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A Review on Enteric Coated Granules

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Abstract: Enteric coated granules are solid unit dosage forms intended for oral administration that are engineered to bypass the stomach and release the drug into the small intestine. "enteric" indicates small intestine; As a result, enteric coatings stop medication from being released before it reaches the small intestine. The majority of enteric coatings function by providing a coated surface that is stable at the stomach's highly acidic pH but rapidly degrades at a less acidic (relatively more basic) pH. These materials include fatty acids, waxes, shellac, plastics, and plant fibers. The ideal properties of enteric coatings, their advantages and disadvantages, the various polymers used, their chemical structures, the selection and mechanism of drugs, and the manufacturing and evaluation of enteric coated granules are all covered in this review. Due to their advantages over conventional drug delivery systems—longer dosing intervals and increased patient compliance—these have recently piqued the interest of numerous formulators. The study provides an overview of the most recent developments in this field.

Key words: Evaluation, ideal properties, the mechanism, and methods of enteric coated granules.

I. INTRODUCTION

Granules are substances made up of dry, solid aggregates of powder particles that are strong enough to resist handling. They are designed to be taken orally. Before administration, some are chewed, some are swallowed whole, and some are dissolved or dispersed in water or another appropriate liquid.

Granules include one or more active ingredients, excipients, and, if required, flavouring agents and colourants that have been approved by the appropriate authority. Granules can be found in preparations with one dosage or multiple doses. A device capable of measuring the specified amount is used to administer each dose of a multidose preparation.

Several categories of granules may be distinguished:

- effervescent granules;
- coated granules;
- gastro-resistant granules;
- modified-release granules.

1.1 Granules Coating are typically coated with one or more layers of mixes of different excipients in coated granules, which are typically multidose formulations.

1.1.1. Primary components involved in granules coating

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

1.1.2 Process Design & Control for Coatings

The majority of coating techniques include spraying a coating solution over the granules while they are being stirred around in a fluid bed, pan, etc. A thin layer that sticks to each granules is created as the solution is sprayed. The coating can either be applied once to form the coating or it can be applied many times to form the coating in layers. Pans that rotate for coating are frequently utilised in the pharmaceutical business. In the pan, which is normally tilted at an angle from the horizontal, uncoated granules are first inserted. The liquid coating solution is then added to the pan while the granules tumble. The liquid part of the coating solution is then evaporated by blowing air over the surface of the tottering granules. A fluid bed coater, in contrast, works by circulating air through a bed of granules at a speed that supports and separates the granules as independent units. The granules are sprayed with the coating mixture once separation has occurred. [1-7]

The coating procedure typically consists of the following phases and is batch operated:

- 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

1.1.3 Coating equipment A modern granules coating system combines several components:

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

1.3 Granules coating's benefits and drawbacks

Granules coating benefits include following the intricate shapes of embossed characters or emblems, not causing granules to clump together during the coating process, and being sturdy and robust enough to withstand handling.

Pills need coatings to give them a smoother finish, making big pills simpler to swallow, and to cover up the bad taste.

The process of coating a granules is laborious and time-consuming, and it necessitates the skills of a highly qualified specialist. Limitations of sugar coating, such as their comparatively expensive cost, lengthy coating time, and large bulk, have led to the employment of other coating materials.

II. ENTERIC COATING

An enteric coating is a barrier that regulates where oral medication is absorbed in the digestive tract. Enteric coatings stop the release of medication before it reaches the small intestine because the word "enteric" refers to the small intestine. At low pH levels, the enteric coated polymers continue to unionise and are hence insoluble. However, as the GIT's pH rises, the acidic functional groups become ionisable and the polymer swells or dissolves in the fluid there. CAP, CAT, PVAP, HPMCP, fatty acids, waxes, shellac, polymers, and plant fibres are materials used for enteric coatings.

Four factors justify the application of such a coating to a granules, granules or capsule ingredient:

- Defence of active medicinal components against the stomach's acidic environment (e.g. enzymes and certain antibiotics).
- To stop nausea or gastrointestinal distress brought on by a medication because of inflammation (e.g. sodium salicylate).
- To deliver medications in their most concentrated form to the principal site of absorption in the small intestine, where absorption is most effective.
- To give repetitive action a delayed-release component.[8]

To regulate the pH solubility profile of the enteric coated dosage form, the polymer selection and coating layer thickness are crucial.

The most popular stomach ulcer-causing medications, such as aspirin, diclofenac, and naproxen, are usually offered with enteric coatings. Because omeprazole, a medication that inhibits the production of stomach acid, is itself broken down in acid, it usually has an enteric coating around it, either in the form of a granule in the capsules or a granule in the dispersible form. Sulfasalazine is used to treat arthritis as well as Crohn's disease, an inflammatory condition of the intestines. It is frequently administered without an enteric coating for arthritis in order to increase absorption, in contrast to the use for Crohn's disease where it needs to be in the intestines to function.

An antibacterial medicine called ERY-TAB contains erythromycin base in a specifically enteric-coated granules to shield it from gastric acidity's inactivating effects and to enable effective absorption of the antibiotic in the small intestine. Each white oval granules of the ERY-TAB (erythromycin delayed-release granules) ranges in dosage strength from 250 mg to 333 mg to 500 mg of erythromycin as the free base. Enteric coated aspirin is another granules that is offered for sale. For instance, enteric-coated peppermint oil and Micropirin® 75 mg EC granules. such as Colpermin®

2.1 Ideal enteric coating material

- 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
- Ability to be readily printed

2.1.1 Polymers used for enteric coating

- Methyl acrylate-methacrylic acid copolymers
- Cellulose acetate phthalate (CAP)
- Cellulose acetate succinate
- Hydroxypropyl methyl cellulose phthalate
- Hydroxypropyl methyl cellulose acetate succinate (Hypromellose acetate succinate)
- Polyvinyl acetate phthalate (PVAP)
- Methyl methacrylate-methacrylic acid copolymers
- Shellac
- Cellulose acetate taramellite
- Sodium alginate
- Zein
- Aqua-Zein®, which is an aqueous zein formulation containing no alcohol.
- Amylose starch and starch derivatives

- Dextrins

2.2 Limitations

Due to the broad range of pH values and various enzymes found in the GI tract, which the drugs must navigate before reaching the target site, the efficacy and reliability are questioned.

III. OBJECTIVE

The goal of the current research is to provide information about enteric coated granules as well as gastro-resistant drug delivery systems in general. Due to their advantages over traditional drug delivery systems, these have recently piqued the attention of many formulators. The study gives a summary of the most recent developments in this field.[11]

IV. MECHANISM OF ENTERIC COATED TIME-RELEASE PRESS COATED (ETP) GRANULES

ETP granules are made up of three layers: an enteric coating layer, a press-coated swellable hydrophobic polymer layer, and a drug-containing core granules with a rapid release function (HPC, HPC). (acid resistance function).[12,13] Due to the outer enteric coating layer's resistance to acid, the granules does not discharge the medication in the stomach. After stomach emptying, the enteric coating layer disintegrates quickly, and the press coated polymer (HPC) layer starts to deteriorate slowly. Since there is no drug release period (lag phase) after gastric emptying, rapid drug release happens when the erosion front hits the core granules, which takes a long time.

V. METHOD OF MANUFACTURING ENTERIC COATED BY SPRAY COATING TECHNIQUE

Wet granulation was used to make the granules. Drug and additional excipients were passed through #80, and then enough binding agent was gently added to create dough mass. The bulk was sieved through # 8 before being dried at 45°C for about an hour. The granules were then passed through # 20 before being lubricated with magnesium stearate. A shallow concave plain/plain punch was used to compress the mixed mixture into granules with a weight of 250 mg each, a thickness of 4.46± 0.21 mm, and a diameter of 7.9 mm.

Cellulose was dissolved in 50 ml of isopropyl alcohol and a weighed quantity of pectin was dissolved in 50 ml of water. After thoroughly combining the two solutions to create a homogeneous mixture, PEG-6000 was introduced as a plasticizer. 5.1.2 covering for cores The compressed pills are coated with enteric using the traditional coating pan method. The coating of the granules was done in a pan coater at 50 rpm, 50ºC, and a flow rate of 10 ml/min. Spraying was used to apply the coating, and it was then cured. With the proper pressure, these liquids are sprayed over the granules. The coated pills are secondarily dried in a tray dryer after being initially dried with a heat blower.

5.1 Coating methodology

With one spray gun and a standard coating tray, granules were coated. Alcohol 95% was originally used to clean the coating pan. Core granules weighing 3.5 kg were chosen as the batch quantity for coating. The coating pan was filled with the core pills. Using a dryer and air compressor, granules centres were pre-heated to a temperature of about 40 °C. Throughout the full coating process, warm air (up to 50–55°C) was blown into the coating pan. Enteric coating solution was put into the spray cannon, which was operating at the right flow rate. Under an appropriate air pressure (87.0-116.0 psi) 6-8 bar, seal coating dispersion was sprayed onto the falling cores while the pan was in motion. blow drying pills while the air heater was turned off.

5.2 Further thoughts

- A constant negative air pressure must be kept in the pan. (More air out than in).
- Always give the tailpipe temperature at least 15 minutes to stabilise after startup before adjusting fluid and/or air flows.
- If there is any tackiness or sticking, decrease the spray rate of the coating solution by 15% for the first 1% weight gain in order to achieve the highest enteric quality and adhesion between the core and enteric interface.
- Once delivery of the coating solution has started, maintain a consistent flow rate.
- When coating, keep gun tips in the open position. (Colorcon).

Tables 1 and 2 list the coating conditions and parameters

Table no: -1 Parameters of coating process

Equipment	Erweka Coating Pan
Substrate	50 mg Erythromycin stearate granules
Pan Charge	3.5 Kg
Dispersion solid content	15.0% (w/w)
Pan speed	14 rpm
Inlet Temperature	52-58ºC
Exhaust air temperature	40-42ºC
Bed Temperature	35-40ºC
Spray rate	50 g/min.
Distance between spray gun and granules bed	15 cm
Coating time	160 min

Table no: -2 Parameters of coating formulation

Parameters	**Coating**
Theoretical weight gain (mg)	10 ± 2%
Polyethylene glycol (PEG 6000)	1.4% (w/w)
Deionized water	72.5% (w/w)

6. Evaluation of granules [16]

6.1 Measurement of the angle of repose

The angle of repose was determined by the funnel method. The determination of angle of repose by this method is referred to as static angle of repose. Angle of repose is an indirect method of quantifying powder flow ability; because of their relationship with inter particle cohesion. A static heap will slide when the angle of inclination is large enough to overcome frictional forces and stop when gravitational forces balance the forces. The sides of heap will make an angle with horizontal which is called angle of repose.[17] Powder is poured onto the centre of the dish from the funnel that can be raised vertically until the maximum cone height (h) is obtained. The angle of repose can be calculated by the given formulae. $\alpha = \tan^{-1}$ (h/r), where h is height of pile and r is radius of pile. This was done thrice, from that average angle of repose and standard deviation was calculated.

6.2 Pore/Bulk density

The apparent true density (ρb) was measured by pouring the pre weighed (M) blend into a graduated cylinder. The bulk volume (Vb) of the blend was determined by this method. Then the true density was determined by the given below formulae. ρb = M/Vb This was done thrice, from that average true density and standard deviation was calculated.

6.3 Tap density

The measured cylinder containing a known mass (M) of blend was tapped for a fixed time, and the minimum volume (Vt) occupied in the cylinder was measured. The tapped density was calculated by the formulae mentioned below. Tap density = M/Vt This was done thrice, from that average tap density and standard deviation was calculated.

6.4 Porosity [18] The porosity of voids and of the powder is defined as the ratio of void volume to the bulk volume of the packaging. E= (Vb-Vp)/Vb=1 - (Vp/Vb)

6.5 Carr's Index

Based on the apparent bulk density and the tapped density, the percentage compressibility of the bulk drug was determined by using the following formula. %Compressibility = tapped density - bulk density/tapped density X100

6.6 Hausner's Ratio

The ratio of tapped density to bulk density of the powders is called the Hausner's ratio.

CONCLUSION

We can infer from the summary above that enteric coating is used on granules to prevent first pass metabolism, gastric irritation, and degradation while also directing the medication to the target intestines. Streptococcal infections of the oesophagus (strep throat), skin, and lungs (pneumonias) caused by Streptococcal pneumoniae, Mycoplasma pneumoniae, and Legionella pneumophila can all be treated with enteric-coated granules. (Legionnaires disease). To regulate the pH solubility profile of the enteric coated dosage form, the polymer selection and coating layer thickness are crucial. When creating enteric coated dosage forms, drugs with a low oral bioavailability (50%), a short biological half-life (about 3 hours), and sufficient protein binding are favoured.

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