmacological/ therapeutic effect is related substance on the bio molecule that it interacts with.

1) Physical Properties :Physical property of drug is responsible for its action

2) Chemical Properties : The drug react extracellularly according to simple chemical reactions like neutralization, chelation, oxidation etc.

Various Physico-Chemical Properties are

- Solubility
- Partition Coefficient
- Dissociation constant
- Hydrogen Bonding
- Ionization of Drug
- Redox Potential
- Complication
- Surface activity
- Protein binding
- Isosterism

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

4. Principles of Medicinal Chemistry by Kadam SS, Mahadik KR, Bothara KG, Vol. I & II, 10th Edition, Nirali Prakashan.

Lecture No: 3

Name of topic/lesson – General considerations

Subtopic: stereo chemical aspect of drug action.

Objective: To study the stereo chemical aspect of drug action.

Topic Outcomes: At the end of topic you should be

1. Able to study the stereoisomer's.

2. Different types of isomers.

Stereochemistry, a sub discipline of chemistry, involves the study of the relative spatial arrangement of atoms that form the structure of molecules and their manipulation. Study of stereochemistry focuses on stereoisomer's, which by definition have the same molecular formula and sequence of bonded atoms (constitution), but differ in the three-dimensional orientations of their atoms in space. For this reason, it is also known as 3D chemistry—the prefix "stereo-" means "three-dimensionality".

An important branch of stereochemistry is the study of choral molecules. Stereochemistry spans the entire spectrum of organic, inorganic, biological, physical and especially supramolecular chemistry.

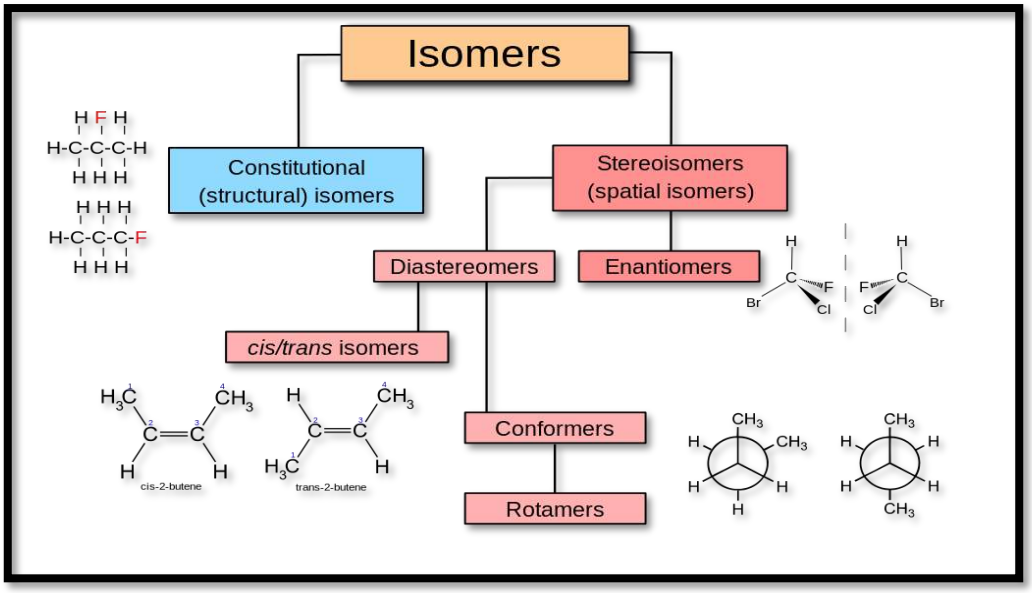

Fig. Different types of Isomers

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 4

Name of topic/lesson – General considerations

Subtopic: Bioisosterism.

Objective: To study the Bioisosterim.

Topic Outcomes: At the end of topic you should be

1. Able to study the bioisosterism and examples.

2. Different classification of bioisosteres and applications .

bioisosteres are chemical substituents or groups with similar physical or chemical properties which produce broadly similar biological properties to another chemical compound. In drug design, the purpose of exchanging one bioisostere for another is to enhance the desired biological or physical properties of a compound without making significant changes in chemical structure. the main use of this term and its techniques are related to pharmaceutical sciences. Bioisosterism is used to reduce toxicity, change bioavailability, or modify the activity of the lead compound, and may alter the metabolism of the lead.

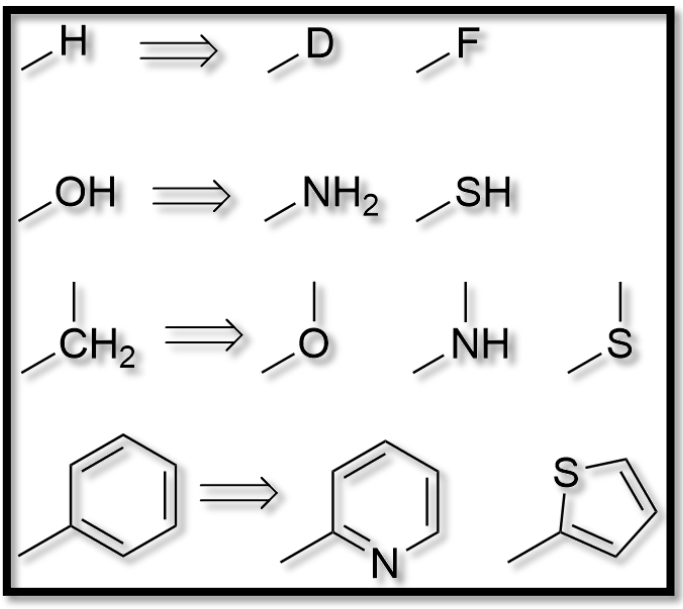

Fig . Classical Bioisosteres

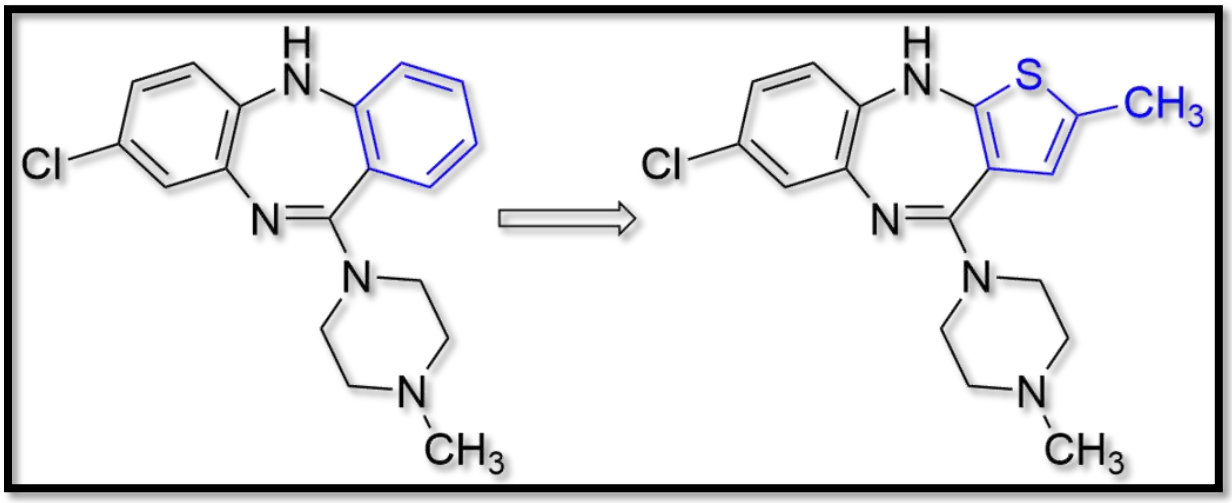

Fig. Non-classical bioisosteres

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

4. Principles of Medicinal Chemistry by Kadam SS, Mahadik KR, Bothara KG, Vol. I & II, 10th Edition, Nirali Prakashan.

Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 5

Name of topic/lesson – General considerations

Subtopic: Introduction to drug absorption.

Objective: To study (ADMET) absorption, distribution, metabolism, excretion and toxicity.

Topic Outcomes: At the end of topic you should be:

1. Able to study (ADMET) process of drug.

2. Toxicity of different drugs.

ADME

Is abbreviation in pharmacokinetics and pharmacology for"absorption, distribution, metabolis -m, and excretion", and describes the disposition of a pharmaceutical compound within an organism. The four criteria all influence the drug levels and kinetics of drug exposure to the tissues and hence influence the performance and pharmacological activity of the compound as a drug.

Absorption:

compound to reach a tissue, it usually must be taken into the bloodstream - often via mucous surfaces like the digestive tract (intestinal absorption) - before being taken up by the target cells. Factors such as poor compound solubility, gastric emptying time, intestinal transit time, chemical instability in the stomach, and inability to permeate the intestinal wall can all reduce the extent to which a drug is absorbed after oral administration.

Distribution:

Distribution is defined as the reversible transfer of a drug between one compartments to another. Some factors affecting drug distribution include regional blood flow rates, molecular size, polarity and binding to serum proteins, forming a complex. Distribution can be a serious problem at some natural barriers like the blood–brain barrier.

Metabolism:

Compounds begin to break down as soon as they enter the body. The majority of small-molecule drug metabolism is carried out in the liver by redox enzymes, termed cytochrome P450 enzymes. As metabolism occurs, the initial (parent) compound is converted to new compounds called metabolites. When metabolites are pharmacologically inert, metabolism deactivates the administered dose of parent drug and this usually reduces the effects on the body. Metabolites may also be pharmacologically active, sometimes more so than the parent drug .

Excretion:

Compounds and their metabolites need to be removed from the body via excretion, usually through the kidneys (urine) or in the feces. Unless excretion is complete, accumulation of foreign substances can adversely affect normal metabolism. There are three main sites where drug excretion occurs.

Excretion of drugs by the kidney involves 3 main mechanisms:

- Glomerular filtration of unbound drug.
- Active secretion of (free & protein-bound) drug by transporters (e.g. anions such as urate, penicillin, glucuronide, sulfate conjugates)or captions such as choline, histamine.
- Filtrate 100-fold concentrated in tubules for a favorable concentration gradient so that it may be secreted by passive diffusion and passed out through the urine.

Toxicity:

sometimes, the potential or real toxicity of the compound is taken into account (**ADME-Tox** or **ADMET**). Parameters used to characterize toxicity include the median lethal dose (LD_{50}) and therapeutic index.

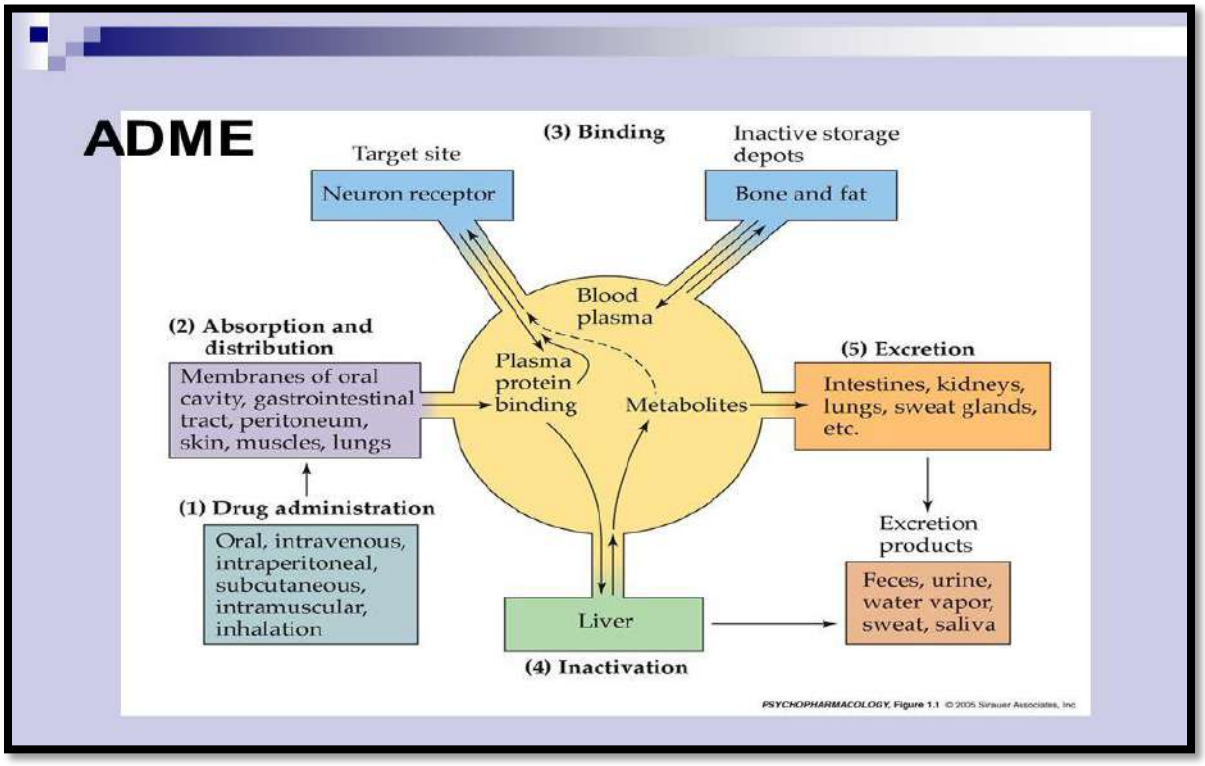

Fig. ADME Process

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture No: 6

Name of topic/lesson – General considerations

Subtopic: Protein binding.

Objective: To study Protein binding.

Topic Outcomes: At the end of topic you should be:

1. Able to study plasma protein binding of drug.

2. process of protein binding.

Plasma protein binding refers to the degree to which medications attach to proteins within the blood. A drug's efficiency may be affected by the degree to which it binds. The less bound a drug is, the more efficiently it can traverse cell membranes or diffuse. Common blood proteins that drugs bind to are human serum albumin, lipoprotein, glycoprotein, and α, β, and γ globulins.

A drug in blood exists in two forms: bound and unbound. Depending on a specific drug's affinity for plasma protein, a proportion of the drug may become bound to plasma proteins, with the remainder being unbound. If the protein binding is reversible, then a chemical equilibrium will exist between the bound and unbound states, such that:

Protein + drug ⇌ Protein-drug complex

Notably, it is the unbound fraction which exhibits pharmacologic effects. It is also the fraction that may be metabolized and/or excreted. For example, the "fraction bound" of the anticoagulant warfarin is 97%. This means that of the amount of warfarin in the blood, 97% is bound to plasma proteins. The remaining 3% (the fraction unbound) is the fraction that is actually active and may be excreted. Note that this does not mean that 97% of the plasma proteins are bound with drug.

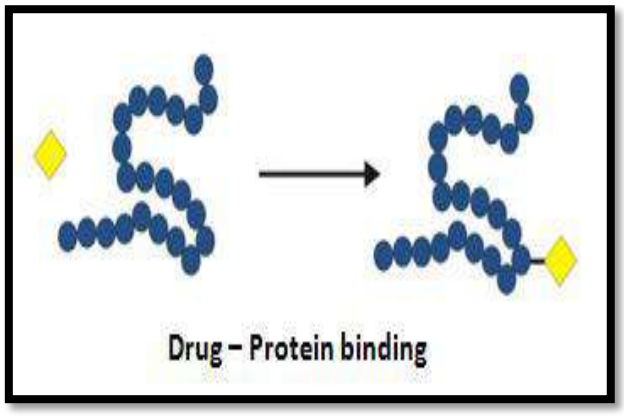

Fig. protein binding

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 7

Name of topic/lesson – General considerations

Subtopic: Blood brain barrier.

Objective: To study Blood brain barrier.

Topic Outcomes: At the end of topic you should be:

1. Able to draw structure of blood brain barrier.

2. Different function of blood brain barrier.

The **blood–brain barrier** (**BBB**) is a highly selective semi permeable border that separates the circulating blood from the brain and extracellular fluid in the central nervous system (CNS). The blood–brain barrier is formed by endothelial cells of the capillary wall, astrocyte end-feet ensheathing the capillary, and pericytes embedded in the capillary basement membrane.[2] This system allows the passage of some molecules by passive diffusion, as well as the selective transport of molecules such as glucose, water and amino acids that are crucial to neural function.

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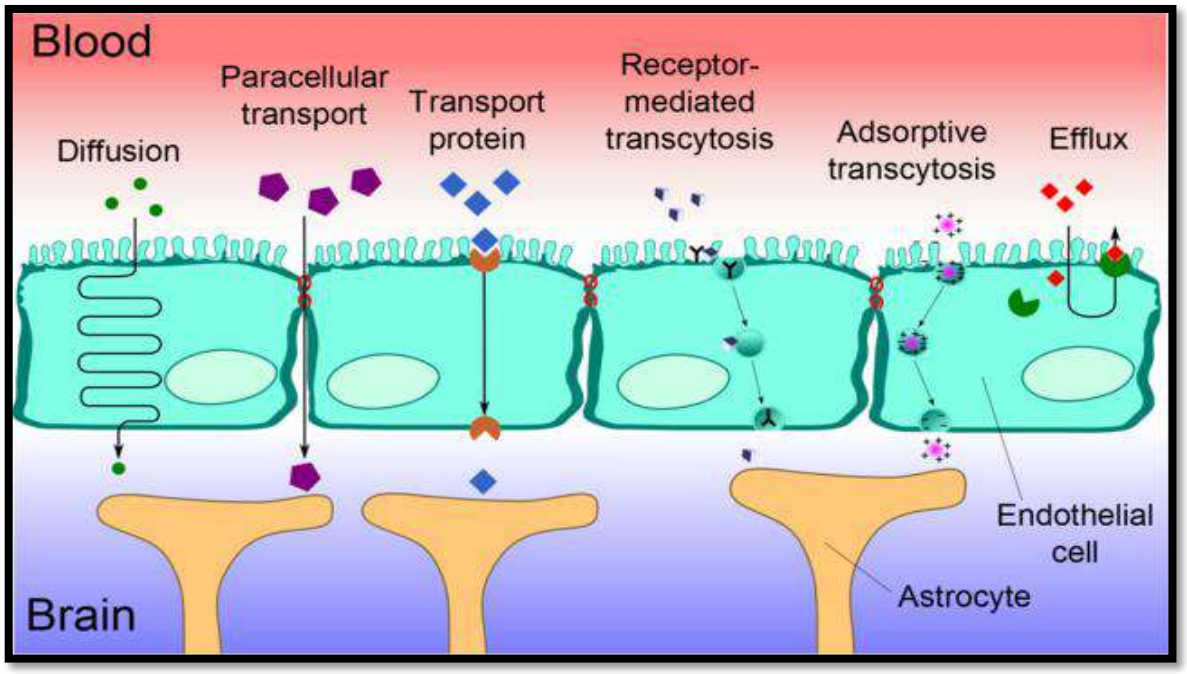

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Fig. Blood brain barrier.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 8

Name of topic/lesson - Receptors.

Subtopic: Introduction to Receptors.

Objective: To study the receptors.

Topic Outcomes: At the end of topic you should be:

1. Able to draw structure of receptor.

2. Different functions of receptor.

receptors are chemical structures, composed of protein, that receive and transduce signals that may be integrated into biological systems.These signals are typically chemical messengers, which bind to a receptor, they cause some form of cellular/tissue response, e.g. a change in the electrical activity of a cell. There are three main ways the action of the receptor can be classified: relay of signal, amplification, or integration.[2] Relaying sends the signal onward, amplification increases the effect of a single ligand, and integration allows the signal to be incorporated into another biochemical pathway.

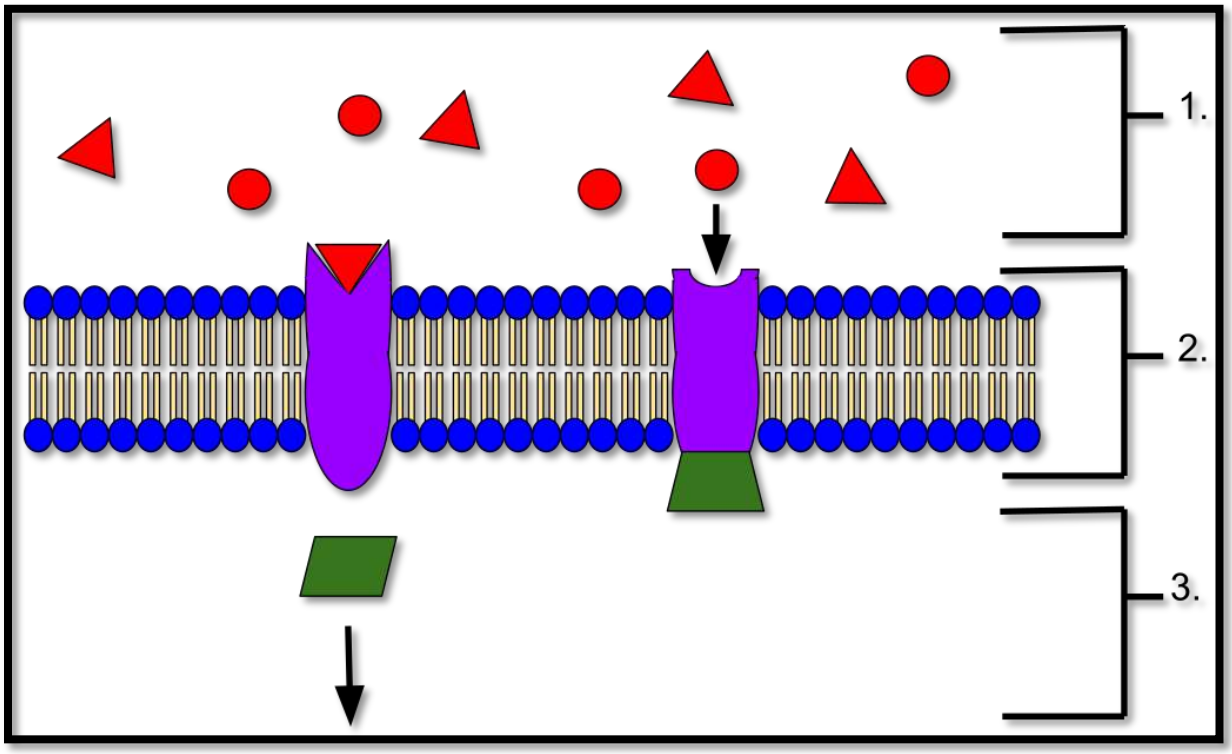

Fig. Receptors

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 9

Name of topic/lesson - Receptors.

Subtopic: Types of receptor

Objective: To study types of the receptors.

Topic Outcomes: At the end of topic you should be:

1. Able to study types of receptor and struture.

2. Different functions of receptor.

Receptors are very diverse and include the following major categories,

Type 1: Ligand-gated ion channels (ionotropic receptors)

Type 2: G protein-coupled receptors (metabotropic receptors)

Type 3: Kinase-linked and related receptors (see "Receptor tyrosine kinase" and "Enzyme-linked receptor"

Type 4: Nuclear receptors

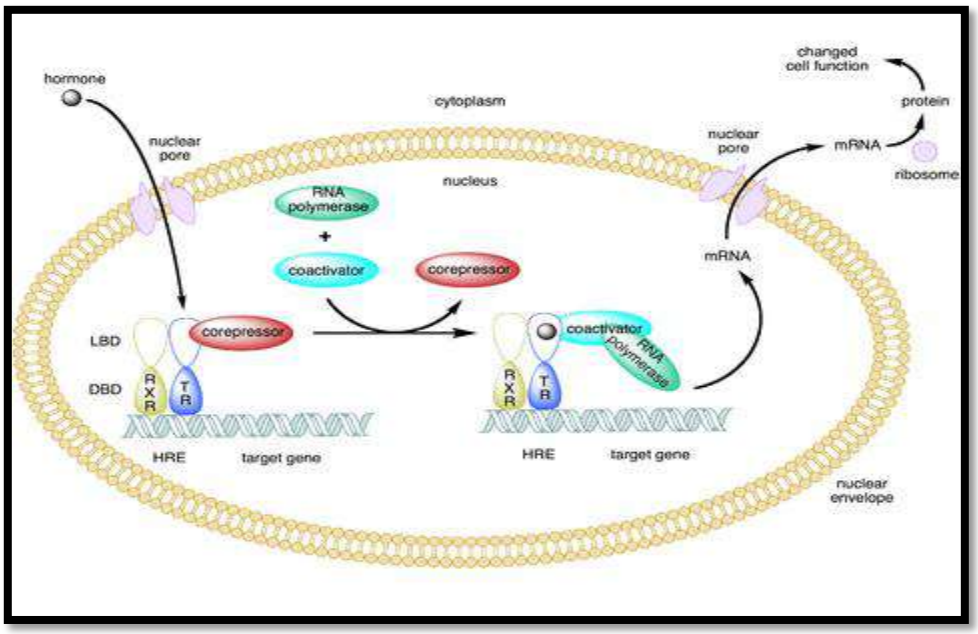

*Fig. **Nuclear receptors***

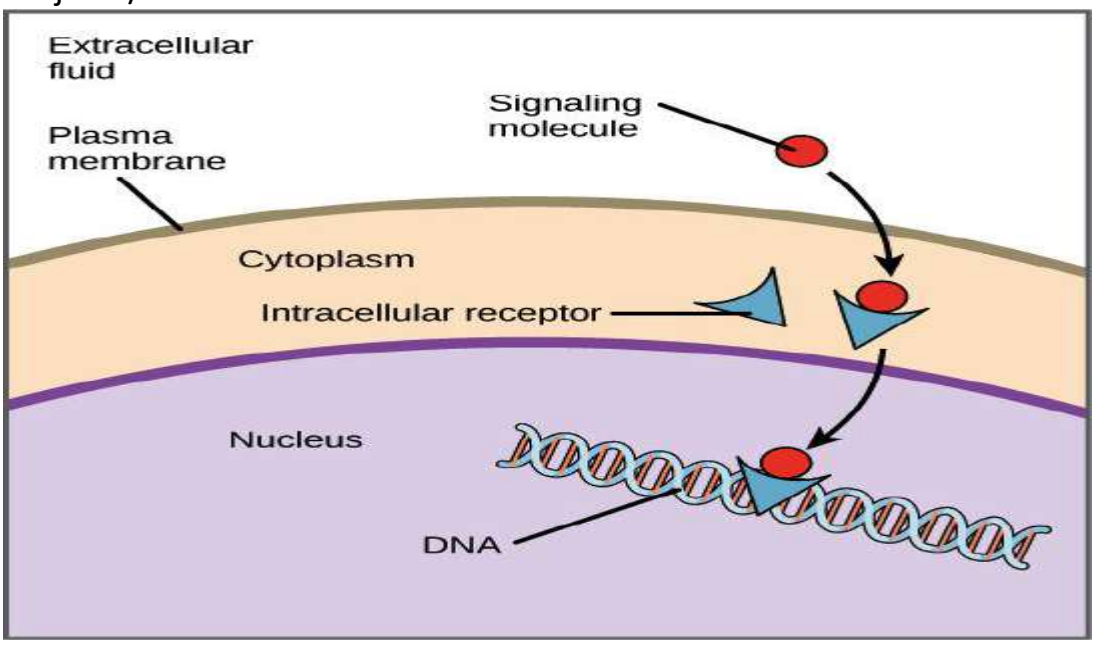

Fig: Ligand-gated ion channels

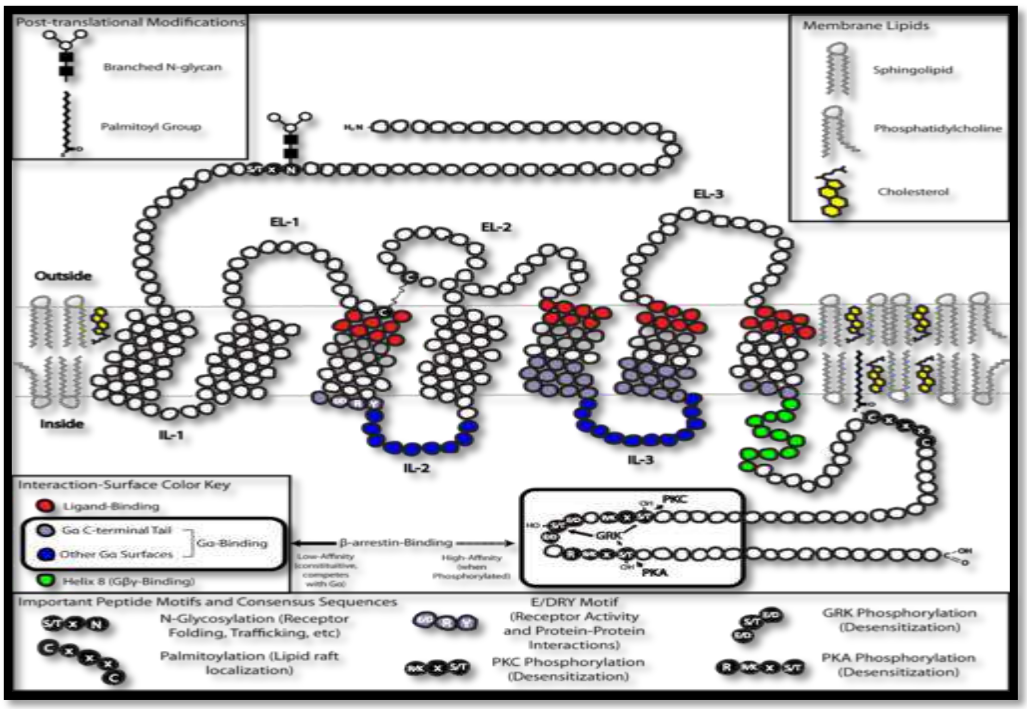

Fig. G protein-coupled receptors

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 10

Name of topic/lesson - Receptors.

Subtopic: Receptors as drug targets, structure, function & signal transduction.

Objective: To study types of the receptors drug targets.

Topic Outcomes: At the end of topic you should be:

1. Able to study types of receptor drug target and struture.

2. Different functions of signal transduction.

Interactions involved in the drug–receptor complex are the same forces experienced by all interacting organic molecules. These include:- covalent bonding, ionic (electrostatic) interactions, ion–dipole and dipole–dipole interactions, hydrogen bonding, charge-transfer interactions, hydrophobic interactions, halogen bonding, and van der Waals interactions.

1. Covalent Bonds : The covalent bond is the strongest bond, generally fromed by sharing of electrons between two atoms. It is formed by a drug–receptor interaction, except with enzymes and DNA. The majority of drugs combine with their receptor by weak molecular interactions.⎫These interactions forms a strong link between the drug and its receptor but individually the interactions are reversible. ⎭ The covalent bonds are important as compare to other bonds.

2. Ionic (or Electrostatic) Interactions :

For protein receptors at physiological pH (pH 7.4), basic groups such as the amino side chains of arginine, lysine are protonated and, therefore, provide a cationic environment. Acidic groups, such as the carboxylic acid side chains of aspartic acid and glutamic acid, are deprotonated to give anionic groups.

3. Ion–Dipole and Dipole–Dipole Interactions :

As a result of the greater electronegativity of atoms such as oxygen, nitrogen, sulfur, and halogens relative to that of carbon, C–X bonds in drugs and receptors, where X is an electronegative atom, will have an asymmetric distribution of electrons; this produces electronic dipoles.

4. Hydrogen Bonds :

Hydrogen bonds are a type of dipole–dipole interaction formed between the proton of a group X–H, where X is an electronegative atom, and one or more other electronegative atoms (Y) containing a pair of non-bonded electrons.

5. Charge–Transfer Complexes :

When a molecule (or group) that is a good electron donor comes into contact with a molecule (or group) that is a good electron acceptor, the donor may transfer some of its charge to the acceptor. This forms a charge-transfer complex.

6. Halogen Bonding :

It has now been well established that a covalently bonded halogen atom can act as an electron acceptor (Lewis acid) to undergo halogen bonding with an electron-rich donor atom, such as O, N, or S. These interactions can govern the conformation of molecules in the binding site of proteins.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 11

Name of topic/lesson - Receptors.

Subtopic-Intracellular cyclic nucleotides and other mediators of biological response.

Objective: To study intracellular cyclic nucleotides and other mediators of biological response.

Topic Outcomes: At the end of topic you should be:

1. Able to study intracellular cyclic nucleotides and other mediators of biological response.

2. Functions of intracellular cyclic nucleotides and other mediators of biological response.

Cyclic nucleotide–gated ion channels or CNG channels are ion channels that function in response to the binding of cyclic nucleotides. CNG channels are nonselective cation channels that are found in the membranes of various tissue and cell types, and are significant in sensory transduction as well as cellular development. Their function can be the result of a combination of the binding of cyclic nucleotides (cGMP and cAMP) and either a depolarization or a hyperpolarization event.

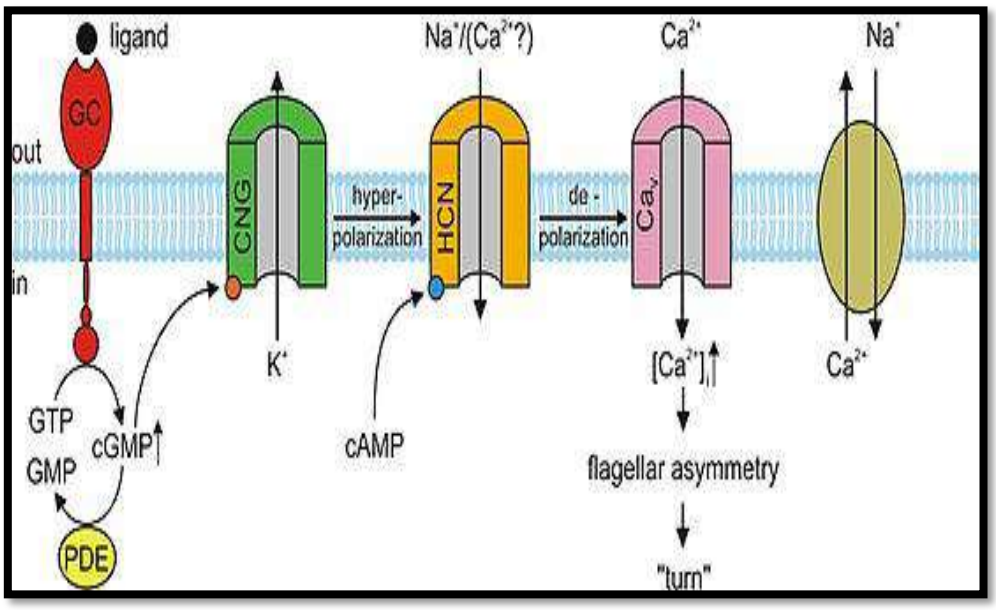

Fig. cyclic nucleotide–gated ion channels

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 12

Name of topic/lesson - Receptors.

Subtopic- Drug- Receptor mechanism including signal transduction.

Objective: To study Drug- Receptor mechanism including signal transduction

Topic Outcomes: At the end of topic you should be:

1. Able to study Drug- Receptor mechanism including signal transduction.

2. Functions and structure of signal transduction.

Signal transduction is the process by which a chemical or physical signal is transmitted through a cell as a series of molecular events, most commonly protein phosphorylation catalyzed by protein kinases, which ultimately results in a cellular response. Proteins responsible for detecting stimuli are generally termed receptors, although in some cases the term sensor is used.

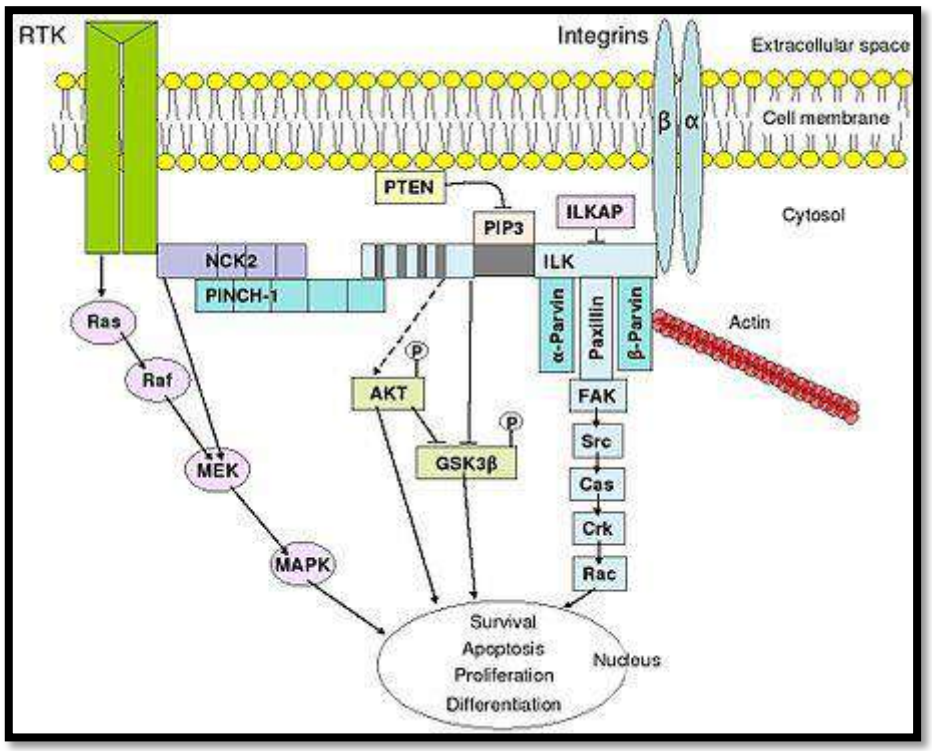

***Fig.* Signal transduction**

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 13

Name of topic/lesson - Adrenergic agent.

Subtopic-Introduction.

Objective: To study the adrenergic agent.

Topic Outcomes: At the end of topic you should be:

1. Able to study the adrenergic agent.

2.Structure of adrenergic agent.

Sympathomimetic drugs (also known as **adrenergic drugs** and **adrenergic amines**) are stimulant compounds which mimic the effects of endogenous agonists of the sympathetic nervous system. The primary endogenous agonists of the sympathetic nervous system are the catecholamines (i.e., epinephrine [adrenaline], norepinephrine [noradrenaline], and dopamine), which function as both neurotransmitters and hormones. Sympathomimetic drugs are used to treat cardiac arrest and low blood pressure, or even delay premature labor, among other things.

Mechanism of action:

The mechanisms of sympathomimetic drugs can be direct-acting (direct interaction between drug and receptor), such as α-adrenergic agonists, β-adrenergic agonists, and dopaminergic agonists; or indirect-acting (interaction not between drug and receptor), such as MAOIs, COMT inhibitors, release stimulants, and reuptake inhibitors that increase the levels of endogenous catecholamines.

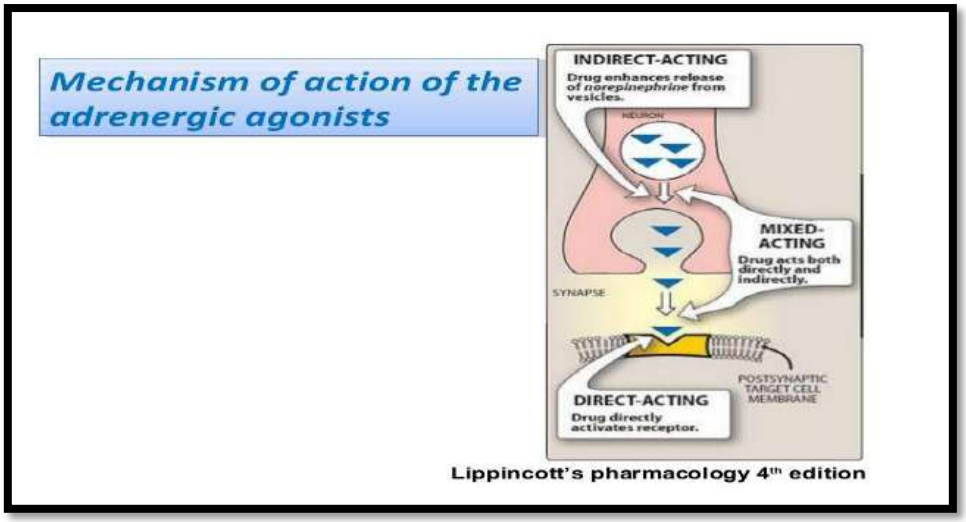

Fig. Mechanism of action of adrenergic agent.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 14

Name of topic/lesson - Adrenergic agent.

Subtopic- Adrenergic agonist.

Objective: To study the different types adrenergic agonist.

Topic Outcomes: At the end of topic you should be:

1. Able to study different types of adrenergic agonist.

2.Classification of adrenergic agonist.

An **adrenergic agonist** is a drug that stimulates a response from the adrenergic receptors. The five main categories of adrenergic receptors are: α_1, α_2, β_1, β_2, and β_3, although there are more subtypes, and agonists vary in specificity between these receptors, and may be classified respectively. However, there are also other mechanisms of adrenergic agonism. Epinephrine and norepinephrine are endogenous and broad-spectrum. More selective agonists are more useful in pharmacology.

An *adrenergic* agent is a drug, or other substance, which has effects similar to, or the same as, epinephrine (adrenaline). Thus, it is a kind of sympathomimetic agent. Alternatively, it may refer to something which is susceptible to epinephrine, or similar substances, such as a biological receptor (specifically, the adrenergic receptors).

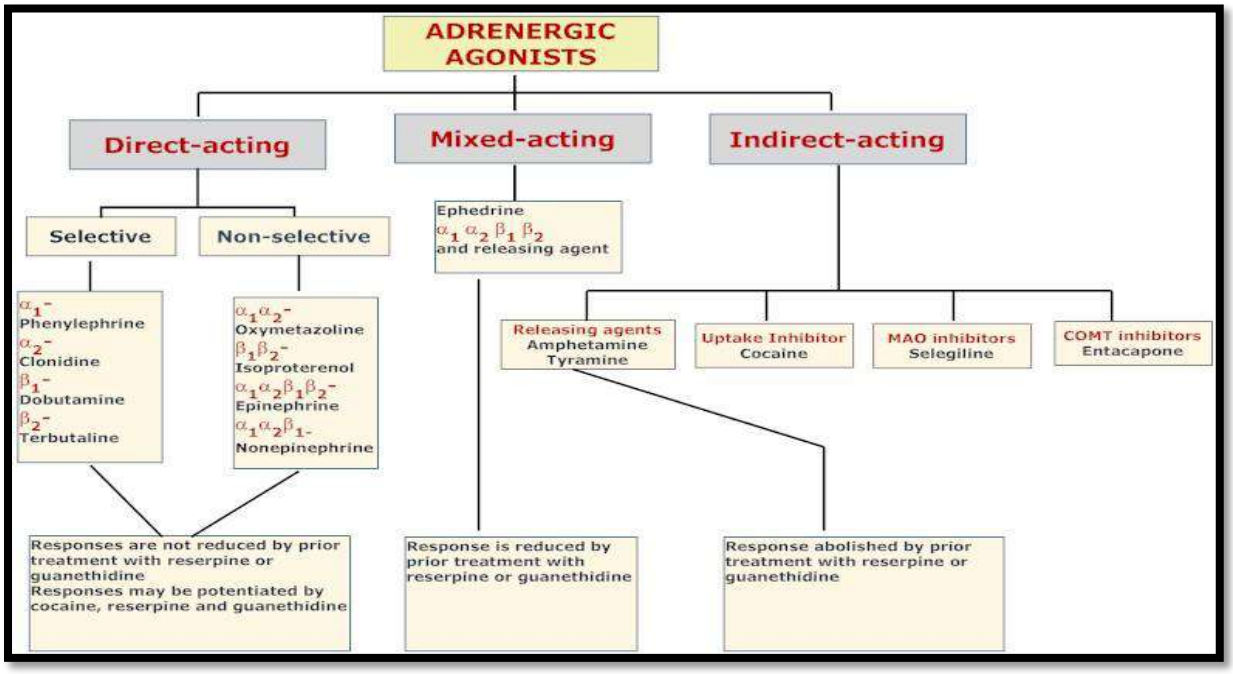

Fig. Classification of adrenergic agonists.

References:

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Lecture No: 15

Name of topic/lesson - Adrenergic agent.

Subtopic- Adrenergic agonist.

Objective: To study the different types adrenergic agonist and their examples.

Topic Outcomes: At the end of topic you should be:

1. Able to study different types of adrenergic agonist and examples.

2.Able to draw different strutures.

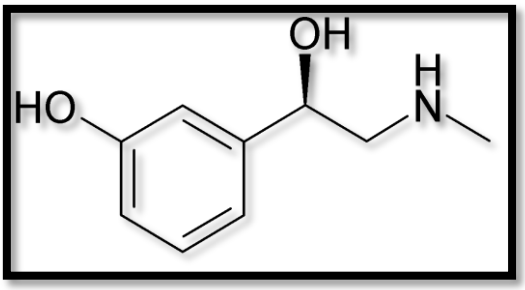

Fig .phenylephrine.

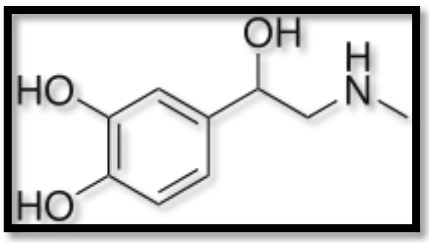

Fig.Epinephrine.

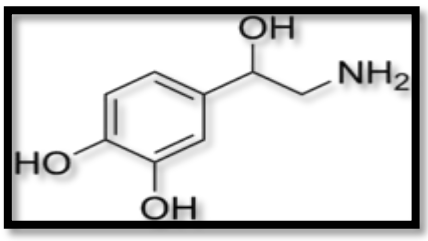

Fig.Norepinephrine.

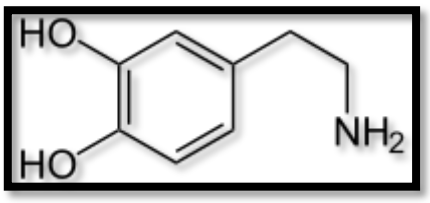

Fig.Dopamine.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

4. Principles of Medicinal Chemistry by Kadam SS, Mahadik KR, Bothara KG, Vol. I & II, 10th Edition, Nirali Prakashan.

Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 16

Name of topic/lesson - Adrenergic agent.

Subtopic-Adrenergic antagonist.

Objective: To study the different types adrenergic antagonist.

Topic Outcomes: At the end of topic you should be:

1. Able to study different types of adrenergic antagonist.

2.Different classification of adrenergic antagonist.

An **adrenergic antagonist** is a drug that inhibits the function of adrenergic receptors. There are five adrenergic receptors, which are divided into two groups. The first group of receptors are the beta (β) adrenergic receptors. There are β_1, β_2, and β_3 receptors. The second group contains the alpha (α) adrenoreceptors. There are only α_1 and α_2 receptors. Adrenergic receptors are located near the heart, kidneys, lungs, and gastrointestinal tract.[1] There are also α-adreno receptors that are located on vascular smooth muscle.

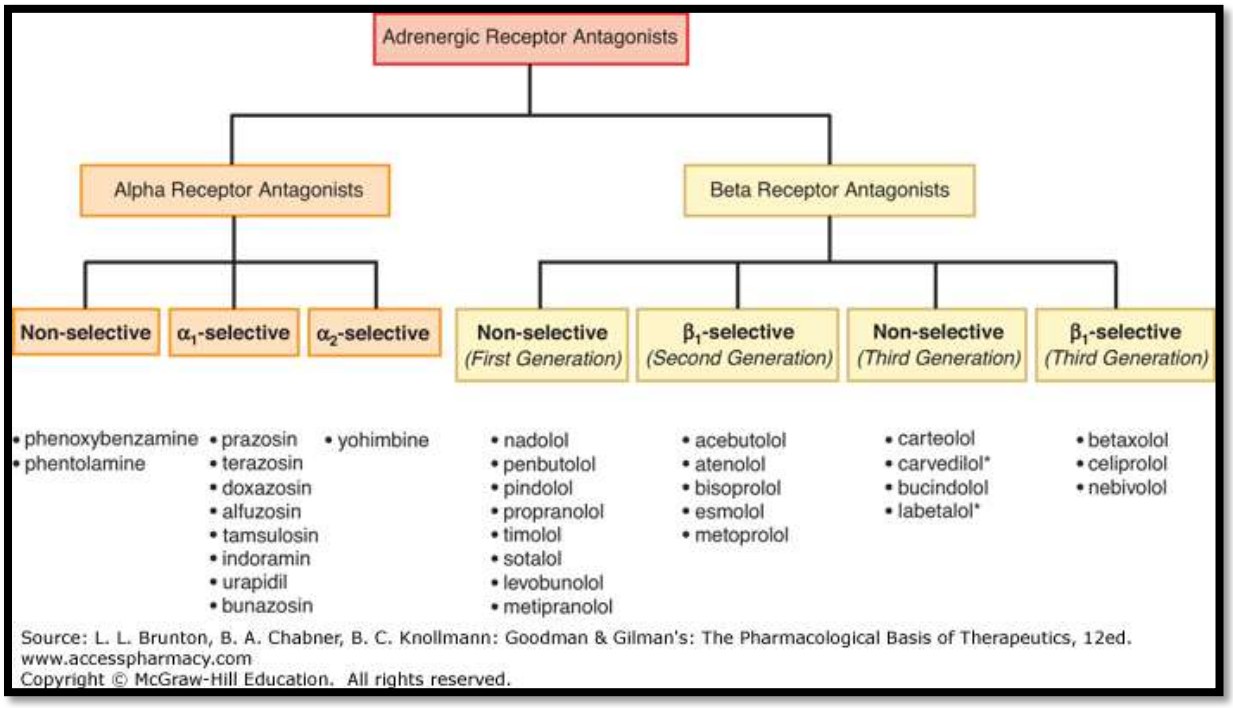

Fig. Classification of adrenergic antagonist.

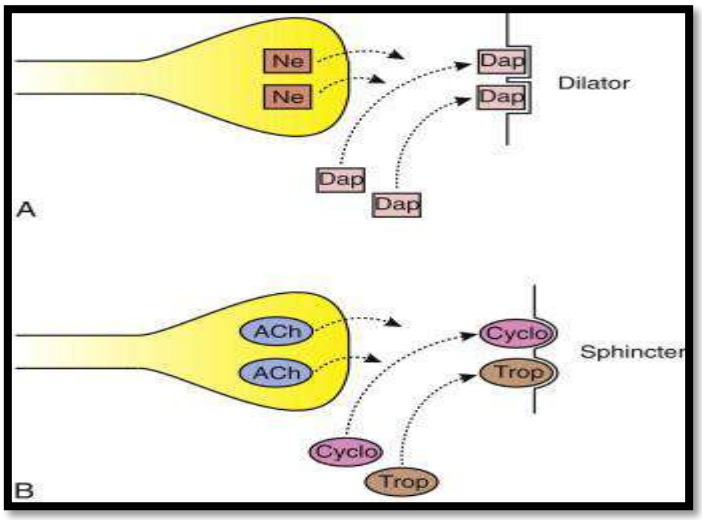

Fig. Adrenergic antagonist mechanism of action.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 17

Name of topic/lesson - Adrenergic agent.

Subtopic-Adrenergic antagonist.

Objective: To study the different types adrenergic antagonist and their examples.

Topic Outcomes: At the end of topic you should be:

1. Able to study different types of adrenergic antagonist and their examples.

2. Able to draw different strutures.

a) Alpha blockers:

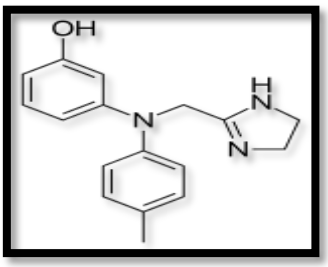

Fig.Phentolamine

Its primary action is vasodilation due to α_1 blockade. Non-selective α-blockers can cause a much more pronounced reflex tachycardia than the selective α_1 blockers. Like the selective $\alpha_1$blockers, phentolamine causes a relaxation of systemic vasculature, leading to hypotension. This hypotension is sensed by the baroreceptor reflex, which results in increased sympathetic nerve firing on the heart, releasing norepinephrine.

b) Beta blockers:

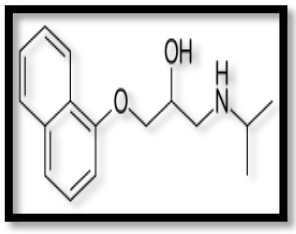

Fig.Propranolol

Propranolol is a medication of the beta blocker class. It is used to treat high blood pressure, a number of types of irregular heart rate, thyrotoxicosis, capillary hemangiomas, performance anxiety, and essential tremors.

c) Mixed action:

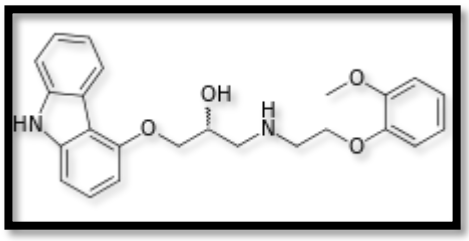

Fig.Carvedilol

Carvedilol is a medication used to treat high blood pressure, congestive heart failure(CHF), and left ventricular dysfunction in people who are otherwise stable.[1] For high blood pressure, it is generally a second-line treatment.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 18

Name of topic/lesson - Adrenergic agent.

Subtopic-Biosynthesis.

Objective: To study the Biosynthesis of adrenergic agent.

Topic Outcomes: At the end of topic you should be:

1. Able to study the biosynthesis of catecholamine.

2. Able to draw different strutures.

Adrenergic (more precisely 'Noradrenergic') transmission is restricted to the sympathetic division of the ANS. There are three closely related endogenous catecholamines (CAs). Noradrenaline (NA) It acts as transmitter at postganglionic sympathetic sites (except sweat glands, hair follicles and some vasodilator fibres) and in certain areas of brain. Adrenaline (Adr) It is secreted by adrenal medulla and may have a transmitter role in the brain. Dopamine (DA) It is a major transmitter in basal ganglia, limbic system, CTZ, anterior pituitary, etc. and in a limited manner in the periphery.

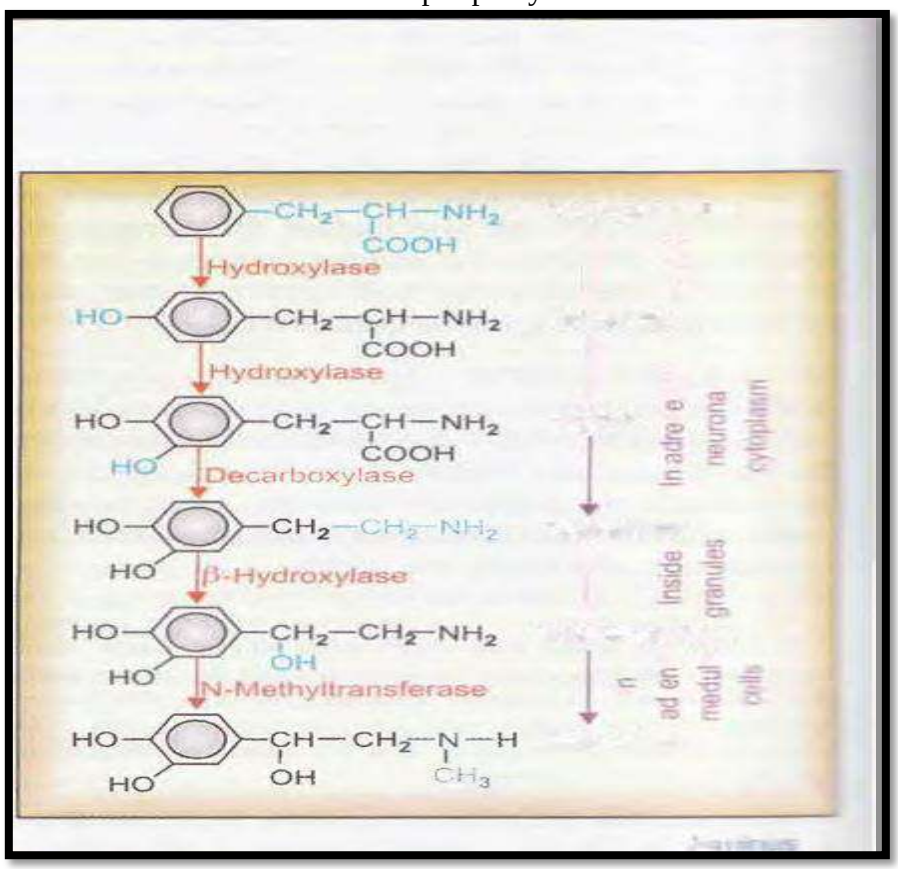

Fig.Synthesis of catecholamines (CAs).

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture No: 19

Name of topic/lesson - Adrenergic agent.

Subtopic-Release and metabolism of noradrenaline.

Objective: To study the Release and metabolism of noradrenaline.

Topic Outcomes: At the end of topic you should be:

1. Able to study the release mechanism of noradrenaline.
2. Able to draw metabolism pathway of noradrenaline.

Inside the brain norepinephrine functions as a neurotransmitter, and is controlled by a set of mechanisms common to all monoamine neurotransmitters. After synthesis, norepinephrine is transported from the cytosolinto synaptic vesicles by the vesicular monoamine transporter (VMAT). Norepinephrine is stored in these vesicles until it is ejected into the synaptic cleft, typically after an action potential causes the vesicles to release their contents directly into the synaptic cleft through a process called exocytosis.

Once in the synapse, norepinephrine binds to and activates receptors. After an action potential, the norepinephrine molecules quickly become unbound from their receptors. They are then absorbed back into the presynaptic cell, via reuptake mediated primarily by the norepinephrine transporter (NET). Once back in the cytosol, norepinephrine can either be broken down by monoamine oxidase or repackaged into vesicles by VMAT, making it available for future release.

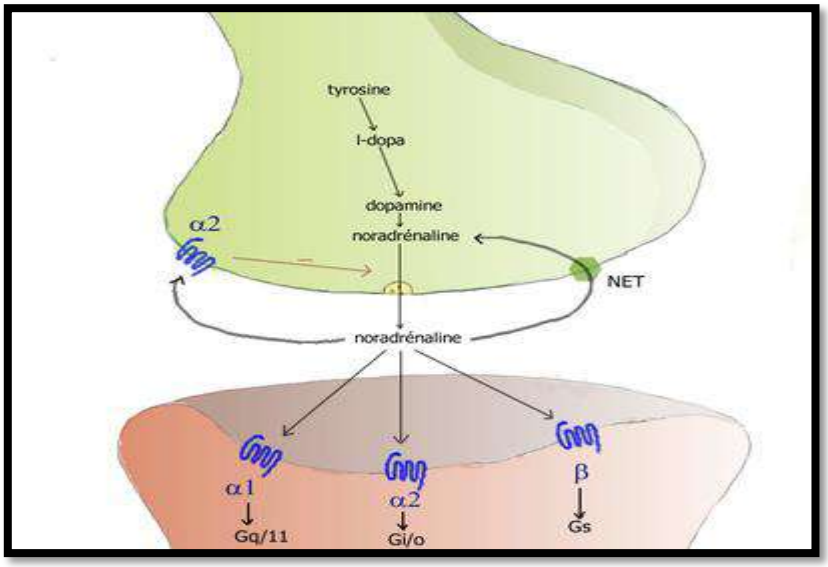

Fig. Release and metabolism of noradrenaline.

Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 20

Name of topic/lesson - Adrenergic agent.

Subtopic-Receptor subtypes and their structural features.

Objective: To study the -Receptor subtypes and their structural features.

Topic Outcomes: At the end of topic you should be:

1. Able to study the types and their subtypes.

2. Able to draw classsification and structures.

The **adrenergic receptors** or **adrenoceptors** are a class of G protein-coupled receptors that are targets of many catecholamines like norepinephrine (noradrenaline) and epinephrine (adrenaline) produced by the body, but also many medications like beta blockers, $\beta_2$agonists and α_2 agonists, which are used to treat high blood pressure and asthma. There are two main groups of adrenoreceptors, α and β, with 9 subtypes in total:

- α are divided to α_1 (a G_q coupled receptor) and α_2 (a G_i coupled receptor):
  - α_1 has 3 subtypes: α_{1A}, α_{1B} and α_{1D}
  - α_2 has 3 subtypes: α_{2A}, α_{2B} and α_{2C}
- β are divided to β_1, β_2 and β_3. All 3 are coupled to G_s proteins, but β_2 and β_3 also couple to G_i

G_i and G_s are linked to adenylyl cyclase. Agonist binding thus causes a rise in the intracellular concentration of the second messenger (Gi inhibits the production of cAMP) cAMP. Downstream effectors of cAMP include cAMP-dependent protein kinase (PKA), which mediates some of the intracellular events following hormone binding.

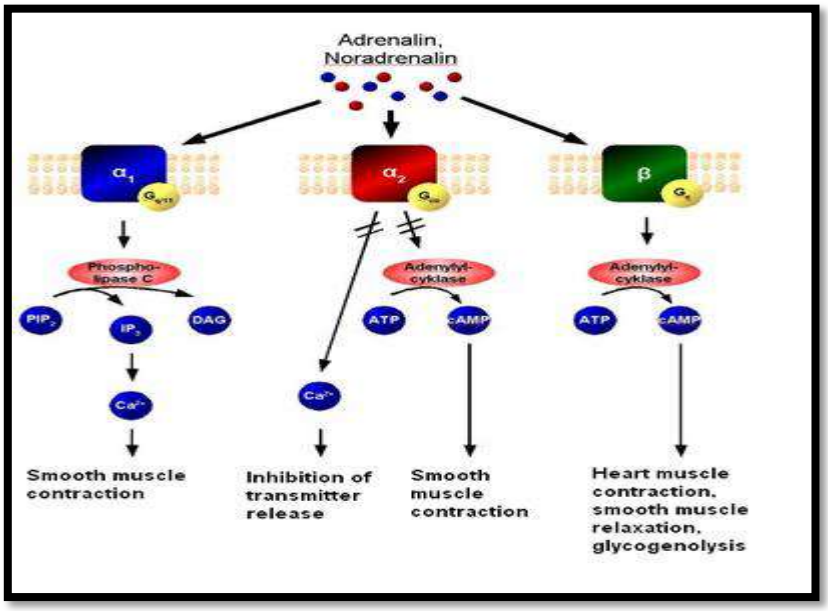

Fig. mechanism of adrenoreceptors.

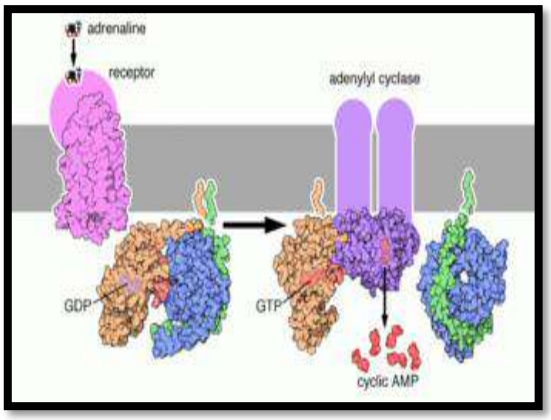

Fig. Adrenergic receptor.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 21

Name of topic/lesson - Cholinergic agent.

Subtopic-Introduction.

Objective: To study the Cholinergic agent.

Topic Outcomes: At the end of topic you should be:

1. Able to define cholinergic agent and drug.

2. Able to draw mechanism of action of cholinergic agent.

Cholinergic agents are compounds which mimic the action of acetylcholine. A **parasympathomimetic drug**, sometimes called a **cholinomimetic drug**, is a substance that stimulates the parasympathetic nervous system (PSNS). These chemicals are also called cholinergic drugs because acetylcholine (ACh) is the neurotransmitter used by the PSNS. Chemicals in this family can act either directly by stimulating the nicotinic or muscarinic receptors (thus mimicking acetylcholine), or indirectly by inhibiting cholinesterase, promoting acetylcholine release, or other mechanisms.

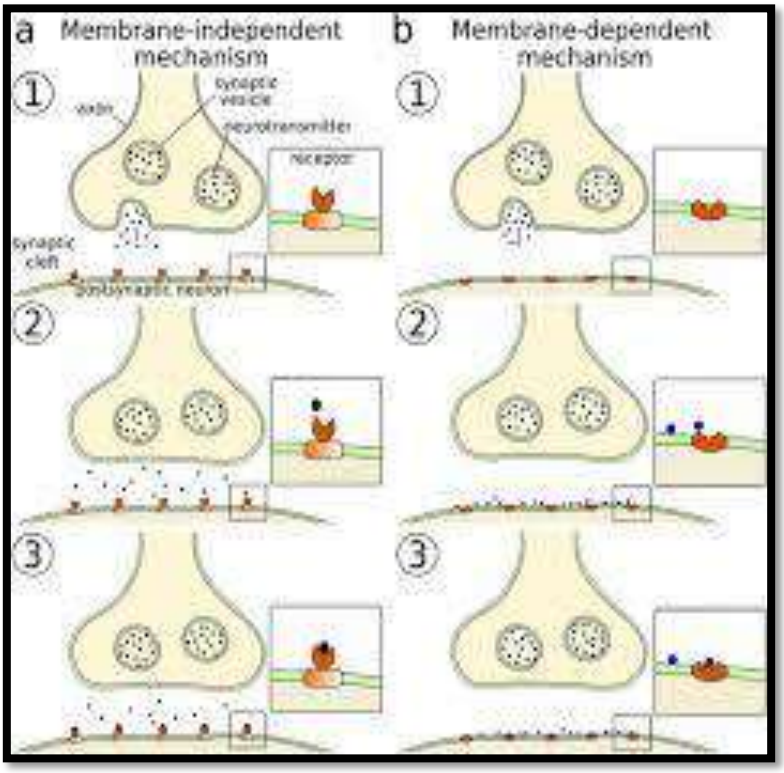

Fig. Mechanism of action of cholinergic agent.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 22

Name of topic/lesson - Cholinergic agent.

Subtopic-Biosynthesis.

Objective: To study the biosynthesis of Cholinergic agent.

Topic Outcomes: At the end of topic you should be:

1. Able to study biosynthesis cholinergic agent and drug.
2. Able to draw biosynthesis of cholinergic agent.

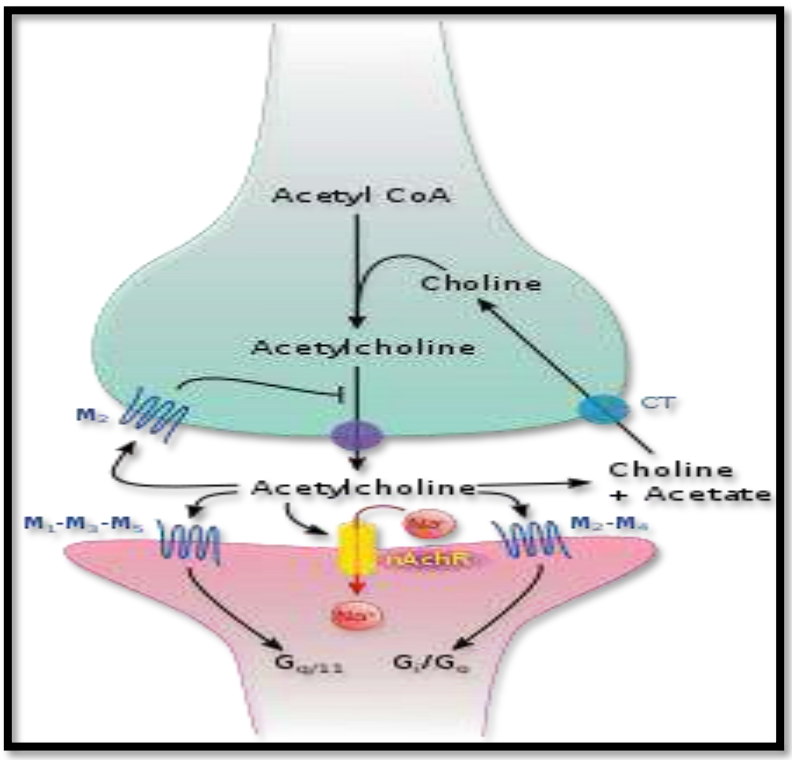

Fig. Biosynthesis of cholinergic agent.

Choline acetyltransferase (commonly abbreviated as **ChAT**, but sometimes **CAT**) is a transferase enzyme responsible for the synthesis of the neurotransmitter acetylcholine. ChAT catalyzes the transfer of an acetyl group from the coenzyme acetyl-CoA to choline, yielding acetylcholine (ACh). ChAT is found in high concentration in cholinergic neurons, both in the central nervous system(CNS) and peripheral nervous system (PNS). As with most nerve terminal proteins, ChAT is produced in the body of the neuron and is transported to the nerve terminal, where its concentration is highest.

Presence of ChAT in a nerve cell classifies this cell as a "cholinergic" neuron. In humans, the choline acetyltransferase enzyme is encoded by the *CHAT* gen**e.**

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture No: 23

Name of topic/lesson - Cholinergic agent.

Subtopic-Release and metabolism of acteylcholine.

Objective: To study the Release and metabolism of acteylcholine.

Topic Outcomes: At the end of topic you should be:

1. Able to study Release and metabolism of acteylcholine and drug.
2. Able to draw structure of Release and metabolism of acteylcholine**.**

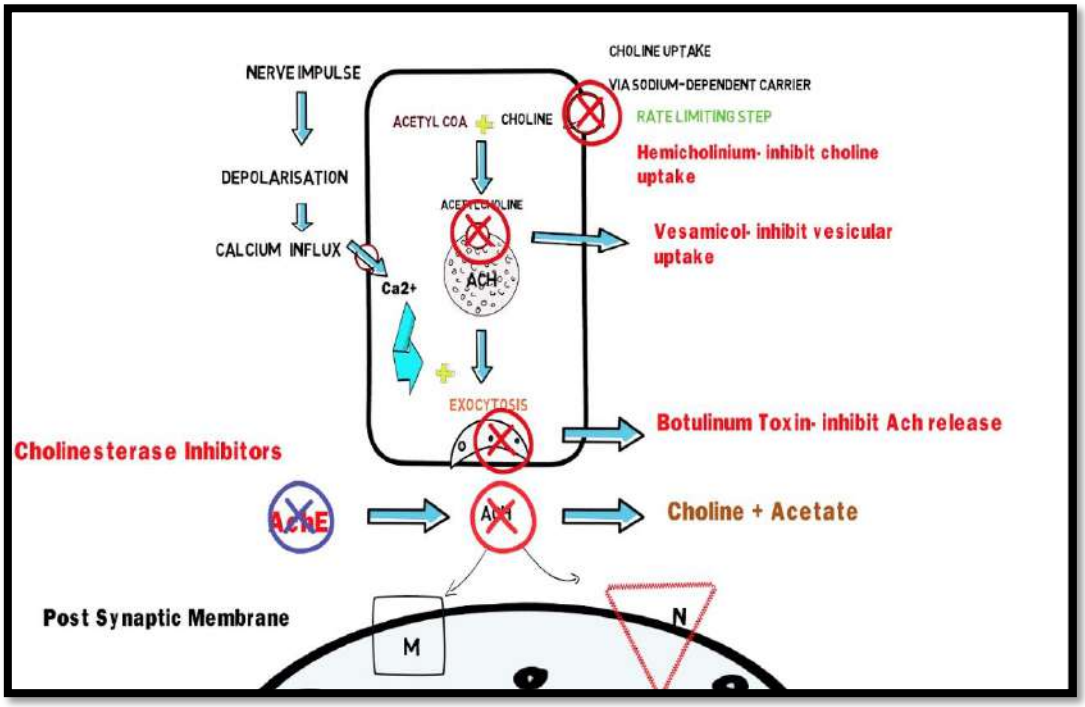

Fig. Release and metabolism of acetylcholine.

ACh is released from the presynaptic neuron into the synaptic cleft and binds to ACh receptors on the post-synaptic membrane, relaying the signal from the nerve. AChE, also located on the post-synaptic membrane, terminates the signal transmission by hydrolyzing ACh. The liberated choline is taken up again by the pre-synaptic neuron and ACh is synthesized by combining with acetyl-CoA through the action of choline acetyltransferase.

Metabolism of acetylchoine done by the acetylcholinesterase enzyme which are located at post synaptic cell region. these enzymes responsible for metabolism and release of acetylcholine from synaptic vessel.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture No: 24

Name of topic/lesson - Cholinergic agent.

Subtopic-Cholinergic receptors.

Objective: To study the different types of Cholinergic receptors

Topic Outcomes: At the end of topic you should be:

1. Able to study the classification of cholinergic receptors.
2. Able to draw structure of cholinergic receptors.

Cholinergic receptors function in signal transduction of the somatic and autonomic nervous system. The receptors are named because they are activated by the ligand acetylcholine. These receptors are subdivided into nicotinic and muscarinic receptors which are named secondary to separate activating ligands that contributed to their study. Nicotinic receptors are responsive to the agonist nicotine, while muscarinic receptors are responsive to muscarine. While both nicotinic and muscarinic receptors are activated in response to the ligand binding of acetylcholine, their mechanism of activation differs significantly. As mentioned, nicotinic receptors are ionotropic. This means activation of the receptor leads to the formation of an ion channel within the cell membrane, known as a ligand-gated ion channel.

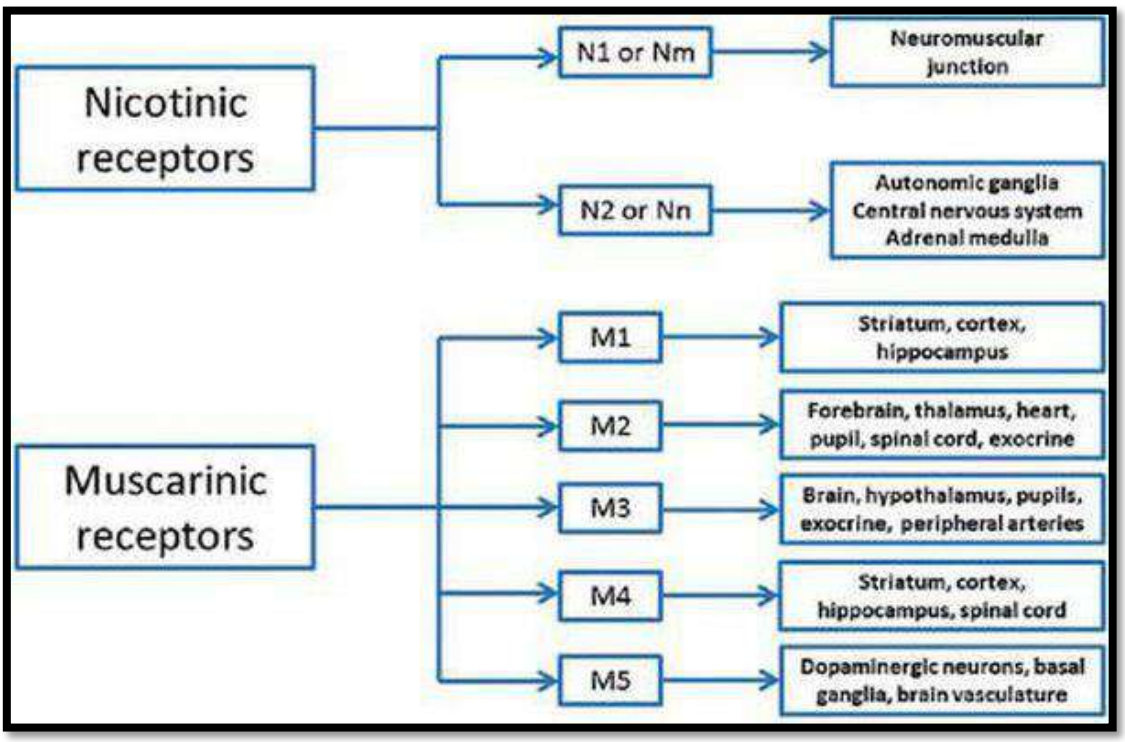

Fig. Types of cholinergic receptors.

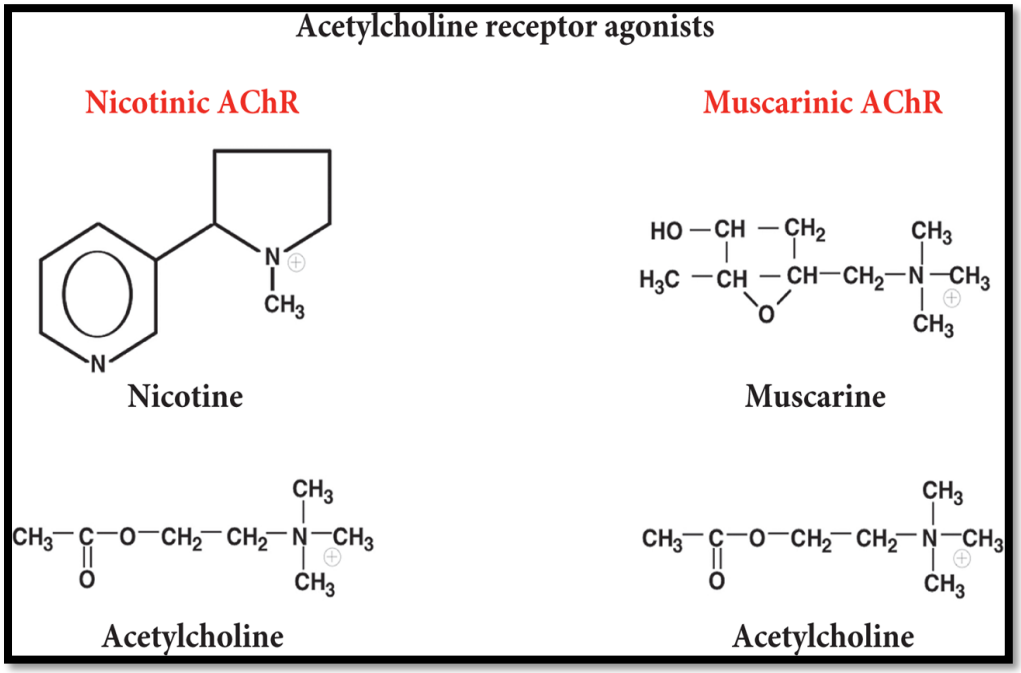

Fig. Examples of cholinergic receptors.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 25

Name of topic/lesson - Cholinergic agent.

Subtopic-Cholinergic agonists.

Objective: To study the Classification and types of cholinergic agonist.

Topic Outcomes: At the end of topic you should be:

1. Able to study the cholinergic agonists and their types.
2. Able to draw different structure of cholinergic agonists.

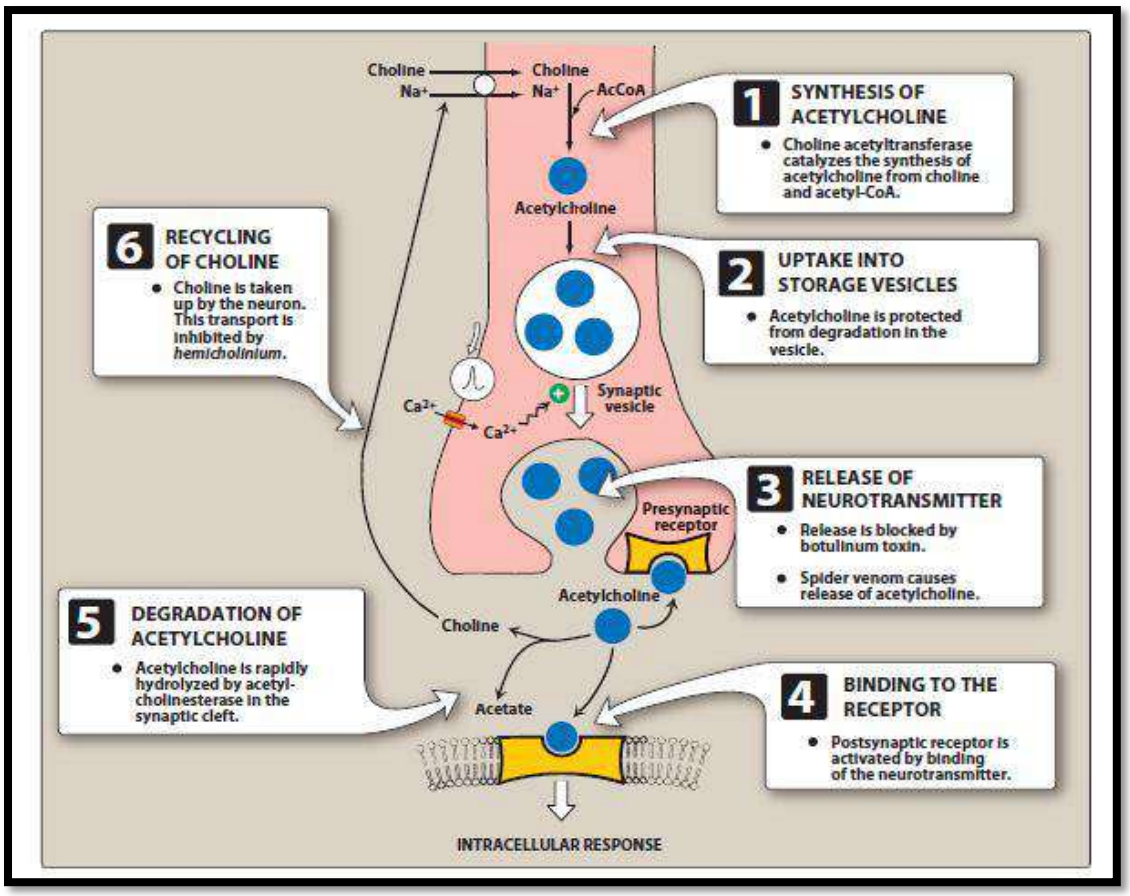

Fig. Cholinergic agonist.

muscarinic agonist is an agent that activates the activity of the muscarinic acetylcholine receptor. The muscarinic receptor has different subtypes, labelled M1-M5, allowing for further differentiation. A **nicotinic agonist** is a drug that mimics the action of acetylcholine (ACh) at nicotinic acetylcholine receptors (nAChRs). The nAChR is named for its affinity for nicotine.

Examples include nicotine (by definition), acetylcholine (the endogenous agonist of nAChRs), choline, epibatidine, lobeline, varenicline and cytisine.

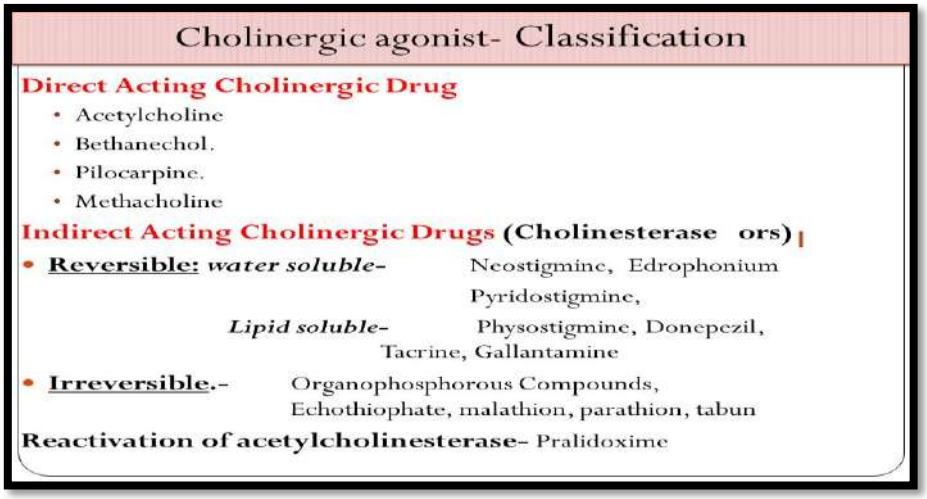

Fig.classification ofcholineric agonist.

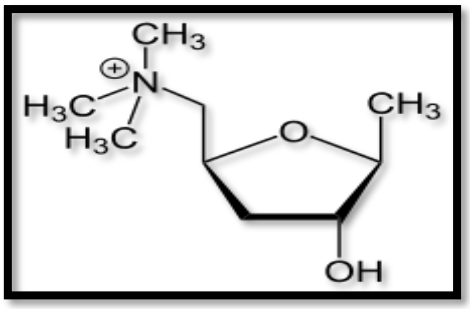

Fig. muscarinic agonist.

References:

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 26

Name of topic/lesson - Cholinergic agent.

Subtopic-Cholinergic antagonist.

Objective: To study the classification and types of cholinergic antagonist.

Topic Outcomes: At the end of topic you should be:

1. Able to study the cholinergic antagonist and their types.
2. Able to draw structure of cholinergic antagonist.

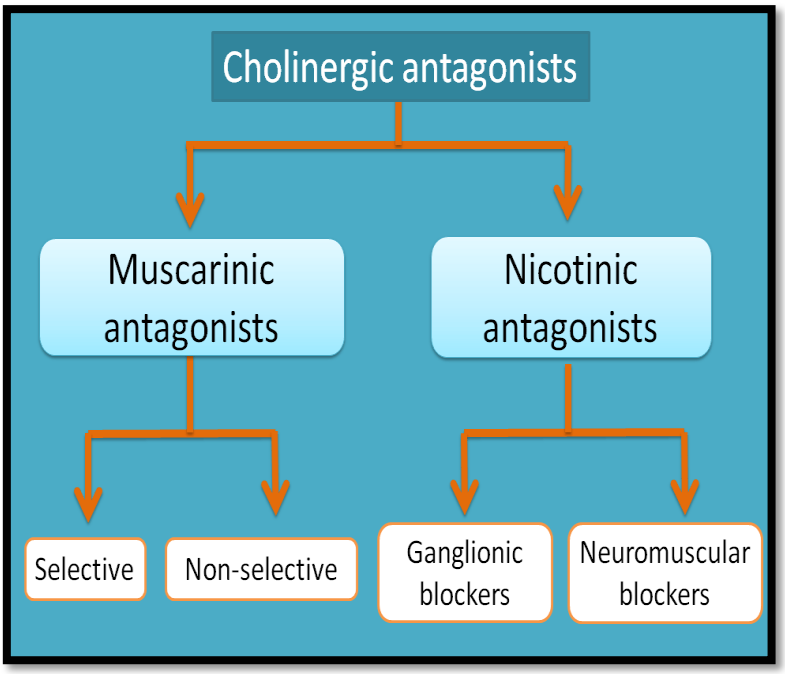

Fig. classification of cholinergic antagonist.

A **muscarinic receptor antagonist** (**MRA**) is a type of anticholinergic agent that blocks the activity of the muscarinic acetylcholine receptor. Acetylcholine (often abbreviated **ACh**) is a neurotransmitter whose receptor is a protein found in synapses and other cell membranes. Besides responding to their primary neurochemical, neurotransmitter receptors can be sensitive to a variety of other molecules.

A **nicotinic antagonist** is a type of anticholinergic drug that inhibits the action of acetylcholine (ACh) at nicotinic acetylcholine receptors. These compounds are mainly used for peripheral muscle paralysis in surgery, the classical agent of this type being tubocurarine, but some centrally acting compounds such as bupropion, mecamylamine,

and 18-methoxycoronaridine block nicotinic acetylcholine receptors in the brain and have been proposed for treating nicotine addiction.

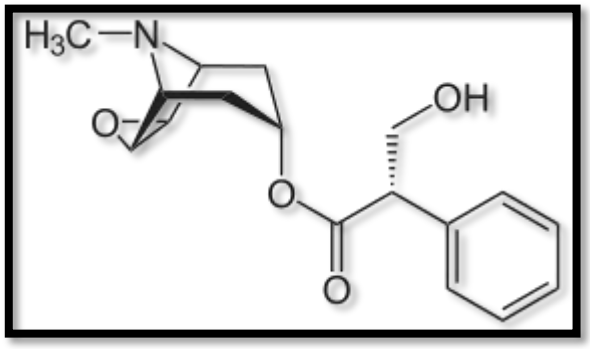

Fig. Muscarinic antagonist.

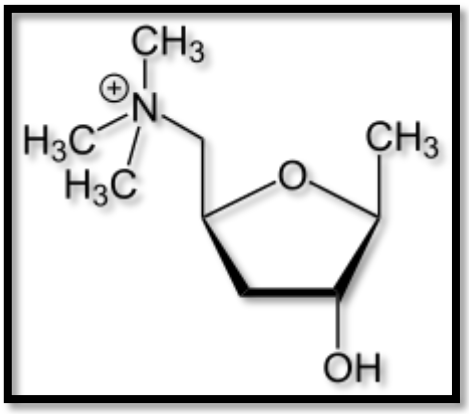

Fig. Muscarinic agonist.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 27

Name of topic/lesson - Cholinergic agent.

Subtopic-Acetylcholinesterase inhibitors.

Objective: To study the Acetylcholinesterase inhibitors.

Topic Outcomes: At the end of topic you should be:

1. Able to study the acetylcholinesterase inhibitors.

2. Able to draw the inhibition of acetylcholinesterase inhibitors.

acetylcholinesterase inhibitor (**AChEI**) or **anti-cholinesterase** is a chemical or a drug that inhibits the acetylcholinesterase enzyme from breaking down acetylcholine, thereby increasing both the level and duration of action of the neurotransmitter acetylcholine. Acetylcholinesterase inhibitors are classified as reversible, irreversible, or quasi-irreversible (also called pseudo-irreversible).

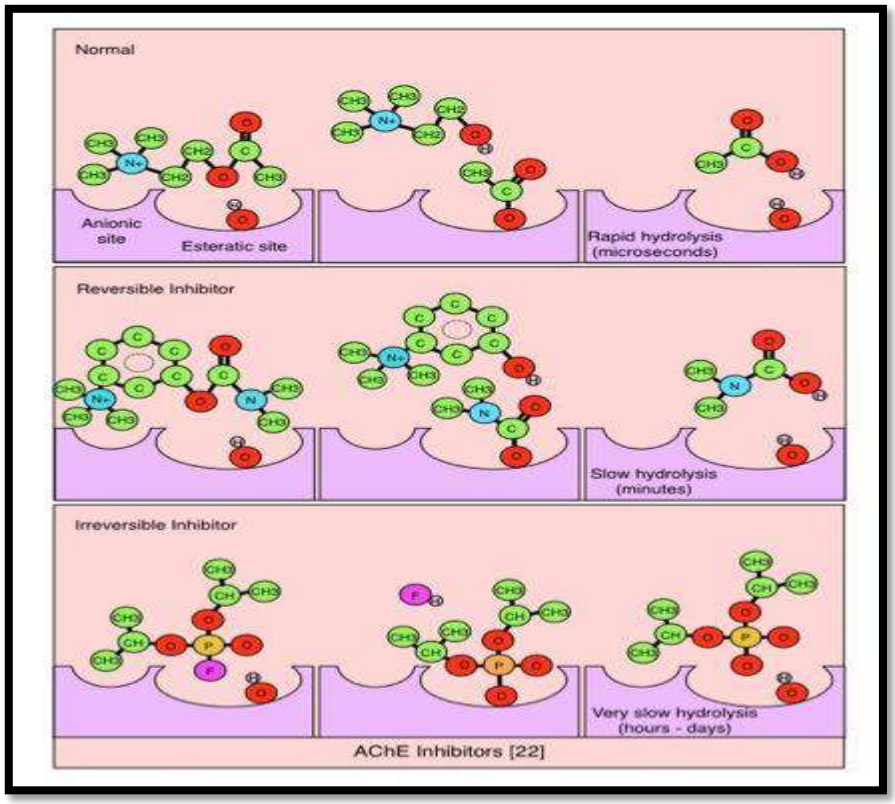

Fig. acetylcholinesterase inhibitors.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

4. Principles of Medicinal Chemistry by Kadam SS, Mahadik KR, Bothara KG, Vol. I & II, 10th Edition, Nirali Prakashan.

Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 28

Name of topic/lesson - Cholinergic agent.

Subtopic- Ganglionic blockers.

Objective: To study the Ganglionic blockers.

Topic Outcomes: At the end of topic you should be:

1. Able to study the ganglionic blockers and drug.

2. Able to draw structure of ganglionic blockers.

A **ganglionic blocker** (or **ganglioplegic**) is a type of medication that inhibits transmission between preganglionic and postganglionic neurons in the Autonomic Nervous System, often by acting as a nicotinic receptor antagonist. Nicotinic acetylcholine receptors are found on skeletal muscle, but also within the route of transmission for the parasympathetic and sympathetic nervous system (which together comprise the autonomic nervous system). More specifically, nicotinic receptors are found within the ganglia of the autonomic nervous system, allowing outgoing signals to be transmitted from the presynaptic to the postsynaptic cells. Thus, for example, blocking nicotinic acetylcholine receptors blocks both sympathetic (excitatory) and parasympathetic (calming) stimulation of the heart. The nicotinic antagonist hexamethonium, for example, does this by blocking the transmission of outgoing signals across the autonomic ganglia at the postsynaptic nicotinic acetylcholine receptor.

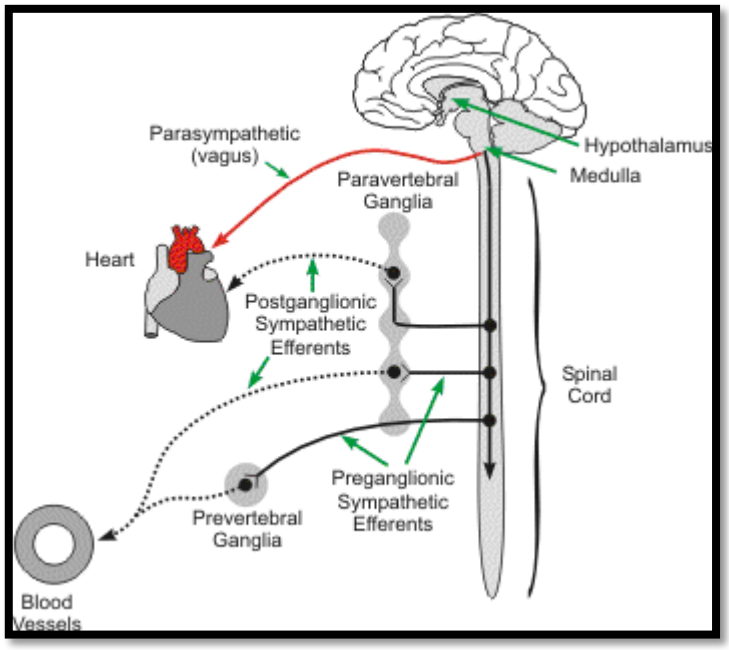

Fig. Ganglionic blockers.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 29

Name of topic/lesson - Cholinergic agent.

Subtopic- Neuromuscular blockers.

Objective: To study the Neuromuscular blockers.

Topic Outcomes: At the end of topic you should be:

1. Able to study the neuromuscular blockers and drug.

2. Able to draw structure of neuromuscular blockers.

Neuromuscular-blocking drugs block neuromuscular transmission at the neuromuscular junction, causing paralysis of the affected skeletal muscles. This is accomplished either by acting presynaptically via the inhibition of acetylcholine (ACh) synthesis or release or by acting postsynaptically at the acetylcholine receptors of the motor nerve end-plate. While some drugs act presynaptically (such as botulinum toxin and tetanus toxin), those of current clinical importance work postsynaptically.

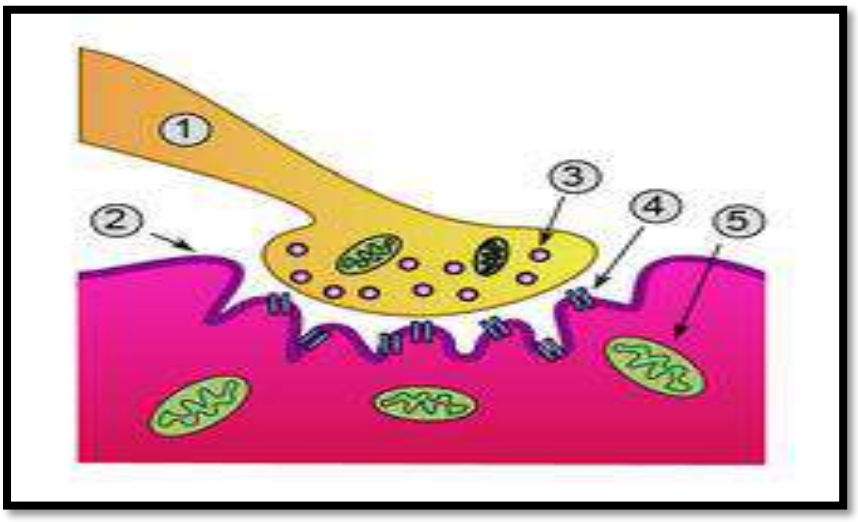

Fig.Neuromuscular-blocking drugs

Mechanism of action: Quaternary muscle relaxants bind to the nicotinic acetylcholine receptor and inhibit or interfere with the binding and effect of ACh to the receptor.
Each ACh-receptor has two receptive sites and activation of the receptor requires binding to both of them. Each receptor site is located at one of the two α-subunits of the receptor. Each receptive site has two subsites, an anionic site that binds to
the cationic ammonium head and a site that binds to the blocking agent by donating
a hydrogen bond.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 30

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Introduction.

Objective: To study the Drugs affecting cardiovascular system.

Topic Outcomes: At the end of topic you should be:

1. Able to study the drug affected by CVS.

2. Able to draw structure of the CVS drugs.

Cardiovascular disease (**CVD**) is a class of diseases that involve the heart or blood vessels. CVD includes coronary artery diseases (CAD) such as angina and myocardial infarction (commonly known as a heart attack). Other CVDs include stroke, heart failure, hypertensive heart disease, rheumatic heart disease, cardiomyopathy, heart arrhythmia, congenital heart disease, valvular heart disease, carditis, aortic aneurysms, peripheral artery disease, thromboembolic disease, and venous thrombosis.

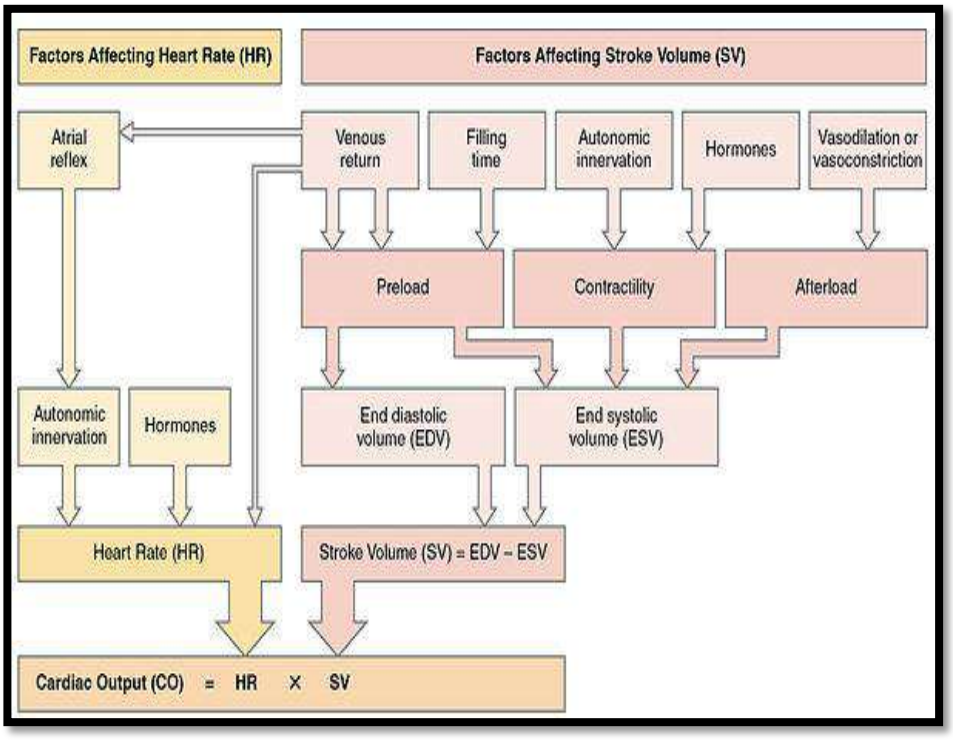

Fig.Cardiac physiology

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 31

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Cardiotonic agents.

Objective: To study the cardiotoinic agent and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the cardiotonic agent.

2. Able to draw mechanism of action of cardiotonic agent.

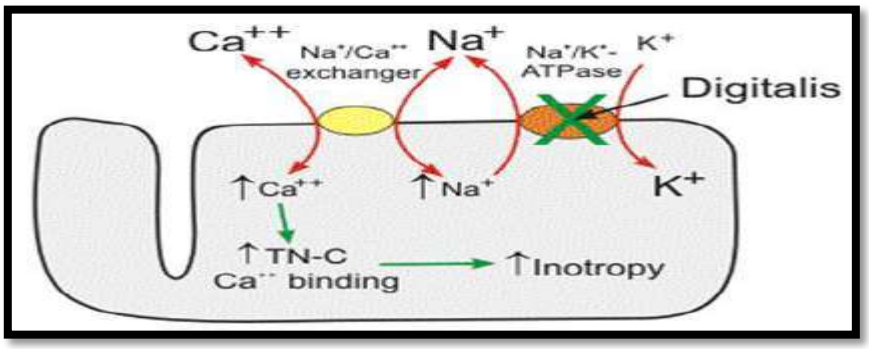
Cardiotonic agents are drugs used to increase the contractility and output in a hypodynamic heart without propotionate increase in 02 consumption .Commonly used in the treatment of heart failure (HF).Cardiotonic (inotropic) drugs affect the intracellular calcium levels in the heart muscle, leading to increased contractility. This increase in contraction strength leads to increased cardiac output, which causes increased renal blood flow and increased urine production**.**

TYPES:

1. Cardiac glycoside.
2.Phosphodiesterase inhibitors.

Mechanism of action:

Digitalis compounds are potent inhibitors of cellular Na^+/K^+-ATPase. This ion transport system moves sodium ions out of the cell and brings potassium ions into the cell. This transport function is necessary for cell survival because sodium diffusion into the cell and potassium diffusion out of the cell down their concentration gradients would reduce their concentration differences (gradients) across the cell membrane over time. Loss of these ion gradients would lead to cellular depolarization and loss of the negative membrane potential that is required for normal cell function. The Na^+/K^+-ATPase also plays an active role in the membrane potential.



Fig, Mechanism of action.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture No: 32

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Cardiotonic agents.

Objective: To study the cardiotoinic agent and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the cardiotonic agent.

2. Able to draw different structure of cardiotonic agent.

Chemical structure of cardiac glycosides:

CGs contain non-sugar part (aglycon or genin) which is considered to be cyclopentanoperhydrophenantrene ring connected with 5-membered lactonic cycle (groups of cardenolids) or 6-membered nonsaturated lactonic cycle (groups of bufadienolids) and sugar part (glycon). The main CGs are considered to be cardenolids. Sugar part consists of widely spread sugars (D-glucose, D-fructose, D-xylose, L-ramnose) and sugars which are specific and only in CGs (D-digitoxose, D-cymarose, D-oleandrose). The CGs, which contain specific sugar, are metabolized in the liver very slowly, so they have long period of action.

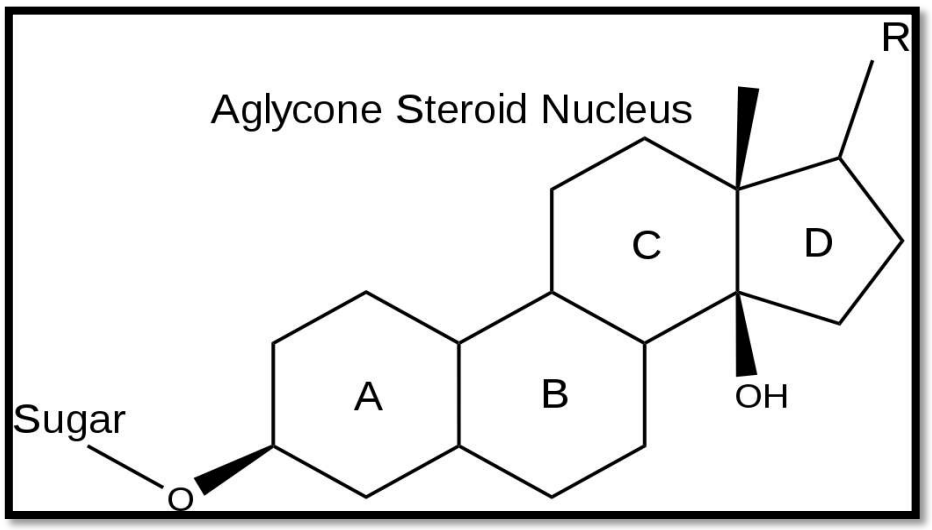

Fig.G.S of cardiac glycosides.

Classification of CGs :

CGs are classified according to their level of polarity. There are 3 groups:

1. Polar CGs (hydrophilic)- Strophanthine, Corglycone

2. With intermediate polarity - Digoxine, Celanide

3. Non polar CGs – Digitoxine, Gitoxine

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 33

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anti anginal agents.

Objective: To study the Anti-anginal agent and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the anti anginal agent.

2. Able to draw different structure of anti-anginal agent.

It is a pain syndrome due to induction of an adverse oxygen supply/demand situation in a portion of myocardium. Antianginal drugs are used to help restore the appropriate supply-and-demand ratio in oxygen delivery to the myocardium.

Classification;

Nitrates:

a. short acting nitrates

Eg: Glyceryl trinitrate (Nitroglycerine)

b.Long acting nitrates

Eg; Isosorbide dinitrate (sorbitrate)

Beta-BLOCKERS:

Eg; Atenelol, Propanalol

Calcium channel blockers:

a. phenyl alkamine

Eg: verapamil

b. benzothiazepine

Eg: Diltiazem

c. Dihydropyridines

Eg: Nifidipine, Amlodipine

Potassium channel openers:

Eg: Nicorandil

• OTHers

Eg: Ivabradine

Mechanism of action:

The nitrates relax and dilate veins, arteries, and capillaries, allowing increased blood fl ow through the vessels and lowering systemic blood pressure because of a drop in resistance.Nitrates decreases the preload and afterload.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture No: 34

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anyianginal agents.

Objective: To study the Anti-anginal agent and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the anti-anginal agent.

2. Able to draw different structure of antianginal agent.

a)Nitrates :

Nitrates cause vasodilation[1] of the venous capacitance vessels by stimulating the endothelium-derived relaxing factor (EDRF). Used to relieve both exertional and vasospastic angina by allowing venous pooling, reducing the pressure in the ventricles and so reducing wall tension and oxygen requirements in, the heart.

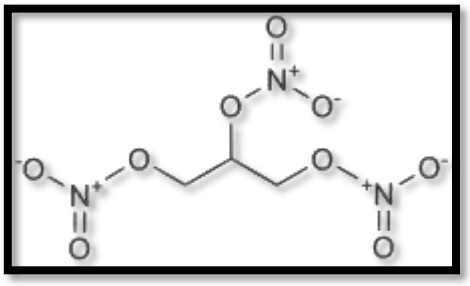

Fig. ***Nitroglycerin.***

b)Beta blockers:

Beta blockers are used in the prophylaxis[2] of exertional angina by reducing the myocardial oxygen demand below the level that would provoke an angina attack.

They are contraindicated in variant angina and can precipitate heart failure. They are also contraindicated in severe asthmatics due to bronchoconstriction, and should be used cautiously in diabetics as they can mask symptoms of hypoglycemia.

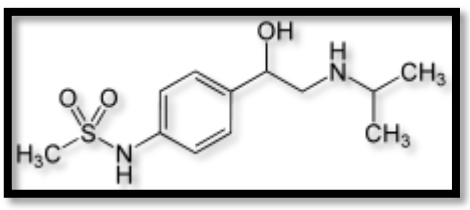

Fig. Sotalol

c)Calcium channel blockers:

Calcium ion (Ca^{++})antagonists (Calcium channel blockers) are used in the treatment of chronic stable angina, and most effectively in the treatment of variant angina (directly preventing coronary artery vasospasm). They are not used in the treatment of unstable angina

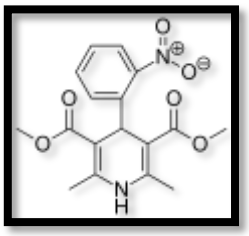

Fig. Nifedipine

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 35

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anti-arrhythemic agents.

Objective: To study the Anti-arrhythemic agents and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the Anti-arrhythemic agents.

2. Able to draw different structure of Anti-arrhythemic agents.

Antiarrhythmic agents, also known as **cardiac dysrhythmia medications**, are a group of pharmaceuticals that are used to suppress abnormal rhythms of the heart (cardiac arrhythmias), such as atrial fibrillation, atrial flutter, ventricular tachycardia, and ventricular fibrillation.

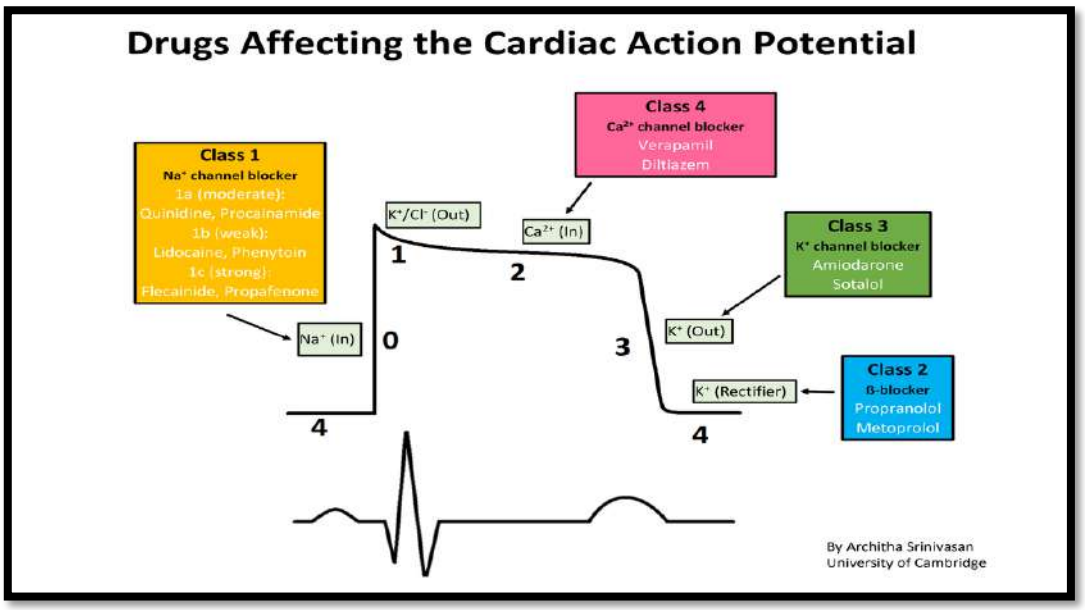

Fig. Drugs affecting cardiac action.

The Vaughan Williams classification was introduced in 1970 by Miles Vaughan Williams.[1]

Miles was the tutor for Pharmacology at Hertford College, Oxford; one of his students, Bramah N. Singh, contributed to the development of the classification system, and had a subsequent eminent career in the United States; the system is therefore sometimes known as the **Singh-Vaughan Williams classification**.

The five main classes in the Vaughan Williams classification of antiarrhythmic agents are:

- **Class I** agents interfere with the sodium (Na^+) channel.

- **Class II** agents are anti-sympathetic nervous system agents. Most agents in this class are beta blockers.
- **Class III** agents affect potassium (K^+) efflux.
- **Class IV** agents affect calcium channels and the AV node.
- **Class V** agents work by other or unknown mechanisms.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 36

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anti-arrhythemic agents.

Objective: To study the Anti-arrhythemic agents and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the Anti-arrhythemic agents.
2. Able to draw different structure of Anti-arrhythemic agents.

a)class I:

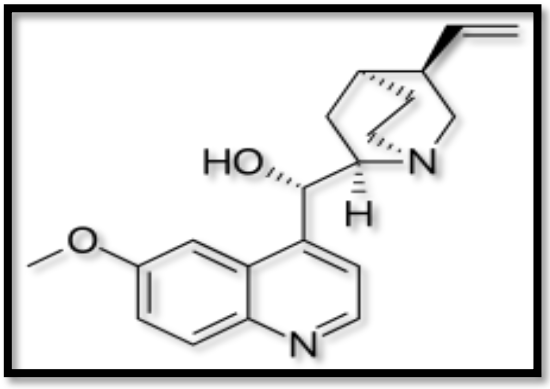

Fig. Quinidine.

b) class II:

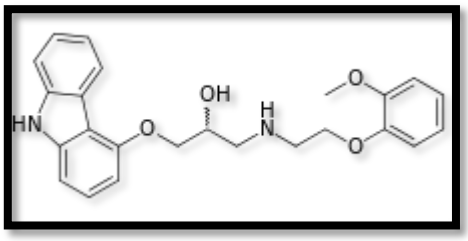

Fig. Carvedilol.

c) class III:

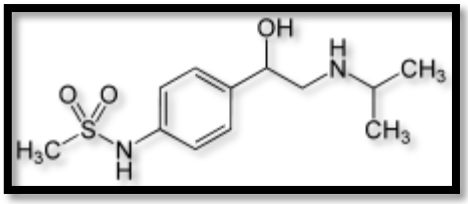

Fig. Sotalol.

d) class IV:

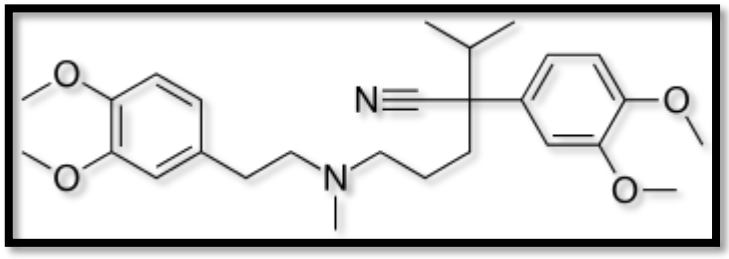

Fig. Verapamil.

e) class V:

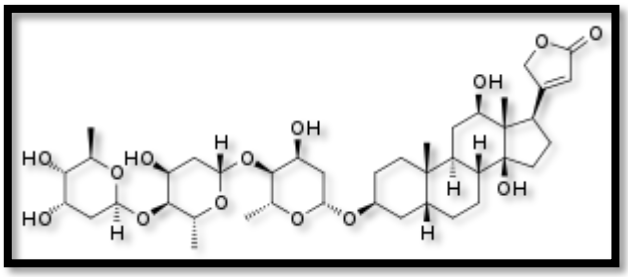

Fig. Digoxin.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 37

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anti-hypertensive agents.

Objective: To study the Anti-hypertensive agents and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the Anti-hypertensive agents.
2. Able to draw different structure of Anti-hypertensive agents.

Antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischaemic heart disease by 21%, and reduce the likelihood of dementia, heart failure, and mortality from cardiovascular disease. There are many classes of antihypertensives, which lower blood pressure by different means. Among the most important and most widely used drugs are thiazide diuretics, calcium channel blockers, ACE inhibitors, angiotensin II receptor antagonists (ARBs), and beta blockers**.**

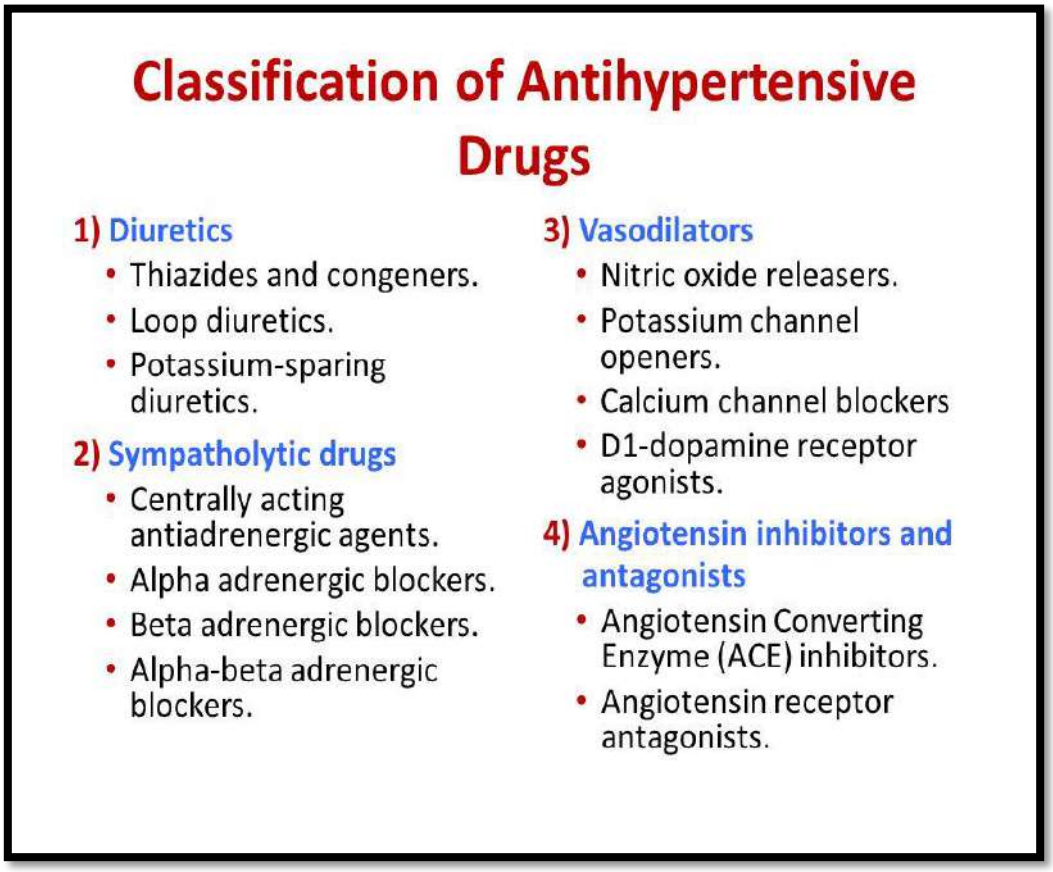

Fig. Classification of antihypertensive drugs.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 38

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anti-hypertensive agents.

Objective: To study the Anti-hypertensive agents and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the Anti-hypertensive agents.
2. Able to draw different structure of Anti-hypertensive agents.

a) Diuretics:

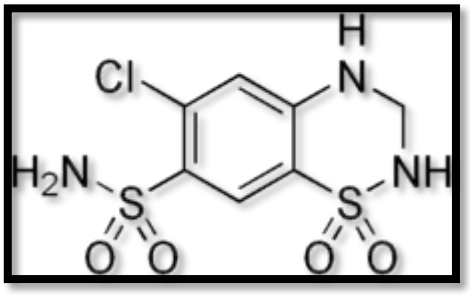

***Fig. Hydrochlorothiazide*.**

b)Calcium channel blockers:

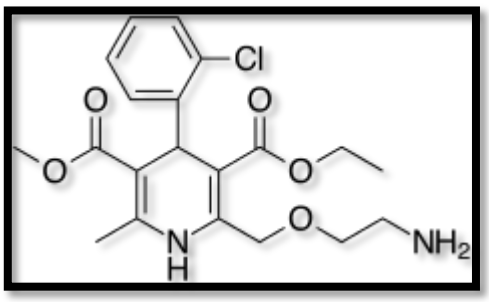

Fig. Amlodipine

c)ACE inhibitors:

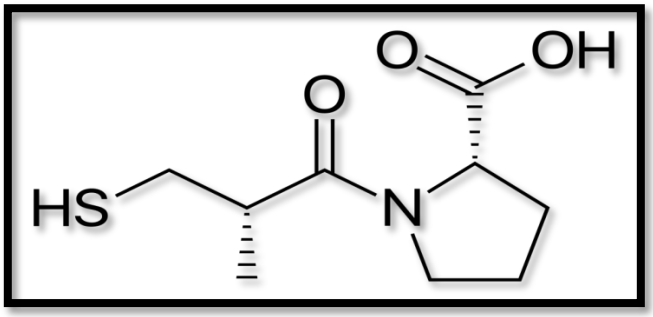

Fig.Captopril

References:-

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 39

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Antihyperlipidemic agents.

Objective: To study the Antihyperlipidemic agents.and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the Antihyperlipidemic agents**.**

2. Able to draw different structure of Antihyperlipidemic agents**.**.

Hyperlipidemia is abnormally elevated levels of any or all lipids or lipoproteins in the blood.[2] It is the most common form of dyslipidemia (which includes any abnormal lipid levels).

Lipids (water-insoluble molecules) are transported in a protein capsule. The size of that capsule, or lipoprotein, determines its density. The lipoprotein density and type of apolipoproteins it contains determines the fate of the particle and its influence on metabolism.

Hyperlipidemias are divided into primary and secondary subtypes. Primary hyperlipidemia is usually due to genetic causes (such as a mutation in a receptor protein), while secondary hyperlipidemia arises due to other underlying causes such as diabetes.

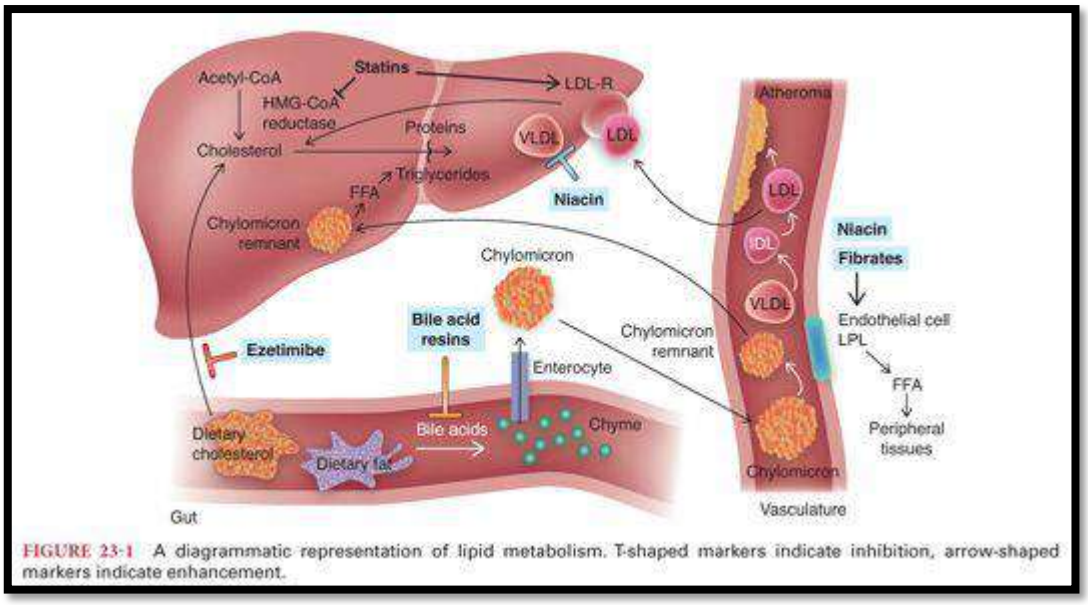

FIGURE 23-1 A diagrammatic representation of lipid metabolism. T-shaped markers indicate inhibition, arrow-shaped markers indicate enhancement.

Fig.Lipid lowering agent.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

4. Principles of Medicinal Chemistry by Kadam SS, Mahadik KR, Bothara KG, Vol. I & II, 10th Edition, Nirali Prakashan.

Lecture No: 40

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Anti-hyperlipidemic agents.

Objective: To study the Anti-hyperlipidemic agents and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the Anti-hyperlipidemic agent.

2. Able to draw different structure of antihyperlipidemic agent..

MECHANISMS OF ACTION OF HYPOLIPIDEMIC DRUGS

MAIN GOAL is to DECREASE LDL concentration or INCREASE HDL concentration in plasma (OR BOTH)

A. Inhibit HMG-CoA reductase

B. Inhibit intestinal absorption of cholesterol

C. Bind bile acids

D. Inhibit VLDL synthesis and/or secretion

E. Stimulate lipoprotein lipase

F. Inhibit LDL oxidation

Ezetimibe is a medication used to treat high blood cholesterol and certain other lipid abnormalities.[1] Generally it is used together with dietary changes and a statin.[2] Alone, it is less preferred than a statin

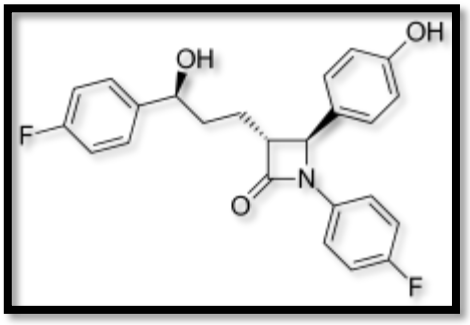

Fig. Ezetimibe

Lomitapide (INN, marketed as Juxtapid in the US and as Lojuxta in the EU) is a drug used as a lipid-lowering agent for the treatment of familial hypercholesterolemia, developed by Aegerion Pharmaceuticals.[1] It has been tested in clinical trials as single treatment and in combinations with atorvastatin, ezetimibe and fenofibrate.

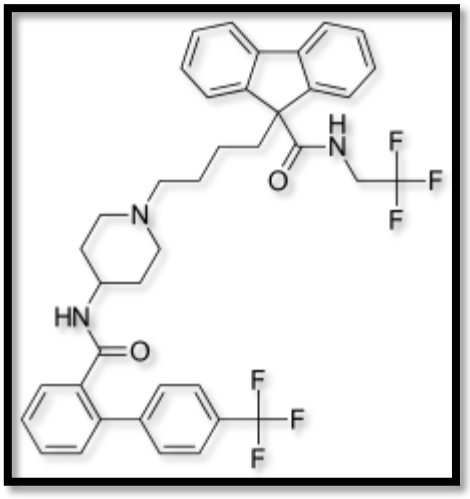

Fig. Lomitapide

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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Lecture No: 41

Name of topic/lesson - Drugs affecting cardiovascular system.

Subtopic-Calcium channel blockers.

Objective: To study the cardiotoinic agent and classification.

Topic Outcomes: At the end of topic you should be:

1. Able to study the cardiotonic agent.

2. Able to draw different structure of cardiotonic agent.

Calcium channel blockers (CCB), calcium channel antagonists or calcium antagonists are a group of medications that disrupt the movement of calcium (Ca^{2+}) through calcium channels.[3] Calcium channel blockers are used as antihypertensive drugs, i.e., as medications to decrease blood pressure in patients with hypertension.

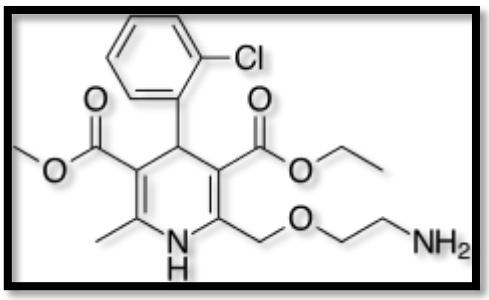

Fig.Amlodipine

Amlodipine, sold under the brand name **Norvasc** among others, is a medication used to treat high blood pressure and coronary artery disease.[3]While not typically recommended in heart failure, amlodipine may be used if other medications are not sufficient for treating high blood pressure or heart-related chest pain.

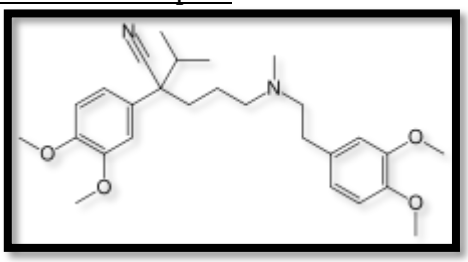

Fig.verapamil

Phenylalkylamine calcium channel blockers are relatively selective for myocardium, reduce myocardial oxygen demand and reverse coronary vasospasm, and are often used to treat angina.

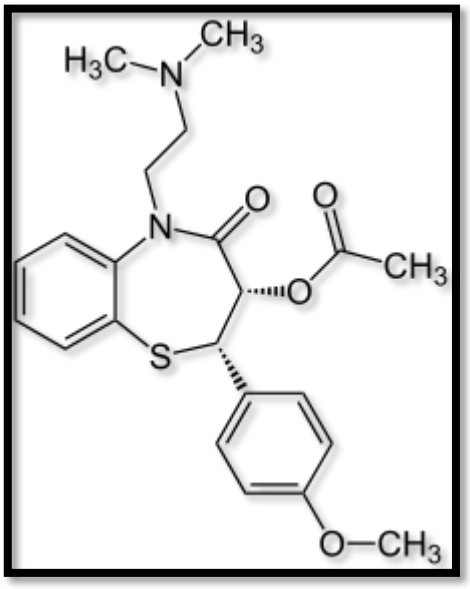

Fig.Diltiazam

Benzothiazepine calcium channel blockers belong to the benzothiazepine class of compounds and are an intermediate class between phenylalkylamine and dihydropyridines in their selectivity for vascular calcium channels. By having both cardiac depressant and vasodilator actions, benzothiazepines are able to reduce arterial pressure without producing the same degree of reflex cardiac stimulation caused by dihydropyridines.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

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Lecture No: 42

Name of topic/lesson - Diuretic agents.

Subtopic-Introduction.
Objective: To study Diuretic agents.

Topic Outcomes: At the end of topic you should be:

1. Able to study function of diuretic agent.

2.Diuretics and their site of action.

A **diuretic** is any substance that promotes diuresis, the increased production of urine. This includes forced diuresis. There are several categories of diuretics. All diuretics increase the excretion of water from bodies, although each class does so in a distinct way. Alternatively, an antidiuretic, such as vasopressin (antidiuretic hormone), is an agent or drug which reduces the excretion of water in urine. diuretics are used to treat heart failure, liver cirrhosis, hypertension, influenza, water poisoning, and certain kidney diseases. Some diuretics, such as acetazolamide, help to make the urine more alkaline and are helpful in increasing excretion of substances such as aspirin in cases of overdose or poisoning. Diuretics are sometimes abused by people with an eating disorder, especially people with bulimia nervosa, with the goal of losing weight.

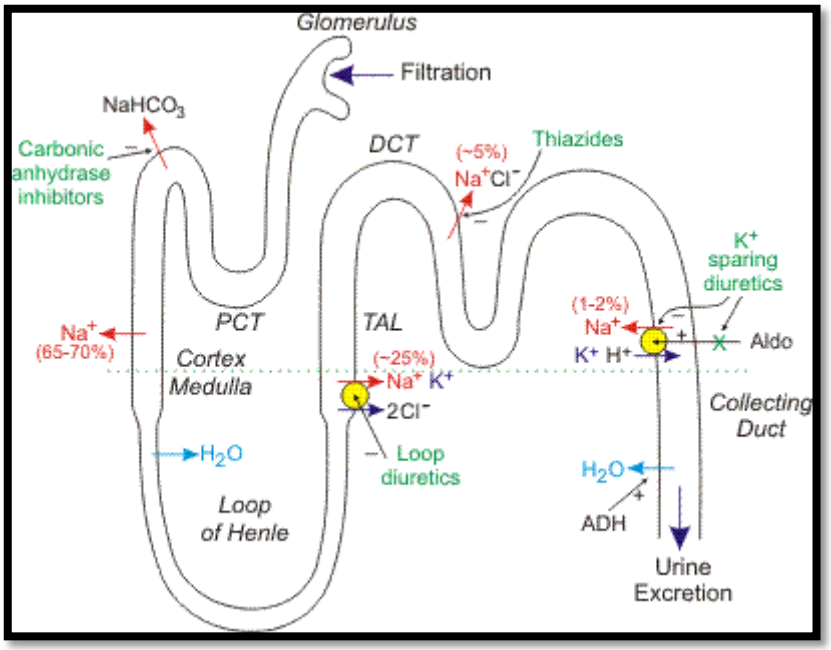

Fig. Diuretic and their site of action.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 43

Name of topic/lesson - Diuretic agents.

Subtopic-Types of diuretic agent.

Objective: To study different types/classification Diuretic agents.

Topic Outcomes: At the end of topic you should be:

1. Able to study different types of diuretic agent.

2.Able to draw different sturucture of diuretic agents.

Chemical classification of diuretic agent involved:

a) Osmotic diuretics.

b) Carbonic anhydrous inhibitor.

c) Thiazide diuretics.

d) Loop diuretis.

e) Potassium sparing diuretics.

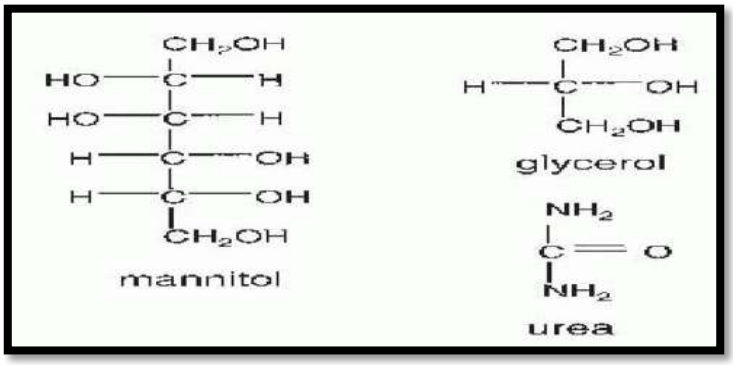

Fig. Osmotic diuretics.

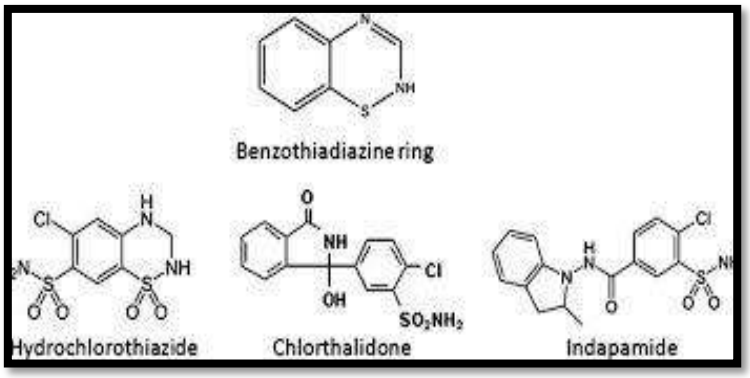

Fig. Thiazide diuretics.

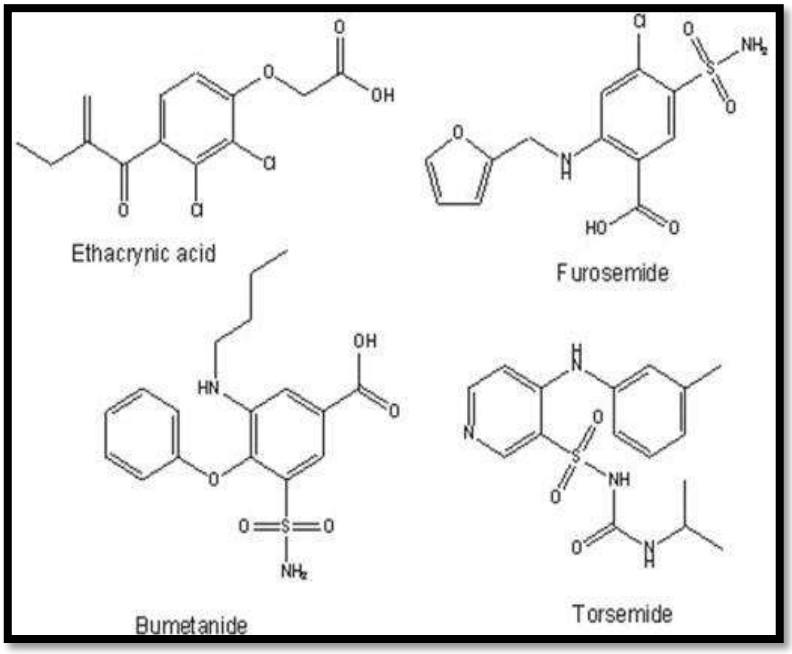

Fig. Loop diuretics.

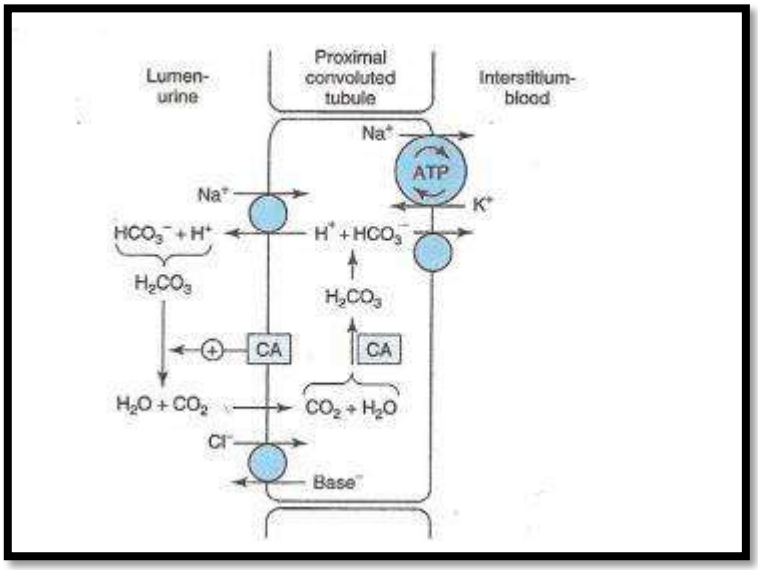

Fig. Carbonic unhydrous inhibitors.

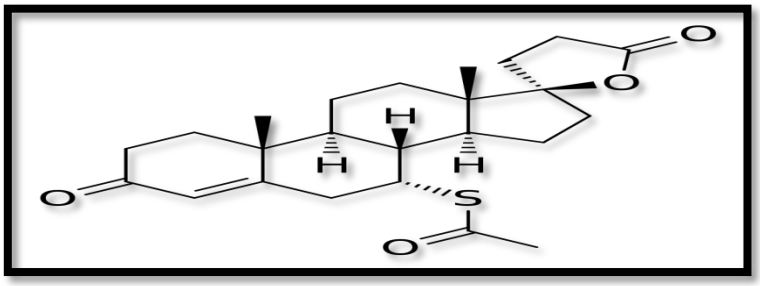

Fig. Potassium sparing diuretics.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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Lecture No: 44

Name of topic/lesson - Diuretic agents.

Subtopic-SAR of thiazide diuretics.

Objective: To study SAR Diuretic agents.

Topic Outcomes: At the end of topic you should be:

1. Able to study the structural activity relationship of thiazide diuretic .

1. 2.Able to draw different sturucture and chemical classification of thiazide diuretic .

SAR of thiazide diuretics:

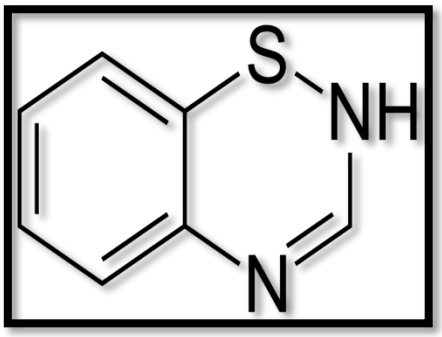

Fig. G.S of Thiazide

- The position 2 can tolerate the presence of small alkyl groups such as methyl. Substituents in 3 position determines the potency,duration of action.
- Loss of c-c double bond between 3&4 positions of nucleus increases diuretic potency approximately three to ten fold.
- Direct substitution of the 4,5 or 8 position with an alkyl group usually results in diminished diuretic activity.
- Substitution of the 6-position with an activating group is essential for diuretic activity The best substituent's include Cl,Br,CF3 and No2 groups.
- The sulphamoyl group in the7-position is a prerequisite for diuretic activity.

chemical classification of thiazide diuretic :

a) 1st generation of thiazide .e.g Chlorothiazide.

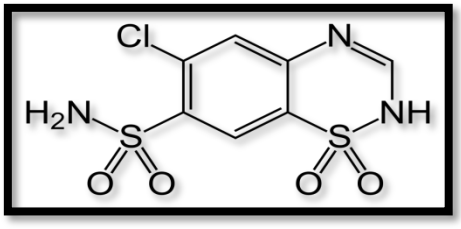

Fig. Chlorothiazide.

b) 2nd generation of thiazide.e.g. Hydrocholorothiazide.

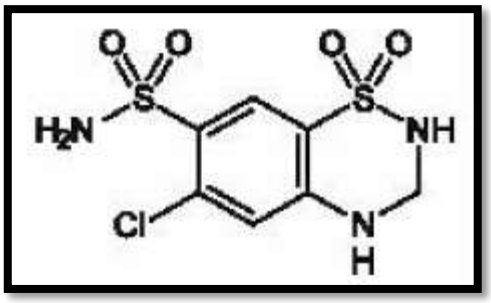

Fig. Hydrocholorothiazide.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

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Lecture synopsis Sub: Medicinal Chemistry-I

Subject I/C: M.K. Munde

Lecture No: 45

Name of topic/lesson - Diuretic agents.

Subtopic-SAR of Loop diuretics.

Objective: To study SAR Loop diuretics.

Topic Outcomes: At the end of topic you should be:

1. Able to study the structural activity relationship of loop diuretic .

2.Able to draw different sturucture of loop diuretic .

Loop diuretics selectively inhibit Nail reabsorption in the thick ascending limb of the loop of Henley. Due to the large Nail absorptive capacity of this segment and the fact that diuresis is not limited by development of acidosis, as it is with the carbonic anhydrate inhibitors, these drugs are the most efficacious diuretic agents available.
The two prototypical drugs of this group are **furosemide and ethacrynic acid.**

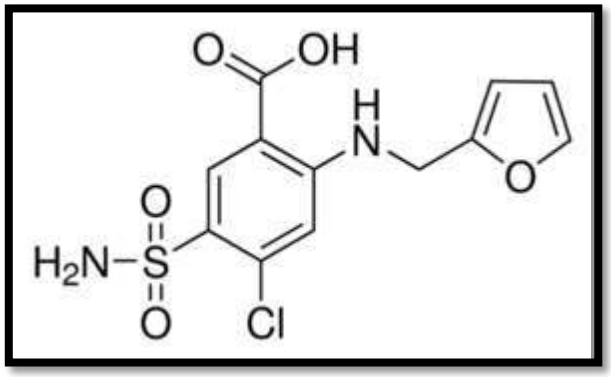

Fig. furosemide.

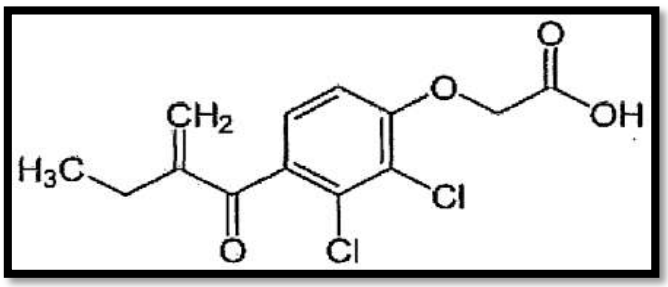

Fig. ethacrynic acid.

SAR of loop diuretics:

- They are either 5-sulphamoyl-2-amino benzoic acid or 5- sulphamoyl-3-amino benzoic acid derivatives.
- The carbonyl group at C-1 provides optimal diuretic activity.
- The substitution of activating group (X) in the position 4 by Cl, alkoxy, aniline, benzyl, or benzoyl group at 4th position increases the diuretic activity.
- The presence of sulphamoyl group in the 5th position is essential for activity.
- The two series of 5-sulphamoyl benzoic acid differ in the nature of the functional group that substituted in 2nd and 3rd position.
- The presence of furfuryl, phenyl, and thienyl methyl group at 2nd amino group of 5-sulphomoyl -2-amino benzoic acid gives maximum diuretic activity.
- The wide range of alkyl group can be substituted at 3rd amino group of 5-sulfamoyl-3-amino been- azoic acid without modifying the optimal diuretic activity.
- A molecule with a weakly acidic group to direct the drug to the kidney and an alkylation moiety to react with sulphydryl groups and lipophilic groups seemed to provide the best combination of a diuretic in the class.

References:

1. Wilson and Griswold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, Lippincott Co. Philadelphia.

2. Foye's Principles of Medicinal Chemistry by Lemke, 6th edition, Lippincott William Wilkins.

3. Burger's Medicinal Chemistry by Wolff ME, John Wiley & Sons, New York

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