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A SCIENTIFIC REVIEW ON ENTERIC COATED TABLET

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ABSTRACT

Tablet coating is one of the oldest pharmaceutical processes still is existence. Coating is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form in order to confer specific benefits over uncoated variety. It involves application of a sugar or polymeric coat on the tablet. Enteric coated means a tablet or capsule or the other form of oral medication which is layered with a defensive coating. This coating is used to fortify the stomach from unwanted effects or detrimental effects of a medication. Most enteric coatings work by presenting a coated surface that is stable at the highly acidic p^H found in the stomach, but breaks down rapidly at a less acidic (relatively more basic) p^H. Materials used for enteric coatings includeCAP, CAT, PVAP and HPMCP. So in order to obtain a gastro resistant drug it should have entericcoating and suitable polymers for the dosage form. Different polymers were used in enteric coating like cellulose acetate phthalate, polyvinyl acetate phthalate, hydroxyl propyl methyl cellulose. The present review describes enteric coating, their ideal properties, various polymers used, methods of manufacturing and evaluation of enteric coated tablets study provides an overview of the recent advances that have taken place in this arena.

KEYWORDS: Enteric coated tablet, Evaluation, Ideal Properties, Mechanism and Methods of entericcoated tablets.

INTRODUCTION

A tablet can be defined as solid, flat or biconcave disc (also available in various shapes) prepared by compressing a drug or a mixture of drugs with or without suitable diluents. Tablets are solid dosage forms containing medicinal substances with or without suitable diluents. They are the most widely preferred form of medication both by pharmaceutical manufacturer as well as physicians and patients. They offer safe and convenient ways of active pharmaceutical ingredients (API) administration with excellent physicochemical stability in comparison to some other dosageforms, and also provide means of accurate dosing. They can be mass produced with robust quality controls and offer different branding possibilities by means of coloured film coating, different shapes, sizes or logos.

The three process involved in the manufacturing of tablets are: wet granulation, dry granulation, direct compression.

Tablet manufacturing methods - advantages and limitations

Method	Advantages	Limitations
Direct compression	• Cost effectiveness, stability. • Faster dissolution, Simplified validation. • Simple, economical process. • No heat or moisture, so good for unstable compounds.	• Not suitable for all API generally limited to lower dose compounds. • Segregation potential. • Expensive excipients.
Wet granulation	• Robust process suitable for most compounds. • Increases and improves the uniformity of powder density. • Reduces air entrapment. • Imparts flow ability to a formulation. • Can reduce elasticity problems. • Coating surface with hydrophilic polymer	• Expensive: time and energy consuming process. • Specialized equipment required. • Stability issues for moisture sensitive and thermolabile API with aqueous granulation.

	can improve wettability.	
	• Binds API with excipient, thus reducing segregation potential.	
Wet granulation (non-aqueous)	• Suitable for moisture sensitiveAPI • Vacuum drying techniques can remove/reduce need for heat.	• Expensive equipment • Needs organic facility • Solvent recovery issues Health and environment issues.
Dry granulation (slugging or roll compaction)	• Eliminates exposure to moistureand drying. • Slugging may be used for moisture and heat sensitive material.	• Dusty procedure • Not suitable for all compounds • Slow process.

Types of tablets

The tablet dosage form is a versatile drug delivery system. Different types of tablet formulations are available, which could be broadly classified based on:

(1) Route of administration such as tablets for oral delivery, sublingual delivery, buccal delivery, rectal delivery or vaginal delivery, and

(2) Formulation characteristics such as immediate release tablets, effervescent tablets, melt-in mouth or fast dissolving tablets, delayed release or extended release tablets. [1-2]

Enteric coating of tabletstablet coating

Coated tablet are defined as tablets covered with one or more layers of mixture of various substances such as natural or synthetic resins, gums, inactive and insoluble filler, sugar, plasticiser, waxes, authorized colouring material and sometimes flavouring material. Coating may also contain active ingredient. Coating is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form in order to confer specific benefits over uncoated variety. Coating may be applied to a wide range of oral solid dosage form, such as particles, powders, granules, crystals, pellets and tablets.

When coating composition is applied to a batch of tablets in a coating pan, the tablet surfaces become covered with a tacky polymeric film. Before the tablet surface dries, the appliedcoating changes from a sticky liquid to tacky semisolid, and eventually to a non-stick dry Surfacepans. The entire coating process is conducted in a series of mechanically operated acorn-shaped coating pans of galvanized iron stainless steel or copper. The smaller pans are used for experimental, developmental, and pilot plant operations, the larger pans for industrial production.[3]

Advantages of tablet coatig

- To avoid irritation of oesophagus and stomach.
- To avoid inactivation of drug in the stomach.
- To modify the drug release.
- To improve patient compliance.
- To mask the bitter taste.

Disadvantages of tablet coating

- Disadvantages of sugar coating such as relatively high cost, long coating time and high bulk haveled to the use of other coating materials.
- However the process of coating is tedious and time-consuming and it requires the expertise of highly skilled technician.[4]

Primary components involved in tablet coating

- Tablet properties.
- Coating process.
- Coating equipment's.
- Parameters of the coating process.
- Facility and ancillary equipment's.
- Automation in coating processes.

Coating process

It is most desirable that the coating should be uniform and should not crack under stress. Hence, various techniques were designed for the application of the coating on the tablet surface. Generally, the coating solutions are sprayed onto the uncoated tablets as the tablets are being agitated in a pan, fluid bed, etc. As the solution is being applied, a thin film is formed which sticks to each tablet. The liquid portion of the coating solution is then evaporated by passing air over the surface of the tumbling pans. The coating may be formed either by a single application or may be developed in layers through the use of multiple spraying cycles. Rotating coating pans are oftenused in the pharmaceutical industry.[5]

The coating may be formed by a single application or may be built up in layers through theuse of multiple spraying cycles. Uncoated tablets are placed in the pan and the liquid coating solution is introduced into the pan while the tablets are tumbling.

Objectives of coating

The objectives of tablet coating are as follows:

- To prolong the shelf life of the drug.
- To enhance ease of swallowing large dose forms.
- To retard loss of volatile ingredients.
- To modify and/or control the rate of drug release as in repeat-action, delayed release (entericcoated) and sustain-release products.

- To incorporate incompatible drugs together in a single dosage form.
- Increasing the mechanical strength of the dosage form.[3,5]

Recent trends in tablet coating technique

- ❖ Electrostatic dry coating.
- ❖ Magnetically assisted impaction coating (MAIC).
- ❖ Aqueous film coating technology.
- ❖ Supercell coating technology.

Tablet coating defects with causes and their remedies.

Sl. no	Tablet defects	Definition	Causes	Remedies
1	Chipping	It occurs when theedges of the tablets, during subsequent	Coating solution.Dry granules.	That can make the tabletsbrittle and promote capping.
		handling and coatingoperations and it isdefects where thefilm becomes chipped and dented.	More binding	
2	Twinning	This is the term which was used forthe tablets that stick together, and it's a common issue Associated with capsule shaped tablets.	Low pan speed. Improper shape of tablets. High spray rate.	The change is almostimpossible to see, but it prevents the twinning problems. In some case, it is necessary to modify the design of the tooling by very slightly changing the radius.
3	Blistering	It is local detachmentof film from the solution forming blister.	Blistering occurs because ofentrapment of gases in film because of overheating during spraying.	Milder drying conditionsare warranted in this case.
4	Blushing	It is defects best described as whitish specks or haziness inthe film.	It is thought to be due to precipitated polymer exacerbated by the use of high coating temperature at or above the thermal gelation temperature of the polymers.	----------
5	Mottling	It is defined as unequal distribution of colour on a tablet, with light or darkareas standing out in an otherwise uniform surface.	Improper mixing of colourbinding solution. Large particle size. When the drug substance is coloured and excipients are white or colourless	Coating solution prepare properly in sufficient quantity.

Enteric coated

The enteric coated polymers remain unionize at low pH, and therefore remain insoluble. But as the pH increases in the GIT, the acidic functional groups are capable of ionization, and the polymer swells or becomes soluble in the intestinal fluid. Materials used for enteric coatings include Eudragit L-100, PEG-400, CAP, CAT, PVAP and HPMCP, fatty acids, waxes, shellac, plastics and plant fibres. Enteric coating covers various ideal properties such as resistance to gastric fluids, susceptible/ permeable to intestinal fluid, compatibility with most coating solution components and the drug substrate, formation of continuous film, nontoxic, cheap and ease of application. Polymers were selected based on the dissolution pH ranging from 4.5 – 7.0.

An enteric coating is a barrier that controls the location of oral medication in the digestive system where it is absorbed. The word "enteric" indicates small intestine; therefore enteric coatings prevent release of medication before it reaches the small intestine. The enteric coated polymers remain unionise at low p^H, and therefore remain insoluble. But as the pH increases in the GIT, the acidic functional groups are capable of ionisation, and the polymer swells or becomes soluble in the intestinal fluid.[6]

There are four reasons for putting such a coating on a tablet or capsule ingredient:

- Protection of active pharmaceutical ingredients, from the acidic environment of the stomach (e.g. enzymes and certain antibiotics).
- To prevent gastric distress or nausea from a drug due to irritation (e.g. sodium salicylate).
- For the delivery of drugs that are optimally absorbed in the small intestine to their primary absorption site in their most concentrated form.
- To provide a delayed-release component for repeat action.
- Required for minimizing first pass metabolism of drugs.

Reasons for performing enteric coating:

The possible reasons are.

a. Protection of active pharmaceutical ingredients, from the acidic environment of the stomach. (e.g. Enzymes and certain antibiotics)
b. To prevent gastric distress or nausea from a drug due to irritation. (e.g. sodium salicylate)
c. For the delivery of drugs that are optimally

absorbed in the small intestine to their primary absorption site in their most concentrated form.

d. To provide a delayed-release component for repeat action.
e. Required for minimizing first pass metabolism of drug.[7]

Need of enteric coating:

- To protect the stomach from the drug.
- To protect the drug from the stomach.
- To protect the acid liable drugs from the gastric fluid.
- To forbid gastric distress or nausea due to irritation from a drug.[8]

Advantages of enteric coating tablets

- Protect the drug from the stomach.
- Protect the acid liable drugs from the gastric fluid e. g. enzymes and certain antibiotics.
- Coatings are necessary for tablets that have an unpleasant taste, and a smoother finishmakes large tablets easier to swallow.
- Forbid gastric distress or nausea due to irritation from a drug, e.g., sodium salicylate.

Disadvantages of enteric coating tablet:

- Process is tedious.
- Time-consuming.
- Requires the expertise of highly skilled technician.[6]

Important reasons for enteric coating:

- To protect the stomach from the drug.
- To protect the drug from the stomach.
- To release the drug after the stomach e .g. in the intestine.
- To protect the acid liable drugs from the gastric fluid e. g. enzymes and certain antibiotics.
- To forbid gastric distress or nausea due to irritation from a drug, e.g. sodium salicylate.
- To deliver drugs intended for local action in the intestines, e. g. intestinal antiseptics could be delivered to their site of action in a concentrated form.
- Need for minimizing first pass metabolism.
- To extend a delayed release component for repeat-action tablets.(8)

Mechanism of drug release from enteric coating:

All enteric polymers possess ionizable acid groups, usually a free carboxylic acid from a phthalic moiety. The equilibrium between unionized insoluble polymer and ionized soluble polymer will be determined by the p^H of the medium and the p^{Ka} of the polymer. The Henderson- Hassel Bach equation can be used to predict the ratio of ionized to unionized polymer based on these two parameters, i.e.

P^H- P^{Ka}=log [Concentration ionized form/ Concentration unionized form].(9)

Ideal enteric coating materials should have the followingproperties:

* Resistance to gastric fluids.
* Ready susceptibility to or permeability to intestinal fluids.
* Compatibility with most coating solution components and the drug substrates.
* The film should not change on aging.
* Formation of continuous film.
* Non-toxicity, cheap and ease of application.
* Low cost.
* Ease of application without specialized equipment.[4]

Enteric coating materials:

Enteric coatings polymers are selectively insoluble substances. They won't dissolve in theacidic juices of the stomach, but they will when they reach the higher pH of the small intestine. Most enteric coatings won't dissolve in solutions with a pH lower than 5.5.

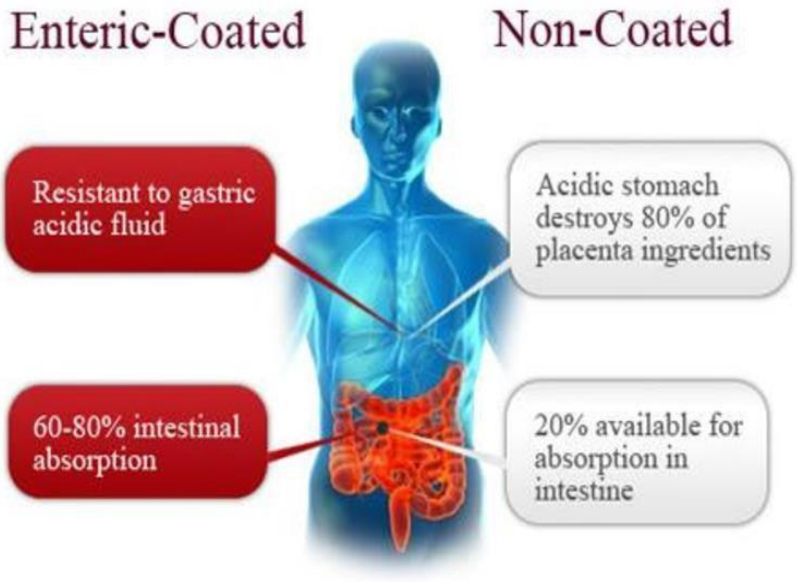
Commonly-used enteric coating polymers:

* Meth acrylic acid copolymers.
* Cellulose acetate (and its succinate and phthalate version).
* Polymethacrylic acid/acrylic acid copolymer.
* Hydroxypropyl methyl cellulose phthalate (HPMCP).
* Polyvinyl acetate phthalate (PVAP).
* Hydroxyl ethyl cellulose phthalate.
* Cellulose acetate tetra hydro phthalate.
* Sodium carboxymethyl cellulose.
* Eudragit L-100-55.

The earliest enteric coatings utilized formalized gelatine, this was unreliable because of the polymerization of gelatine could not be accurately controlled. Another was shellac, disadvantage was polymerization with time, and resulting in poor dissolution of the coating. The most extensively used polymers are CAP, PVAP. The most recently used polymers are HPMCP, Methacrylic acid copolymers.

- **Cellulose Acetate Phthalate (CAP):** Effective enteric coating, it only dissolves above pH 6 and may delay drug release longer than desired. It is permeable to moisture and simulated gastric fluid in comparison with other enteric polymers and it is susceptible to hydrolytic breakdown on storage. Its properties determine that it is hygroscopic, which makes it vulnerable to solubility and penetration of moisture into GI fluid.
- **Poly Vinyl Acetate Phthalate (PVAP):** Less permeable to moisture and simulated gastric juice, it is more stable to hydrolysis on storage. Enteric dosage forms coated with PVAP disintegrates at p^H5.[10]

Composition of Coating Solution	*Enteric Coating*	*Non-enteric Coating*
Polymer	Cellulose acetate phthalate, shellac, eudragits, hydroxypropyl methyl cellulose acetate	Ethyl cellulose, methyl cellulose, HPMC, and PVP
Solvent	Ethanol, acetone, rectified spirit, and isopropyl alcohol	
Plasticizers	PEG 200, PEG 400, and diethyl phthalate	
Coloring agents	FD&C approved colors	
Opacifying agents	Titanium dioxide, aluminum hydroxide, and purified talc	
Flavoring agents	Optional	
Surfactants	Optional	
Polishing agents	Beeswax/Carnauba wax, acetone, and alcohol	



Method of manufacturing enteric coated tablet

Preparation of core tablet:

All the ingredients are passed through sieve #80 and properly mixed together in air tight plastic container. The mixed ingredients are evaluated for precompression parameters, the blend of mixture to be compressed by direct compression in rotary tablet punching machine. The weightof the tablets was adjusted.

Preparation of enteric coated tablet (By dipping method):

The compressed tablets will be coated with enteric polymer solution by dipping method. Desired tablet coating continued the dipping and weight gain was achieved. The coated tablets were studied for its weight variation, thickness, uniformity of drug content and *in vitro* dissolution study. In this, cores to be coated are a held in a suitable device eg: baskets.

Coating is applied by dipping tablet into coating liquid then wet tablets are dried in conventional coating pans. Alternate dipping and drying steps can be repeated several times untilthe desired coating is achieved.

Evaluation of Core and Coated tablets:

- Hardness
- Uniformity of weight.
- Friability.
- Drug content study.
- FT-IR analysis.
- Differential scanning calorimetric (DSC) analysis.
- *In vitro* dissolution studies.
- Disintegration test.
- Acid uptake test.

Hardness test

Tablets require certain amount of strength or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping. Hardness can be defined as the strength ofthe tablet to withstand the pressure applied. In this test, a tablet was laced between two anvils,force was applied to the anvils and the crushing strength that just causes the tablet to break isrecorded.

It was measured using Monsanto tablet hardness tester. The values were expressed in kg/cm3.

Thickness

Tablet thickness is an important parameter to be controlled to facilitate packaging. Tablet thickness, at constant compressive load, varies with changes in die fill, with particle size distribution and packing of the particle mix being compressed. Tablet thickness must be controlled within a ±5% variation of a standard value. The thickness of the tablets was measured by using digital Vernier callipers. The thickness was denoted in millimetre.

Friability

Friability is a measure of the resistance of the tablet to abrasion. The friability of tablets was determined by using Roche friabilator. The percentage friability of the tablets were calculated bythe formula.

$$\% \text{ Friability (F)} = \frac{WO - Wf}{Wf} \times 100$$

Where,

WO = Initial weight of tablets Wf = Final weight of tablets.

***In vitro* dissolution studies:**

The objective of *in vitro* dissolution testing is to evaluate the variables that effect the rateand extent of release of a drug substance from the finished dosage form, and in turn, the *in vivo* performance of the drug product.

CONCLUSION

Coating of the pharmaceutical dosage form is a wonderful advantage and remarkable development in recent decades to the enhancement of the quality of the solid dosage form. Several development techniques have come to market to elegance the look, reduction of the error, stability of the tablet and easy way to control and operate. Each technique has its own set of benefits and drawbacks. This technology has undergone significant development and advancement in terms of energy consumption, film processing, and drying quality. From the above review, we can conclude that tablets are made enteric-coated for avoiding the first pass metabolism, gastric irritation and degradation and to direct the drug to the target intestines. The choice of the polymer and the thickness of the coated layer are critical to control the pH solubility profile of the enteric coated dosage form. Drugs which are having low oral bioavailability (<50%), short biological half-life (about 3 hrs) and an adequate protein binding that are preferred while formulating enteric coated dosage form. This dosage form is preferred as it is very convenient and easy to formulate, cost- effective and does not require high cost equipment. For that reason, this dosage form has been gaining so much attention nowadays. In the future, there is still a lot of opportunities for improvement in coating technique. More research into better coating solvents, drying techniques,and spaying methods is required.

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