

## Lec 4: Tablet Coating

# Tablet Coating

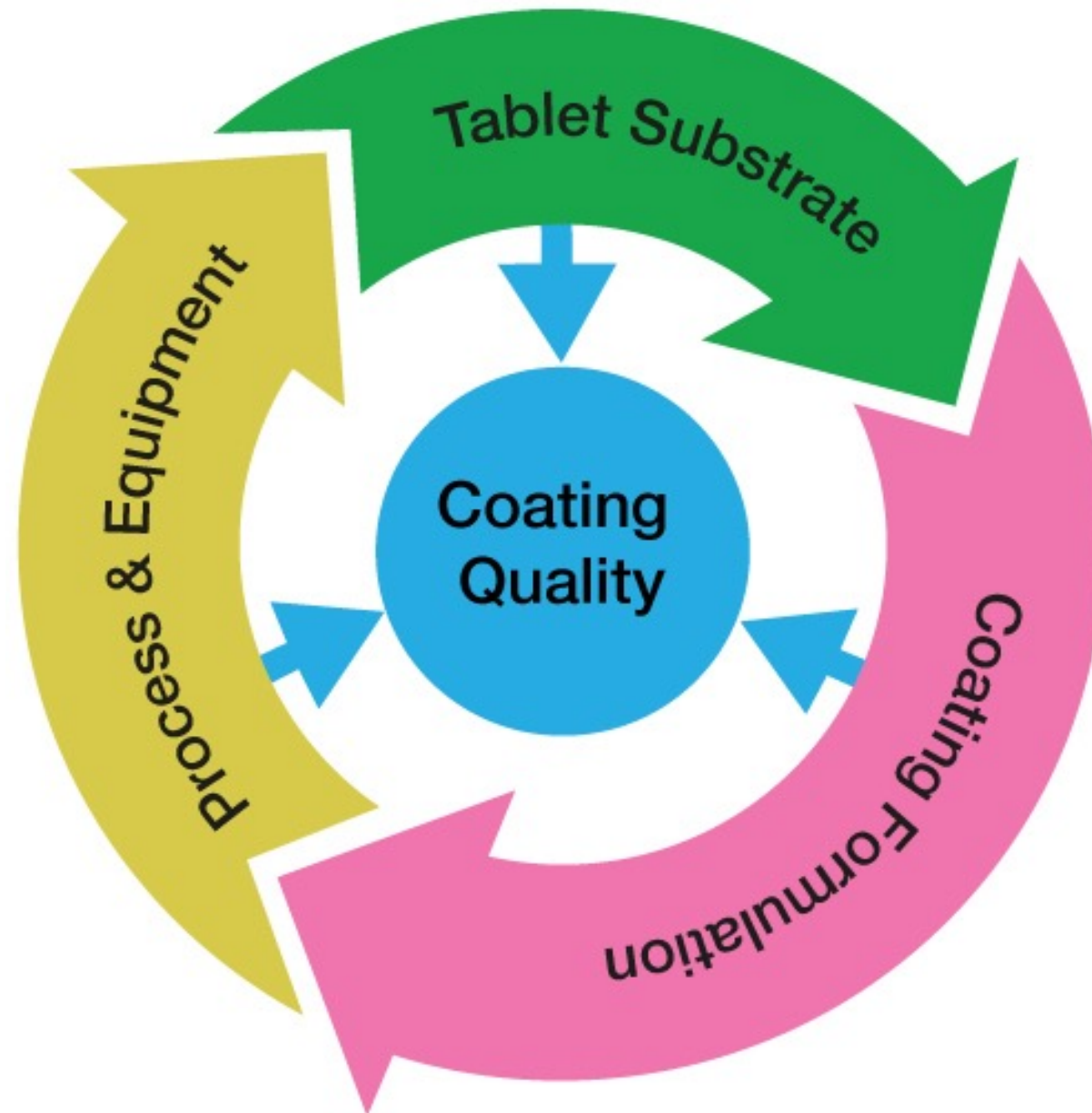
- Tablet coating is adapted from the food preservation process.
- The first air suspension coater was created by Dr. Dale Wurster in 1950.
- He introduced **airflow** in the tablet coating machine and the perforated coating pans.
- His work resulted in the first reproducible and uniform tablet coating.



# Tablet Coating Principles

- Tablet coating is an **additional** step that increases cost; therefore, the decision to coat a tablet is usually based on one or more of the following reasons:
  1. To **minimize** undesirable **taste, odor, or color** of the drug.
  2. To provide physical and chemical **protection** for the drug.
  3. To **control the release** of the drug from the tablet.
  4. To **protect** the drug from the **gastric environment** of the stomach with an acid-resistant enteric coating.
  5. To improve the pharmaceutical **elegance** by use of special colors and contrasting printing.
  6. To assist tablet **movement and mobility**, especially for patients with dysphagia while swallowing.

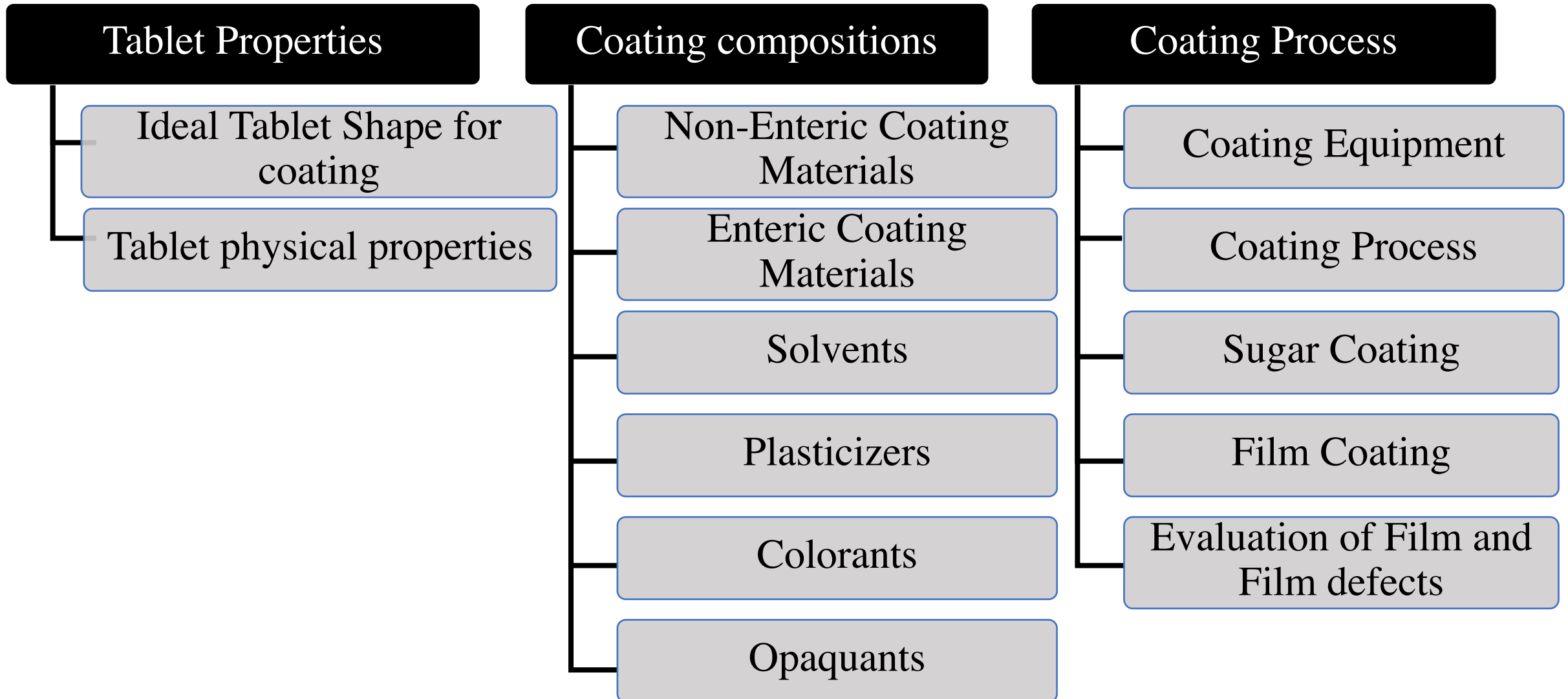
# Tablet Coating Process





# Tablet Coating

Three main parts in studying tablet coating:



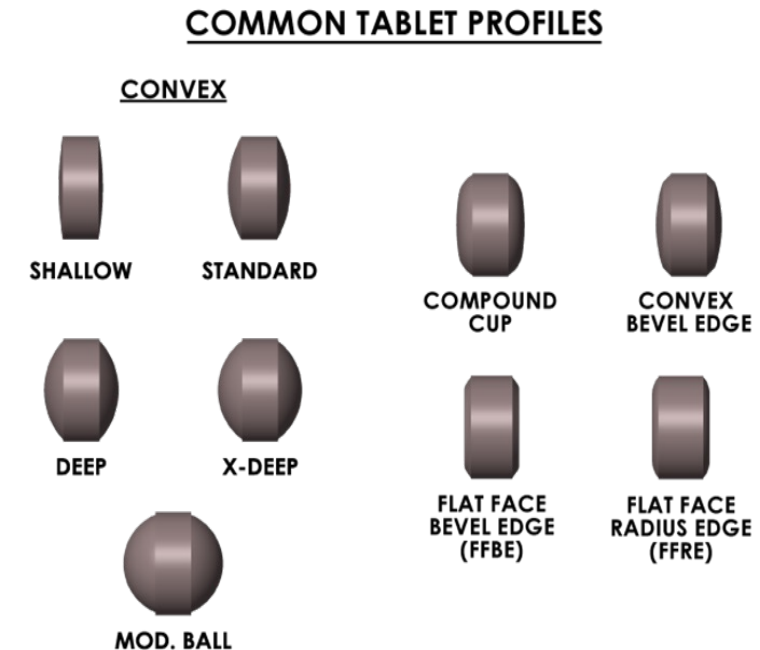
# Preferred Tablet Properties for Coating

1. Tablets must possess the proper **physical characteristics**:
  - To withstand the intense **mechanical stress** that results from striking other tablets and the walls of the coating machine, the tablet must be strong enough to **resist abrasion and chipping**.
2. Tablet **shape should be intact and free of imperfections**:
3. Tablet **surfaces** that are **brittle**, soften in the presence of heat, or **affected by the coating** compositions tend to become **rough** in the early phase of the coating process and are unacceptable for film coating.



# Preferred Tablet Properties for Coating

4. The **physical shape** of the tablet is important.
- The coating includes covering the tablet with a **tacky** polymeric material that before becoming completely dry will form tacky semisolid and eventually to a nontacky dry surface.
  - **So**, tablets need constant movement inside the coating machine, or tablet agglomeration can occur.
  - The **ideal tablet shape** for coating is the **sphere** which allows the tablet to **roll freely** in the coating pan with minimal tablet-to-tablet contact.



# Preferred Tablet Properties for Coating

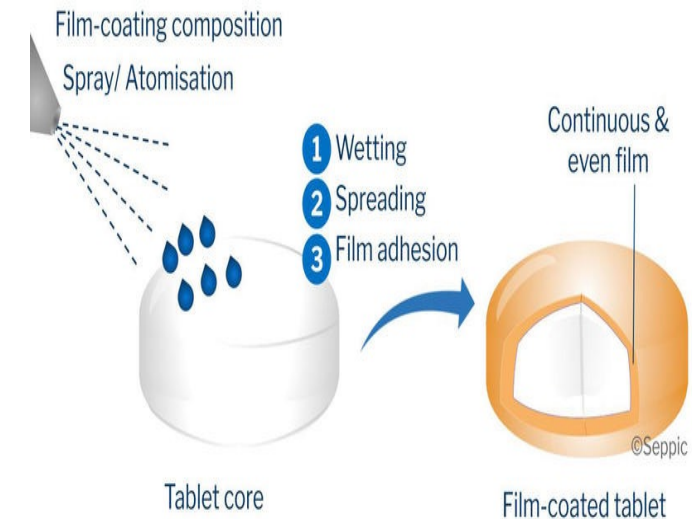
- The **worst** shape is a **square flat-faced** tablet in which coating materials would collect between the surfaces to glue them together.
  - That's **why** coated tablets usually have round surfaces.
5. Tablet surface **hydrophobicity/hydrophilicity** should match that of the coating materials.
- Coating materials must **wet** the tablet surface.
  - For this reason, **surfactant** may be added to the coating solution.





# Coating Compositions

- Coating material can form a **physical deposition** on the surface of the tablet such as sugar and wax coating.
- **Coating materials** should have the following **properties**:
  1. **Soluble** in solvent for coating preparation.
  2. Able to produce **elegant-looking** products.
  3. **Stability** in the presence of heat, light, moisture, air, and the substrate being coated. Film properties should not change with aging.



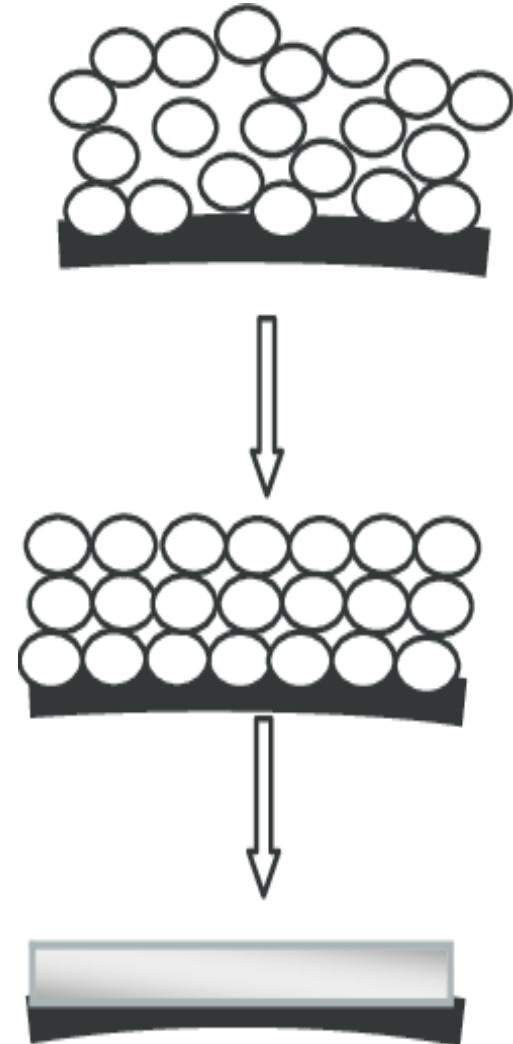
# Coating Compositions

4. Essentially **no** taste, odor, or color.
  5. **Compatibility** with common coating solution additives.
  6. **Nontoxic** and pharmacologically **inert**.
  7. Should not tend to **bridge/fill** the debossed tablet surfaces.
  8. **Resistance** to cracking.
- Note: **No** coating material fulfills all requirements of an ideal coating material.



# Coating Compositions: Film Forming Materials

- Polymers are used to form the film around the tablet.
- Can be classified into **non-enteric** and **enteric** materials.
- Examples:
- **Non-enteric Materials:** these materials tend to solubilize inside the GI tract and release the drug.
  - a. Hydroxypropyl methylcellulose (HPMC).
  - b. Ethyl Cellulose (EC).
- **Enteric materials:** these materials tend to solubilize depending on the pH of the GI tract.
  - a. Hydroxypropyl Methyl Cellulose Phthalate (HPMCP).
  - b. Cellulose Acetate Phthalate.
  - c. Acrylate Polymers.



# Non enteric Materials (Non Functional FC)

- **Hydroxypropyl methylcellulose (HPMC):**
- Available in different viscosity grades.
- This polymer is the **material of choice** for air suspension and pan-spray coating systems.
- It is **close to be an ideal** coating polymer for film coating. The reasons for that are:
  1. **Solubility** of the polymer in **organic and aqueous** solvents.
  2. **Noninterference** with tablet disintegration and drug availability.
  3. **Flexibility** (chip resistance) and **absence** of taste and odor.
  4. **Stability** in the presence of heat, light, air and moisture.
  5. Ability to **incorporate color** and other additives into the film without difficulty.



# Hydroxypropyl methylcellulose (HPMC):

## Non Ideal properties:

- When used alone it tend to bridge and fill debossed tablet surfaces.
- That is why its usually incorporated in a mixture with other polymer or plasticizers to eliminate bridging or filling problem.

# Non enteric Materials (Non Functional FC)

- **Ethyl Cellulose (EC):**
- This material is **completely insoluble** in **water and gastrointestinal** fluids and thus **cannot be used alone** for tablet coating.
  - It is usually **combined with water-soluble polymers, e.g., HPMC**, to prepare films with reduced water solubility.
- **Advantages:** The polymer is soluble in various **organic solvents** and is nontoxic, colorless, odorless, tasteless, and **quite stable** to most environmental conditions.
- **Disadvantages:**
- EC without plasticizers tend to be **brittle**.

# Enteric Materials

- The most important **reasons** for enteric coating are:
  1. To **protect the drug** from the stomach, e.g., enzymes and certain antibiotics.
  2. To **protect the stomach** from the drug, e.g., salicylates.
  3. To **deliver drugs** optimally absorbed in the **small intestine** to their primary absorption site in their most concentrated form.
  4. To **provide a delayed-release** component for repeat-action tablets.



# Enteric Materials

- **Ideal** enteric coating material should have the following properties:
  1. **Resistance** to gastric fluids.
  2. **Ready susceptibility** or permeability to intestinal fluids.
  3. **Compatibility** with the most coating solution component and the drug substrates.
  4. **Stability** alone and in coating solutions.
  5. **Formation** of a continuous (uninterrupted) film.
  6. **No** toxicity.
  7. **Reasonable** cost.
  8. **Ease of application** without specialized equipment.



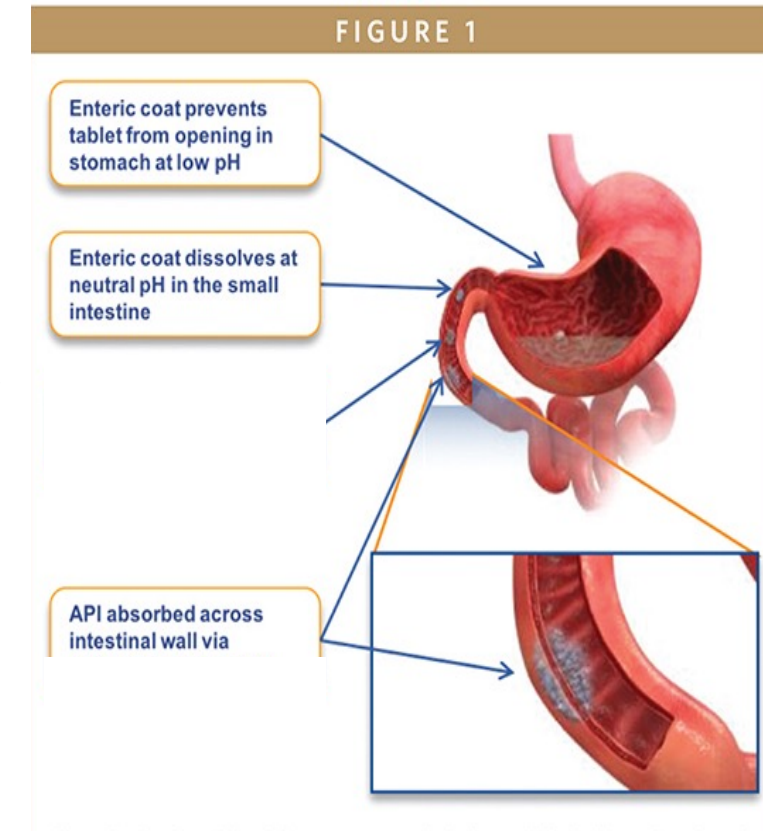
# Enteric Materials (mechanism)

- The pH of the stomach varies from 1-5.
- Enteric materials are either (mechanism of action):
  1. **water-resistance** → digested or emulsified by intestinal juices.
  2. **pH-sensitive** materials. slowly swell and fall apart when solvated or become permeable near and above pH 5.
- Usually, the enteric formulation is a **combination** of the enteric technique above to achieve the desired action.  
**Because** all available enteric material falls short in some aspects.



# Challenges for Enteric Coated Tablet

- All enteric-coated tablets must pass the USP disintegration test where the tablet has to stay intact for at least 1 hour and disintegrate within 2 hours (for most tablets).
- Passing the test does not mean guaranteeing optimal bioavailability. Several other **challenges** will face enteric coated tablets inside the body:
  1. The pH of the stomach varies from 1-5. Some patients are having achlorhydria or hypochlorhydria.
  2. The amount of gastric fluids may vary between individuals; and for the same individual from time to time.



# Challenges for Enteric coated tablet

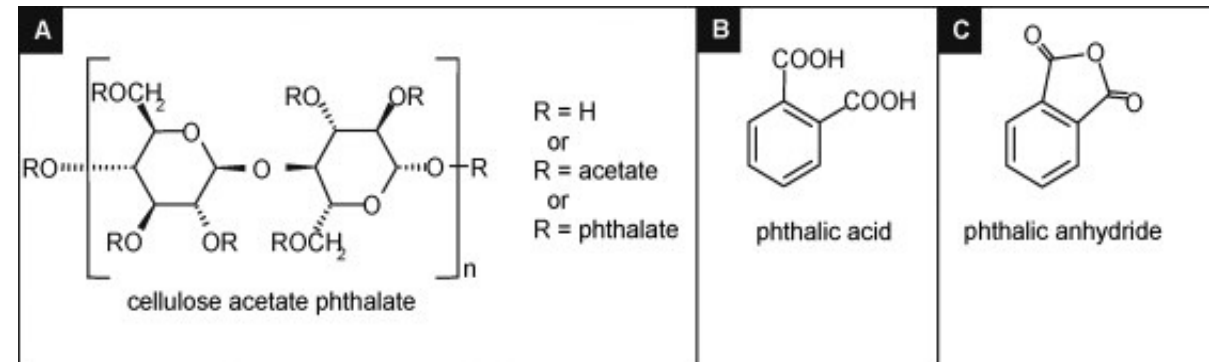
3. USP test does not require testing the drug amount in solution during the disintegration test. In some cases, the drug can **escape before tablet breakage** so the tablet **will pass the USP test** but may **fail** to protect the GI tract.
4. Some enteric-coated techniques use **retardant polymer** which depends on **hydrophobicity and is not pH dependent**.
  - In this case, the polymer needs time to solubilize and allow the drug to release so if the tablet travels so fast in the GI tract it may not have enough time to solubilize and the tablet will **fail** to release its contents.

# Coating Compositions: Enteric Materials

- **Cellulose Acetate Phthalate (CAP):**
- It has been used widely in the industry.
- **Disadvantage**
  - Dissolving only **above pH 6** and possibly **delaying the absorption of drugs**.
  - It is also hygroscopic and relatively permeable to moisture and gastric fluids. There may be a **premature release of some drugs**.
  - CAP films are **brittle** and require some adjuvants to achieve better film.



GIT region	pH of that region
Stomach	1.5 in fasting and 2-5 in fed condition
<b>Small intestine pH</b>	
Duodenum	6.1 in fasting and 5.4 in fed condition
Jejunum	5.4
Ileum	7.8
Large intestine	5.5-7
Rectum	7-8





# Enteric Materials

- **Acrylate polymers (Eudragit):**
- These polymers produce films that are resistant to gastric fluid and are soluble in GIT fluid at pH 6-7.
- **Hydroxy Propyl Methyl Cellulose Phthalate (HPMCP):**
- These polymers dissolve at a lower pH (pH 5-5.5) and this solubility **may** result in higher bioavailability of some drugs.

# Coating Compositions: Solvents

- To **dissolve** or **disperse** polymer and other additives.
- **Ideal** solvent:
  1. It Should **dissolve** or disperse the polymer system.
  2. It should **easily disperse other coating** solution components into the solvent system.
  3. Small concentrations of polymers (2 to 10 %) should **not** result in an extremely **viscous solution**, which will create coating problems.
  4. It should be colorless, tasteless, odorless, inexpensive, non-toxic, inert, and nonflammable.
  5. It should have a **rapid drying rate**.
  6. It should have **no environmental impact**.

# Solvents

- The **most widely used** solvents (either alone or in combination) are **water**, **ethanol**, **chloroform**, and acetone.
- Because of environmental and economic considerations, **water is the solvent of choice**; however, several polymers cannot be applied as aqueous solutions.

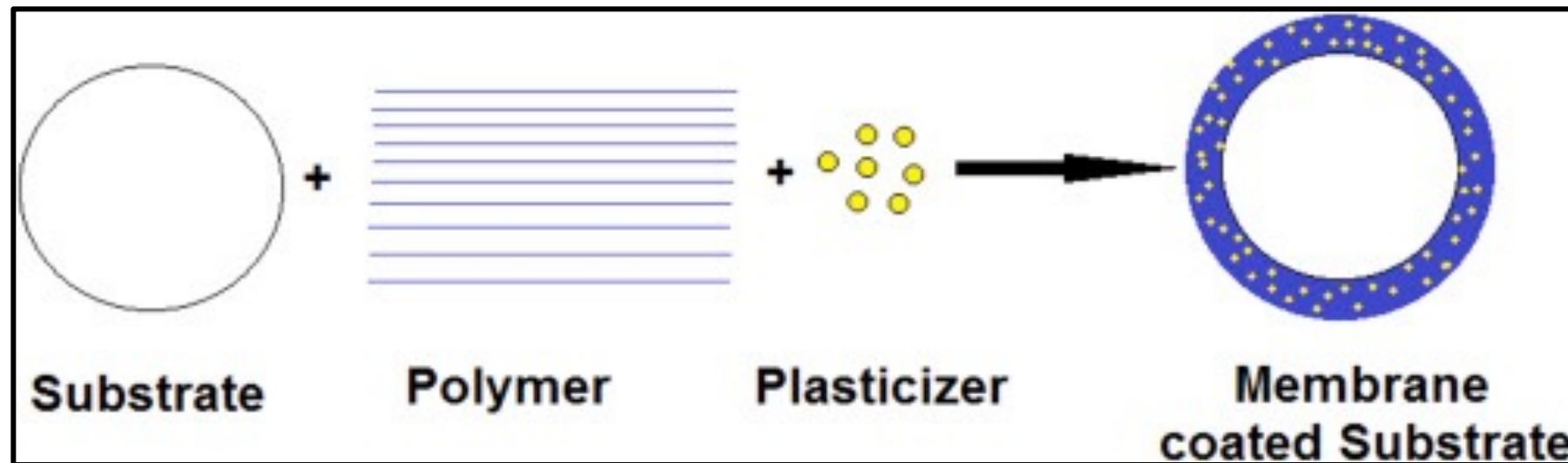
# Coating Compositions: Plasticizers

- A plasticizer is a **non-volatile material** that when incorporated with the film former, improves the **flexibility** and **adhesion** properties of the resulting film.
- **Without** a plasticizer, most of the **polymers tend to pack together** in a rigid three-dimensional honeycomb arrangement.
- When used in the correct proportion, the plasticizers **impart flexibility** to the polymer by **decreasing** their molecular rigidity.
- A **combination of plasticizers** may be needed to achieve the desired effect.
- The concentration of the plasticizer(s) depends on many factors including the **polymer type method of application, and the manufacture's recommendation.**



# Coating Compositions: Plasticizers

- Recommended levels of plasticizers can range from **1-50%** w/w of the film former.
- Some of the commonly used plasticizers are **castor oil**, **glycerin**, low molecular weight polyethylene glycol (**PEG**) (**200-400 series**), **Tweens**, and **Spans**.
- In **aqueous coating**, water-soluble plasticizers, e.g., PEG are used.
- Conversely, castor oil and Spans are used primarily for **organic coating** solutions.



# Coating Compositions: Colorants

- They may be **soluble** in the solvent or **suspended** as insoluble powders.
- **Lakes pigments** have **become the colorants of choice** for sugar or film coating systems, as more reproducible colors are achieved.
  - Lakes pigments will produce a more evenly distributed color every time.

# Coating Compositions: Opaquants

- These are **very fine** inorganic powders used in the coating solutions to provide **more pastel colors** and increase film coverage.
- These opaquants can **provide a white coating or mask the color** of the tablet core.
- Colorants are much **more expensive** than opaquants and **less colorant** is required when opaquants are used.
- The most commonly used material for this purpose is **titanium dioxide**.

# Coating Process

- Tablet coating is the application of coating materials to moving tablets with the concurrent use of **heated air** to facilitate the evaporation of the solvent.
1. The distribution of the coating materials is done by the continuous movement of the tablets in the coating pan.
    - During the coating process, the tablets move through an application zone (in front of the nozzle) in which a portion of the tablets receive some of the coating materials.
  2. With the help of **hot air**, the tablets are mostly in the **drying phase** and are recycled repeatedly through the application zone until the desired coat is achieved.



# Coating Equipment



# 1- Conventional Pan System

- It consists of a spherical pan mounted angularly on a stand. The pan is rotated by a motor.
- **Heated air** is directed into the tablet bed and is exhausted by means of ducts.
- The coating materials (**solution**) are applied to the tablets by either **ladling** or **spraying** on the rotating tablets.
- Using **spraying** is preferred because:
  - a) It is **faster**.
  - b) Distributes the coating materials **more evenly**.
  - c) Reduces the **drying time**.



## 2- Perforated Pan System

- It is the **most widely** used machine in tablet coating.
- It consists of a **perforated drum** that rotates in a closed chamber.
  - Drying air is passed through the tablets and is exhausted through perforations in the drum.
- Perforated pan coaters are **efficient with high coating capacity** and **can be automated** completely for both the sugar and film coating processes.
- The coating solution is applied to the surface of the rotating bed of tablets through **spraying nozzles** that are positioned inside the drum.
- <https://youtu.be/SXEduweiViw>







## Types of Coating & Processing



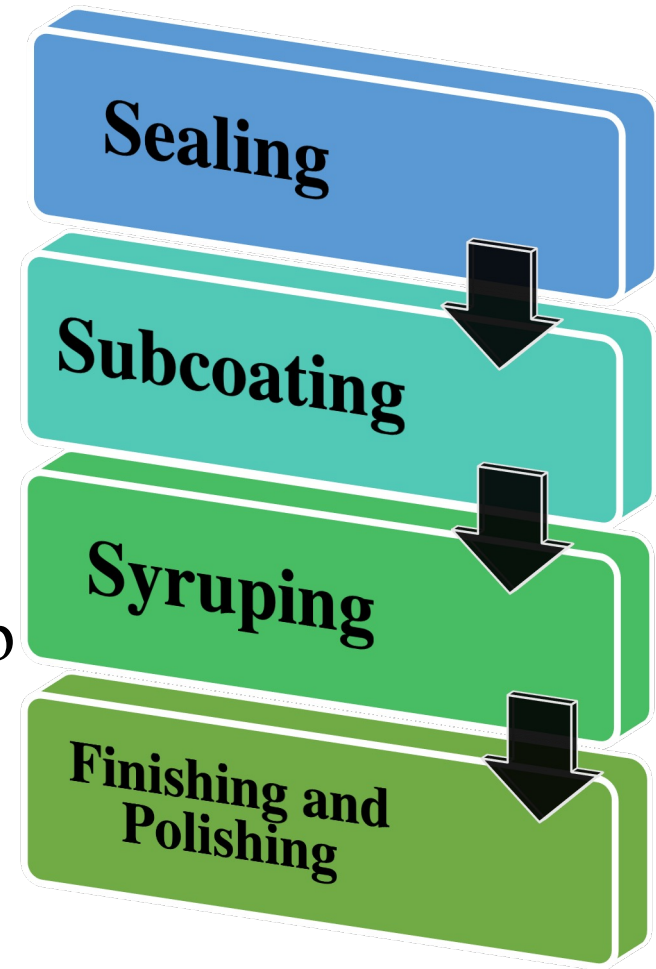
# Sugar Coating

- It **was** commonly used in the past, although it may be used nowadays due to the **excellent appearance** it gives to tablets.
- The sugar coating involves several steps, the duration of which ranges from a **few hours to several days**. → **needs time**
- A successful product greatly **depends on** the **skill of the operator**. This is especially true in the **pan-ladling** method in which the coating solution is poured over the tablets.



# Sugar Coating

- The sugar-coating process involves the following steps: **sealing, sub-coating, syruping (smoothing), finishing and polishing.**
- **Sealing (Seal Coating):**
- To **prevent moisture penetration** into the tablet core, a sealing coat is applied.
- **Without** a sealing coat, the overwetted tablets would absorb excess moisture, leading to **tablet softening** or disintegration and affecting the physical and chemical **stability** of the finished product.

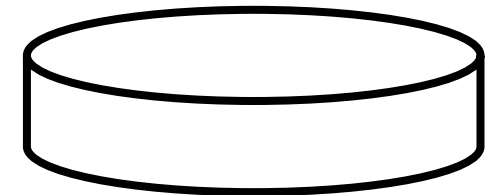




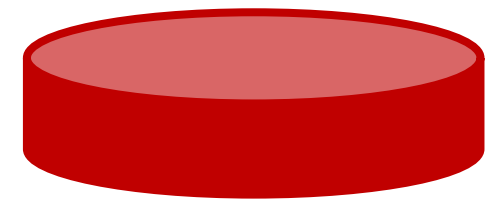
# Sugar Coating Process: Seal Coating

- **Shellac** is an effective sealing agent, **but** tablet disintegration and **dissolution** times **may prolong upon aging** because of the polymerization of the shellac.
- **Zein** is another material that has been used as an effective sealing agent. Prolongation of **dissolution** times has **not** been reported for zein on aging.

Original Tablet

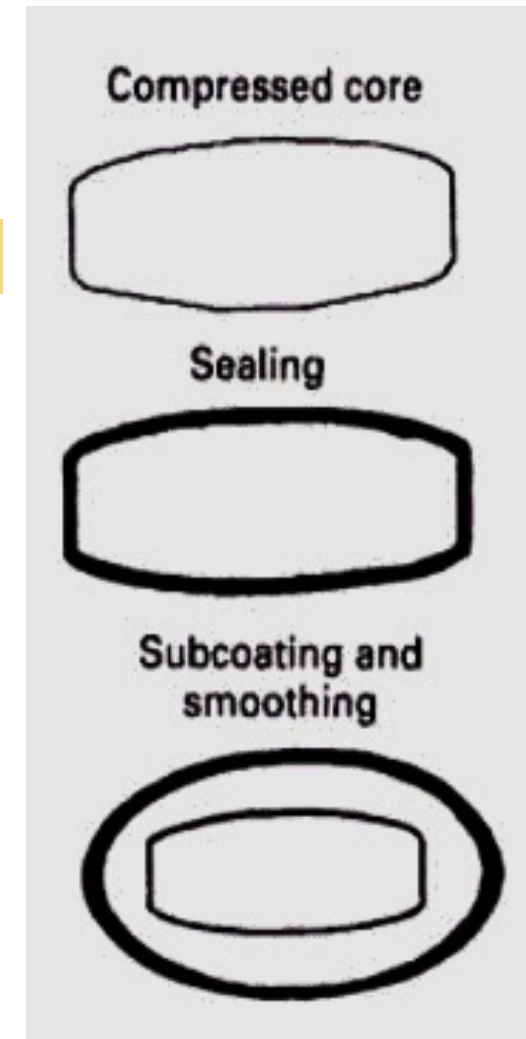


Sealed Tablet



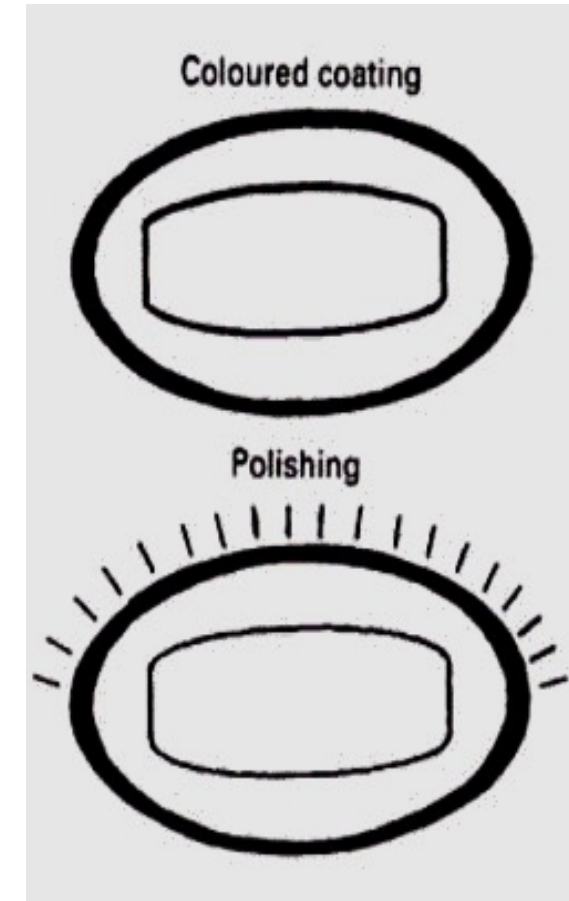
# Sugar Coating Process: Subcoating

- The subcoating is applied **to round the edges** and build up the tablet size. Sugar coating **can increase the tablet weight** by 50-100%.
- The subcoating step consists of applying a **sticky binder solution** (e.g. gelatin or **sugar** solution) to the tablets **followed** by a dusting of a subcoating powder (e.g. talc powder) and then drying.
- Subsequent sub-coats are applied in the same manner until the desired thickness is achieved.
- **Note:** *any coat should **not** be applied unless the previous one is completely **dry**.*



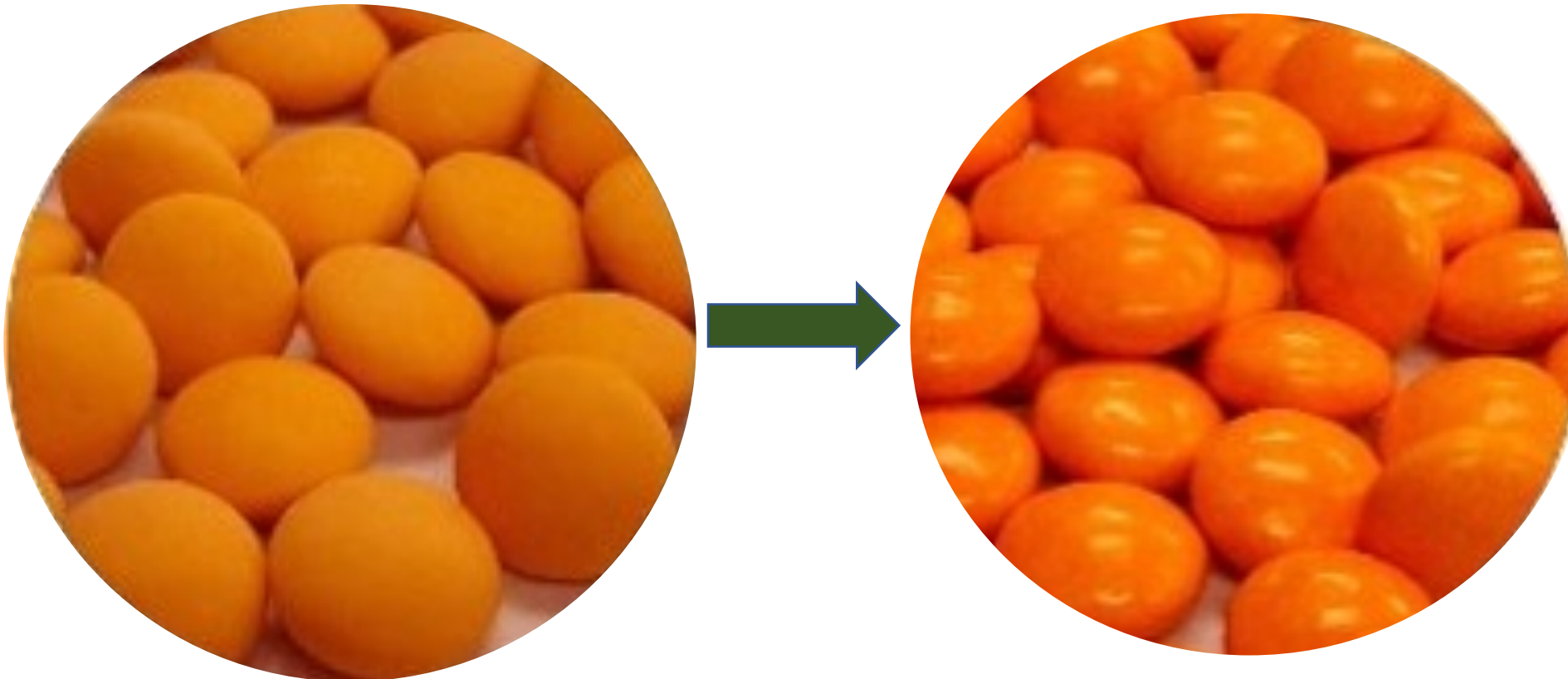
# Sugar Coating Process: Syrup (smoothing/coloring) Coating

- The purpose of this step is:
  1. **To hide** the imperfections in the tablet surface caused by the sub-coating step **and**
  2. **To impart** the **desired color** to the tablet.
- This step perhaps requires the **most skill**.
- The first syrup coats usually contain some suspended powders and are called “**grossing syrups**”.
  - In general, no color is added until the tablets are **quite smooth because** premature application to rough tablets can produce a **mottled** appearance in the final tablets.
- In the subsequent syruping steps, syrup solutions containing the **dye** are applied until the final size and color are achieved.



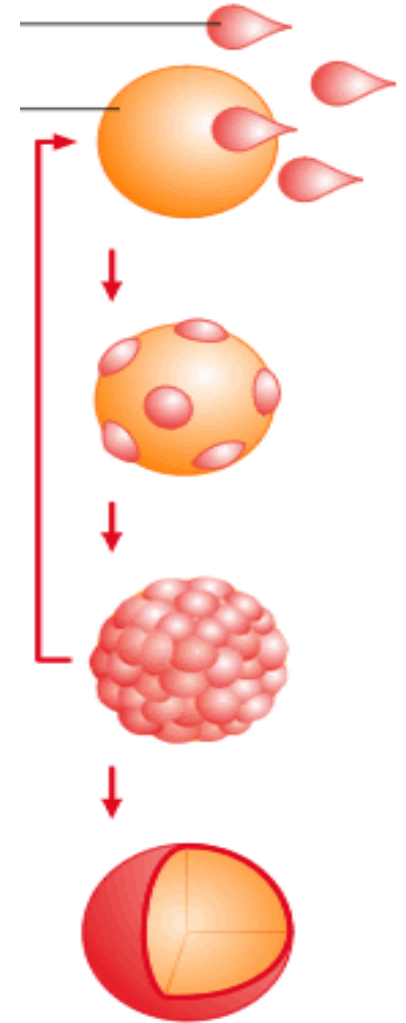
# Sugar Coating Process: Finishing and Polishing

- **Finishing:** in the finishing step, a few **clear coats** of syrup may be applied.
- **Polishing:** the desired luster (gloss) is obtained in this step. The tablets can be polished in clean coating pans by using certain **wax** (e.g. beeswax, carnauba wax).



# Film Coating Process

- It is **preferred** over sugar coating because:
  1. It is **faster**.
  2. More **economic**.
  3. **The versatility** of film-forming polymers that can be used
  4. It slightly increases the final tablet weight (**only 2-5%**).
- Film coating involves the same equipment and methods as in sugar coating, as follows:





# Pan Spray Method for Film Coating

- The introduction of spraying equipment was an evolution in the film coating process.
- Spraying allows an important advantage **which is automatic control** of the liquid application.



# Pan Spray Method: Control Variables

- Whatever the coating is carried out in, a conventional or perforated pan, certain process variables should be controlled to ensure good product quality.

1. **Pan variables**: the pan **shape**, **load**, and **rotational speed** all affect the mixing of the tablets.

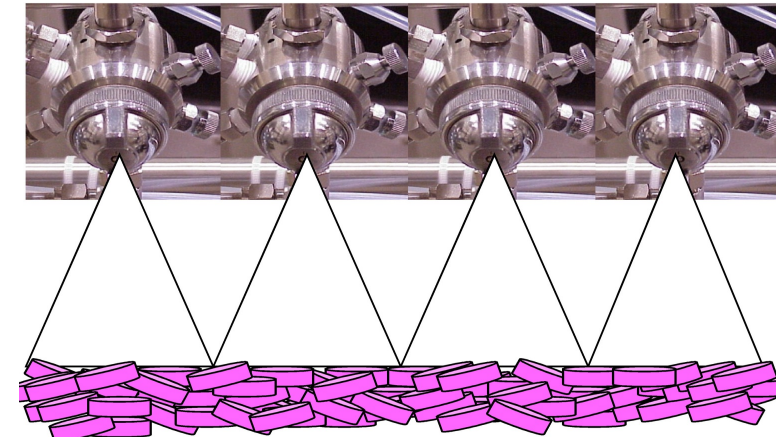
- Uniform mixing is essential for depositing the same quantity of the film on each tablet.
- Speeds that are **too slow** may cause **localized overwetting**, resulting in tablets sticking.
- Speeds that are **too high** may **not** allow **enough time** for drying before the same tablets are reintroduced under the spray; which results in **rough tablets**.

# Pan Spray Method Control Variables

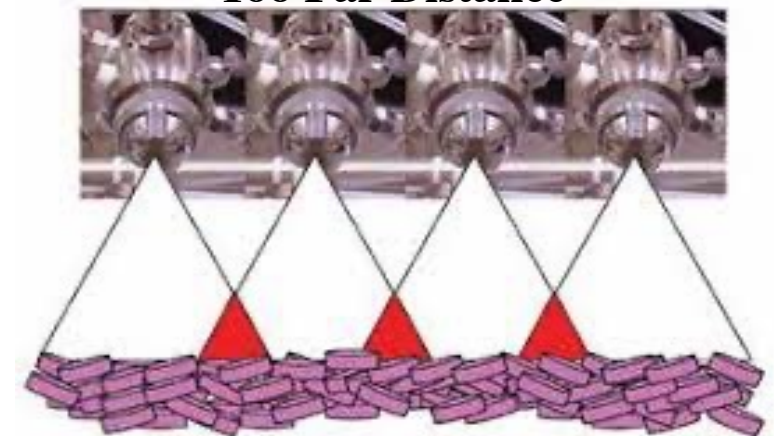
2. **Spray variables:** the spray variables to be controlled:

- a) The **rate** of liquid application.
- b) The **degree (size and size distribution)** of atomization.
  - Atomization that is **too fine** leads to some droplets drying before reaching the surface → **rough tablet** or excess dust in the pan.
  - **Too large** an atomization will lead to **overwetting**.
- c) **Nozzle to bed distance** (affects the amount of coating solution applied to a tablet each time it passes in front of it).

**Correct Distance**



**Too Far Distance**



# Pan Spray Method: Control Variables

## 3. Drying air variables:

- The **temperature, volume, and rate** are parameters of the process air that need to be controlled to obtain an optimum drying environment.
  - The **heat sensitivity** of the **film-forming material and tablet core** largely determines the upper temperature that can be applied.
- The temperature applied is between 50-90 °C (for most drugs).

# Evaluations of Coated Tablets

- **Will involve:**
- Evaluation of the **general appearance** such as color (hue and continuity), size, and physical defects on the coating
- **Performance** of the tablet: drug release characteristics, long-term stability of coated product.
- In general, visual inspection is sufficient to define relative coated tablet quality.
- **A practical qualitative** measure of the resistance of a coated tablet to abrasion can be obtained by merely **rubbing the coated tablet on a white sheet of paper**. Strong films remain intact and no color is transferred to the paper; **very soft coats** are readily "erased" from the tablet surface to the paper.



# Film Defects

- Variations in formulation and processing may result in unacceptable quality defects in the film coating.
1. **Sticking and picking:** **overwetting** or excessive film **tackiness** causes the tablets to stick to each other or the coating pan.
    - On drying, the point of contact of the film may remain adhered to the **pan or another tablet**.
  2. **Roughness:** a rough or gritty surface is a defect often observed when the coating is applied by a **spray**. Some of the droplets may **dry too rapidly** before reaching the tablet bed resulting in a deposit on a tablet surface.





# Film Defects

3. **Orange peel effects**: inadequate **spreading** of the coating solution before drying caused a bumpy or “orange peel” effect on the coating.
  - This indicates spreading is impeded by: 1- **too rapid** drying or 2- high solution **viscosity**.
4. **Bridging and filling**: during drying, the film may shrink and pull away from the sharp corners resulting in a “**bridging**” of the surface depression.
  - This problem results from **inadequate plasticizers**.
    - Adjusting the amount of plasticizer or using another one will solve the problem.



# Film Defects

- **Blistering:** When coated tablets require further drying in ovens, the solvent from the core is too rapidly evaporated, and the effect of high temperature on the strength, elasticity, and adhesion of the film may result in blistering.
- ➔ **solution:** Milder drying will solve this problem.



**Blistering**