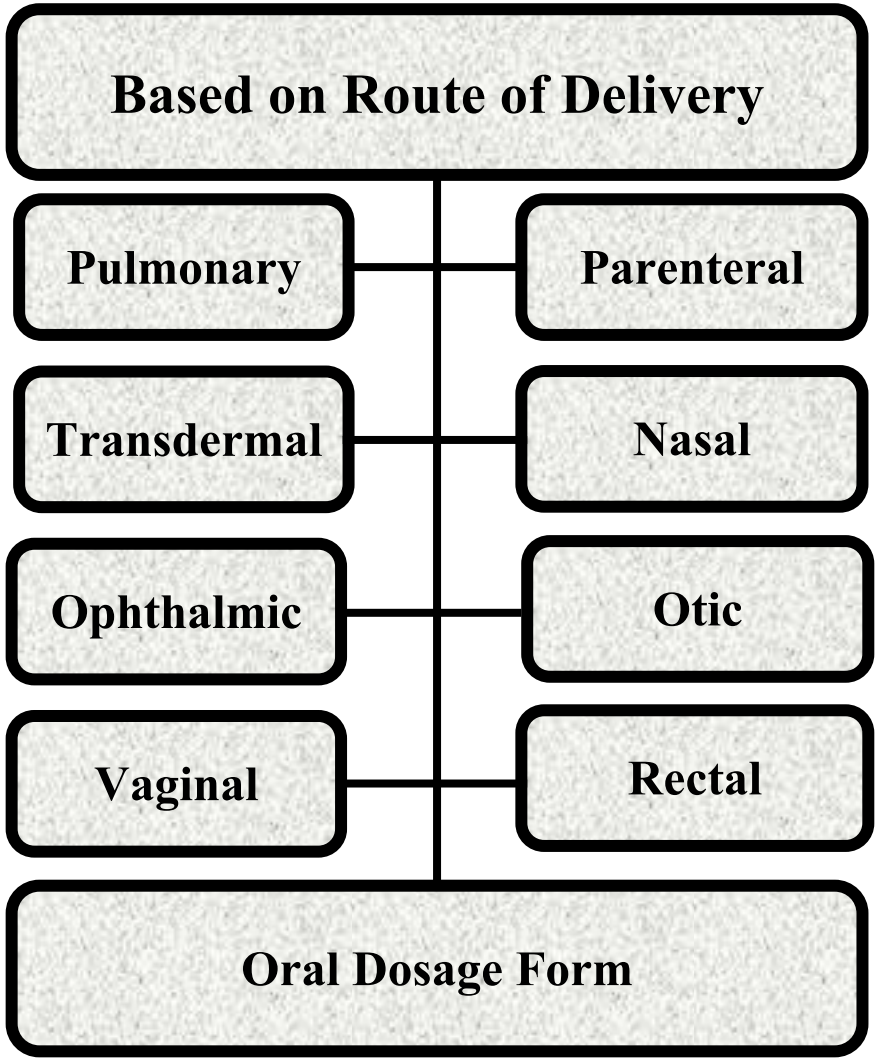
Lecture 1:

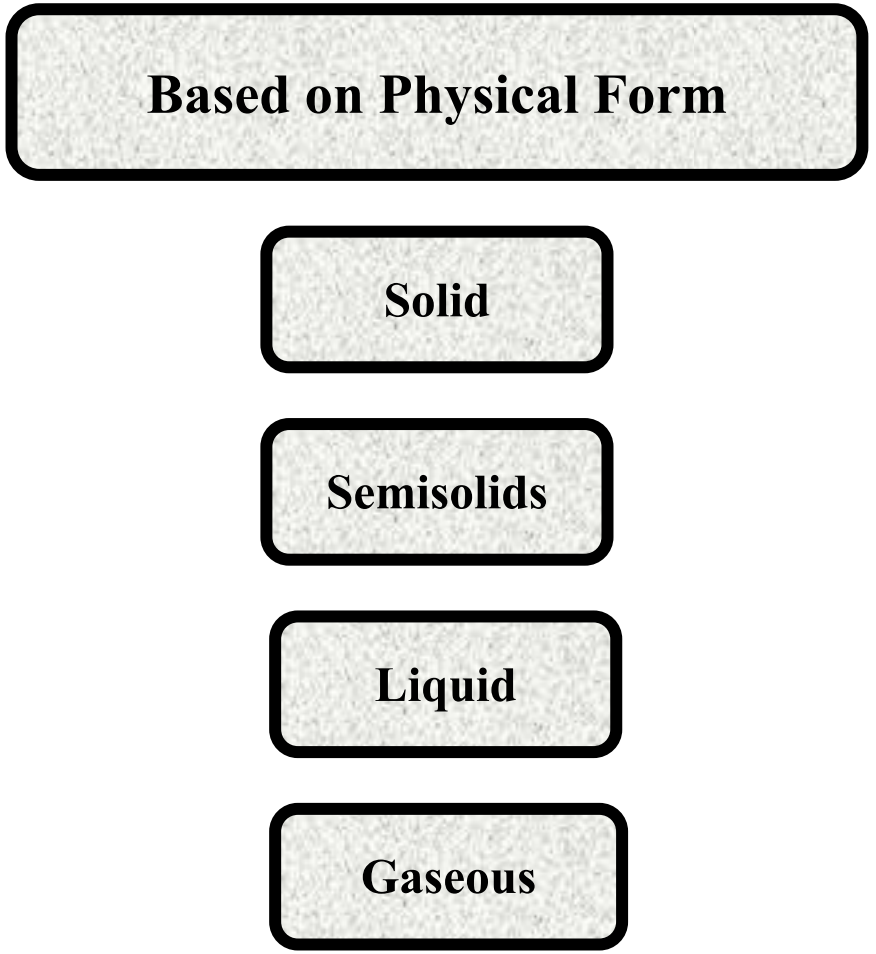
Tablet Dosage Forms

What is Pharmaceutical Dosage Form

- Define as a combination of **drug** (active pharmaceutical ingredient (API)) and **excipients** in a certain configuration.
- **Drug**: is the active pharmaceutical material that can alter the biological condition
- **Excipients:** inactive materials that do various actions during manufacturing, storage, and use of formulations
- **Advantages of the Dosage Forms:**
  - Able to **deliver the right amount** of drug in a convenient way that is relatively easy to be delivered and acceptable by patient
  - Enables **control of drug delivery** like fast onset, extended-release

Classification of Dosage Forms





Stages in Manufacturing a Dosage Form

A- Pre-formulation stage: preliminary studies to identify

1. **Physical and chemical properties** of the medicinal substance which will indicate the efficacy and bioavailability of the candidate dosage form.
2. Evaluation of particle size, solubility, stability, excipient compatibility, and crystal/surface properties

Stages in Manufacturing a Dosage Form (continue)

B- Biopharmaceutical studies: to discover the rate and extent at which candidate drug will be available at the site of action, this includes:

- **Pharmacodynamic studies**: or the effect of the **drug on the body** which studies therapeutic effect, toxic effect, and adverse drug reaction.
- **Pharmacokinetic Studies**: Effect of the **body on drug**. Studies the absorption, distribution, metabolism, and Excretion.
- **Product analysis**: make several candidate dosage forms and test bioavailability, pharmacokinetic (effect of the body on the drug), preferred dosage form, and required dose.
- **Other studies**: include patient compliance, cost of manufacturing, and stability of the final dosage form.

C- Formulation and development: involve the actual formulation of the desired dosage form

Tablet Dosage form

- The **oral route** is the most important method of administering drugs for systemic effects
- About **90 % of drugs** are administered orally
- Tablets are the **most common** form of orally administered dosage forms
- Tablet as other dosage form consists of API and excipients
- Tablets may vary in size, shape, weight, hardness, thickness, disintegration, and dissolution characteristics and in other aspects, depending on their intended use and method of manufacture.
- Tablets are usually **prepared by compression**

Advantages of Tablet

1. **Unit Dosage Form** (accurate dose): In syrup for example dose is designed to be contained in each 5 or 30 ml so the patient is asked to measure their dose by tea/tablespoonful which can be missed by 20-50%
2. They are the **lightest** and most **compact** of all oral dosage forms.
3. **Easy to handle**, store, and dispense tamperproof dosage form
4. Easier than capsules in **shipping and packaging**
5. Manufacturing **cost is lower** than most other dosage forms.
6. **Identification of tablets** is potentially the simplest and cheapest, requiring no additional processing steps when employing an embossed or monogrammed punch face.

Advantages of Tablet

7. They may provide the **greatest ease of swallowing** with the least tendency for "hang-up" above the stomach, especially when coated (requires that tablet disintegration is not excessively rapid).
8. They are better **suite to large-scale** production than other unit oral forms.
9. They have the best combine properties of chemical, mechanical and microbiologic **stability** of all the oral forms.
10. Their **release profile is easy to control** and manipulate

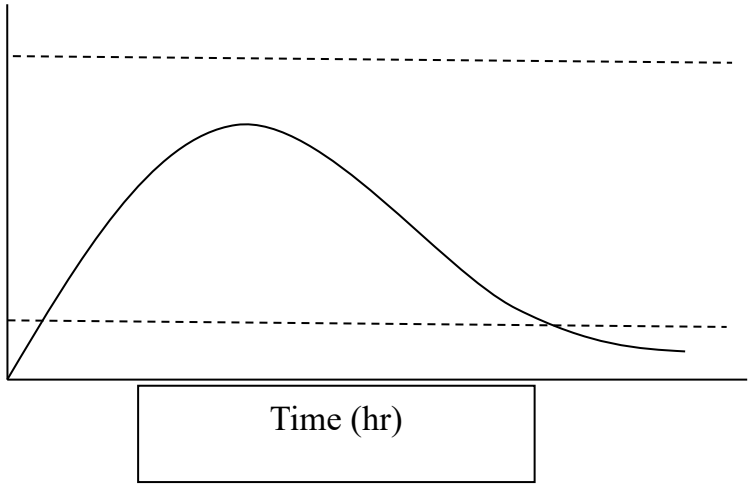
Disadvantages of Tablet

1. Some drugs **resist compression** into the dense compact. Owing to their amorphous nature or flocculent, and low-density character.
2. **Not ideal to hide the bad taste** or smell of some API. In addition, drugs that are **sensitive to oxygen** or atmospheric moisture may require encapsulation or entrapment prior to compression (if possible).
3. Difficult to formulate for drugs **with poor wetting properties**, and **slow dissolution properties (will be difficult for other dosage forms too)**.
4. Some **drugs degrade if administered** orally (will be difficult for other dosage forms too)

Types of Tablets

- **Tablet ingested orally:**

1. **Compressed tablet (plain tablet)**: uncoated tablet designed for **rapid disintegration**
   - Tablets in this category are usually intended to provide rapid disintegration and drug release.
   - Most tablets containing drugs intended for local GI effects (such as antacids and adsorbents) are of this type
   - Also intended for systemic circulation, especially for acidic drugs that best dissolve in the upper GI tract such as ibuprofen.



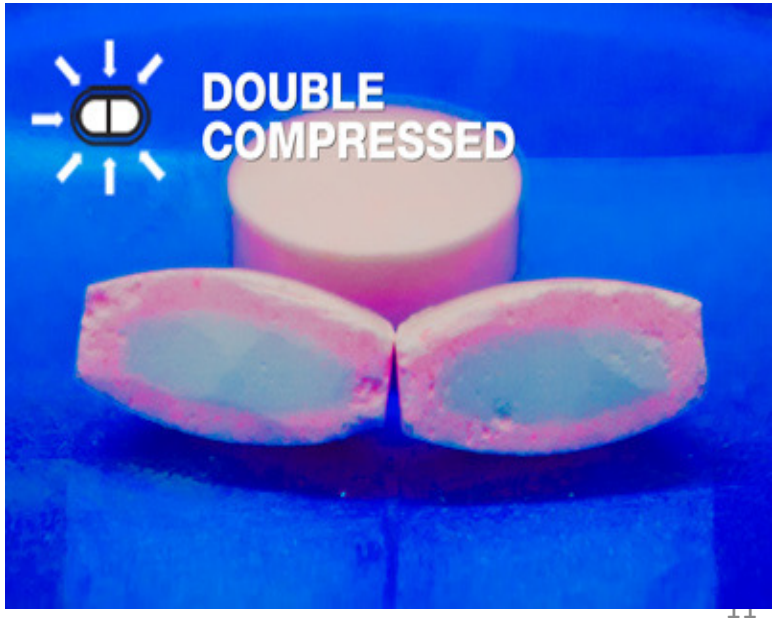
Tablet ingested orally (continue)

2. Multiple compressed tablets :

- **Two classes**: Layered tablets, and compression-coated tablets (tablets within a tablet)
- Tablets contain two or more components **separated from each other**
- Formulated by **1-** light compression for each layer then **2-** a final full compression for the whole tablet
- **This type is prepared to**:

a) To separate physically or chemically **incompatible** ingredients or,

b) To **produce multiple or prolonged** action products.



Multiple compressed tablets

- **Drawbacks (disadvantages)**:
- **Production speed is lower** than for compressed tablets, especially for compression-coated tablets.
- It is difficult to **control the release** of each layer especially if one layer is designed to disintegrate in the stomach and the other in the gastrointestinal tract. **Because** the blood level will be highly related to gastric emptying time which is variable
- This is **why** few multiple compressed tablets are marketed.

Tablet ingested orally (continue)

3. Chewable tablets:

- It is to be chewed in the mouth before ingestion and is **not** intended to be swallowed intact.
- It is mainly made for **children** and people who have **difficulty swallowing** the intact tablet.
- **For example**, chewable aspirin for children and antacid tablets.
- **Bitter or foul-tasting** drugs **are not good** candidates for this type of tablet. (disadvantage)
- For antacid tablets, **chewable tablet** provides two advantages:

a. The dose of most antacids is large, so the typical antacid tablet would be too large to swallow. So, it is better for **patient compliance**.

b. The activity of the antacid is related to its **particle size** → if the tablet is chewed before swallowing, better acid neutralization may be possible from a given antacid dose.

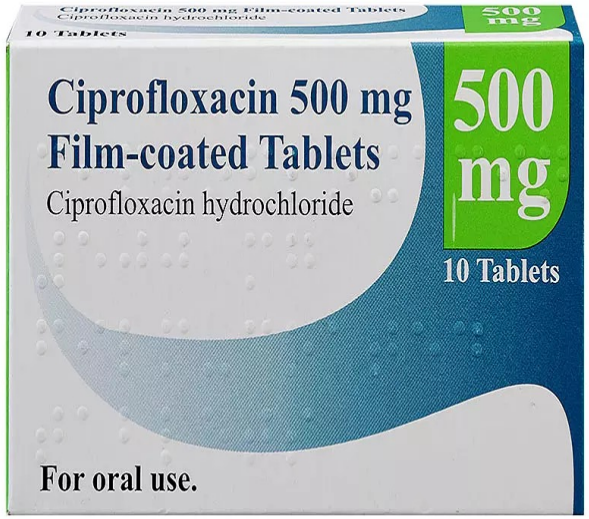
Tablet ingested orally (continue)

4. Sugar-coated tablets:

- The tablet is coated with a thin layer (can be colored) of sugar to produce an **elegant tablet** and to **hide the smell or test** of some medications.
- The coating is water soluble and quickly dissolves after swallowing
- Example flu-out® tablet

5. Film-coated tablets:

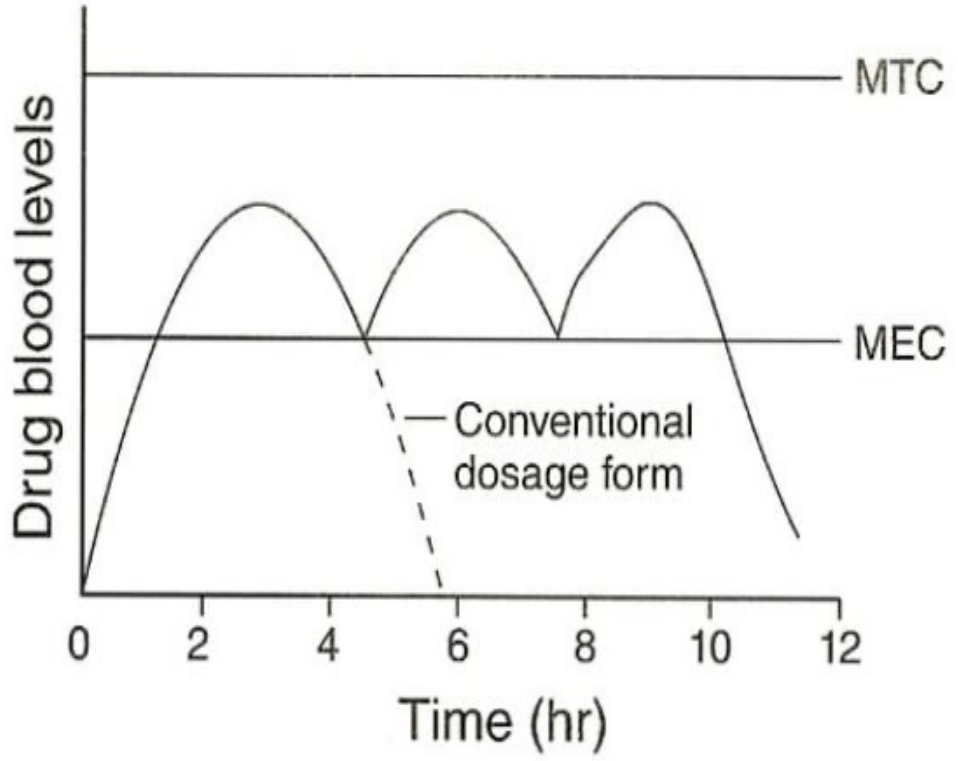
- Developed as an alternative way for enteric and sugar coating.
- It produces an elegant tablet and offers some control of the drug release profile.



Tablet ingested orally (continue)

6. Repeated action tablets :

- One type of extended-release dosage form
- Specific type of multiple compressed tablets
- Designed that each layer release their component at specific time
- Example some antiallergic medications



Tablet ingested orally (continue)

7. Delayed action and enteric-coated tablets :

- These tablets are covered with a shell
- This shell does not dissolve in gastric acid but it will dissolve in the small or large intestine to give the desired effects
- These are usually used to **protect the stomach** from the irritation caused by some medications such as aspirin.
- It is also applied to drugs that can be destroyed by gastric acid

Tablets Used in the Oral Cavity

1. Buccal and sublingual tablets:

- The most common type in this category.
- These tablets are designed to **dissolve and release** their active component rapidly and in a small volume to be absorbed via the oral mucosa.
- Drugs pass **directly to the systemic** circulation and avoid first-pass metabolism.
- Results in a **more rapid onset** of drug action.
- An example of that is the nitroglycerine tablet (angised®) for angina.

Tablets Used in Oral Cavity (continue)

2. Troches and lozenges:

- Used in the oral cavity and intended to exert their effect in the mouth or throat.
- Troches are prepared **by compression**.
- These two types are designed to **dissolve slowly** in the mouth and **not** to disintegrate

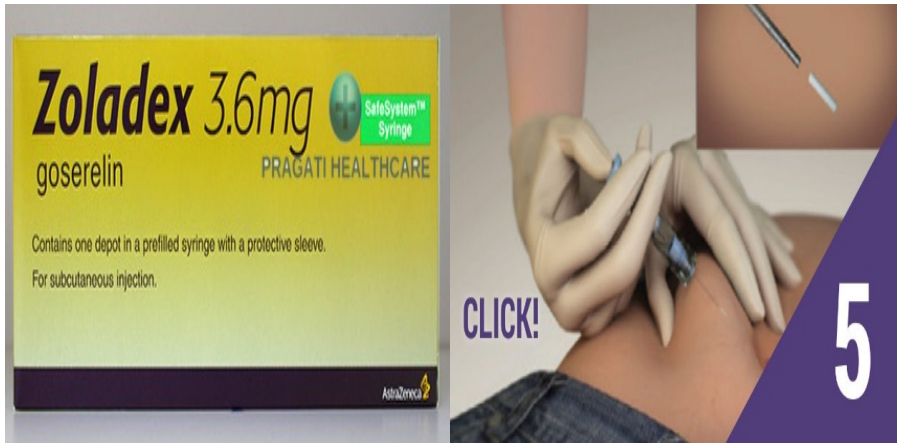
3. Dental cones:

- Minor tablet form and designed to be placed in empty space after tooth extraction.
- Provides **slower releasing antibacterial** agent or to reduce bleeding.

Tablets Administered by Other Routes

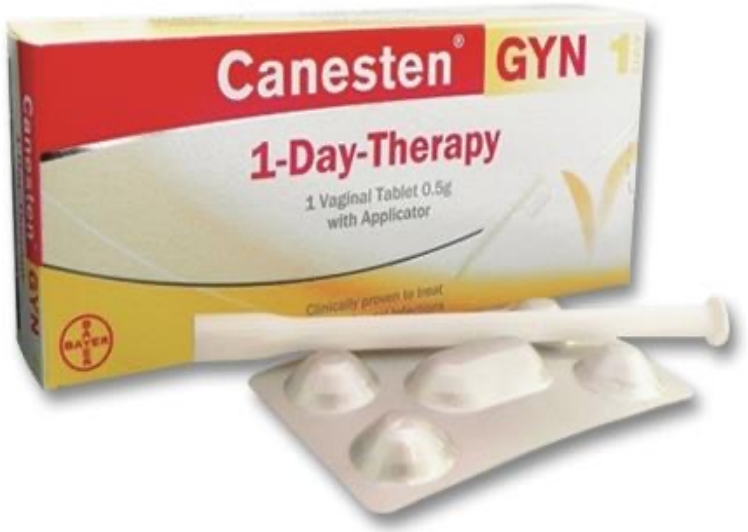
1- Implantation tablets:

- **Depot tablets are** designed for **subcutaneous** implantation and to release their product over a prolongated time.
- Usually small and cylindric, or rosette-shaped forms, and are typically **not more than 8** mm in length.
- These tablets are administered using a special syringe or may require a surgical procedure



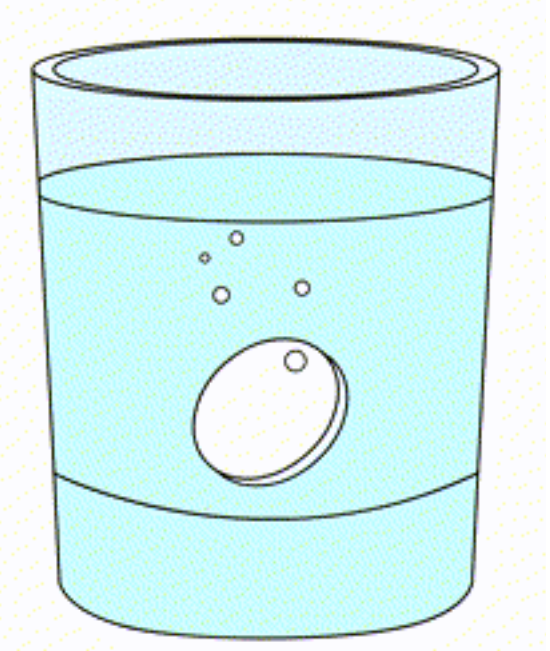
2- Vaginal tablets:

- Designed to undergo **slow dissolution** and drug release in the vaginal cavity
- They are usually oval and come with an applicator



Tablet Used to Prepare Solutions

1- Effervescent tablets:



- Designed to **make solution rapidly** with simultaneous release of carbon dioxide (CO_2).
- These tablets usually contain citric acid plus sodium bicarbonate.
- **The advantages**:

1. They are highly **accepted by patients.**
2. Provide an **accurate dose compare** to liquid dosage form.
3. Can be **designed to protect stomach**, where the PH of the resulted solution can be adjusted.

- **Disadvantage** They are relatively complicated to manufacture and store.

Tablet Used to Prepare Solutions (continue)

2- Dispensing tablets:

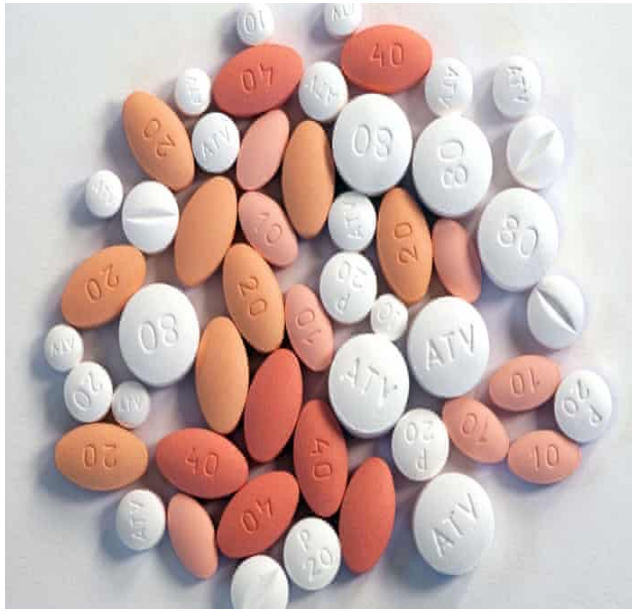
- An **old form** of tablets that were used by the pharmacist to prepare a drug solution at a specific concentration.
- It **contains a larger amount of active ingredient** than usual tablets.

3- Hypodermic tablets:

- Contains **water-soluble drugs** that are designed to be added to sterile water to prepare a solution for injection.
- Due to the advancement in manufacturing of injection dosage forms, this type of tablet is no longer used nowadays.

Ideal Tablet

1. **Elegant products** have their own identity while free of defects such as chips, cracks, discoloration, or contamination.
2. Should **withstand the rigors of mechanical shocks** encountered in its production, packaging, shipping, and dispensing.
3. Should have the **chemical and physical stability** to maintain its physical attributes over time (during shelf life).
4. Must be **able to release the medicinal agent**(s) in the body in a predictable and reproducible manner.
5. Have **suitable chemical stability** over time that does not allow alteration of the medicinal agent(s).



Tablet Ingredients

- **Properties of tablet ingredients**:

1. **Nontoxic and legal** in the countries where the product is to be marketed
2. Must be **commercially available**
3. **Reasonable cost**
4. Must **not be contraindicated themselves** (e.g. sucrose) or because of the component (e.g. sodium) in any segment of the population.
5. Must be **physiologically inert** (for excipients)
6. Must be **physically and chemically stable themselves** or in combination with the drugs(s) and other tablet components.
7. **Free** of unacceptable microbiological contaminations.
8. **Must be color compatible** (must not produce any off-color appearance).
9. Must **not alter bioavailability** (for excipients)

Tablets Excipients

X

Excipient Type	Definition	Example
Antioxidant	Agent that inhibits oxidation and thus is used to prevent deterioration of preparations by oxidative process	Ascorbic acid, butylated hydroxyanisole, butylated hydroxytoluene, propyl gallate, sodium ascorbate, sodium bisulfite,
Tablet anti-adherent	Agent that prevents the sticking of tablet formulation ingredients to punches and dies during tablet production	Magnesium stearate, talc
Tablet binder	Substance used to cause adhesion of powder particles in tablet granulations	Acacia, carboxymethylcellulose, ethyl cellulose gelatin, methylcellulose, pregelatinized starch

Tablets Excipients

X

Excipient Type	Definition	Example
Tablet diluent	Inert substance used as filler to create desired bulk, flow properties, and compression characteristics in preparation of tablets	Dibasic calcium phosphate, kaolin, lactose, mannitol, microcrystalline cellulose, powdered cellulose, precipitated calcium carbonate, sorbitol, starch
Tablet disintegrant	Used in solid dosage forms to promote disruption of solid mass into smaller particles which are more readily dispersed or dissolved	Alginic acid, carboxymethylcellulose calcium, microcrystalline cellulose, polacrilin potassium, sodium alginate, sodium starch glycollate, starch

Tablets Excipients

X

Excipient Type	Definition	Example
Tablet glidant	**Agent used in tablet and capsule formulations to improve flow properties of powder mixture**	**Colloidal silica, corn starch, talc**
Tablet lubricant	**Substance used in tablet formulations to reduce friction during tablet compression**	**Calcium stearate, magnesium stearate, mineral oil, stearic acid, zinc stearate**