Introduction to medicinal chemistry

Med Chem I
كيمياء دوائية (1)

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Introduction to medicinal chemistry
Introduction to medicinal chemistry (Cont.)

• Like any science, the development of medicinal chemistry depends on

  Ideas + knowledge + tools

• The discoveries in medicinal chemistry were usually achieved by either of two kinds of people

1. Genius of predictive logic, who have opened a new field by interpreting correctly a few well-placed experiments, whether they pertained to the design or the mechanism of action of drugs.

2. Those who have varied patiently the chemical structures of physiologically active compounds until a useful drug could be evolved as a tool in medicine.

Burger 1970

• The primary objective of medicinal chemistry is the design and discovery of new compounds that are suitable for use as drugs.

• This process involves a team of workers from a wide range of disciplines such as chemistry, biology, biochemistry, pharmacology, mathematics, medicine and computing, amongst others.

• The medicinal compounds can be referred as drugs. However, drugs are usually used to refer to those medicinal compounds which have potential for abuse like morphine and heroin.
Question) What are drugs and what are drug parameters?

Answer)

Drugs are strictly defined as chemical substances that are used to prevent or cure diseases in humans, animals and plants.

The activity of a drug is its pharmacological effect on the subject (e.g. analgesic or β-blocker).

The potency of a drug is the quantitative measure of the activity.

The duration of action of a drug is the period of time during which the activity is exerted at certain potency range.

Other terms include

The side effect of a drug is the unwanted pharmacological effect (e.g. tachycardia, palpitation).

The tolerance to a drug is the resistance (tachyphylaxis) occurs when a drug is no longer effective in controlling a medical condition.
Is it food, drug or poison?

- Drugs act by interfering with biological processes, so no drug is completely safe.

- **Food can act like a drug.** Junk foods and fizzy drinks have been blamed for causing hyperactivity in children. It is believed that junk foods have high concentrations of certain amino acids which can be converted in the body to neurotransmitters.

- **Poison can act like a drug** if used in small quantities, e.g. cytotoxic compounds used to treat cancers. Remember pharmacy logo.

- **Drug can act as food**, example taking vitamin C as additive to juices.

- **Drug can act as poison** if taken in excess, for example overdose of paracetamol may cause coma and death

- **Food act as poison.** Example taking high salty food.

- **Poison act as food ……..**

Figure 1.1 Aspirin and paracetamol
Introduction to medicinal chemistry (Cont.)

- Mid- to late 20th century has seen many discoveries that help in understanding the chemistry of disease states, biological structures and metabolic processes.
- Humans were able to understand
  
  **Drug transportation across membranes**
  - Hydrophilic drug
  - Hydrophobic
  - Very hydrophobic

**Drug mode of action (receptor binding)**
- Drug A binds to receptor
- Drug B cannot bind to receptor

**Drug distribution throughout body**

**Drug metabolism**
Question)

How people know there are biological receptors?

Answers)

Only molecules of similar structures produce similar biological activities. Thus, there should be a receptor which recognizes the structural differences.
Introduction to medicinal chemistry (Cont.)

DEVELOPMENT OF MEDICINAL CHEMISTRY: PSYCHOLOGICAL AGENTS

- A anti-tuberculosis compound has antidepressant effect ??????

Iproniazid

Hmmm,
- It is weakly basic
- It has aromatic ring
- It has hyrazide group
- It is hydrophobic

Sooo,
Other compounds which have similar properties may have similar antidepressant effects.........
Discovery of tricyclic antidepressant chlorpromazine (Phenothiazines) in 1950 followed by imipramine (dibenzazepine) in 1957 and zimelidene in 1957.
New drugs can also be isolated as human metabolites, then subjected to further chemical modification to prepare new analogues.
Introduction to medicinal chemistry (Cont.)

Development of Medicinal Chemistry: Hormones

- New drugs can also be isolated as human metabolites, then subjected to further chemical modification to prepare new analogues.

Adrenal cortex

CNS

Biosynthetic pathway

Epinephrine

Norepinephrine

Dopamine

Dopa

Discovery of propranolol antihypertensive agent

Discovery of apomorphine to be used as sympathomimetics and for Parkinsonism

Used as supplement for biosynthesis of dopamine in Parkinsonism
- Dynamics is everywhere.
- Drug kinetics includes dynamics.

Note: Drug-receptor interaction theory is in absorption, distribution, metabolism and excretion. Regardless whether the receptor is specific or not.
Introduction to medicinal chemistry (Cont.)

- Physicochemical properties of drug controls almost all pharmacokinetics and pharmacodynamics.

**Physicochemical prop**

E.g. Make drug more lipophilic

**Pharmacodynamics**

- Dissociates slowly from fatty tissue: +

**Pharmacokinetics**

- Long duration of action: +
Physicochemical properties

Pharmacodynamics

Pharmacokinetics