

1 4 ⇒ History And Development of Medicinal Chemistry:

- Medicinal chemistry is the branch of pharmaceutical chemistry that deals with design, development and synthesis of newer medicinal active agents and study of structure Activity Relationship of medicinal active molecules.
- Medicinal chemistry is a science that interlink with chemistry and biology.
- It involves aspects of biological, medical and pharmaceutical sciences.
- It is concerned with invention, discovery, designed, identification, preparation of biologically active agents and their metabolism.
- It includes synthesis, structure Activity Relationship, receptor interaction and

ADME. [Absorption, Distribution, Metabolism and Excretion]

→ Medicinal chemistry involves study of properties of drugs like solubility, ionization, partition coefficient, hydrogen bonding, bioisosterism, etc.

• History and development of Medicinal Chemistry:-

→ In Egypt, India and China, plants were used to treat various diseases.

→ The use of plants was recorded by Hippocrates, Dioscorides, and Galenus.

→ The traditional use of plants is recorded in various "pharmacopoeias" and "Materia Medica".

→ In 17th and 18th century some newer plants were used to treat various diseases in Europe.

→ Hippocrates:- [450 B.C.]

• He was the founder of Modern Chemistry.

• According to him, "Disease is a pathological process and its treatment by a drug is not a magic, this treatment has a scientific base."

• The earliest reference of medicinal preparation was came from India [Rig Veda] and in China from Materia Medica [2500-3000 B.C.]

→ After that in India, a large no. of medicinal prepara. in Ayurveda was reported by physicians like "Charaka", "Shushruta" and "Vagabhatt".

→ The Chinese emperor "Shen Nung" [2735 B.C.] has compiled a book of herbs

→ The 19th century was regarded as the

Birth of Modern Medicinal Chemistry.

- In the beginning of 19th century, no. of alkaloids were isolated, this includes Morphine [1803], quinine [1823] and Atropine [1833].
- After 1860, the principles of organic chemistry were used to synthesize the synthetic and semi-synthetic derivatives from plant origin.
 - for eg:- Aspirin synthesized from Salicin in 1899.
 - Benzocaine synthesized from Cocaine in 1892.
- These syntheses have improved the biological activity due to this scientist believed that there was a relationship betⁿ chemical structure and biological activity, these give rise to SAR studies.
- In 1869, Crum Brown and Fraser had proposed that molecule can produce some signals and body cells can respond to this kind of signals.
- In 1890, Ehrlich had given idea of specific receptors for active compounds and proposed "Lock and Key" theory.
- The first phase of Medicinal Chemistry was introduced in betⁿ 1890 - 1940, these includes effective drugs for the treatment of infectious diseases like Typhoid, Malaria, Hepatitis, tuberculosis, tetanus etc.
- Dale and Abiquist has proposed receptor sub-type for cholinergic and Adrenergic

receptors.

- During this period some synthetic Anti-malarial drugs like Pamaquine (1926), Mepacrine (1932) and chloroquine (1943) were developed as Anti-malarial agents to replace quinine alkaloids.
- During 2nd world war, some powerful Anti-infective agents like Sulphonamides, Penicillin, Tetracyclines, Chloramphenicol, streptomycin etc were developed to save life of soldiers.
- The 2nd phase of Modern medicinal chemistry was bet'n 1940-1980, during that all the drugs for all the diseases were developed.
- The period 1945 to 1965 was considered as "Golden Era" in the medicinal chemistry.
- During this period, corticosteroids, oral contraceptives, Anti-psychotics, Anti-Depressant, Hypoglycemic agents were developed.
- In 1960, the drug Thalidomide had shown the teratogenic effect, this made new drug registration and regulation more tight.
- In 1964, Quantification of SAR was given by Hansch.
- During last 3 decades, A novel development and advancement occurred in Medicinal Chemistry and these includes QSAR, molecular modeling, computer Aided drug design, fragment library, homology modeling, Highthroughput screening etc.
- This makes, a researcher to invent newer drugs for particular diseases within less time period.

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* Sedatives And Hypnotics:-

→ Sedatives:- The Agents that cause reduction of spontaneous motor Activity (mental and physical both) and cause Drowsiness without inducing sleep are known as Sedatives.

→ They are more slowly acting drugs.

→ Hypnotics:- The agents that produce or maintain sleep are known as Hypnotics.

→ They are quicker in action.

Sedative $\xrightarrow[\text{high dose}]{\text{low dose}}$ Hypnotic

• In low dose, same drug will work as sedative and in high dose same drug will act as hypnotic.

→ These agents are used as Muscle relaxant, Anticonvulsants and Anti-anxiety agents.

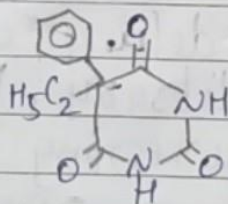
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Wednesday

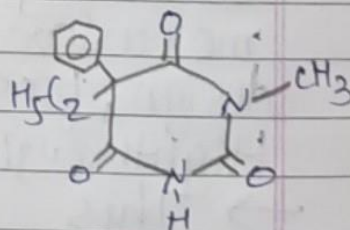
* Classification :-

1) Barbituric Acid derivatives:-

a) Longer Acting:- Phenobarbital, Mephobarbital



Phenobarbital

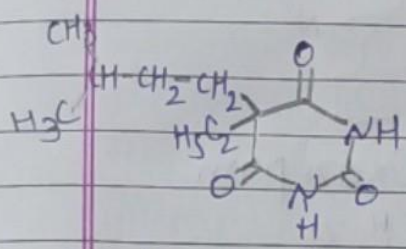


Mephobarbital

→ action remains greater/more than 6 hrs.

b) Intermediate acting:- (3-5 hrs)

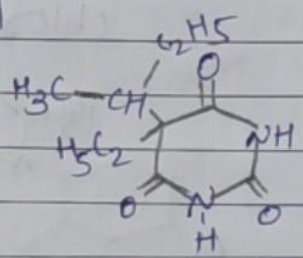
Allobarbitol, Amobarbitol



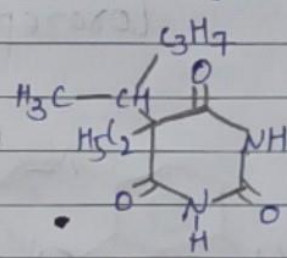
Amobarbitol

c) Short acting:- (Less than 3 hours)

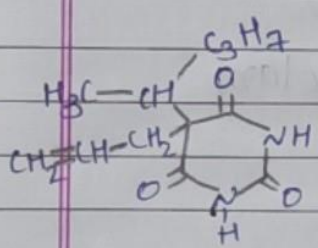
Hexobarbitol, secobarbitol, butobarbitol, Pentobarbitol



Butobarbitol



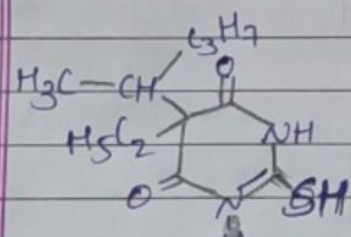
Pentobarbitol



secobarbitol

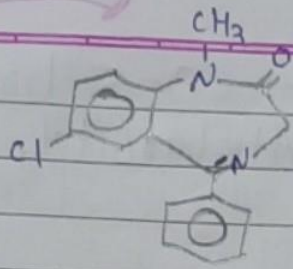
d) Ultrashort acting:- (within seconds)

Thiopental, Thiamylal

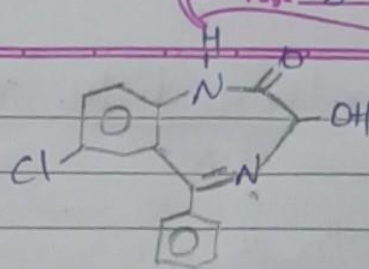


Thiopental

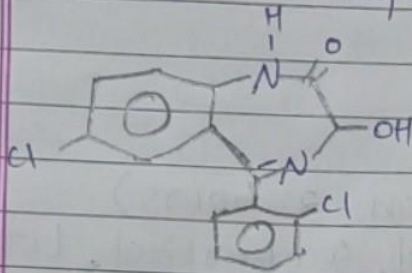
2) Benzodiazepines:- Diazepam, Oxazepam, Lorazepam, Nitrazepam, Chlorthalidone, Chlorthalidone, Alprazolam.



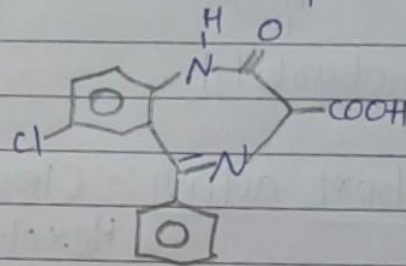
Diazepam



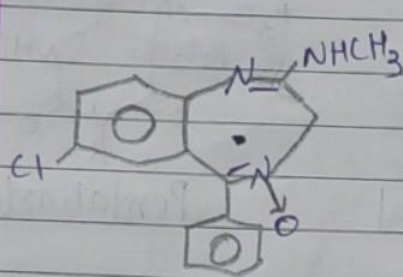
Oxazepam



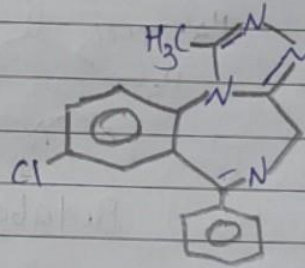
Lorazepam



chlorthalidone



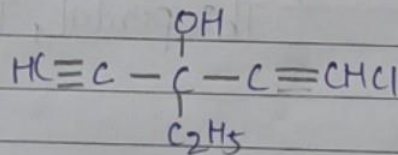
Chlordiazepoxide



Alprazolam

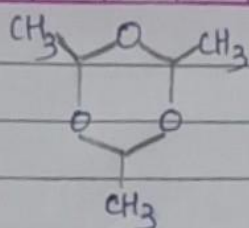
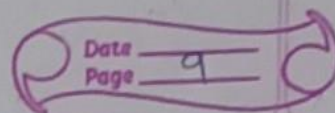
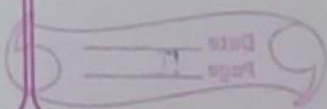
3) Miscellaneous:-

a) Alcohol derivatives:- Ethanol, Bromoethanol, ethchlorvynol

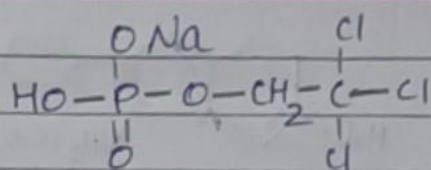


Ethchlorvynol

b) Aldehydes:- Paraldehyde, chloral hydrate, Trichloro sodium

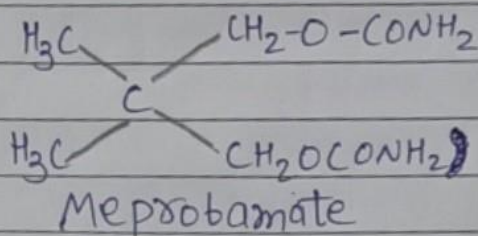


Paraldehyde



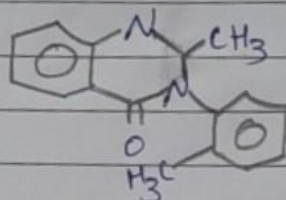
Triclofos sodium

c) Carbamate derivatives: - Ethionamide, Meprobamate



Meprobamate

d) Quinazoline derivatives: - Methaqualone

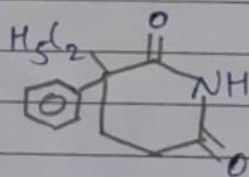


methaqualone

e) Bromide derivatives: - NaBr, KBr, NH₄Br

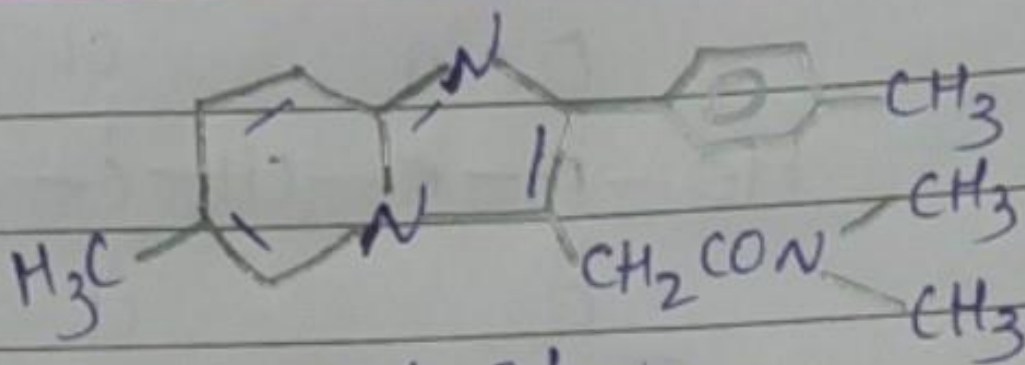
f) plant derivatives: - Radix valeriana

g) Amide derivatives: - Glutethimide



Glutethimide

h) Newer drugs: - Zopiclone, Zolpidem



Zolpidem