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RESEARCH ARTICLE

HYDRODYNAMICALLY BALANCED SYSTEMS AS NOVEL GASTRORETENTIVE DRUG DELIVERY SYSTEM-A CURRENT STATUS

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ABSTRACT

As we all know about world trending towards the novel drug delivery systems because of site specific effect, minimal toxicity and increase the half life of drugs, and also improve the bioavailability of different types of drugs. Oral administration of the drug is the most effective method for administering medication because of its ease of administration, patient adherence, and patient capacitance, among other advantages. There have been many different strategies developed for the purpose of increasing the gastro retentive time. Some examples of these strategies are the high-density system, the floating system, the swelling and expanding system, and the mucoadhesive and bio-adhesive systems. The easiest and most effective Gastroretentive dosage form is called the Hydrodynamically Balanced System (HBS);the primary purpose of this article review is to concentrate on the mechanism of the HBS system along with its advantages, disadvantages, and future toward a hydrodynamically balanced sheet.

Key words: *Gastro retentive drug delivery system, GIT, Gastric emptying time, Hydrodynamically Balanced System (HBS).*

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INTRODUCTION

Despite the significant advancements that have been done in the field of drug delivery, there are still some problems; the oral administration of medications (therapeutic agents) is still the method that is most commonly used. Gastro retentive drug delivery system (GRDDS) is a unique and Novel approach which has been developed for use in this industry (Alluri, 2020). The term "gastro retentive drug delivery system" (GRDDS) refers to a method that focuses on site-specific release of the drug in the upper gastrointestinal tract (GIT) for local or systemic effects. This method is beneficial for increasing the bioavailability of a drug as well as its therapeutic efficacy (Gadge, 2019). Due to the fact that drugs that are easily taken up (absorbed) from the gastrointestinal tract as well as those with short half-lives are rapidly eliminated from the systemic circulation, frequent dosing is required for these types of medications. To find a solution to this issue, researchers are developing gastroretentive drug delivery systems. These systems implement an excellent plasma drug concentration for prolonged periods of time, thereby reducing the number of times a dose needs to be administered (Pant, 2016).

STOMACH- Anatomy & Overview: The adult stomach has a capacity of between 1000 and 1500 milliliters and stomach is the most dilated part of the digestive tract. It is positioned in the area between the lower end of the oesophagus and the beginning of the duodenum, which is the initial part of the small intestine. Both neural and hormonal signals are involved in the regulation of gastric motility. The enteric nervous system, in addition to the parasympathetic (primarily the vagus nerve), sympathetic, and sympathetic nervous systems, are the primary sources of nervous control (Daniels, 2005).

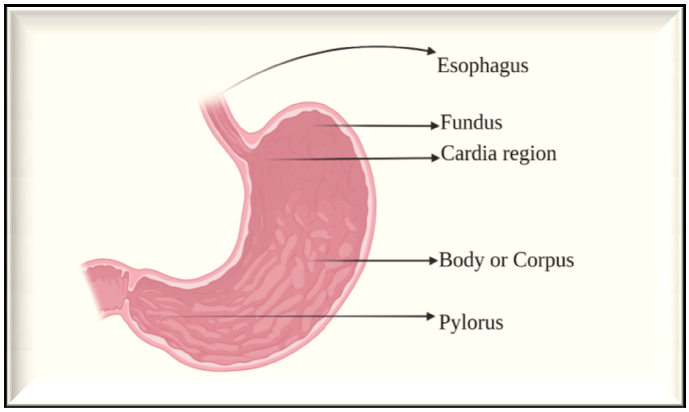

Figure 1. Functional Parts of Stomach

The stomach is divided into the following sections: [5]

There are total 4 main parts of the stomach, which are as follows:

1) Cardiac region (with cardiac sphincter)
2) Fundus
3) Body or Corpus
4) Pyloric region
   a.Pyloric antrum
   b.Pylorus
   c.Pyloric canal
   d.Pyloric sphincter

Gastroretentive Drug Delivery System [GRDDS]: The term "gastroretentive drug delivery system"(GRDDS) refers to dosage forms that have the ability to be retained in the stomach (Dr. M.M. Khan). For several hours, these systems can remain in the stomach and significantly extend the time that a drug remains in the stomach (Jasim, 2021). Following oral administration, this delivery method would be retained in the stomach. As a result, the drug will be released slowly and steadily into the gastrointestinal tract (GIT), where it can be absorbed over time (Rathee, 2012).

Gastroretentive Techniques:

Following are the techniques included in the Gastroretentive systems: (Ganesh, 2011).

a) Floating system
b) Effervescent system
c) Non-effervescent system
d) Hydrodynamically balanced system
e) Gas generating system
   i. Raft-forming system
   ii. Low density system
   iii. Bio/mucoadhesive system
   iv. Swelling system, etc.

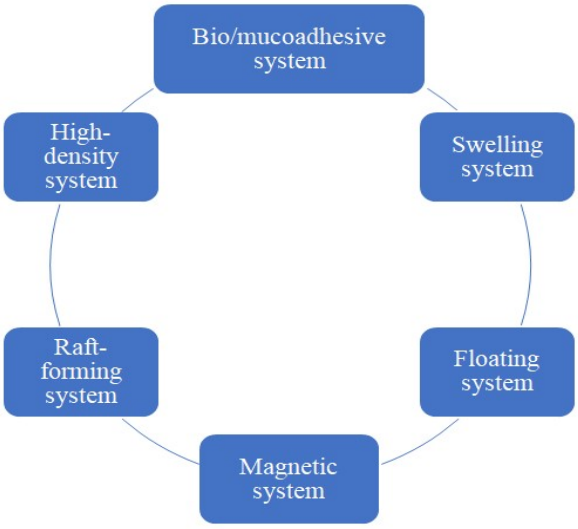

Figure 1. Different types of GRDDs

1) **Floating system:** The mechanism that manages the pharmacokinetic release rate of a medication to a specific site in a gastro-retentive drug delivery system (FDDS) is referred to as the FDDS. This is done in order to produce the desired pharmacological effect. FDDS, also known as hydro-dynamically balanced systems (HBS), are low-density systems that float above the contents of the stomach and remain there for an extended period of time, thereby releasing the pharmacological component at the pace that is required. Floating over the stomach's contents makes the time spent in gastro-retention last longer and makes fluctuations less severe (Lodh, 2020).
2) **Swelling system:** In reality, the swelling drug delivery system, also known as GRDDs and abbreviated as SDDS, is a different kind of the gastroretentive drug delivery systems. In this method, the medicine (tablet) that is swallowed causes the stomach to expand, and because of this, the medicine (tablet) is unable to pass through the pyloric sphincter and is instead kept in the stomach (Aslam, 2014).
3) **Bio/mucoadhesive system:** Mucoadhesion is a process in which two aspects, one of which is biological in origin, are held together for lengthy periods of time by interfacial forces. This condition is known as mucoadhesion. Mucoadhesion is utilised when a bond is created with a mucosal surface, whereas bioadhesion refers to sticky interactions with any biological or biologically generated substance (Nikalje, 2012).
4) **High-density system:** High-density systems have a density larger than that of gastric fluids (1.004 g/cm3) and so sink to the bottom of the stomach fluids and achieve gastric retention, most likely as a result of enhanced resistance to the gastric contractions due to their high density. Barium sulphate, zinc oxide, iron oxide, iron powder, and titanium dioxide are typical excipients utilised to guarantee a suitably high density of these systems. Typically, the dose forms documented in the literature are pellets or tablets with a high density (Vrettos, 2021).
5) **Raft-forming system:** The Raft Forming System, which is a Gastroretentive drug delivery system, was designed in order to increase this gastric retention time. This solves some of the problems that we have with other methods of taking medication, and as therapeutic efficacy will improve, it will also be easier to administer floating dosage forms into patients. And so, a floating Raft System that is promising has been figured out and accomplished. This system might be suitable for some of the population, such as paediatrics, as well as other people who have difficulty taking controlled medication in solid form, and this could lead to improved patient compliance and efficacy (Patel and Vaishnav, 2020).
6) **Magnetic system:** These systems take the form of small gastroretentive capsules that contain a magnetic material. The material's expulsion from the stomach is prevented by the interaction of the magnetic material with a sufficiently powerful magnet that is applied to the surface of the body in the region where the stomach is located. The actual usefulness of such systems is questionable despite the numerous reports of successful tests. This is due to the fact that the intended outcomes can only be accomplished if the magnet position is picked with very high precision in order to produce the desired results. It is likely that the creation of new magnetic field sources that may be applied readily will result in an improvement to this notion (Sowmya, 2019).

Gastric motility pattern & Gastric emptying time: Gastrointestinal (GI) motility is the coordinated contractions and relaxations of the GI muscles required to move food from the mouth to the anus (Punati, 2017). The gastric emptying rate (gastrointestinal transit time) quantifies the rate at which the stomach empties its entire content into the duodenum. The stomach performs a phenomenal function by quickly absorbing large quantities of foods with varying physical and chemical compositions. Human stomachs can expand 10 to 15 times their volume in the absence of a substantial increase in intragastric pressure (Goyal, 2019). It is common knowledge that the stomach has the potential to act as a 'depot' for sustained release (SR) dose forms, the release of which can be influenced by the amount of time it takes for the stomach to empty. Even while the process of stomach emptying happens throughout both fasting and fed stages, the pattern of motility that occurs during these two statesis very different from one another. When the individual is in a fasting condition, it is defined by a series of electrical events that occur between the digestion processes (Journal, 2012).

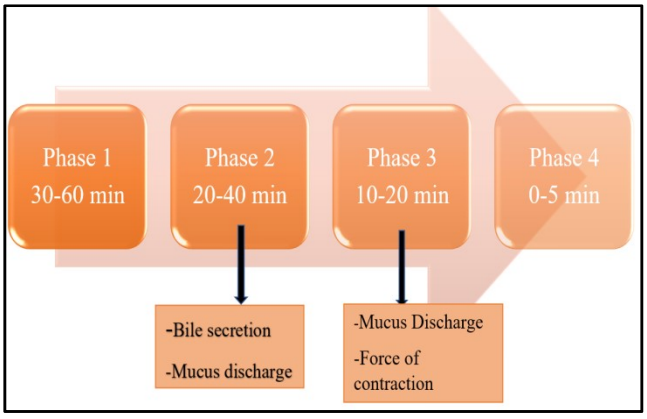

Figure 2. Gastric emptying time with phases

Phase 1- Phase 1 (the basic phase) lasts 30 to 60 minutes and contractions are infrequent.

Phase 2- Phase 2 (Preburst phase) lasts between 20 and 40 minutes and is characterised by sporadic action potentials and contractions.

Phase 3- Phase 3 (Burst phase) lasts between 10 and 20 minutes and is characterised by intense, regular contractions.

Phase 4- The fourth phase lasts between 0 and 5 minutes and occurs between the second and first phases of two consecutive cycles.[19]

Factors affecting Gastric emptying time:[20]

There are a number of factors that can influence the rate at which the stomach empties, and consequently the amount of time that oral dose forms are retained in the stomach.

1] Density
2] Size
3] Shape of dosage form
4] Simultaneous consumption of food and its nature
5] Both the total number of calories and how often they are consumed

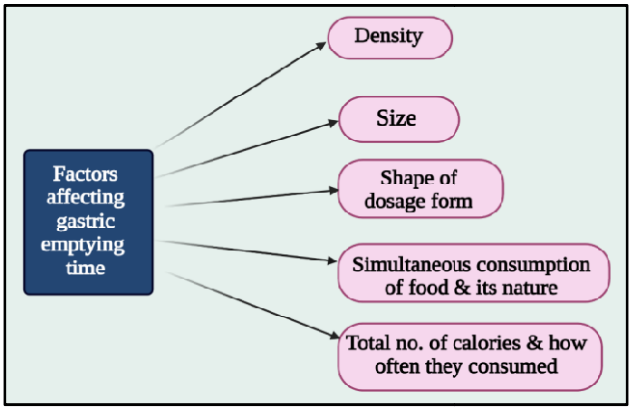

Figure 3. Factors Affecting Gastric Emptying Time

Advantages of GRDDS:

1] Compared to the administration of nongastroretentive drug delivery, this gastroretentive drug delivery strategy can significantly increase the bioavailability of therapeutic agents, particularly those that are metabolised in the upper GIT.
2] Gastroretentive drug delivery can prolong and sustain drug release in the stomach and small intestine. They treat stomach and small intestine disorders (Adibkia, 2013).
3] These systems increase the bioavailability of drugs metabolised in the upper GI tract, like riboflavin and levodopa. By increasing gastric residence time, gastroretentive dosage forms help reduce dosing frequency for drugs with a short half-life (Vinchurkar, 2021).
4] Delivery of drugs through the gastrointestinal tract can reduce the amount of interference from the body, resulting in increased drug efficacy (Pant, 2016).

Disadvantages: (Pant, 2016)

1] GRDDS cannot include drugs with poor acid stability, low solubility, or gastric mucosa irritation.
2] Floating systems require high stomach fluid levels to work effectively. This dosage form requires more water.
3] Swellable dosage form must swell before stomach exit and be larger than pylorus aperture. It must resist Phase III MMC housekeeper waves.
4] Floating systems require high stomach fluid levels to work effectively. This dosage form requires more water.

Difference between Conventional DDS and Gastroretentive DDS

Table 1. Difference between Conventional DDS and Gastroretentive DDS [24], [12]

Sr. No.	Parameters	Conventional DDS	Gastroretentive DDS
1.	Patient compliance	Less	Improves patient toxicity
2.	Toxicity	High	Low
3.	Dose dumping	High risk	Low risk
4.	Drug with narrow absorption window in small intestine	Not suitable	Suitable
5.	Drug which degrades in the colon	Not advantageous	Very advantageous
6.	Drug having rapid absorption through GIT	Not advantageous	Very advantageous

Hydrodynamically Balanced System: The history of the HBS (Hydrodynamically balanced system) system began in 1978 when Sheth and Tossounian designed, developed, and described the system for the first time. The easiest and most effective gastroretentive dosage form is called the Hydrodynamically Balanced System (HBS). HBS is made up of gel-forming polymers, and the drug is encapsulated inside of a hard gelatin capsule shell. The shell of the swollen hydrogel is formed either through immersion in the solution (in vitro) or swallowing (in vivo), depending on the method (Soni, 2018). Based on the findings of the pharmacokinetic studies, HBS has been determined to be theformulation that is most ideally suited for the particular application at hand, which requires a slow and consistent delivery (Erni, 1987). The goal of hydrodynamically balanced systems, also known as HBS, is to increase the amount of time that a dosage formspends in the gastro intestinal tract, which in turn helpsto improveabsorption. These types of delivery systems are ideal for medications that are more soluble in an acidic environment and also for medications that have a specific site of absorption in the upper part of the small intestine. to stay in the stomach for a considerable amount of time. It is required that the dosage form have a bulk density that is lower than 1 (Amit, 2011). Since itopride hydrochloride is a prokinetic medicine and its principal site of action is the stomach and also in the pH range of 3.5 to 5.5, It would be beneficial to design an itopride hydrochloride drug delivery system that floats. This would make it easier for the body to absorb the drug**.** The produced tablets of each formulation were tested for a variety of characteristics, including physical characteristics, assay, swelling index, in-vitro drug release, total floating time, floating lag time, tablet density, hardness, and friability.

Classification of the Hydrodynamically balanced system:

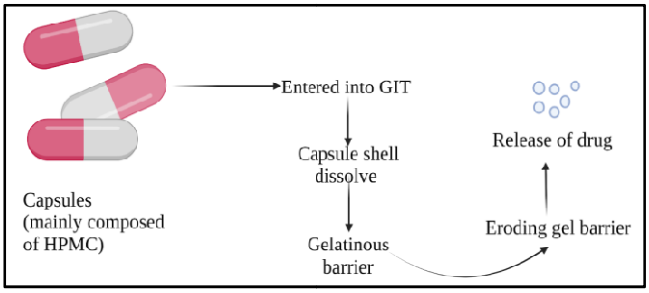

Figure 5. Systematic illustration of HBS mechanism

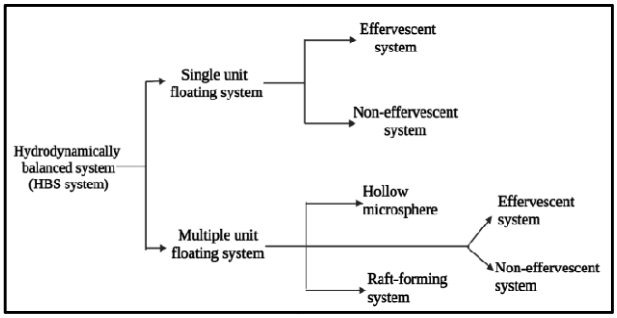

Figure 6. Classification of HBS system

Advantages of HBS:[27]

1] Gastric retention time limits sustained oral controlled-release drug absorption. FDDS spend several hours in the stomach to increase GRT. Thus, prolonging the GRT increases drug absorption.
2] By favourably affecting the way in which the active agent is absorbed, FDDS increases the bioavailability of the active agent.
3] FDDS enhances stomach pharmacotherapy by means of local drug release, which results in high drug levels at the gastric mucosa and lowers the risk of gastric cancer.
4] FDDS can serve as carriers for antiviral, antifungal, and antibacterial agents (GIT). Absorption window describes these drugs.
5] Formulating highly potent drugs as FDDS improves their safety margin leading to good control of plasma levels and expulsion of the floating system after complete drug release, which reduces suppression of the drug's activity by the body (counter activity) and minimises adverse activity at the colon.

Disadvantages of HBS:[28]

1] There is a requirement for an increased quantity of fluids in the stomach.
2] Unsuitable for medications like those that have a difficult time dissolving in gastric fluid.
3] Irritating to the digestive tract.

HBS (Hydrodynamically balanced system) in oral drug delivery system: The Hydrodynamically Balanced System, also known as the HBS, is an oral dosage form (capsule or tablet) that is intended to increase the amount of time that the dosage form spends residing within the gastrointestinal tract. It is a formulation of a medication that contains gel-forming hydrocolloids with the intention of remaining buoyant on the contents of the stomach. This not only extends the amount of time that the drug spends in the gastrointestinal tract, but it does so in a region of the gastrointestinal tract that increases the likelihood of the drug inward at the site of absorption in a dissolved state, making it ready for absorption. Dissolving of the medicine and its release from the capsule while it is still present in the fluids of the stomach both taking places at the pH of the stomach. These processes occur under conditions that are able to be regulated to a satisfactory degree. Further regulation of the pH of the microenvironment is possible through the formulation of pharmaceuticals [29]. Granules, powders, capsules, tablets, laminated films, and hollow microspheres have all been utilised in the development of a variety of buoyant delivery systems. The following are some examples of various drugs that have been formulated as various forms of FDDS.[30] If the gastric fluid density is greater than that of the medication, it will float on the proximal surface of the stomach content, allowing for maximum drug release before being emptied into the small intestine. Gastric fluid is 1g/cm3. If a medicine has a lower density than gastric fluid, it floats; otherwise, it sinks. For the most part, this system can make use of formulations that have a narrow absorption window, solubility that is pH-dependent, and active transport absorption either by the upper or lower part of the smaller intestine [31].

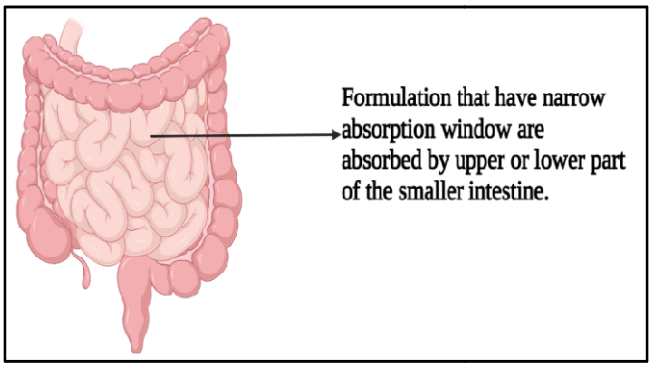

Figure 8. Absorption from small intestine

Novel hydrodynamically balanced system

Future Potential: The FDDS method can be utilised for a variety of potential active agents that have a narrow absorption window. These include antiviral, antifungal, and antibiotic agents (sulphonamides, quinolones, penicillins, cephalosporins, aminoglycosides, and tetracyclines) that are absorbed from very specific regions of the GI tract. The development of these agents has been halted due to a lack of appropriate pharmaceutical technologies. The quantitative efficiency of floating delivery methods in the fasted and fed states as well as the link between prolonged GRT and SR/PK features were investigated. Floating Drug Delivery Systems, also known as FDDS, have been created in order to lengthen the amount of time that drugs spend in the stomach (GRT)[32]. Using a magnetic field to keep the dosage form within the stomach was proposed as an additional new method. Magnetically active components would be included in the dose form. It was necessary to install an external magnet on the abdomen over the stomach in order to keep the supplied medication in place. This delivery system's lack of patient compliance was one of its primary drawbacks in vivo, despite its revolutionary design[33]. Understanding polymer behaviour and its role in formulation is essential for the logical construction of the gastroretentive dosage form. This is especially true when seen from the perspective of formulation. In addition, the selection of an acceptable concentration of polymer is also an extremely critical step in theprocess of formulating such dosage forms. In this context, the quality by design (QbD) approach can be an effective instrument for examining the effects of formulation and process variables on the essential quality characteristics of GRDDS. There has been a considerable revolution in the understanding and control of the manufacturing process, which has significantly contributed to a reduction in the risk of product failure as a result of the deployment of the QbD approach in pharmaceutical fields [34].

Examples: Klausner et al created a Levodopa GRDDS using unfolding polymeric membranes with enlarged diameters and great stiffness. Carbidopa-pretreated beagles were studied in vivo. X-rays were used to locate the formulated formulation in the GI tract. Blood samples were also tested for the active medication. The optimised GRDDS of Levodopa maintained therapeutic concentrations (>500 mg/ml) for 9 h. Mean absorption time was longer than non-GR controlled release-particles and oral solution [33].

Table 2. Marketed products of FDDS:[37]

Sr. No	Marketed products
1.	Madopar HBS (Prolopa HBS)
2.	Valrelease
3.	5-mg Valium tablet
4.	Topalkan
5.	Almagate FlotCoat

Future Aspects: In recent years, substantial scientific and technological advancements have been made in the discovery and application of a rate-controlled oral drug delivery system. These advancements have been made possible as a result of a number of factors. These advancements have been made probable by the successful overcoming of physiological challenges, such as a short GRT and unpredictable GET. Current methods for extending the GRT include the floating drug delivery system (FDDS), which is also referred to as the hydrodynamically balanced system (HBS), the swelling and expanding system, the polymeric bioadhesive system, the modified-shape system, the high-density system, and various other delayed gastric emptying devices. FDDS has developed into a highly effective method for managing the release of a variety of medications. It is possible that the management of gastrointestinal (GI) transit profiles will be the primary emphasis for the next two decades, and that this will lead to the development of new medications with expanded therapeutic applications and significant advantages for patients. Even though there are a number of issues that need to be resolved before prolonged gastric retention can be achieved, a

significant number of businesses are working toward commercializing this method [26].

CONCLUSION

Most medications are primarily absorbed in the stomach, but due to variations in gastric emptying rates, certain pharmaceuticals pass throughout the stomach without being absorbed, leading to a variety of absorption patterns. The development of different delivery systems that remain inside the stomach for the predefined amount of time as a result of advancements in pharmaceutical technology has improved drug absorption. A useful method for increasing drug bioavailability and optimizing' the delivery of medications with a limited window of absorption and low solubility is the gastro retentive drug delivery system. The manipulation of controlled oral drug distribution seems to be most successfully accomplished using delayed stomach emptying rates and buoyancy principles. Since there has been a sharp rise in interest in this field in recent years, it is likely that this will result in the creation of effective dosage forms.

REFERENCES

Alluri, R., Sai, A., S. Aeila, and T. M. Sai, "GASTRORETENTIVE DRUG DELIVERY SYSTEM-AN OVERVIEW," no. January, 2020, doi: 10.20959/wjpps20201-15243.

Gadge, G., V. Sabale, A. Khade, and U. Mahajan, "Current Approaches on Gastro Retentive Drug Delivery System: An Overview," *Int. J. Pharm. Res. Technol.*, vol. 9, no. 2, pp. 16–28, 2019, doi: 10.31838/ijprt/09.02.04.

Pant, S., A. Badola, and P. Kothiyal, "A review on gastroretentive drug delivery system," *Indian J. Pharm. Biol. Res.*, vol. 4, no. 2, pp. 01–10, 2016, doi: 10.30750/ijpbr.4.2.1.

Daniels I. R. and W. H. Allum, "The Anatomy and Physiology of the Stomach," *Up. Gastrointest. Surg.*, pp. 17–37, 2005, doi: 10.1007/1-84628-066-4_2.

"Dr. M.M. Khan, Physiology Of Stomach, part 1.pdf." .

Faizi, S. M., S. R. Wasankar, P. N. Rathi, S. N. Lateef, A. Borade, and A. Ahmed, "Development and evaluation of gastroretentive microspheres of cefixime," *Indian J. Pharm. Educ. Res.*, vol. 48, no. 1, pp. 49–55, 2014, doi: 10.5530/ijper.48.1.8.

Jasim, I. K., A. A. Abdulrasool, and S. N. Abd-Alhammid, "Nanosponge based gastroretentive drug delivery system of 5-fluorouracil for gastric cancer targeting," *Int. J. Drug Deliv. Technol.*, vol. 11, no. 3, pp. 958–963, 2021, doi: 10.25258/ijddt.11.3.52.

Rathee, P., S. Rathee, A. Nanda, and A. Hooda, "Gastroretentive Drug Delivery Systems : A Review of Formulation Approaches DELIVERY SYSTEMS," vol. 1, no. 8, 2012.

Ganesh, N. S.S. M. Ambale, B. Ramesh, and K. B. Deshpande, "An overview on limitations of gastroretentive drug delivery system," *Int. J. Pharm. Sci. Rev. Res.*, vol. 8, no. 2, pp. 133–139, 2011.

Lodh, H. S. FR, P. K. Chourasia, and H. A. Pardhe, "Floating Drug Delivery System: A Brief Review," *Am. J. PharmTech Res.*, vol. 10, no. 4, pp. 103–122, 2020, doi: 10.46624/ajptr.2020.v10.i4.010.

Aslam, R. Y. Mehmood, S. Khan, and H. Yousaf, "Techniques and polymers used to design gastroretentive drug delivery systems - a review.," *World J. Pharm. Pharm. Sci.*, vol. 3, no. 12, pp. 97–110, 2014.

Nikalje, A. P., S. Tiwari, and S. Kamble, "Mucoadhesive: as oral controlled gastroretentive drug delivery system.," *Int. J. Res. Pharm. Sci. (Jaipur, India)*, vol. 2, no. 3, pp. 32–59, 2012.

Vrettos, N. N. C. J. Roberts, and Z. Zhu, "Gastroretentive technologies in tandem with controlled-release strategies: A potent answer to oral drug bioavailability and patient compliance implications," *Pharmaceutics*, vol. 13, no. 10, 2021, doi: 10.3390/pharmaceutics13101591.

Patel R. and G. Vaishnav, "Raft Forming System - Gastroretentive drug delivery system," *Int. J. Adv. Eng. Manag. Sci.*, vol. 6, no. 12, pp. 515–519, 2020, doi: 10.22161/ijaems.612.5.

Sowmya, B., S. Arvapalli, and A. V. S. S. S. Gupta, "World Journal of Pharmaceutical A REVIEW ON GASTRORETENTIVE DRUG DELIVERY SYSTEM," vol. 5, no. 4, pp. 101–110, 2019.

Punati J. *et al.*, "Gastrointestinal Motility Physiology," 2017.

Goyal, R. K., Y. Guo, and H. Mashimo, "Advances in the physiology of gastric emptying," *Neurogastroenterol. Motil.*, vol. 31, no. 4, pp. 1–14, 2019, doi: 10.1111/nmo.13546.

Journal, I., O. F. Pharmaceutical, and C. Sciences, "Review Article Gastric Retentive Controlled Drug Delivery : An Overview," vol. 1, no. 1, pp. 156–163, 2012.

Jassal, M., U. Nautiyal, J. Kundlas, and D. Singh, "A review: Gastroretentive drug delivery system (grdds)," *Indian J. Pharm. Biol. Res.*, vol. 3, no. 01, 2015, doi: 10.30750/ijpbr.3.1.13.

Streubel, A., J. Siepmann, and R. Bodmeier, "Gastroretentive drug delivery systems," *Expert Opin. Drug Deliv.*, vol. 3, no. 2, pp. 217–233, 2006, doi: 10.1517/17425247.3.2.217.

Adibkia, K., S. Ghanbarzadeh, G. Mohammadi, R. B. Atashgah, and A. Sabzevari, "Gastro retentive drug delivery systems: A review," *J. Reports Pharm. Sci.*, vol. 2, no. 2, pp. 190–204, 2013, doi: 10.5897/ajpp2015.4307.

Vinchurkar, K. *et al.*, "Features & Facts of Gastroretentive Drug Delivery System-A Review Gastroretentive İlaç Dağıtım Sisteminin Özellikleri ve Gerçekleri-Bir İnceleme Short title: Gastroretentive Drug Delivery System," 2021, doi: 10.4274/tjps.galenos.2021.44959.

Soni, S., V. Ram, and A. Verma, "Updates on Approaches to Increase the Residence Time of Drug in the Stomach for Site Specific Delivery: Brief Review," *Int. Curr. Pharm. J.*, vol. 6, no. 11, pp. 81–91, 2018, doi: 10.3329/icpj.v6i11.36436.

Erni W. and K. Held, "The hydrodynamically balanced system: A novel principle of controlled drug release: (with 2 color plates)," *European Neurology*, vol. 27. pp. 21–27, 1987, doi: 10.1159/000116171.

Amit, J. K., R. Rammulrajsinh, D. Sonali, P. Kinal, and A. Pradeep, "Hydrodynamically balanced systems (HBS): Innovative approach of gastroretention: A review," *Int. J. PharmTech Res.*, vol. 3, no. 3, pp. 1495–1508, 2011.

M. Amit Gupta, V. Aarti Belgamwar, S. Prashant Wake, P. Trivesh Rathi, and D. R. Mundhada, "Design and development of hydrodynamically balanced tablet of itopride," *J. Chem. Pharm. Res.*, vol. 3, no. 6, pp. 856–864, 2011.

Kristl, J., S. Baumgartner, F. Vrecer, and A. Rotar, "Formulation and evaluation of hydrodynamically balanced matrix systems," *Farm. Vestn.*, vol. 48, no. SPEC. ISS., pp. 264–265, 1997.

Retention, G. and E. Systems, "FLOATING DRUG DELIVERY SYSTEMS: ENHANCE GASTRIC RESIDENCE TIME R. Santosh Kumar, Ganesh Sai Myneni AN ALTERNATIVE APPROACH TO," vol. 8, no. 01, 2018.

Preziosi, P., "Drug development," *Compr. Med. Chem. II*, vol. 2, no. 2, pp. 173–202, 2006, doi: 10.1201/9780429022951-10.

Singh, A. K. and N. Sharma, "Future outlook hydrodynamic drug delivery system of solid oral dosage form: Review," *IP Int. J. Compr. Adv. Pharmacol.*, vol. 6, no. 3, pp. 96–101, 2021, doi: 10.18231/j.ijcaap.2021.018.

Yadav, P. H., D. P. Kardile, M. T. Deshmukh, and R. V. Shete, "Hydrodynamically Balanced System: A Review," *J. Drug Deliv. Ther.*, vol. 11, no. 1-s, pp. 147–153, 2021, doi: 10.22270/jddt.v11i1-s.4548.

Shashank, C., K. Prabha, S. Sunil, and A. Vipin Kumar, "Approaches to increase the gastric residence time: Floating drug delivery systems- A review," *Asian J. Pharm. Clin. Res.*, vol. 6, no. 3, pp. 1–9, 2013.

Mandal, U. K., B. Chatterjee, and F. G. Senjoti, "Gastro-retentive drug delivery systems and their in vivo success: A recent update," *Asian J. Pharm. Sci.*, vol. 11, no. 5, pp. 575–584, 2016, doi: 10.1016/j.ajps.2016.04.007.

Tripathi, J., P. Thapa, R. Maharjan, and S. H. Jeong, "Current state and future perspectives on gastroretentive drug delivery systems," *Pharmaceutics*, vol. 11, no. 4, pp. 1–22, 2019, doi: 10.3390/ pharmaceutics11040193.

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