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AN OVERVIEW ON VARIOUS TYPES OF GASTRORETENTIVE DRUG DELIVERY SYSTEM

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Gastro retentive drug delivery system is one of the approaches to achieve controlled drug delivery. The gastro retentive drug delivery system is a way to prolong residence time of active pharmaceutical ingredient in gastrointestinal tract. It is also applied for targeting drug in upper gastrointestinal tract for generating local and systemic effect. Controlled drug delivery creates a window of absorption that release drug for a longer duration of time before reaching absorption site. Gastro retentive drug delivery systems have gained wide variation of oral drug distribution in the area of late. It includes all the approaches that keep the dosage form in the stomach for a longer duration of time. This also enables sustained release of active pharmaceutical ingredient which in turn overcomes many limitations of conventional drug delivery systems. It has begun tremendous advances in the field of gastro-retention to meet controlled release of drugs.

Aim of research. The main aim of this survey to prolong the gastric retention dosage form in the stomach and improve the medication concentration in the stomach.

Material and Method. To prepare this manuscript, various keywords were searched in different search engines such as Google, Yahoo, Bing etc. The available information in public domain was collected and classified according to delivery system. This review paper aim to provide complete information about different delivery systems related to Gastro retentive drug delivery systems (GRDDS). It is also applied for targeting drug in upper gastrointestinal tract for generating local and systemic effect.

Result. After going through various literatures, it can be said that the GRDDS can improve local bioavailability and therapeutic efficacy and dosing frequency possible reduction in dose size. This paper is focused on various physiological contemplation and obtainable formulation approaches for development of gastro retentive drug delivery system.

Conclusions. This article discusses various types of GRDDS and their approaches. The gastric retentive drug delivery systems improve drug absorption. Prolonged gastric retention time of therapeutic mutations provide several benefits such as improving absorption, bioavailability and enhance the therapeutic action of drug

Keywords: gastric emptying, gastro retentive drug delivery system (GRDDS), floating drug delivery system, biomucoadhesive system

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1. Introduction

Floating drug delivery system is also popularly known by the name of hydro dynamically controlled system. Basically the floating dosage form is of very low density, which enable drug to float in gastric media in stomach this results in increasing the residence time of drug in stomach without affecting gastric emptying rate in whole. The dosage form keep floating on gastric content and release drug in slow manner at desired rate, resulting in increased gastric retentive time in the stomach. It also helps in reducing the drug concentration variation in plasma. In spite of having many advantages, this dosage form suffers number of disadvantages such as unpredictable gastric emptying – time, variation of gastric emptying time from person to person, small gastrointestinal transit time (8–12 h), and number of drugs have absorption windows in upper part of small intestine [1]. The formulation scientists have to take care of these many number of challenges while designing a gastro retentive drug delivery systems. Apart from this the main challenge that one face is of shorter gastric residence time (GIT), which is unpredictable and changes depending on number of factors. To be able to design GRDDS in a better way, a thorough knowledge and understanding

of anatomy and physiology of GIT is necessary [2]. Gastric emptying states were fed along with fasting. The available literature shows that orally administered controlled drug delivery systems suffer from two major challenges low gastric residence time (GRT) and uncertain GRT [3]. Drugs with solubility in high alkaline PH of intestine, can be delivered using gastro retentive drug delivery systems. Gastro retentive drug delivery system is reported to have increased the solubility of such drugs [4]. GRDDS is also used for drugs that degrade in colonic region. It is also beneficial for:

- Improving bioavailability of drug increasing therapeutic efficiency of drug.
- Reducing dose of drug.
- Maintaining uniform concentration of blood [5].
- Reducing fluctuation in therapeutic concentration of drug.

2. Importance of GRDDS in the field of pharmaceuticals

Immediate release oral delivery systems is most widely used to treat disease, there are absorbed at specific site only. Number of disadvantage of immediate release dosage form makes it necessary to develop gastro-retentive drug delivery systems. These systems will help

in keeping drug at specific site for longer duration of time.

This is achieved by maintaining the dosage form in the stomach and drug is being released at specific location in stomach, duodenum and intestine in controlled action. The below structure (Fig. 1) are shown in various parts of human stomach [6].

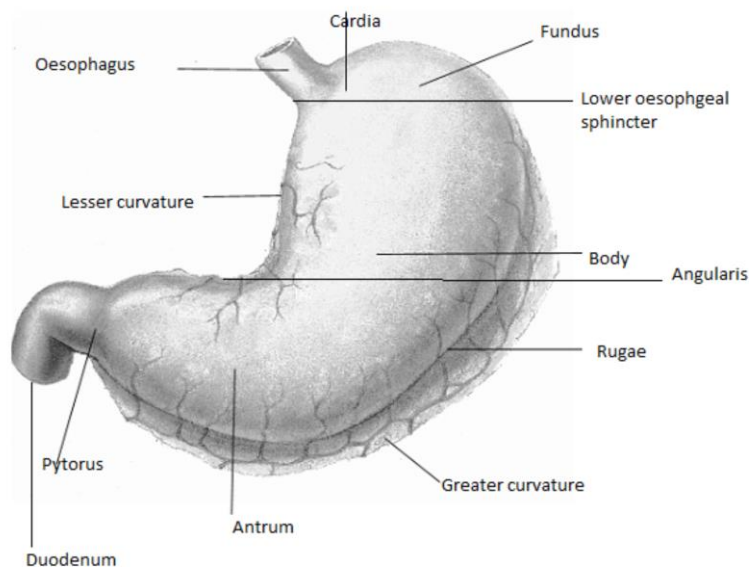


Fig. 1. Various parts of human stomach

3. GRDD system advantages

Gastro retentive drug delivery systems having various type of benefits in several areas, they are following:

1. It improves drug delivery and drug absorption
2. By this method controlled amount of drug can be delivered [7]
3. It has a local action on stomach [8]
4. It minimizes the mucosal irritation
5. Increases first pass biotransformation
6. Ease of administration and improved patient compliance
7. Low frequency of dosing
8. Improves therapeutic efficacy [5]
9. Sustained release dosage form helps in avoiding gastric irritation [9].

GRDDS shows some sort of disadvantages:

Following are the disadvantages of gastro retentive drug delivery system:

- Floating drug delivery systems require high fluid level in stomach to float and work effectively [1]
- Drugs that absorb selectively in colon, e.g. corticosteroids [1]
- Drugs that have very limited acid solubility (e.g. phenytoin)
- The drug that undergoes a significant first pass metabolism (e.g. nifedipine)
- The needs for high levels of abdominal fluids for the delivery system to float and function efficiently [10]
- The presence of food is required to delay gastric emptying [11]

Factor affecting of GRDDS

The factors that affect the gastro retentive system for the gastric retention time of dosage forms are:

Shape and size of dosage form

– The average gastric residence time of non-floating dosage forms is highly variable and depends on their size, which may be large, medium and small units.

– Most sizes should be more than 7.5 mm in diameter [12, 13].

Density of dosage form

– Low density dosage form can float at the surface of gastric content. High density dosage form sinks and remains at bottom of stomach. Density of dosage form should be less than 1.0gm/cm^3 to make the float at the surface of gastric content [14].

Age

– GRT is higher in chorion patients and lower in newborn and children. Age above 70 (>70) now displays GRT [15].

Posture

– GRT may vary between supine and conscientious ambulance states [16].

Gender

– Males have higher GRT than females [16].

Nature of the meal

– Meal with high amount of fatty acid reduces the gastric retention time. This happens due to changes in gastric motility [17].

Frequency of food ingestion

– When food is ingested frequency, GRT increase subsequently. This happens due to low frequency of migrating myoelectric cycle [1].

4. Other drawbacks associated with specific type of GRDDS given are [18]

High density system: this technology find very difficult to deliver large amount of drug at specific site. Moreover, this systems is not get accepted by pharmaceutical industry. This may be the reason due to which these type of systems are yet not available in market.

Floating system: the amount of gastric content is one of the most important literature for floating systems. Level of fluid is also one of the important factor for floating fluid level must be high for making dosage form float at surface [19, 20].

Expandable system: these are dosage form which comes in contact of gastric fluid expands and remain there for a longer duration of time. However, these dosage forms have certain limitation. Blocking of gastric passage is one of them. They are difficult to manufacture and are not economical. Storage of the dosage forms are also challenging due to presence of hydrolysable and bio degradable polymers [21].

Mucoadhesive system and bioadhesive system: Epithelial cell are renewed continuously after mucoadhesive and bioadhesive dosage form detached from mucosa. Rapid turnover can get of mucus and peristaltic movement of stomach cause this detachment [22, 23].

Magnetic system: attainment of patient compliance is a major challenge for this type of dosage form.

5. Strategies for delaying drug transit through GIT:

Physiological system. It uses natural ingredients or fat derivatives such as tri ethanolamine myristate, which stimulate duodenal or jejunal receptors to gastric emptying [1, 24].

Pharmaceutical system.

First two approaches are not used due to toxicity problems. The various pharmaceutical approaches are:

Gastro retentive dosage form.

The dosage forms that can be maintained in the stomach are called GRDF. Over the last two decades, numerous of GRDF have been designed to prolong gastric residence time. The below Table 1 shown are transit time of dosage form across the GIT [25].

Table 1

Transit time of dosage form across the GIT				
No.	Dosage form	Small intestine	Stomach	Total transit time (hour)
1.	Tablet	3.1±0.4	2.7±1.5	5.8
2.	Capsule	3.2±0.8	0.8±1.2	4.0
3.	Pellets	3.4±0.1	1.2±1.3	4.6
4.	Solution	4.1±0.5	0.3±0.1	4.4

6. Type of gastro retentive dosage forms and approaches:

Floating system:

Floating drug delivery system (FDDS)

Floating drug delivery systems are believed to have lower density than gastric contents. This enables them to float on the gastric content.

Effervescent system

Non effervescent system:

- Alginate beads
- Hydrodynamically balanced system
- Microporous compartment
- Microballoons or hollow microspheres [18].

Floating drug delivery system:

Floating drug delivery systems utilizes following two systems to float at the surface of gastric content:

- Effervescent system;
- Non effervescent system.

Effervescent system and non effervescent system of intra-gastric floating drug delivery devices are shown in Fig. 2 [24, 26].

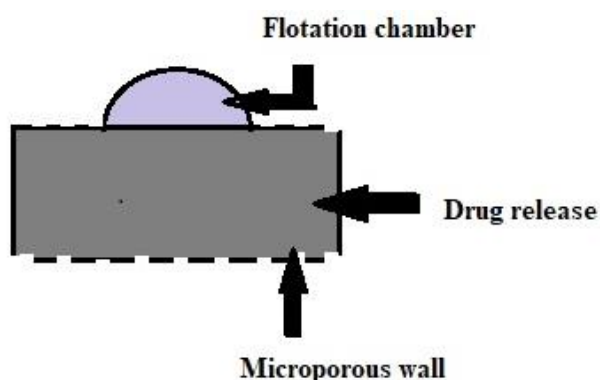


Fig. 2. Graphical representation of intra-gastric floating drug delivery device

6.1. Effervescent floating system

Swellable polymers and various effervescent forming chemicals are used for formulating this kind of systems. They are planned so that when in contact with the acidic gastric substance, CO₂ is freed and gets entangled in swollen hydrocolloids, which gives lightness to the measurement dosage forms [27]. Floatation of

drug delivery system in the stomach loaded up with vacuum, air, or an inert gas [28, 29]. Gas can be brought into the floating chamber by the volatilization of a natural dissolvable (organic solvent) (e.g., ether or cyclopentane) or by the CO₂ delivered because of a floating responses between organic acids and carbonate–bicarbonate salts [30, 31]. These devices contain a hollow deformable unit that changes over from a fallen to an extended position and comes back to the crumbled position after a pre decided measure of time to allow the unconstrained discharge of thin floatable system from the stomach [4]. Proportion of sodium carbonate and citric acid should ideally be 1:0.76 for optimum gas production [18].

6.2 Non effervescent floating system

These systems uses higher amount of one of more gels (20–75 %) and highly swellable cellulosic hydrocolloids. Few extensively used cellulosic hydrocolloids are hydroxyethyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, sodium carboxymethyl cellulose [32]. Polysaccharides or matrix forming polymers are also used for preparing and are incorporated into tablets and capsules. Few examples of such compounds are polyacrylates, polycarbophil, and polystyrene [33]. One these systems are exposed in gastric fluid, these gels are hydrated. These hydrated gels along with other polymers form a colloidal gel barrier [34, 35]. These barriers thus formed, controls fluid penetration into the system and thereby control the release of drug from the systems [28, 36, 37]. The following approaches are used to design in the intra-gastric floating systems [4].

Alginate beads

These are dosage forms are prepared by freeze drying of calcium alginate. Spherical beads are prepared by dropping sodium alginate solution into aqueous solution of calcium chloride [38]. This causes precipitation of calcium alginate. The calcium alginate beads were compared to solid beads [39, 40]. It was observed that the beads were prolonging residence time. The GRT in the case of solid beads was found to be 1 hour whereas with calcium alginate beads, GRT of 5.5 hour was observed [18, 41].

Hydrodynamically balanced intragastric delivery system (HBS)

Hydrodynamically adjusted gastrointestinal drug delivery system, either in the form of capsules or tablets, they are intended to prolonged gastrointestinal time in a zone of the GI tract to maximize the drug, increasing the absorption site in arrangement state and subsequently, prepared for ingestion [42]. These system are contains to drug with gel-forming hydrocolloids intended to stay light on the stomach content [5, 43]. This type of systems utilizes one or more hydrophilic polymers such as hydrophilic polymers are - hydroxypropyl methylcellulose (HPMC), hydroxethyl cellulose (HEC), hydroxypropyl cellulose (HPC), sodium carboxymethyl cellulose (NaCMC), polycarbophil. The representation of hydrodynamically balanced intragastric delivery are explain in figure 3 [44, 45].

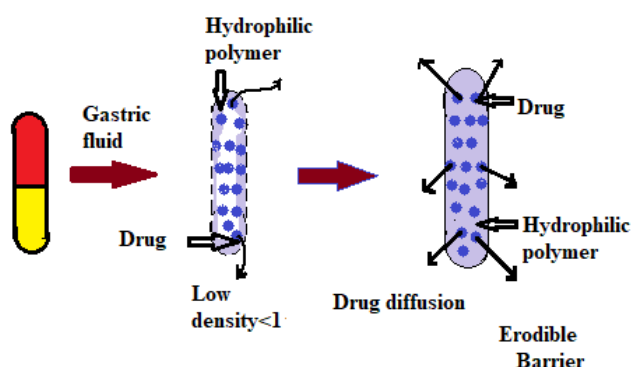


Fig. 3. Representation of hydrodynamically balanced intragastric delivery system (HBS)

Microporous compartment

In this type of systems, drug is kept into a micro compartment with pores on top and bottom walls, and peripheral wall is completely sealed. This sealing prevents contact of gastric surface and drug reservoir [46, 47].

When these systems are administered, air gels get entrapped in flotation chamber. This enables delivery systems to float on gastric content. Gastric fluids, through the pores enter into the systems. The drug gels dissolved is the fluid and transport continuously into the intestine for absorption [48].

Microballoons or hollow microspheres

Micro balloons or hollow microspheres are filled with drugs in their other polymer layer. Solvent evaporation and solvent diffusion methods used for utilizing polymer were used for preparing microballoons or hollow microspheres [46]. Few polymers that are utilized for preparing such systems are polycarbonate, cellulose acetate, calcium alginate, Eudragit S, etc. [39, 49, 50]. The such systems developed floats uniformly on the surface of gastric content for more than 12 hours. Hollow microspheres are considered to be one of the most promising floating systems as they are combined with the advantages of multi-unit and float much [6].

Non-floating system

This type of system are retained is stomach with number of mechanisms. Other than, floating of delivery. These systems are maintained in the stomach by many mechanisms but not by floating [51, 52]. Non-floating system are further subdivided:

- a) Sinking (High density) drug delivery system
- b) Bioadhesive / mucoadhesive system

- c) Magnetic system
- d) Unfoldable system [53].

Bio adhesive & mucoadhesive system

The bio adhesive and mucoadhesive system are drug delivery systems. They are used as a delivery device within the lumen to increasing the absorption of drug into a site of specific method [54].

The bioadhesive system adheres to the epithelial cell surface or mucus in stomach. These is done with the help of polymers which have mucoadhesive properties. Bioadhesive system increase the affinity and time duration of adhesion between the dosage form and biological membrane [55, 56]. Bioadhesive delivery system is also reported to have increased bioavailability [57]. The mucoadhesive drug delivery systems consist of a mucoadhesive polymers, which adheres to the gastric mucosal surface and prolong its gastric retention in the GIT [58, 59]. The mucus creates the ability to adhere to the gel layer. These polymers can be natural such as sodium alginate, gelatin, guar gum, etc., or semisynthetic polymers such as HPMC, carbopol, sodium carboxy methyl cellulose [5, 6, 9]. There are number of natural occurring mucilages which are reported to have mucoadhesive properties [60, 61]. These mucilages were studied for checking their ability to formulate various dosage form and reported accordingly in literatures [62–64].

Hydration-mediated adhesion

Some polymers are hydrophilic in nature causing large amount of water to disperse and become viscous, leading to bio-adhesive. Prolonged gastro-retention of the bio and muco-adhesive drug delivery system is controlled by the dissolution rate of the polymer [22].

Bonding-mediated adhesion

This type adhesion, the polymers used in system enables adhesion of system to mucus or epithelial cell surface. This type of binding includes various mechanisms which include physical, chemical and mechanical binding. Physical or mechanical bonding that may result from deposition and inclusion of the adhesive material into the crevices of the mucosa [65, 66]. Chemical bonds may be either covalent or ionic nature [6, 67].

Receptor-mediated adhesion

Receptor-mediated adhesion polymers are those that have the ability to bind specific receptor sites on the cell surface. Receptor mediated events act as a potential variant in bio and muco-adhesion, therefore enhance gastric retention of dosage forms [6].

Swelling /Expanding system

Subsequent to being gulped, these dosage forms swell to a size that keeps away from their entrance through the pylorus [33]. In this method, as a result, the dosage form is maintained in the stomach for a long time. These systems are at some point referred for plug point system. As a rule, they will stay halted at the pyloric sphincter [68]. These polymeric cross sections remain in the gastric gloom for a couple of hours even in the few worked state. Proceeded and controlled drug release may be accomplished by selecting a polymer with the right sub-atomic weight and swelling properties [4, 69]. When exposed to gastric fluid, the polymer swallows water and becomes swollen. The broad swelling of these polymers is an after effect of the presence of physical-chemical

cross links in the hydrophilic polymer organize [70, 71]. These cross linking of polymers maintain the physical integrity of dosage form and thus retard the rate of dissolution [72]. The degree of cross linking between the polymeric chain decides the extent and duration of swelling. High degree of cross linking results in maintenance of physical integrity of dosage form for a longer period of time [73]. This also retards the swelling of the dosage

form. Low level of cross linking results in faster dissolution of polymer and at the same time, the dosage form swelling capacity is increased [74]. Therefore, a balance between the swelling and dissolution is always sought for better formulation development. Figure 4 explains a relationship between degree of cross linking and swelling behaviour dosage form and figure 5 is shown swella-ble system of drug [75, 35].

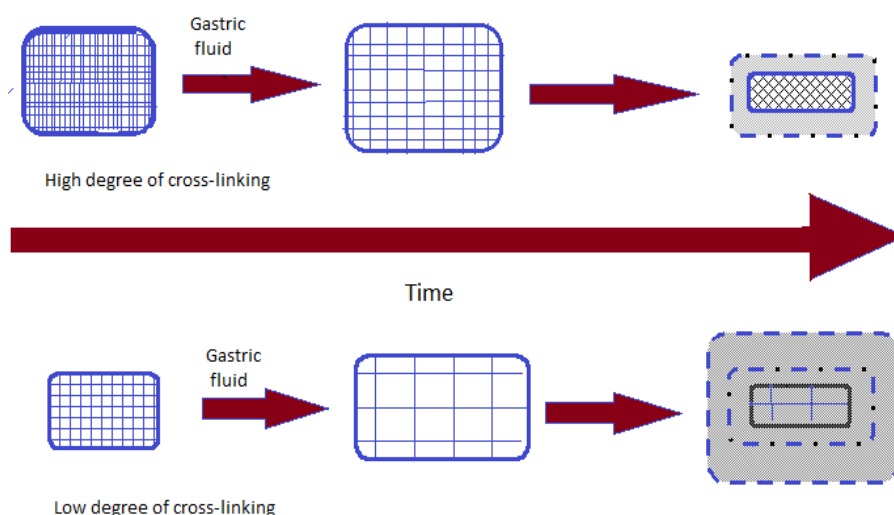


Fig. 4. Relationship between the degree of cross-linking of the polymeric chains and the swelling behaviour of swelling system

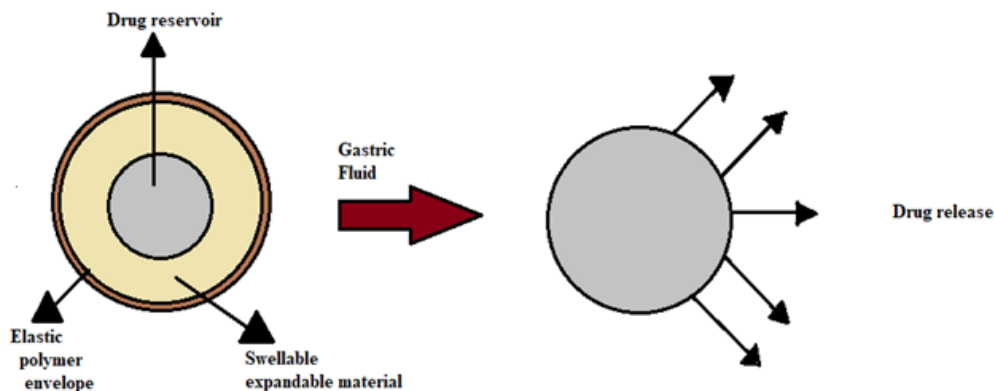


Fig. 5. Swella-ble system of drug

6.3. Expandable system

Expandable systems have initiated to be designed from last 3 decades.

The expanded form that the stomach received and inhibits the pathway and finally another short form that the stomach received, when retention is no longer needed, i.e. after the GRDF releases its active ingredient [25], the expandable dosage form is administered to the stomach and it inhibits the pathway. In the mean time, this expandable delivery system release small delivery system, when no further retention is needed [76]. This small delivery then releases its active ingredients. These gastro-retentive dosage forms GRDFs are swallowed easily [77]. This reaches stomach and, wells considerably and is retained [37, 78]. These only for a longer duration of

time with each release of active ingredient, their size reduce continuously [21, 79].

Magnetic system

Magnetic field is the driving force of this type of system. In this type of system, a small magnet is placed inside the dosage form. Another magnet is placed on the abdomen. By using the external magnet, dosage form are made to reside at GIT. By this way gastric residence time is increased in this type of system [9, 34, 80].

Superporous hydrogel

Superporous hydrogel are swella-ble systems, these are differ adequately from the conventional types to justify separate and classification. With pore sizes between 10 nm to 10 μm , the absorption of water by con-

ventional hydrogels to reach equilibrium state during which early withdrawal can occur in h dosage form. Superporous hydrogels, average orifice size > 100 µm, and due to rapid watering by capillary wetting through swell, abundant open pores to create equilibrium with in one minute [81]. These dosage forms swell to form a larger size and have sufficient mechanical strength to withstand pressure of gastric contraction [25, 82].

Raft technology

The raft technology have established much consideration for the delivery of drug delivery for gastrointestinal disorders and infections. A meaning of raft is a flat structure, typically made of planks, logs that floats on water and is used for transport or as a platform for swimmers. This raft floats on gastric fluids due to low

bulk density developed by the preparation of carbon dioxide. Usually, the raft technology have a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of CO₂ to make the system less dense and float on the gastric fluids [83].

Frame tablets (or tablets with an insoluble skeleton) – for their production, auxiliary substances are used that form a network structure (matrix), in which the drug is included.

7. In – vivo studies literatures

There are number of literatures which reports in–vivo studies of gastro–retentive drug delivery system. Table 2 summarizes few literatures which reports in vivo study GRDDS.

Table 2.

In vivo study of gastro retentive drug delivery system

Animal	Drug	Rout of drug administration	Formulation	Dose	Reference
Albino rats	Eprosartan mesylate	Oral	microballoon formulation	1mg/kg	[84]
Wistar rats	Eprosartan mesylate	Oral	Solid dispersion	10mg/kg	[85]
Male rats	amoxicillin	Oral	mucoadhesive microspheres	Not available	[86]
Albino rabbits	5-fluorouracil	Oral	Floating film (capsules)	0.341 ± 0.110 to 0.717 ± 0.031 mm	[55]
New Zealand rabbits	ofloxacin	Oral	Floating pellets	100 mg	[87]
Albino rats	pentoxifylline	Oral	Floating tablet	30±1 mg	[88]
Wistar rats	metronidazole	Oral	Muco adhesive floating tablet	250 mg	[88]
Healthy volunteers	levofloxacin	Oral	floating mini-tablets	140 mg	[51]
Healthy human volunteers	ofloxacin	Oral	Floating tablet	400 mg	[89]
Male beagle dogs	Pregabalin	Oral	Gastro- floating sustained-release tablet & capsules	(75 mg per capsule & 82.5 mg per tablet)	

8. Conclusion

According to various published literature and detailed investigations on viable products, it can be concluded that the gastro-retentive drug delivery systems includes advancement, needs and their approaches. Gastro-retentive drug delivery system is an approach to keep drug at specific site of GIT for longer duration of time and target the drug in upper GIT. Issue of drug

solubility can be also be addressed by developing gastro retentive drug delivery system as it allows dosage form to reside at absorption site for a longer period. Gastric retentive drug delivery systems improve drug absorption. Prolonged gastric retention time of therapeutic mutations provide several benefits such as improving absorption, bioavailability and enhance the therapeutic action of drug.

References

1. Jassal, M., Nautiyal, U., Kundlas, J., Singh, D. (2015). A review: Gastroretentive drug delivery system (grdds). Indian Journal of Pharmaceutical and Biological Research, 3 (01). doi: <http://doi.org/10.30750/ijpbr.3.1.13>
2. Shah, H. P., Prajapati, S. T., Patel, C. N. (2017). Gastroretentive drug delivery systems: from conception to commercial success. Journal of Critical Reviews, 4 (2), 10. doi: <http://doi.org/10.30750/ijpbr.3.1.13>
3. Jagdale, S. C., Agavekar, A. J., Pandya, S. V., Kuchekar, B. S., Chabukswar, A. R. (2009). Formulation and Evaluation of Gastroretentive Drug Delivery System of Propranolol Hydrochloride. AAPS PharmSciTech, 10 (3). doi: <http://doi.org/10.1208/s12249-009-9300-8>
4. Neumann, M., Schneider, F., Koziolok, M., Garbacz, G., Weitschies, W. (2017). A novel mechanical antrum model for the prediction of the gastroretentive potential of dosage forms. International Journal of Pharmaceutics, 530 (1-2), 63–70. doi: <http://doi.org/10.1016/j.ijpharm.2017.07.067>
5. Satinderkakar, R. S., Shallusandhan. (2015). Gastroretentive drug delivery systems: A review. African Journal of Pharmacy and Pharmacology, 9 (12), 405–417. doi: <http://doi.org/10.5897/ajpp2015.4307>

6. More, S., Gavali, K., Doke, O., Kasgawade, P. (2018). Gastroretentive drug delivery system. *Journal of Drug Delivery and Therapeutics*, 8 (4), 24–35. doi: <http://doi.org/10.22270/jddt.v8i4.1788>
7. Wagh, P. K., Ahirrao, S. P., K. S. J. (2018). Gastroretentive drug delivery systems: a review on expandable system. *Indian Journal of Drugs*, 6 (3), 142–15.
8. Ramdas, T. D., Hosmani, A., Somwanshi B. S. (2015). Raft Technology for Gastro Retentive Drug Delivery. *Human Journals*, 3 (1), 233–252. Available at: <http://ijppr.humanjournals.com/wp-content/uploads/2015/04/17.Ramdas-T.-Dolas-Dr.-Avinash-Hosmani-and-Sachin-B.-Somwanshi.pdf>
9. Yadav, S., Nk, N., Jeyabalan, G., Gupta, M. (2016). Review Article Gastroretentive drug delivery system : a concise review. *International Journal of Research in Pharmacy and Science*, 6 (2), 19–24. Available at: <https://pdfs.semanticscholar.org/348f/26a81ec520b40ff9928c6f35b66eb050a57c.pdf>
10. Ananthakumar, R., Chitra, K., Satheshkumar, S. (2018). Review Article A review on applications of natural polymers in gastroretentive drug delivery system. *Drug Invention Today*, 10 (3), 285–289. Available at: <http://jprsolutions.info/files/final-file-5aef1766975766.44615667.pdf>
11. Rathod, H. J., Mehta, D. P., Yadav, J. S. (2016). A review on Gastroretentive Drug Delivery Systems. *PharmaTutor*, 4 (7), 29–40.
12. Prajapati, V. D., Jani, G. K., Khutliwala, T. A., Zala, B. S. (2013). Raft forming system—An upcoming approach of gastroretentive drug delivery system. *Journal of Controlled Release*, 168 (2), 151–165. doi: <http://doi.org/10.1016/j.jconrel.2013.02.028>
13. Pasupathi A., Anjana, M. N. (2020). Review Article An Updated Review on Gastroretentive Drug Delivery System: An Approach to Enhance Gastric Retention. *International Journal of Pharmaceutical Sciences Review and Research*, 61 (4), 78–83. Available at: <https://globalresearchonline.net/journalcontents/v61-1/14.pdf>
14. Nayak A. K., M. R. (2010). Gastro retentive drug delivery systems: A review. *Asian Journal of Pharmaceutical and Clinical Research*, 3 (1), 190–204.
15. Derle, D., Lahane, A. L. (2019). Gastroretentive drug delivery system. *European of Biomedical and Pharmaceutical Sciences*, 6 (1), 263–270. Available at: https://storage.googleapis.com/journal-uploads/ejbps/article_issue/volume_6_january_issue_1/1546247842.pdf
16. Siraj, S., Molvi, K. I., Nazim, S. (2013). Various Perspectives of Gastroretentive Drug Delivery System: A Review. *American Journal of Advanced Drug Delivery*, 1 (4), 443–451. Available at: <https://www.imedpub.com/articles/various-perspectives-of-gastroretentive-drug-delivery-system-a-review.pdf>
17. Badoni, A., Ojha, A., Gnanarajan, G., Kothiyal, P. (2012). Review On Gastro Retentive Drug Delivery System. *The Pharma Innovation Journal*, 1 (8), 32–42. Available at: <http://www.thepharmajournal.com/archives/2012/vol1issue8/PartA/4.1.pdf>
18. Sharma, D., Sharma, A. (2014). Gastroretentive drug delivery system - a mini review. *Asian Pacific Journal of Health Sciences*, 1 (2), 80–89. doi: <http://doi.org/10.21276/apjhs.2014.1.2.9>
19. Chandan, K. B., Raghavendra, K. G., Suresh Kumar, J. N., Satyanarayana, V., Naga, P. K. (2015). Design Formulation and Evaluation of Ranitidine HCl Gastro Retentive Floating Tablets. *International Journal of Pharma Research and Health Sciences*, 3 (5), 862s–873s. Available at: <http://www.pharmahealthsciences.net/pdfs/volume3-issue5/S-6-vol3-issue5-drchandankumarbrahma.pdf>
20. Vo, A. Q., Feng, X., Pimparade, M., Ye, X., Kim, D. W., Martin, S. T., Repka, M. A. (2017). Dual-mechanism gastroretentive drug delivery system loaded with an amorphous solid dispersion prepared by hot-melt extrusion. *European Journal of Pharmaceutical Sciences*, 102, 71–84. doi: <http://doi.org/10.1016/j.ejps.2017.02.040>
21. Ullah, M. B., Karim, M. R., Alam, M. S., Hassan, M. R., Bhuiyan, M. A., Rana, M. S. (2018). Formulation and In vitro Evaluation of Unfolding Type Expandable Gastroretentive Film of Enalapril Maleate. *Bangladesh Pharmaceutical Journal*, 20 (2), 148–156. doi: <http://doi.org/10.3329/bpj.v20i2.37868>
22. Patil, H., Tiwari, R. V., Repka, M. A. (2016). Recent advancements in mucoadhesive floating drug delivery systems: A mini-review. *Journal of Drug Delivery Science and Technology*, 31, 65–71. doi: <http://doi.org/10.1016/j.jddst.2015.12.002>
23. Wu, Y., Zhang, W., Huang, J., Luo, Z., Li, J., Wang, L., Di, L. (2020). Mucoadhesive improvement of alginate microspheres as potential gastroretentive delivery carrier by blending with *Bletilla striata* polysaccharide. *International Journal of Biological Macromolecules*, 156, 1191–1201. doi: <http://doi.org/10.1016/j.ijbiomac.2019.11.156>
24. Tripathi, Thapa, Maharjan, Jeong. (2019). Current State and Future Perspectives on Gastroretentive Drug Delivery Systems. *Pharmaceutics*, 11 (4), 193. doi: <http://doi.org/10.3390/pharmaceutics11040193>
25. Pawar, V. K., Kansal, S., Garg, G., Awasthi, R., Singodia, D., Kulkarni, G. T. (2010). Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. *Drug Delivery*, 18 (2), 97–110. doi: <http://doi.org/10.3109/10717544.2010.520354>
26. Chanda, R., Roy, A., Bahadur, S., Saha, S., Das, S., Choudhury, A. (2010). Floating Drug Delivery: A Potential Alternative To Conventional Therapy. *International Journal of PharmTech Research*, 2 (1), 49–59.
27. Shah, S. H., Patel, J. K., Patel, N. V. (2009). Stomach specific floating drug delivery system: A review. *International Journal of PharmTech Research*, 1(3), 623–633. Available at: <http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.631.1457&rep=rep1&type=pdf>
28. Lalge, R., Thipsay, P., Shankar, V. K., Maurya, A., Pimparade, M., Bandari, S. et. al. (2019). Preparation and evaluation of cefuroxime axetil gastro-retentive floating drug delivery system via hot melt extrusion technology. *International Journal of Pharmaceutics*, 566, 520–531. doi: <http://doi.org/10.1016/j.ijpharm.2019.06.021>
29. Sivaneswari, S., Karthikeyan, E., Chandana, P. J. (2017). Novel expandable gastro retentive system by unfolding mechanism of levetiracetam using simple lattice design – Formulation optimization and in vitro evaluation. *Bulletin of Faculty of Pharmacy, Cairo University*, 55 (1), 63–72. doi: <http://doi.org/10.1016/j.bfopcu.2017.02.003>
30. Shaik, T., Sundaram, M. A., Umasankar, K., June, M. (2014). Review on gastroretentive drug delivery system. *International Journal of Research in Pharmaceutical and Nano Sciences*, 3 (3), 177–185. Available at: http://ijrpns.com/article/REVIEW%20ON%20GASTRORETENTIVE%20DRUG%20DELIVERY_SYSTEM.pdf
31. Raza, A., Hayat, U., Wang, H.-J., Wang, J.-Y. (2020). Preparation and evaluation of captopril loaded gastro-retentive zein based porous floating tablets. *International Journal of Pharmaceutics*, 579, 119185. doi: <http://doi.org/10.1016/j.ijpharm.2020.119185>
32. Praveen, R., Prasad Verma, P. R., Venkatesan, J., Yoon, D.-H., Kim, S.-K., Singh, S. K. (2017). In vitro and in vivo evaluation of gastro-retentive carvedilol loaded chitosan beads using Gastroplus™. *International Journal of Biological Macromolecules*, 102, 642–650. doi: <http://doi.org/10.1016/j.ijbiomac.2017.04.067>

33. Porwal, A., Dwivedi, H., Pathak, K. (2017). Decades of research in drug targeting using gastroretentive drug delivery systems for antihypertensive therapy. *Brazilian Journal of Pharmaceutical Sciences*, 53 (3). doi: <http://doi.org/10.1590/s2175-97902017000300173>
34. Reddy, B. V., Navaneetha, K., Deepthi, P. S. A. (2013). Gastroretentive Drug Delivery System- A Review. *Journal of Global Trends in Pharmaceutical Sciences*, 4 (1), 1018–1033. Available at: <https://www.jgtps.com/admin/uploads/PmvF2t.pdf>
35. Matharu, A. S., Motto, M. G., Patel, M. R., Simonelli, A. P., Dave, R. H. (2011). Evaluation of Hydroxypropyl Methylcellulose Matrix Systems as Swellable Gastro-Retentive Drug Delivery Systems (GRDDS). *Journal of Pharmaceutical Sciences*, 100 (1), 150–163. doi: <http://doi.org/10.1002/jps.22252>
36. Li, Z., Xu, H., Li, S., Li, Q., Zhang, W., Ye, T. et. al. (2014). A novel gastro-floating multiparticulate system for dipyrindamole (DIP) based on a porous and low-density matrix core: In vitro and in vivo evaluation. *International Journal of Pharmaceutics*, 461 (1-2), 540–548. doi: <http://doi.org/10.1016/j.ijpharm.2013.12.024>
37. Kotreka, U. K., Adeyeye, M. C. (2011). Gastroretentive Floating Drug-Delivery Systems: A Critical Review. *Critical Reviews™ in Therapeutic Drug Carrier Systems*, 28 (1), 47–99. doi: <http://doi.org/10.1615/critrevtherdrugcarriersyst.v28.i1.20>
38. Kumar, L., Sharma, A. (2019). Gastro Retentive Floating Microsphere: A Review. *Journal of Pharmaceutical Science and Bioscientific Research*, 9 (227), 142–148. Available at: http://www.jpsbr.org/volume_9/JPSBR_Vol_9_Issue_1_html_files/JPSBR19RS2012.pdf
39. Kumar, R., Kamboj, S., Chandra, A., Gautam, P. K., Sharma, V. K. (2016). Microballoons: An Advance Avenue for Gastroretentive Drug Delivery System- A Review. *UK Journal of Pharmaceutical Biosciences*, 4 (4), 29–40. doi: <http://doi.org/10.20510/ukjpb/4/i4/110644>
40. Thanziya, F., Ar, S., Vinayak, K. (2019). Review Article A Review On Gastroretentive Floating Beads. *International Journal of Pharma And Chemical Research*, 5 (2), 89–95. Available at: <http://www.ijpacr.com/files/13-04-2019/12.pdf>
41. Das, M., Giri, T. K. (2020). Hydrogels based on gellan gum in cell delivery and drug delivery. *Journal of Drug Delivery Science and Technology*, 56, 101586. doi: <http://doi.org/10.1016/j.jddst.2020.101586>
42. Gupta, S., Singh, S. (2014). Multiple unit system: an approach towards gastroretention. *Journal of Biological & Scientific Opinion*, 2 (2), 188–195. doi: <http://doi.org/10.7897/2321-6328.02242>
43. Manmohan, Shukla, T. P., Mathur, A., Upadhyay, N., Sharma, S. (2011). A review on gastroretentive drug delivery system: an emerging approach to improve the gastric residence time of solid dosage forms. *International Journal Of Pharmaceutical Sciences Review And Research*, 8 (2), 176–182. Available at: <https://globalresearchonline.net/journalcontents/volume8issue2/Article-029.pdf>
44. Mayavanshi, A. V., Gajjar, S. S. (2008). Floating drug delivery to increase gastric retention of drugs: A Review. *Research Journal of Pharmacy and Technology*, 1 (4), 55–61. doi: <http://rjptonline.org/AbstractView.aspx?PID=2008-1-4-63>
45. Tomar, A., Upadhyay, A., Gupta, S. K., Kumar, S. (2019). An Overview on Gastroretentive Drug Delivery System: Current Approaches and Advancements. *Current Research in Pharmaceutical Sciences*, 9 (1), 12–16. doi: <http://doi.org/10.24092/crps.2019.090102>
46. Kockisch, S., Rees, G. D., Tsibouklis, J., Smart, J. D. (2005). Mucoadhesive, triclosan-loaded polymer microspheres for application to the oral cavity: preparation and controlled release characteristics. *European Journal of Pharmaceutics and Biopharmaceutics*, 59 (1), 207–216. doi: <http://doi.org/10.1016/j.ejpb.2004.07.007>
47. Kumar, R. M., Shatyanarayan, B., Paladugu, N. D., Muddasar, S. (2013). A Comprehensive Review On Gastro Retentive Drug. *Acta Chimica And Pharmaceutica India*, 3 (2), 149–164.
48. Potekar, P. M., Mulla, J. A. S., Doijad, R. C. (2017). Gastro-Retentive Drug Delivery Systems: A Review. *Indian Journal of Novel Drug Delivery*, 9 (3), 159–166.
49. Goud, M. S. C., Pandey, V. P. (2016). Review Article On Gastroretentive Drug Delivery System. *International Journal of Pharmacy and Biological Sciences*, 6 (3), 158–165.
50. Kawade, A. V. (2019). A review of microballoons: An advance technique for Gastroretentive drug delivery system. *International Journal of Research in Pharmacy and Pharmaceutical Sciences*, 4 (4), 3–4.
51. Shakya, R., Thapa, P., Saha, R. N. (2013). In vitro and in vivo evaluation of gastroretentive floating drug delivery system of ofloxacin. *Asian Journal of Pharmaceutical Sciences*, 8 (3), 191–198. doi: <http://doi.org/10.1016/j.ajps.2013.07.025>
52. Tort, S., Han, D., Steckl, A. J. (2020). Self-inflating floating nanofiber membranes for controlled drug delivery. *International Journal of Pharmaceutics*, 579, 119164. doi: <http://doi.org/10.1016/j.ijpharm.2020.119164>
53. Chudiwal, V., Shahi, S., Chudiwal, S., Ahale, D. (2018). Innovative Technologies for Gastro-Retentive Drug Delivery Systems. *Global Journal of Pharmacy & Pharmaceutical Sciences*, 4 (5). doi: <http://doi.org/10.19080/GJPPS.2018.04.555650>
54. Singh, B., Garg, B., Bhatowa, R., Kapil, R., Saini, S., Beg, S. (2017). Systematic development of a gastroretentive fixed dose combination of lamivudine and zidovudine for increased patient compliance. *Journal of Drug Delivery Science and Technology*, 37, 204–215. doi: <http://doi.org/10.1016/j.jddst.2016.12.014>
55. Zhang, C., Tang, J., Liu, D., Li, X., Cheng, L., Tang, X. (2016). Design and evaluation of an innovative floating and bioadhesive multiparticulate drug delivery system based on hollow structure. *International Journal of Pharmaceutics*, 503 (1-2), 41–55. doi: <http://doi.org/10.1016/j.ijpharm.2016.02.045>
56. Malik, R., Garg, T., Goyal, A. K., Rath, G. (2014). Polymeric nanofibers: targeted gastro-retentive drug delivery systems. *Journal of Drug Targeting*, 23 (2), 109–124. doi: <http://doi.org/10.3109/1061186x.2014.965715>
57. Bahadur, S., Chanda, R., Roy, A., Choudhury, A., Das, S., Saha, S. (2008). Preparation and Evaluation of Mucoadhesive Microcapsules of Captopril for Oral Controlled Release. *International Journal of PharmTech Research*, 1 (2), 100–105.
58. Chen, N., Niu, J., Li, Q., Li, J., chen, X., Ren, Y. et. al. (2019). Development and evaluation of a new gastroretentive drug delivery system: Nanomicelles-loaded floating mucoadhesive beads. *Journal of Drug Delivery Science and Technology*, 51, 485–492. doi: <http://doi.org/10.1016/j.jddst.2019.03.024>
59. Jhansee, M., Kumar, D. A. (2013). Recent Advances. *Gastro Retentive Drug Delivery System : A Review*, 26–28.
60. Bahadur, S., Saha, S., Das, S. (2010). Formulation of terbutaline sulphate mucoadhesive sustained release oral tablets from natural materials and in vitro-in vivo evaluation. *Asian Journal of Pharmaceutical Sciences*, 5 (4), 168–174.
61. Bahadur, S., Roy, A., Chanda, R., Baghel, P., Saha, S., Choudhury, A. (2016). Assessment of Some Phytochemical and Physicochemical Properties of Fenugreek Seed Mucilage. *Research Journal of Pharmacy and Technology*, 9 (9), 1321–1324. doi: <http://doi.org/10.5958/0974-360x.2016.00251.1>

62. Bahadur, S., Roy, A., Baghel, P., Chanda, R. (2016). Formulation of Glipizide Tablets using Fenugreek Seed Mucilage: Optimization by Factorial Design. *Asian Journal of Pharmaceutics*, 10 (4), 662–668. doi: <http://doi.org/10.22377/ajp.v10i04.906>
63. Bahadur, S., Roy, A., Baghel, P., Choudhury, A., Saha, S., Chanda, R. (2018). Formulation and evaluation of glipizide tablets utilizing Hibiscus rosasinensis leaves mucilage. *Indonesian Journal of Pharmacy*, 29 (1), 23–28. doi: <http://doi.org/10.14499/indonesianjpharm29iss1pp23>
64. Janardhan, D., Lingam, M., Mohan, C. K., Venkateswarlu, V. (2008). Formulation and In vitro evaluation of gastro retentive drug delivery system Formulation and in vitro Evaluation of Gastroretentive Drug Delivery System for Ranitidine Hydrochloride. *International Journal of Pharmaceutical Science and Nanotechnology*, 1 (3), 227–232.
65. Ami, M., Hejal, P., Yogi, P. (2012). Review Article Advancements In Controlled Release Gastroretentive Drug Delivery System : A Review. *Journal Of Drug Delivery And Thera*, 2 (3), 12–21.
66. Khan, R. (2013). Gastroretentive drug delivery system – a review. *International Journal Of Pharma And Bio Sciences*, 4 (2), 630–646.
67. Prinderre, P., Sauzet, C., Fuxen, C. (2011). Advances in gastro retentive drug-delivery systems. *Expert Opinion on Drug Delivery*, 8 (9), 1189–1203. doi: <http://doi.org/10.1517/17425247.2011.592828>
68. Hwang, K.-M., Nguyen, T.-T., Seok, S. H., Jo, H.-I., Cho, C.-H., Hwang, K.-M. et. al. (2019). Swellable and porous bilayer tablet for gastroretentive drug delivery: Preparation and in vitro-in vivo evaluation. *International Journal of Pharmaceutics*, 572, 118783. doi: <http://doi.org/10.1016/j.ijpharm.2019.118783>
69. Chavanpatil, M. D., Jain, P., Chaudhari, S., Shear, R., Vavia, P. R. (2006). Novel sustained release, swellable and bioadhesive gastroretentive drug delivery system for ofloxacin. *International Journal of Pharmaceutics*, 316 (1-2), 86–92. doi: <http://doi.org/10.1016/j.ijpharm.2006.02.038>
70. Gaikwad, S. S., Avari, J. G. (2019). Improved bioavailability of Azelnidipine gastro retentive tablets-optimization and in-vivo assessment. *Materials Science and Engineering: C*, 103, 109800. doi: <http://doi.org/10.1016/j.msec.2019.109800>
71. Pant, S., Badola, A., Khotiyal, P. (2016). Review Article A Review On Gastroretentive Drug Delivery System. *International Journal Of Research And Development in Pharmacy and Life Sciences*, 5 (4), 2178–2187.
72. Balkrishana, V. Y., Ajinath, S. H., Singh, K. H., Gokul, T. S., Govindrao, J. A., Road, T. (2020). Formulation and evaluation of gastro retentive extended release formulation of metformin hydrochloride. *GSC Advanced Research and Reviews*, 2 (2), 8–17. doi: <http://doi.org/10.30574/gscarr.2020.2.2.0003>
73. Singh, S., Bhavesh, S., Nayak, S., Bothara, S. (2013). Formulation and Evaluation of Leveteracetam Extended Release Tablets. *International Journal of Pharmaceutical Sciences and Nanotechnology*, 6 (1), 1958–1965. doi: <http://doi.org/10.37285/ijpsn.2013.6.1.6>
74. Streubel, A., Siepmann, J., Bodmeier, R. (2006). Gastroretentive drug delivery systems. *Expert Opinion on Drug Delivery*, 3 (2), 217–233. doi: <http://doi.org/10.1517/17425247.3.2.217>
75. Shep, S., Dodiya, S., Lahoti, S., Mayee, R. (2011). Swelling system: a novel approach towards gastroretentive drug delivery system. *Indo Global Journal of Pharmaceutical Sciences*, 1 (3), 234–242. Available at: <http://iglobaljournal.com/wp-content/uploads/2011/12/4.-Santosh-Shep-et-al.pdf>
76. Shinde, A. J., Swami, K. B., More, H. N. (2017). Formulation and optimization of expandable gastroretentive tablet of diltiazem hydrochloride using factorial design. *Asian Journal of Pharmaceutics*, 11 (1), S24–S36. doi: <http://doi.org/10.22377/ajp.v11i01.1085>
77. Shah Sunil Kumar, Kumar Neeraj, C. N. (2018). Formulation and Optimization of Expandable Gastro Retentive Floating Matrix Tablet of Mosapridecitrate Using Factorial Design. *International Journal of Pharmacy and Pharmaceutical Research*, 12 (1), 78–96.
78. Dehghan, M., Kha, F. (2009). Gastroretentive drug delivery systems: a patent perspective. *International Journal of Health Research*, 2 (1), 23–44. doi: <http://doi.org/10.4314/ijhr.v2i1.55385>
79. Rimawi, I. B., Muqedi, R. H., Kanaze, F. I. (2019). Development of Gabapentin Expandable Gastroretentive Controlled Drug Delivery System. *Scientific Reports*, 9 (1), 1–12. doi: <http://doi.org/10.1038/s41598-019-48260-8>
80. Jaimini, M., Tanwar, Y. S., Srivastava, B. (2012). Formulation and Characterization Of Gastroretentive Drug Delivery System Of Losartan Potassium. *International Current Pharmaceutical Journal*, 2 (1), 11–17. doi: <http://doi.org/10.3329/icpj.v2i1.12872>
81. Gupta, R., Tripathi, P., Bhardwaj, P., Mahor, A. (2018). Recent advances in gastro retentive drug delivery systems and its application on treatment of H. Pylori infections. *Journal of Analytical & Pharmaceutical Research*, 7 (4), 404–410. doi: <http://doi.org/10.15406/japlr.2018.07.00258>
82. Kumari, P. V. K., Sharmila, M., Rao, Y. S. (2020). Super Porous Hydrogels : A Review. 32 (13), 153–165. doi: <http://doi.org/10.9734/jpri/2020/v32i1330595>
83. Sundari, P. P., Gangadhari, R., Srinivas, P. (2015). Formulation and evaluation of sustained release floating microballoons of eprosartan mesylate. *World Journal of Pharmaceutical Research*, 4 (9), 2260–2271.
84. Dangre, P. V., Godbole, M. D., Ingale, P. V., Mahapatra, D. K. (2016). Improved Dissolution and Bioavailability of Eprosartan Mesylate Formulated as Solid Dispersions using Conventional Methods. *Indian Journal of Pharmaceutical Education and Research*, 50 (3s), S209–S217. doi: <http://doi.org/10.5530/ijper.50.3.31>
85. Zhao, S., Lv, Y., Zhang, J. Bin, Wang, B., Lv, G. J., Ma, X. J. (2014). Gastroretentive drug delivery systems for the treatment of Helicobacter pylori. *World Journal of Gastroenterology*, 20 (28), 9321–9329.
86. Bhardwaj, P., Singh, R., Swarup, A. (2014). Development and characterization of newer floating film bearing 5-fluorouracil as a model drug. *Journal of Drug Delivery Science and Technology*, 24 (5), 486–490. doi: [http://doi.org/10.1016/s1773-2247\(14\)50092-5](http://doi.org/10.1016/s1773-2247(14)50092-5)
87. Rahim, S. A., Carter, P., Elkordy, A. A. (2017). Influence of calcium carbonate and sodium carbonate gassing agents on pentoxifylline floating tablets properties. *Powder Technology*, 322, 65–74. doi: <http://doi.org/10.1016/j.powtec.2017.09.001>
88. El-Zahaby, S. A., Kassem, A. A., El-Kamel, A. H. (2014). Design and evaluation of gastroretentive levofloxacin floating mini-tablets-in-capsule system for eradication of Helicobacter pylori. *Saudi Pharmaceutical Journal*, 22 (6), 570–579. doi: <http://doi.org/10.1016/j.jsps.2014.02.009>
89. Qin, C., Wu, M., Xu, S., Wang, X., Shi, W., Dong, Y. et. al. (2018). Design and optimization of gastro-floating sustained-release tablet of pregabalin: In vitro and in vivo evaluation. *International Journal of Pharmaceutics*, 545 (1-2), 37–44. doi: <http://doi.org/10.1016/j.ijpharm.2018.04.011>

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