JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Strategies for Prolonged Gastric Retention: An Overview of GRDDS Technologies

Divvala Monika[1], M.Gayatri Devi [2*] , Nagamani.B[3], Dr. P. Uma Devi[4]

[1,2*,3,4] Department of Pharmaceutics ,Viswanadha Institute of Pharmaceutical Sciences, Visakhapatnam 531173, Andhra Pradesh, India.

[2.]Department of Pharmaceutics ,Viswanadha Institute of Pharmaceutical Sciences, Visakhapatnam 531173, Andhra Pradesh, India.

Corresponding Author Email: gayatri.minnu@gmail.com

Abstract

Gastroretentive drug delivery systems (GRDDS) represent a promising advancement in oral drug administration, particularly for drugs with narrow absorption windows, pH-sensitive stability, or local gastric action. These systems aim to enhance drug bioavailability by prolonging gastric residence time, thereby ensuring controlled and site-specific drug release. This review explores the anatomical and physiological considerations of the stomach relevant to GRDDS development, discusses the types of drugs suited for such systems, and outlines the key limitations and factors affecting gastric retention. Various GRDDS technologies are examined, including loading systems, high-density systems, mucoadhesive systems, expandable systems, super porous hydrogels, and magnetic systems, each with distinct mechanisms to achieve prolonged retention. The review also emphasizes material selection, formulation challenges, and evaluation methods for GRDDS. Overall, GRDDS hold significant potential in improving therapeutic outcomes, patient compliance, and targeted delivery, especially for drugs with limited bioavailability in the lower gastrointestinal tract.

Keywords: Gastroretentive Drug Delivery Systems (GRDDS), Gastric Retention, Controlled

Release , Floating Drug Delivery , Mucoadhesive Systems, Bioavailability ,Swelling Systems ,Magnetic Systems ,High-Density Dosage Forms
,Oral Drug Delivery ,Gastric Residence Time ,Site - Specific Delivery

INTRODUCTION:

Oral administration is popular despite continuous improvement in drug delivery approaches owing to patient comfort and ease of administration. Controlled release drug delivery systems are designed for oral administration. These drug delivery systems release the medication in a predetermined, predictable, and controlled way. They are not suitable for drugs with low bioavailability due to stability or absorption issues.[1] These problems can get better through modern approaches, which are designed to increase the residence of such drugs in the stomach for an extended time. Such drug delivery systems are called gastroretentive drug delivery systems (GRDDS). GRDDS are suitable for those drugs, which are absorbed from the stomach (e.g. albuterol),[2]labile at alkaline pH (e.g. ranitidine and metformin),[3] poorly soluble at alkaline pH (e.g. furosemide and diazepam),[4] and having a narrow window of absorption (e.g. riboflavin and levodopa).[5]

Some of the common advantages associated with use of GRDDS include improved patient compliance by reducing the frequency of dosing; improved therapeutic efficacy of drugs with a short half-life; site-specific delivery of medications; sustained and controlled release of drugs in the stomach; enhanced residence time of drugs at the absorption site; improved bioavailability from the gastrointestinal tract; avoiding dose dumping of medicines.[6]

To develop GRDDS, different materials like ion-exchange resins, mucoadhesives, high-density materials, raft forming substances, magnetic substances, and super porous hydrogels are used.[7,8]

This review provides a concise account of various attributes of recently developed approaches for GRDDS.

Anatomy and physiology of the stomach:

Knowledge about the anatomy and physiology of the stomach is essential for the successful formulation of gastroretentive dosage forms. Anatomically, the stomach is divided into three areas: the proximal portion toward the esophagus is fundus, followed by the body, which serves as a storage site for engulfed food, and the antrum, the last part that connects the body to the small intestine. Antrum helps in churning action and in gastric emptying.[9]

In a fasting state, a sequence of contractions occurs cyclically through the stomach and intestine every 120-180 min, called the migrating myoelectric cycle. It is further divided into four phases. The pattern of contraction changes in a fed state is termed as the digestive motility pattern.[10]

This pattern comprises phase 1- (basal phase); phase 2- (pre burst phase); phase 3- (burst phase); and phase 4.[11]

.

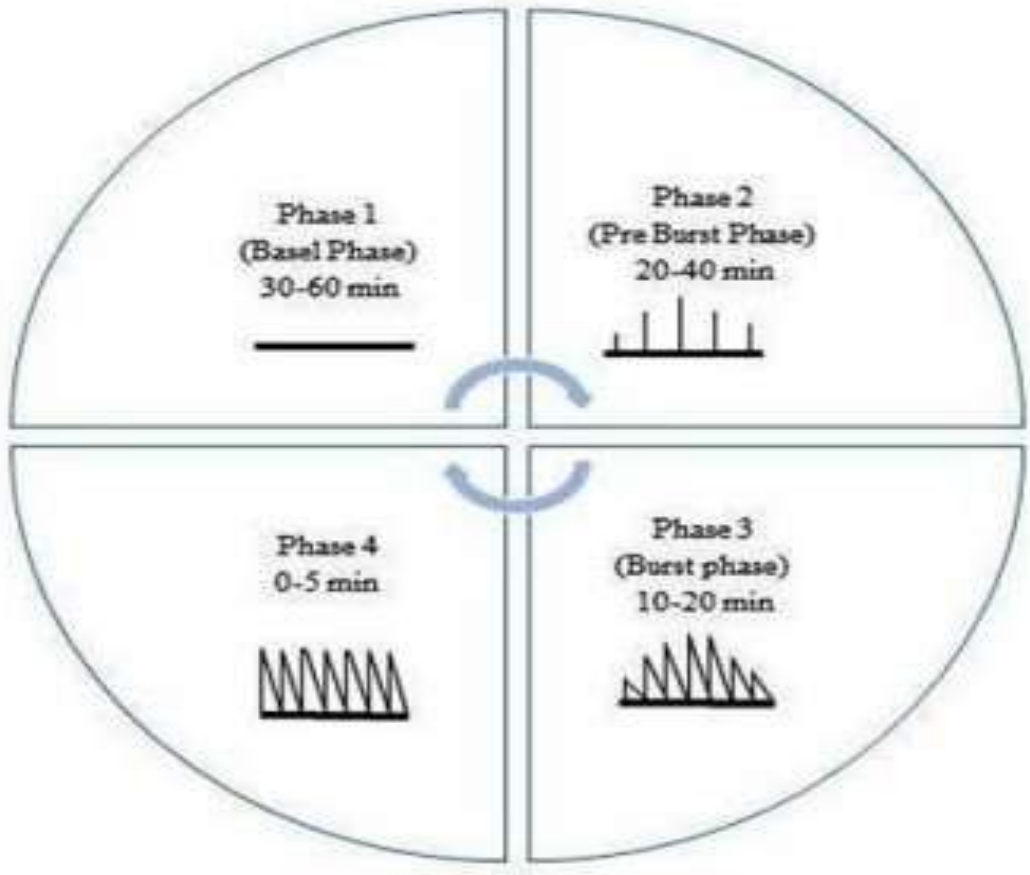

Figure 1: Motility pattern in the Gastrointestinal tract

Potential candidates for gastro retentive drug delivery system:

1. Drugs that are primarily absorbed in the stomach egg Ampicillin.

2. Drugs that are poorly soluble in alkaline pH egg Furosemide, Diazepam.

3. Drugs that have narrow absorption window egg Levodopa, Methotrexate.

4. Drugs that degrade in the colon egg. Ranitidine, Metformin HCL.

5. Drugs that disturb normal colonic microbes egg Antibiotics against Helicobacter pylori.

6. Drugs rapidly absorbed from the GI tract egg Tetracycline.

7. Drugs acting locally in the stomach[12]

Limitations of gastro retentive drug delivery system:

1. Aspirin and NSAIDS can cause gastric lesions and slow release of such drugs in the stomach is unwanted.

2. Drugs such as isosorbide denigrate which are equally absorbed throughout the GIT will not benefit from incorporation into a gastric retention system.

3. Bioadhesion in the acidic environment and high turnover of mucus may raise questions about the effectiveness of the technique

4. Physical integrity of the system is a very important and primary requirement for the success of the system.

5. High variability in gastric emptying time due to variations in emptying process, unpredictable bio availability.[13,14]

Factors affecting gastric retention time of the dosage form

Density- the density of the dosage form should be less than that of the gastric contents (1.004g/ml).

Size- Dosage form having diameter of more than 7.5mm have more gastric residence time than that of 9.9mm diameter dosage form.

Fed or unfed state- Under fasting conditions, the gi motility is characterized by periods of strong

motor activity that occurs every 1.5-2 hrs. The MMC sweeps undigested material from the stomach and if the timing of the formulation coincides with that of MMC, the GRT of the unit can be very short, however in fast state MMC is delayed and GET is longer.

Nature of Meal- Feeding of indigestible polymers or fatty acids can change the motility pattern of the stomach to a fed state,thus decreasing gastric emptying rate and prolonging drug release.

Caloric Content- GRT can be increased by 4-10 with a meal that is high in protein and fat.

Frequency of Feed- The GRT can be increased over 400 min when successive meals given are compared with the single meal due to low frequency of MMC.

Gender- Mean ambulatory GRT in male (3.4hrs) is less compared with the age and race matched female counterparts (4.6hrs) regardless of height, weight and body surface.

Age- People with age more than 70 have a significantly longer GRT. Concomitant drug administration- anticholinergic like atropine and propantheline, opiates like codeine can prolong GRT[9-13].

Classification of GRDF:

a) High-density system

b) Floating system

c) Expandable system

d) Super porous hydrogels

e) Mucoadhesive bioadhesive system

F) Magnetic system

High Density System:

This approach involves formulation of dosage forms with density that must exceed density of normal stomach content 1.004g/ml. These formulations are prepared by coating drugs on a heavy core or mixed with heavy inert material such as iron powder, zinc oxide, titanium dioxide, and

barium sulphate. The resultant pellets can be coated with diffusion controlled membrane[15]

Floating or Low-Density System:

by their low densities, FDDS remain afloat above the gastric contents for prolonged periods and provide continuous release of the drug. These systems in particular have been extensively studied because they do not adversely affect the motility of

the GIT. Their dominance over the other types of GRRDS is also evident from the large number of floating dosage forms being commercialized and marketed worldwide.[16]

Volatile liquid containing system The GRT of a drug delivery system can be sustained by incorporating an inflatable chamber, which contains a liquid e.g. ether, cyclopentane, that bases at body temperature to cause the inflation of the chamber in the stomach. The device may also consist of a bio erodible plug made up of Polyvinyl alcohol, Polyethylene, etc. that gradually dissolves causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable systems from the stomach[17]

Gas-Generating Systems:

These buoyant delivery systems utilize effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO2, which gets trapped in the jellied hydrocolloid layer of the system thus decreasing its specific gravity and making it lose over gastric content.

Non-Effervescent FDDS:

The Non-effervescent FDDS is based on the mechanism of swelling of polymer or bioadhesion to the mucosal layer in the GI tract. The most commonly used excipients in non-effervescent FDDS are gel-forming or highly swell able cellulose-type hydrocolloids, hydrophilic gums, polysaccharides, and matrix-forming materials such as polycarbonate, polyacrylate, polymethacrylate, polystyrene as well as bioadhesive polymers such as Chitosan.[18]

Mucoadhesive systems:

Mucoadhesive drug delivery systems contain a mucoadhesive polymer that adheres to the gastric mucosal surface and prolongs its gastric retention in the git. The capability to adhere to the mucus gel layer makes mucoadhesive polymers very useful excipients in the GRRDS. These polymers can be natural such as sodium alginate, gelatine, guar gum, etc. semisynthetic polymers such as HPMC, carpool, sodium carboxymethyl cellulose[19.] The adhesion of polymers with mucous membrane may be mediated by hydration, bonding, or receptor-mediated. In hydration-mediated adhesion, the hydrophilic polymer becomes sticky and mucoadhesive upon hydration. Bonding mediated involves mechanical or chemical bonding. Chemical bonds may involve ionic or covalent bonds or van der Waal forces between the polymer molecule and the mucous membrane. Receptor-mediated adhesion takes place between certain polymers and specific receptors expressed on gastric cells. The polymers can be cationic or anionic or neutral[20.]

Swelling System:

These are the dosage forms, which after swallowing swells to such an extent that their exit from the pylorus is prevented as a result; the dosage form is retained in the stomach for a prolonged period. These systems are called as plug type systems as they tend to remain lodged at the pyloric sphincter. The formulations are designed for gastric retention and controlled delivery of drugs in the gastric cavity, such formulations remain in the gastric cavities for several hours even in the fed

state. Controlled and sustained release may be achieved by selection of proper molecular weight polymer, and swelling of the polymers retard the release[21.] On coming in contact with gastric fluid the polymer imbibes water and swells. The extensive swelling of these polymers is due to the presence of physical-chemical cross-links in the hydrophilic polymer network. These cross-links prevent the dissolution of the polymer and hence maintain the physical integrity of the dosage form. An optimum cross-linking, which maintains a balance between the swelling and the dissolution, should be maintained. Aguilera developed a polymeric coating system that formed an outer membrane on the conventional tablets. In the dissolution media, the membrane detached from

the core and swelled to form a balloon that kept the unit loating. The size of the units increased by three to six-folds, thus the floating ability as well as the increased dimension offered the system gastro retentive property[22]

Magnetic System:

This system is based on the simple idea that the dosage form contains a small internal magnet and a magnet placed on the abdomen over the position of the stomach. Using an extracorporeal magnet, the gastric residence time of the dosage form can be enhanced for a prolonged period.[23]

Advantages and applications of gastroretentive delivery systems:

Gastroretentive dosage forms release the drug in a controlled manner to their specific site of action.[24] These systems help increase the bioavailability of drugs

that get metabolized in the upper part of the gastrointestinal tract, such as riboflavin and levodopa, etc.[25,26] For drugs that have a short half-life, gastroretentive dosage forms help reduce the dosing frequency and improve patient compliance by enhancing GRT. Also, they provide a sustained and prolonged release of drugs in the stomach and intestine, which are helpful in local therapy.[27,28,29]

Conclusion:

Gastroretentive drug delivery systems (GRDDS) offer a strategic approach to enhance the bioavailability and therapeutic efficacy of drugs with absorption windows in the upper gastrointestinal tract. By prolonging gastric residence time, these systems can achieve controlled, sustained, and localized drug release, improving treatment outcomes and patient compliance. Various technological approaches—including loating systems, mucoadhesive formulations, high-density systems, expandable matrices, and magnetic devices—provide diverse solutions for overcoming challenges associated with rapid gastric emptying and poor drug solubility at intestinal pH levels. However, limitations such as variability in gastric emptying, patient-specific physiological factors, and formulation integrity must be carefully addressed during development. Continued research and innovation in polymer science, drug formulation, and device engineering

will further reine GRDDS and expand their clinical applicability for a wide range of drugs.

References:

1. Schneider F, Koziolek M, Weitschies W. In vitro and in vivo test methods for the evaluation of gastroretentive dosage forms. Pharmaceutics. 2019;11:416.

2. Boulton DW, Fawcett JP. Enantioselective disposition of albuterol in humans. Clin Rev Allergy Immunol. 1996;14:115–138.

3. Chandira RM, Palanisamy P, Jaykar B. Formulation and evaluation of bilayer floating tablets of metformin hydrochloride. Int Res J Pharm. 2012;3:257–267.

4. Menon A, Ritschel WA, Sakr A. Development and evaluation of a monolithic floating dosage form for furosemide. J Pharm Sci. 1994;83:239–245.

5. Levy G, Jusko WJ. Factors affecting the absorption of riboflavin in man. J Pharm Sci. 1966;55:285–289.

6. Badoni A, Ojha A, Gnanarajan G, Kothiyal P. Review on gastroretentive drug delivery system. J Pharm Innov. 2012;1:32–42.

7. Malpure PS, Chavan BR, Maru AD, Badhane JS, Thakare EB, Sonawane PS. Gastroretentive drug delivery systems. World J Pharm Pharm Sci. 2019;8:506–528.

8. Kumar M, Kaushik D. An Overview on various approaches and recent patents on gastroretentive drug delivery systems. Recent Pat Drug Deliv Formul. 2018;12:84–92.

9. Pound AU, Shendge R, Pote AK. Current approaches on gastroretentive drug delivery systems. J Drug Deliv Ther. 2020;10:139–146.

10. GundaRK. Formulation development and evaluation of gastroretentive drug delivery systems. A review. J Pharm Res. 2017;8:11–20.

11. More S, Gavali K, Doke O, Kasgawadek P. Gastroretentive drug delivery system. J Drug Deliv Ther. 2018;8:24–35.

12. Subrahmanyam CVS, Setty JT. Laboratory manual of physical Pharmaceutics. Vallabh Prakashan

2002; pg no 212.

13. Vinod KR, Vasa S, Anbazhagan S. Approaches for gastroretentive drug delivery, IJABPT, 2008;589-601.

14. Pawar V.K, Shashwat K, Garg G, Awasthi R. Gastroretentive dosage form: A review with special emphasis on floating drug delivery systems, Informa Healthcare 2011;18(2):97-110

15. Waterman KC. A critical review of gastric retentive controlled drug delivery. Pharmaceutical Development and Technology, 2007;12: 1-10.

16. Kotreka U and Adeyeye MC. Gastroretentive floating drug delivery system a review. Therapeutic Drug Carrier System, 2011; 28(1):47-99.

17. Jamil F, Sunil K, Sharma S, Vishvakarma P, Singh L. Review on stomach specific drug delivery: development and evaluation. IJRPBS, 2011;2(4):1427-1433.

18. Talukder R, Fassihi R. Gastroretentive delivery systems. Drug development and industrial pharmacy,2004;30(10):1019-1028.

19. Krogel I and Bodmeier R. loathing or pulsatile drug delivery system based on coated effervescent cores. International Journal of Pharmaceutics, 1999;187:175-184.

20. Groning R, Heun C. Oral dosage forms with controlled gastrointestinal transit drug delivery, 1984;10(4):527-539.

21. Agyilirah GA, Green M, Ducret R. Evaluation of gastric retention properties of cross linked polymer-coated tablets versus those of non disintegrating tablets. Int J Pharma. 1991; 75:241-247

22. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled release system for gastric retention. Pharmaceutical Research,1997;14(6):815-819

23. Girish S, Sonar, Devendra K, Jain, Dhananjay M. Preparation and invitro evaluation of bilayer floating bioadhesive tablets of Rosiglitazone Maleate. Asian Journal of Pharmaceutical Sciences.2007;2(4):161-169.

24. Wadher KJ, Kakde RB, Umekar MJ. Formulation and evaluation of a sustained-release tablet of metformin hydrochloride using hydrophilic synthetic and hydrophobic natural polymers. Indian J Pharm

Sci. 2011;73:208–215.

25. Rudraswamy-Math NR, Gupta VR. Formulation and evaluation of gastroretentive controlled release tablets of alfuzosin hydrochloride. Pak J Pharm Sci. 2015;28:2147–2152.

26. Sonani NG, Hiremath SP, Dasankoppa FS, Jamakhandi VG, Sreenivas SA. Design and evaluation of gastroretentive mucoadhesive cephalexin tablets. Pharm Dev Technol. 2010;15:178–183.

27. Gangurde HH, Chordiya MA, Tamizharasi S, Senthilkumaran K, Sivakumar T. Formulation and evaluation of sustained release bioadhesive tablets of ofloxacin using 3(2) factorial design. Int J Pharm Investig. 2011;1:148–156.

28. Gattani SG, Londhe SG, Chalikwar SS, Amrutkar JR. Formulation and evaluation of gastroretentive drug delivery of verapamil hydrochloride. Eur J Parenter Pharm Sci. 2010;15:125–129.

29. Saritha D, Sathish D, Rao YM. Formulation and evaluation of gastoretentive floating tablets of domperidone maleate. J Appl Pharm Sci. 2012;2:68–73.