Coating of tablets and multiparticulates

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Coating of tablets and multiparticulates

- Tablet coating is the application of a coating material to the exterior of a tablet with the intention of conferring benefits and properties to the dosage form over the uncoated variety.

- Coating can be applied to:
  - Tablets (the most commonly coated dosage form)
  - Capsules
  - Multiparticulates
  - Drug crystals

Coating of tablets and multiparticulates

Types of coating

There are three main types of coating:

1. Film coating: for tablets, multiparticulates, capsules, ..
2. Sugar coating
3. Press (Compression) coating

2 & 3 For tablets only

Film coated tablets

Sugar coated tablets

Features	Sugar coating	Film coating
Tablets		
Appearance	Rounded with high degree of polish	Retains contour of original core Usually not as shiny as sugar coat types
Weight increase due to coating materials	30–50%	2–3%
Logo or ‘breaklines’	Not possible	Possible
Other solid dosage forms	Coating possible but little industrial importance	Coating of multiparticulates very important in modified-release forms
Process		
Stages	Multistage process	Usually single stage
Typical batch coating time	8 hours, but easily longer	1.5–2 hours
Functional coatings	Not usually possible apart from gastro-resistant (enteric) coating	Easily adaptable for controlled release

Reasons for coating of tablets and multiparticulates

1. To provide protection of drug from environment, especially light and moisture
2. To mask taste, odor or color of the drug
3. Masking any batch difference in the appearance of raw materials
4. To modify drug release:
   - Delayed release (ex. enteric coating to protect the drug from the gastric environment of the stomach or the stomach from irritation caused by some drugs)
   - Extended release properties.
5. To aid in identification of product (i.e.colored coating)
6. To improve tablet elegancy
7. To facilitate tablet swallowing
8. To enable easier handling during high-speed filling and packaging of the coated product (improve product flow, increase mechanical strength, minimize dust formation)

Film coating

- Film coating is the most modern and generally used method nowadays.
- Nearly all newly launched coated products are film coated rather than sugar coated.
- Depending on the materials used in coating it is either for:
  - immediate release (non-functional coating) or
  - modified (delayed or extended) release (functional coating).

Film coating

Advantages of film coating

1) Reduction in coating time
2) Usually single stage
3) Small increase in tablet weight
4) No significant increase in disintegration time
5) Less chipping and cracking

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Film coating

Coating suspension formulation

- Polymer (Film former)
- Plasticizer
- Color
- Solvent

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Film coating polymers

Ideal characteristics of a film forming polymer

Solubility

- Polymer solubility is important for two reasons:
  - It determines the behavior of coated product in the GIT.
  - It determines the solubility of the coating in a chosen solvent system
- Film coatings that are used in immediate release products have usually good solubility in aqueous fluids, while those used form modified release have limited or no solubility in aqueous media.

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Film coating polymers

Ideal characteristics of a film forming polymer

Viscosity

- Polymers applied as solutions in a selected solvent should have relatively low viscosity.

- High viscosity complicates the product transfer of the coating liquid from the storage vessel to the spray guns, and subsequent atomization.

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Film coating polymers

Ideal characteristics of a film forming polymer

Permeability

- Film coating can be used to optimize the shelf-life of a tablet preparation, as some polymers are efficient barriers against the permeability of water vapour or other atmospheric gases.
- These properties vary widely between the individual polymers.

➢ Polymers for extended release coating should be permeable to water (and drug in conventional systems)

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Film coating polymers

Ideal characteristics of a film forming polymer

Mechanical strength

Film-coating polymers should possess suitable characteristics with respect to:

- *Film strength*, which greatly affects the ability of the coating to resist the mechanical stresses to which it will be exposed during the coating process and during subsequent handling of the coated product.
- *Film flexibility*, which imparts similar benefits to film strength and minimizes film cracking during handling or subsequent storage.
- *Film adhesion*, which is necessary to ensure that the coating remains adherent to the surface of the dosage form right up to the point of being taken by the patient.

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Film coating polymers

Ideal characteristics of a film forming polymer

The film forming material (polymer) should also have the following characteristics:

- It should be capable of producing a continuous elegant and smooth film.
- It should be essentially with no color, taste or odor.
- It should be compatible with common coating additives
- It should be nontoxic and pharmacologically inert
- It should be stable in the presence of heat, light, moisture , air, and the substrate being coated (no change with aging).

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Film coating

- Combination of polymers may be used to modify the film properties.
- Many water insoluble polymers are available as aqueous dispersions.
- Some polymers are efficient barriers against the permeability of water vapor and atmospheric gases, therefore they can be used to increase the shelf-life of tablets

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Types of film forming polymers

Polymers for immediate release

- Cellulose derivatives
  - Hydroxypropyl methylcellulose
    - Soluble in aqueous media and organic solvents
    - Form good films
  - Methylcellulose
  - Hydroxypropylcellulose
  - Hydroxyethylcellulose
  - Methylhydroxyethylcellulose
- Vinyl derivatives
  - Povidone (polyvinyl pyrrolidone, PVP)
  - Copovidone (A copolymer of vinyl pyrrolidone and vinylacetate)
  - Polyvinyl alcohol (PVA): exhibits good barrier properties to environmental gases and water vapor
- Polyethylene glycols
- Aminoalkyl methacrylate copolymers (Eudragit E®)

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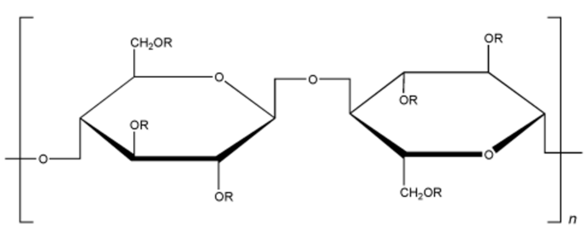
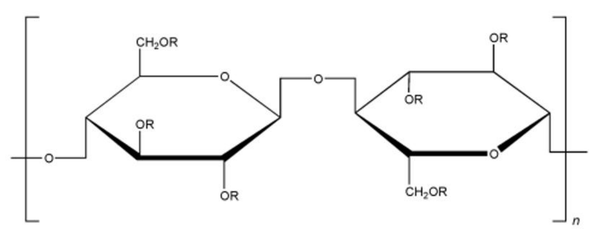


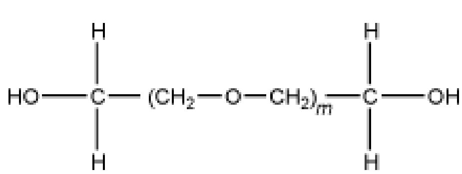
where R is H, CH_3, or $CH_3CH(OH)CH_2$

Hydroxypropyl methylcellulose (Hypromellose, HPMC)



R is H or $[CH_2CH(CH_3)O]_mH$

Hydroxypropylcellulose



Polyethylene glycols

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Types of film forming polymers

Sustained release polymers

- Cellulose derivatives
  - Ethylcellulose
  - Cellulose esters (cellulose acetate, cellulose acetate butyrate)
- Methylmethacrylate copolymers (Eudragit RS®, Eudragit RL®)
- Silicon elastomers
- Polyvinyl acetate

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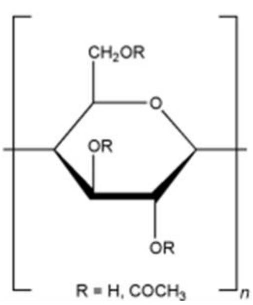
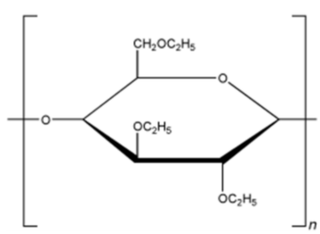
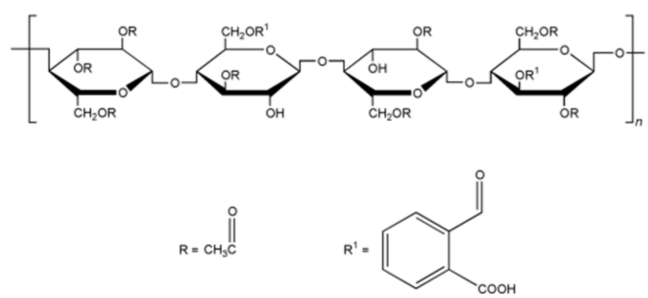


Cellulose acetate



Ethylcellulose



Cellulose acetate phthalate

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Types of film forming polymers

Enteric materials

- Phthalate esters
  - Cellulose acetate phthalate (CAP)
  - Polyvinyl acetate phthalate (PVAP)
  - Hydroxypropyl methycellulose phthalate
- Cellulose acetate trimellitate (CAT)
- Methacrylic acid copolymers (Eudragit L®, Eudragit S®)
- Carboxymethyl ethylcellulose (CMEC)
- Hydroxypropyl methycellulose acetate succinate (HPMCAS)

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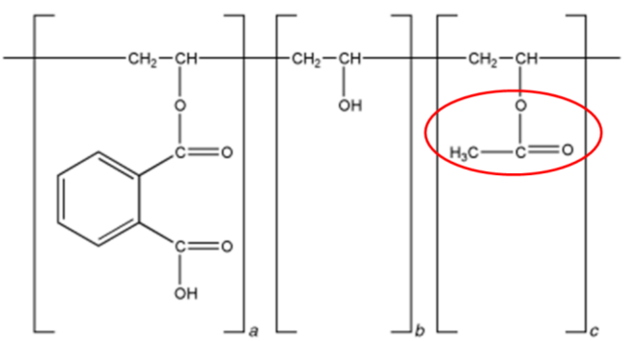
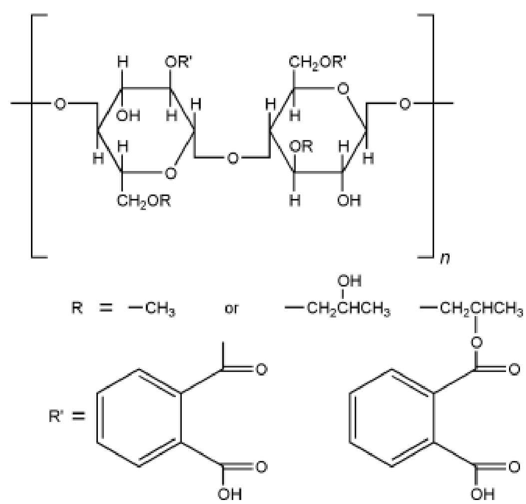


Polyvinyl acetate phthalate

Depending on the phthalyl content, *a* will vary with *b* in mole percent. The acetyl content *c* remains constant depending on the starting material.



Hydroxypropyl methylcellulose phthalate

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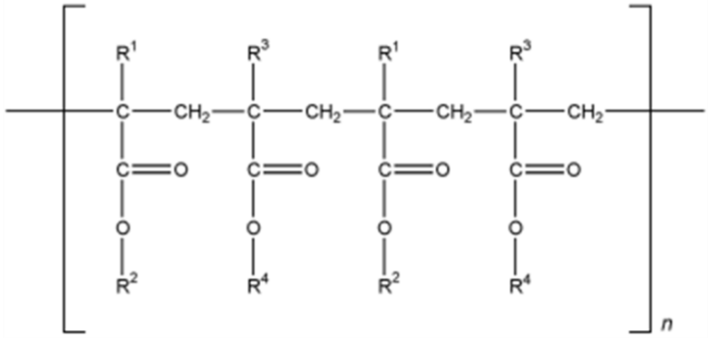

For *Eudragit E*:
R1, R3 = CH3
R2 = CH2CH2N(CH3)2
R4 = CH3, C4H9

For *Eudragit L* and *Eudragit S*:
R1, R3 = CH3
R2 = H
R4 = CH3

For *Eudragit RL* and *Eudragit RS*:
R1 = H, CH3
R2 = CH3, C2H5
R3 = CH3
R4 = CH2CH2N(CH3)3+Cl–

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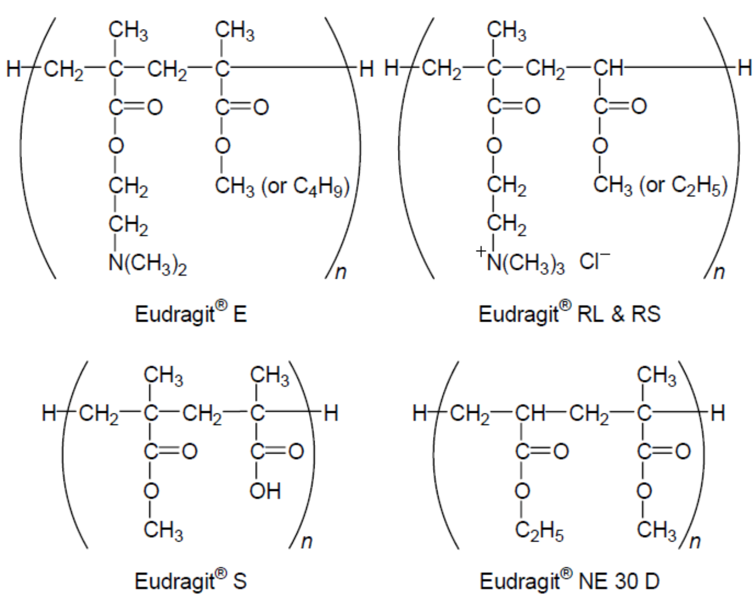

Figure 4.3 Strutctures of selected Eudragits®.

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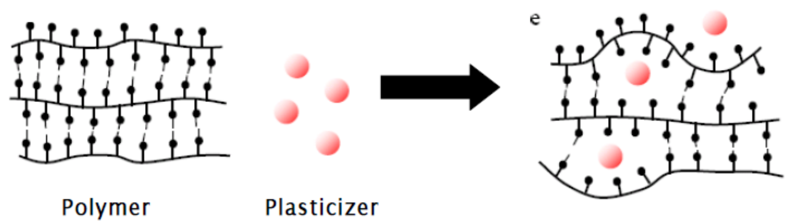
Plasticizer

- These are agents used to improve the quality (flexibility, adhesion) of film.
- They decrease film brittleness.
- They should be soluble in the solvent used to dissolve the polymer.
- **Mechanism**: They interpose themselves on a molecular scale between the polymer strands thus permit them to move more freely.



Plasticizer

- Examples
  - Polyhydric alcohols: Polyethylene glycols, Propylene glycol, Glycerin
  - Oils: Castor oil, coconut oil, mineral oil
  - Surfactants: Polysorbates (Tweens), Sorbitan esters (Spans)
  - Organic esters: Diethyl phthalate, Glyceryl triacetate (Triacetin), Triethylcitrate, acetyltriethylcitrate.

Colorants

- Pharmaceutically acceptable colors are available in both water soluble forms (dyes) and water insoluble forms (pigments)
- Pigments have advantages over water soluble colors:
  - More stable towards light
  - Provide better opacity and covering power
  - Optimize the impermeability of the film to vapor
- Examples: iron oxide pigments, titanium dioxide and aluminum lakes.

Solvent

- In the past, polymers were dissolved in organic solvents (methanol, ethanol, chloroform, isopropanol, acetone, methylethylketone and methylene chloride).
- Modern techniques now rely on water as a solvent because of the disadvantages of organic solvents which include:
  - Environmental side effects
  - Safety (toxicity, explosion)
  - Financial
  - Solvent residues in the film (impurities)

Aqueous polymeric dispersions

- Industrially, specialized dispersions of water insoluble polymers are frequently used.
- They permit aqueous processing of water-insoluble polymers.

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Aqueous polymeric dispersions

Examples

Material trade name	**Polymer**	**Use**
Aquacoat ECD®, Surelease®	Ethylcellulose	Sustained release coating
Eudragit® RS 30 D, Eudragit® RL 30 D, Eudragit® NE 30 D	Methylmethacrylate copolymers	Sustained release coating
Kollicoat® SR 30 D	Polyvinylacetate	Sustained release coating
Eudragit L 30 D-55 Eudragit FS 30D	Methacrylic acid copolymers	Enteric coating
Aquacoat® cPD	Cellulose acetate phthalate	Enteric coating

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Film coating process

- Fundamental requirements of tablet coating system include:

1) Adequate means of atomizing the spray liquid for application to the tablet cores
2) Adequate mixing and agitation of the tablet bed
3) Sufficient heat input in the form of drying air for solvent evaporation
4) Good exhaust facilities to remove dust and evaporated solvent.

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Film coating process

Film is usually applied by:

- Pan coating
  - Standard coating pan
  - Perforated coating pan
- Fluidized bed (Air suspension) coating

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Film coating process

Conventional pan system

- The standard coating pan consists of a circular metal pan mounted angularly on a stand.
- Heated air is directed into the pan and onto the tablet bed surface and is exhausted by means of ducts positioned through the front of the pan.
- The coating formula is added either by pouring or by spraying (Nowadays spraying is the most commonly used method).
- Spraying system is used to spray the liquid coating materials, which produce faster, and more even distribution of the solution or suspension.

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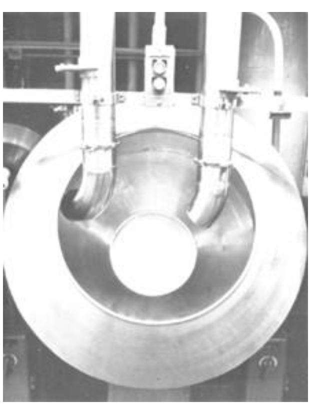

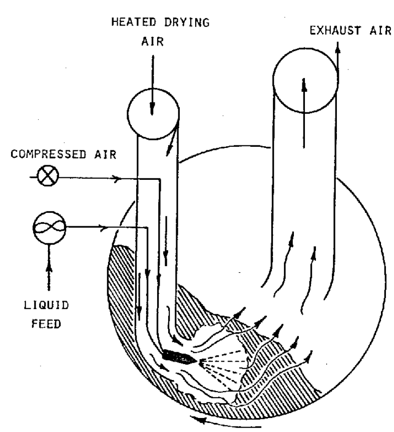

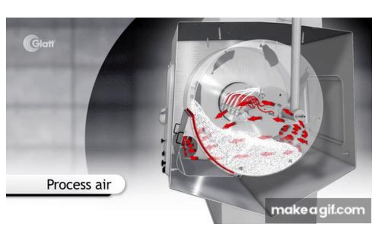

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Film coating process

- A significant improvement in the drying efficiency of the standard coating pan is achieved by:
  - The immersion sword
  - The immersion tube system
  - The Pellegrini pan

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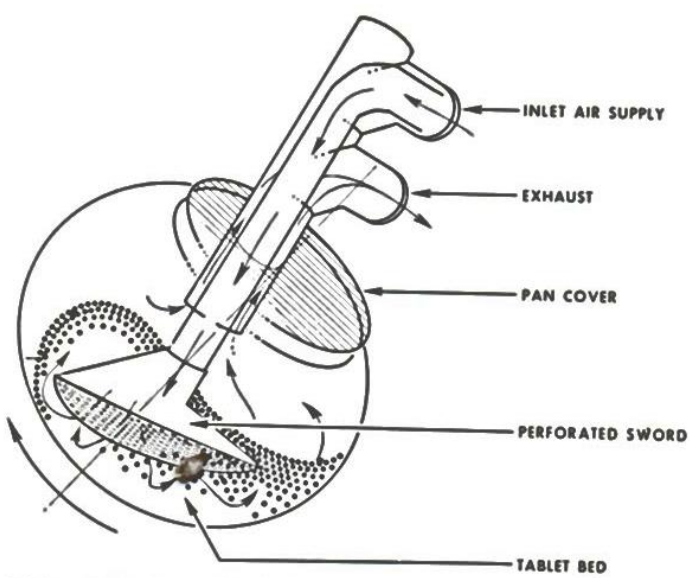

FIG. 12-7. *Simplified diagram of Glatt immersion-sword system.*

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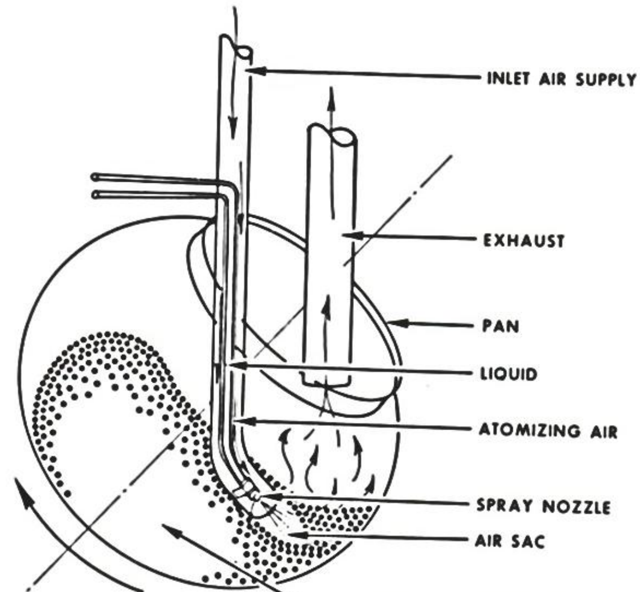

FIG. 12-8. *Diagram of immersion-tube system. (From Demmer et al.[5])*

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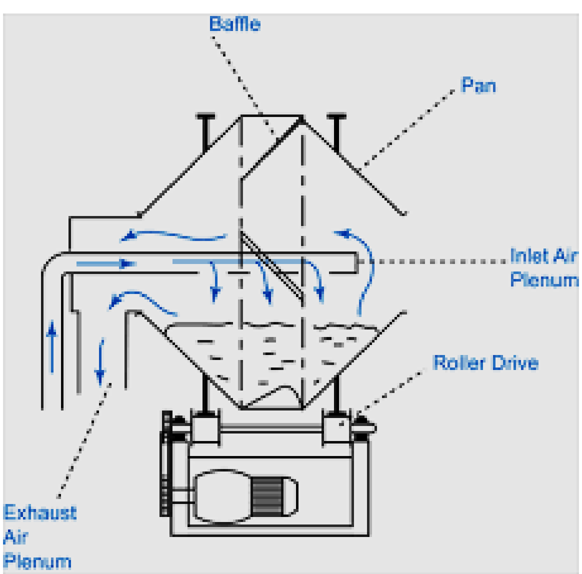

Pelligrini pan coater (enclosed)

Pellegrini coating pan

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Film coating process

Perforated Pan Systems

- In general, all equipment of this type consists of a perforated or partially perforated drum that is rotated onto its horizontal axis in an enclosed housing. Examples on this type are
- **Accela Cota** and **Hi-coater**. In these coaters, the drying air is directed into the drum is passed through the tablet bed and exhausted through perforations in the drum
- **Driacoater** the drying air can be directed from inside the drum through the tablet bed and out an exhaust duct. The coating system is applied to the surface of the rotating beds of tablets through spraying nozzles or by pouring via distribution pipes.

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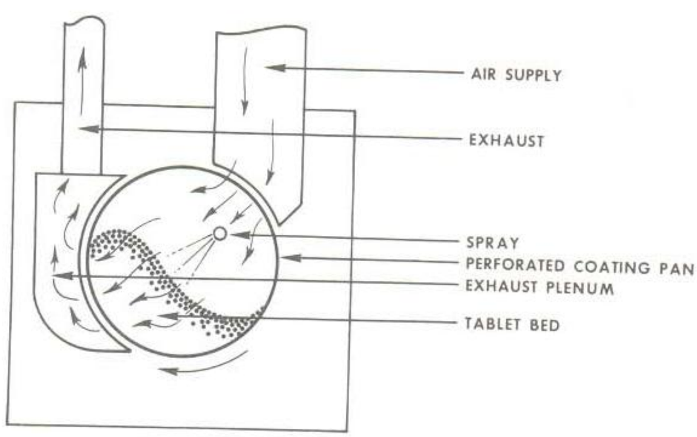

FIG. 12-9. *Simplified diagram of Accela-Cota system.*

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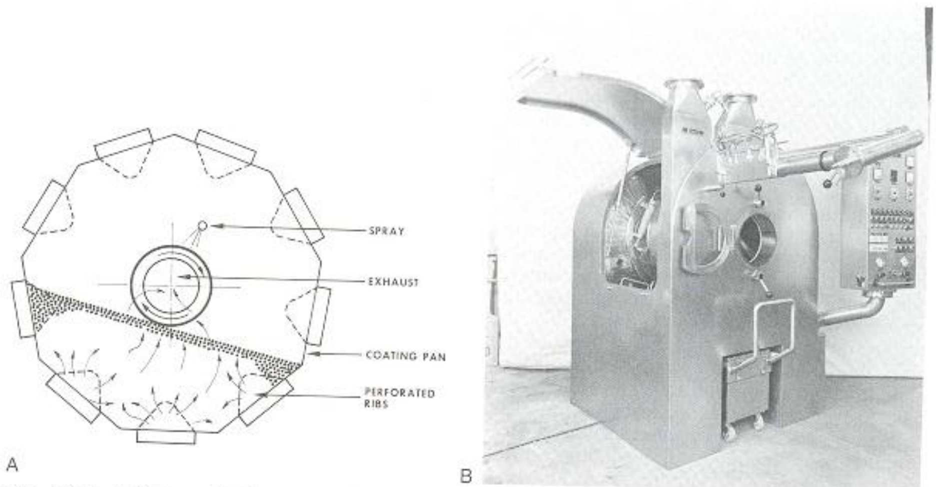

FIG. 12-11. A, *Diagram of Driacoater pan.* B, *Glatt coater.* (*Courtesy of Glatt Air Techniques Inc., Ramsey, NJ.*)

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Film coating process

Pan coating

1) Charge the pan with tablets and operate the drying air and exhaust as required.
2) When the tablets begin to tumble, half of the coating solution is applied in thin steady stream while exhaust is working.
3) Air and temperature should be controlled to allow uniform spread of solution before drying.
4) When the tablets are dried the air should be reduced and fourth of the solution is added in a thin stream.
5) The rest of solution is added at interval of 5 - 10 min.

- Process variables include pan variables (shape, rotational speed and baffling), Spray variables (degree of atomization, spraying rate) and process air variables (temperature, rate ..)

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Spray application systems

- The two basic systems used to apply a finely divided (atomized) spray onto tablets are:
  – High pressure airless
  – Low pressure air atomized

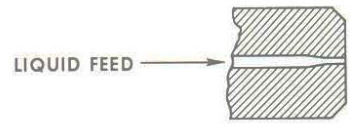

FIG. 12-14. *Simplified diagram of a high-pressure, airless nozzle.*

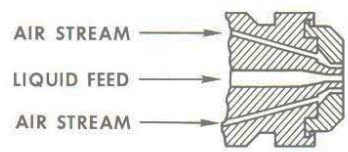

FIG. 12-15. *Simplified diagram of a low-pressure, air-atomized nozzle.*

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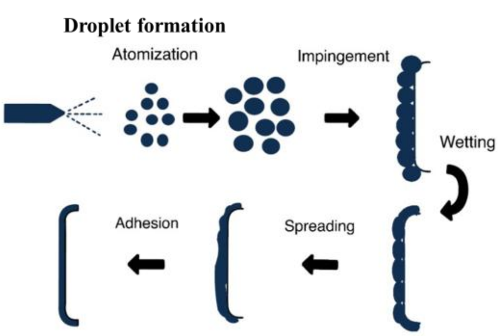
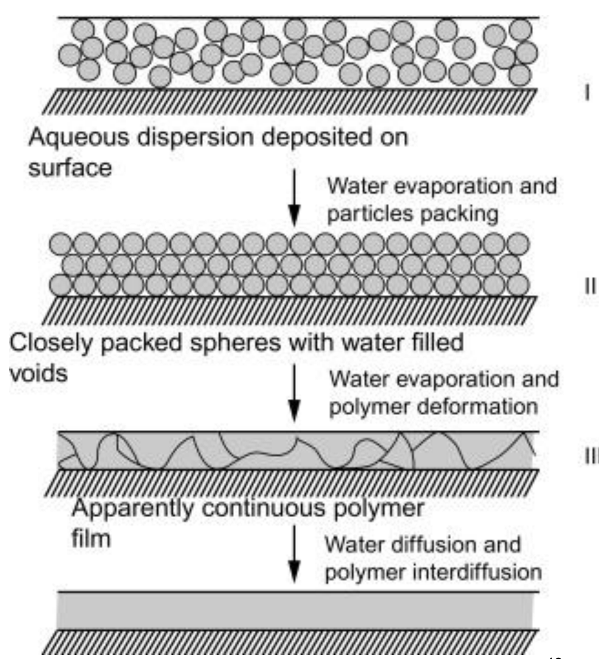


Coalescence



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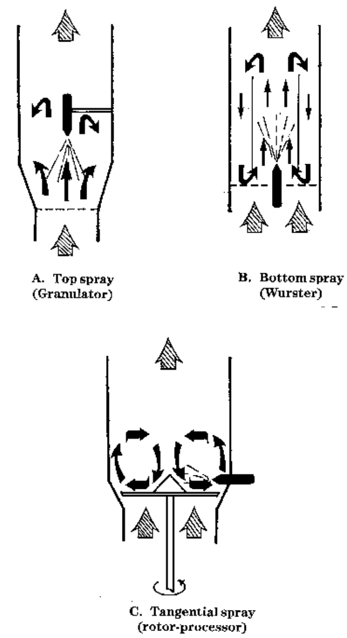
Film coating process

Fluidized-bed (Air suspension) coating

- In this technique tablets are kept in motion inside a chamber by blowing hot air. At the same time coating solution is applied by an atomizing nozzle.



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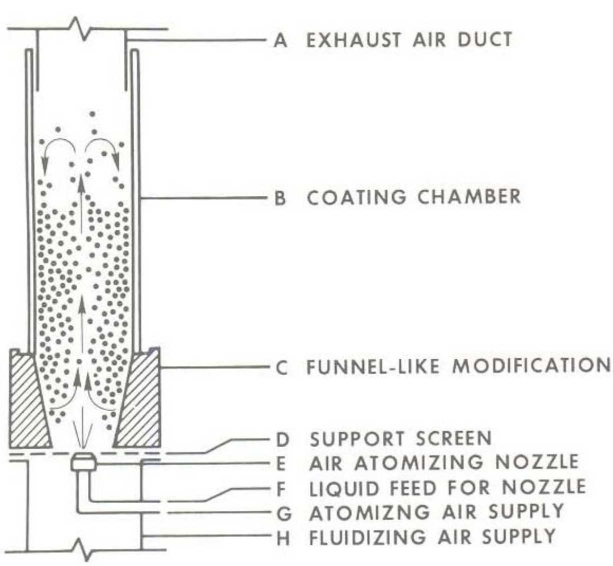
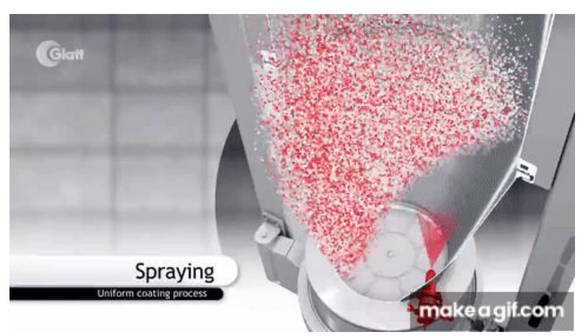


FIG. 12-12. *Diagram of a fluidized bed coater.*



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Ideal characteristics of film-coated tablets

1. Film coated tablets should display an even coverage of film and color.
2. There should be no abrasions of tablet edges or crowns.
3. Logos and break lines should be distinct and not filled.
4. The tablet must be compliant with finished product specifications and any relevant compendial requirements.

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Coating faults and film defects

- Variations in formulation and processing conditions may result in unacceptable quality defects in the film coating. These defects include:

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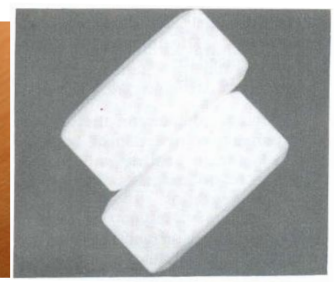
Coating faults and film defects

Picking and twining

- Overwetting and inadequate drying conditions will cause tablets to stick to each other or to the coating pan.
- Common problem with flat or capsule-shaped tablets



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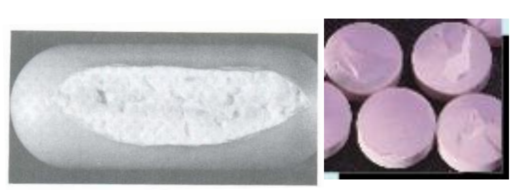
Coating faults and film defects

Cracking and peeling

- Film cracking occurs if the internal stresses exceed the tensile strength of the film.
- Film peeling may also occur.
- This problem is usually overcome by improving mechanical properties of the film by:
  - Using higher molecular weight polymers or polymer blends.
  - adjusting plasticizer type or concentration.

Film cracking



Film peeling

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Coating faults and film defects

Blistering

- This results from too rapid evaporation of the solvent from the core
- Milder drying conditions are indicated in this case

Bridging

- During drying, the film may shrink and pull away from the sharp corners of an intagliation or bisect.
- Increasing the plasticizer content or changing the plasticizer can decrease the incidence of bridging

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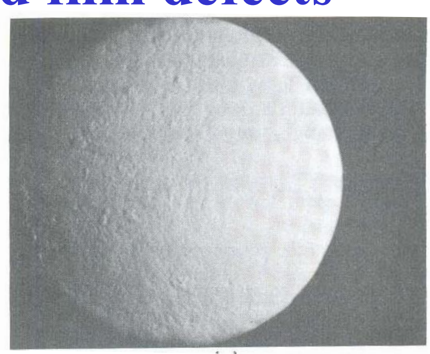
Coating faults and film defects

Orange peel effects



- Inadequate spreading of the coating solution before drying causes a bumpy or "orange peel" effect on the coating
- Causes:
  - Two rapid drying
  - High solution viscosity

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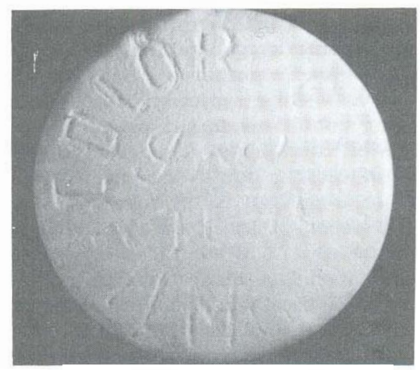
Coating faults and film defects

Bridging of logos

- Partial or complete detachment of the coating in the region of the logo.
- This can be solved through formulatio of the coating formula by:
  - Improving film adhesion
  - Reducing stress within the film



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Coating faults and film defects

Color variation

- This problem may result from:
  - Uneven spray pattern
  - Improper mixing
  - Insufficient coating

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Sugar coating

- Sugar coating is the traditional method of coating tablets
- It involves successive application of sucrose based solutions to tablet cores.
- It is less common nowadays than film coating
- It takes time from hours to few days.
- The increase in tablet weight is 30-50 %
- In general the equipments used in film coating can, with suitable modification, be used for sugar-coating techniques.
- Methods of applying the coating syrup include manually using a ladle or by spraying.

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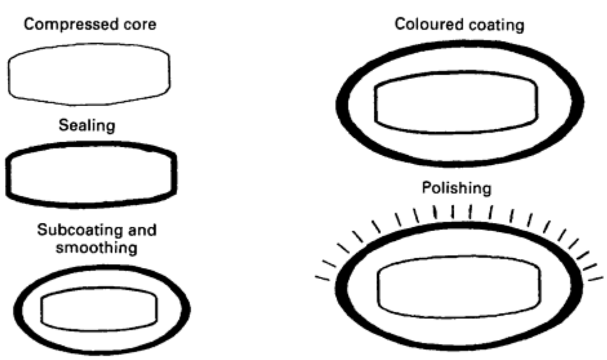
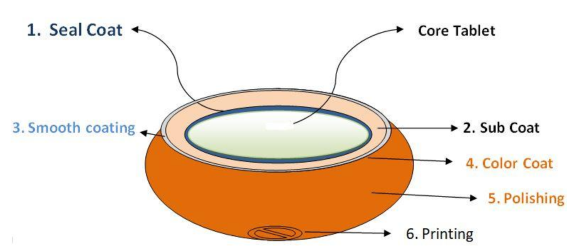
The stages in sugar coating





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Sugar coating

1. Sealing of the tablet core

- A seal coat is applied to prevent moisture penetration into the tablet core (especially needed in pan-ladling processes).
- In spray processes, it is possible to adjust the application of the subcoats and coat so that localized overwetting does not occur and therefore no need for sealing.

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Sugar coating

Examples of materials used in sealing:

- Shellac
  - This is a purified resinous secretion of the insect *Laccifer lacca.*
  - It suffers from occasional supply problems and quality variation.
  - there are also stability problems associated with increased disintegration and dissolution times on storage.
- Zein (extracted from corn gluten meal)
- cellulose acetate phthalate
- polyvinyl acetate phthalate

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Sugar coating

2. Subcoating

- The subcoating is applied to round the edges and build up the tablet size
- The process is usually performed by applying sticky solution of sugar, gelatin or acacia to the tablet and then adding (dusting) the subcoating powder (bulking agent) such as calcium carbonate or talc to the tablets and then drying
- Subsequent subcoats are applied in the same manner until the tablet edges have been covered and the desired thickness is achieved
- For spray processes, a subcoating suspension containing both binder and the subcoating powder is sprayed intermittently on the tablet bed

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Sugar coating

3. Smoothing

- Tablets will have a rough surface after subcoating.
- The purpose of this step is to remove the imperfections in the tablet surface (rough surface) caused by subcoating process.
- In this step, few sugar syrup coats are applied (the first usually contains some suspended particles and called grossing syrup).

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Sugar coating

4. Coloring

- In general colors should be added when the tablets become quite smooth.
- Syrup solutions containing the dye are applied until the final size and color are achieved.
- In the final syruping or finishing step, a few clear coats of syrup may be applied.

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Sugar coating

5. Polishing

- Tablets are moved to the polishing pan and solutions of beeswax or carnauba wax in suitable volatile solvent are applied until the tablets become shiny.

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Sugar coating

6. Printing

- It is a common practice to identify all oral solid dosage forms with a manufacturers logo, product name, dosage strength or other appropriate code.

- For sugar coating such identification can be done only by printing using special edible inks.

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Sugar coating problems

Cracking, chipping and splitting of coat

- Sugar coatings are inherently brittle.
- Tablet cores that expand cause cracking.
- Expansion may result from:
  - Moisture sorption
  - Stress relaxation of the core
- Addition of small quantity of polymer often helps to improve structure integrity.

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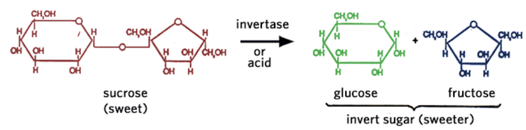
Sugar coating problems

Twinning

- Results from drying after sticking of tablets.

Non drying coating

- This a result of sugar inversion.



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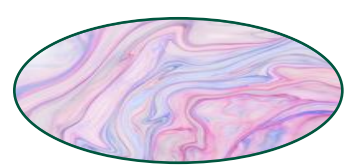
Sugar coating problems

Uneven color

Causes:

- Poor distribution of coating liquids.
- Color migration of water soluble dyes while the coating is dried.
- Unevenness of the surface of the subcoat.
- Excessive drying between color application can cause erosion of the color layer



➢ ***Marbling***

➢ Itmay result from rough surface after smoothing so that the thichkness of polish layer varies

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Sugar coating problems

Blooming and sweating

- This result from residual moisture.
- This mositure can diffuse out and affect the product quality.
- Moderate levels of moisture egress causes the polish to take on a fogged (fade) appearance (**Blooming**).
- Higher levels of moisture egress the moisture may appear like beads of perspiration (**Sweating**) which may cause tablets stored in closed containers to stick.

BLOOMING: FADING OR DULLING OF A TABLET COLOR AFTER A PROLONGED PERIOD OF STORAGE AT A HIGH TEMPERATURE

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Press coating

- The technology of press coating differs from the film and sugar coating techniques.
- Press coating involves the compaction of granular material around already performed core using compressing equipment (specialized tableting machine) similar to that used for the core itself.

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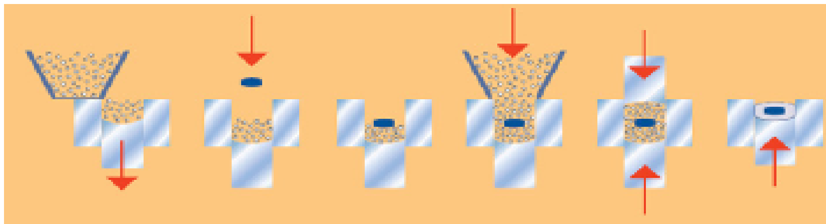

I: Prefilling the half amounts of outer coating materials into the die.
II: Putting the inner core tablet on the powder bed of outer coating materials.
III. Centering.
IV: Filling the residual half amounts of outer coating materials.
V. Compression
VI. Ejection of press-coated tablet from the die.

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Press coating

- Press coating is used mainly to separate chemically incompatible drugs.
- Two steps of press coating can be used for perfect separation between two ingredients by an inert middle layer.
- There has been increased use of compression coatings for the purpose of modified release products (e.g. Adalat® CC).
- The disadvantages of the process arise from the complexities of the mechanism used in the compressing machine.

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Standards for coated tablets

- In general pharmacopeias have similar requirements for coated and uncoated tablets, the difference being that:
  - Film coated tablets must comply with the uniformity of mass test unless otherwise justified and authorized.
  - Disintegration test
    - Immediate release tablets
      - Film coated: 30 min (except for enteric)
      - Other types of coating: 60 min
      - The test may be repeated using 0.1 N HCl in the event that any tablets fail to disintegrate in the presence of water.
    - Enteric coated tablets
      - A challenge test in acidic medium (e.g. 0.1 N HCl for 1.5 - 2 hours) is done, where no disintegration should occur. Then the tablets are transferred to buffered medium where disintegration should occur within 45-60 min

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Coating of multiparticulates

- Multiparticulates, often referred to as "pellets" or "beads" possess many benefits compared to conventional non-disintegrating tablets.

- They may be used in extended release or delayed release dosage forms.

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Coating of multiparticulates

Advantages of multiparticulates:

- Their small size (typically 0.5-2 mm) allows them to pass through the pyloric valve. Therefore, the GIT transit is more consistent than that of tablets.
- They allow the release to be optimized for individual drugs in a system delivering two or more active drugs.
- They are less likely to suffer from problems associated with film failure or poor coating uniformity.
- Whole non-disintegrating tablets can potentially lodge in restriction within the GIT and this can lead to ulcerative mucosal damage.

Types of multiparticulate

- **Drug crystals**
  - They should have appropriate size and shape
- **Irregular granules**
  - These can be coated but it is difficult to achieve uniform coating thickness.
- **Spheronized granules**
  - These can be prepared by extrusion/spheronization or rotor granulation.
- **Drug loaded nonpareils**
  - These are preformed spherical particles about 1 mm in diameter consisting primarily of sucrose and starch.
  - The drug (dissolved or suspended in a suitable solvent containing also a polymer binder is usually sprayed onto the surface of nonpareils and then they are film coated.
- **Minitablets** (1-2 mm)

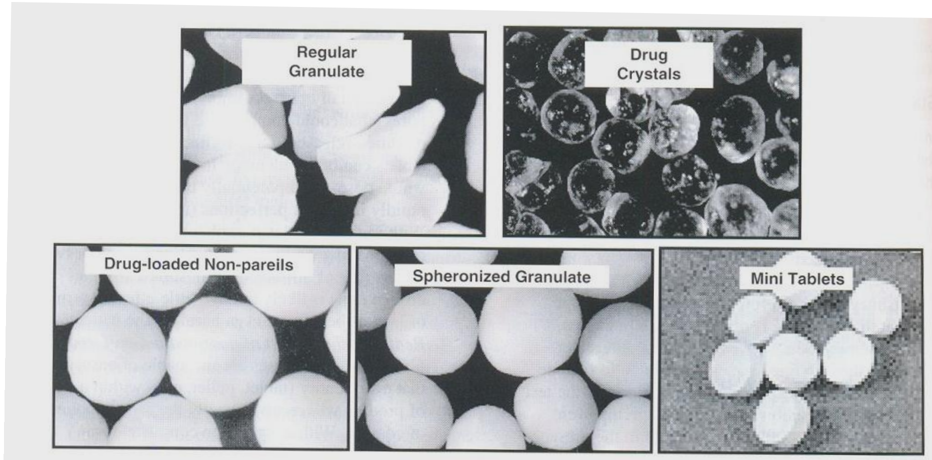

Fig. 33.10 Examples of film-coated multiparticulates.

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Process for coating multiparticulates

- Traditionally multiparticulates were coated using pan coating processes.
- Today fluidized bed coating is preferred because of their ability to:
  - Enable discrete coating while minimizing the risk of agglomeration
  - Ensure that coatings are uniformely deposited on the surface of each multiparticulate in the batch.

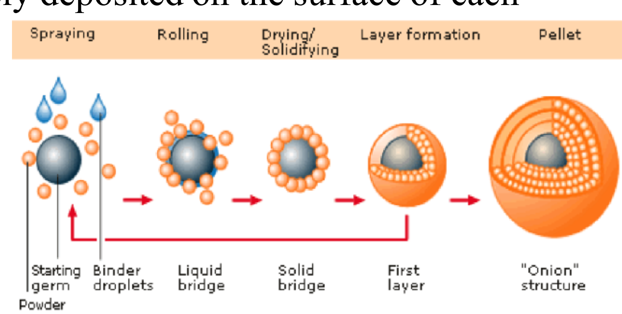

Fig. 2: Principle of Powder layering

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Other coating methods and technologies

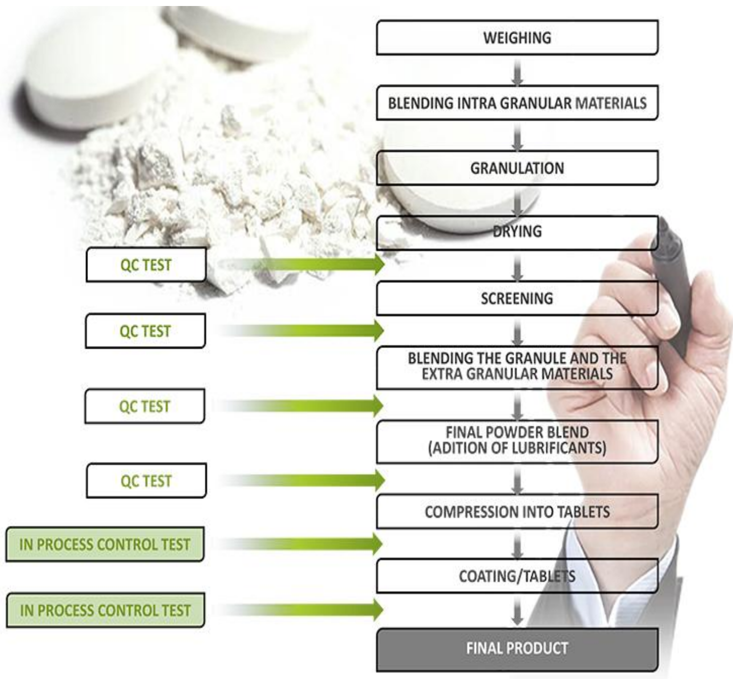
- **Dip coating**
  - Tablets are coated by dipping into coating solution.
  - Not commonly used nowadays.

- **Hot melt coating**
  - Melt is sprayed and not solution
  - Materials used (M.P. 55 -65 °C): beeswax, synthetic monoglyceride and diglycerides, synthetic spermaceti.
  - Fluidized-bed coating is preferable.

- **Electrostatic powder coating process**
  - Uses principles similar to those used in photocopying.

Gelatin-coated tablets

- A recent innovation is the gelatin-coated tablet.
- Advantages:
  - It allows the coated product to be about one-third smaller than a capsule filled with an equivalent amount of powder.
  - The gelatin coating facilitates swallowing,
  - Gelatin-coated tablets are more tamper evident than unsealed capsules.



Types of Quality control tests

1.Official tests

- Weight variation test
- Drug content
- Disintegration time test
- Dissolution test

2.Unofficial tests

- Thickness
- Hardness
- Friability
- Organoleptic characters

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Parameters and frequency of In Process Checks for Tablets (Coating & Polishing Stage) TABLE C

Tablets for In process frequency and sample size during Coating & Polishing				
Sr. No	In Process Parameter	In process checks by Production	In process checks by QA	Sample Quantity in No.
1	Physical Appearance	After each coating cycle/ every 30 min and at the end of lot/ batch and after polishing.	QA person shall be done in-process checks as per instruction given in BMR.	20
2	Average Weight	After each coating cycle/ every 30 min and at the end of lot/ batch and after polishing.		20
3	Thickness	Coated tablets after polishing of lot/ batch.		10
4	Tablets Breaking force (If applicable)	Coated tablets after polishing of lot/ batch.		10
5	Disintegration Time.	Coated tablets after polishing of lot/ batch.		6
6	Diameter	Coated tablets after polishing of lot/ batch.		10
7	LOD of Tablets	Coated tablets after coating of lot/ batch.		No. of tablets equivalents to 10 gm.
8	Inlet, outlet Temperature, Spray rate, Pan RPM and weight gain	After each coating cycle/ every 30 min and at the end of lot		20

Note: In process checks shall be carried out after machine stoppage or breakdown.

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Sugar coating example

Subcoating Solutions	*Formula Variation* I	II	III	
Gelatin	60 g	5.4 kg		
Acacia	60 g	2.7 kg	450 g	
Sugar, cane	1500 g	53.7 kg		
Syrup, corn			450 g	15
Syrup, USP			3.785 L	
Water, distilled	1.0 L	44.3 kg		

Subcoating Powders	*Formula Variation* I	II	III	IV	V	VI	
Kaolin		225 kg					
Dextrin		112 kg	185 kg				
Cocoa powder		60 kg					
Calcium carbonate, pptd			480 kg		7.72 kg		
Sugar, cane, powdered	4.1 kg	112 kg	240 kg	40 kg	0.9 kg	180 g	8
Acacia, powdered	0.12 kg			6 kg		1 g	(
Starch, corn	1.35 kg				0.9 kg	60 g	
Talc, USP	0.23 kg					1 g	
Calcium sulfate, NF							8

Syrup Solutions	*Grossing Syrups* I	II	III	*Heavy Syrups* I	II	*Regular Syr* I
Colorant	q.s. ad	q.s. ad	q.s. ad	q.s. ad	q.s. ad	q.s. ad
Subcoating powder	22.7 kg					
Calcium carbonate, light		7.75 kg	69 g			
Sugar, cane, powder	136 kg	22.7 kg	572 g	2.73 kg	181 kg	85 g
Starch, corn		1.36 kg	69 g			
Syrup, USP		22.7 L		3.785 L	256 kg	
Water, distilled	76 kg		290 ml			q.s. 100 ml

Polishing Solutions	*Formula Variation* I
Wax, carnauba, yellow	0.09 kg
Beeswax, white	0.09 kg
Wax, paraffin	0.02 kg
Naphtha	3.785 L

Film coating example

Function	INGREDIENT	TABLET CORE/ COATING %	QUANTITY (mg)
	Tablet core		
API	Cyclophosphamide monohydrate	22	53,45 (50 mg anhydrous)
DC vehicle (Diluent/Binder)	Microcrystalline cellulose (Vivapur®)	43	102,00
DC vehicle (Diluent/Binder)	Anhydrous dibasic calcium phosphate (Anhydrous Encompress®)	31	75,00
Disintegrant	Sodium starch glycolate (Explotab®)	2,5	6,00
Glidant	Colloidal anhydrous silica (Aerosil®)	0,5	1,15
Lubricant	Magnesium stearate	1	2,40
	Coating		
Plasticizer	Sorbitol	17	5,60
Solvent/Plasticizer	Glycerol	68	22,42
Film-forming agent	Povidone (Kollidon®)	5,2	1,72
Coloring agent	FD&C Blue No. 1 (E133) Aluminum lake	0,09	0,03
Opacifier	Titanium dioxide	0,7	0,23
Solvent	Water	9	3,00

Tablet core: 240 mg
Coating: 30 mg
Total: 270 mg

Figure 9. Formulation of cyclophosphamide sorbitol film-coated tablets.