Pharmacology

Mid Material – Lecture 1

Introduction to Pharmacology

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Pharmacology

Pharmakon = Drug; Logos = Science

• **Pharmacology** can be defined as 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.

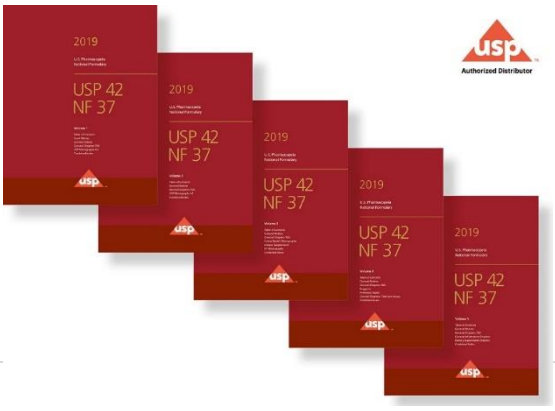
Drug

• A term of varied usage.

- **Medicine**: any substance with the potential to prevent or cure disease or enhance physical or mental welfare.
  - We talk about the drugs in **general**, about the outcomes of the drug
- **Pharmacology**: any chemical agent that alters the biochemical or physiological processes of tissues or organisms (a substance that is listed in the pharmacopeia).
  - It's more **specific**, we talk about the process of the drug.

Pharmacopeia

- A book describing drugs, chemicals, and medicinal preparations: issued by an officially recognized authority and serving as a standard.
- It contains: Information about the drugs, descriptions, how to use, how to prepare, main reasons for use.
- E.g. British pharmacopeia (BP) and United state pharmacopeia (USP).



British Pharmacopoeia Volume III

Formulated Preparations: Specific Monographs

Paracetamol Tablets

General Notices

Action and use

Analgesic; antipyretic.

DEFINITION

Paracetamol Tablets contain Paracetamol.

The tablets comply with the requirements stated under Tablets and with the following requirements.

Content of paracetamol, $C_8H_9NO_2$

95.0 to 105.0% of the stated amount. **Margin of error = 5% for paracetamol**

IDENTIFICATION

Extract a quantity of the powdered tablets containing 0.5 g of Paracetamol with 20 ml of *acetone*, filter, evaporate the filtrate to dryness and dry at 105°. The residue complies with the following tests.

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of paracetamol (*RS 258*).

Major objective of drug treatment

- To have a drug at the **site of action** in a **proper concentration** that is good enough to **reverse a defect** without producing **side or toxic effects**.
- We should give the drug in the right way so it reaches the site of the action and at the appropriate concentrations.
- Not supra-therapeutic that leads to toxicity.
- Not sub-therapeutic that doesn't give the action required.

Drug classification

1. Drug source.
2. The need for prescription.
3. Therapeutic use.
4. Pharmacological category.
5. Physiological system targeted by the drugs.
6. Chemical nature.
7. Drugs to treat common vs. rare diseases.

1. Drug Source

A. **Natural**: Plants (atropine, digoxin), Animals (insulin), Human (growth hormone), Microorganisms (Penicillin, streptomycin and many other antibiotics)
B. **Minerals**: Liquid paraffin, magnesium sulfate, magnesium trisilicate, kaolin, etc.
C. **Genetic engineering:** Human insulin, human growth hormone etc.
D. **Semisynthetic**: (human insulin)
E. **Synthetic**: (agonists; antagonists) most common, and now used widely more than those of other sources.

2. The need for prescription

A. **Prescription drugs**: Are used under only medical supervision and dispensed by an order of medical practitioner only.

- Any drug that has a potential for abuse, EX: Antibiotics, their misuse (overuse) leads to *increase bacterial or antibiotic resistance.*

B. **OTC (Over the Counter) drugs:** Can be sold over the counter without prescription

- Drugs that have little potential of abuse.
- It differs among different countries.

3. Therapeutic use

A. **Anti-hypertensive drugs:** Atenolol, Furosemide, Amlodipine, Ramipril (*Same therapeutic use, but different physiological activity*).
B. **Anti-microbial drugs:** Amoxicillin, Ciprofloxacin, sulfamethoxazole
C. **Anesthetics**: Ketamine, isoflurane, xylazine
D. **hypoglycemic drugs:** Insulin, Metformin, Linagliptin, Pioglitazone
E. **Anticoagulants:** Warfarin, Heparin, Rivaroxaban

4. pharmacological action

- This should be precise.
  - **Atenolol**: Beta blocker (BB)
  - **Furosemide**: Loop diuretic
  - **Amlodipine**: Calcium channel blocker (CCB)
  - **Ramipril**: Angiotensin converting enzyme inhibitor (ACEI)

5. Physiological systems targeted by the drug

- **Drugs acting on respiratory system:** Selective beta-2 adrenergic receptors agonists (Albuterol) – Bronchodilator for Asthma.
- **Drugs acting on gastrointestinal tract:** Proton pumps inhibitors (omeprazole)

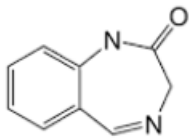
6. Chemical Nature

- Common chemical groups or structures can be used to classify drugs that have similarity in their pharmacological profile.

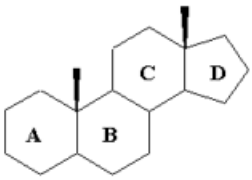
Ex: Alprazolam, which is an oral benzodiazepine.

They have the same nucleus but different side chains.

Benzodiazepines



Steroids



6. Drugs to treat common vs. rare diseases

A. **Essential Medicines**, as defined by the WHO are those drugs that satisfy the health care needs of the majority of the population; they should therefore be available at all times in adequate amounts and in appropriate dosage forms, at a price the community can afford.
   - **Ex**: Antibiotics and pain killers.
   - Used because of frequent exposure to infections.
   - For common disease that have high frequency and vast majority of population get advantage from them (Wider availability).

B. **Orphan Drugs:** These are drugs or biological products for diagnosis/treatment/prevention of a rare disease or condition, or a more common disease (endemic only in resource poor countries) for which there is no reasonable expectation that the cost of developing and marketing it will be recovered from the sales of that drug.
E.g. sodium nitrite (cystic fibrosis), fomepizole (antidote for methanol poisoning), liposomal amphotericin B (pulmonary fungal infection) and many more.

Main branches of pharmacology

- Pharmacokinetics
- Pharmacodynamics
- Toxicology
- Pharmacotherapy
- Clinical pharmacology
- Pharmacogenetics
- Pharmacogenomics
- Chemotherapy
- Pharmacognosy
- Pharmacoeconomics
- Pharmacoepidemiology

Branches of pharmacology usually answer all of the following questions:

- How much of a drug to give? Dose
- How frequent a drug should be given? Related to the biological half-life ($t_{1/2}$)
- When to give it? Before or after meals; at bed time, PRN...
- How to give it? Route of administration

- The **dosage regimen** definition is "Decision of drug administration regarding formulation, route of administration, drug dose, dosing interval and treatment duration."

Pharmacokinetics

- The branch of pharmacology concerned with the movement of drugs within the body.
- Deals with ADME process i.e. what the body does to the drug

Pharmacodynamics

- The branch of pharmacology concerned with the effects of drugs and the mechanism of their action
- Drug's plasma concentration, its response and duration of action i.e. What the drug does to the body and how.

Toxicology

- **T**he branch of pharmacology that deals with the undesirable effects of chemicals on living systems, from individual cells to humans to complex ecosystems.

Pharmacotherapy

- It is the clinical application of pharmacodynamics and pharmacokinetics for treatment

Clinical pharmacology

- Medical discipline which combines pharmacological and clinical expertise with the ultimate goal of improving efficacy and safety in the clinical use of drugs.

Pharmacogenetics and pharmacogenomics

- *pharmacogenetics* usually refers to how variation in one single gene influences the response to a single drug. *Pharmacogenomics* is a broader term, which studies how all of the genes (the genome) can influence responses to drugs.
- The distinction however, is arbitrary and both terms can be used interchangeably

Chemotherapy

- The treatment of disease by means of chemicals that have a specific toxic effect upon the disease producing microorganisms or that selectively destroy cancerous tissue
- We usually use the word *Chemotherapy* referring to **cancer**, while it actually refers to any drug that has toxicity (Chemically) on microorganisms (Antibiotics) or on cells like cancer cells.

Pharmacognosy

- The study about the physical, chemical, biochemical, and biological implications of natural products for medicinal or health benefit purposes.

Pharmacoeconomics

- The branch of economics that uses cost-benefit, cost-effectiveness, cost-minimization, cost-of-illness and cost-utility analyses to compare pharmaceutical products and treatment strategies.

Pharmacoepidemiology

- The study of the utilization and effects of drugs in large numbers of people; it provides an estimate of the probability of beneficial effects of a drug in a population and the probability of adverse effects. It can be called a bridge science spanning both clinical pharmacology and epidemiology.

Dosage forms

- It is the physical form of drug product that is suitable for administration to man. It contains specified dose or amount of drug in a specified quantity or unit of the formulation.
  A. Solid
  B. Semi-solid
  C. Liquid
  D. Gas

Solid

- Tablets Capsules Powder

- The capsule may contain powder or small particles but the whole thing with its shell is called a capsule.
- Powder can be used **topically** it can be also reconstituted and then injected into the blood, also some kinds of drugs are not stable in the liquid form so we store it in the powder (solid & dry) form till the using time (we reconstitute it).
- A tablet may contain a very small amount from the drug substance itself (like 10 micrograms) and another suitable substance to make it a bit bigger and swallowable.
- It (The tablet) might be coated (ex. With sugar) in a shell to give it a colour or taste or to make it slowly absorbed so it won't be completely broken down at one place (high does at that place only), And it can be uncoated.

Semi-solid

- Creams
- Ointments
- Paste
- Gel
- Suppositories

1. **Creams** are more aqueous and watery (*easily dissolved in water when washing it*)while ointments are more <u>oily in nature</u> which gives it a relatively **longer contact time**, so we give it when the injured area is more exposed also ointments have a **moisturizing like function** so for example when a dryness in the skin leads to an infection ,ointments are a very good option to treat both dryness and the infection itself .
2. **Pastes** are similar to creams but highly concentrated and they are relatively thick in nature so it's <u>less spreadable</u> (*Can't diffuse easily*).
3. **Eye Gels** have <u>longer contact time</u> than eye drops.
4. **Suppositories** are <u>semi solid</u> because they dissolve very easily when in contact with the body (at body temp).

- In cases of skin pigmentation (*skin discoloration*); the medications used are relatively of strong effect on skin that is why it is preferable to give pastes in such cases so that we prevent the diffusion of these medications to other areas of skin.

Liquid

- Monophasic
  - ➢ Syrup
  - ➢ Solution

- Biphasic
  - ➢ Suspension
  - ➢ Emulsion

- **Monophasic drugs** are completely dissolved in the solution (*Once looking to bottle you see no particles in it*).
- **Syrups** are more sugary than solutions and it also have longer contact time *(i.e., cough medicines are usually syrups*).
- Biphasic drug; it is seen in one of the two ways:
  1. **Solid** suspended in **liquid** solution
  2. **liquid** suspended in **liquid** solution.

Gas

- Inhalers

Routes of administration

- In order for the drugs to exert their effect, they should reach to the site of action or receptor to produce the effect.
- This is a complex process
- This involves the release of the drug from the dosage form, absorption, distribution, metabolism and elimination (pharmacokinetics will be discussed in details later)
- Routes of administration (*the way in which the drug is taken*) depends on:

1. The properties of the drug itself and the route of absorption (ex. Some drugs are degraded completely in the GI system so it doesn't reach the blood so it can't be taken orally), so is to ensure that the drug reach the site of action in order to produce the desirable effects
2. It depends also on the patient:
   - kids can't swallow tablets.
   - Stroke patients usually have what is called **Dysphagia** (difficulty in swallowing).

Main routes of administrations

1. Buccal and Sublingual
2. Oral
3. Inhalational
4. Parenteral
5. Topical
6. Rectal
7. Transdermal (Patches).

Buccal and sublingual

- **Buccal**: between the inner cheeks and the gums.
- **Sublingual**: under the tongue.
- Solid (tablet) or liquid (spray) dosage form
- They are **systemic drugs**, once the drug is absorbed it reaches (enter) systemic circulation directly.
- Drug absorbed from the buccal cavity (highly vascular) and the presence of saliva fasten the dissolution in case of tablet dosage form, so that the absorption rate is relatively fast.
- **Advantages**:
    1. Quick onset of action
    2. Avoid first pass effect
    3. Can be used for unconscious patients

Oral

- Used for local or systematic effect
- Solid or liquid dosage forms
- Drug absorbed from the GI tract
- Most common
- **Advantages**:
    A. Simplest rout
    B. Self-administration
- **Disadvantages**:
    A. Slow onset of action
    B. Absorption issues
    C. Drug destruction by GIT enzymes
    D. First pass effect
    E. Food-drug interaction
    F. Unsuitable for unconscious or vomiting patients

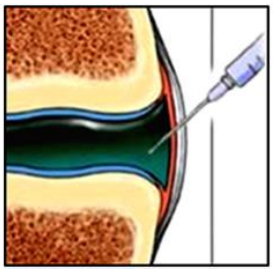
Inhalational

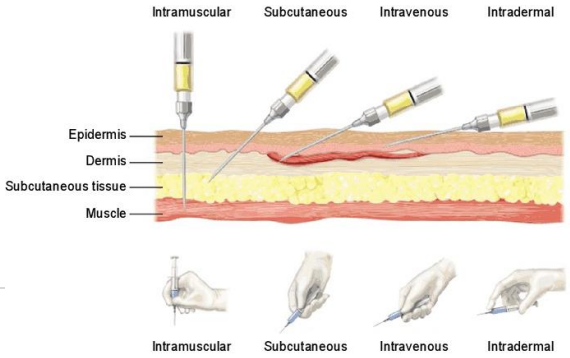
- Used for local (predominantly) or systematic effects
- Solid (powder), liquid or gas dosage forms
- Mostly used for respiratory conditions such as asthma
- **inhalation** is usually used *locally* to treat diseases, most commonly ***asthma*** and ***COPD*** (that we'll know more about when we study the respiratory system).
- **inhalers** could also be used to give *systematic effects;* the drug gets absorbed through the lung to the blood circulation and then moves with the blood to the sites of action.
- because the effects of it is usually local and inhaled <u>directly</u> to the lung, it *doesn't* go through the GI tract, so it *doesn't* undergo destruction or liver metabolism, and so the dosage of the drug that we need is *less* when used locally to give the same effect.
- we can *avoid* <u>systematic side effects</u> in **inhalation** and that's due to it not going through the circulation and not reaching the blood and different tissues. (as opposed to **oral**)
- Its effect is *instant*, for an example:
  When asthma patients have difficulty in breathing and they take the inhaler **Ventolin** (trade name for albuterol or salbutamol) the bronchi dilate instantly and breathing goes back to normal, that is due to the fact that it *didn't* need the process to through the blood and reach the target, it instantly reached the site of action (the lung).

- **Advantages**:
  A. Smaller dose than oral route
  B. is used to give the same effect
  C. Lower incidence of side effects
  D. Rapid onset of action
- **Disadvantages:**
  A. Local side effects (inhaled corticosteroids)
     In chronic diseases such as **Asthma** and **COPD**, the patient uses inhalers for a long period of time to control their diseases, and because asthma inhalers are corticosteroids & usually having steroids in them, after using them for some time steroids accumulate in the oral cavity resulting in *local fungal infection*. As a doctor, you should be advising your patients using any inhaler with **cortisone** in it to rinse their mouth after using the inhaler to prevent that infection.
  B. Not easy to use in children
     Explaining it to a child is hard because of its complicated instruction.

Parenteral

- Drugs are given by a rout out of the alimentary canal most commonly by injections
  A. Intradermal is superficial injection and it is used for diagnostic tests for allergy and vaccines
  B. Subcutaneous injection used for drugs that cannot be given orally. It gives quick onset and prolonged action (insulin)
  C. Intramuscular used for solutions (aqueous and oil) and for suspensions.
  D. Intravenous injection used for aqueous solutions only (antibiotics and parenteral products).
  E. Intraarticular injection used in arthritis patients to administer corticosteroids.





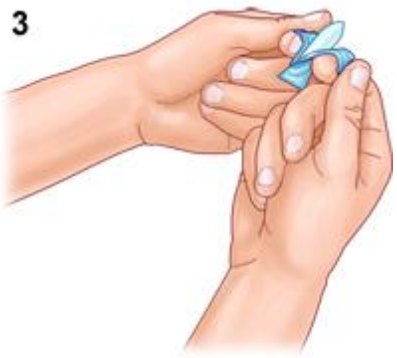
1. Immunologists use **intradermal injection** to know what is causing a patient allergy and that is through giving them *allergens* usually in the back in *small* doses to know exactly what is causing the allergic reaction.
2. **Subcutaneous injection** (slightly deeper) is given in the fatty tissue, it solves the issue of some drugs (when given by oral administration) being unstable in the GI tract because some of them *break down* in the GI therefore it won't be useful, giving it in this way gives a *fast effect* while still *sustaining the release*; solving another problem because the sudden release of some drugs to the blood (*insulin* in this case) can be harmful and lead to *hypoglycemia* (can cause coma)
   - The **subcutaneous injection** effects are important (<u>rapid onset of action</u> & <u>sustained release</u>)
3. **Intramuscular injection (IM)** features:
   a. we can give <u>bigger</u> doses of the drug in this way.
      (e.g. 3-5 mL injections cannot be given intradermally or subcutaneously)
   b. it can be a either an aqueous drug (water-soluble) or it can be oily (lipid-soluble).
   c. we can give <u>Biphasic liquids</u> (suspensions with solid *particles*) through this injection.
      Meanwhile giving it in the vein (IV) can cause some issues like blood clots.
4. **Intravenous injection (IV)** can be given in huge amounts to patients (in liters; such as in **Parenteral Nutrition**) as long as it is an aqueous solution otherwise it will cause *clotting*.
5. **Intraarticular injection** is given in the *joints* to avoid systemic side effects that would be caused by *cortisone* or other components.

Topical

- Can be cream, ointment, gel, paste or lotion for external use.
- Easy to use
- It is usually for local use.

Rectal

- Used for local or systematic effect
- Rectal = suppositories.
- Solid, liquid or semi-solid dosage forms
- Drug <u>absorbed from the rectum</u> (3 veins)
- High bioavailability (but not 100%)
- **Advantages**:
  A. Can be used for vomiting of unconscious patients, children, elderly or mentally disturbed and patients with dysphagia
  B. Can be used for local action (laxatives)

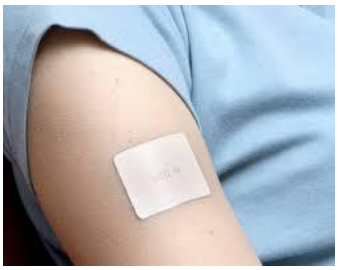


- **Disadvantages**:
  A. Less convenient than oral rout
  B. Lower patient acceptability

- Rectal effect can be:
- local (e.g. enemas are used for constipation/to give a laxative effect)
- systemic (e.g. paracetamol for children if they can't take it orally due to vomiting)
- fast absorption due to 3 rectal veins; Two of the three veins in the rectum are directly in contact with the systemic circulation and the third one is in contact with the portal vein (to the liver); therefore 2/3 of the drug are directly absorbed and 1/3 is metabolized, that's why it has high bioavailability (but not 100%).

Transdermal

- Applied to the skin and deliver a controlled dose of a drug over a specified period of time to produce systemic effect (nicotine patches).
- =>Most important transdermal use are the **nicotine patches** helping smokers to quit smoking by giving them controlled amounts of nicotine that diffuse from the patch through the skin to the blood circulation(systemic); sustained release, replaced each day.



Test Yourself

Overdose midterm selected questions:

1. What is the 'Orphan drug'?
   a) Drug with cheap price
   b) Drugs used to prevent & treat rare diseases.
   c) Work on orphan receptors
   d) More than one answer is correct

   Correct answer: B

Vagus midterm selected questions:

2. A 35-year-old patient came to your clinic suffering from psoriasis. after looking into his case, you decided that giving local Dithranol will be the best strategy for treatment of this patient. if you know that Dithranol is a corrosive drug that local irritation when applied to the skin, which one of the following dosage forms would be the best for this drug administration to minimize this side effect on the intact skin?

   Answer: Dithranol paste