INTRODUCTION OF PHARMACOLOGY

- Pharmacology is the science of drugs
- The word "pharmacology" is derived from the two words
  Greek :Pharmakon, which means "drug"
  logus, which means "science."
  i.e science of drugs
- it deals with interaction of exogenously(बाहरी रूप से) administered(किसी के द्वारा दिया जाना) chemical molecules with living systems, and any single chemical substance which can produce a biological response(called drug).
- It cover all aspects of knowledge about drugs, but mainly those are effective and safe in use for medicinal purposes.
- **Drug** -Drugs are chemicals of low molecular masses (~100 – 500u). These interact with macromolecular targets and produce a biological response. When the biological response is therapeutic and useful, these chemicals are called medicines and are used in diagnosis, prevention and treatment of diseases.

  Or
- World Health Organization (WHO) in 1966 defined drugs as any substance or product which is used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient, either therapeutic or diagnostic benefits.

- **Definition**- Pharmacology is the science of the study of substances that interact with living systems through chemical processes, especially by binding to regulatory molecules and activating or inhibiting normal body processes.

  Or

  Pharmacology is a discipline of science concerned with the study of medications and their effects on biological systems, or the study of how drugs function in the body (sometimes known as 'drug activities').
- Pharmacology deals with the knowledge of drugs, their sources, biochemical and physiological effects, mechanism of action, and therapeutic(चिकित्सीय) uses of drug
- Pharmacology studies the effects of drugs and how they exert their effects. For example, paracetamol can reduce body temperature in case of fever by inhibiting an enzyme known as cyclooxygenase in CNS, which is responsible for the synthesis of a number of inflammatory mediators. Penicillin cures certain bacterial infections by disrupting the synthesis of bacterial cell walls by inhibiting a key enzyme.
- The general pharmacology involves the aspects(पहलू) of - sources of drugs, route of administration of drugs, absorption of drugs and factors affecting them, their distribution, biotransformation, and excretion, the mechanism by which the drug is acting with receptor, toxicity of drug and preclinical and clinical evaluation

❖ **TOPIC COVERED UNDER GENERAL PHARMACOLOGY**

1. Branches of Pharmacology
2. Some definition
3. Sources of drugs
4. Drug nomenclature
5. Regulatory oversight
6. The drug development and approval process
7. Classification of drugs
8. Pharmacotherapeutics
9. Drug information source
10. Essential medicine list
11. Prescription writing
12. Medication errors
13. Irrational, non-essential and hazardous drugs in the market
14. Fixed dose combination
15. The menace of the fake drugs-consequences, causes and possible solution.

1) BRANCHES OF PHARMACOLOGY

Pharmacology contain two main branches: 1) pharmacokinetics and 2) pharmacodynamics.

i) **Pharmacokinetics (what body does to drug):**

- In this we study movement of drug, their absorption, distribution, metabolism, and excretion
- The study of what happens to the drug in the body is called pharmacokinetics.
- For example, *chlorpromazine* is absorbed at a faster rate by the parenteral route than the oral route; it binds with plasma and tissue protein and it is metabolized into the liver and is excreted in 15 to 30 hours.

ii) **Pharmacodynamics (what drug does to body):**

- In this we study the physiological and biochemical effects of drugs and their mechanism of action at organ system/subcellular/macromolecular levels,
- e.g.-Adrenaline ➔ interaction with adrenoceptors ➔ G-protein mediated stimulation of cell membrane bound adenylyl cyclase ➔ increased intracellular cyclic 3 ',5' AMP ➔ cardiac stimulation, hepatic glycogenolysis and hyperglycaemia, etc.

1.1)Other branches

i) **Pharmacotherapeutics:**

- It deals with clinical application of the pharmacokinetic and pharmacodynamic knowledge of the drug, in finding a cure of diseases or relief of symptoms.
- It includes use of drugs in the treatment, diagnosis, or prevention of a disease or in alteration of physiological functions for the benefit of the recipient.

ii) **Toxicology:**

- It is a science of poisons.
- Poisons are substances that are harmful and dangerous or show fatal symptoms in animals and human beings
- Many drugs in large dose act as poisons, for example, *aspirin* in less dose acts as an anticoagulant by inhibiting thromboxane A2, thus, it is useful for heart patients but in high dose causes ulceration and can lead to fatal bleeding.

iii) **Chemotherapy:**

- It is concerned with the effect of drug upon microorganisms and parasites, living and multiplying in living organisms.
- It is now also useful for the treatment of cancer by targeting cancerous cells.

iv) **Clinical pharmacology**:

- It deal with drugs and their clinical use.
- It gives useful data about the potency, usefulness, doses, and toxicity of new drugs for their safe clinical use.

v) **Pharmacoepidemiology**:

- It is a study of the effect of the drugs on population.

vi) **Pharmacoeconomics**:

- It is a branch of pharmacology which studies the cost effectiveness of drug treatment and cost of medications, particularly among certain groups such as elderly and AIDS patients.

vii) **Pharmacogenetics**:

- It is the study of the genetic variation that gives rise to differing response to drugs among individuals or populations.
- Some patients respond to certain drugs with greater than usual sensitivity to standard doses.
- Screening of individuals for a variety of such differences before prescribing may help in individualized therapy.

viii) **Pharmacogenomics**:

- It is the application of genomic technologies to drug discovery and further characterization of older drugs.

ix) **Pharmacognosy**:

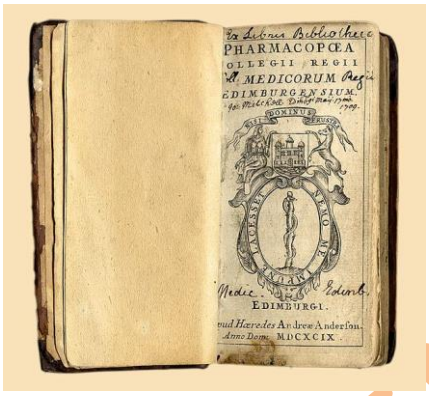
- It deals with the study of the sources of drugs derived from plants and animal origin.

x) **Pharmacy**:
- It is the art and science of compounding or preparing suitable dosage forms for administration of drugs in man and animals and dispensing drugs.
- It also includes identification, selection, collection, purification, isolation, standardization, and quality control of medicinal substances.

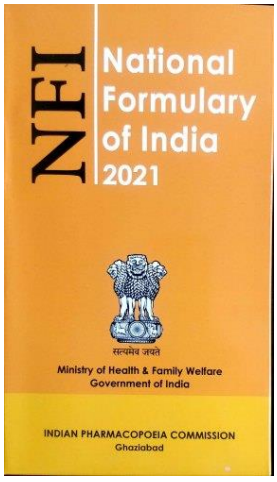
xi) **Clinical pharmacy**:
- It is a health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health, wellness, and disease prevention.

2) DEFINITIONS

i) Pharmacopoeia:
- It is an official reference containing a selected list of the established drugs and medicinal preparations with descriptions of their physical properties and tests for their identity, purity, and potency.
- It defines the standards of preparations.
- A few famous pharmacopoeia and other reference books are the
  - i) British pharmacopoeia (BP),
  - ii) Indian Pharmacopoeia (IP),
  - iii) International Pharmacopoeia (IP), and
  - iv) Unites States Pharmacopoeia (USP).



ii) National formulary:
- It provides product information on drugs available to prescribers in respective countries/states/health systems.
- For example,
  - i) National Formulary of India is published by Government of India, and
  - ii) British National Formulary (BNF) is jointly published by British Medical Association (BMA) and the Royal Pharmaceutical Society.



iii) Essential medicines:
- WHO defines Essential Medicines as those that satisfy the priority healthcare needs of the population.
- 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.

iv) **Orphan drugs**:

- These are the drugs for diagnosis, prevention, and treatment of a **rare disease** or a **more common disease** (but **endemic only** in poor countries), for the manufacturing and marketing of these drugs Pharmaceutical industries shows little interest because they are used for only a small number of patients, that means huge financial losses for the companies.
- Rare diseases which occur in small patient populations thus are "orphaned" by the pharmaceutical industry—that is, only a few approved drug treatment options available are called "orphan diseases."
- **A drug used to treat, prevent, or diagnose an orphan disease is called orphan drug.**
- Rare diseases or orphan diseases are those that present at the maximum 6% to 8% of the world population, for example,
  - genetic diseases—infantile spinal muscular atrophy,
  - cystic fibrosis, patent ductus arteriosus(PDA),
  - lysosomal storage disorders,
  - familial adenomatous polyposis (FAP), and
  - acute intermittent porphyria.
- Some of the examples of orphaned drugs are
  - *miglustat* used for Type 1 Gaucher disease,
  - *iloprost* for pulmonary arterial hypertension in patients with NYHA Class III or IV symptoms,
  - *bosanten* for WHO Class II–IV symptoms,
  - *pegvisomant* used for cromegaly, and
  - *busulfan* used for allogeneic hematopoietic progenitor cell transplantation for chronic myelogenous leukemia.
- Various countries have enacted laws in this regard and provide incentives and support for drug development.

3) Sources of drugs

- Drugs are obtained mainly from plants, animals, microbes, and mineral sources.
- Nowadays, a majority of therapeutically used drugs are produced from synthetic or semisynthetic products.
- Various sources are given as follows
  - i) Animal sources:
    - Insulin, heparin, gonadotrophins, thyroid extract, and antitoxic sera (for example, antisnake venom).
  - ii) Minerals:
    - Liquid paraffin, ferrous sulfate, magnesium sulfate, magnesium trisilicate, kaolin, etc.
  - iii) Microorganisms—
    - bacteria and fungi: *Penicillin, streptomycin, erythromycin, polymixin B, bacitracin, chloramphenicol, nystatin, griseofulvin.*
    - Apart from antibiotics obtained from microorganisms, other products that are also produced by microorganisms include streptokinase, an enzyme from gram-positive cocci (Streptococcus pyogenes), and vitamin B_{12} (cyanocobalamin), produced from Streptomyces griseus.
  - iv) Human beings:
    - These products are obtained from human beings.
    - For example, immunoglobulins from blood, growth hormone from the pituitary gland, placental extract from placenta, and chorionic gonadotropin from the urine of pregnant women.
  - v) Synthetic compounds:
    - Analgesics, antimicrobials, hypnotics, anticancer drugs, etc.
  - vi) Genetic engineering:
    - Human insulin, growth hormone, etc.
  - vii) Hybridoma technique:
    - Monoclonal antibodies, etc.
  - viii) Plant sources:
    - The pharmacologically active components in vegetable drugs are given in the following text.

(a) Alkaloids:

- These are water-soluble salts of water-insoluble nitrogenous compounds.
- Some of the important alkaloids are as follows:
  - → Cinchona (Cinchona officinalis): *Quinine*, etc.
  - → Rauwolfia serpentina (root): *Reserpine*.
  - → Coca (Erythroxylum coca): *Cocaine*.
  - → Opium (Papaver somniferum): *Morphine* group.
  - → Belladonna (Atropa belladonna): *Atropine* group.

(b) Glycosides:

- These are ether-like organic structure combined with sugars. The non-sugar component is called aglycone or genin.
- The important glycosides are as follows:
  - → Digitalis (Digitalis purpurea, Digitalis lanata): *Digoxin*, etc.
  - → Senna (Cassia acutifolia): *Sennoside*, etc.
  - → Stropanthus (Strophanthus kombe): *Stropanthin*, etc.

(c) Oils:

(1) Fixed oils:

- These are glycerides of oleic, palmitic, and stearic acids. Mostly fixed oils are edible and used for cooking.
- The fixed oils used as drug are as follows:
  - → Castor (Ricinus communis): Castor oil.
  - → Olive (Olea europaea): Olive oil.
  - → Cocoa butter (Theobroma cacao): Theobroma oil used as emollient in skin cream and making suppositories.

(2) Volatile oils:

- These are essential oils which contain the hydrocarbon terpene.
- The important volatile oils are as follows:
  - → Turpentine oil, from species of pines, used as a counterirritant.
  - → Lemon oil (from citrus limon), used as a flavoring agent.
  - → Peppermint, cardamom, ginger, and fennel used as carminative and flavoring agents.
  - → Eucalyptus oil used for relieving congestion.
  - → Oil of clove mainly useful in toothache for relieving pain.

(d) Resins:

- These are oxidized or polymerized volatile oils.
- The different types of resins are as follows:
  - → Oleoresins: A mixture of volatile oils and resins. Male fern extract used for tapeworm infestation.
  - → Gum resins: Asafoetida, used as carminative and antispasmodic.
  - → Oleo gum resin: Myrrh—it has a local stimulant and antiseptic properties and generally used in mouthwash.
  - → Balsams: Benzoin, used internally as expectorant and externally as astringent.
  - → Balsam Tolu, used as stimulating expectorant.

(e) Gums:

- These are the secretory products of plants.
- On hydrolysis, they yield simple sugar-like polysaccharides.
- They are pharmacologically inert substances and mainly employed as a suspending and emulsifying agent in various pharmaceutical products.
- The widely used preparations are gum acacia and tragacanth.

(f) Tannins:

- These are non-nitrogenous constituents of plant.
- Chemically, these are phenolic derivatives and are characterized by their astringent action.
- Tannins are generally used in the treatment of diarrhoea and burns.
- The important plants which contain tannins are Hirda (in combination form “Triphala”), Amla, Behera, Ashoka bark, Black catechu, etc.

4) DRUG NOMENCLATURE/NAMING OF DRUGS

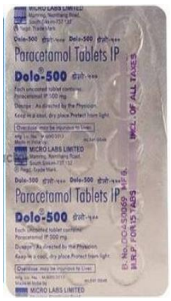
- The three broad name classifications of drugs are as follows:
  - → Chemical/molecular/scientific name
  - → International nonproprietary/generic/approved name
  - → Proprietary/brand/trade name

(i) **Chemical/molecular/scientific name**:

- It is the chemical/ molecular structure of the drug and shows the structure in terms of atoms and molecules accompanied by a diagram of the chemical structure.
- Chemical or scientific names are complex, long, can be difficult to pronounce, and are useful to a few technically trained personnel.
- For example, acetyl-p-amino-phenol is a chemical name for *paracetamol*.
- This name is not suitable for routine use by medical professionals or common people.
- However, this name is very helpful for the discovery of new compounds.

(ii) **International nonproprietary/generic/approved name:**

- Non-proprietary mean- not registered not protected by trademark or patent or copyright.



- The International Nonproprietary Name (INN) is an official generic and nonproprietary name given to a pharmaceutical drug—that is, this is the abbreviated(संक्षिप्त) and approved name of the drug.
- International nonproprietary names provide a unique standard name for each active ingredient, thus making communication more precise and avoid prescribing errors.
- Each drug's INN is unique.
- Drugs from the same therapeutic or chemical class are usually given names with the same *stem*. –
  - *sartan* for angiotensin blockers (for example, *losartan*),
  - *-azepam* suffix for benzodiazepines (for example, *lorazepam* and *diazepam*),
  - *-pril* for ACE inhibitors (for example, *captopril*), and
  - *ase* for enzymes (for example, *alteplase*).
- The nature of a drug can be easily identified by studying the suffix.
- WHO has laid down the general principles in naming a drug by the nonproprietary name.
- However, the nonproprietary name may sometimes vary from country to country.
- Usually, the British Approved Name (BAN) and the INN coincide, and where the two differed, the BAN was modified to match the INN with some exception where the nonproprietary name of some drugs in UK (BAN) and USA (USAN) is different.
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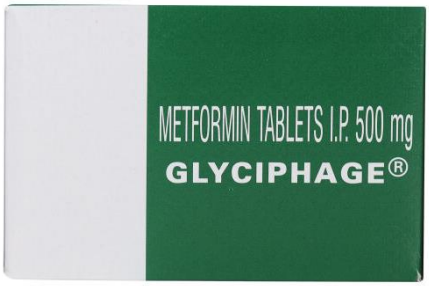
BRITISH APPROVED NAMES(BAN)	UNITED STATES APPROVED NAMES(USAN)
Adrenaline	Epinephrine
Dexamphetamine	Dextroamphetamine
Ergotametrine	Ergonovine
Glyceryl trinitrate	Nitroglycerine
Hyoscine	Scopolamine
Isoprenaline	Isoproterenol
Lignocaine	Lidocaine
Paracetamol	Acetaminophen
Phenobarbitone	Phenobarbital
Rifampicin	Rifampin
Thiopentone	Thiopental
Salbutamol	Albuterol
Frusemide	Furosemide

- The generic name can be used by anyone and it removes the confusion of giving several names to the same drug with the same chemical structure regardless of who manufactures them.
- A generic drug name is not capitalized, for example, *aspirin* and *paracetamol*.

(iii) Proprietary/brand/trade name:

- These are names given to the drug by the manufacturing and marketing company.
- The innovator company can then exclusively market and sell this "brand-name" product during the patent protection period.
- Copyright laws prevent any other person from using the brand name. On expiry of the patent life, a branded-name drug product is eligible to be manufactured and marketed as a "generic drug."
- Trade name refers to a particular company and appears with the sign ® at its upper right corner which indicates that the name is registered and its production is restricted to that pharmaceutical company as the sole owner. For example, antidiabetic drug metfromin marketed as Glyciphage ; *metformin* is a generic name whereas Glyciphage is a brand name.



- One drug can have so many trade/brand names, for example, *paracetamol* (*acetaminophen*) has more than 30 trade names; some of these are Crocin, Panadol, Calpol, etc.
- A **generic medicine** is a legitimately produced medicine that is an exact copy of the innovator/originator product (branded medicine) and performs in exactly the same way.
- Though brand-name drug and its generic version must have the same active ingredient, dosage, strength, usage directions, safety, quality, performance, and use, it may differ in inactive ingredients, preservatives, colour, shape, taste, and packaging.
- For example, generic and brand name drugs must meet the exact same standards for equivalency in effectiveness, safety profile, and quality except cost. The difference in cost between a generic and a brand-name drug is mainly due to a difference in the development costs as manufacturers of the generic versions do not incur expenses on developing and marketing the generic version which is required for a new drug; thus, the manufacturers can produce the drug at a lower unit cost and sell it for less. Further, the competition keeps the prices of generic medicines down.

5) REGULATORY OVERSIGHT (नियमो की निगरानी)

- The Drug Regulatory Authority (DRA) oversees(देखरेख) the approval and regulation of drugs.
- For a drug to be prescribe in market, the manufacturer needs the approval of the DRA—that is, product licenses (known formally as Marketing Authorisations). Product licence permitting license holders to sell medicinal products in market.
- To get that approval, the manufacturer must fulfil the criteria of drug's safety and effectiveness according to specified in law and agency regulations, ensure that its manufacturing plant passes DRA inspection, and obtain DRA approval for the drug's labelling—that is, every license for a medicinal product contains information about the approved uses of the drug, including prescribing information for physicians, for example, dosage forms, packaging, therapeutic indications, doses, route of administration, contraindications, precautions for use or special warnings, adverse drug reactions, drug interactions, and patient brochures(An information brochure **tells patients, healthcare users and their families about the care that is being offered, and adds to the information given verbally by the healthcare professional**).
- Almost all countries have established Drug Regulatory Authorities to assure the safety and effectiveness of Investigational New Drugs (IND) through the evaluation of clinical pharmacology and biopharmaceutics (physicochemical properties of a drug in dosage form and the pharmacology, toxicology, or clinical response observed after its administration) data in support in the New Drug Application (NDA) and license application review programs.
- Regulatory oversight is necessary to prevent anyone from selling or freely advertising the benefit and safety including products containing *cocaine* or opioids (for example, *morphine*).
- DRA is responsible for approval of new drugs, and medical devices as well as oversight of the drugs and medical devices already available in the market. This includes both prescription drugs and over-the-counter (OTC) drugs (drugs that do not require a prescription).
- Also, "dietary supplements" such as vitamins, amino acids, mineral, and herbal medication, even though most of these products have significant pharmacologic activity, are not regulated.