

Section 7

Coating

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General Introduction

Evolution of the Coating Process

Early in the history of medicine, pills were first coated with a mucilage of *Plantago psyllium*, and subsequently with gold or silver. Coating with honey and sugar was further developed in order to mask the unpleasant and bitter taste encountered as the pill was taken into the buccal cavity and swallowed, while coating with gold or silver was specially prepared for people of high political status. In the 19th century, sugar became a major ingredient for candy products. Other natural products such as shellac, zein, and gum arabic were commonly used in the pharmaceutical industry. However, such materials were later replaced by semi- or fully-synthetic substances, which are available on the market today. These products have consistent quality and are available in more precisely defined grades. Due to health concerns, especially with diabetic patients and children, sugar is sometimes replaced by more suitable non-tooth decaying, semi-synthetic materials.¹

Purpose of Tablet Coating

The purpose of tablet coating^{1,2} is to:

1. Enhance palatability and mask the unpleasant taste and odor of the active drug substance
2. Increase the stability of an active drug substance during exposure to light, moisture and atmospheric oxygen
3. Increase the mechanical integrity of the tablet during manufacturing, packaging (i.e. to reduce friction and increase the production rate during high-speed processing) and shipping
4. Enhance the elegance and glossy appearance of the tablet core
5. Protect the patient's clothes and hands from staining due to a colored or migrating active drug substance
6. Modify the drug release profile, such as with an enteric coating, sustained release coating, osmotic pump, etc.
7. Avoid side effects caused by the active drug substance (i.e. prevention of gastric irritation by employing an enteric polymer coating)
8. Avoid incompatibility of active drug substances by physical separation of the incompatibles into the core and coat
9. Identify the product using a coating unique to a particular manufacturer

Types of Pharmaceutical Coating Processes

Sugar Coating

Overview

The sugar coat was developed primarily from technologies employed in the confectionery industry, which have been optimized over the years, and are still widely used today. Development of Brufen® by Boots (United Kingdom) was a major milestone in the development of sugar coating technology through the use of spray sugar coating. Sugar-coating processes result in nearly doubling the weight of the original tablet core; therefore batch sizes are calculated based on the finished tablet weight after coating. However, the use of modern spraying systems has resulted in a dramatic reduction in the final product weight. Moreover, the airflow velocity and processing temperature are very critical in achieving a pharmaceutically elegant finished product.²

Raw Materials

Coating Formers

Coating formers, which form the coating due to their mass and cohesion, typically consist of sugars, binders and fillers.

a). *Sucrose, other sugars, and sugar alcohols:*

Sucrose is used primarily as a coating material in concentrations ranging between 50-60%, since syrups with a sugar content of less than 65% are stable at room temperature without crystallization occurring. Aqueous solubility of sucrose is increased by the use of heat.

Due to major concerns in using the products in diabetic patients, and the fact that they cause dental caries, other sugars and sugar alcohols are used to replace sucrose. These include glucose, lactose, maltitol, mannitol, isomalt, sorbitol, xylitol, and sugar mixtures such as invert sugar and starch sugars.

b). *Binders:*

The function of a binder is to increase the strength and elasticity of the coating by forming bonds and thus a coherent matrix. Examples of binders include polyvinyl acetate (PVA), polyvinyl pyrrolidone (PVP), acacia gum, gelatin, agar-agar, sodium alginate, carboxymethyl starch, dextrans, cellulose ethers, and starches.

c). *Fillers:*

A filler builds up the structure and adds mass to the coatings. Examples of fillers include kaolin, dextrin, precipitated calcium carbonate, powdered acacia, corn starch, talc and calcium sulfate.

Colorants

A colorant adds color to the coatings and covers imperfections which may appear in the tablet core. Examples of colorants include pigments (titanium dioxide or other inorganic coloring agents), dyes, and lakes.

Flavors

Flavoring agents are used to improve and enhance the acceptability and palatability of the dosage form in order to maximize patient compliance. Examples include naturally and synthetically derived agents (cinnamon, fruit flavors, etc.).

Lubricants, Glidants, and Antiadherents

These materials reduce friction between the individual sugar-coated cores and thus prevent dust formation during the drying step. Examples of lubricants, glidants and antiadherents include talc and colloidal silicon dioxide.

Smoothing Agents

The function of a smoothing agent is to smooth out the surface of the coatings by lubricating and binding the fines that may be created during the coating process. An example of a smoothing agent is a combination of syrup and acacia gum.

Polishing Agents

A polishing agent enhances the reflectivity and intensity of the color of the coatings. It can either be incorporated into the smoothing agent or applied onto the smooth surfaces of the coated product. Examples of polishing agents include beeswax and carnauba wax.

Suspension Stabilizers

A suspension stabilizer prevents phase separation or sedimentation of the coating suspension while it is being applied during the coating process. Examples of suspension stabilizers used include surface active agents (emulsifying agents, bentonite) or thickening agents. However, the limitation of thickening agents is based on the viscosity of the coating suspension.

Processing Steps

Sugar coating layers are built up during processing by repetition of the application, distribution, and drying steps. Three types of sugar coating techniques are commonly used:

a). *Plain sugar coating (application of syrup at room temperature):*

This coating technique includes 3 steps: application of coating formulation onto the cores, distribution of formulation on the core surfaces, and drying to increase the strength of each coating layer. However, the time required for distribution and drying is critical to obtain a smooth even coating.

b). *Two-component coating or lamination process (application of a syrup or binder solution first in a slight excess amount, and then dusting with a powder to bind the excess solution):*

Compared to the plain sugar coating technique, the two-component coating is a more complicated technique involving two steps of application of solution and powder. In order to obtain a high volume increase within a short period of time, adjustment must be made between powder and liquid quantities and performed by skillful operators.

c). *Hot sugar coating (application of heated syrup):*

For the hot sugar coating technique, syrup is heated above room temperature to reduce the viscosity of the syrup. Therefore, a higher sugar content formulation can be used, with gelatin as a binder, and less water has to be removed during the drying process. However, the temperature used during the process must be controlled since the gelatin is prone to hydrolysis at temperatures above 60° C. Attempts to prevent sugar crystallization during processing may make this technique more complicated and more expensive since all equipment parts used must be insulated and heated.¹

Sealing (Protective Coating)

The main purpose of the sealing layer application is to protect the cores from subsequent damage, especially for water-sensitive cores in which an additional protective film often is applied prior to subcoating, and for gastro-sensitive cores in which gastro-resistant layers are incorporated. In some cases, if the film layers are poor primers, a binder layer must be applied in order to ensure adhesion of the subsequent coatings. Seal coating materials include shellac, cellulose acetate phthalate (CAP), zein, and synthetic resins.

Subcoating

The main purpose of applying the subcoating layer is to facilitate rounding of the sharp edges of the cores. There are two techniques for the subcoating application:

a). *Liquid/powder (traditional method)*

Subcoating syrups, which are suitable for layering or subcoating, typically contain sugar syrup and a larger proportion of glutinous binders such as polyvinylpyrrolidone (PVP), acacia gum, gelatin, sodium carboxymethyl-cellulose (NaCMC), hydroxyethyl cellulose (HEC), hydroxyethyl ethylcellulose (HEEC), hydroxyethyl hydroxypropylcellulose (HEHPC), or polyvinyl acetate (PVA) in levels up to 10%. In contrast, subcoating powders consist of coating formers including inorganic and organic solids, such as talc, calcium carbonate or corn starch. This method of application requires skilled personnel to monitor the process since the amount of powder and liquid used for subcoating is critical.

Example of a subcoating and dusting syrup:³

<i>Ingredients</i>	<i>%</i>
Silicon dioxide	1
Gelatin	1-5
Acacia gum	2-4
NaCMC	1
Sucrose	63
Water	33

Example of a subcoating or dusting powder:⁴

<i>Ingredients</i>	<i>%</i>
Silicon dioxide	5
Talc	10
Wheat starch	10
Sucrose	75

b). *Suspension*

The subcoating suspension consists of calcium carbonate, talc, acacia gum and titanium dioxide (white pigment) suspended in water. The application of the subcoating as a suspension is considered to be more feasible than the traditional method.

Example of a subcoating suspension:⁵

<i>Ingredients</i>	<i>%</i>
Sucrose	40
Calcium carbonate	20
Talc (asbestos-free)	12
Gum acacia (powdered)	2
Titanium dioxide	1
Distilled water	25

After the sealing and subcoating steps, a dusting powder composed of particles less than about 10 µm in diameter is applied slowly during the drying phase so that it remains plastic over a longer period of time, to facilitate rounding of the edges of the tablet core. In some cases, requiring a rapid build-up of coating without employing any dusting steps, filler syrup layers containing a high proportion of sugar or other solids with suspension stabilizers to prevent sedimentation may be applied.

Example of a filling syrup:⁶

<i>Ingredients</i>	<i>%</i>
Calcium carbonate	20
Dextrin	1.5
Titanium dioxide	1
Talc	7.5
Sucrose	48
Water	22

Smoothing

The main purpose of smoothing is to reduce the surface roughness prior to achieving glossing on the smooth surface during the polishing step. A *glossing syrup* usually contains suspended powders, such as diluted colorants, to provide a base for the coloring and finishing steps.

Coloring and Finishing

Coloring is a critical step of the sugar coating process since the layers must be applied onto evenly rounded and uniformly coated cores with correct matching of the color between lots. Pigments provide better covering power than dyes, therefore, only a small amount of pigment

is needed to complete the coloring step. A white pigment, titanium dioxide, is typically used in the coloring layers.

Example of pigmented syrups:⁷

<i>Ingredients</i>	<i>%</i>
Color pigment	0-3.7
Acacia	1.2
Titanium dioxide	0-3.7
Sucrose	61.8
Water	33.3

<i>Ingredients</i>	<i>%</i>
Sucrose	58-66
Gelatin or acacia gum	0.5-1
Polyethylene glycol (PEG) or PEG fatty acid ester	1-3
Colloidal silica	0.5-1
Titanium dioxide	0.05-0.1
Dyes, pigments	qs
Water qs to	100.00

Polishing

The main purpose of polishing is to obtain a transparent, glossy and reflective coating with no opalescence or cloudiness remaining from previous steps. Therefore, the polishing step can intensify the colors and eliminate white reflections visible from the tablet. Additionally, it makes the product more stable upon storage. The polishing step can be performed by incorporating waxes, fats, or lacquers into the final coating layer.

In some products, printing on the high-gloss surface is performed to provide unique product identification.

Example of polishing and finishing solutions:⁸

<i>Ingredients</i>	<i>%</i>
Carnauba wax	0.52
Paraffin wax	0.06
PEG	0.02
Trichloroethylene	99.4

In some cases, uniform coating layers may be applied using a combination of ingredients with different functions, as a single syrup formulation. This process is a more economical and practical way to coat different core shapes, and permits the use of pigments to provide a uniform color. In fact, uniform coloring can be obtained with only a few coating layers. A typical single syrup formulation for coating is;¹

Film Coating

A film coating is defined as a thin and uniform polymer based coat of about 20 to 100 μm in thickness, which is applied to the surface of substrates such as tablets, granules, powder, capsules, multiparticulates or pellets.⁵

Compared to sugar coating, film coating provides more flexibility with the ability to coat a variety of substrates, other than just compressed tablets. Although the first tablet film coating appeared in 1930, the first commercially available film coated tablet was not produced until 1954 by Abbott Laboratories using a fluidized bed coating column with a Wurster insert and an organic solvent system.²

Advantages of Film Coating

1. Enhance the elegance and glossy appearance of the dosage form
2. Obtain legible logo and product identification after coating. Product information can be engraved on the tablet core
3. Improve mechanical integrity and resistance of the dosage form upon handling and shipping from manufacturing site to patients
4. Modify the pharmaceutical function of the dosage form, especially for enteric or modified release coating
5. Increase flexibility in types of formulations coated and processing equipment required
6. Minimal weight increase (about 2-3 % of tablet core weight) compared to a sizeable increase when using a sugar coating (doubling the weight of tablet core)
7. Significantly reduced processing time, with increased process efficiency and output
8. Minimize dusting^{2,5}

Typical Film Coating Formulation Components

Polymers

Polymers are flexible linear macromolecules having a molecular weight range between 10,000 and several million daltons. Polymers consist of a number of repeating units in the structure.

Ideal properties for polymers used in film coating include:

- a) solubility in a wide range of solvent systems in order to allow flexibility in formulations
- b) ability to produce films with excellent mechanical properties
- c) stability against light, oxygen, hydrolysis
- d) low toxicity
- e) optimum dissolution in the gastrointestinal tract.⁵

Coating polymers can be categorized into two types:

- a) non-functional or conventional film coating polymers, which can be used as a coating to improve the appearance, improve the handling, and prevent dusting of dosage forms;
- b) functional coating polymers, which can be used to modify the pharmaceutical function of the dosage forms, especially with enteric or modified release coatings.

Characteristics of concern for polymers used during the coating process include solubility, solution viscosity, film permeability, mechanical properties (i.e. tensile strength, elastic modulus, work of failure, strain), and so on. For the coating application, the polymer frequently is dissolved in a suitable solvent, such as water or a non-aqueous organic solvent. However, some water-insoluble polymers are available commercially as an aqueous dispersion, which permits aqueous film coating, and are particularly useful for modified release coating applications. Based on the method of preparation, polymer dispersions can be classified into two types: true latexes and pseudolatexes.

Comparison of True Latexes and Pseudolatexes²

Type	True Latex	Pseudolatex
Description	Very fine dispersion of polymer in an aqueous phase	Fine dispersion of polymer in an aqueous phase
Particle size range (nm)	10-1000	10-1000
Method of preparation	Emulsion polymerization of monomer, initiator, and catalyst	-Produced from the polymer, by mechanical means - Free of residual monomer and traces of initiators
Examples	Acrylate polymers (Eudragit® L100-55, and Eudragit® NE30D, Röhm Pharma GmbH)	Ethylcellulose dispersion (Aquacoat® ECD, FMC BioPolymer)

For an aqueous polymeric dispersion, film formation can occur when the polymer in a wet state is present as a number of discrete particles. Those particles come close to each other due to the capillary action of the film of water around the particles. They then make contact, deform, coalesce, and finally fuse together to form a discrete film. Lehmann⁹ recommended that the coating temperature during the application process should be about 10-20°C above the minimum film-forming temperature (MFT) in order to ensure the optimum conditions for film formation. The MFT is the minimum temperature above which film formation will occur under specific conditions and is dependent on the temperature at which the polymer changes from a hard glassy amorphous state to a softer rubbery state. This change in state is defined as the glass transition temperature (T_g) of the polymer. Moreover, the glass transition temperature of such a polymer can be lowered by the incorporation of a plasticizer into the polymer solution or dispersion.

Plasticizers

Plasticizers are low molecular weight organic solvents with high boiling points. They are used to alter the physical properties of a polymer (i.e. hard or brittle) and render it more flexible and softer to function as a film-coating material. Generally, there are some similar chemical features (i.e. functional groups) between a polymer and its plasticizer. Plasticizers are normally used at concentrations between 15-35% based on

polymer weight. Plasticizers also have a significant influence on mechanical properties of the film. Specifically, they can reduce cohesive intermolecular forces along the polymer chains and enhance flexibility by increasing strain or film elongation and decreasing tensile strength and elastic modulus of the polymer.

Additionally, they influence the permeability characteristics of the film, especially to water vapor, as well as lowering the glass transition temperature of the polymer to allow a more feasible coating process. Plasticizers also possess solvent power to insure compatibility with the polymer. Plasticization time (i.e. mixing time of plasticizer with polymer) and plasticizer level influence the nature of the polymer films.¹⁰ Three types of plasticizers are commonly used in coating processes:

- a). *Polyols: water miscible*
Glycerol (glycerin)
Propylene glycol (PG)
Polyethylene glycol (PEG 200-6000 grades)
- b). *Organic esters:*
Diethyl phthalate (DEP) - water insoluble
Dibutyl phthalate (DBP) - water insoluble
Dibutyl sebacate (DBS)- water insoluble
Triethyl citrate (TEC)-water miscible
Acetyltriethyl citrate (ATEC) - water insoluble
Acetyltributyl citrate (ATBC) - water insoluble
Tributyl citrate (TBC) - water insoluble
Triacetin (glyceryl triacetate; TA)-water miscible

-
- c). *Oils/glycerides: water insoluble*
Castor oil
Distilled acetylated monoglycerides (AMG)
Fractionated coconut oil

Pigments or Opacifiers

Pigments or opacifiers are used in film coating to:

- Enable product identification
- Protect the active ingredient against light by optimizing the opacifying properties of pigments
- Modify the gas permeability of a film
- Decrease the risk of counterfeiting the product

However, the use of pigments and opacifiers could be omitted from the formulation if a clear coating is required.

Vehicles or Solvents

Solvents and vehicles play an important role in carrying the coating materials to the surface of the product core. They include water, alcohols, ketones, esters, and chlorinated hydrocarbons. The type of vehicle or solvent used during the coating process can be used to classify the type of film coating into an organic film coating (non-aqueous film coating), or an aqueous film coating. These types of coatings will be discussed in later sections. Necessarily, the solvent has to interact intimately with the selected polymer in order to allow both film adhesion and mechanical strength to be optimized.

Other Components

Other components are used occasionally in low concentrations for specific formulations such as processing auxiliary substances or drug release modifiers. Flavors may be included in some oral formulations to make them more palatable. Adhesion enhancers (e.g. saccharides such as polydextrose, maltodextrin, and lactose) are used to increase the adhesion of cellulosic systems to the substrate as well as improve stability towards light, for unstable colors).¹¹

Surfactants or dissolution enhancers (i.e. xanthan gum with Eudragit® NE30D coated theophylline granules)¹², as well as pore-forming agents (e.g. sucrose or sodium chloride with ethylcellulose-coated salicylic acid tablets)¹³ can be used to enhance the dissolution of the final dosage forms. Anti-tacking agents/glidants (e.g. talc, magnesium stearate, kaolin, glyceryl monostearate) typically are used to reduce sticking during film formation. Additionally, some film coatings may contain an active ingredient, such as preservative (i.e. sorbic acid), antifoaming agents (i.e. dimethylpolysiloxane), stabilizing agents, or waxes.

Types of Film Coating

Organic Solvent Systems

Overview

Due to environmental, safety and health-related concerns, the use of organic-based coatings has decreased recently with the advent of aqueous-based coatings. Additionally, the introduction of newly-developed coating equipment and the development of new film coating raw materials which can be applied in aqueous media, as solutions or dispersions, foster a more practical operation with aqueous-based coating systems. Similarly, some newer forms of older polymers previously used for organic-based systems have been transformed by manufacturers into different forms that allow the formulators to choose a more suitable form for aqueous-based coatings.

Disadvantages

1. Environmental, fire and toxicity hazards
2. Requires flameproof equipment to reduce hazardous working environment for the operator.
3. Residual solvent from coating process.
4. Requires solvent recovery systems.
5. High cost of the process due to the required use of special safety equipment with organic solvents.

Aqueous Coating Systems

Overview

Recently, the trend in coating has favored aqueous film coating since organic solvent systems require a high capital outlay in equipment and solvents, the limitation of chlorinated hydrocarbons use by regulatory authorities, the environmental concern for pollution, and the development of perforated coating pans and spraying systems, which allow application of more sophisticated coating materials.

Immediate Release Coatings

Pharmaceutical Applications

- Mask the unpleasant taste and odor of drug;
- Protect the active drug substance from exposure to light, moisture and atmospheric oxygen;
- Enhance the elegance and glossy appearance of the dosage form;
- Improve mechanical integrity of the dosage forms upon handling from manufacturing site to patients;
- Prevent dosage forms from dusting.

Polymers Used for Conventional Film Coating

Cellulose Ethers

Cellulose ethers are a major group of polymers used in the film coating process. Method of preparation, type of substitution groups, degree of substitution (DS), molar substitution (MS), polymer chain length, size and extent of branching have significant effects on polymer properties with respect to their solubility, thermal gel point, molecular weight and solution viscosity. There are four types of cellulose ethers specified in the USP17: HPMC 2910, HPMC 2208, HPMC 2906, and HPMC 1828. The number designations define the methoxy/hydroxypropoxy ranges of the respective HPMC.

Commonly used cellulose ethers for film coating and their properties are:

Hydroxypropyl methylcellulose (HPMC)

HPMC is soluble in both aqueous and organic solvent. It provides aqueously clear soluble films. Color coating with addition of pigment is possible.

Hydroxypropyl cellulose (HPC)

HPC is soluble in both aqueous and alcoholic solvents. HPC films tend to be tacky and weak, and are usually used in

combination with other polymers to provide additional adhesion to the substrate.

Hydroxyethyl cellulose (HEC)

HEC is soluble in water, insoluble in organic solvents.

Sample Formulation

Cellulosic coating formulation²

<i>Ingredients</i>	<i>%w/w</i>
HPMC (5 mPa, polymer)	7.5
PEG 400 (plasticizer)	1.6
Iron oxide yellow (pigment/opacifier)	0.6
Titanium dioxide (pigment/opacifier)	3.0
Purified water (vehicle)	87.3

Cellulosic Based Coatings

Recently, FMC BioPolymer introduced LustreClear™ which is a microcrystalline cellulose/carrageenan-based coating system. LustreClear is supplied in powder form and is a completely water-based system. It has an advantage over the cellulose ethers in that it is easy to disperse and non-foaming during hydration for faster preparation. Although a clear coat, color coating, upon addition of pigments/lakes, is feasible. LustreClear films exhibit good adherence and no logo bridging.

Coating Formulation

<i>Ingredients</i>	<i>%w/w</i>
LustreClear	9.0
Purified water	91.0

Acrylic Polymers

This group of various synthetic polymers, methacrylic aminoester copolymer, has diverse functionality in film coating. They can be used for rapidly disintegrating coatings, taste and odor masking, colored or transparent coatings, etc., and are available as the Eudragit® products from Röhm Pharma.

Modified Release Film Coatings

This type of film coating provides a delayed release action for a drug from a coated dosage form in the acidic environment of the stomach, but readily releases the drug once it passes into more basic pH environment of the upper intestine (i.e. duodenum). Enteric release dosage forms avoid side effects (i.e. nausea, vomiting) caused by irritation of some active drugs to the gastric mucosa, and prevent destruction of some drugs by gastric enzymes and the acid environment of the gastric fluid. The USP has specified this type of dosage form as a *delayed-released* dosage form. An enteric coating remains intact at a low pH but will undergo dissolution at a higher pH and allow the release of active ingredient from the dosage form.

Polymers Used for Enteric Release Film Coating

Cellulose Acetate Phthalate (CAP)

This polymer is widely used in enteric film coating. It is a white, free-flowing powder with a slight odor of acetic acid. According to USP¹⁷ specifications, CAP should contain 21.5-26.0% w/w acetyl content and 30.0-36.0 % w/w phthalyl content. The USP also requires a maximum limit on the quantity of free acid and loss on drying or water content since both parameters can accelerate hydrolysis of CAP. Additionally, due to their chemical composition, most of the phthalate-based enteric coating polymers are unstable upon storage. CAP is insoluble in water, alcohols, and chlorinate hydrocarbons, but has greater than 10% solubility in acetone, acetone/ethanol (1:1), acetone/methanol (1:1,1:3), acetone/methylene chloride (1:3), ethyl acetate/isopropyl alcohol (1:1).

CAP is available as a white powder from Eastman Chemical Co.

CAP Coating Formulation

<i>Ingredients</i>	<i>%w/w</i>
CAP	5.0
Glycerol triacetate	1.0
Isopropyl alcohol	17.0
Dichloromethane	68.5
Water	8.5

CAP is also available as a 30% solids dispersion (latex) as Aquacoat® CPD from FMC BioPolymer. Aquacoat CPD is employed as an aqueous enteric coating for tablets, beads, both hard and soft gelatin capsules and in wet granulation.

CAP Latex Coating Formulation

<i>Ingredients</i>	<i>Suspension (g)</i>	<i>Solids (g)</i>
Aquacoat® CPD	100.0	30.0 (76.9%)
DEP	9.0	9.0 (23.1%)
Purified water	151.0	-----
	260.0	39.0 (100%)

Polyvinyl Acetate Phthalate (PVAP)

The USP has specified a total phthalate content in PVAP of between 55-62 %w/w. The final polymer composition is also controlled by a viscosity specification and a limit of 5% water content. Compared to CAP, PVAP is less susceptible to hydrolysis, which minimizes or limits the content of free phthalic acid and other free acids. PVAP is soluble in methanol, methanol/methylene chloride, 95% ethanol, ethanol/water (85:15).

Shellac

This naturally occurring polymer is produced from a purified resinous secretion of the insect *Laccifer lacca*. It can be modified to meet certain specifications. In the past shellac was used widely in a variety of applications, especially as a sealer coat prior to sugar coating, enteric coating, or modified release coating. Due to its many drawbacks including inconsistent supply, variation in quality (common with a natural product), and stability problems associated with an increase in disintegration and dissolution times upon storage, shellac is not often used

in coating today. Shellac is insoluble in water, but soluble in alkaline media, and moderately soluble in warm ethanol.

Methacrylic Acid Copolymers

This group of polymers contains free carboxylic acid groups, and therefore can be used for enteric coating purposes by forming salts with alkalis. Methacrylic acid copolymers are soluble at pH values greater than 5.5.

Additives:

- Plasticizer is recommended.
- Pigments and opacifiers to reduce sticky nature of the polymers since they are likely to bind with large quantities of pigments.
- Polyethylene glycols (PEG) to provide a glossy appearance to the final product and stabilize the water-dispersible form (e.g. Eudragit® L30D).

The methacrylic acid copolymers are available as various grades of Eudragit® by Röhm Pharma.

Cellulose Acetate Trimellitate (CAT)

CAT polymer has similar properties to CAP polymer, especially solubility. In addition, CAT has an additional carboxylic acid group on the aromatic ring and dissolves at a pH of 5.5.¹⁴ To obtain the best enteric coating results from aqueous processing, ammoniated solutions of CAT in water are recommended.

Additives:

- Recommended plasticizers: triacetin, acetylated monoglyceride, diethyl phthalate (DEP)

CAT is available as a white powder from Eastman Chemical Co.

Hydroxypropyl Methylcellulose Phthalate (HPMCP)

HPMCP characteristics, particularly at the pH where dissolution occurs, are determined by the degree of substitution of the three substituent groups (i.e. methoxy, hydroxypropoxy, and carboxybenzoyl). Basically, this polymer is prepared from phthalic acid-treated HPMC. There are two types of substitution specified in the USP: HPMCP 200731 (20%w/w methoxy, 7%w/w hydroxypropoxy, and 31%w/w carboxybenzoyl) HPMCP 220824 (22%w/w methoxy, 8%w/w hydroxypropoxy, and 24%w/w carboxybenzoyl).

Solubility:

- insoluble in water
- soluble in aqueous alkaline media, acetone/water (95:5), acetone/methanol (1:1), acetone/-ethanol (1:1), or methylene chloride/ethanol (1:1)

Additives:

- Recommended plasticizers include triacetin, acetylated monoglyceride and DEP.

HPMCP is commercially available from Eastman Chemical Co. and Shin-Etsu.

Sustained Released Coatings

Polymers Used for Sustained Release Film Coating

Ethylcellulose (EC)

Ethylcellulose is insoluble in water. It was used extensively in organic solvent-based coatings in combination with other water soluble polymers, especially HPMC or polyethylene glycols (PEG), in order to provide a more hydrophilic nature to the EC film and promote drug diffusion through pores or channels. It provides additional gloss and shine to the tablet surface and optimizes film toughness to minimize surface imperfections caused by handling. It is preferred for modified release coatings because it is odorless, tasteless, and

has a high degree of stability to light and heat under normal storage conditions. The USP specifies an ethoxy content between 44.0-51.0 %w/w. The water dispersible form of EC provides significant advantages and makes processing of water insoluble polymers from an aqueous-based system possible.

Some commercially available products:

- Powder, Aqualon®, Aqualon Division, Hercules Inc. and Dow Chemical Co.

It is available in a wide range of viscosity and substitution types for a wide range of applications.

Aqueous Dispersion

Aquacoat® ECD is a 30% by weight aqueous dispersion (latex) of ethylcellulose polymer. The dispersion contains ethylcellulose (polymer), cetyl alcohol (stabilizer) and sodium lauryl sulfate (stabilizer/emulsifier). A plasticizer (e.g., DBS, DEP, Triacetin, Myvacet and TEC) is recommended. Aquacoat ECD, in addition to being used for sustained release film coating, can also be used for taste-masking and as a moisture barrier/sealant. The dispersion, in combination with water soluble polymers such as HPMC, can also be employed to produce elegant film coated tablets having all the positive attributes of aqueous film-coated tablets.

Ethylcellulose Latex Coating Formulation

<i>Ingredients</i>	<i>Suspension (g)</i>	<i>Solids (g)</i>
Aquacoat® ECD	100.0	30.0 (80.6%)
DBS	7.2	7.2 (19.4%)
Water	16.8	-----
	<u>124.0</u>	<u>37.2 (100.%)</u>

Methacrylate Ester Copolymers

Solubility:

This group of polymers is neutral and insoluble over the entire physiological pH range due to their completely esterified structure, thus the lack of free carboxylic acid groups (i.e. it is a pH independent polymer). However, their modified release application can be realized based on their ability to swell and being permeable to water and dissolved substances.

Additives include hydrophilic materials (i.e. soluble cellulose ethers, PEG) to achieve desirable release profiles.

The methacrylate ester copolymers are available in several grades to promote the desired release profiles as the Eudragit® products from Röhm Pharma.

Conclusion

Coatings play a multifunctional role in formulations depending on the desired properties of the dosage form. Recent advances in coating equipment, processes, and materials have created significant improvements in coating technology. The type of coating process chosen depends upon the type of coating that is to be applied, the durability of the tablet core, stability of the dosage form, and the economics of the process. However, recent trends in the coating technology have favored aqueous film coating because of its wide application, low environmental concerns, efficiency of the process, and wide commercial availability of coating materials.

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