Introduction to Pharmacology

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- Pharmacology is the science of drugs (Greek: Pharmacon=Drug;logos=is course)
- In a broad sence it deals with interaction of exogenously administered chemical molecules (drugs) with living systems.
- It encompasses all aspects of knowledge about drugs
- but most importantly those that are relevant to effective and safe use for medicinal purposes.

History of Pharmacology:

- For thousands of years most drugs were crude natural products of
  - unknown composition
  - and limited efficacy.
- Only the overt effects of these substances on the body were known (But MoA is unknown)
- In 1847 in Germany Pharmacology as an experimental science was produced by Rudolf Buchheim.

- In the later part of the 19th century, Oswald Schmiedeberg-- propounded some of the **fundamental concepts in pharmacology**.

Father of pharmacology

- Since then drugs have been
  - purified,
  - chemically characterized,
  - vast variety of highly potent and selective new drugs have been developed.
  - mechanism of action including molecular target of many drugs has been elucidated

- The two main divisions of pharmacology are pharmacodynamics and pharmacokinetics.

- **Pharmacodynamics** (Greek: dynamcs-power)

  What the drug does to the body.

- This includes physiological and biochemical effects of drugs and their mechanism of action at organ **system/subcellular/macromolecular levels**.

- e.g Adrenaline: interact with adrenoceptors

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  G-protein mediated stimulation of membrane bound adenylyl cyclase

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  Increased intracellular cyclic 3',5' AMP

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  Cardiac stimulation, hepatic glycogenolysis and hyperglycaemia etc.

- **Pharmacokinetics** (Greek: Kinesis-movement)

  What the body does to the drug.

- This includes
  - absorption,
  - distribution, binding/localization,/ storage,
  - biotransformation
  - and excretion of the drug.

Eg. Pharmacokinetics of Paracetamol

- Paracetamol is rapidly and almost completely absorbed (1)
- 25% bound to plasma proteins and rest is almost uniformly distributed (2) in the body.
- Metabolized (3) in the liver- by glucuronide and sulfate conjugation

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  inactive metabolites → excreted (4) in urine
- **t1/2** of 2-3 hours and a **clearance** value of 5 ml / kg/ min.

IMPORTANT DEFINITIONS

- **Drug** (French: Drogue - a dry herb): It is the single active chemical entity present in a medicine that is used for diagnosis, prevention, treatment/ cure of a disease.

- This disease oriented definition of drug does not include contraceptives or use of drugs for improvement of health.

- The **WHO** (1966) has given a more comprehensive definition:-

- "**Drug** is any substance or product that is used or is intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient."

- The term '**drugs**' is being also used to mean addictive/ abused / illicit substances.

- Some other important aspects of pharmacology are:
- **Pharmacotherapeutics:**

  It is the application of pharmacological information together with knowledge of the disease for its prevention, mitigation or cure.

- It includes selection of the
  - most appropriate drug,
  - dosage and duration of treatment
  - taking into account the specific features of a patient are a part of pharmacotherapeutics.

- **Clinical pharmacology:**

  It is the scientific study of drugs in man.

- It includes
  - Pharmacodynamic and pharmacokinetic investigation in healthy volunteers and in patients,
  - Evaluation of efficacy and safety of drugs,
  - Comparative trials with other forms of treatment,
  - adverse effects etc.

- The **aim of clinical pharmacology**

  To generate data for optimum use of drugs and the practice of 'evidence based medicine'.

- **Chemotherapy:**

  It is the treatment of systemic infection/ malignancy with specific drugs that have selective toxicity for the infecting organism/ Malignant cell with no /minimal effects on the host cells.

Drugs in general, can thus be divided into:

- **Pharmacodynamic agents:**

  These are designed to have pharmacodynamic effects in the recipient.

- **Chemotherapeutic agents:**
  - These are designed to inhibit/ kill invading parasite/ malignant cell
  - no/minimal pharmacodynamic effects in the recipient.

- **Pharmacy:**

  It is the art and science of compounding and dispensing drugs or preparing suitable dosage forms for administration of drugs to man or animals.

- It includes
  - Collection and identification,
  - Purification
  - isolation,
  - synthesis,
  - standardization and quality control of medicinal substances

- **Pharmaceutics**:

  The large scale manufacture of drugs is called as Pharmaceutics.

- **Toxicology:**

  It is the study of poisonous effect of drugs and other chemicals (household, environmental pollutant, industrial, agricultural, homocidal) with emphasis on detection, prevention and treatment of poisonings.

- It also includes the study of adverse effects of drugs

DRUG NOMENCLATURE

- A drug generally has 3 type of names:

  (a) **Chemical name:**

  - It describes the substance chemically, e.g. 1-(Isopropylamino)-3-(1-naphthlloxy) propan-2-ol for propranolol.

  - This is cumbersome and not suitable for use in prescribrng.

- **B. code name** e.g. RO 15-1788 (later named flumazenil) may be assigned by the manufacturer for convenience and simplicity before an approved name is coined.

(C) Non-proprietary name: It is the name accepted by a competent scientific body or authority e. g. the United States Adopted Name (USAN) by the USAN council.

- Similarly there is the British Approved name (BAN) of a drug.

- The nonproprietary names of newer drugs are kept uniform by an agreement to use the Recommended International Nonproprietary Name (rINN) in all member countries of the WHO.

- However, many older drugs still have more than one non-proprietary names e.g. 'meperidine' and 'pethidine' or 'lidocaine' and'lignocaine' for the same drugs.

- Until the drug is included in a pharmacopoeia, the nonproprietary name may also be called the approved name.

Official Name:

- After its appearance in the official publication, it becomes the official name.

- The term generic name is used in place of nonproprietary name.

(D) Proprietary (Brand) name:

- It is the name assigned by the manufacturer(s) and is his property or trade mark.

- One drug may have multiple proprietary names, e.g. ALTOL, & ATEN etc.

- Brand names are designed to be catchy, short, easy to remember and often suggestive,
- e.g. LoPRESOR suggesting drug for lowering blood pressure.
- Brand names generally differ in different countries, e.g. timolol maleate eye drops are marKeted as TIMOPTIC in USA but as GLUCOMOL in India.

- Even the same manufacfurer may market the same drug under different brand names in different countries.
- In addition, combined formulations have their own multiple brand names.
- This is responsible for much confusion in drug nomenclature.

- There are many arguments for using the nonproprietary name in prescribing the drugs due to its:

  - Uniformity,

  - Convenience,

  - Economy,

  - And better comprehension (propranolol, sotalol etc).

- However, when it is important to ensure consistency of the product in terms of quality and bioavailability, etc.

- and when official control over quality of manufactured products is not rigorous,

it is better to prescribe by the dependable brand name.

Essential Medicines

- The WHO has defined **Essential Drugs** (medicines) as "those that satisfy the priority healthcare needs of the population".

- They are selected with due regard to
  - public health relevance,
  - evidence on efficacy and safety,
  - and comparative cost effectiveness.

Essential medicines

- **Essential medicines:** are intended to be available within the context of functioning health systems
  - At all times and in adequate amounts,
  - In appropriate dosage forms, with assured quality and adequate information,
  - And at a price the individual and the community can afford.

How essential medicines ?

- It has been realized that
  - only a handful of drugs out of the multitude available can meet the health care needs of majority of the people in any country,
  - And that many well tested and cheaper drugs are equally (or more) efficacious and safe as their newer more expensive congeners.

- For optimum utilization of resources, goverment (especially in developing countries) should concentrate on these drugs by identifying them as essential medicines.

- The WHO has laid down criteria to guide selection of an essential medicine.

  (a) Adequate data on its efficacy and safety should be available from clinical studies.

  (b) It should be available in a form in which quality, including bioavailability and stability on storage can be assured.

  (c) Its choice should depend upon:

  - pattem of prevalent diseases;
  - availability of facilities and trained personal
  - financial resources
  - genetic, demographic and environmental factors.

(d) In case of two or more similar medicines, choice should be made on the basis of their relative efficacy, safety, quality, price and availability.

- Cost-benefit ratio should be a major consideration.

(e) Choice may also be influenced by comparative pharmacokinetic properties and local facilities for manufacfure and storage

(f) Most essential medicines should be single compounds.

- **Fixed ratio combination** - included only when
  - dosage of each ingradient meets the requirements of a defined population group,
  - the combination has a proven advantage in
    - therapeutic effect, safety, adherence
    - or in decreasing the emergence of drug resistance.

- (g) Selection of essential medicines should be a continuous process which should take into account the
  - changing priorities for public health action,
  - epidemiological conditions as well as availability of better medicines/ formulations
  - progress in pharmacological knowledge.

- To guide the member countries, the WHO brought out its first Model List of Essential Drugs along with their dosage forms and strengths in 1977

- This has been revised from time to time and the current is the 15th list (2007).

National List of Essential Medicines (India)

- India produced Its National Essential Drugs List in 1996 and has revised it in 2003 with the title " National List of Essential Medicines".

- This includes 354 medicines which are considered to be adequate to meet the priority healthcare needs of the general population of the country.

- Adoption of the essential medicines list for procurement and supply of medicines has resulted in

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  improved availability of medicines, cost saving and more rational use of drugs.

Orphan Drugs

- These are drugs or biological products for diagnosis/ treatment and prevention of a rare disease or condition or a more common disease (endemic only in poor country) for which there is no reasonable expectation that the cost of developing and marketing will be recover from the sales of that drug.

- The list includes
  - sodium nitrite
  - fomepizole
  - liposomal amphotericin B
  - digoxin immune Fab (digoxin antibody)
  - liothyronin (T3) and many more.

- Though these drugs may be life saving for some patients they are commercially dfficult to obtain.

- Government in developed countries offer tax benefits and other incentives to pharmaceutical companies for developing and marketing orphan drugs (eg. Orphan Drug Act in USA)