Coating of tablets & multiparticulates
DEFINITION

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.
In its widest sense the technology is also applicable to multi-particulate systems intended for modified-release applications. To a much lesser extent coatings may also be applied to hard-shell and soft elastic capsules.
Types of tablet coating

- Three main types are in use:
  - Film coating
  - Sugar coating
  - Press coating
Reasons for coating tablets

1. Ingredients may need protection from the environment, particularly light and moisture.

2. Many drugs have a bitter or otherwise unpleasant taste, coating is an efficient way to mask such tastes. Tablets that are coated are also somewhat easier to swallow than uncoated tablets.
3- Coloured coatings also mask any batch differences in the appearance of raw materials and hence allay patient concern over tablets of differing appearance.

4- Coatings may be optimized with respect to colouration and gloss to aid in their sales appeal or to reinforce a marketing brand identification.

5- Coloured coatings aid in the rapid identification of product by the manufacturer, the dispensing pharmacist and the patient.
6-Coating tablets facilitates their handling on high-speed automatic filling and packaging equipment. Very often coating confers an added mechanical strength to the tablet core. Cross-contamination is also reduced in the manufacturing plant, as ‘dusting’ from tablets is eliminated by coating.

7-Functional film coatings are used to impart enteric or controlled-release properties to the coated tablet or, more usually, to coated multiparticulates.
• FILM COATING

Nearly all newly launched coated products are film coated rather than sugar coated, for the reasons given in Table 1.
<table>
<thead>
<tr>
<th>Features</th>
<th>Sugar coating</th>
<th>Film coating</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tablets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Rounded with high degree of polish</td>
<td>Retains contour of original core. Usually not as shiny as sugar coat types</td>
</tr>
<tr>
<td>Weight increase due to coating materials</td>
<td>30–50%</td>
<td>2–3%</td>
</tr>
<tr>
<td>Logo or ‘break’ lines</td>
<td>Not possible</td>
<td>Possible</td>
</tr>
<tr>
<td>Other solid dosage forms</td>
<td>Coating possible but little industrial importance</td>
<td>Coating of multiparticulates very important in modified release forms</td>
</tr>
<tr>
<td><strong>Process</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stages</td>
<td>Multistage process</td>
<td>Usually single stage</td>
</tr>
<tr>
<td>Typical batch coating time</td>
<td>Eight hours, but easily longer</td>
<td>1.5–2 hours</td>
</tr>
<tr>
<td>Functional coatings</td>
<td>Not usually possible apart from enteric coating</td>
<td>Easily adaptable for controlled release</td>
</tr>
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</table>
Process description

• Film coating involves the deposition, usually by a spray method, of a thin film of polymer surrounding the tablet core.

• The coating liquid (solution or suspension) contains a polymer in a suitable liquid medium together with other ingredients such as pigments and plasticizers.
• This solution is sprayed on to a rotating, mixed tablet bed or fluid bed. The drying conditions permit the removal of the solvent so as to leave a thin deposition of coating material around each tablet core.
Coating suspension formulation

- Typically this comprises:
  - Polymer
  - Plasticizer
  - Colourants
  - Solvent.
Ideal characteristics of a film coating polymer

- **Solubility**
- For conventional film coating the polymer should have good solubility in aqueous fluids to facilitate the dissolution of the active ingredient from the finished dosage form. However, where a modified-release action is required then a polymer system of low water solubility or permeability will be chosen.
• **Viscosity**
• polymers should have a low viscosity for a given concentration. This will permit the easy, trouble-free spraying of their solutions in industrial film coating equipment.
• **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.
• **Mechanical properties**

polymer chosen for a film coat formulation must be:

• one with **adequate strength** to withstand the impact and abrasion encountered in normal handling. **Insufficient** coating strength will be demonstrated by the development of cracks and other imperfections in the coating.

• It should be mentioned that the polymer chosen must also **comply** with the relevant regulatory and pharmacopoeial requirements current in the intended marketing area.
Types of polymer available

- Cellulose derivatives
- Hydroxypropyl methylcellulose
- methylcellulose and hydroxypropyl cellulose.
- Methacrylate amino ester copolymers
• Aqueous polymer dispersion

• Industrially, specialized dispersions of water-insoluble polymers such as ethylcellulose and ammonio methacrylate copolymers for use in aqueous media are frequently encountered in the coating of beads and granules for use in modified-release preparations.

• The advantage of these materials is that they permit the aqueous processing of otherwise water-insoluble polymers, with the consequent benefits of this method of processing.
• Plasticizers

• Plasticizers are generally added to film coating formulations to modify the **physical properties** of the polymer to make it more usable. One important property is their ability to decrease film brittleness.

• Examples of plasticizers are:
  • polyols, such as polyethylene glycol 400
  • organic esters, such as diethyl phthalate
  • oils/glycerides, such as fractionated coconut oil.

In general, only water-miscible plasticizers can be used for aqueous-based spray systems.
• Colourants
  • Any permitted colourants in a film coat formula are invariably water-insoluble colours (pigments). Pigments have certain advantages over water-soluble colours: they tend to be more chemically stable towards light, provide better opacity and covering power, and optimize the impermeability of a given film to water vapour.

Examples of colourants are:
  • iron oxide pigments
  • titanium dioxide
  • aluminium Lakes.
Solvents

Modern techniques now rely on water as a polymer solvent because of the significant drawbacks that readily became apparent with the use of organic solvents. The disadvantages of organic solvents for the process:

• 1. Environmental: the venting of untreated organic solvent vapor into the atmosphere is ecologically unacceptable, and efficient solvent vapor removal from gaseous effluent is expensive.
• 2. **Safety**: organic solvents provide explosion, fire and toxic hazards to plant operators.

• 3. **Financial**: the use of organic solvents necessitates the building of flame- and explosion-proof facilities. Ingredient cost is also comparatively high, and the associated costs of storage and quality control must also be taken in to consideration.

• 4. **Solvent residues**: for a given process the amount of residual organic solvent in the film must be investigated. With increasing regulatory pressure this will become an area for additional control in the future.
• Process details

• The vast majority of film-coated tablets are produced by a process which involves the atomization (spraying) of the coating solution or suspension on to a bed of tablets.

• Figure 2 shows one of the most widely used pieces of equipment for film coating,
Basic process requirements for film coating

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 to Provide the **latent heat of** evaporation of the solvent. This is particularly important with aqueous-based spraying.

4. **good exhaust facilities** to remove dust- and solvent-laden air.
• Ideal characteristics of film-coated tablets

• Film-coated tablets should display

  • an even coverage of film and colour.

  • no abiasion of tablet edges or crowns.

  • Logos and break lines should be distinct and not filled in.

  • The tablet must also be within specifications and any relevant compendial requirements.
Coating faults
These arise from two distinct causes:

1. **Processing**: for example, inadequate drying conditions will permit coating previously deposited on the tablet surface to stick against neighbouring tablets. When parted, this will reveal the original core surface underneath.

2. **Formulation faults**: film cracking or ‘bridging’ of break lines are examples of this type. After taking due account of the mechanical properties of the film, reformulation will almost certainly be successful in overcoming the problem.
SUGAR COATING

- Sugar coating is a multistage process and can be divided into the following steps:

1. Sealing of the tablet cores
2. Subcoating
3. Smoothing
4. Colouring
5. Polishing
6. Printing.
Initially the tablet cores to be sugar coated are sealed against the entry of water by the application of a water-impermeable polymer. Shellac has traditionally been used for this purpose and is indeed still used today, although more reliable materials, such as cellulose acetate phthalate and polyvinyl acetate phthalate, also find favor.
To attain the typically rounded profile of a sugar coated tablet, the sealed tablet core must be built up to gain the desired profile. This process of subcoating is usually performed by adding bulking agents such as calcium carbonate or talc to the applied sucrose solutions. A gum such as acacia is also added to the applied suspension.
• the subcoated tablets will have to be made smooth before the next stage can be commenced. This is accomplished by the application of a few coats of sucrose syrup.

• Nearly all sugar-coated tablets are coloured as appearance is usually considered to be of great importance with this dosage form. The pigments used are those permitted by the national legislation of the country where the products are to be marketed.
• After the colour-coating stage the tablets will require a separate polishing stage for them to acquire an acceptable appearance. Several methods can be used, but commonly beeswax and carnauba wax are used in the process.

• To facilitate identification sugar-coated tablets are usually printed with a manufacturer’s logo or code.
• Process details

• Typically tablets are sugar coated by a panning technique. The simplest form would be a traditional sugar-coating pan with a supply of drying air (preferably of variable temperature and thermostatically controlled) and a fan-assisted extract to remove dust- and moisture-laden air.

• Methods of applying the coating syrup include manually using a ladle, and, automatic control. In modern equipment some form of automatic control is available for the application of coating syrups.
• Ideal characteristics of sugar-coated tablets

• 1-tablets must comply with finished product specifications and any appropriate compendial requirements.

• 2- Sugar-coated tablets should ideally be of a perfectly smooth rounded contour with even colour coverage. Most manufacturers take advantage of the aesthetic appeal of a sugar-coated tablet and polish to a high gloss.

• 3-Any printing should be distinct, with no smudging or broken print.
Coating faults

These are usually associated with process defects, such as splitting of the coat on storage, caused by inadequate drying during the coating application.
• PRESS COATING

involves the compaction of granular material around an

already preformed core using compression equipment

similar to that used for the core itself,. 
press coating is used

- to separate chemically incompatible materials, one or more being placed in the core and the other(s) in the coating layer. However, there is still an interface contact left between the two layers. In cases where even this is important then the process of pre-coating can be taken one stage further. It is possible to apply two press coatings to a tablet core using suitable equipment. This equipment produces press-coated tablets with perfect separation between active core and coating, as the two can be separated by an inert middle layer.
FUNCTIONAL COATINGS

tablet coatings that perform a pharmaceutical function, such as conferring controlled or enteric release on the dosage form.

- Controlled-release coatings
  - Film coating provides an extremely effective way of conferring a controlled-release aspect to a tablet or, more usually, a multiparticulate system.
• After coating these particles are filled into hard gelatin shells, or occasionally compressed directly into tablets by a process which permits minimal rupture of the applied film.

• The coatings involved use polymers with restricted water solubility or permeability, and include ethylcellulose and modified acrylate derivatives.
Multiparticulates commonly referred to as ‘pellets’ or ‘beads’, find favor over conventional non-disintegrating tablets for controlled release use, owing to a number of factors:

1. Their small size (typically 0.7—2.00 mm) allows them to pass through the constricted pyloric sphincter and distribute themselves along the gastrointestinal tract. This tends to overcome the disadvantage that whole tablets have of a rather irregular passage through the gastrointestinal tract and consequent irregular absorption
2. Whole, non-disintegrating tablets can be liable to lodge in restrictions within the gastrointestinal tract, and this can lead to ulcerative damage to the gastric mucosa as the drug solution is leached out from the tablet. Because of their small size, this is not a problem with multiparticulates.

3. Should an individual bead or pellet fail and release all of its contents at once the patient would not be exposed to any undue risk. This is certainly not the case if a non-disintegrating tablet failed, when the consequences would potentially be serious.
Types of multiparticulate

Extruded/spheroflized granulates

Produced in modified granulating equipment, with the drug granulation extruded through a mesh or other device under pressure to form small granulates which are subsequently spheronized.

Non-pareils These are sucrose spheres which are coated with the drug plus an adhesive water-soluble polymer (Fig 28.4). After their formation and any necessary intermediate steps such as drying, they may be coated with the controlled-release coating.
Fig. Differences between multiparticulate types.
• Mechanisms of drug release from multiparticulates

• Diffusion

• On contact with the aqueous fluids of the gastrointestinal tract, water will enter the interior of the particle by diffusion. Dissolution of the drug will occur and drug solution will diffuse across the controlled-release coat to the exterior.
Erosion

Some coatings can be designed to erode gradually with time, thereby releasing the drug contained within the pellet.

- Osmosis

In allowing water to enter, an osmotic pressure can be built up within the interior of the pellet. Drug solution will be forced out of the pellet to the exterior.
Enteric coating

This technique is used to protect the tablet core from disintegration in the acid environment of the stomach for one or more of the following reasons:

1. Prevention of acid attack on active constituents unstable at low pH
2. To protect the stomach from the irritant effect of certain drugs
3. To facilitate absorption of a drug that is preferentially absorbed distal to the stomach
Polymer are insoluble in aqueous media at low pH, but as the pH rises they experience a sharp, well defined increase in solubility at a specific pH.

Enteric coating is possible using both sugar- and film-coating techniques.
• **Enteric film coating**

The enteric polymers (CAP, PVAP, suitable acrylic derivative) are capable of forming a direct film in a film-coating process. Sufficient weight of enteric polymer must be used to ensure an efficient enteric effect. This is normally two or three times that required for a simple film coating.
Enteric sugar coating

The sealing coat is modified to comprise one of the enteric polymers in sufficient quantity to pass the enteric test for disintegration. The subcoating and subsequent coating steps are then as for conventional sugar coating.
• **STANDARDS FOR COATED TABLETS**

1. **Film-coated tablets** must comply with the **uniformity of mass** test unless otherwise justified and authorized.

2. Film-coated tablets comply with the **disintegration test** for uncoated tablets except that the apparatus is operated for 30 minutes. The requirement for coated tablets other than film coated is modified to include a 60-minute operating time. Furthermore, the test may be repeated using 0.1 N HCl in the event that any tablets fail to disintegrate in the presence of water.