Tablet coating

Lecture 10

DEVELOPMENT OF FILM COATING FORMULATIONS

The development of film coating formulations depend on the answer to the following questions:

1. What is the purpose of coating (either masking taste, odor or color, or control release of drug)?
2. What tab. size, shape or color constraints must be placed on the developmental work?

- In pharmaceutical industry, the colour, shape and size of the final coated tablet is important for marketing and these properties have a significant influence on the decisions.

DEVELOPMENT OF FILM COATING FORMULATIONS

- Film formulations can be preliminarily tested by spraying or casting films. Through the preparation of a series of films with slight changes in formula ingredients, it is possible to eliminate the obvious physical incompatibilities and poor film combinations rather quickly.
- The physical appearance of these films can provide evidence of potential colorant or opaquant separation. Lack of colour uniformity within the film could suggest that the insoluble additives have not been properly suspended or that some interaction has occurred between the ingredients.

DEVELOPMENT OF FILM COATING FORMULATIONS

In addition, films can be submitted for the following tests:

1. **Water vapor permeability**

If the coating is used to provide some physical protection for a tab. containing a water unstable drug; then the film's water vapor permeability should be assessed.

2. **Film tensile strength**

This test is applied by putting on a force at constant rate on film strips to evaluate their elasticity and tensile strength/breaking stress.

Uses: evaluate conc. of plasticizers or additives

Ex: coating composition that yield brittle films must be plasticized to obtain more flexible films that is acceptable for tab. coating.

Coated tab. evaluations

This involves studying the film and film-tab. surface interaction by the following test methods:

a. **Adhesion test** (using tensile-strength tester) to measure the force required to peel film from tab. surface.
b. **Diametral crushing strength** (using tab. hardness tester) to compare resistance of uncoated and film coated tab. to crushing.
c. **The rate of tab. disintegration and/or dissolution** unless the coating is used to control release of drug, it should have minimum effect on tab. disintegration or dissolution.

d. **Stability studies** to determine the effect of temp. and humidity changes on the film (by applying elevated humidity on film tab. and measure tab. wt. gain to get information on the protection provided by the film).

e. **Investigation of film surface roughness, hardness and color** either by visual inspection or using instruments (a practical qualitative measure of the resistant of a coated tablet to abrasion can be obtained by rubbing the coated tab. on a white sheet of paper. Resilient films remain intact and no color is transferred to the paper; but very soft film coatings are readily erased from the tab. surface to the paper).

Coating formula optimization

Optimization known as minor modification in a basic formula which has been several benefits like:

a. improving adhesion of coat to core.
b. increasing coating hardness.
c. improving any property of the coating that the formulator deems deficient.

Ex: changes in polymer to plasticizer ratio or addition of different plasticizers or polymers are important modifications.

Materials used in film coating

No commercially available material fulfills all requirements of an ideal coating materials but an **ideal film coating materials should have the following attributes:**

1. Solubility in solvent of choice.
2. Solubility for intended use like freely soluble in water, slow water solubility or pH-dependent solubility (enteric coated)
3. Produce elegant looking product.
4. Stability with aging, heat, light, moisture and air.
5. No color, taste or odor.
6. Compatibility with coating solution additives.
7. No toxicity and no pharmacologic activity and easily applicable to tab.
8. Resistance to cracking.
9. No bridging or filling of the debossed tab. surfaces by the film former
10. Ease of printing on high speed equipment.

Film formers (non-enteric and enteric materials)

Non-enteric materials

Most common polymers used for film coating:

Hydroxypropylmethylcellulose, USP (HPMC)

This polymer is prepared by reacting alkali-treated cellulose first with methyl chloride to introduce methoxy groups and then with propylene oxide to introduce propylene glycol ether groups. The resulting products are commercially available in different viscosity grades.

Best used in: air suspension and pan-spray coating systems

Widely spread due to:

1. Solubility in GI fluid and in organic & aq. solvents.
2. Non-interference with tab. disintegration and drug availability.
3. Flexibility, chip resistance, and absence of taste or odor.
4. Stability in the presence of heat, light, air and reasonable levels of moisture.
5. Ability to Incorporate color and other additives into the film without difficulty.

- **HPMC closely approaches the desired properties of an ideal polymer for film coating.**

- **When used alone:** has the tendency to bridge or fill debossed tab. surfaces.
- **Mixture of HPMC with other polymers or plasticizers:** eliminate bridging or filling problems.

Ethylcellulose, NF (EC)

Manufactured by the reaction of ethyl chloride or ethyl sulfate with cellulose dissolved in sodium hydroxide. Different viscosity grades are available depending on degree of ethoxy substitution.

Properties:

1. Completely insoluble in H_2O and GI fluids and thus cannot be used alone for tablet coating.
2. It is usually combined with water soluble additives, e.g. (HPMC) to prepare films with reduced water solubility properties (S.R) to coat tab. and fine particles.
3. Soluble in organic solvents.
4. Non-toxic, odorless, colorless.
5. Stable to most environmental conditions.

- Unplasticized EC films are brittle and require film modifiers to obtain an acceptable film formulation.

NEW TYPE: developed aq. dispersion of EC **(Aquacoat)**

Hydroxypropylcellulose

Note: prepared from treatment of cellulose with sodium hydroxide followed by reaction with Propylene oxide.

Properties:

1. Soluble in water below 40°C (insoluble >45°C), GI fluids and many polar organic solvents.
2. Tacky as dries from solution system, so desirable for **subcoat** but not for color or gloss coat.
3. Producing very flexible films.
4. Not used alone but used in combination with other polymers to improve film characteristics.

Povidone, USP

Synthetic polymer, have 4 viscosity grades (K-15, K-30, K-60, K-90) and these values represent variety in M.wt respectively.

USES:

1. **As a tab. coating and as a binder (mostly used in industry is k-30)**
2. **Improve dispersion of colorants in coating solutions to get a more uniformly colored film.**

Properties and modification:

a. Soluble in organic solvents, water, GI and intestinal fluids but can be modified by cross-linked with other materials to produce films with enteric properties.

b. Extremely tacky and can be modified by using plasticizers, suspended powder or other polymers.

Sodium carboxymethylcellulose, USP (Na CMC)

Available in low, medium, high, and extra high viscosity grades.

Properties:

1. Easily dispersed in water to form colloidal solutions but insoluble in organic solvents.
2. Films prepared are brittle.
3. Partially dried films are tacky but modified with additives.

Polyethylene glycols (PEG)

Manufactured by the reaction of ethylene glycol with ethylene oxide in the presence of NaOH at elevated temp. and under pressure.

Uses:

1. In film coating a wide variety of M.wts are available. High M.wt. PEG (900-8000) are white, waxy solids used in combination with other polymers to modify film properties. Coats produced with high M.wt PEG can be (hard, smooth, tasteless and non-toxic but sensitive to elevated temp.).

2. As plasticizers for coating solution films when using low M.wt. (200-600) liquid PEGs.

Acrylate polymers (Eudragit)

Eudragit E (cationic polymer)

Freely soluble in gastric fluid up to pH 5 and expandable above pH 5.

Available as organic sol., solid material and aq. dispersion.

Eudragit RL and RS

Available only as organic sol. and solid materials.

Produce films for the delayed-action preparations similar to EC formulations.

Enteric materials

Important reasons for enteric coating are as follows:

1. Protect acid-labile drugs from gastric fluids e.g. certain antibiotics.
2. Prevent gastric distress or nausea due to irritation from drugs e.g. sodium salicylate.
3. Deliver drugs intended for local action in the intestines e.g. intestinal antiseptics delivered to their site of action in a concentrated form and bypass sys. absorption in the stomach.
4. Deliver drugs that are absorbed in small intestine in their concentrated form.
5. Provide delayed release for repeat-action tab.

Ideal enteric coating material properties:

1. Resistance to gastric fluids.
2. Ready permeability to intestinal fluids.
3. Compatibility with most coating solution components and the drug substrates.
4. Stability alone and in coating solutions, so it shouldn't change upon aging.
5. Formation of continuous (uninterrupted) film.
6. Non-toxicity.
7. Low cost.
8. Ease of application without specialized equipment.
9. Ability to be readily printed or to allow film to be applied to debossed tab.

Important notes:

Polymers or materials used to achieve enteric coating range from **water-resistant films to pH-sensitive materials** (some are digested or emulsified by intestinal juices and some slowly swell and fall apart when solvated).

Difficulties encountered in enteric formulations:

- **Passing the disintegration test:** enteric coated tab in gastric fluid show no disintegration, cracking or softening after 1 hr., while within 2 hr. period in intestinal fluids all tab disintegrate.
- **pH-sensitive materials:** acid labile drugs protected from pH 1-5 while the enteric polymer should dissolve or become permeable near and above pH 5 when approaching pylorus.
- **pH-independent solubility polymers:** which act by mechanical hydrophobicity to provide enteric effect, the film might so thick that if the dosage form travels too fast through the GIT, solubilization in intestinal fluids may never be achieved.

Cellulose acetate phthalate (CAP)

Disadvantages of CAP films:

1. **Dissolving only above pH 6** so delaying drug absorption.
2. **Hygroscopic and relatively permeable to moisture and gastric fluids.**
3. **Susceptible to hydrolytic removal** of phthalic and acetic acids so changing film properties.
4. **Brittle** and therefore formulated with adjuvants to achieve better enteric film.

- Development of aqueous enteric coating called **Aquateric** coating. It is composed of solid or semisolid polymer spheres of CAP with an average particle size of 0.2 micron.

Acrylate polymers (Eudrgit L and Eudragit S)

Properties:

1. **Both resistance to GI fluids and soluble at pH 6 and 7 respectively.**
2. **Eudragit L** (available as organic sol., solid or aq. dispersion) while **Eudragit S** (available as organic sol. and solid).

Hydroxypropyl methylcellulose phthalate, NF

Marketed as HPMCP 50, 55 and 55S (HP-50, HP-55, HP-55S)

Properties:

1. **Dissolves at a lower pH (5 to 5.5)** than CAP or acrylate copolymers, so this may result in higher bioavailability of some drugs.
2. **Quite stable** compared with CAP because of their absence of labile acetyl groups.

For general enteric preparations, HP-55 is recommended.

Polyvinyl acetate phthalate (PVAP)

Note: Made from esterification of partially hydrolyzed PVA with phthalic anhydride.

Properties: Similar to HP-55 in stability and pH-dependent solubility.

Solvents

Ideal solvent system considerations:

a. Dissolve or disperse the polymer system.
b. Easily disperse other coating sol. components into solvent system.
c. Colorless, tasteless, odorless, inexpensive, non-toxic, inert, and inflammable.
d. Rapid drying rate (the ability to coat 300kg load in 3-5 hrs.).
e. No environmental impact.
f. Small conc. of polymers (2-10%) shouldn't result in too viscous sol. sys. (> 300 cps), thus creating process problems.

E.g. of solvents used alone or in combination (water, ethanol, methanol, chloroform, acetone, methylene chloride, methylethyl ketone and isopropanol).

Plasticizers

The quality of a film can be modified using "internal" or "external" plasticizing techniques.

Internal: related to the chemical modification of the basic polymer that alters the physical properties of the polymer by controlling degree and type of substitution in addition to chain length.

External: act as additives to the coating solution formula and it can be either nonvolatile liquid or another polymer, which can be incorporated with the primary polymeric film former that changes flexibility, tensile strength or adhesion properties of film.

NOTE: To be effective it should be soluble in solvent sys. and partially soluble or miscible with film former.

E.g. aqueous coat required water soluble plasticizers like PEG (200, 400), PG and glycerin.

Organic coat required castor oil or span.

- The choice of plasticizer depends on the ability to solvate the polymer and alter polymer-polymer interactions (impart flexibility by relieving molecular rigidity).
- The type of plasticizer and its ratio to polymer can be optimized to achieve desired film properties.
- Viscosity of the plasticizer will affect film permeability, flexibility, solubility, taste, and its toxicity, compatibility with other coating solution components and stability of the film.

Conc. of plasticizer (1-50%) it depends on: Polymer chemistry, method of application and the presence of additives.

Colorants

Either soluble in solvents or suspended as insoluble powders to achieve distinctive color and elegance to a dosage form:

1. **Suspended insoluble powders:** using fine powder colorants (<10 microns) to achieve proper distribution in coating solution. In general, the suspended colorants must be milled in the coating solution to attain a uniform dispersion of the colorants.

E.g. FD&C (Food Drug and Cosmetic) or D&C (Drug and Cosmetic) colorants. These are synthetic dyes or lakes of dyes.. **Lakes have become the colorants of choice for sugar or film coating as more reproducible tablet colors are attainable. Lakes contain 10-30% of the pure dye content.**

2. **Coating solution:** used without milling like Opalux (sugar coat), Opaspray (film coat) and opadry (complete film coat conc.).

E.g. inorganic materials (iron oxide) and natural colorants (chlorophyll).

Conc. of colorants in coating solution depends on:

Color shade desired, type of dye and conc. of opaquant-extenders. Very light shade uses (<0.01%) while dark color uses (>2%), lakes required more conc. since contain less colorants.

Opaquant-Extenders

Very fine inorganic powders used in coating solution to provide:

i. **More pastel colors and increase coverage**

ii. **White coating or masking the color of tab. core.**

- **Colorants are much more expensive than these inorganic materials and effectively less colorant is required when opaquant are used.**

E.g. titanium dioxide, talc, aluminum silicate, Mg oxide, calcium sulfate, Mg carbonate and aluminum hydroxide.

Miscellaneous coating solution components

To provide unique characteristics for D.F. Like:

Flavors and sweeteners: mask odor or enhance taste.

Surfactants: solubilize immiscible or insoluble ingredients or facilitate faster dissolution of coat.

Antioxidants: stabilize a dye system to oxidation or color change.

Antimicrobials: prevent microbial growth during preparation and storage.

Film defects

Sticking and picking: overwetting or excessive film tackiness causes tab. to stick (pick) to each other or to coating pan and resulting for small exposed area of core.

Solution: reduction in liquid application rate or increase in drying air temp. and air volume.

Roughness: roughness or gritty surface when coating applied by a spray due to drying of droplets rapidly before reaching tab. bed or due to increase in pigment and polymer conc. in the coating solution.

Solution: moving of nozzle closer to tab. bed or reducing degree of atomization.

Orange-peel effects or bumpy: inadequate spreading of viscous sol. or too rapid drying.

Solution: thinning the sol. with additional solvent

Bridging and filling:

Bridging during drying, the film shrink and pull away from the corners of an intagliation or bisect.

Solution: increasing plasticizer content or changing the plasticizer.

Filling either by applying too much sol. resulting in a thick film the fills the bisect or by applying sol. too fast so overwetting may cause the liquid to quickly fill and retained in bisect.

Solution: monitoring fluid application rate and thorough mixing of tab in pan.

Blistering: effect of high temp. on strength, elasticity, adhesion and rapid evaporation of solvent from the core when further drying of coated tab is required.

Solution: using mild drying conditions.

Hazing/Dull film: also called **bloom** and it occurs when:

1. Using too high temp. for formulation and cellulosic polymers are applied out of aq. media.
2. Coated tab are exposed to high humidity conditions and partial solvation of film occurs.

Color variation: occurs due to improper mixing, uneven spray pattern and insufficient coating resulting to the migration of soluble dyes, plasticizers and other additives during drying so a mottled or spotted coat appear.

Solution: use of lake dyes and reformulation with different plasticizers or additives.

Cracking: internal stress in film exceed tensile strength of film.

Solution: increasing tensile strength by using high M.wt. polymers or polymer blends. Also, internal stress minimized by adjusting plasticizer type and conc. and pigment type and conc.