ejpmr, 2016,3(4), 135-144

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 3294-3211

EJPMR

A DETAIL UNDERSTANDING OF ENTERIC COATED TABLET: MANUFACTURING AND EVALUATION

Sushama Pole, Suryaprakash Maurya, Pooja Hasnale, Nitin Rathod, Sharayu Bendale, Dr. Nilesh M. Khutle**

Assistant Professor, Department of Pharmaceutics, Dr. L.H. Hiranandani College of Pharmacy, Ulhasnagar, Maharashtra, India. Pin-421003.

***Correspondence for Author: Dr. Nilesh M. Khutle**

Assistant Professor, Department of Pharmaceutics, Dr. L.H. Hiranandani College of Pharmacy, Ulhasnagar, Maharashtra, India. Pin-421003.

Article Received on 03/02/2016 **Article Revised on 25/02/2016** **Article Accepted on 16/03/2016**

ABSTRACT

The tablet coating is perhaps one of the oldest pharmaceutical process still in existence. Enteric-coated tablets are delayed-release tablets that are intended to resist the gastric fluid and to release their active substance in the intestinal fluid. Coating of tablet with suitable enteric coating material required to disintegrate and release the drug in intestine depending upon the compactness and percent content of additives. Materials used for enteric coatings include CAP, CAT, PVAP and HPMCP, fatty acids, waxes, shellac, plastics and plant fibres. The present review describes enteric coating, their ideal properties, benefits and limitation, various polymers used, their chemical structure, criteria for drug selection and mechanism, methods of manufacturing and evaluation of enteric coated tablets. Most enteric coating works by presenting a surface that is stable at the highly acidic p^H found in stomach, but breaks down rapidly at a less acidic p^H. For e.g. they will not dissolve in the acidic juices of the stomach (p^H -3), but will in the alkaline (p^H 7-9) environment present in the small intestine. Enteric coating protect the stomach against drugs which causes gastric irritation also protect the drug which is unstable in gastric fluids.

KEYWORD: Enteric coated tablet, Ideal properties, Method and Mechanism of enteric-coated tablet, Evaluation of Core and coated tablets.

INTRODUCTION

Tablet as dosage form[1]

A tablet is a pharmaceutical dosage form. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid. Tablets Dosage form is one of a most preferred dosage form all over the world. Almost all drug molecules can be formulated in a tablet and process of manufacturing of tablets is very simple, and is very flexible.

Tablet Coating[1]

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 that broadly ranges from facilitating product identification to modifying drug release from the dosage form. After making a good tablet, one must often coat it. Coating may be applied to a wide range of oral solid dosage form, including tablets, capsules, multiparticulates and drug crystals. 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 applied coating changes from a sticky liquid to tacky semisolid, and eventually to a non-sticky dry Surface pans. 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.

Basic Principles involve in Tablet Coating[1]

Tablet coating is the application of coating composition to moving bed of tablets with concurrent use of heated air to facilitate evaporation of solvent.

I. Solution in which influences the release pattern as little as possible and does not markedly change the appearance.
II. Modified release with specific requirement and release mechanism adapted to body function in the digestive tract.
III. Colour coating which provides insulation.
IV. To incorporate another drug or formula adjuvant in the coating to avoid chemical incompatibilities or to provide sequential drug release.

Coating Process Design & Control: In most coating methods, when the tablets are being agitated in a pan, fluid bed, etc. at that time spraying on tablets by coating solution takes place. As the solution is being sprayed, a thin film is formed that adheres directly to each tablet. The coating may either be formed by a single application or may be built up in layers through the use of multiple spraying cycles.[4] Firstly, uncoated tablets are placed in the pan, which is typically tilted at an angle from the horizontal, and then the liquid coating solution is introduced into the pan while the tablets are tumbling. By passing air over the surface of the tumbling tablets, the liquid portion of the coating solution is then evaporated. In comparison, a fluid bed coater operates by passing air through a bed of tablets at a velocity sufficient to support and separate the tablets as individual units. Once separation takes place, then the tablets are sprayed with the coating composition.[1-7] The coating process is usually a batch operating task consisting of the following phases:

- Identification of batch and Recipe selection (film or sugar coating)
- Loading/Dispensing (accurate dosing of all required raw materials)
- Warming
- Spraying (Both application and rolling are carried out simultaneously)
- Drying
- Cooling
- Unloading

Coating equipment: A modern tablet coating system combines several components

- A coating pan
- A spraying system
- An air handling unit
- A dust collector

Advantages of Tablet Coating[1]

1. Tablet coatings must be stable and strong enough to survive the handling of the tablet, must not make tablets stick together during the coating process, and must follow the fine contours of embossed characters or logos on tablets.

2. Coatings can also facilitate printing on tablets, if required. Coatings are necessary for tablets that have an unpleasant taste, and a smoother finish makes large tablets easier to swallow.

Disadvantages of Tablet Coating[1]

1)Disadvantages of coating such as relatively high cost, long coating time and high bulk have led to the use of other coating materials.

2)This process is tedious and time-consuming and it requires the expertise of highly skilled technician.[7]

ENTERIC COATING

A tablet that has a special outer covering designed to dissolve in the small intestine. Once the enteric-coating is dissolved the tablet disintegrates and the active ingredient can be absorbed by the patient.

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 un-ionize at low P^H, and therefore remain insoluble. But as the P^H 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 CAP, CAT, PVAP and HPMCP, fatty acids, waxes, shellac, plastics and plant fibers. 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.[8]

The choice of the polymer and the thickness of the coated layer are critical to control the p^H solubility profile of the enteric coated dosage form. The most common drugs which cause stomach ulcers like aspirin, diclofenac and naproxen are frequently available with enteric coatings. Omeprazole, which is a drug which stops the stomach from producing acid, is itself broken down in acid and therefore the drug generally has an enteric coating around it either as a granule in the capsules or as a granule in the dispersible form. Sulfasalazine is used either for the treatment of Crohn's disease which is inflammation of the intestines or for the treatment of arthritis. When used for Crohn's disease where it is needed in the intestines to work, it is given with an enteric coating whereas for arthritis it is very often given without an enteric coating so that it can be absorbed more quickly.

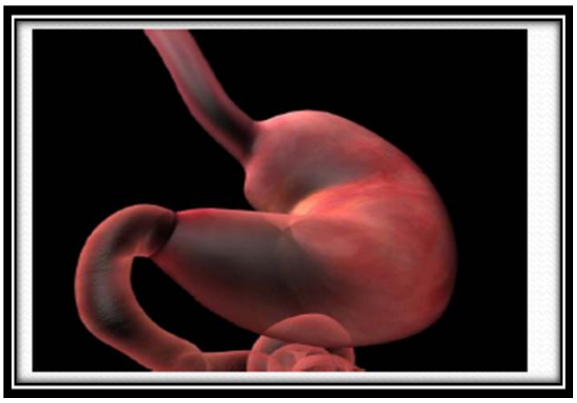
ENTERIC COATING- NESSESARY

1. After Taking a Typical Supplement

The tablet is swallowed and travels down the oesophagus to the stomach.

In the stomach the tablet is churned and gyrated in highly acidic digestive Secretions with p^H (1-4), for 45 minute to 2 hours.

If there is anything left of tablet, it will be passed through the duodenum to the small intestine.



Highly Acidic Environment.

2. Fate of Uncoated Tablets
Stomach acid breaks down tablets to prematurely release active ingredients (enzyme).

The highly acidic environment of the stomach destroys the majority of the enzyme's activities.

If the tablet is of poor quality (contains Binder and fillers) the product may pass through both the stomach and intestine with no absorption.

PROPERTIES OF ENTERIC COATING MATERIAL
1. Resistance and susceptibility
2. Stability and compatibility
3. Low cost and non-toxicity
4. Ease of application without specialized equipment.
5. Ability to be readily printed or to allow film to be applied to debossed tablet.
6. Formation of continuous (uninterrupted) film.

Primary Component Involved In Enteric Coated Tablets Formulation
1. Manufacture of Tablet core.
2. Coating Composition
a) Polymers.
b) Plasticizer.
c) Solvent.
d) Colorant.

3. Coating process
A) Coating Equipment
a) A coating pan.
b) A spraying system.
c) An air handling system.
d) A dust collector.
B) Process Parameter.

4. Coating Problems.
5. Evaluation parameters for coated tablets
a) Hardness
b) Friability
c) Weight Variation
d) Disintegration Time
e) Thickness
f) Drug content studies
g) In vitro drug release studies

Process of Manufacturing Enteric Coated Tablet[14]
Method used in manufacturing of tablet
Direct compression and Wet Granulation are two most commonly used technique for manufacturing of tablets.

A) Direct compression
Direct compression is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pre-treatment of the powder blend by wet or dry granulation procedure is required. The advantage of direct compression include saving in energy, equipment, material and handling cost. The disadvantage include segregation problem, content uniformity problem and dust generation.

B) Wet Granulation Process
Wet granulation is the most widely used process of agglomeration in pharmaceutical industry is wet granulation. Wet granulation process simply involves wet massing of the powder blend with a granulating liquid, wet sizing and drying.

Important steps involved in the wet granulation
i) Mixing of the drug(s) and excipients.
ii) Preparation of binder solution.
iii) Mixing of binder solution with powder mixture to form wet mass.
iv) Drying of moist granules.
v) Mixing of screened granules with disintegrant, glidant and lubricant.

Advantages
i) Permits mechanical handling of powders without loss of mix quality.
ii) Improves the flow of powders by increasing particle size and sphericity.
iii) Increases and improves the uniformity of powder density and cohesion during and after compaction.
iv) Reduces air entrapment and the level of dust and cross-contamination.
v) Allows for the addition of a liquid phase to powders (wet process only).
vi) Makes hydrophobic surfaces hydrophilic.

Limitation of wet granulation
i) The greatest disadvantage of wet granulation is its cost. It is an expensive process because of labour, time, equipment, energy and space requirements.
ii) Loss of material during various stages of processing.

iii) Stability may be major concern for moisture sensitive or thermo labile drugs.
iv) Multiple processing steps add complexity and make validation and control difficult.
v) An inherent limitation of wet granulation is that any incompatibility between formulation components is aggravated.

C) Dry granulation

In dry granulation process the powder mixture is compressed without the use of heat and solvent. It is the least desirable of all methods of granulation. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain a granules. Two methods are used for dry granulation. The more widely used method is slugging, where the powder is recompressed and the resulting tablet or slug are milled to yield the Granules.

Process of Manufacturer of Enteric Coated Tablet[5][6][7][9]

After the forming of tablet core, the tablet core are first coated with separating layer and then with the enteric coating layer. The Enteric coated formulation usually contains the following component

a) Polymer.
b) Plasticizer.
c) Solvent.
d) Colorant.

Polymers

Definition: Polymers are substance containing a large number of structural units joined by the same type of linkage. These substances often form into a chain-like structure starch, cellulose, and rubber all possess, polymeric properties.

An ideal enteric coated material should have the following properties

1. Resistance to gastric fluids.
2. Ready susceptibility to or permeability to intestinal fluids.
3. Compatibility with most coating solution components and the drug substrates.
4. Stability alone and in coating solutions. The films should not change on aging.
5. Formation of a continuous (uninterrupted) film.
6. Nontoxicity.
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 tablets.

With an acid-resistant property, enteric coating polymers generally possess free carboxylic acid groups on the polymer backbone. They are insoluble in acidic media but become deprotonated and dissolved in basic media at p^H nearly neutral values (p^H>5).

Classification of Polymers

Enteric coating polymers can be classified into 3 groups based on chemical compositions as listed below.

1. Polymethacrylates

Methacrylic acid/ethyl acrylate.

2. Cellulose esters

- Cellulose acetate phthalate (CAP).
- Cellulose acetate trimellitate (CAT).
- Cellulose acetate succinate.
- Hydroxypropylmethylcellulose acetate succinate (HPMCAS)/ hypromellose acetate succinate.
- Hydroxypropyl methylcellulose phthalate.

3. Polyvinyl derivatives

Polyvinyl Acetate Phthalate (PVAP)

Solubility of the polymers depends on the number of carboxylic acid groups varied in the composition. Commercial enteric coating polymers are available as powder, aqueous dispersion.

1) Polymethacrylates

(Methacrylic acid/ethyl acrylate)

Two forms of commercially available enteric acrylic resins are Eudragit L and Eudragit S both resins produces film that are resistant to gastric fluid. Eudragit L and Eudragit S are soluble in intestinal fluid at p^H 6 to 7 respectively. Eudragit L are available as an organic solution, solid, or aqueous dispersion. Eudragit S are available as an organic solution and solid.

2) Cellulose esters

Cellulose esters has been widely used in the industry. CAP has the disadvantage of dissolving only above the p^H 6, and possibly delaying the absorption of drugs. It is also hygroscopic and relatively permeable to moisture and gastric fluid, in comparison with other enteric polymers.FMC corporation has developed a patented aqueous enteric coating called 'Aquateric'.Aquateric coating is a reconstituted colloidal dispersion of latex particles. It is composed of solid or semisolid polymer spheres of cellulose acetate phthalate ranging in size from 0.05 to 3 microns with an average particle size of 0.2 micron.HPMCP-50, 55,55S these are derived from Hydroxy propyl cellulose, these polymers dissolves at low p^H (5 to 5.5) than CAP or acrylic co-polymers. These polymers are quite stable compared with CAP because of their absence of labile acetyl groups.

3) Polyvinyl Derivatives

Polyvinyl acetate phthalate (PVAP)

Polyvinyl acetate phthalate (PVAP) is manufactured by the esterification of a partially hydrolyzed Polyvinyl acetate with phthlicanhydride. this polymers is similar to HP-55 in stability and p^H-dependent solubility. It is supply as ready-to-use or ready-to-disperse enteric systems.

Threshold pH of commonly used enteric polymers

Sr.No	Enteric Polymers	Optimum pH Dissolution
1	Polyvinyl acetate phthalate (PVAP)	5.0
2	Cellulose acetate trimelitate (CAT)	5.5
3	Hydroxypropyl Methylcellulose phthalate (HPMCP)	> 5.5
4	Hydroxypropylmethylcellulose acetate succinate (HPMCAS)	>6.0
5	Methacrylie acid copolymer, Type C (Eudragit L100-55)	> 6.0
6	Methacrylic acid copolymer dispersion (Eudragit L30D-55)	> 5
7	Methacrylic acid copolymer, Type A	> 6.0
8	(Eudragit®L-100 and Eudragist L12,5)	---
9	Cellulose acetate phthalate (CAP) (Aquateric)	6.0
10	Methacrylic acid copolymer, Type B	> 7.0
11	Eudragist S-100 and Eudragit S12,5	---

Plasticizer: Success of enteric coating efficiency mostly relies on the addition of plasticizers. Plasticizers are a group of auxiliary components that improve elasticity of the polymeric film.

Plasticizer function

- Plasticizers reduce the minimum film forming temperature (MFFT) of the polymers.
- Softening the polymeric film at lower temperature.
- Improves the spreadability of the polymer on the surface of the coating substrates.
- Generates a smoother surface texture of the coating layer.
- A wide range of plasticizers are available to the formulator such as phthalate esters, phosphate esters, other esters like citrates, stearates, sebacate, oleate, adipate etc. oils, glycerol, glycols etc.

The type of plasticizer should be selected carefully as it influences the film brittleness, compatibility with the coating substrates and product stability. Hydrophilic plasticizer, triethyl citrate, is reported to improve the property of Eudragit L 30 D-55 film in the soft gelatin capsule formulations regardless of the type of filled liquid whereas hydrophobic plasticizer, tributyl citrate, gives satisfactory enteric protection only with hydrophobic filled liquid. The latter plasticizer could migrate to the hydrophobic filled liquid upon storage, resulting in the reduction of the enteric protection.

Properties of Plasticizer

1. PEG (Polyethylene Glycol)

These are hydrophilic substances and soluble in water. PEGs are used alone as hydrophilic plasticizers in enteric coating. Rate of release of water soluble drugs decreases with increase in the molecular weight of PEGs. The PEG with molecular weight of 6000 and above decreases plasticizing effect and increases lubricants effect. Migration of PEG can occur from the tablet enteric coating leading to interactions with core compounds.

2. TEC (Triethyl Citrate)

It is citric acid ethyl esters, Also known as Citroflex 2.
It is principally used as plasticizer, Miscible with water.
It is effectively used in aqueous based coating in oral sustained or enteric coated tablets.

3. Oils /Glycerides

a) Castor Oils.
b) Acetylated monoglycerides.
c) Fractionated coconut oil.

Solvent: Solvents are used to dissolve or disperse the polymers and other additives and convey them to Substrate surface.

a) Water.
b) Alcohols.
c) Ketones.
d) Esters.
e) Chlorinated Hydrocarbons.

Ideal requirement are summarized below

Should be either dissolve/disperse polymer system.
i) Should easily disperse other additives into solvent system.
ii)
iii) Small concentration of polymers (2-10%) should not in an extremely viscous solution system creating processing problems.
iv)
v) Should be colourless, tasteless, odourless, inexpensive, inert, nontoxic and non-flammable.
vi) Rapid drying rate.
vii) No environmental pollution.

Additives: The properties and composition of other components of the film coating formulation also need to be considered and optimized to get the most desired effects without affecting the quality of the film. Various other components which could be used in coating formulation are:

1. Pigments/Colorant

The commonly used colorants in coating are water soluble dyes. However, the overall colour effect of these dyes depend on the dye concentration at a particular point, thickness of film at that point and the residual moisture content in the film at that point. As these parameters can differ from tablet to tablet, the colour

difference among various tablets within the same batch may become very visible.

2. Opacifier
The opacity of the film depends on the difference between the refractive index of the polymer and other components of the coating formulation. The lake colours used in enteric coating has refractive index similar to that of various polymers, thus the opacity of lake colours is very poor.eg Titanium Oxide.

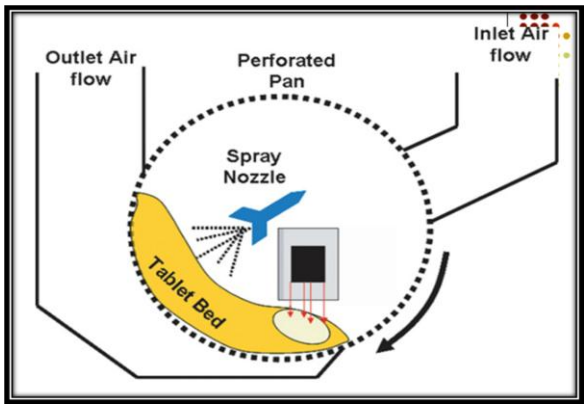
3. Anti-tacking agent
The most commonly used anti- tacking agent is Talc, which if used in higher concentration tends to settle down from the coating suspension, thus affecting the composition of suspension during the coating process.

Coating Tablet Process and Equipment[10][11]
Coating Technology is used extensively in the pharmaceutical industry, e.g. for the application of non-functional or functional coats (aesthetic, protective or rate controlling polymer films) and for the deposition of Active Pharmaceutical Ingredients (APIs) onto nonpareils (multi-particulate dosage forms). In addition to efficient techniques for API layering of multi-particulate systems, an accurate method of coating objects 3 to 30 mm in length with APIs is also desired in the pharmaceutical industry as this is the size range of most single-unit solid dosage forms. e.g. in terms of coating speed and accuracy/uniformity, particularly for the deposition of low dose API onto single unit tablet dosage forms which requires a greater degree of accuracy than can be achieved using current tablet coating technique.

Objectives
To determine the accuracy and uniformity of the coating method in applying small amounts (theoretical doses of 200 and 400 micrograms per tablet) of an API onto conventional tablets.

The coating process is usually a batch driven task consisting of the following phases
a. Batch identification and Recipe selection.
b. Loading/Dispensing (accurate dosing of all required raw materials).
c. Warming/Preheating.
d. Spraying (application and rolling are carried out simultaneously).
e. Drying.
f. Cooling.
g. Unloading.

Tablet coating equipment may include
a. Spray guns.
b. Coating pan.
c. Polishing pan.
d. Solution tanks.
e. Blenders and mixers.
f. Homogenizers.
g. Mills.
h. Peristaltic pumps.
i. Fans.
j. Steam jackets



A Simple Diagram Of A Tablet Coating System

A) COATING PAN
Coating pans are used to form an aqueous or organic film around any kind of pellets and tablets or micro granules. These pans are also widely used to sugar-coat tablets. A coating pan is an essential requirement in pharmaceutical applications. Different coating techniques are applied in pharmaceutical industry.

Working: Tablets are continuously fed into a coating drum at a controlled rate. A high volume of process air heats the tablets at the time of entering and moving in the drum. Coating solution is applied through a series of spray guns as the product moves down the length of the coating drum. The tablets are homogeneously mixed for a uniform coating/weight gain. Shallow bed depth of the pan allows the tablet/pellets to pass through the spraying zone and finally discharged from the exhaust end of the coating drum and transported through a conveyor belt for collection, storage, inspection and packaging. These machines ensure consistent exterior coating.

Salient features of Coating Pan are as follows
- Usually, temperature can be controlled with the help of temperature controller.
- Compact hot air blower with inlet air damping arrangement, is generally there in different coating pans.
- Mounting facility is available for easy change from coating pan to polishing pan.
- Coating pans do not require any foundation and are able to install on pre-leveled floor.
- Flameproof type of construction is optional.

B) SPRAY GUNS
The spray guns create a fine mist of coating solution that dries just after it contacts the tablet. The liquid spray coating dried onto the tablets by heated air drawn through the tablet bed from an inlet fan. The air flow is regulated for temperature and volume to provide

controlled drying and extracting rates, and at the same time, maintaining the drum pressure slightly negative relative to the room in order to provide a completely isolated process atmosphere for the operator.

COATING PROCESS[10] [11]

1. Tablet coating takes place in a controlled atmosphere inside a perforated rotating drum. Once you load a batch of tablets into the coating pan, you need to preheat the tablets and allow time for dust and tablet flash to exit the pan. Angled baffles fitted into the drum and air flow inside the drum provide means of mixing the tablet bed. As a result, the tablets are lifted and turned from the sides into the centre of the drum, exposing each tablet surface to an even amount of deposited/sprayed coating. Once the temperature of the outlet air reaches 42° to 46°C, usually within 15 minutes, spraying can begin.
2. The spray guns create a fine mist of coating solution that dries just after it contacts the tablet. The liquid spray coating dried onto the tablets by heated air drawn through the tablet bed from an inlet fan. The air flow is regulated for temperature and volume to provide controlled drying and extracting rates, and at the same time, maintaining the drum pressure slightly negative relative to the room in order to provide a completely isolated process atmosphere for the operator.
3. As the water evaporates, it leaves the solids behind to form a thin film on the tablet. The key to tablet coating is to get the surface slightly wet and immediately dry. Remember: apply the coating in many short, fast exposures, not in long, slow exposures.
4. Once the base coating is applied, you can increase the rate of solution addition and the pan speed proportionately. Typically, it takes about 20 minutes before increasing the spray rate and pan speed significantly.
5. Tablets that are very porous may require an initial spray rate that is slower than the average of 100 millilitres per minute per gun. Be sure to monitor spraying to see whether the spray pattern changes. If it does, there is likely a build-up of solids on the gun tips. Correct this only by cleaning the tips, which means stopping the spray and the pan.
6. The enteric coating solution dries on the tablet surface because there is a constant supply of hot air entering the drum and passing through the drum's perforations into the bed of tablets. Over time, the film builds layer after layer of solids.
7. After finished applying the solution and drying it, the tablets must cool.

For coatings to adhere properly, the tablets must remain at a specific temperature, the solution must be applied at a consistent rate, and the motion of the tablets must be active yet tranquil. Disrupt any of these conditions, and this will produce a defective tablet.

Parameters Influences in Tablet Coating Process

Tablet coating is a complex process that is affected by many variables. Some of those variables can be evaluated or controlled, others can't.

Here are some of the parameters you should check when evaluating coating process to determine the source of defective coated tablets.

1. Control: Many problems occur in coating, such as temperature, pan pressure, spray rates, and atomization pressure. But, the tablet's surface temperature can be measure with additional tools (out from the coating equipment) by using infra red thermometer (laser thermometer).

2. Tablet quality: Tablets must have the proper porosity, surface, hardness, and moisture content.

3. Waiting period. Most tablets cannot be coated immediately after they've been compressed. The energy within the tablets is still fairly high and they are still warm. In addition, tablet hardness changes over 24 to 48 hours. Let the tablets rest at least that long before you coat them meanwhile you can check the uncoated tablet for assay, dissolution or other specification by quality control. After the QC released the tablet, then you can start the coating process.

4. **Batch size**. Variation in batch size changes the required pan speed, gun geometry, spray rates, and temperature. The more your batch sizes vary the more quality issues that will arise in the coating process. Usually, the greater batch size or the greater number of tablets in pan coating the pan speed to spin faster. Vice versa, if the number of tablets or the smaller the batch size, pan speeds spin also reduced.

5. **Coating Solution preparation**. Prepare coating solutions the same way, regardless of the batch, the shift, or the operator. Track the solution temperature, mixer speed, and storage time. Better if you had standard operation procedure for the coating solution manufacturing.

6. Spray gun calibration. Should calibrate or check the calibration of the guns every time you change products. This means checking the gun's overall condition and its filter, nozzle alignment, and needle condition.

7. **Spray Gun Position/Geometry**. Geometry refers to the gun-to-gun alignment, gun-to-tablet bed alignment, and distance from the gun to the end of the pan. Furthermore, make sure all the guns are pointed in exactly the same direction and are maintaining the same spray pattern. Make certain that the tubing and connections are tight and do not interfere with alignment.

8. **Gun nozzles**. The spray gun nozzles must be kept clean and free of product build-up. Use a flashlight

during coating to look into the cabinet and check the nozzles.

9. **Pan loading**. A visual inspection is critical when coating tablets that are friable or that chip or break easily. That's why, while loading the tablets, tablets that are broken, capped, chipped, or covered with black specks. Then to check it one by one, as long as eyes can see. Which will help pinpoint the source of any defects that occur. Also check the tablets during initial pan rotation, or after preheating.

10. Cleaning. Make sure cleaned and dried each component of the spraying system before re-installing it after a product changeover.

In tablet coating, small changes in almost any parameter can lead to big differences in results.[10]

COATING TABLET DEFECTS[13] [14]

Here is a list of common defects associated with coated tablets and some likely causes and the remedies.

1) Picking and sticking: This is when the coating removes a piece of the tablet from the core. Over wetting or excessive film tackiness causes tablets to stick to each other or to the coating pan. On drying, at the point of contact, a piece of the film may remain adhered to the pan or to another tablet, giving a "picked" appearance to the tablet surface and resulting in a small exposed area of the core. It is caused by over-wetting the tablets, by under-drying, or by poor tablet quality.

Remedy: A reduction in the liquid application rate or increase in the drying air temperature and air volume usually solves this problem. Excessive tackiness may be an indication of a poor formulation.

2) Twinning: This is the term for two tablets that stick together, and it's a common problem with capsule shaped tablets.

Remedy: Assuming you don't wish to change the tablet shape, you can solve this problem by balancing the pan speed and spray rate. Try reducing the spray rate or increasing the pan speed. In some cases, it is necessary to modify the design of the tooling by very slightly changing the radius. The change is almost impossible to see, but it prevents the twinning problem.

3) Colour Variation: This problem can be caused by processing conditions or the formulation. Improper mixing, uneven spray pattern and insufficient coating may result in colour variation. The migration of soluble dyes, plasticizers and other additives during drying may give the coating a mottled or spotted appearance.

Remedy: The use of lake dyes eliminates dye migration. A reformulation with different plasticizers and additives is the best way to solve film instabilities caused by the ingredients.

4) Orange Peel: This refers to a coating texture that resembles the surface of an orange. Inadequate spreading of the coating solution before drying causes a bumpy or "orange-peel" effect on the coating. It is usually the result of high atomization pressure in combination with spray rates that are too high. This also indicates that spreading is impeded by too rapid drying or by high solution viscosity.

Remedy: Thinning the solution with additional solvent may correct this problem.

5) Mottled colour: This can happen when the coating solution is improperly prepared, the actual spray rate differs from the target rate, the tablet cores are cold, or the drying rate is out of specification.

6) Capping and Lamination

This is when the tablet separates in laminar fashion. Capping is partial or complete separation of top or bottom crowns of tablet main body. Lamination is separation of a tablet into two or more distinct layers. Friability test can be used to reveal these problems.

The problem stems from improper tablet compression, but it may not reveal itself until you start coating. How you operate the coating system, however, can exacerbate the problem.

Remedy: Be careful not to over-dry the tablets in the preheating stage. That can make the tablets brittle and promote capping.

7) Roughness

A rough or gritty surface is a defect often observed when coating is applied by a spray. Some of the droplets may dry too rapidly before reaching the tablet bed, resulting in the deposits on the tablet surface of "spray dried" particles instead of finely divided droplets of coating solution.

Surface roughness also increases with pigment concentration and polymer concentration in the coating solution.

Remedy: Moving the nozzle closer to the tablet bed and reducing the degree of atomization can decrease the roughness due to "spray drying".

Evaluation Parameters Of Core Tablets[15][16]

1) Flow properties of blend

Density

A quantity of 2 gm of powder from each formula, previously lightly shaken to break any Agglomerates formed, was introduced into a 10 ml measuring cylinder. After the initial Volume was observed, the cylinder was allowed to fall under its own weight onto a hard Surface from the height of 2.5 cm at 2 sec intervals. The tapping

was continued until no further change in volume was noted. Both bulk density (BD) and tapped density (TD) were determined.

Compressibility Index: Compressibility is the ability of powder to decrease in volume under pressure. Compressibility is a measure that is obtained from density determinations.

Hausner's ratio: It is usually determined from the ratio between the tapped density (TD) and the bulk density (BD).

Angle of Repose

Angle of repose (θ) is the maximum angle possible between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel method and is the measure of the flowability of powder/granules.

Evaluation Parameters For Core and Coated Tablet[15] [16]

Weight variation: Twenty tablets are weighed individually and the average weight is calculated. The individual tablet weights are then compared to the average weight.

Thickness: The thickness of individual tablets may be measured with a micrometer, which permits accurate measurements and provides information of the variation between tablets.

Hardness: Hardness was determined by taking six tablets from each formulation, using a Monsanto Hardness Tester.

Friability: It is usually measured by the use of the Roche friabilator. A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus. After four minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability.

Disintegration Test

The disintegration test is carried out using the disintegration tester which consists of a basket- rack holding 6 plastic tubes, open at the top and bottom, the bottom of the tube is covered by a 10 mesh screen. The basket is immersed in a bath of suitable liquid held at $37^{o}C$, preferably in a 1L beaker.

In-vitro dissolution study

The dissolution test was performed using USP dissolution testing apparatus 2 (paddle method); Medium - 0.067M Phosphate buffer, pH 6.8; Volume- 1000 ml; Temperature- 37ºC; RPM – 50; Time intervals- 10, 20, 30 and 45 mins. Absorbance of these solutions was measured at the wavelength of UV-248nm. Separately inject equal volumes (about 10 µl) of the dissolution medium as blank, standard preparation and sample preparation into chromatograph, and the chromatograms was recorded and measure the peak area responses for the analyte peak.

CONCLUSION

Enteric coating protect the stomach against drugs which causes gastric irritation. Enteric coating protect the drug which is unstable in gastric fluids. Enteric coating provide a delayed- release component for repeat action tablets. Enteric coated tablets resist the action of the acidic stomach fluids and pass through it before the coating can dissolve thus protecting the gastric mucosa from the irritating effects of the ingredients in the tablets e.g. Aspirin. However, this coating dissolves in the neutral or alkaline milieu of the intestine and the active ingredients become available for absorption into the blood stream. Enteric coating solution may also contain other ingredients which may aid in the application of the coating material to the tablet or to improve the character of the coating. These may be such ingredients as polymers, surfactants, plasticizers, antifoaming agents, solubilizing agents, colouring agents. Enteric release coating consist of P^{H} sensitive polymers, which means the coating remains intact in the acidic environment of stomach and then solubilizes in the more alkaline environment of small intestine.

REFERENCES

1. Aulton ME, Pharm. Acta. Helv., 1981; 56(4–5): 133–136.
2. Indian Pharmacopoeia, 4th edition New Delhi, Controller of Publications, 1996; A-80, 82.
3. Leon Lachman, Herbert A, Liberman, Kaing Joseph L., The theory and practice of industrial pharmacy, Varghese publishing house, Bombay, 3rd edition, 293-295.
4. Chein YW. Novel Drug Delivery System Marcel Dekker Inc. New York., 1992; 14: 139-196.
5. Chakraborty Sumit, Sarkar Sibaji and Debnath Sujit Kumar, "Formulation Development and Evaluation of Pantoprazole Enteric Coated Tablets", International Journal of Chem Tech Research, 2009; 1(3): 663-666.
6. Bozdag S., Çalis S., and Sumnu M., "Formulation and Stability Evaluation of Enteric-Coated Omeprazole Formulations", S.T.P. Pharma Sciences, 1999; 9(4): 321-327
7. Kamble Rupesh S., Kajale Archana D., Giradkar Keshao P., Bakade BV., Channawar MA., Chandewar AV., "Formulation and Development of Enteric Coated Dosage form using Ketorolac Tromethamine", International Journal of Pharmaceutical Research and Development, 2010; 2(8): 126-135.
8. Willemijntje A., Hoogerwerf, Pasricha Pankaj Jay Pharmacotherapy of Gastric Acidity, Peptic Ulcers, and Gastroesophageal Reflux Disease. "Goodman & Gilman's The Pharmacological Basis of Therapeutics" 11th ed., 2006; 623-634.

9. Philip Anil K. and Philip Betty, Colon Targeted Drug Delivery Systems: A Review on Primary and Novel Approaches, Oman Medical Journal, 2010; 25(02): 70-78.
10. Leon Lachman, Herbert A, Liberman, Kaing Joseph L., The theory and practice of industrial pharmacy, Varghese publishing house, Bombay, 3rd edition, 293-295.
11. Eurotherm. Invensys. The Tablet Coating Process, 2012, Aug 18. Available from http//www.eurotherm.com/industries/life sciences/applications/tablet-coating/
12. Kibbe A.H. (Ed.), Handbook of Pharmaceutical Excipients (Pharmaceutical Press, London, UK, 2000; 501–504.
13. Shah A. Coating Tablet Defect: The Cause and The remedies, Coating Polymers, 2011, [cited 2012 Aug, 05] available from http:/vikram thermo. blogspot in/2011/06/picking and sticking.html?go back=gde_3292037_member_56911500.
14. Picta. R Problems Associated With Tablet Manufacturing, 2011, [cited 2012 July17] Available from http:/www.pharmainfo.net/rajapicta 1023/blog/problem-associated –tablet-manufacturing.
15. D. Raju, J. Padmavathy, V. Sai, D. Saravanan and I. Aparna Lakshmi, Formulation and development of enteric coated tablets of prednisolone as a colon targeted drug delivery, IJPSR, 2011; 2(3): 685-690.
16. Patil Ajit, Payghan Santosh and Disouza John, Formulation and Evaluation of Enteric coated tablets of Azithromycin dihydrate, International Journal of Chem Tech Research, 2011; 3(3): 1479-1484.