24. Coating of Pharmaceutical Dosage Forms

The coating of pharmaceutical solid dosage forms, especially the surface of tablets, has been practiced for about 150 years. In many cases the coating is a commonly used procedure, although it is applied on a functionally completed dosage form and requires an additional expense. Benefits of the coating process include:

• Increases stability by protecting the active substance from external influences such as air, humidity and light.
• Masks the unpleasant taste and smell.
• Allows the patient to swallow the medicine more easily.
• Makes it easy to recognize the product during manufacturing or during patient use.
• Minimizes the risk of interference between incompatible components.
• Provides mechanical integrity of the product.
• Enteric coating allows modification of active substance release in the form of repeated action and controlled release.

Different methods can be applied in coating the pharmaceutical solid dosage forms according to the core to be coated and the coating material to be used. For example; sugar coating, film coating, hot melt coating, compression coating and so on.

The structure to which the coating is applied is called the core or substrate. The core types may be crystals, various types of granules, micropellets, tablets, hard gelatin capsules, and soft gelatin capsules. The features expected from the core and the points to note are:

• The core should be resistant to rotation, friction, impact during coating and should be of appropriate hardness. This stiffness should not affect the biological function of the dosage form in reverse.

• If the tablets are to be used as a core, they must be convex and must be compressed with deep concave punches to prevent them from sticking to the top, to ensure that the corners and edges are covered properly.

• Adhesion of the coating layer requires that the core surfaces are smooth (close to the spherical shape of the particle to be coated in the particulate system) and do not contain dust.

• Determine whether the materials forming the core are heat sensitive due to the heat applied in the process.

• The interaction between the core and the coating must be investigated.

25.1 Film Coating

Film coating is the formation of a polymer-based thin layer on a suitable core. The resulting film coating has a thickness of 20-200 μm. The main advantages of the film coating are:

• Reduction in the amount of coating applied,
• Faster processing,
• Process efficiency and increased yield,
• Increased flexibility in the optimization of formulations as a result of the diversity of coating materials and systems,
• A simpler operation, also provided by automation,
• Applicability to various pharmaceutical forms (such as tablets, active substance crystals, granules, capsules, inert beads, nonpareils, powders).

The film coating of pharmaceutical products is divided into two groups in terms of their effect on the active substance release:

1- Functional film coating: Coatings applied to modify active substance release. For example; enteric coatings, controlled release coatings (membrane-depot systems and osmotic controlled systems).
2- Non-functional film coating: Coatings applied to improve the appearance of the product, to facilitate swallowing, to mask the taste or to increase the stability.

The major components of the film coating formulations are polymers, plasticizers, solvents and coloring agents.

Polymers: Depending on their solubility, solutions are used at 10-15% concentration in water or organic solvents. A more recent approach is the use of water-based dispersions of water-insoluble polymers to counteract the environmental and human health side effects of organic solvents. These dispersions contain polymer at 20-30% concentration and are semi-colloidal with particle diameters of 1-1000 nm, they are present in the form of ready-made dispersions (latexes and pseudolates) in milk appearance or micronized powder which can be dispersed in water afterwards.

Cellulose derivatives (HPMC, HPC, MC, EC, Na-CMC), vinyl polymers (PVP) and acrylic polymers (Eudragit E and NE etc.) can be used for film coating. For the enteric coating, acid esters of the above polymers (CAP, CAT, PVAP, HPMC-P, HPMCAS, Eudragit L and S etc.) are used. Acrylic polymers (such as Eudragit RS and RL) and EC can be used for controlled release.

Plasticizers: They are used to increase the flexibility of the coating, to reduce the risk of film breakage and to increase adherence to the filament core. Polymers should be compatible and should not be volatile. Examples of plasticizers are glycerin, propylene glycol, PEGs, triacetin, diethylphthalate and acetylated monoglycerides.

Solvents: Solvents, alcohols, ketones, chlorinated hydrocarbons and suds used in film coating. Solvents are an aid in applying the polymers to the core. A good interaction between the polymers and the solvents is required in terms of the formation of the film coating and the mechanical properties.

As coloring agents, pigments and especially lacquers are preferred over water-soluble paints.

Film coating formulations are applied by spray-atomization techniques. Initially, conventional coating pans were used, but factors such as inadequate drying conditions, the need for fully closed systems, especially when using organic solvents, and the inability to mix the cores, have led to the design and use of modified coating pans to eliminate these deficiencies (Pellegrini Pan, Glatt Pan, Accela-Cota as). Although the fluidized-bed method has been developed for the rapid drying of powders / granules and has been a used system, the Wurster process has been widely used for the last 20 years especially for the coating of tablets as well as particulate materials (Fig. 25.1). The three basic systems used in this method are:

• Top spray granulator
• Bottom spray, Wurster column
• Tangential spray, rotor processor

The choice of these systems depends on the desired function and structure of the coating to be applied.

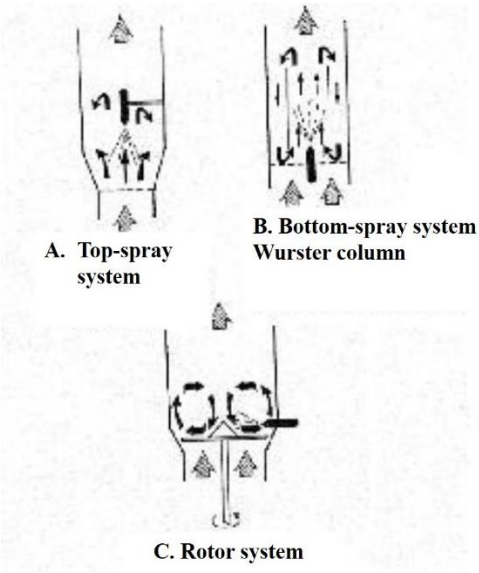

Figure 25.1. Schematic presentation of 3 basic processes applied in film coating by fluid bed method *[Limmer, D. (ed.), Remington:The Science and Practice of Pharmacy, 20th Ed., pg.894-902, 2000, Lippincott Williams & Wilkins, Baltimore]*.

25.2. Sugar Coatings of Tablets, Production of Dragee

The sugar coating process is perhaps the earliest pharmaceutical process that has taken its source from the confectionery industry and is still being applied. Despite the modernization and automation in recent years, this process is considered as an art than a science. The process steps and the complexity of the formulations to be applied make it difficult to complete the transition to automation. However, it is still applied as a process with high repeatability in terms of quality and performance, in line with Good Manufacturing Practice (GMP) requirements.

At the end of the process, the main sugar coating material used is sucrose because it is non-sticky, dry, smooth and provides high quality coverage. Other materials are sugar alcohols such as maltitol, sorbitol, and xylitol, which have a lower glucose, isomalt, lactose-sucrose mix and lower insulin load than other sugars.

Other materials are fillers ($CaCO_3$, starch, talc, TiO_2, $CaSO_4$.$2H_2O$, $CaHPO_4.2H_2O$, Ca-lactate.$5H_2O$) such as binders (such as acacia gum, carboxymethyl starch, cellulose ethers, gelatin, PVA, PVP, Na-alginate) which increase the elasticity and resistance of the coating. Lubricants such as talc are used to reduce friction between the coated cores and to prevent dust formation during the drying phase. Thickening agents to prevent sedimentation of the coating suspension; the surfactant may be introduced into the coating formulation as a wetting and dispersing agent. Color, taste and fragrance materials are other adjuncts used to increase the usability of the product.

The coating process is a repetitive application of the process steps. The processes performed when forming layer is;

• application of the coating formulation in portions on the cores,
• waiting for a while when the cores are in motion for homogenous distribution of the applied portion,
• drying for crystallization of the layer,

A sugar coating process involves the sequential formation of five layers:

1) Protective coating (sealing): In order to provide physical / chemical stability of the core material in contact with aqueous coating formulations and to prevent interaction of some core components with

coating, the polymer-based materials are applied several times in the form of pouring or spraying. Solutions of polymers such as shellac, zein, HPMC, PVP, PVAP and CAP in organic solvents in concentrations of 15-30% w / v are used for this purpose.

2-Subcoating: It provides rounding of tablet edges and causes 50-100% increase of tablet weight. The subcoating process is repeated until the tablet edges are rolled and the desired thickness is reached, in the order of application and drying of the binder solution and the dusting mixture. Drying speed is a critical parameter that affects the plastic properties of the coating. Initial short drying periods require a longer period, especially towards the end of the process.

3- Smoothing: In order to cover the roughness of the tablet surface formed during the undercoating, it is applied as a suspension in filler such as $CaCO_3$, starch and talc in syrup solution. A small amount of colorant can be added to this suspension for a good color base.

4- Color coating: Mixtures of the coloring agents in the syrup solution are applied.
It is also possible that the formulations of steps 2, 3 and 4 are combined into a single formulation. This is called "uniform coating".

5 - Polishing: The application of waxes (such as carnauba wax) that are dusted with sugar-coated tablets in coating pans or canvas coated lacquers, or warm solutions in organic solvents of these waxes.
Coating pans are used for the sugar coating process. Typically in such a coating pan there are systems used to provide the air to dry the tablets, to remove moisture and dust. Figure 25.2 shows a conventional coating pan. With the modification of these pans, many coating types of equipments have been created.

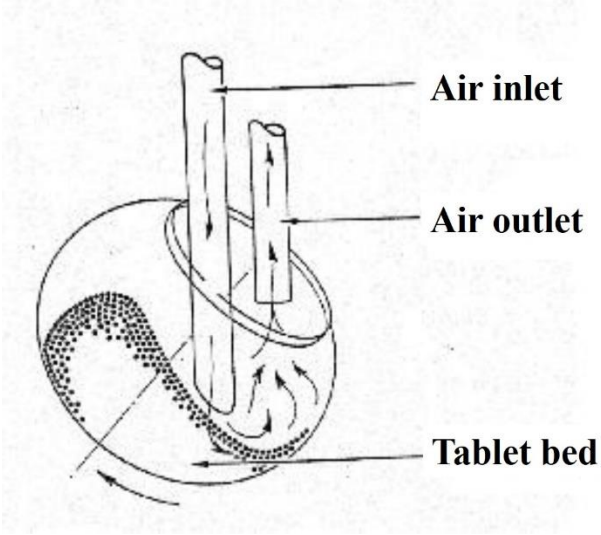

Figure 25.2. The appearance of a classic coating pan [Lachman, L., et al., The Theory and Practice of Industrial Pharmacy, 3rd Ed., Pg.346-373, 1986, Lea Febiger, Philadelphia].

25.3. Controls of Coated Dosage Forms

1. Color, appearance,
2. Disintegration test (EP5),
3. Dissolution test (EP5),
4. Content uniformity (EP5),
5. Mass homogeneity (EP5),
6. Microbial quality determination (EP5).

Some of the additional tests that can be applied to film-coated dosage forms are:

7. Determine the swelling degree of the coating,
8. pH-dependent dissolution behavior,

9. The determination of solvent residues,
10. Examination of surface appearance,
11. Determination of film adhesion.

Practice 25.1.

1. Protective coating

Cellulose acetate phthalate (CAP)		10.0 g
Propylene glycol		3.0 g
Methylene chloride		48.0 ml
Alcohol	q.s.	100.0 ml
	Prepare 20 ml.	

Preparation:
CAP is dissolved in methylene chloride. Propylene glycol is added and mixed then completed to 100 ml with alcohol.

Application:
1. Weigh 60 g tablet and put in a pan, heat to 30 ° C while rotating.
2. The protective coating solution is sprayed onto the rotating tablets 3 times (with about 1 ml per application). Allow 5-10 minutes between applications for drying tablets. If the tablets stick to each other, a sufficient amount of talc is dusted to prevent this. Care is taken to disperse the solution homogeneously. The temperature is kept at 30 ° C during application.

2. Subcoating

Subcoating solution		
Gelatin		2.0 g
Acacia gum		5.0 g
Sugar		50.0 g
Distile water	q.s.	100.0 g
	Prepare 40 g.	

Preparation:
Sugar is dissolved in half of the required water. Gelatin and acacia gum are swelled in ¼ portions of cold water and are added into the hot sugar solution. Care should be taken that air bubbles do not form during mixing. The mixture is brought to the desired weight with water. This solution is covered with a watch glass on a water bath and kept at 50 ° C.
Dusting mix of the subcoating

Titanium dioxide	1.0 g
Sugar (powdered)	38.0 g
Talc	61.0 g
Prepare at 1/10 ratio.	

Preparation:
The powders are mixed and sieved from a thin sieve.

Application:
1. Add 1.5 ml of warm subcoating solution homogeneously to the tablets to which the protective coating has been applied in the rotating pan without applying heat and air. In subsequent applications a total of 10 coatings, 1 ml each time, is applied. Allow at least 5 minutes between each application to ensure adequate drying. If there is adhesion between the tablets, a dusting mix is dispensed to the tablets to provide free rotation and to prevent sticking.

2. After the application of the final coating, air is introduced into the tub until the tablets dry (30 - 40 ° C). If necessary drying can be carried out in a drying cabinet at 40 ° C.

3. Smoothing coating

Calcium carbonate	10.0 g
Corn starch	17.0 g
Syrup (50% w / w sugar)	73.0 g
Prepare 50 g.	

Preparation:
Calcium carbonate and corn starch are mixed in mortar. The syrup is gradually added and the powders are dispersed homogeneously in this syrup. This resulting suspension should not be heated.

Application:
1. Before starting, the dust adhering to the pan wall is cleaned. Tablets with a subcoating but not a proper appearance are placed in the pan. The pan is rotated and the temperature of the tablets is brought to about 50 ° C.
2. Apply a sufficient amount of coating suspension (15-25 drops) onto the tablets. As this dispersion dries faster, care must be taken to disperse it rapidly and uniformly. When the tablets are dried and a slightly dusty surface appearance is observed, redispersing is applied. In this way, 5-15 coatings are applied until the tablet surfaces are smooth.

4. Color coating

Coloring matter	q.s.
Sugar (powdered)	85.0 g
Distiled water q.s.	100.0 ml

Preparation:
Sugar is dissolved in distilled water by heating and the coloring agent is added.

Application:
1. Rotate the pan and heat the tablets to 50^{o}C; store at this temperature.
2. Color coating solution is applied. The surface of the tablets is again color coated before starting to become slightly dull. In this way coating is applied 5 times. (For a good color base, the coloring matter can also be added to the smoothing coating dispersion).
3. Heat application is terminated and 3-4 coatings are applied. Each coating is applied just before the surfaces of the tablets do not become dull and become dusty.
4. The pan is stopped after the last coating and is operated intermittently in every few minutes. The tablets are left in the pan and left overnight for slow drying.

5. Polishing

The painted cores are put into the polishing pan and then the operation is started. Powdered carnauba wax or wax is added. Processing is continued until proper brightness is obtained.

Questions
1. Write down the amounts of the powder mixture and each of the coating mixture you have used.
2. Weigh 10 tablets then calculate average weight, standard deviation and relative standard deviations.
3. Weigh 10 samples from the dragees you have prepared, then calculate average weight, standard deviation and relative standard deviations.
4. Find the average weight of the cores and coatings and calculate how much of those values correspond to the percentages of the dragees.
5. Write your suggestions while preparing dragee.