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“ADVANCEMENT IN ENTERIC COATED TABLETS: MECHANISMS, FORMULATION, AND CHARACTERIZATION FOR ORAL SITE-SPECIFIC DRUG DELIVERY”

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Abstract: This review delves into the intricate world of delayed-release coated tablets, elucidating their pivotal role in oral site-specific drug delivery systems. The influence of pharmacokinetics and pharmacodynamic traits on administration routes, particularly oral medication, is explored. Despite the prevalence of conventional oral dosage forms like capsules and tablets, concerns around drug toxicity and effectiveness have paved the way for novel drug delivery strategies. The focus turns to the significance of enteric coatings in facilitating drug delivery into the intestinal area, overcoming challenges posed by the gastrointestinal tract's microenvironment. Strategies like pH-sensitive drug release and time-controlled drug release have emerged to tackle these obstacles, exhibiting promising potential but also encountering variability in drug delivery due to individual gastric emptying times. The paper delves into the essentials of enteric coating materials, highlighting their attributes, composition, and ideal characteristics for effective drug protection and release. It evaluates newer materials for tablet coating and enumerates the advantages and disadvantages of enteric coatings, offering a comprehensive analysis of their mechanisms, equipment used, recent trends, coating processes, and potential defects. Additionally, the review encompasses pre- and post-compression characteristics of tablets, emphasizing the importance of factors like powder characteristics, tablet thickness, weight consistency, hardness, friability, disintegration time, and drug content uniformity.

Keywords: Oral Site Specific Delivery, Delayed Release, Enteric Coated Tablet, Polymers, Recent Trend In Coating, Mechanism And Methods For Enteric Coating, Evaluation

Introduction

The medication's pharmacokinetics and pharmacodynamic characteristics influence the route of administration in addition to convenience and compliance ^[1]. Most popular method of medicine administration is oral. Due to its benefits, including non-invasiveness, patient compliance, and ease of medication delivery, it is the most favoured method ^[2]. Due to knowledge of drug toxicity and ineffectiveness when delivered orally via conventional means in the form of capsules or tablet form, these dosage forms appear more inviting ^[3]. The tablet is the most commonly adopted dosage form lately in use because of its

ease of self administration, compactness, and relatively ease of the production process^[4]. Before a medicine to get into the systemic circulation after oral delivery, it must first get over an array of barriers. Drug plasma levels following oral administration may be insignificant due to physico-chemical characteristics of the drug, such as low water solubility or large molecular mass and aggregation. To get around these obstacles, a number of solutions have been devised^[5].

Oral site specific drug delivery system:

In order to improve systemic absorption of medications that are unstable in the stomach and to treat a number of bowel illnesses locally, oral site-specific drug delivery devices have garnered a lot of attention recently. However, the gastrointestinal tract's microenvironment and different absorption pathways typically provide challenges for formulation scientists working to create and optimise oral drug delivery systems. Applying an enteric coating to a solid dosage form could facilitate the delivery of a medicinal substance into the intestinal area. The past ten years have seen the effort and publication of a number of strategies to create novel ways for site-specific drug release, such as pH-sensitive drug release and time-controlled drug release. Among these are the release systems with time constraints, including dosage formulations with sustained or delayed release show great promise. However, these dosage forms may exhibit considerable interpatient variability in the site of drug delivery due to the potentially wide variance in the gastric emptying time of these forms in humans. Conversely, enteric-coated dosage forms and other pH-sensitive delivery systems provide a straightforward and useful method of intestinal medication distribution^[6,7].

The first delayed release pharmacological product, modified release (MR) formulations were created in the 1880s and have since revolutionised how patients receive their medications^[8]. Typical medication administration via oral modalities are known to have an expedient drug release. Contrary to this, modified release dosage forms not only enable the upkeep of therapeutic drug levels with minimal variations but also the reduction of the regularity of drug administration doses^[9]. Drugs featuring delayed release are ones which disseminate their active ingredients into the body periodically, primarily in the small intestine. Such methods have been developed to release the medicine primarily at a certain location in the GIT. The medications included in such a system include those that are:

- i. Metabolized in the stomach or by intestinal enzymes
- ii. Known in order to generate gastric distress
- iii. Absorbed from an isolated intestinal site;
- iv. Intended to exert local repercussions at a particular git site^[10].

Coating is a technique wherein a tablet's outer surface is covered using suitable material^[11]. In addition to providing medication considerable physical and chemical protection, the coating also alters the drug's release characteristics^[12].

Enteric Coating^[13,14]

An enteric coating is a obstacle that delays oral medications from dissolving in the stomach and encourages their dissolution in the intestine, where they are absorbed. Since the word "enteric" corresponds to the small intestine, enteric coatings limit medicine release before it reaches the small intestine. A pH level that is low causes the enteric coated polymers keep on being unionised and insoluble. But as the pH in the GIT escalates, the acidic functional groups might ionise and the polymer swells or dissolves in the intestinal fluid. Fatty acids, waxes, shellac, polymers, and plant fibres count among the components used in the manufacture of enteric coatings. The desirable characteristics of an enteric coating are characterised by being resistant to GI fluids, susceptible to or permeable to intestinal fluid, compatible with the majority of coating solution ingredients and the drug substrate, forming a continuous film, nontoxic, affordable, and simple to use. Shellac (esters of aleurtic acid), cellulose acetate phthalate (CAP), poly(methacrylic acid-co-methyl acrylate), cellulose acetate trimellitate (CAT), poly(vinyl acetate phthalate) (PVAP), and hydroxypropyl methylcellulose phthalate (HPMCP) constitute certain of the polymers employed in enteric coating. Based on the dissolving pH range of 4.5 to 7.0, polymers were specified.

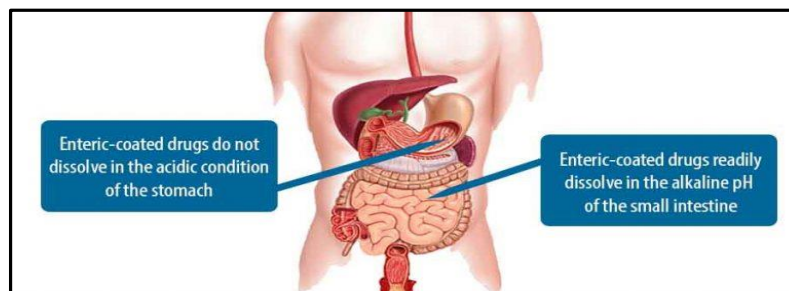


fig no 1. enteric coated drug in git

Need for Enteric Coating ^[15]

Enteric coating is important for the following reasons:

- To shield the medication from stomach acid
- To release the medication in the intestines or elsewhere after the stomach
- To prevent certain antibiotics and enzymes from reacting with the stomach juice and destroying acid-sensitive medicines
- To prohibit nausea or gastrointestinal distress brought on by a drug's irritant, such as sodium salicylate,
- To administer medications designed to have a local effect in the intestines, such as intestinal antiseptics
- May be focused and sent to the area where they would work.
- The requirement to reduce first pass metabolism.
- To prolong a delayed release component for a tablet with a repeat action

Ideal Characteristics of Enteric Coating Material ^{[16]:}

- It should be resistance to stomach juices.
- Rapid permeability or sensitivity to intestinal secretions.
- Compatible with the majority of medication ingredients and coating solution components.
- Stability both by itself and within coating solutions.
- The continuous, uninterrupted film's formation.
- Lack of Toxicity.
- Low price.
- Simplicity of use without specialised tools.
- Capability to print easily or to enable film application on tablets without embosses.
- In liquids with a pH of less than 5.5, the majority of enteric coatings should not disintegrate.

Composition of Enteric Coating ^{[14,17]:}

0.01%–10% resin and 0.01%–10% polymer make up an enteric coating composition. A pharmaceutical, nutraceutical, fruit, vegetable, agricultural, or industrial product can be used as a substrate. The enteric coating composition can be applied to it to create an enteric coating.

table no.1. constituents of enteric coating

Constituents	Examples
Resin	Shellac
Polymer	Alginate
Plasticizer	Triethyl citrate
Preservatives	Sorbates
Detackifying agent	Monosterate
Lubricant	Palmitic acid
Colorant	FD & c lake yellow

New Materials for Tablet Coating

- Zein
- Aqua zein®, which is an aqueous zein formulation containing no alcohol.
- Amylose starch and starch derivatives
- Dextrin's

Advantages Of Enteric Coating ^[18,19]

1. Protects Sensitive Ingredients: Shields drugs from stomach acid to prevent early breakdown.
2. Improves Absorption: Releases medication in the small intestine for better absorption.
3. Reduces Stomach Irritation: Minimizes discomfort caused by some drugs.
4. Controls Release: Allows for a gradual drug release, reducing the need for frequent dosing.
5. Hides Bad Taste or Odor: Masks the unpleasant taste or smell of some medicines.
6. Prevents Interactions: Lowers the risk of drug interactions by releasing in the small intestine.
7. Boosts Stability: Protects drugs from moisture and light, extending their shelf life.
8. Lessens Side Effects: Reduces stomach-related side effects for certain medications.

Disadvantages of enteric coating ^[20]

1. Complex process.
2. It requires time.
3. Needs a technician with advanced training.

Mechanism Of Enteric Coating ^[21]

ETP tablets are made up of three layers: an enteric coating layer (acid resistance function), a press-coated swellable hydrophobic polymer layer (Hydroxy propyl cellulose layer, or HPC), and a drug-containing core tablet (for rapid release). Due to the outer enteric coating layer's resilience to acid, the tablet does not dissolve and release the medication in the stomach. Following emptying of the stomach the enteric coating layer disintegrates, and the layers of press coated polymers (HPC) are gradually worn away by intestinal fluid. Since there is no drug release period (lag phase) after gastric emptying, rapid drug release happens when the erosion front reaches the core tablets, that utilises a long time

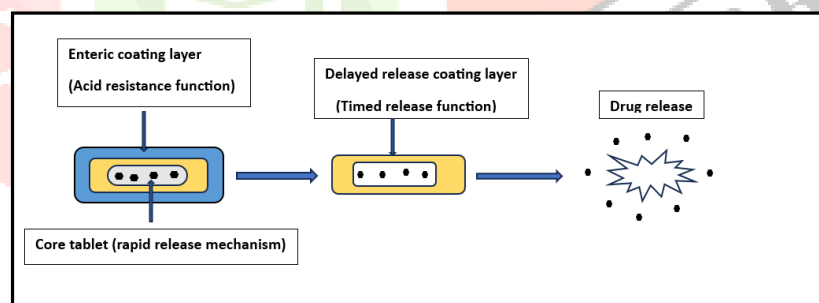


fig no.2. mechanism of drug release from enteric coating

Equipment used for tablet coating ^{[22]:}

A modern coating system combines several components

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

Recent trends in tablet coating technique ^[23]

- Electrostatic dry coating
- Magnetically assisted impaction coating (MAIC)

- Aqueous film coating technology
- SUPERCELL coating technology

Coating process ^[24,25]

The vast majority of coating techniques include spraying coating solutions onto the tablets while they are being stirred around in a fluid bed, pan, etc. A thin coating is created as the solution is sprayed and can be applied all at once or in phases. In the pharmaceutical sector, rotating pans are frequently employed. The pan, which is normally positioned at an angle from horizontal, is filled with uncoated tablets, and the liquid coating solution is evaporating by blowing air over their surfaces. A fluid bed coater, in contrast, works by blowing air over the surfaces of the turning tablets. In contrast, a fluid bed coater works by forcing air through a bed of tablets at an adequate pace to coat the medication.

Defects in tablet coating ^[26,27]

1. Blistering
2. Blooming/Dull film
3. Blushing
4. Chipping/ Edge Erosion
5. Cratering
6. Cracking/Splitting
7. Color variation
8. Core Erosion/ Surface Erosion
9. Discoloration
10. Logo Bridging
11. Logo In-filling /Break Lines In-filling
12. Orange Peel (Roughness)
13. Pitting
14. Peeling
15. Sticking and Picking
16. Scuffing of Film-coated Tablets
17. Twinning
18. Tablet Breakage

Pre-Compression Characteristics ^[28-30]:

Powder utilised for compression of core tablet were assessed for various rheological properties such bulk density, tapped density, compressibility index, flow properties (angle of repose) by utilising standard procedures.

Bulk Density: Using a measuring cylinder and a bulk density device the volume and weight of the entire batch of powder were measured.

$$\text{Bulk density} = \text{Total weight} / \text{Total bulk volume}$$

Tapped Density: Tapped density is calculated as : Total weight / Total volume after tapping. Tapped density was calculated by taking the powder in a measuring cylinder, the volume of powder after 100 tappings, and the weight of the total powder.

Compressibility Index: To determine the compressibility index, the powder was placed in a measuring cylinder, the volume (V₀) was noted before tapping, and the volume (V) was noted once more after 100 taps. V₀ is the volume of the powder or the powder before tapping; the compressibility index is $(1 - V/V_0) \times 100$. V is the powder volume/powder after 100 taps..

Angle of Repose (Ø): The height and radius of the powder heap were measured in order to calculate the angle of repose. The bottom of a cut system funnel was fastened at a height of 5 cm from the plane and fixed to a stand. Powder was poured into a funnel and allowed to flow naturally while the height and radius of the

powder mound were measured. These studies were conducted both before and after lubricants/glidants were added.

$\text{Tan } (\emptyset) = h/r = \text{height of powder pile.}$

Post compression characterization of tablets ^[31,32] :

Tablets were assessed using industry-standard techniques for their thickness, weight consistency, hardness, friability, disintegration time, and dissolving profiles.

Thickness: A vernier calliper calibrated in terms of micrometres use to measure the thickness of the tablets.

Weight Consistency: Ten tablets were taken, and each was weighed separately. Standard deviation, percent coefficient of variance, and average weight were computed.

Test for Hardness: A Pfizer hardness tester use to gauge the hardness of prepared tablets.

Friability Test: The friability of the tablets examined using the Roche Friabilator. Five pills were precisely weighed, added to the tumbling chamber, and rotated there for five minutes at a speed of 25 rpm. Tablets were weighed once more, and the formula below was used to calculate the percentage weight reduction.

$\% \text{ Friability} = \frac{\text{Initial wt of tablets} - \text{Final wt of tablets}}{\text{Initial wt of tablets}} \times 100$

Disintegration Time: Using a USP disintegration apparatus, a disintegration test for core tablets in 0.1N HCl was conducted at 37 °C.

Drug Content Uniformity: Three randomly chosen tablets from each batch were correctly weighed and ground into a powder in a clean, dry glass mortar and pestle. A 100 mL volumetric flask containing distilled water received 100 mg of medication powder, which was then added, bringing the total volume to 100 mL. The solution was filtered, occasionally stirred for 24 hours, and then analysed for drug concentration at a maximum wavelength of 256.5 nm using distilled water as a blank.

Characterization test for coated tablets ^[33,34]:

Weight gain: The tablets were assessed for their percentage weight gain. After coating the known-weight core tablet, the weight was once more taken. The algorithm below was used to compute the percentage weight gain.

$\% \text{ Weight Gain} = \frac{W2 - W1}{W1} \times 100$

Coating Thickness: The tablets' coating thickness was assessed using a vernier calliper, the core tablet's thickness was measured in terms of micrometers.

In vitro dissolution studies: Coated tablets were tested using a USP XXIV type 1 (basket) device for in vitro dissolution studies. The dissolution media, which included 900 mL of liquid, was swirled at 100 revolutions per minute while remaining at a constant temperature of 37 0.5 °C. The tablet was stored in a basket inside the jars.

Stability Studies: The ability of a certain formulation, in a specific container, to remain within its physical, chemical, therapeutic, and toxicological requirements is considered a drug's level of stability

Conclusion:

The evolution of delayed-release coated tablets has revolutionized drug delivery mechanisms, offering precise targeting and enhanced absorption. Enteric coatings, with their ability to shield drugs from stomach acid and release them in the intestines, have opened avenues for improved therapeutic outcomes and reduced side

effects. While the advantages of enteric coatings are substantial, the complexities in their processes and the need for specialized equipment pose challenges. Nonetheless, the continuous research and innovation in coating materials and techniques offer promising prospects for refining oral site-specific drug delivery systems. This comprehensive review underscores the critical role of delayed-release coated tablets in navigating the intricate pathways of oral drug delivery, paving the way for advancements that optimize drug efficacy and patient compliance.

References

1. Kim, J. and De Jesus, O., 2021. Medication routes of administration.
2. Alqahtani, M.S., Kazi, M., Alsenaidy, M.A. and Ahmad, M.Z., 2021. Advances in oral drug delivery. *Frontiers in pharmacology*, 12, p.618411.
3. Murugesan, S., Gowramma, B., Lakshmanan, K., Reddy Karri, V.V.S. and Radhakrishnan, A., 2020. Oral modified drug release solid dosage form with special reference to design; an overview. *Current Drug Research Reviews Formerly: Current Drug Abuse Reviews*, 12(1), pp.16-25.
4. Nyol, S. and Gupta, M.M., 2013. Immediate drug release dosage form: a review. *Journal of Drug Delivery and Therapeutics*, 3(2).
5. Werle, M., Takeuchi, H. and Bernkop-Schnürch, A., 2009. Modified chitosans for oral drug delivery. *Journal of pharmaceutical sciences*, 98(5), pp.1643-1656.
6. Fukui, E., Miyamura, N., Uemura, K. and Kobayashi, M., 2000. Preparation of enteric coated timed-release press-coated tablets and evaluation of their function by in vitro and in vivo tests for colon targeting. *International journal of pharmaceutics*, 204(1-2), pp.7-15.
7. Nair, A.B., Gupta, R., Kumria, R., Jacob, S. and Attimarad, M., 2010. Formulation and evaluation of enteric coated tablets of proton pump inhibitor. *Journal of basic and clinical pharmacy*, 1(4), p.215.
8. Trenfield, S.J. and Basit, A.W., 2020. Modified drug release: current strategies and novel technologies for oral drug delivery. In *Nanotechnology for oral drug delivery* (pp. 177-197). Academic Press.
9. Gujral, G., Kapoor, D. and Jaimini, M., 2018. An updated review on modified release tablets. *Journal of Drug Delivery and Therapeutics*, 8(4), pp.5-9.
10. Brahmankar, D.M., Jaiswal, S.B., 2017. *Biopharmaceutics and Pharmacokinetics*. Vallabh Prakashan. 3rd Edition. page no. 24-27
11. Arora, R., Rathore, K.S. and Bharakatiya, M., 2019. An overview on tablet coating. *Asian Journal of Pharmaceutical Research and Development*, 7(4), pp.89-92.
12. Gaikwad, S.S. and Kshirsagar, S.J., 2020. Review on Tablet in Tablet techniques. *Beni-Suef University Journal of Basic and Applied Sciences*, 9, pp.1-7.
13. MP, S.C., Prasobh, G.R., Remya, S.B., Aparna, P., Saranya, S. and Blessy, M.R., *International Journal of Modern Pharmaceutical Research*.
14. Sawalkar, P.D., Dr. Rajurkar, V.G., Prof. Munde, V.S., 2023. *International Journal of Pharmaceutical Research and Applications*, pp.1811-1820.
15. Palshikar, P., Sharma, A., Chauhan, C.S. and Kamble, R., 2013. Preparation and evaluation of enteric coated tablet of sodium valproate. *Int J Res Pharm Chem*, 3(3), pp.583-590.
16. Anamika., Agarwal, A., Agarwal, R., Bhardwaj, P., Sabreen, M. 2022. A review: formulation and evaluation of coating tablet. *International Journal Of Curent Science*. pp.2250-1770
17. Mounica, P., Pavani, S. and Mounica Rani, P., 2018. A review on recent advances in enteric coating and enteric polymers. *World J. Pharm. Res*, 7, pp.475-495.
18. Hussan, S.D., Santanu, R., Verma, P. and Bhandari, V., 2012. A review on recent advances of enteric coating. *IOSR J Pharm*, 2(6), pp.05-11.
19. Aurora, J., Talwar, N. and Pathak, V., 2006. Colonic drug delivery challenges and opportunities-an overview. *European Gastroenterology Review*, 1, pp.1-4.
20. Gobinath, T., 2014. *Formulation and evaluation of enteric coated tablets of Pantoprazole* (Doctoral dissertation, JKK Nattraja College of Pharmacy, Komarapalayam).
21. Patil, G.D., Tambe, K.P., Shirsat, S.P. and Patil, P.A., 2021. Review on enteric coated polymers. *Research Journal of Pharmaceutical Dosage Forms and Technology*, 13(1), pp.82-85.
22. Zaid, A.N., 2020. A comprehensive review on pharmaceutical film coating: past, present, and future. *Drug Design, Development and Therapy*, pp.4613-4623.
23. Ankit, G., Ajay, B., Kumar, K.M., Neetu, K. and Bihani, S.G.L., 2012. Tablet Coating techniques: Concepts and recent trends. *Int. Res. J. Pharm*, 3(9), pp.50-58.

24. Salawi, A., 2022. Pharmaceutical Coating and Its Different Approaches, a Review. *Polymers*, 14(16), p.3318.
25. Fotovvati, B., Namdari, N. and Dehghanhadikolaei, A., 2019. On coating techniques for surface protection: A review. *Journal of Manufacturing and Materials processing*, 3(1), p.28.
26. Lippincot Williams And Wilkins. 2005. Remington's The Science and Practice of Pharmacy. Volume-I. 21st ed. Indian Edition, 929-938
27. Arora, R., Rathore, K.S. and Bharakatiya, M., 2019. An overview on tablet coating. *Asian Journal of Pharmaceutical Research and Development*, 7(4), pp.89-92.
28. Shingala, H., Rangpariya, A., Rupapara, H., Parmar, A. and Kotadiya, M., 2023. FORMULATION, DEVELOPMENT AND EVALUATION OF POLYHERBAL ANTI UROLITHIATIC TABLET BY WET GRANULATION METHOD FOR ANTI-UROLITHIATIC ACTIVITY.
29. Kang, S.J. and Kim, J.E., 2023. Development of Clinically Optimized Sitagliptin and Dapagliflozin Complex Tablets: Pre-Formulation, Formulation, and Human Bioequivalence Studies. *Pharmaceutics*, 15(4), p.1246.
30. Venugopalaiah P, Prakash KB, Ramesh Y, Alagusundaram M. Formulation and evaluation of extended-release tablets of trimetazidine HCL.
31. Chaturvedi, H., Garg, A. and Rathore, U.S., 2017. Post-compression evaluation parameters for tablets-an overview. *Eur J Pharm Med Res [Internet]*, 4(11), pp.526-30.
32. Butola, M., Bhatt, V., Nainwal, N., Jakhmola, V., Dobhal, K. and Ale, Y., 2023. Preparation and Evaluation of Polymer Fused Metformin Hydrochloride Sustained Release Tablet. *Ind. J. Pharm. Edu. Res*, 57(3), pp.711-717.
33. Chavan, P.M. and Ughade, S., 2018. Preparation, characterization and evaluation of tablet for colonic delivery. *INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH*, 9(5), pp.2027-2033.
34. Singh, A., Bansal, M., Gupta, R.K. and Sharma, D., 2023. Formulation and Evaluation of Enteric Coated Tablet of Aceclofenac. *International Journal of Health Advancement and Clinical Research (tz)*, 1(1).

