TABLET COATING 2

Lec. 9

Development of Film Coating Formulations

The development of film coating formulations depend on the following:

1. Purpose of coating (either masking taste, odor or color, or control release of drug).
2. Tab. size, shape or color constraints put on the developmental work.

DEVELOPMENT OF FILM COATING FORMULATIONS

1. **Water vapor permeability**

Coating is used to provide some physical protection for tab. containing a water unstable drug; thus give a way for assessing water vapor permeability.

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.**

3. 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 coat used for control release of drug so min. 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 instrument or visual inspection (by rubbing a film coated tab. on white sheet paper to determine that no color, no abrasion or very soft film erased from the tab. surface to the paper).

4. 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: Colorants and opaquant conc. fixed to achieve predetermined shade. Also 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 of the tab. surfaces with the film former
10. Ease of printing on high speed equipment.

Film formers (non-enteric and enteric)

Non-enteric materials

Most common polymers used for film coating:

Hydroxypropyl methylcellulose, USP (HPMC)

Note: This polymer is prepared by reacting alkaline treated cellulose with CH4Cl to indroduce methoxy gps and then with propylene oxide to indroduce P.G. ether. grs so introducing this polymer in diff. viscosity.

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. No interference with tab. disintegration and drug availability.
3. Flexibility, chip resistance, and absence of taste or odor.
4. Stability in heat, light, air and reasonable levels of moisture.
5. Incorporate with color and other additives into the film without difficulty.

Closed to properties of ideal polymer due to:

a. **Used alone:** tendency to bridge or fill debossed tab. surfaces.
b. **Mixture of HPMC with other polymers or plasticizers:** eliminate bridging or filling problems.
c. **Used considerably in glossing solutions.**

Ethylcellulose, NF (EC)

Note: prepared by reacting EC dissolved in NAOH with ethyl chloride or ethyl sulfate. Thus degree of viscosity depends on degree of ethoxy substitution.

Properties:

1. **Completely insoluble in H_2O and GI fluids**
2. **Not used alone** but combined with water soluble additives (HPMC) to prepare S.R. films with water solubility properties to coat tab. and fine particles.
3. **Soluble in organic solvents.**
4. **Non-toxic, odorless, colorless.**
5. **Stable** to most environmental conditions.

NEW TYPE: developed aq. dispersion of EC **(Aquacoat)** these **pseudolatex systems** are **high-solids with low viscosity** produced by developing unplasticized EC films that are brittle and required film modifiers to obtain an acceptable film formulation.

Hydroxypropylcellulose

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

Properties:

1. Soluble in water at 40°C (insoluble >45°C),GI fluids and many polar organic solvents.
2. Tacky as dries from solution system so desire 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

Note: 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. **Tab. coat and binder (mostly used in industry is k-30)**
2. **Improve dispersion of colorants in coat solution to get uniform 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 but adhere well to tab.
3. Partially dried films are tacky but modified with additives.
4. Conversion to aq. film coating improved usefulness in coating systems.

Polyethylene glycols (PEG)

Note: reaction of ethylene glycol with ethylene oxide in the presence of NAOH at elevated temp. and pressure.

Uses:

1. Film coating when using high M.wt. (900-8000) solid waxes PEGs in combination with cellulose acetate phthalate (but soluble in gastric fluids). Also consider [hard, smooth, tasteless, non-toxic and sensitive to elevated temp.].
2. 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 and permeable above pH 5.

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

Eudragit RL and RS

Available as organic sol. and solid

Used as delayed release films (pH-independent) similar to EC.

Enteric materials

Important reasons for enteric coating are as follows:

1. Protect acid-labile drugs from gastric fluids e.g. enzymes and 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 conc. form and bypass sys. absorption in the stomach.
4. Deliver drugs that are absorbed in small intestine in their conc. 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 solution, so it shouldn't change upon aging.
5. Formation of cont. (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 deboss ed tab.

Important notes:

Polymers or materials used to achieve enteric coating should be either **water-resistant films or pH-sensitive materials** (they either digest by enzymes or emulsified by intestinal juices and/or may slowly swell and fall apart when solvated).

E.g. 1. water resistant: enteric coated tab in gastric fluid show no disintegration, cracking or softening after 1 hr., while after 2 hr. period in intestinal fluids all tab disintegrate.

2. pH-sensitive materials: acid labile drugs protected from pH 1-5 while the enteric polymer start to dissolve or permeable near and above pH 5 when approaching pylorus.

3. pH-independent polymers: they depend on hydrophobicity to provide enteric effect, the film is thick so protect from gastric juice and begin to solubilize in intestine but solubility of drug and their diffusion may not be achieved.

Cellulose acetate phthalate (CAP)

Disadvantages of CAP films:

1. Dissolve above pH 6 so delay drug absorption.
2. Hygroscopic and permeable to moisture and gastric fluids.
3. Susceptible to hydrolysis by removal of phthalic and acetic acids so changing film properties.
4. Brittle and formulated with hydrophobic film forming materials or adjuvants to achieve better enteric film.

Developed for Aquateric coating to exceed these disadvantages.

Acrylate polymers (Eudrgit L and Eudragit S)

Properties:

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

Hydroxypropyl methylcellulose, NF

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

Properties:

1. **Dissolve at pH 5 to 5.5** so this solubility characteristic result in higher bioavailability of some drugs.
2. **Quite stable** compared with CAP because of their absence of labile acetyl groups.

Polyvinyl acetate phthalate (PVAP)

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

Properties: **Similar to HP-55 in stability and pH-independent 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 (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)

- **Water (aq. system) is the best but sometimes drugs may hydrolyze so using of non-aq.-solvent based coating in sugar coat while it is not preferred in film coating.**

Plasticizers

Quality of film modified by using internal and external plasticizers:

Internal: can alter chemical modification and physical properties of basic polymer by controlling degree and type of substitution also chain length.

External: act as additives and it can be either non-volatile liquid or another polymer, which can be incorporated with 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. aq. coat **required water soluble plasticizers like PEG 200, 400 PG and glycerin.**

Organic coat **required castor oil, span, tween and organic acid esters.**

Choose of plasticizers depend on:

1. Ability to solvate polymer and alter polymer-polymer interactions.
2. Ability to impart flexibility by relieving molecular rigidity.
3. Type and its ratio to polymer to achieve desired film coating.
4. Viscosity that effect film permeability, flexibility, solubility, taste, toxicity, compatibility with other coating sol. and stability of coat film.

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

Colorants

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

1. **Suspended insoluble powders:** using fine powder colorants (<10 м) or milled to achieve proper distribution in coating solution.

E.g. FD&C (Food Drug and Cosmetic) or D&C (Drug and Cosmetic) colorants are synthetic dyes or lake of dyes (water insoluble) **like alumina or talc**. Used for sugar or film coat and contain 10-30% pure dye.

2. **Coating solution:** used without milling like Oalux (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. Since 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** (since colorants are expensive and less effective in presence of opaquants).

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

E.g. **titanium dioxide, talc, aluminum silicate, Mg oxide, sulfate, 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.

Quality Control

After coating: tab. check for:

A. Color (hue and continuity)
B. Size
C. Appearance
D. Physical defects in coating affect performance or stability

In-vitro tests include:

A. Dissolution and disintegration.
B. Mechanical strength.
C. Resistance to chipping and cracking during handling.

In-vivo test including bioavailability test to perform availability of drug affected by minor changes in conc. of ingredients either the core or film due to storage or aging.

Stability Testing

Stability testing determines the effect of time (aging) and storage conditions on physical and chemical stability of coated product like color change and chemical degradation.

The stability program designed as:

1. Determining shelf life or expiration date of the coated product under normal storage conditions in its intended package by having at least 2 years expiration and must conform to all standards of performance and potency after manufacture.
2. Determine product stability at elevated or accelerated storage conditions in relation to temp., humidity and light exposure to study degradation rate of active ingredient and to project expiration date for the product stored under ambient conditions by using Arrhenius relationship.

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 stresses minimized by adjusting plasticizer type and conc. and pigment type and conc.

Specialized Coatings

Compression coating: finished product is tab. within tab. by using specialized machines.

Advantages:

a. used for core tab. that cannot tolerate organic solvents or water.
b. taste masking or to provide delayed or enteric release.
c. separate incompatible ingredients.

Electrostatic coating: is an efficient method of spraying coat with strongly opposite electrostatic charges onto conductive substrate thus complete and uniform coat of corners and intagliation on substrate is achieved.

Disadv: limited method for tab coating.

Dip coating: coat is applied to tab. core by dipping them into the coating liquid then dried in conventional coating pan and repeated for several times to obtain desired coating.

disadvantages: lack speed, versatility and reliability of spray coating techniques.

Vacuum film coating: is a new coating procedure by employing specially designed baffled hot water jacketed pan and sealed to achieve vacuum system.

Mech.: tab placed in pan and air is replaced by nitrogen before desired vacuum achieved then coating sol. applied with airless spray system and evaporation occurs in heated pan and removed by vacuum system.

Adv.: no high velocity heated air so low energy requirements and high efficiency coating also organic solvents used safely and effectively with minimum environmental concern.


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