International Journal of Pharmaceutics and Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Review Article

A CURRENT REVIEW ON GASTRORETENTIVE DRUG DELIVERY SYSTEM

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***Article History:**

Received: 17/07/2024
Revised: 10/08/2024
Accepted: 21/08/2024

ABSTRACT

Oral route is the most appropriate and preferred route for systemic or local delivery of any drug. The gastro retentive dosage forms (GRDFs) is a very long-term time used to improve treatment with several important drugs. To overcome these limitations, various approaches have been proposed to increase the gastric retention time of the delivery system in the upper part of gastrointestinal tract. Gastroretentive dosage form (GRDF) prolongs the GRT by targeting site-specific drug release in upper part of GIT. To formulate GRDDS various approaches like floating drug delivery systems, non-effervescent drug delivery systems, high density drug delivery systems, bioadhesive systems, magnetic systems, expandable systems etc. The purpose of this article is to compile the recent literature with special focus on various gastroretentive approaches and examined with their advantages and disadvantages. In order to understand various physiological difficulties to achieve gastric retention, we have summarized important factors controlling gastric retention. Finally the evaluation parameters of gastroretentive drug delivery systems and their application are covered in detail. Although tremendous advances have been seen in oral controlled drug delivery system in the last two decades, this system has been of limited success in the case of drugs with a poor absorption window throughout the GIT (Gastro Intestinal Tract).

Keywords: Gastro Retentive Dosage Forms, GRDDS, Gastrointestinal tract, floating drug delivery systems.

INTRODUCTION

Gastro retentive drug delivery systems is a type of system which prolongs the residence of administered drug in the gastric region for several hours thereby the bioavailability and solubility of challenging drugs may gets enhanced, and improves the patient compliance. Gastric emptying delaying conceptual mechanisms of mucoadhesion, flotation and sedimentation supports the gastro retentive drug delivery systems (Shweta *et al*., 2005). Thereby gastro retentive drug delivery systems enhance the absorption of drugs in the gastrointestinal tract drug by improving the contact time with the small intestinal mucosa. Gastric retention based drug delivery systems in turn provide a newer therapeutic possibilities and substantial benefits for researchers. Gastro retentive drug delivery systems may reduces the drug wastage. Gastro retentive drug delivery systems offer a controlled drug delivery profile with effective plasma drug concentration, reduces dosing frequency and minimizing plasma fluctuations (Arunachalam *et al*., 2011).

Drugs suitable for gastro retentive drug delivery formulations include drugs that have

low absorption in the lower part of the GIT, unstable, poorly soluble at alkaline pH, short half-life, and show local activity at the upper part of the intestine (Julu *et al*., 2019). Due to the sustained/controlled release effect gastro retentive drug delivery formulations minimizes the mucosal irritation which may provides a desired plasma drug concentration and prevent drug fluctuations without causing dose dumping. Unstable drugs can also be delivered by this approach. The various approaches utilized in gastro retentive drug delivery system includes extended gastric residence time, low-density (floating), high-density (sinking), expandable (swelling), and mucoadhesive systems.

The better understanding on the anatomy and physiology of the stomach (specifically proximal stomach- fundus and body; and the distal stomach- antrum and pylorus) plays a crucial role for the successful development of the gastro retentive dosage form. The critical factors which affect the gastro retentive drug delivery systems are size/ shape/density of gastro retentive formulations, caloric density, factors associated with patients etc. The passage through the pyloric antrum can be prevented by an increase in the size of the dosage form. The lower density of gastro retentive drug delivery formulations than that of gastric fluids favors the floating capacity of the gastro retentive formulations. Caloric density of the ingested food increases the gastro retentive property, herein the gastric emptying rate also gets affected by the gastro retentive formulations. The other factors related to patient such as gender, age, illness, and emotional state also influences the delivery of gastro retentive formulations. Diseases conditions of Parkinson's disease, diabetes also influence the gastric emptying rate. Elderly patients and males have superior gastric emptying rate compared to females and younger's. In addition factors influencing the delivery of gastro retentive formulations works by accelerating or delaying gastric emptying in other related conditions of fear and apprehension, acute /chronic diseases, trauma, drugs, and surgery. The gastroretentive dosage formulation has been regulated by various factors such as polymer types (nonionic, cationic, and anionic polymers), polymer composition, viscosity grade, polymer molecular weight, and drug solubility.

Physiology of Stomach

Before designing the gastroretentive formulation, it is important to understand the overall anatomy and physiology of stomach. Stomach is divided into proximal and distal stomach. Proximal stomach includes fundus and body, while distal stomach includes antrum and pylorus. The fundamental function of the stomach is to store food and grind it properly so that it can release in duodenum. Fundus and Body act as reservoir for foods and antrum act as pump that assist gastric emptying through propelling action. The mobilitic action of stomach is known as Migrating Myoelectric Complex. Gastric emptying occurs both in fed and unfed or fasting state but the pattern in gastric emptying for both the state varies drastically. During fed state, gastric emptying rate is delayed as motor activity generates after 5-10 min of food intake and continue till food remain in stomach while fasted state shows an interdigestive sequence of electrical events in both stomach and small intestine for every 90-120 min in cyclic manner. In this phase the

diameter of pylorus increases to approx. 19mm. The particles which are smaller than the diameter of pyloric sphincter transfer easily from pylorus to duodenum (Arora *et al*., 2005; Patil and Datta, 2013).

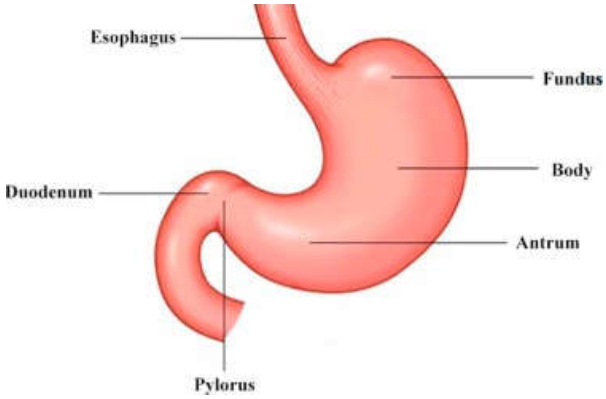

Figure 1: Physiology of Stomach

Physicochemical properties of GRDDS

Physicochemical properties of GRDDS include density, size, and shape of the dosage form, which play major roles in the formulation of GRDDS. The dosage forms having a density lower than the gastric contents can float to the surface, while high-density systems sink to the bottom of the stomach. For an ideal formulation, the density should be in the range of 1.0-2.5 g/cm^3. Dosage forms having a diameter of more than 7.5 mm show better gastric residence time (GRT). Circular, spherical or tetrahedron-shaped devices show excellent gastroretentive properties (Tomar *et al*., 2019).

Physiological factors affecting retention of GRDDS in the stomach:

The most important factors controlling the gastric retention time of dosage forms include fed or unfed state, nature of the meal, caloric content, and frequency of feeding. In the case of a fasting environment, gastric retention time is less due to the increase in GI motility. Emptying of gastric content occurs due to peristalsis. If peristalsis coincides with dosage form administration, the gastric residence is short. However, after meals, peristalsis is delayed and may help increase the gastric residence of the formulation. A high-calorie meal containing proteins, fats, and fibrous compounds increases gastric retention time. In the case of multiple meals, the gastric retention is more than a single meal due to persistent inhibition of peristalsis. Also, some other factors, such as sex and age, affect gastric retention. Compared with males, females have a slower gastric emptying time irrespective of height, weight, and body surface. A person at the age of more than 70 exhibits longer GRT. In comparison, neonates show less GRT compared with geriatric patients (Chudiwal *et al*., 2017).

Advantages of GRDDs

1. Enhanced bioavailability.
2. Enhanced first-pass biotransformation.
3. Sustained drug delivery/reduced frequency of dosing.
4. Targeted therapy for local ailments in the upper GIT.
5. Reduced fluctuations of drug concentration.
6. Minimization of fluctuations in drug concentration.
7. Reduced counter-activity of the body.
8. Extended time over critical (effective) concentration and Minimized adverse activity at the colon.
9. Site specific drug delivery and Improvement of bioavailability and therapeutic efficacy of the drugs and possible reduction of dose e.g. Furosemide.
10. Maintenance of constant therapeutic levels over a prolonged period and thus reduction in fluctuation in therapeutic levels minimizing the risk of resistance E.g. beta-lactam antibiotics (penicillin's and Cephalosporin's).

11. The controlled, slow delivery of drug form gastro retentive dosage form provides sufficient local action at the diseased site, thus minimizing or eliminating systemic exposure of drugs.
12. Gastro retentive dosage forms minimize the fluctuation of drug concentrations and effects. This feature is of special importance for drug with a narrow therapeutic index.
13. Minimize the counter activity of the body leading to higher drug efficiency (Mayavanshi and Gajjar, 2008; Deshpande *et al*., 1996).

Disadvantages of GRDDs

1. Unsuitable for drugs with limited acid solubility. E.g. Phenytoin
2. Unsuitable for drugs that is unstable in acidic environment. E.g. Erythromycin
3. Drugs that irritates or causes gastric lesions on slow release. e.g. Aspirin and NSAID's
4. Drugs that absorb selectively in colon. E.g. Corticosteroid
5. Drugs that absorb equally well through GIT. E.g. Isosorbide dinitrate, Nifidipine
6. Floating drug delivery systems require high fluid level in stomach to float.
7. Some drugs present in the floating system causes irritation to gastric mucosa (Nayak *et al*., 2010).

Factors affecting the Gastroretentive system:

There are various factors which affect the GRDDS:

- Density – Gastric retention time of drug is depend on the density. The density is always less than that of gastric content.
- Size - The drugs which have diameter of more than 7.5 mm have more gastric resistance time as compared to drugs of diameter 9.5 mm.
- Shape of dosage form – The tetrahedron and ring shaped dosage foam have longer period than other dosage foam of same size.
- Nature of meal - Presence of food in the stomach affects the gastroretentive drug delivery system. Feeding of indigestiable polymers or fatty acid salts can change the mortality pattern of the stomach to the fed state, thus decreasing the gastric emptying rate and prolong drug release.
- Caloric content - The GRT can be increased with meal contain high protein and fats upto 4 to 10 hours.
- Frequency of feed – the GRT can increased over 400 minutes when successive meal are given as compared with a single meal due to the low frequency of MMC (migrating motor complex).
- Age – The GRT can be longer to the elderly people , mostly over the of 70.
- Posture – GRT can vary between supine and upright ambulatory states of the patients.
- Biological factors - Diabetes and Crohn's disease, etc.
- Concomitant drug administration - Floating time is affected by antichilonergics drugs such as atropine and propantheline, opiates like codein etc (Doshi and Tank, 2012; Arora *et al*., 2000).

Approaches to achieve gastric retention

Different approaches have been used to achieve or to increase the gastric retention of oral dosage forms in the stomach. Some of the drugs are formulated as single dosage or some are formulated as multi-component dosage forms. GRDDS can be classified in following approaches (Figure 2):

- High density system
- Bioadhesive/mucoadhesive system

- Raft forming system
- Magnetic system
- Floating/low density system
  - Effervescent system
  - Non effervscent system
- Expanding system
  - Swelling system
  - Unfoldable system

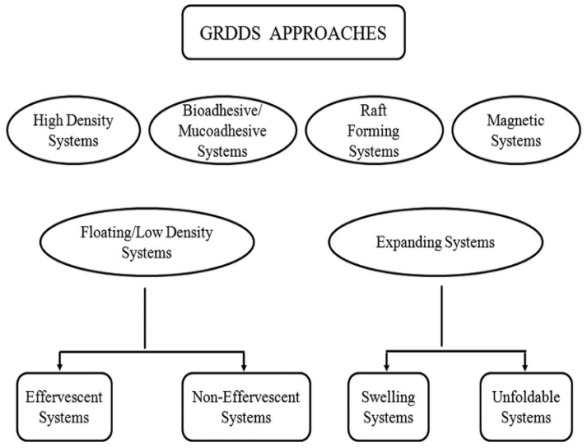

Figure 2: Approaches to gastric retention delivery system

High density system

In this dosage forms the density of formulation is higher than the density of the normal stomach content (Figure 3). These dosage forms are prepared by coating the drug with the heavy core or mixed with heavy inert material such as zinc powder, iron oxide, titanium dioxide etc. These system have some drawbacks like difficul to manufacture in large amount due to intract with gastric fluid to release its drug content and also this system is not availiable in the market (Singh and Kim, 2006).

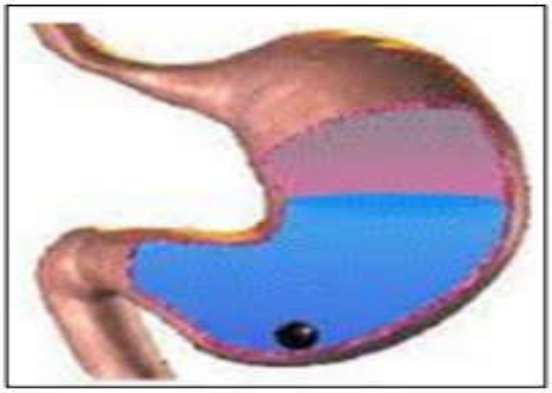

Figure 3: High density system

Bioadhesive/mucoadhesive system

In mucoadhesive system, drugs contain mucoadhesive polymers which binds to the gastric mucosal surface and increases its GRT in the GIT (Figure 4). The mucoadhesive polymers are very useful exicipient in the GRDDS. These polymers can be natural or can be synthetic. Natural polymers are sodium alginate, gelatin, guar gum, tara gum, karaya gum. Synthetic polymers are HPMC, carbopol, vinyl pyrolidine, sodium carboxyl methylcellulose (Talukder and Fassihi, 2004).

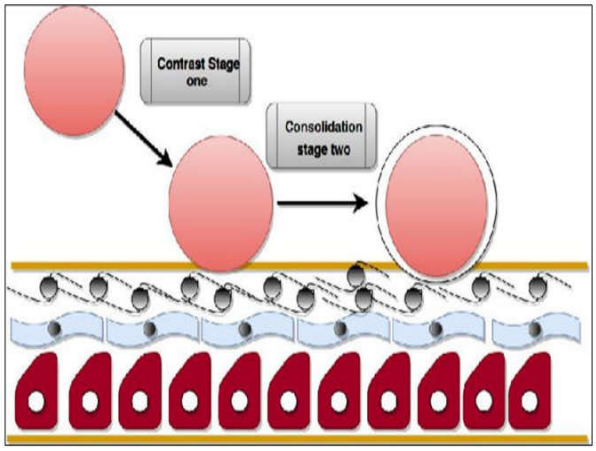

Figure 4: Bioadhesive/mucoadhesive system

Raft forming system

Raft forming system is not only helpful for sustained release drug but also useful for pediatric and geriatric patients. This system is also used in the liquid dosage form.

Sustained and prolonged release of drug, good stabiity and bioavailiability makes the gaft forming sysetem very suitable for gastric retention of the drug (Figure 5). Nowadays raft forming system has received much attention for the delivery of antacids and drug delivery for GIT infections and disorders (Prajapati *et al*., 2013).

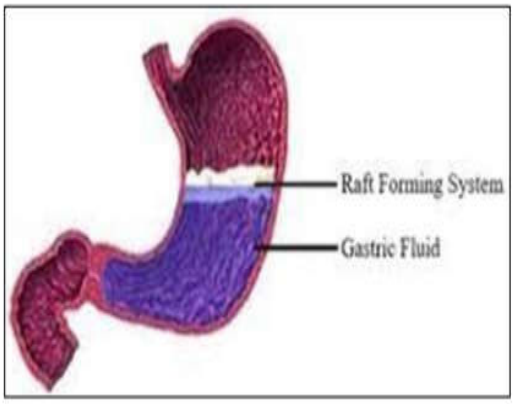

Figure 5: Raft forming system

Magnetic system

In the magnetic system, the dosage form contain a small internal magnet or a magnet placed on the abdomen over the position of the stomach (Figure 6). They guided them to the oesophagus with an external magnet for the initial 2 minutes and almost all the granules were retained in the region after 2 hours (Kakar *et al*., 2013; Ito *et al*., 1990).

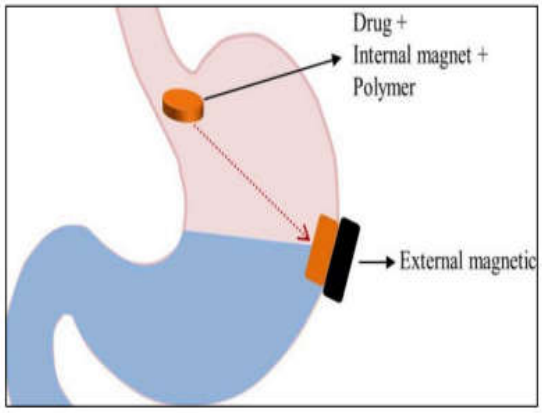

Figure 6: Magnetic system

Floating/ low density system

By the name low density system, these drugs remains float above the gastric contents for prolong period of time and provide continuous release of the drug (Figure 7). These system are broadly used due to less or no adverse affect in the GIT. These dosage forms are also known as gas powered system, which can float in the contents of the stomach and release the drug in a controlled manner for prolonged period of time. This system is also known as hypodynamically balanced systems (Waterman, 2007; Rathee *et al*., 2012; Sauzet *et al*., 2009).

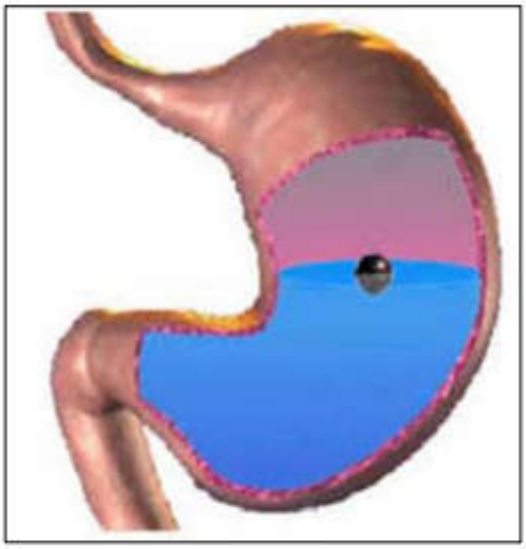

Figure 7: Floating or low density system

Floating system are of two types:

- **Effervescent system**
- **Non- effervescent system**

Effervescent system

When these drugs come in contact with gastric juice of stomach, carbondioxide gas is released. This provide buoyancy to the dosage form that float on the gastric fluid. These effervescent system have further divided into different types:

Volatile liquid containing system

The GRT of a drug delivery system can be sustained by incorporating an inflatable chamber, which contain a liquid. eg. Ether, cyclopentane, that gasifies at body temperature to cause the inflatation of the chamber in the stomach. The device made up of Polyvinyl alcohol, Polyethylene that gradually dissolves causing the inflatable chamber to release gas and collapse after a predetermined time to permit the spontaneous ejection of the inflatable system from the stomach.

Gas generating system

These system utilize effervescent reactions between carbonate/bicarbonate salts and citric/tartaric acid to liberate CO_2, which gets intrapper in the jellified layer of the system thus decreasing its specific gravity and making it float over gastric content.

Non effervescent system

The non effervescent system is based on the mechanism of swelling of polymer to mucosal layer in GIT. The most commonly used exicipients are hydrophilic gums, polysaccharides and matrix forming materials such as polycarbonate, polyacryate, as well as bioadhesive molecule such as Chitosan (Prassanakumara *et al*., 2012; Jamil *et al*., 2011).

Expanding/swelling system:

These dosage form after administrated to such an extent that it prevents to passage through the pyrolus, as a result the dosage form is remained in the stomach for a prolong period of time (Figure 8). These system are also called as plug type system because they remain have the tendency to lodged at the pyrolic sphincter. These formulations are designed for gastric retention and controlled delivery system for drugs in gastric cavity. Sustained and controlled release drug may be achieved by selecting a polymer with proper molecule weight and swelling property. When it comes in contact with gastric fluid the polymer imbibes water ad swell. The extensive swelling of these polymers is a result of the presence of physical-chemical crosslinks in the hydrophillic polymer network (Groning and Heun, 1984; Agyilirah *et al*., 1991).

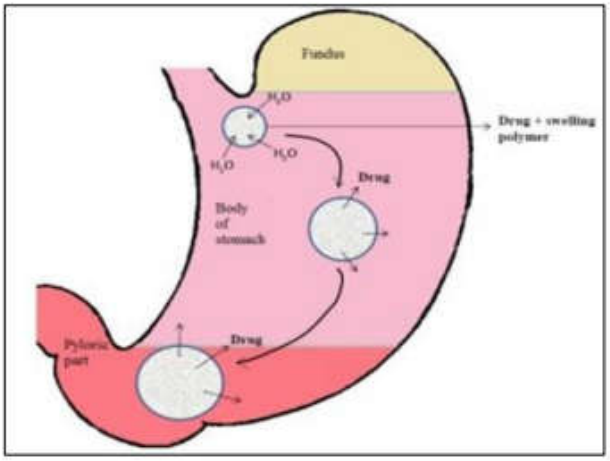

Figure 8: Expanding /swelling system

Methods of Preparation of Gastro-Retentive Multiparticulate System:

Solvent Evaporation Method

To construct the hollow inner core of a floating multiparticulate dosage form, solvent diffusion and evaporation processes can be used. The drug is either dissolved or disseminated in the polymer solution, which has been dissolved in an organic solvent. The medicine solution is then used to create oil in water emulsion by being emulsified into an aqueous phase with the proper ingredient (surfactants/polymer). After the formation of a stable emulsion, the organic solvent is evaporated either by raising the temperature under

pressure or by constant stirring (Kale *et al*., 2001; Muthuamy *et al*., 2005). The elimination of the solvent causes polymer precipitation at the oil/water interface of droplets, producing cavities and hollowing them out to give them floating qualities. For the development of such systems, polymers such as cellulose acetate, chitosan, Eudragit, Acrycoat, Methocil, polyacrylates, polyvinyl acetate, carbopol, agar, polyethylene oxide, and polycarbonates have been investigated (Streubel *et al*., 2002).

Ionotropic Gelation Method

Ionotropic gelation is supported by poly electrolytes' capacity to cross link in the presence of opposing ions to form beads. The ion tropic gelation technique has become popular with the use of alginates, gellan gum, chitosan, and carboxymethyl cellulose for medication and cell encapsulation (Streubel *et al*., 2003). Despite having the property of coating on the drug core and acting as release rate retardants, natural poly electrolytes contain some anions in their chemical structure. By interacting with polyvalent cations, these anions create meshwork structures and promote gelation by attaching primarily to anion blocks. Dropping a drug-loaded polymeric solution into an aqueous solution comprising polyvalent cations yields the hydrogel beads (Gaba *et al*., 2008).

Emulsion Solvent Diffusion Method

The affinity between the drug and the organic solvent is stronger in the emulsion solvent diffusion method than between the organic solvent and the aqueous solvent. Despite the fact that the organic solvent is miscible, the medication is dissolved in it and the solution is dispersed in the aqueous solvent, resulting in emulsion droplets. The organic solvent gradually diffuses out of the emulsion droplets into the surrounding aqueous phase, while the aqueous phase diffuses into the droplets that crystallise the medication.

Novel Method for Foam Powder

A novel multi-particulate gastroretentive drug delivery method based on low-density foam powder has also been presented and tested in vitro (Streubel *et al*., 2002). Floating microparticles were created using an oil-in-water solvent extraction / evaporation process using polypropylene foam powder, verapamil hydrochloride (as the model drug) and Eudragit RS, ethyl cellulose, or poly (methyl methacrylate). Methylene chloride was used to dissolve the medication and the polymer that controlled the release rate. Within this organic phase, polypropylene foam powder was then dissolved. The resultant suspension was then emulsified in an external aqueous poly (vinyl alcohol) solution and stirred to allow microparticle formulation. Themicroparticles were sieved, rinsed with water, and dried in a desiccator because they were irregular in shape and highly porous. Importantly, the drug encapsulation efficiency was high and nearly independent of the system's theoretical loading. Good in-vitro floating behaviour was seen in all cases. Surprisingly, the examined compositions produced a wide range of release patterns. Further research focused on the creation of a better production procedure

for this sort of low density, foam-based, floating microparticle, as well as the demonstration of the system's in vitro performance (Streubel *et al*., 2003). The proposed innovative preparation technique has several advantages, including quick processing periods, no exposure of the materials to high temperatures, the opportunity to avoid harmful organic solvents, and high encapsulation efficiencies. Floating microparticles were made by soaking microporous foam particles in an organic solution of the drug and polymer, followed by drying (Singh and Kim, 2000). In most cases, good in-vitro floating behaviour was observed, and a wide range of drug release patterns could be created by altering the drug loading and type of second polymer (Heng and Wong, 2003).

Melt Granulation Technique

Melt granulation is a method that produces granules by adding either a molten binder or a solid binder that melts throughout the operation. This is also known as melt agglomeration or thermoplastic granulation (Chokshi and Zia, 2004; Breitenbach, 2002; Kidokoro *et al*., 2003; Parashar *et al*., 2019).

Principle of Melt granulation:

The process of granulation consists of a combination of three phases:

a. Wetting and nucleation,

Wetting and Nucleation process

During the nucleation process, the binder comes into contact with the powder bed, resulting in the production of tiny agglomerates. mSchafer and Mathiesen propose two nucleation mechanisms.

Immersion

When the size of the molten binder droplets is larger than that of the small solid particles, nucleation by immersion takes place.

Fine solid particles are deposited onto the surfaces of molten binder droplets as immersion progresses.

Distribution

A molten binding liquid is applied to the surfaces of tiny solid particles using the distribution method.

The collision of the wetted particles produces the nuclei.

Small binder droplet size, low binder viscosity, and large shearing pressures are often favourable circumstances for nucleation via the distribution approach.

b. Coalescence step

In order to increase the success of fusion nuclei, it involves nuclei with leftover surface liquid.

The surface liquid gives the nuclei plasticity and is necessary for the nuclei's surface to deform for coalescence as well as to facilitate granulation rounding.

c. Attrition and breakage

Attrition and breakage are granulation fragmentation phenomena that are solidified by tray cooling to ambient temperature without the need for tumbling drying.

As a result, breaking is known to play a more important role in influencing the final parameters of the melt granulation during the granulation phase.

Requirements of Melt granulation

In general, a meltable binder concentration of 10-30% w/w in comparison to fine solid particles is utilized. A meltable binder suited for granulation has a melting point that is typically between 50-100°C

Hydrophilic meltable binders are employed in the preparation of immediate-release dosage forms, whereas hydrophobic meltable binders are preferred in the preparation of prolonged-release formulations.

Fine solid particle melting points should be at least 20°C higher than the maximum processing temperature.

Meltable Binders

Its physical and chemical stability.It must be solid at room temperature and melt between 40 and 80°C.

Its hydrophilic-lipophilic balance (HLB) ensures proper active ingredient release.

There are two type of Meltable binder:

a) Hydrophilic meltable binders

b) Hydrophobic meltable binder

Evaluation Parameters:

Buoyancy Lag Time:

It is determined in order to know the time taken by the dosage form to float on the top of the dissolution medium, after it is placed in the medium.

Floating Time:

It is the time taken by the dosage form to float continuously on the dissolution media. This test is usually performed in SGF-Simulated Gastric Fluid in which the temperature is maintained at 37ºC.

Specific Gravity / Density: Density is usually determined by the displacement method, in which Benzene used as displacement medium.

Swelling Index:

After immersion of swelling dosage form into SGF at 370C, dosage form is removed out at regular interval and dimensional changes are measured in terms of increase in tablet thickness /diameter with time.

Water Uptake:

It is an indirect measurement of swelling property of swellable matrix. Here dosage form is removed out at regular interval and weight changes are determined with respect to time. So it is also termed as Weight Gain (Bagul *et al*., 2012).

Water uptake = WU = (Wt – Wo) * 100 / Wo

Where, Wt = weight of dosage form at time t

Wo = initial weight of dosage form

Weight variation:

According to USP the weight variation test done by weighing 20 tablets individually. And then calculating the average weight and comparing the individual tablet weights to the average. Not more than 2 tablets can exceed the limit.

Hardness & friability:

Hardness is defined as the “force required to break a tablet in diametric compression test.” Hardness is also known as the tablet crushing strength. The devices which are used to test hardness are Monsanto tester, strong Cobb tester, Pfizer tester, etc. Friability of tablets can be determined by using Roche Friabilator. In this, a pre-weighed tablet sample is placed, which is then operated for 100 revolutions (Bagul *et al*., 2012).

***In-vitro* dissolution tests:**

In- vitro dissolution test is generally performed by using USP apparatus with paddle and GRDDS is placed normally as per other conventional tablets. But sometimes as the vessel is large and paddles are at bottom,

there is much lesser paddle force acts on floating dosage form which generally floats on surface. If the floating dosage form does not rotate may not give proper result and also may not give reproducible result. Different types of transformation in dissolution assembly have made to produce reproducible results. They are as shown in following (Figure 9).

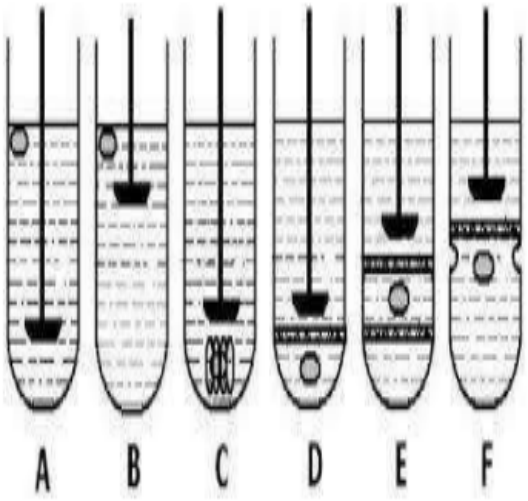

Figure 9: Reproducible results

Applications and rationale use of GRDDS

Sustained Drug Delivery: GRDDS float on the gastric contents over a prolonged period of time, as these systems have bulk density <1 (Goswami *et al*., 2020).

Site-Specific Drug delivery: This delivery system is very useful for drugs that are absorbed from the stomach or the proximal part of the small intestine, especially with respect to their application for the treatment of *H. Pylori* infections (Dixit, 2011).

Absorption Enhancement: This is important in the case of drugs that are absorbed from the upper part if the GIT and by formulating this type of drugs as GRDDS can improve the poor bioavailability, thereby maximising their absorption (Bhardwaj *et al*., 2011).

CONCLUSION

It can be concluded that GRDDs offers various potential advantages for drugs with poor bioavailability due their absorption is restricted to the upper gastrointestinal tract and they can be delivered efficiently thereby maximizing their absorption and enhancing absolute bioavailability. Growing understanding of impact of GIT physiology on drug delivery will ensure development of an increasing number of drug delivery system to optimize drug delivery of molecules exhibiting regional variability in drug absorption. Hence gastro retentive drug delivery systems may be found to be more efficacious for the delivery of drugs to the systemic circulation.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Agyilirah, G.A., Green, M. & Ducret, R. (1991) Evaluation of gastric retention properties of cross linked polymer-coated tablet versus those of non-disintegrating tablets. *International Journal of Pharmaceutics*, 75, 241–247.
- Amit, N., Ruma, M. & Biswarup, D. (2010) Gastro retentive drug delivery system [Review]. *Asian Journal of Pharmaceutical Research*, 3, 2–10.
- Arora, S., Ali, J., Ahuja, A., Khar, R.K. & Baboota, S. (2005) Floating drug delivery systems: A review. *AAPS PharmSciTech*, 6, E372–E390.
- Arora S, Ali J, Ahuja A, Khar RK and Baboota S. Floating Drug Delivery

Systems: A Review. AAPS Pharm. Sci. Tech. 2005; 6 (3): E372-E390.

- Arora, S., Javed, A., Ahuja, A., Khar, R.K. & Baboota, S. (2000) Floating drug delivery system: A review. *AAPS PharmSciTech*, 6, 372–390.
- Arunachalam, M. Karthikeyan, Kishore Konam, Pottabathula Hari Prasad, S. Sethuraman, S. Ashutoshkumar, S. Manidipa (2011) Floating drug delivery systems: A review. *International Journal of Research in Pharmaceutical Sciences*, 2, 76–83.
- Bagul, U.S., Patil, R.V., Shirsath, Y.A., Nikam, A.J. & Gujar, K.N. (2012) Stomach specific drug delivery systems: A review. *Int. J. Pharm. Res Dev.*, 4, 147–150.
- Bhardwaj, L., Sharma, P.K. & Malviya, R. (2011) A short review on gastro retentive formulations for stomach specific drug delivery: Special emphasis on floating in situ gel systems. *African Journal of Basic and Applied Sciences*, 3, 300–312.
- Breitenbach, J. (2002) Melt Extrusion: From Process to Drug Delivery Technology. *European Journal of Pharmaceutics and Biopharmaceutics*, 54, 107–117.
- Chokshi, R. & Zia, H. (2004) Hot melt extrusion technique, A review. *Iranian Journal of Pharmaceutical Research*, 3, 3–16.
- Chudiwal, V., Shahi, S., Chudiwal, S. & Ahale, D. (2017) Innovative technologies for gastro-retentive. *Asian Journal of Pharmaceutical Research*, 6, 22–28.
- Deshpande, A.A., Shah, N.H., Rhodes, C.T. & Malick, A.W. (1996) Controlled Release Drug Delivery Systems for prolonged gastric residence; An overview. *Pharmaceutical Research*, 22, 531–539.
- Dixit, N. (2011) Floating drug delivery system. *Journal of Current Pharmaceutical Research*, 7, 6–20.
- Doshi, S.M. & Tank, H.M. (2012) Gastro retention- An innovation ver conventional poorly soluble drugs: A review. *International Journal of Phharmaceutical and Chemical Sciences*, 1, 859–866.
- Gaba, P., Gaba, M., Garg, R. & Gupta, G.D. (2008) Floating microspheres, A [Review]. *Pharmainfo.net*, 6, 121–123.
- Goswami, A., Jain, D.N.K. & Goyal, D.M. (2020) An updated review on gastro retentive drug delivery system. *International Journal of Pharmaceutical Sciences Review and Research*, 65, 45–51.
- Groning, R. & Heun, G. (1984) Oral dosage forms with controlled gastrointestinal transit. *Drug Development and Industrial Pharmacy*, 10, 527–539.
- Heng, W.S. & Wong, T.W. (2003) Melt Processes for Oral Solid Dosage Forms. *Pharmaceutical Technology*, 1–6.
- Ito, R., Machida, Y., Sannan, T. & Nagai, T. (1990) Magnetic granules: A novel system for specific drug delivery to oesophageal mucosa in oral

administration. *International Journal of Pharmaceutics*, 61, 109–117.

- Jamil, F., Sunil, K., Sharma, S., Vishvakarma, P. & Singh, L. (2011) Review on stomach specific drug delivery: Development and evaluation. *International Journal of Research in Pharmacy and Biosciences*, 2, 1427–1433.
- Kakar, S., Batra, D., Singh, R. & Nautiyal, U. (2013) Magnetic microspheresas magical novel drug delivery system: A review. *Journal of Acute Disease*, 2, 1–12.
- Kale, R., Rao, B.S., Sharm, S. & Ramanmurthy, K.V. (2001) Preparation and Evaluation of Floatable Drug Delivery System of ketorolac tromethamine. *International Journal of Pharmacy*, 64–65.
- Kidokoro, M., Sasaki, K., Haramiishi, Y. & Matahira, N. (2003) Effect of Crystallization Behaviour of polyethylene glycol 6000 on the Properties of Granule Prepared by Fluidized Hot Melt Granulation (FHMG). *Chemical and Pharmaceutical Bulletin*, 51, 487–493.
- Mayavanshi, A.V. & Gajjar, S.S. (2008) Floating drug delivery systems to increase gastric retention of drugs; A review. *Research Journal of Pharmacy and Technology*, 1, 1–4.
- Muthuamy, K., Govindarajan, G. & Ravi, T.K. (2005) Preparation and Evaluation of lansoprazole Floating Micropellets. *Indian Journal of Pharmaceutical Sciences*, 67, 75–79.
- Parashar, A.K., Patel, P., Gupta, A.K., Jain, N.K. & Kurmi, B.D. (2019) Synthesis characterization and in vivo evaluation of pegylated PPI dendrimer for safe and prolonged delivery of insulin. *Drug Delivery Letters*, 9, 248–263.
- Patil, K.K. & Datta, S.A. (2013) Review on floating drug delivery system. *International Journal of Pharmaceutical Sciences Review and Research*, 21, 276–283.
- Prajapati, V.D., Jani, G.K., Khutliwala, T.A. & Zala, B.S. (2013) An upcoming approach for gastroretentive drug delivery system. *Journal of Controlled Release*, 168, 151–165.
- Prassanakumara, J., Ramarao, T. & Jayaveera, K.N. (2012) Modulation of gastro intestinal transit time by floating drug delivery system. *Indo American Journal of Pharmaceutical Research*, 2, 1223–1232.
- Rathee, P., Jain, M., Rathee, S., Nanda, A. & Hooda, A. (2012) Gastroretentive drug delivery system: A review of formulation approaches. *Journal of Pharmaceutical Innovation*, 4, 147–150.
- Sauzet, C. & Claeys -Bruno M, Nicholes M, Kister J, Piccerelle P, Prinderre P (2009) An innovation floating gastro retentive dosage system: Formulation and in vitro evaluation. *International Journal of Pharmaceutics*, 378, 23–29.
- Singh, B. & Kim, K.H. (2006) Floating drug delivery system: An approach to oral control drug delivery system via gastric retention. *Journal of Contolled Release*, 63, 235–259.

- Singh, B.N. & Kim, K.H. (2000) Floating drug delivery systems: An approach to oral controlled drug delivery via gastric retention. *Journal of Controlled Release*, 63, 235–259.
- Streubel, A., Siepmann, J. & Bodmeier, R. (2002) Floating microparticles based on low density foam powder. *International Journal of Pharmaceutics*, 241, 279–292.
- Streubel A, Siepmann J, Bodmeier R, Floating Microparticles Based on Low Density Foam Powder, Int. J. Pharm, 2002, 241, 279-292.
- Streubel, A., Siepmann, J. & Bodmeier, R. (2003) Floating Matrix tablets based on low density foam powder, effects of formulation and processing parameters on drug release. *European Journal of Pharmaceutical Sciences*, 18, 37–45.
- Streubel A, Siepmann J, Bodmeier R. Floating Matrix Tablets Based on Low Density Foam Powder, Effects of Formulation and Processing Parameters on Drug Release, Eur. J. Pharm. Sci, 2003, 18, 37-45.
- Talukder, R. & Fassihi, R. (2004) Gastroretentive delivery systems: A mini review. *Drug Development and Industrial Pharmacy*, 30, 1019–1028.
- Thapa, P., Maharjan, R. & Jeong, S.H. (2019) Julu Tripathi. *Current State and Future Perspectives on Gastroretentive Drug Delivery Systems*.Pharmaceutics, 11, 1–22.
- 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, 12–16.
- Waterman, K.C. (2007) A critical review of the gastric retentive controlled drug delivery. *Pharmaceutical Development and Technology*, 12, 1–10.