Introduction to Medicinal Chemistry

Lecture for: M.Sc chemistry: II sem
Subject: Medicinal Chemistry-II
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Introduction to Medicinal Chemistry

a) History and development of medicinal chemistry

b) Physicochemical properties in relation to:

- ✓ Biological action Ionization
- ✓ Solubility
- ✓ Partition Coefficient
- ✓ Hydrogen bonding
- ✓ Protein binding
- ✓ Chelation
- ✓ Bioisosterism
- ✓ Optical and Geometrical isomerism.

Introduction to Medicinal Chemistry.

Introduction

- ✓ A branch of chemistry in which the features of biological, and pharmaceutical sciences are studied, is termed as medicinal chemistry.
- ✓ The study of invention discovery, design, and preparation of biologically active compounds.
- ✓ Their metabolism, mode of action at the molecular level, and the structure – activity relationships are also covered under this branch.
- ✓ The studies in medicinal chemistry involve a combination organic chemistry with biochemistry, computational chemistry pharmacology , Pharmacognosy molecular biology , statistics , and physical chemistry.
- ✓ Medicinal chemistry is also used to obtain information on complexities arising due to the presence of functional moiety and the effect on the physicochemical properties of 'target-drug molecule' termed as **Structure Activity Relationship** (SAR); and recently it has been given the name of **Quantitative – Structure – Activity Relationship** (QSAR).
- ✓ Developing a new drugs and determining formulations to deliver bio active compounds.

History & Development of Medicinal Chemistry:

History And Development of Medicinal Chemistry:-

> before thousands year ago

-She nung (Chinese emperor) made a Pharmacopoeia

Chaulmoogra fruit	-dysentery & diarrhoea
Emetine (ipecacuanha root)	- amoebiasis
Cocaine and tryptamine	- hallucination

>The 13th – 20th century

-Chemical :analysis techniques were developed

-Pharmacognosy developed

-Synthesis of chemotherapeutic agent were started

Kolbe (1856) synthesized – Acetic acid

Berthelot (1856) synthesized – Methane

Domagk stated rontosil can cure gram positive bacterial infections in human and animals.

History & Development of Medicinal Chemistry:

Medicinal chemistry is a discipline that encloses the design, development, and synthesis of pharmaceutical drugs. The discipline combines expertise from **chemistry**, especially synthetic organic **chemistry**, pharmacology, and other biological sciences.

Drugs of Antiquity (ancient time)

- The therapeutic plants and minerals are in use since the ancient civilization of the Chinese, the Hindus, the Mayans of Central America, and the Mediterranean people of bygone days.
- **Shen Nung** (a Chinese emperor) made a Pharmacopoeia, includind in it ch' ang shang (an anti – malarial alkaloid) and ma huang (from which ephedrind was isolated).
- The native American Indians used chaulmooger fruit .
- For treating dysentery and diarrhoea, the Brazilians used emetine present in the ipecacuanha root; and it is still used in amoebiasis ancient explorers discovered that the south American Indians chewed cocaine containing coca leaves and tryptamine-containing mushoons for hallucination.
- Many of the developments after the 1860s arose from the synthesis of compounds specifically for their **medicinal** action.

What is Medicinal Chemistry?

In medicinal chemistry, the chemist attempts to design and synthesize a medicine or a pharmaceutical agent which will benefit humanity.

Such a compound could also be called a 'drug'. Latin *'ars medicina',* meaning the art of healing.

It involves:

- Synthesis
- Structure –Activity Relationship (SAR)
- Receptor interactions
- Absorption, distribution, metabolism and excretion (ADME)

History of Medicinal Chemistry:

- In early civilizations of Egypt, India & China the plants being used to treat various diseases.
- In beginning of 19th century, the isolation of a no. of alkaloids including:
  - 1803 ⟶ Morphine
  - 1823 ⟶ Quinine
  - 1833 ⟶ Atropine

  Was used in Medicinal Chemistry.
- In 1860:- Synthesize the semi-synthetic/fully synthetic derivatives of these plant origin.

Example:

- 1892 ⟶ Benzocaine from cocaine
- 1899 ⟶ Aspirin from salicin

- In 1869:- **Crum-Brown & Fraser**

  Proposed that cells can respond to the signal from specific molecule
- In 1890:- **Ehrlich**

  Expressed the idea of specific receptor for biologically active compounds.

  Lock and Key relation
- In 1890-1940:- **1st Phase of Modern Medicinal Chemistry.**

  The development of effective drugs for the treatment of Tuberculosis, Typhoid, Malaria, Infective hepatitis, Tetanus, Cholera etc.
- In 1910-1946:- **Dale and Ablquist**

  1st proposed the receptor sub-types for cholinergic receptor.
- In 1936 ⟶ Sulphonamide
- In 1940 ⟶ Penicillin antibiotics
- In 1949 ⟶ Chloramphenicol and Tetracycline

- In 1940-1980:- **2nd Phase of Modern Medicinal Chemistry.**
  Introduction of all modern therapeutic classes.

- In 1945-1965:- **'Golden Era'**
  Many important therapeutic classes of drugs were invented.

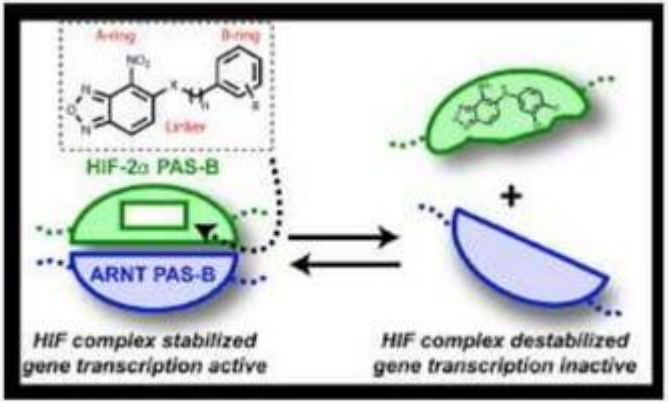
  Examples:-
  - 1949 ⟶ Corticosteroids
  - 1950 ⟶ Antipsychotics
  - 1955 ⟶ Antidepressants
  - 1957 ⟶ Hypoglycemic
  - 1959 ⟶ Contraceptives
  - 1960 ⟶ Benzodiazepines

- In 1960:- The teratogenic effect (Birth of deformed children when mother consumed the drug during pregnancy) came to limelight after thalidomide (Sedative).

- In 1964:- **"Birth of QSAR" By Hansch.**

History & Development of Medicinal Chemistry:

- Although the use of willow bark as a pain-killer was known to the herbalists, the analgesic activity of its constituent salicin 1.1 and of salicylic acid 1.2 were developed in the 1860s and 1870s.
- Exploration in the seventeenth and eighteenth centuries led to the addition of a number of useful tropical plants to those of European origin. The nineteenth century saw the **beginnings** of modern organic chemistry and consequently of medicinal chemistry. Their **development** is intertwined.



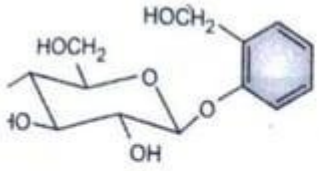


Fig. 1.1 : Salicin

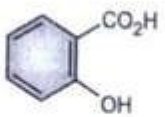


Fig. 1.2 : Salicyclic

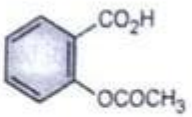


Fig. 1.3 : Aspirin

1.4 R
1.5 R

Fig. 1.4 and 1.

The local anaesthetic action of cocaine was reported in 1884 although its structure was not known at th ications of the dialkylamino esters of aromatic acids modelled on part of the structure of cocaine led to benzo ne (1905). The barbiturates, veronal (1903) and phenobarbital (1911) were introduced as sleeping tablets.

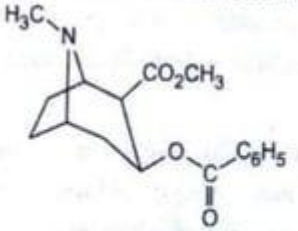


Fig.1.6 : Cocaine

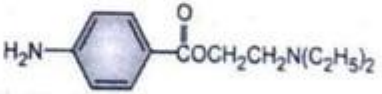


Fig. 1.7 : procaine

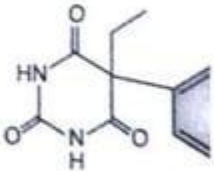


Fig. 1.8 : Phenobarb

Thanks