PHARMACOLOGY

Modified no.

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Oral route

Dosage forms:

- Tablet, Capsule, Powder, Solution, and Suspension.

Advantages:

- Convenient (to most patients)

It is considered the most convenient route of administration.

-self medication, cheap and relatively safe

easy to take and do not require any special equipment.The most cheapest route of administration and NO medication can be considered 100% safe.

-large volume may be given

Doses are typically measured in units such as milligrams (mg), micrograms (mcg).**And in specific cases ,it can reach a gram.**

-does not require maximal sterility

as the gastrointestinal tract has some natural defenses against infection.

Disadvantages: **the most important is the first pass effect ,**

- Absorption is unpredictable.

It is affected by the bioavailability and vd(volume of distribution).

-slow onset of action.

When you take a medication orally, it has to pass through the digestive system, which includes the stomach and the small intestine. This process can slow down the absorption of the drug into the bloodstream.

-impossible to use in unconscious or in vomiting patients.

-some drugs may be destroyed by gastric acidity.

due to- **Physicochemical properties of drugs.** This can reduce the drug's effectivenes

-presence of food or other drugs may interfere with absorption.

It may either slow or fasten its absorption

-Undergoes first-pass metabolism.

After oral administration, drugs pass through the liver before entering the systemic circulation. The liver can metabolize or break down a portion of the drug before it reaches its target site, reducing the drug's potency.A drug which have a high first pass effect ,it ineffective orally

Rectal: involves the insertion of medication into the rectum.

Dosage forms: Ointment, solution, suppository and Jelly

The rectal route of drug administration can act both **locally** (suppositories or creams used to treat conditions like hemorrhoids act locally to alleviate symptoms in that specific region)and **systemically**, depending on the nature of the medication and its intended use.

Advantages:

-Avoids gastric irritation.

This can be advantageous for medications that can cause gastric irritation or those that are sensitive to stomach acid.

-may be used in unconscious patients or vomiting patients or who are unable to swallow and useful in children.

-Avoids first-pass metabolism.

rectal administration bypasses the first-pass metabolism in the liver. This means that a higher fraction of the drug reaches the systemic circulation, potentially leading to a more potent effect. They go rapid metabolism.

Disadvantages:

Inconvenient to the patients (Discomfort), absorption is slow and incomplete, irritation and inflammation to rectal mucosa

The rectal mucosa is sensitive, and certain medications or additives in suppositories may cause irritation or inflammation, leading to discomfort or local side effects.

Sublingual: The dosage is placed under the tongue.

Dosage forms: Tablet, solution and aerosol

Advantages:

-Rapid onset of action.

Medications administered sublingually are absorbed directly into the bloodstream through the highly vascular sublingual mucosa.

- not destroyed by acidity.

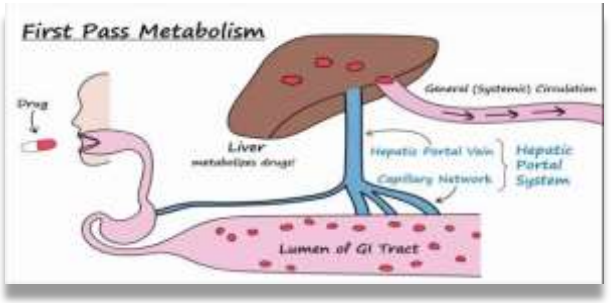
Unlike oral medications, sublingual drugs are not exposed to the acidic environment of the stomach, which can degrade or alter the effectiveness of certain drugs. This can be especially important for acid-sensitive medications.

-avoids first-pass metabolism.

This will increase the drug's bioavailability.

First pass metabolism:

- It means drug metabolism occurring before the drug enters the systemic circulation.
- Results is decreased bioavailability.
- Decreased therapeutic response.



Disadvantages:

-Not suitable for large volume

-poor absorption in vomiting patients.

-bitter or irritant

The taste of sublingual medications can be unpleasant, and some drugs may irritate the sublingual mucosa, potentially leading to discomfort or local side effects.

- water-soluble drugs cannot be given.

Sublingual administration is most effective for drugs that are Lipid-soluble and can be absorbed through the mucous membrane. Water-soluble drugs may not be suitable for this route.

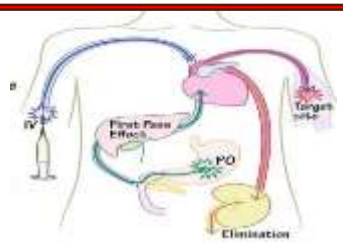
Intravenous:

Dosage forms: Solution

is a method of delivering medications via a direct injection into the bloodstream.

Advantages:

- Bioavailability refers to the percentage of drug that reaches systemic circulation unchanged.



-100% bioavailability.

- no absorption is required.

-fastest onset of action.

I.V drugs act very quickly, often within seconds to minutes, making it ideal for emergency situations or when an immediate therapeutic effect is needed.

-administration of large volume of drug.

Making it suitable for drugs that require high doses or fluids, such as in hydration therapy.

- avoids first-pass metabolism.

Disadvantages:

-Often inconvenient and self medication is not possible.

It requires skilled healthcare professionals, equipment, and monitoring.

- require maximal sterility.

IV procedures demand strict aseptic techniques to prevent infection. Any contamination can lead to serious complications.

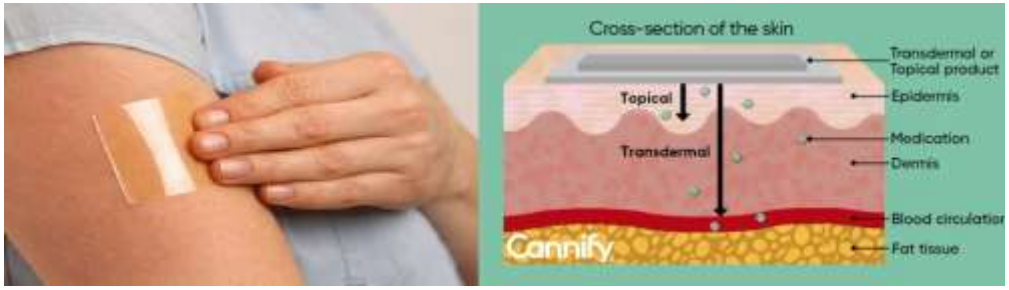
-increased risk of infections.

-difficult to reverse acute adverse effects.

If there are adverse reactions or complications with an I.V-administered drug, it can be challenging to reverse or remove the drug from the system quickly.

Transdermal:

delivering medications through the skin locally via patches.



Dosage forms: Patch

Examples:
-patches for back pain or disc .
-patches that uses for ishemic heart disease

Advantages:

-Used for slow continuous administration.

Transdermal patches are designed for the **slow** and **continuous** release of medication over an extended period, which helps maintain a consistent therapeutic effect.

-prolonged duration of action.

Transdermal administration often results in fewer adverse effects compared to some other routes, as it avoids the digestive system and minimizes fluctuations in drug levels

- no first-pass effect.

-minimal adverse effects.

Patients can benefit from fewer doses, improving adherence to treatment regimens.

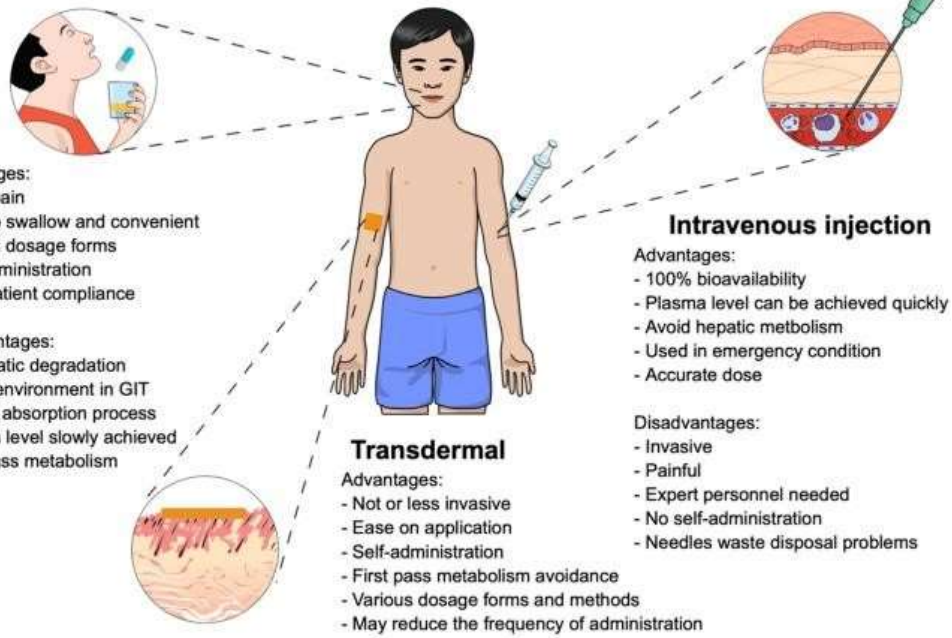
Disadvantages:

-Only a small number of drugs can be used by this route

Only a select number of drugs can effectively penetrate the skin and provide therapeutic levels.

-slow onset of action, could lead to local reactions

local skin reactions, such as irritation, redness, or itching, at the application site.



Oral

Advantages:
- Avoid pain
- Easy to swallow and convenient
- Various dosage forms
- Self-administration
- High patient compliance

Disadvantages:
- Enzymatic degradation
- Acidic environment in GIT
- Longer absorption process
- Plasma level slowly achieved
- First pass metabolism

Intravenous injection

Advantages:
- 100% bioavailability
- Plasma level can be achieved quickly
- Avoid hepatic metbolism
- Used in emergency condition
- Accurate dose

Disadvantages:
- Invasive
- Painful
- Expert personnel needed
- No self-administration
- Needles waste disposal problems

Transdermal

Advantages:
- Not or less invasive
- Ease on application
- Self-administration
- First pass metabolism avoidance
- Various dosage forms and methods
- May reduce the frequency of administration

Disadvantages:
- May cause skin irritation at the application site
- Limited to suitable drugs
- Plasma level may be achieved slowly

Factors affecting the dose

- Age

Pediatric patients often require lower doses per unit of body weight compared to adults due to differences in metabolism and organ function

- Weight

If a patient's weight is larger, the dose of certain medications may also be larger.

- Route of administration

For example, intravenous administration typically delivers the full dose into the bloodstream, while oral administration may require higher doses to compensate for variations in absorption.

- Sex

Males and females can have variations in pharmacokinetics parameters due to physiological and hormonal differences especially the hormonal fluctuations during the menstrual cycle in females , differences in body composition(fat vs muscle) and rate of metabolism and excretion (females have lower rate of metabolism and execration)so females require a lower dose than males.

Factors affecting administration

- Physicochemical properties of drugs

Some drugs may be distroyed by gastric acidity .

- Site of action

Some drugs can not pass the blood brain Barrier in CNS

- Status of patient

- Dosage interval

(**dosage interval**) are determined based on the drug's half-life and therapeutic goals. Short-acting drugs may require more frequent dosing, while long-acting drugs may have extended intervals.

Drug sources:

- Natural

Plants (atropine, digoxin), animals (thyroid hormones; insulin), human (HMG's)

The extraction from animals is associated with allergic reactions because of bacteria and other microbes.

You don't need to know anything about HMG's.

- Semisynthetic (many antibiotics)

Natural but modified in the lab, for example many antibiotics are taken and extracted from a fungus then we modify their structure to minimize side effects, to have better pharmacokinetic properties and to have it in its active form for longer duration of action

- Synthetic (agonists; antagonists)

Antagonists: Drugs that reverse the effect of other drugs (will be discussed later)

Advantages: much purer, less side effects compared to drugs of natural recourses.

Drug nomenclature:

- Chemical name e.g. acetyl salicylic acid

Named according to its chemical structure

- Generic name; nonproprietary; official; approved name...
Aspirin

Named depending on the drug's active ingredient

It is the name that is given to a drug according to its active ingredient that makes it work
Generic name is the most widely used in pharmacology
- Trade name; Proprietary; brand name Remine®; Bufferin®...etc

This name is for prescription purposes, and
it's given by drug companies

** Pharmacokinetic process**

It is the study of what the body does to a drug

Pharmaco**dynamic**: what the drug does to the body.

Pharmaco**kinetics**: what the body does to the drug.

It includes the processes:

- **Absorption**
- **Distribution**
- **Metabolism**
- **Excretion = elimination**

Mathematical representation of these processes:

Drug absorption

Passage of drug from site of administration to circulation and then distributes to reach its target organ (site of action).

Behavior of drugs in the plasma:

- Bioavailability:

The fraction of the given dose that gets into blood

An example: the percentage of the drug that was given orally that reached the blood is 80% the lost is 20%, meaning that the bioavailability= 80% , but if given via IV 100% enters the blood.

NOTE: Drugs with low bioavailability are ineffective given orally.

The bioavailability of an I.V given drug is 100%

- Protein binding:

Represents:

- **A reservoir to the drug**

- **A mean by which drug reaches its site of action**

Some proteins act as carriers to carry the drugs to their designated location

- **A major site of drug-drug interactions**

When a drug interact with another drug, it may increase its binding and therefore increases its activity.
Or it may reduces its binding and subsequently decrease or inhibit its activity

Drugs exists in two forms in the human body:
Free (Active) or bounded (Inactive)

Strongly bound drugs to blood proteins remain longer in blood, have longer $t_{1/2}$ & DOA (Duration of Activation)

**** The free form of the drug, is the form which is active and crosses membranes**

(e.g. 50% of a given drug is albumin bound, means that 50% of the drug which is present in plasma is albumin bound)

Sites of drug absorption:

- Oral mucosa (buccal; sublingual tab.)
- Stomach (aspirin)
- Intestine (major site; iron; vit. B_{12})
- Lungs (general anesthetics)
- Rectum (suppositories)
- Skin (local preparations)

Factors affecting absorption:

molecular weight

- Drug size (Most drugs have MW's between 100 and 1,000)

Drugs are relatively large. But the smaller the drug, the faster its absorbed

- Lipid solubility (major factor)
Lipid/water partition coefficient

The higher the **Lipid/water partition coefficient**, the better absorption. As it could penetrate the cell membrane easier
To find it out. You just need to follow this equation.
Solubility in lipids / the solubility of water

- Degree of ionization or environmental pH:

Henderson-Hasselbalch Equation

$$pH = pKa + \log [A^-]/[HA]$$
$$pH = pKb + \log [BOH]/[B^+]$$

Non ionized/ ionized

Ionization of drugs is the process by which positively or negatively charged ions are formed in a solution
Most of the drugs are organic compounds (weak acids or weak bases).
The organic drugs are not completely ionized in the fluid, they exist in ionized and nonionized forms.

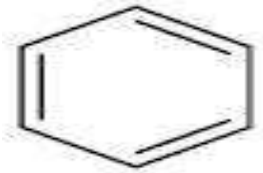
Ionization of drugs depends on the pka of the drug and the pH of the medium

The Ka for an acid or the Kb for a base of a molecule is a measure of its strength as an acid or base

The pK of a drug is the pH at which the concentration of the ionized and non-ionized forms are equal (i.e., 50% ionized and 50% non-ionized)

Polar groups: O; NO_2; COOH; OH...etc.

Nonpolar groups: - S; halogens; Ch_3;



<u>Nonpolar (unionized; lipid soluble) form crosses membranes</u>

Absorbed

<u>Polar (ionized; water soluble form is the pharmacologically active form</u> Not absorbed

Nonpolar (intestine) – nonpolar (to pass blood brain barrier) – polar (active form) – nonpolar (kidney) – polar (secretion)

Changing the polarity is via Ph.

Example:

Sulfanilamide	Sulfathiazole	Sulfacetamide
pKa 10	pKa 7	pKa 6
At pH 7		
		Non ionized
-nilamide	0.1% I	99.9% NI
-thiazole	50% I	50% NI
	50% ionized,	50% non
-cetamide	99% I	1% NI
	ionized	

Polar form, water soluble form, pharmacologically active and doesn't cross the membrane.