



Advanced Pharmaceutical Technology

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**Coating of tablets and
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 multiparticulate 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:
 1. Film coating
 2. Sugar coating
 3. Press coating.
- Of these, **film coating is the major technique**: virtually all new coated products introduced on to the market are film coated.
- **Sugar coating is the more traditional technology** and has seen no real developments in recent years. As a proportion of the total output of coated tablets on a global basis, though, it is **still of some economic importance**.

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.

Factors 2 and 3 aid **patient compliance** with dosage schemes.

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



- This is the more **modern and generally used** technology in tablet coating.
- Nearly all newly launched coated products are film coated rather than sugar coated, for the reasons given in Table 28.1.

Table 28.1 Major differences between sugar and film coating

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 'break' lines	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	Eight hours, but easily longer	1.5–2 hours
Functional coatings	Not usually possible apart from enteric coating	Easily adaptable for controlled release

Process description



Spraying The Tablets

- Film coating involves the deposition, usually by a spray method, of a thin film of polymer surrounding the tablet core.
- It is possible to use conventional panning equipment, but more usually specialized equipment is employed to take advantage of the **fast coating times** and **high degree of automation** possible.
- 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:
 1. Polymer
 2. Plasticizer
 3. Colourants
 4. Solvent.

Ideal characteristics of a film coating polymer

- **Solubility:**

1. 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.
2. However, where a **modified-release** action is required then a **polymer system of low water solubility or permeability** will be chosen.

- **Viscosity:**
- In general, **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:**
- The particular 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

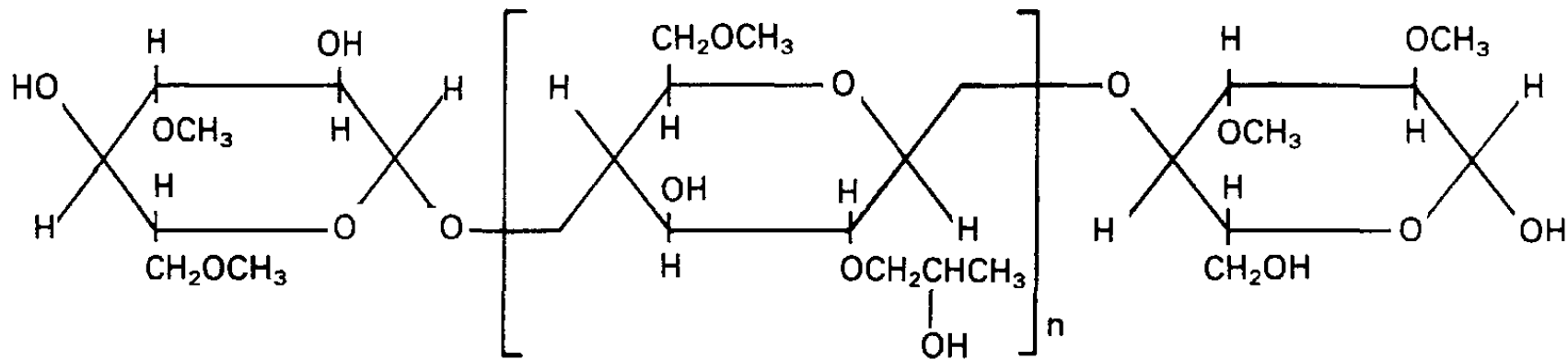
1. Cellulose derivatives
2. Methacrylate amino ester copolymers
3. Ethylcellulose and the ammonio methacrylate copolymers

Cellulose derivatives

- Most are substituted **ethers of cellulose**.
- **Hydroxypropyl methylcellulose** is the most widely used of the cellulosic polymers:
 1. It is **soluble in aqueous** media
 2. forms films which are **mechanically tough** and relatively **easy to apply**.
 3. The **resultant film** can be **clear or coloured** with permitted pigments.
- Other cellulosic derivatives used in film coating are:
 1. Methylcellulose
 2. Hydroxypropyl cellulose.

soluble





Hydroxypropyl methylcellulose

Methacrylate amino ester copolymers

- Basically these polymers are **insoluble in water below pH 4, but in neutral or alkaline media** the films achieve **solubility** by swelling and increased permeability.
- For **simple formulations the disintegration** of the coating can be optimized by the **incorporation of water-soluble materials and also by starches.**
- Chemically an example is the polymer poly(butylmethacrylate) (2-dimethylaminoethyl) methacrylate methylmethacrylate.

- For coatings designed to confer a **modified release** aspect to the final dosage form, **more water-insoluble polymers are used.**



- These include **ethylcellulose** and the **ammonio methacrylate copolymers.**
- Yet another group of polymers is designed to provide an **enteric protection to the dosage form.** This effect is achieved by a pH selectivity of the polymer where it is insoluble at the low pH environment of the stomach yet becomes soluble as the higher pH of the duodenum and the distal portion of the gastrointestinal system is reached.

Aqueous polymer dispersions

- 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.**
- It is generally accepted that the mechanism by which polymers exert their action is for them to **interpose themselves on a molecular scale between the polymer strands.**
- In doing so **they permit these strands to move more freely and allow the polymer to act in a more pliable fashion.**



- **Examples of plasticizers are:**
 1. polyols, such as polyethylene glycol 400
 2. organic esters, such as diethyl phthalate
 3. 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:
 1. they tend to be more chemically stable towards light
 2. provide better opacity and covering power
 3. optimize the impermeability of a given film to water vapour.
- Examples of colourants are:
 1. iron oxide pigments
 2. titanium dioxide
 3. aluminium Lakes.

Solvents

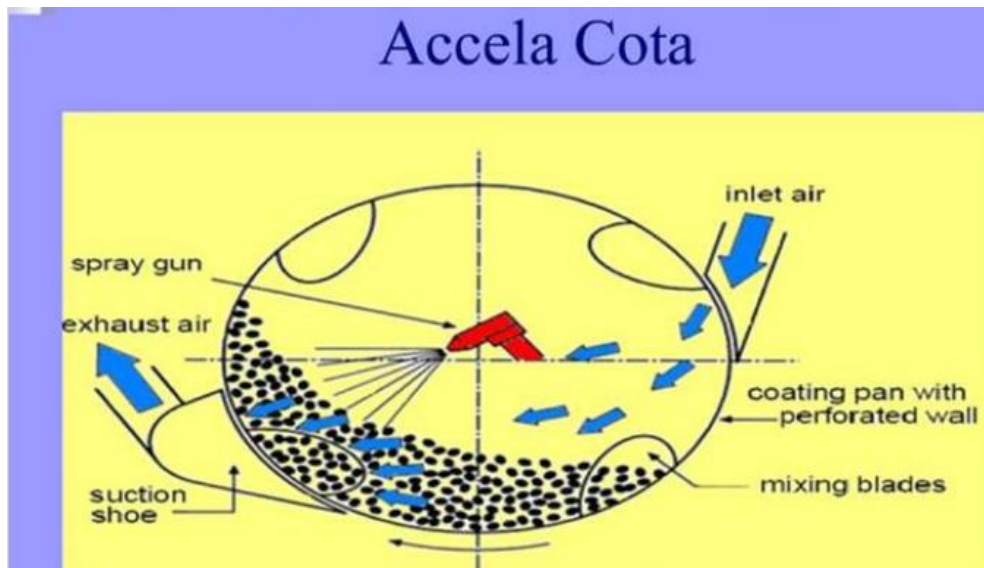
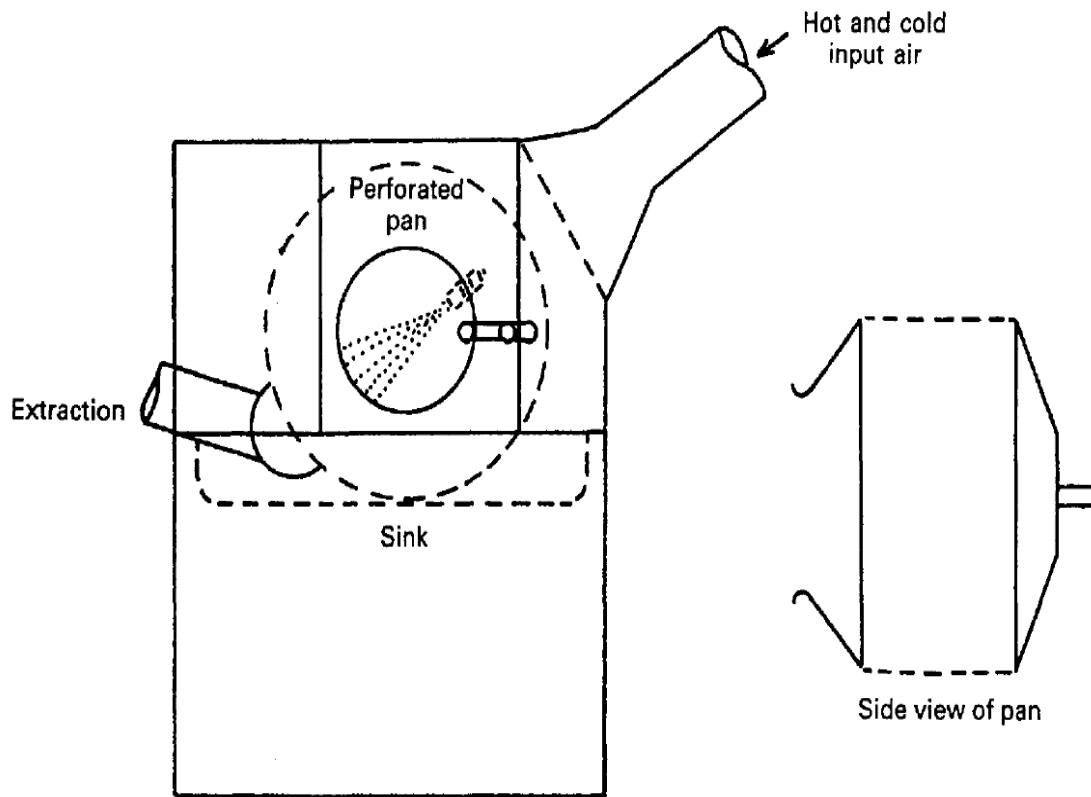
- After the early development of film coating in the 1950s the **polymers used were** invariably **dissolved in an organic solvent.**
- **Modern techniques** now rely on **water** as a solvent because of the significant drawbacks that readily became apparent with the use of organic solvents.

- **The disadvantages of organic solvents:**
- **Environmental:** the venting of untreated organic solvent vapour into the atmosphere is ecologically unacceptable, and efficient solvent vapour removal from gaseous effluent is expensive.
- **Safety:** organic solvents provide explosion, fire and toxic hazards to plant operators.
- **Financial:**
 1. the use of organic solvents necessitates the building of flame- and explosion-proof facilities.
 2. Ingredient cost is also comparatively high,
 3. the associated costs of storage and quality control.
- **Solvent residues:** for a given process the amount of residual organic solvent in the film must be investigated.

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.
- Some examples of equipment suitable for film coating include:
 1. Accela Cota - Manesty Machines, Liverpool, UK
 2. Hi-Coater - Freund Company, Japan
 3. Driacoater - Driam Metallprodukt GmbH, Germany
 4. HTF/150-GS, Italy
 5. IDA - Dumoulin, France.

- Examples of units that function on a fluidized-bed principle include:
 1. Aeromatic-Fielder, Switzerland and UK
 2. Glatt AG, Switzerland and Germany



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:**
 - Spray coating relies upon each core passing through the area of spraying. This is distinct from sugar coating, where each application is spread from tablet to tablet prior to drying;
- 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

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

Coating faults

- These arise from two distinct **causes**:
- **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.
- **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

End of today's lecture

Any
Questions



SUGAR COATING



- Sugar coating may be considered the **traditional method** of coating tablets.
- It involves the **successive application of sucrose-based solutions to tablet cores** in suitable coating equipment.
- Conventional panning equipment with **manual application of syrup has been extensively used**, although more specialized equipment and automated methods are now making an impact on the process.

Stages involved in the production of sugar-coated tablets

- 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.



Sealing

- 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 a great deal today, although **more reliable materials**, such as **cellulose acetate phthalate** and **polyvinyl acetate phthalate**, also **find favour**.

Subcoating

- To attain the typically rounded profile of a sugar coated tablet the sealed tablet core must be built up to gain the desired profile.

critical operation can have a marked effect on tablet quality.

- 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.

Smoothing

- After the correct profile has been obtained the subcoated tablets will almost certainly have a **rough surface**, which 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**.

Colouring

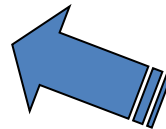
- Nearly all sugar-coated tablets are coloured, as **aesthetic appearance** is usually considered to be of great importance with this dosage form.
- The **pigments used** are those permitted by the national legislation of the country where the products are to be marketed.

Polishing

- 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.

Printing

- To facilitate identification sugar-coated tablets are usually printed with a manufacturer's logo or code.
- The printing process used is an offset gravure in conjunction with special edible inks,



safe to eat

although the inkjet process is starting to make an impact.

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
 1. manually using a ladle,
 2. automatic control.
- In modern equipment some form of automatic control is available for the application of coating syrups.
- **In general, the equipment listed under film coating can, with suitable modification, be used for sugar-coating techniques.**

Ideal characteristics of sugar-coated tablets

1. First the 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

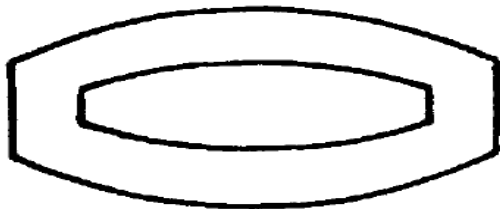
- These are usually associated with process defects, such as **splitting of the coat** on storage, caused by inadequate drying during the coating application.



PRESS COATING



- The technology of press coating differs radically from the previously described film- and sugarcoating techniques.
- Press coating **involves the compaction of granular material around an already preformed core using compressing equipment** similar to that used for the core itself, e.g. **Manesty Drycota**.
- Today press coating is used mainly **to separate chemically incompatible materials**, one or more being placed in the core and the other(s) in the coating layer.



Compaction of granular material around an already preformed core.



- However, there is still an **interface of contact** left between the two layers.
- In cases where even this is important then the process of press coating can be taken one stage further.



- It is possible to apply two press coatings to a tablet core using suitable equipment, e.g. **Manesty Bicota**.
- 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**.

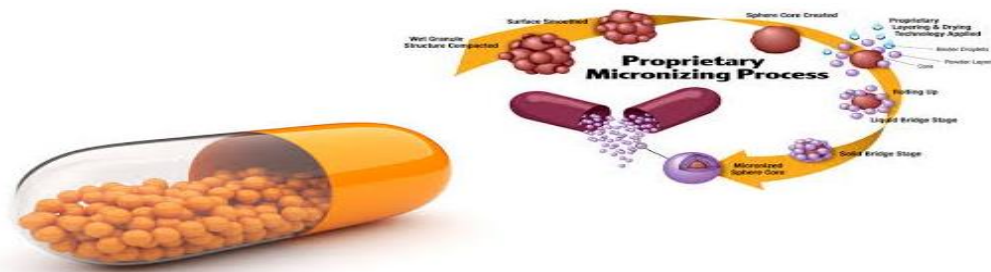
- The formulation and processing of the coating layer **requires some care.**
- Large or irregularly sized agglomerates of granules will **cause the core to tilt** in the second die used for compression of the coating.
- Thus there is the possibility of an incomplete coating, with the core being visible at the tablet surface.
- The **disadvantages** of the process arise from the relative complexities of the mechanism used in the compressing equipment.

FUNCTIONAL COATINGS

- All the coatings described above have been designed as a taste mask, as an identification aid, or indeed for many of the reasons previously discussed for coating tablets.
- There are, however, 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 sorption. These include **ethylcellulose**.



- **Multiparticulates, commonly referred to as 'pellets' or 'beads'**, find favour 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.**

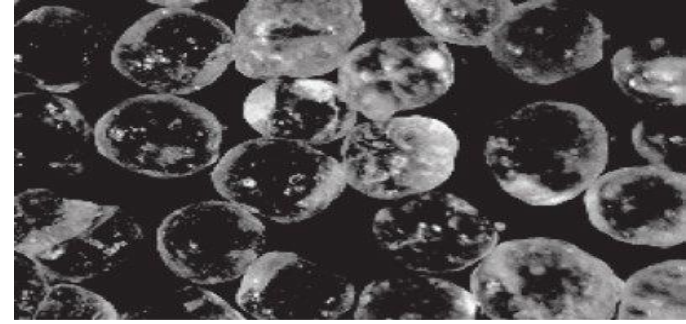
- This is certainly not the case if a non-disintegrating tablet failed, when the consequences would potentially be serious.

Types of multiparticulate

- Drug crystals
- Irregular granules
- Spheronized granulates
- Drug-loaded Non-pareils
- Mini tablets

Drug crystals

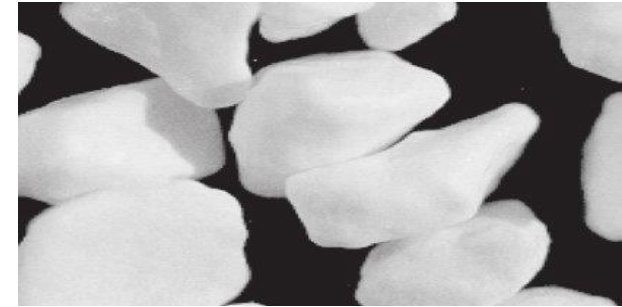
Drug crystals, as long as they are of the appropriate size and shape (elongated or acicular crystals should be avoided), can be directly coated with a modified release film coating.



Irregular granules

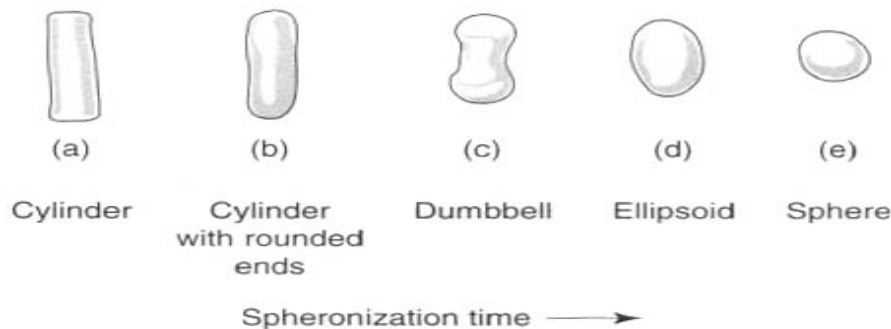
Granulates, such as those regularly used to prepare tablets, can be film coated but

variation in particle size distribution (from batch to batch), as well as the **angular nature of such particles**, can make it difficult to achieve uniform coating thickness around each particle.




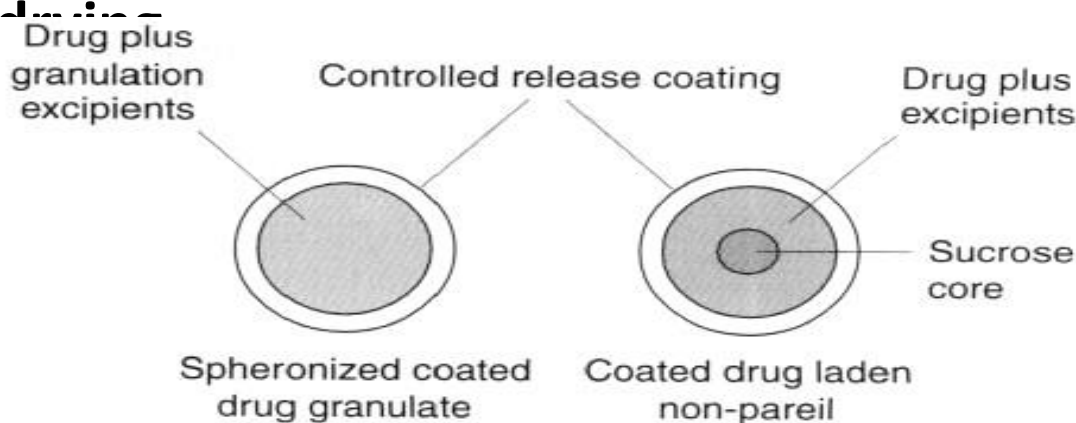
Spheronized granulates

- Spheroidal particles simplify the coating process.
- These are 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



Drug-loaded Non-pareils

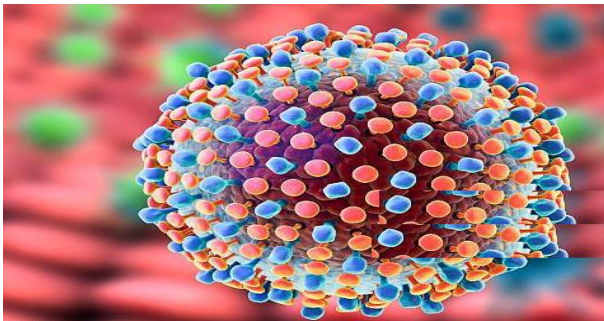
- Another process  producing spheroidal particles involves the application of drug to the surface of placebo pellets, often called *nonpareils*. **spherical particles about 1 mm** in diameter consisting primarily of **sucrose** and **starch**, may also be prepared using **microcrystalline cellulose**.
- **The spheres which are coated with the drug plus an adhesive yet water soluble polymer.**
- After their formation and any necessary intermediate steps such as **granulation**
- they may be **coated**.



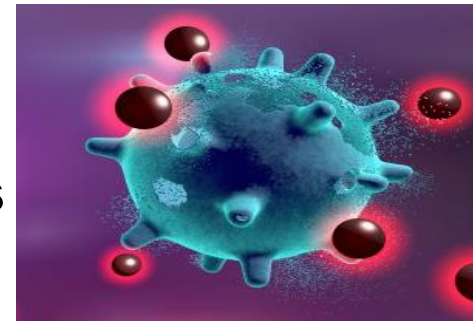
- **Application** of the drug uses either:



1. **A powder-dosing technique** involving alternate dosing of powder (containing the drug substance) and binder liquid onto the surface of the nonpareils **until the required dose of drug has been achieved.**
2. **Spray application of drug**, either suspended or dissolved in a suitable solvent (usually water) containing also a polymer binder (such as **hydroxypropyl methylcellulose or polyvinyl pyrrolidone**) onto the surface of the nonpareils.



Nano- carrier for vaccines



Mini tablets



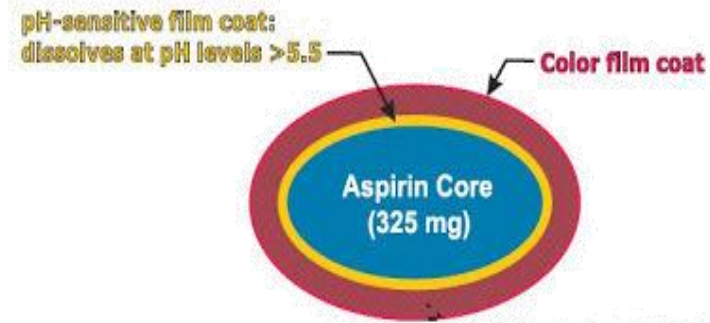
- Many of the other types of multiparticulates described so far suffer from two potential batchwise drawbacks, namely:
 1. **variation in particle size distribution**
 2. **variation in particle shape and surface roughness.**
- Such variability can **result in variable coating thickness** and thus product performance.

This problem can be **overcome** by using mini compressed tablets (typically in the size range of 1–2 mm) produced using a modification of traditional tableting processes.

Mechanisms of drug release from multiparticulates

- Discussed earlier.
 - *Diffusion*
 - *Dissolution*
 - *Erosion*
 - *Osmosis*

Enteric coating

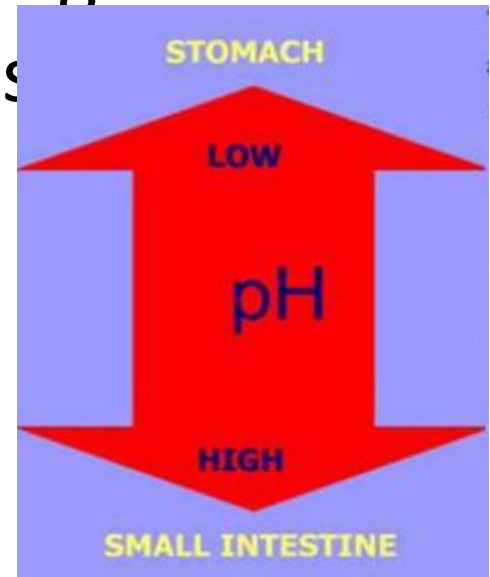


This technique is used to protect the tablet core from disintegration in the acid environment of the stomach for one or more of the following reasons:

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.

- The following **polymers** are among those commonly used for the purposes of coating:

1. Cellulose acetate phthalate
2. Polyvinyl acetate phthalate
3. Suitable acrylic derivatives.



- Because they **possess free carboxylic acid groups** on the polymer backbone, **they exhibit a differential pH solubility profile.**
- They are almost **insoluble in aqueous media at low pH**, but **as the pH rises** they experience a sharp, well denned **increase in solubility** at a specific pH, **e.g. pH 5.2 for cellulose acetate phthalate.**
- **Enteric coating is possible using both sugar- and film-coating techniques.**

Enteric film coating

- The enteric polymers listed 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

- The European Pharmacopoeia has similar requirements for coated and uncoated tablets, the differences being:
 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.**

End of today's lecture

Any
Questions

