Introduction to Medicinal chemistry

→ History and development of medicinal chemistry
→ physicochemical properties in relation to biological action
→ Drug metabolism.

History and Development of Medicinal chemistry

Medicinal chemistry :-

The science that deals with the discovery or design of new therapeutic chemicals and the development of these chemicals into useful medicine.

→ It is also called therapeutic chemistry, pharmaceutical chemistry & pharmacochemistry

→ Medicinal chemistry concerns the discovery
development
interpretation of the mode of
of biologically active compounds
at the molecular level.

Father of Modern Med. chem
* Edward E. Smissman

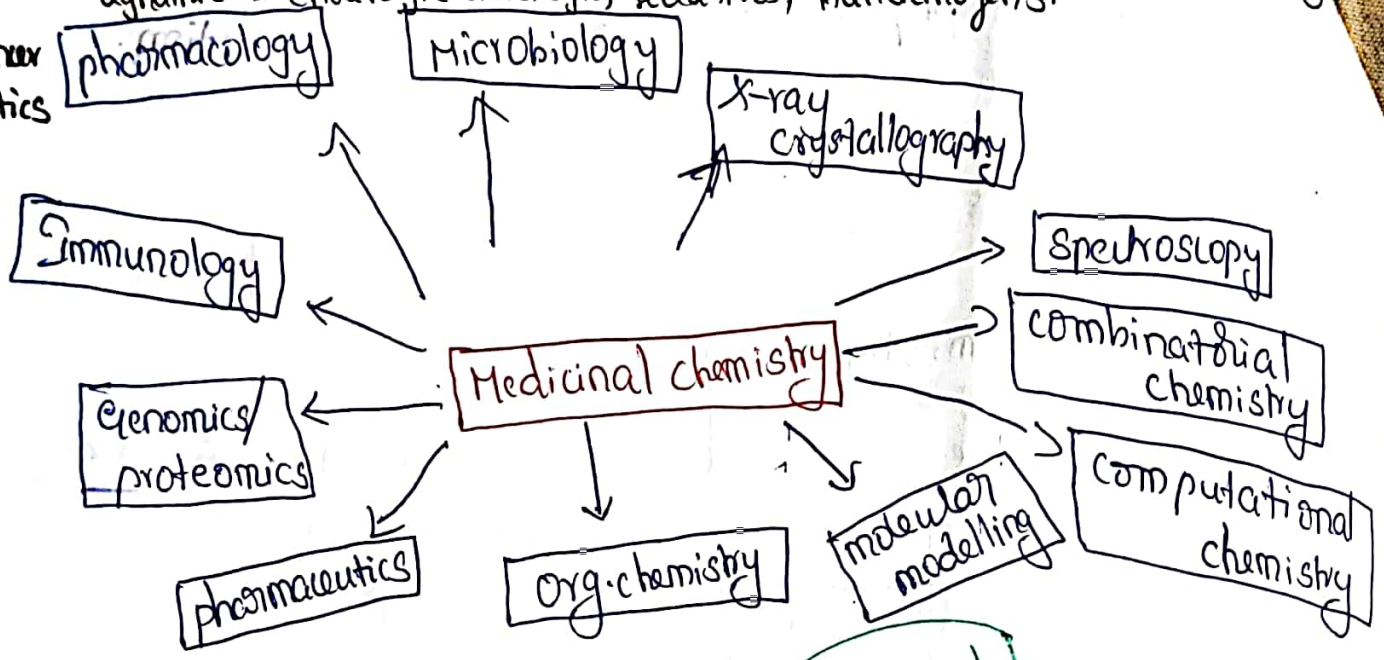
→ Medicinal chemistry is also concerned with the study, identification, and synthesis of metabolic products of drugs and related compounds.

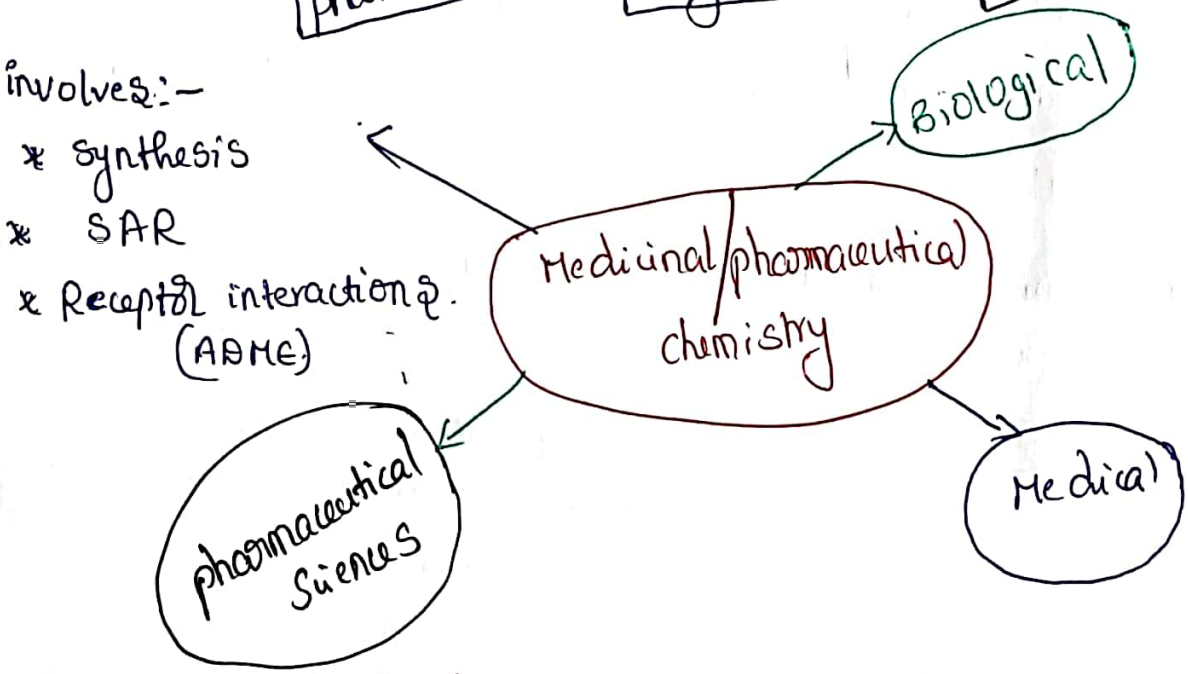
→ Medicinal chemistry is an interdisciplinary research area incorporating different branches of chemistry and biology in the research for better and new drugs (Drug discovery)

Drug:- Any substance which generates biological response. eg: All chemicals other than food that affect living proc

- chemotherapeutic agents
- pharmaco dynamic → cholinergic, adrenergic, sedatives, hallucinogens.
- → miscellaneous → Eg: Local anaesthetics

: Anticancer antibiotics





Role of Medicinal Chemists:-

1. Syn. and characterization of new compounds (leads).
2. Biological assay of the synthesized compounds & determine their effects on biological process.
3. Manipulation of structure of the compound for optimum effect / minimum side effects (Optimization of lead)
4. Study of pharmacokinetic & pharmacodynamic property of drug.
5. Optimization of synthetic route for bulk production.

History of Medicinal chemistry ③

→ The first drug were those from natural sources, extracted principally from higher plants and destined for therapy against infectious diseases.

→ Many centuries before our time, the chinese, Hindus, Maya, and people from the Mediterranean on medicinal herbs.

→ Chang shang – for the treatment of malaria, it is no known that this plant contains alkaloids, such as febrifugine, antimalarial activity.

→ Brazilian indians used to treat dysentry & diarrohea with ipeca root.

→ The incas of peru employed cinchona bark for the fight against fever & malaria. from this plan in 1823 pelletier & caventou extracted quine.

→ Inca also used to chew coca leaves as a stimulant & Euphoriant from this plant in 1859 wohler extracted the LA cocaine.

*. Hippocrates, in the late 5th century B.C recommended application of metallic salts.

* Galen (131-200) – that the use of mixtures of small amounts of natural products could cure all diseases.

* Med. chemistry recieved a large impulse from the discovery made towards the end of 19th century by* paul Ehrlich* (1854-1915), father of chemotherapy

* Emil fischers lock & key theory provides a rational explo of for the Mechanism of action of drugs.

History of Medicinal chemistry

2000 BC Materia Medica 250 vegetables drug & 120 mineral drugs.

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500 BC Egyptial papyrus chers 700 drugs originated from animals/ plants/ minerals.

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Emperor Predrick II issued the Magna carta of pharmacy in 1240

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Syn- of urea 1828 started Organic medicinal chemistry

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Ehrlich "Side chain theory" and chemotherapy & Fischers' lock & key theory

Birth of Modern Med chem 1800.

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Med. chemistry recieved formal recognition in academic pharmacy in 1932.

Objective of medicinal chemistry :-

⑤

Drug discovery - finding a lead.

-> choose a disease
-> choose a drug target
-> identify a bioassay
-> find a lead compound
-> Isolate and purify the lead compound if necessary
-> Determine the structure of the lead compound if necessary

Drug design :-

-> Identify structure-Activity Relationship (SARs)
-> Identify the pharmacophore.
-> Improve target interactions & pharmaco dynamics
-> Improve pharmacokinetic properties.

Medicinal chemistry covers the three stages :-

Discovery step. -> involving choice of target. (Lead compound).
Optimization step -> improvement of lead compound.
Development stage -> continious of improvement of pharmacokinetic properties.

- optimization process takes primarily into acc ~~of~~ the ↑ in potency, selectivity & toxicity.
- Discovery :- production of new active substances.

CADD :- Computer Aided Drug design.
used for rapid assesment of chemical libraries in order to guide and speed up the early-stage development of new active compounds.

Combinatorial chemistry :- Synthetic methods that make it possible that make it large no. of compounds in a single process
this compound libraries can be made as mixtures, sets of individual comp'ds or chemical structures generated by computer ~~chemis~~ software.

Antisense molecules :- Synthetic segments of DNA or RNA, designed to mirror specific messenger RNA (mRNA) sequences and block protein production.

prodrug :- is a medication or compound that, after administration it is metabolized into pharmacologically active drug.
A prodrug may be used to improve how selectively the drug interacts with cells or proces that are not its intended target.

QSAR :- Quantify relationship b/n chemical structure and biological activity. (mathematical relationship).