Available online at www.abhipublications.org
Review Article
ABHI Publications since 2013
International Journal of Pharmacy and Engineering (IJPE)
ISSN 2320-849X

GASTROINTESTINAL FLOATING DRUG DELIVERY SYSTEM: An Overview

Subarna Mahanti[1], Beduin Mahanti[2], Khokan Bera[3*]

[1,2,3] School of Pharmacy (SOP), Techno India University (TIU), Salt Lake, EM-4/1, Sector-V, Kolkata-700091, West Bengal, India,

Abstract

The recent scientific and patented literature concluded that an increased interested in novel dosage forms which retained in the stomach for prolong and predictable period has been shown. Various technological attempts have been made in the research and development of rate - controlled oral drug delivery systems to overcome physiological diversities, as short gastric residence times and unpredictable gastric emptying times using gastro retentive drug delivery system. It is a well-known fact that differences in gastric physiology, such as gastric pH and motility exhibit both intra as well as inter - subject variability demonstrating significant impact on gastric retention time and drug delivery behaviour . Various attempts have been made to develop Gastro Retentive Delivery systems.

Key Words: Floating, gastric motility, mucus membrane, mucosal surface, mucoadhesion

Received: November 01 March 2022, Accepted: March 20th 2022,

Corresponding Author: * , Khokan Bera

School of Pharmacy (SOP), Techno India University (TIU), Salt Lake, EM-4/1, Sector-V, Kolkata-700091, West Bengal, India, E-mail: :kbjadavpur123@gmail.com

Introduction

Gastro Intestinal Floating Drug Delivery System is also termed as Hydrodynamically Balanced System (HBS). This is a low - density system having sufficient tendency to float over the gastric contents and remain in the stomach for an extended period and releases the drug component at the desired rate. Increases gastro - retention time and reduced fluctuation while floating over the gastric contents.It happens during both fasting and fed conditions. An inter- digestive sequence of electrical events take place during the fasting process, which pass every 2-3 hours in both the stomach and intestines. This type of system, after swallowing swells unrestrained via inhibition of gastric fluid to an extentthatit prevents their exit from thestomach.Excipients used most Hydroxypropyl methyl cellulose (HPMC), Polyacrylate polymers, Polyvinyl acetate,Carbopol,Agar, Sodium alginate, Polyethylene oxide and Polycarbonates.Hydrodynamically balanced system wasfirstdesignedbySheth andTossounianin1975, such system contain drug with gel-forming hydrocolloids meant to remain buoyant on the stomach contents. This prolongs GRT and maximizes the amount of drug that reaches its absorption. This system incorporates a high level of one or more gel-forming highly soluble Cellulose type hydrocolloid. Materials commonly used as Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose, Polysaccharide and matrix forming Polymer such as Polyacrylate and Polystyrene.

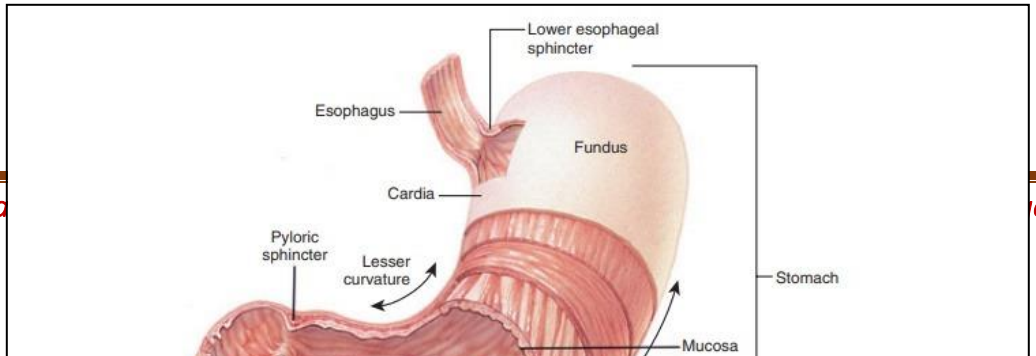

Fig.1:**Physiology of stomach**

Factors Controlling Gastric Retention Time of a Dosage Form

1. Nature of meal
2. Fed or Unfed State
3. Age
4. Frequency
5. Concomitant drug administration
6. Density
7. Size and Shape
8. Caloric Content
9. Gender
10. Posture [1-3]

Classification

The floating system is divided in to two types –

A. Non-effervescent systems

B. Effervescent systems

A. Non-effervescent systems

This type of system, after swallowing swells unrestrained via inhibition of gastric fluid to an extentthatit prevents their exit from thestomach.Excipients used most

Hydroxypropyl methyl cellulose (HPMC), Polyacrylate polymers, Polyvinyl acetate,Carbopol,Agar, Sodium alginate, Polyethylene oxide and Polycarbonates.

This system can be divided into four sub-types –

Colloidal – gel barrier systems / Single layer floating tablets

Hydrodynamically balanced system wasfirstdesignedbyShethandTossounianin 1975, such system contain drug with gel-forming hydrocolloids meant to remain buoyant on the stomach contents. This prolongs GRT and maximizes the amount of drug that reaches its absorption.

This system incorporates a high level of one or more gel-forming highly soluble Cellulose type hydrocolloid. Materials commonly used as Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose, Polysaccharide and matrix forming Polymer such as Polyacrylate and Polystyrene.

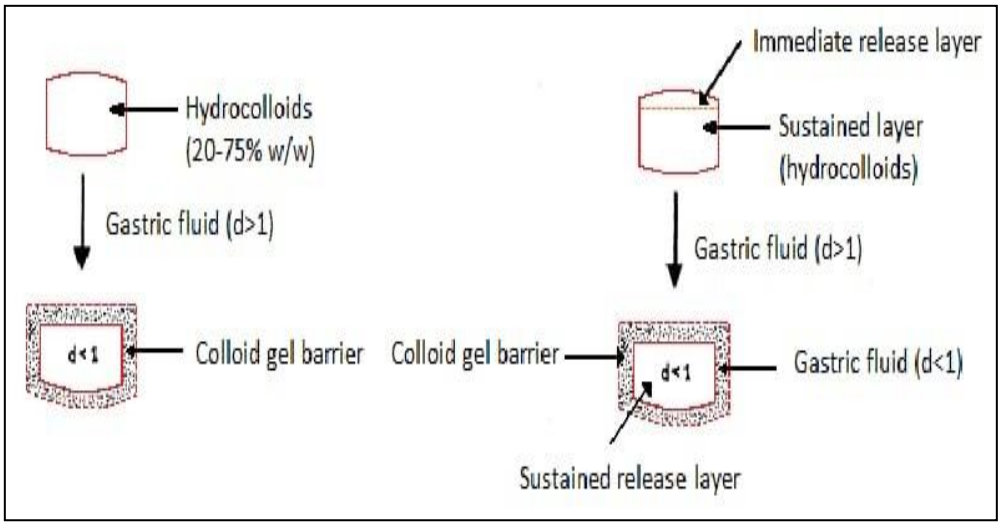

Fig-2: Single layer floating tablets

Microporous compartment system

The technology is based on the encapsulation of drug reservoir in microporous compartment with apertures along its top and bottom walls. The peripheral walls of the drug reservoir compartment are completely sealed to prevent any direct contact of the gastric mucosal surface with the undissolved drug. In stomach the

floatation chamber containing entrapped air causes the delivery system to float over the gastric contents. Gastric fluid enters through apertures, dissolves the drug, and carries the dissolved drug for continuous transport across the intestine for absorption.

Alginate beads

Multi - unit floating dosage forms have been developed from freeze - dried calcium alginate. Spherical beads of approximately 2.5mm in diameter can be prepared by dropping sodium alginate solution into aqueous solution of calcium chloride causing the precipitation of calcium alginate. The beads are separated, snap frozen in liquid nitrogen, and freeze dried at -40^0C for 24 hrs. When compared with solid beads, which gave a short residence, time of 1 hour, and these floating beads gave a prolonged residence time of more than 5.5 hrs.

Hollow microspheres /Micro balloons

Hollow microspheres loaded with ibuprofen in their outer polymer shells were prepared by a novel emulsion – solvent diffusion method. The ethanol: dichloromethane solution of the drug an enteric acrylic polymer was poured into an agitated aqueous solution of PVA that was thermally controlled at 40 degree centigrade. The gas phase generated in dispersed polymer droplet by evaporating of dichloromethane formed an internal cavity in microsphere of polymer with drug. The micro balloons floated continuously over surface of acidic dissolution media containing surfactant for greater than 12 hours in vitro. The drug released was high in pH 7.2 than in pH 6.8. [4-6]

B. Effervescent system

A drug delivery system can be made to float in stomach by incorporating a floating chamber, which may be filled with vacuum, air or inert gas. The gas in

floating chamber can be introduced either by volatilization of an organic solvent or by effervescent reaction between organic acids and bicarbonate salts.

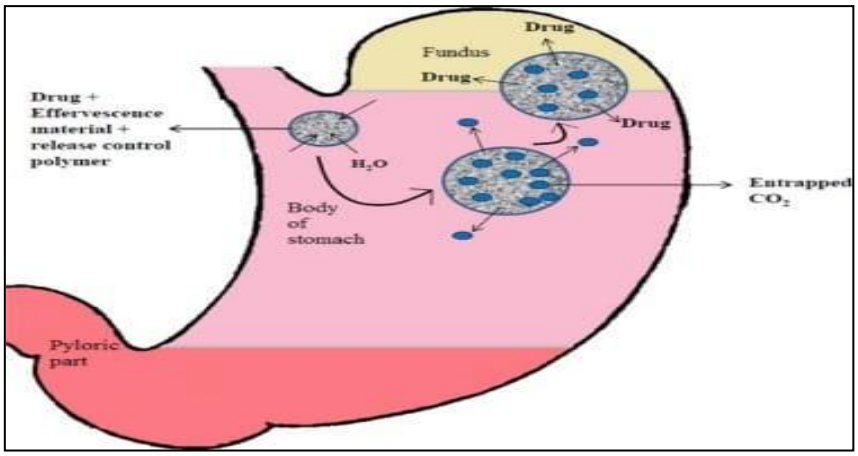

Fig-3: GRDDS based on effervescence

Volatile liquid containing system

The type of systems consists of two chambers separated by an impermeable, pressure responsive, movable bladder. The first chamber contains the drug and the second chamber contains the volatile liquid. The device inflates and the drug is continuously released from the reservoir into the gastric fluid.

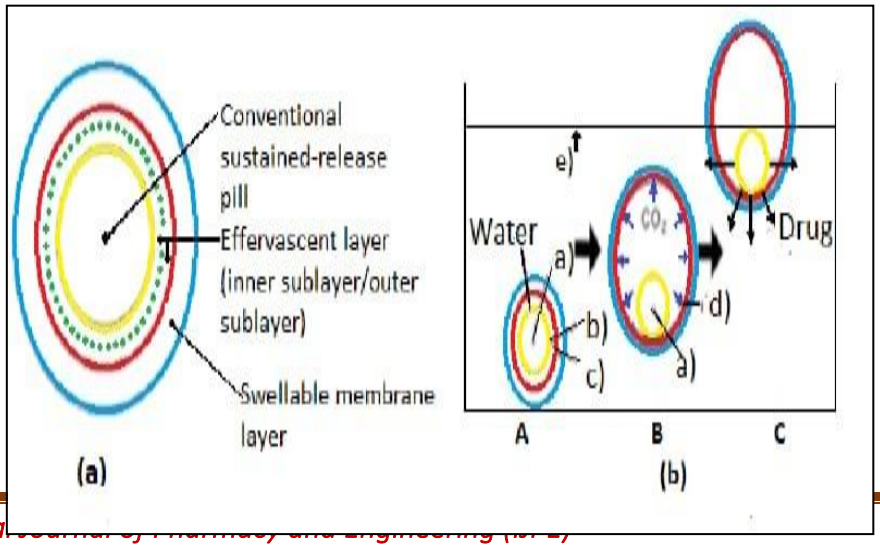

Fig-4: Multiple-unit oral drug delivery system

Gas - generating systems

These buoyant delivery systems utilize effervescent reaction between carbonate/bicarbonate salts and citric / tartaric acid to liberate CO2, which gets entrapped in the gellified hydrocolloid layer of the systems, thus decreasing its specific gravity and making it float over chyme. [7-9]

Methods of Developing Floating Drug Delivery System

Direct compression technique:

It means compressing tablets directly from powder content without altering the substances physical structure itself. Most widely used carriers are Dicalcium trihydrate phosphate, Tricalcium phosphate etc.

Effervescent technique:

An effervescent reaction between organic acid (citric acid) and bicarbonate salts will fill the floating chamber of the drug delivery system with inert gas (CO2).

Wet Granulation Technique:

Involves wet powder massaging, milling or drying. Wet granulation shapes the granules by binding the powders together with an adhesive rather than compacting them.

Inotropic Gelation Technique:

Gelatin of anionic polysaccharide sodium alginate, the primary polymer of natural origin, was accomplished with opposite charged calcium ions with the objective of forming instantaneous micro particles.

***Solvent Evaporation Technique**:*

Continuous phase ability is inadequate to remove the entire amount of liquid dispersal solvent. Solvent evaporates from the dispersal surface to receive hardened microspheres.

Spray Drying Technique:

Involves dispersing the core layer into the liquefied coating content and spraying the core coating mixture into the environment so that the coating is solidified by rapidly evaporating in which the coating material is solubilised.

***Melt Solidification Technique**:*

This method involves emulsifying the molten mass in the aqueous phase followed by cooling it to solidify. Lipids, waxes, polyethylene glycol, etc are the carriers used for this technique.

***Melt Granulation Technique**:*

This method agglomerates the pharmaceutical powders using a meltable binder and does not use water or organic solvents for granulation. [10-12]

Excipients Incorporated in Different Floating Dosage Form

EffervescentAgents: Citric acid, Tartaric acid, Sodium bicarbonate, DI – SGC (Disodiumglycine carbonate) CG (Citro glycine)

ReleaserateRetardants: Talc, Dicalcium phosphate, Magnesium stearate.

InertFattyMaterials: Long chain fatty alcohols, Beeswax, Fatty acids.

ReleaserateAccelerants: Mannitol, Lactose

Hydrocolloids: Acacia, Beta - cyclodextrinGelatin, Alginates, Pectin, HPMC, Carbopol

Buoyancyincreasingagents:

Ethyl alcohol and Polypropylene Foam Powder (AccurelMP)[13-16]

AdvantagesofFloatingDrugDeliverySystem

- FDDS can remain in the stomach for several hours and thereby prolonging the gastric retention time of various drugs.
- Advantages for drugs which are meant for local action in the stomach e.g. antacids
- Formulation of FDDS are useful in intestinal movement and in diarrhoea to hold the drug in floating state in the stomach in order to get comparatively better response.
- By decreasing the dosing frequency FDDS improves patient compliance.
- Treatment of gastrointestinal disorders such as gastroesophageal reflux. [17-18)]

DisadvantagesofFloatingDrugDeliverySystem

- The drug substances which are unstable in the acidic environment of the stomach are not suitable candidates for integration into the systems.
- In these systems the presence of food is usually required to prolong their gastric emptying.
- It is not suitable for drugs which are having stability problem in GIT.
- The drugs which undergo first pass effect and the drugs which are significantly absorbed throughout gastrointestinal tract are only desirable candidate. [19-20]

Application of Floating Drug Delivery System

Enhanced Bioavailability

The bioavailability of riboflavin CR - GRDF is substantially increased compared with the administration of non GRDF CR polymeric formulation.

Sustained delivery of drugs

Oral CR formulations experienced problems in the GIT like gastric residence time. HBS systems that can stay in the stomach for prolonged period and having a bulk density of less than 1 and can float on the gastric contents can usually overcome these problems.

Site specific drug delivery systems

The controlled, gradual drug delivery to the stomach provides appropriate local therapeutic rates and reduces the systemic exposure of the drug. The dosing frequency can be decreased by extended gastric availability from a site driven drug delivery system. e.g., Furosemide and Riboflavin.

Minimized adverse reaction at the colon

Retention of the drug in the stomach in HBS minimizes the amount of drug entering the colon. Unwanted drug activity in the colon region can thus be avoided.

Reduced drug concentration fluctuation

Continuous input of the drug following CR-GRDF administration creates concentrations of the blood drug within a narrower range compared with types of immediate release dosage forms.

Conclusion

Drug absorption in the gastrointestinal tract is a highly variable procedure and prolonging gastric retention of the dosage form extends the time for drug absorption. FDDS promises to be a potential approach for gastric retention. Although there are number of difficulties to be worked out to achieve prolonged gastric retention, many companies are focusing toward commercializing this technique.

References

1. Nayak AK, Maji R, B. Das B. Gastroretentive Drug delivery systems: A Review Asian journal of pharmaceutical and clinical research, 2013.
2. Sharma D, Sharma SK, Kumar AJ. Floating drug delivery system. International journal of pharmaceutical, chemical and biological sciences, 2014; 4(1): 201-207.
3. SK Patil, Ashwini B, Kanavaje Abhijit M, Khade Amol B, and Battase Anil P. A comprehensive review and its possible scope. International journal of pharmacy review and research, 2014; 4(3): 183-189.
4. Sarawade A, Ratnaparkhi MP, and Chaudhari S. Floating drug delivery system: A overview. International Journal of Research and Development in pharmacy and life science, 2014; 3(5): 1106-1115.
5. Sunil AS, Mahale N.B, Salunkhe K.S, Chaudhari. S.R. A review on: Floating drug delivery system. Journal of advanced drug delivery, 2014; 1(2): 96-113.
6. Maheta H, Patel MR, Patel KR, Patel MS. An overview on: floating drug delivery system. ISSN. 2014; 2(3): 61-71.
7. Sharma D, and Sharma A. Gastroretentive drug delivery system. Gastroretentive drug delivery system: A mini review, 2014; 1(2): 80-89.
8. Patil KK, and Saptarshi D. A review on floating drug delivery system. International Journal of pharmaceutical sciences, Review, Research, 2013; 21(1): 276-283.

9. Chaturvedi S, Kumari P, Singh S, and Agarwal VK. Approaches to increase in gastric residence time: Floating drug delivery system. Asian journal of pharmaceutical clinical research, 2013; 6(3): 1-9.
10. Venkataramana M, Arjun VA, Chandrakant M, Raosaheb and Balasaheb AS. Floating drug delivery system to increase in gastric retention of drug. International journal of pharmaceutical chemical sciences, 2013; 2(2): 808-820.
11. Chikahalikar S.S and Wakade R.B. Floating drug delivery system an approach to controlled drug delivery system. International journal of pharmTech research, 2012; 4(4): 1812-1826.
12. Joshi P, Patel P, Modi H .Patel MR, Patel N, A review on gastric retentive drug delivery system, Journal of pharmaceutical science and bioscientific research. (JPSBR), 2013; 2(3): 2012.
13. Gupta P and Gnanarajan PK. Floating Drug Delivery System: A Review. Int. J Pharm Res Rev. 2015; 4(8): 37-44. 2. Shyama SK and Sivakumar R. Floating Drug Delivery System: An Updated Review. Int J Curr Pharm Clinical Res. 2014; 4(3):150-53.
14. Parmar PD, Pande S, Shah HS, Sonara SN and Patel GH. Floating Drug Delivery System: A Novel Approach to Prolong Gastric Retention. World J Pharma Sci. 2014; 3(4): 418-44.
15. Veerareddy PR, Bajjuri S, Sanka K, Jukanti R, Bandari S and Ajmeru RK. Formulation and Evaluation of Gastroretentive Dosage Form of Ofloxacin. Stamford J Pharma Sci. 2011; 4(1): 09-18.
16. Nirmal J, Saisivam S, Peddanna C, Muralidharan S, Godwinkumar S and Nagarajan M. Bi-layer tablets of Atorvastatin Calcium and Nicotinic acid; Formulation and evaluation. Chem Pharm Bulletin. 2008; 56(10): 1455-58.
17. Hamza Yassin El-Said and Mona HA. Design and In Vitro Evaluation of Novel Sustained-Release Double-Layer Tablets of Lornoxicam: Utility of Cyclodextrin

and Xanthan Gum Combination. American Assoc Pharm Scientists. 2009; 10(4):1357-67.

18. Sarojini S and Manavalan R. An overview on various approaches to Gastroretentive dosage forms. Int J Drug Dev Res. 2012; 4(1): 01-1
19. Pawar VK, Kansal S, Garg G, Awasthi R, Singodia D and Kulkarni GT. Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. Drug Deliv. 2010; 18(2): 97-110.
20. Chawla G, Gupta P, Vishal K and Bansal AK. Gastro retention a Means to Address Regional Variability in Intestinal Drug Absorption. Pharm Technol. 2002; 27(7): 50-68.

Received: November 01 March 2022, Accepted: March 20th 2022,

Corresponding Author: * , Khokan Bera

School of Pharmacy (SOP), Techno India University (TIU), Salt Lake, EM-4/1, Sector-V, Kolkata-700091, West Bengal, India, E-mail: :kbjadavpur123@gmail.com