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Review on Gastroretentive Drug Delivery System

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Abstract: *GRDDSs are an innovative tactic in this area (Gastro Retentive Drug Delivery System). GRDDSs can improve the regulated administration of drugs with an absorption window by continuously releasing the drug for a long period before it reaches its absorption site. The aim of this study was to investigate, compile, and succinctly summarise both recent and older literatures, with a focus on methods being applied right now to prolong gastric residency duration. They include of high density systems, floating systems, swelling and expanding systems, bio/mucoadhesive systems, and various delayed gastric emptying devices. The current study briefly discusses the categorization, formulation concerns for gastroretentive drug delivery systems, variables affecting stomach retention, advantages, limitations, and applications. To understand the many physiological hurdles involved in establishing stomach retention, we have highlighted important factors impacting it. Then, we assessed the various gastroretentive techniques that have been devised and developed up to this point, including high density (sinking), floating, bio- or mucoadhesive, expandable, unfoldable, ultra porous hydrogel, and magnetic systems. Additionally, the advantages of gastroretentive medicine administration systems were thoroughly covered.*

Keywords: GRDDS

I. INTRODUCTION

Oral administration is the most feasible and preferred way to get any medication into the systemic circulation. To improve therapeutic advantages such ease of dosage administration, patient compliance, and formulation flexibility, the pharmaceutical industry has recently exhibited a greater interest in oral controlled release drug delivery. Drugs with quick elimination from the systemic circulation and simple absorption from the gastrointestinal tract (GIT) are eliminated from it quickly. To get the intended therapeutic effect, these drugs need to be dosed often. By gradually releasing the medication into the gastrointestinal tract (GIT) and keeping an effective drug concentration in the systemic circulation for a significant length of time, oral sustained-controlled release formulations aim to get around this constraint. After oral administration, such a medicine delivery would be employed and held in the stomach while releasing the drug in a controlled manner, enabling continuous drug delivery to the gastrointestinal tract's absorption sites. (GIT)(1)

A short gastric retention time (GRT) and an unpredictable short stomach emptying time are the two limitations that have the biggest an impact on these drug delivery methods (GET). Due to these limitations, a dosage form's drug release from the absorption zone—the stomach or upper section of the small intestine—may be insufficient, which may lessen the potency of the dose that was provided. In order to offer an oral controlled release dosage form that is site-specific, it is preferable to prolong the drug delivery's time in the stomach. Long-term gastric retention raises the bioavailability of medications, extends the time it takes for them to pass through the stomach, reduces the amount of wasted medicine, and increases the solubility of medications that are less soluble in high pH conditions. Additional local activities in the upper small intestine, such as the therapy of peptic ulcers, may benefit from a prolonged GRT in the stomach. [(1)]

Gastroretentive drug administration is a method to prolong stomach residence time by aiming site-specific medicine release in the upper gastrointestinal tract (GIT) for local or systemic effects. Because they may remain in the stomach area for a long time, medications with gastroretentive dosage forms have substantially longer gastric retention times (GRT). The past few decades have seen the design and development of a variety of gastroretentive drug delivery techniques, such as high density (sinking) systems that are retained in the bottom of the stomach(3), low density (floating) systems that cause buoyancy in gastric fluid, mucoadhesive systems that cause bioadhesion to stomach mucosa, and unfoldable, extendible, or swellable systems that restrict emptying of the dosage forms through the pyloric sphin[(1)]

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In the realm of site-specific oral controlled release drug delivery systems, a number of gastroretentive strategies have lately emerged as leading methodology. These strategies are the subject of the current study.

GRDDS Provide benefits By making such drugs more effective,

Bioavailibility

Therapeutics Efficiency and

Possible reduction of the dose

Maintenance of constatnt Therapeutic levels over a prolonged period and thus reduction in the therapeutic levels

Reduce drug wastage

Improves solubility of drugs that are less soluble at high pH environment (e.g. Weakly Basic drug like domperidone papaverine) (4,5)

II. REVIEW OF LITERATURE

Rabina Aslam and others:

Drugs are delivered via gastroretentive drug delivery methods, which also extend the time that dose forms are retained in the digestive tract.

Amrjeet Daniya-et.al:

Gastric retentive dosage forms have been developed to provide controlled release therapy for drugs with poor absorption in the lower gastrointestinal (GI) tract or for local treatment of problems of the upper GI Tract.

Vivek K Pawar et.al.:

Due to their potential to enhance the efficacy of controlled release systems, gastroretentive dosage forms (GRDF) are receiving a lot of interest. A system that stays in the stomach for a long enough period despite all physiological obstacles, releases active molecules in a regulated way, and is afterwards quickly digested by the body is referred to as an ideal GRDF system. [3,4]

Physiology of Stomach:

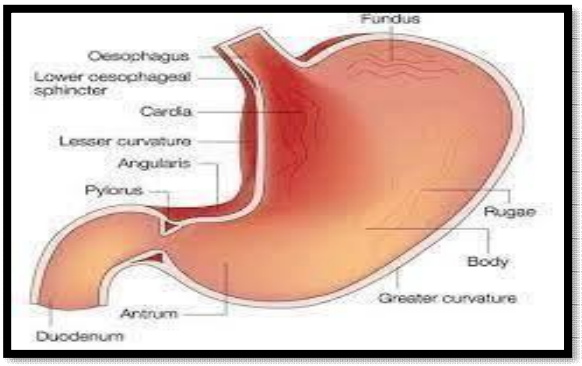
Anatomically, the stomach is divided into three sections. Antrum, Fundus, and Body (pylorus) The fundus and body of the proximal region, which is made up of the fundus and body, serve as a storage area for undigested materials while the antrum is the principal place for mixing motions and acts as a pump for stomach emptying by pushing action. The stomach empties both after eating and when fasting. The phrase "migrating myoelectric cycle" (MMC), which is further divided into four phases, refers to a series of electrical events that take place when fasting and cycle through the stomach and intestine every 2-3 hours. After ingestion, the contraction pattern, sometimes referred to as the digestive motility pattern, changes from a fasted to a fed condition.[6,7]

Phase 1 – (Basic Phase) last from 30-60 min with rare contractinns

Phase 2 – (Preburst Phase) Last for 20-40 min with intermittent actionpotential and conc.

Phase 3 – (Burst Phase) last for 10-20 min which includes intence and regular concentration for short period.

Phase 4 – last for 0-5 min and occurs between phase 2 and 1 of 2 consecutive



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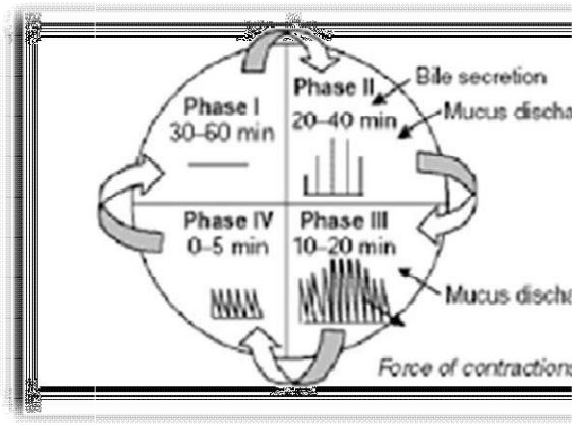
Factor Affecting gastric reaction time of the dosage form:

Density: The dosage form's density should be lower than that of the stomach's contents. (1.004 g/ml)

- More than 7.5 mm in diameter dosage forms have a longer stomach residence period than dosage forms with a 9.9mm diameter.
- Tetrahedron-shaped dosage forms stayed in the stomach longer than other devices of a comparable size. Single or multiple unit formulation? Multiple unit formulation allow coadministration of units with different release profiles or containing incompatible substances and permit a larger margin of safety against dosage form failure than single unit dosage form. They also show a more predictable release profile and insignificant performance impairment caused by unit failure.[11,12]

When fasting, whether in a fed or unfed state, the gi motility is characterised by bursts of vigorous motar activity that happen every 1.5–2 hours. If the time of the formulation and the MMC are the same, the MMC sweeps undigested matter from the stomach, and the GRT of the unit can be extremely short. However, in the fast state, the MMC is delayed and the GRT is prolonged.

- Feeding the stomach with indigestible polymers or fatty acids can cause the stomach's motility pattern to transition to a fed state, slowing down gastric emptying and delaying the release of drugs (11,12)



- A meal heavy in protein and fat can raise calorie content-GRT by 4–10%.

Due to the low frequency of MCC, the GRT might increase by almost 400 minutes when many meals are given in comparison to a single meal.

- Regardless of height, weight, or body surface, the mean ambulatory GRT in males (3.4 hours) is lower than that in their age- and race-matched female counterparts (4.6 hours).
- Age: Individuals older than 70 have much longer GRT.
- Anticholinergic medications like atropine and propetheline, as well as opiates like codeine, might prolong GRT when used concurrently.[11,12]

Potential Drug Candidatev For GRDDS :

- Medications that operate locally in the stomach, such as antacids and misroprostol.
- Drugs with a limited window of absorption in the gastrointestinal tract (GIT), such as L-DOPA Furosemide, riboflavin, aminobenzoic acid, etc.
- Drugs like captopril and ranitidine that are unstable in the intestinal or colonic environment. Metronidazol with HCl.
- Medicines that disrupt the natural flora in the colon, such as antibiotics used to treat Helicobacter pylori.
- Drugs with limited solubility at alkaline pH levels such as verapamil HCl, chlordiazepoxide, and diazepam.(13)

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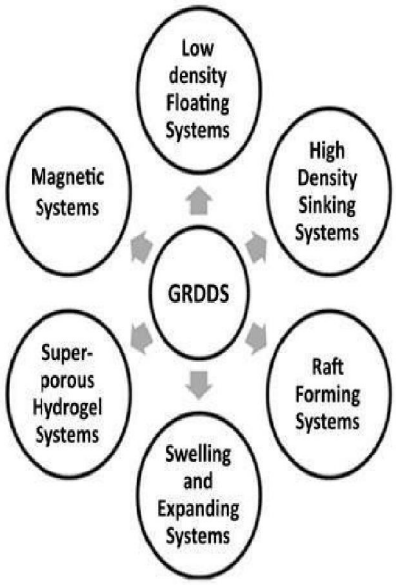
Sr. No.	Terms	Conventional DDs	GRDDs
1	Toxicity	High risk of toxicity	Low risk of toxicity
2	Patient compliance	Less	Improves patient compliance
3	Drug with narrow absorption window in small intestine	Not suitable	Suitable
4	Drug acting locally in stomach	Not much advantageous	Very much advantageous
5	Drug having rapidabsorption through GIT	Not much advantageous	Very much advantageous
6	Drug which degrades in the colon	Not much advantageous	Very much advantageous
7	Dose dumping	High risk of dose dumping	No risk of dose dumping

Drug those are unsuitable for GRDDS

Drugs like phenytoin and others that only very little dissolve in acid.

Medications that are unstable in the stomach, such as erythromycin, etc.

Drugs designed for selective release in the colon, such as corticosteroids and 5-amino salicylic acid, etc.



Types of gastroretentive Dosage form:

High density system:

This method calls for the development of dosage forms with a density greater than that of the contents of a typical stomach (1.04g/ml). These formulations are made by coating the medicine on a substantial support or by combining it with substantial inert substances as iron powder, zinc oxide, titanium dioxide, or barium sulphate. The resulting pellets may have a diffusion-controlled coating. Membrane Because the dry material from which these systems are produced interacts with the stomach fluid to release the medicine they contain, they are technically challenging to make with a high amount of drug. Another issue is that there isn't a system like that on the market..(14)

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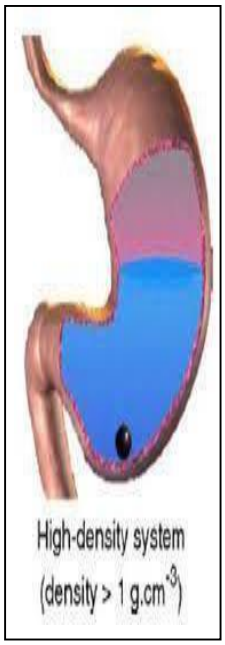
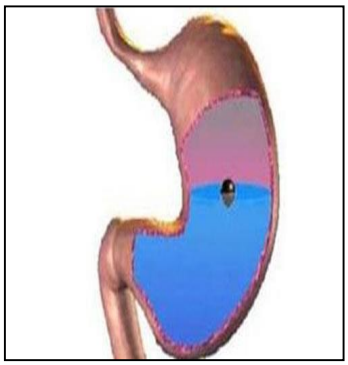
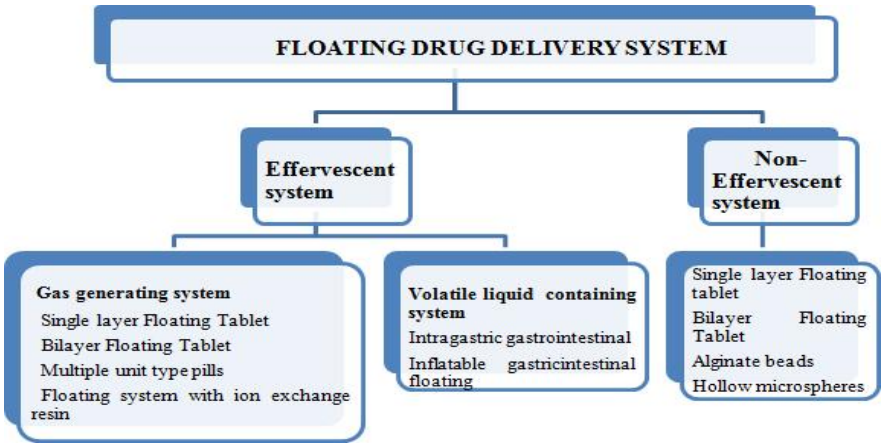


Floating Or Low Density System:

Due to their low densities, FDDS maintain their buoyancy above the stomach contents for extended periods of time and offer continuous medication release. Due to the fact that they have no negative effects on the GIT's motility, these systems in particular have been examined in great detail. Their supremacy over the other types of GRRDS is also demonstrated by the vast array of floating dosage forms that are currently being produced and sold on a global scale.





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Classification of floating drug delivery System

Swelling System:

These are the medications whose swelling upon ingestion prevents their escape from the pylorus, which causes the medication to be held in the stomach for a lengthy time. As they tend to remain trapped at the pyloric sphincter, these systems are known as plug-type systems. By choosing the right molecular weight polymer, controlled and sustained release may be achieved; swelling of the polymers slows the release. The polymer ingests water and expands when it comes into touch with stomach fluid. These polymers considerable swelling is caused by the network of hydrophilic polymers, which contains physical and chemical cross connections. These cross links keep the polymer from dissolving and so preserve the dosage form's physical integrity. The membrane in the dissolving medium split away from the core and formed a bubble that kept the unit afloat. The units' size rose by three to six times, giving the system its gastroretentive feature in addition to its capacity to float.

Mucoadhesive System:

A mucoadhesive polymer used in mucoadhesive medication delivery systems sticks to the stomach mucosal surface and lengthens gastric retention in the gut. The ability of mucoadhesive polymers to cling to the mucus gel layer makes them extremely effective excipients in the GRRDS. Natural polymers include sodium alginate, gelatin, guar gum, and others. Semi-synthetic polymers such sodium carboxymethyl cellulose, carbopol, and HPMC can adhere to mucosal membranes by hydration, bonding, or receptor-mediated mechanisms. When a hydrophilic polymer is hydrated, it transforms into a sticky, mucoadhesive substance. Bonding can be mechanically or chemically mediated. Vander Waal forces or ionic or covalent bonds may also be present in chemical bonding between the polymer molecule and the mucous membrane. Certain polymers and certain receptors expressed on stomach cells adhere via receptor-mediated mechanisms. The polymers might be neutral, anionic, or cationic.

Super Porous Hydrogel Systems

These expandable systems are different enough from the traditional varieties to merit their own categorization. Super porosity hydrogels with an average pore size of >100 micrometres are used in this method to increase gastric retention time (GRT), and they expand to equilibrium size in under a minute as a result of fast water absorption by capillary wetting through a large number of linked open holes. They are designed to have adequate mechanical strength to withstand pressure caused by stomach contraction and expand to a big size (swelling ratio: 100 or higher). The co-formulation of hydrophilic particle material suggests this.

Magnetic System:

A tiny internal magnet is present in the dose form, and a magnet is also applied to the abdomen over the location of the stomach in this method to increase gastric retention time (GRT). Although the magnetic system appears to function, the external magnet needs to be placed precisely, which may limit patient compliance.

Brand Name	Active Ingredient(s)
Cifran OD	Ciprofloxacin
Madopar	Benserazide and L-dopa
Valrelease	Diazepam
Topalkan	Aluminum-magnesium antacid
Cytotec	Misoprostal

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Dosage form	Drug
Floating Tablets	Acetaminophen, Acetylsalicylic acid, Ampicillin, Amoxicillin trihydrate, Atenolol, Captopril, Cinnerzine, Chlorpheniramine maleate, Ciprofloxacin,Diltiazem
Floating Capsules	Chlordiazepoxide HCl, Diazepam, Furosemide, L-DOPA and Benserazide, Nicardipine, Misoprostol, Propranolol
Floating Microspheres	Aspirin, Griseofulvin, p-nitro aniline, Ibuprofen, Terfenadine, Tranilast
Floating Granules	Diclofenac sodium, Indomethacin,
Powders	Several basic drugs

Commonly Used drug in Formulation of Gastroretentive dosage form:
Gastroretentive Products available in the Market:
Ciprofloxacin floating tablet dosage form in gastroresistant dose form:
The current review introduces and investigates the gastroretentive swellable and floating matrix tablet formulation of ciprofloxacin hydrochloride to successfully treat infections caused by susceptible organisms (HCL). The criteria for selecting a drug for a gastroretentive dosage form are met by ciprofloxacin HCl because it has a small absorption window in the stomach and proximal part of the small intestine and is more stable in an acidic environment.

III. MATERIALS AND METHOD

In the creation of ciprofloxacin HCL gastroretentive tablets, various grades of hydroxypropyl methylcellulose were used as suspending and stabilising agents (polymers), alongside sodium starch glycolate (SSG), crospovidon (a disintegrant), sodium bicarbonate (an alkalizing agent), and magnesium stearate (a lubricant).

Ciprofloxacin:

- It is the most potent first generation fluroquinolones active against a broad range of bacteria .
- The most susceptible ones are the gram positive bacilli such as ENTEROBACTERIACEAE and NISEEERIA.
- It is highly effective and bactericidal.
- Effect of antibiotics on Enterobacteriaceae over a relatively long time.
- Having a low mutational resistance frequency.
- Anerobes and protective intestinal streptococci are widespread.
- Active against a variety of aminoglycosides and beta-lactamsresistance bacteria.
- Less active against the acidic pH.

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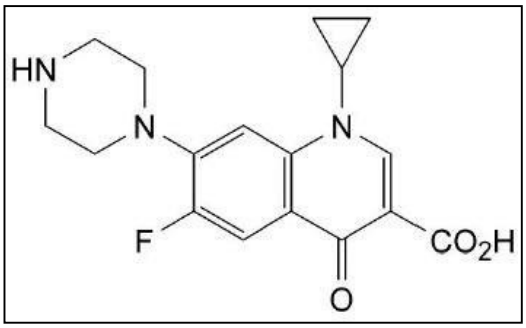
Chemical Structure



Chemical Name:
cyclopropyl-6-fluoro-4-oxo-7-piperazin-1-ylquinoline-3-carboxylic acid

Mechanism of Action:
The fluoroquinolone medication class includes the bactericidal antibiotic ciprofloxacin. By blocking the bacterial enzymes DNA topoisomerase and DNA-gyrase, it prevents DNA replication.

Use:

- Used to treat the urinary tract infection.
- Bacterial gastroenteritis
- Bone, soft tissue, gynaecological and
- wound infection
- Cancroid
- Gonorrhea
- Meningitis
- Respiratory infection
- Tuberculosis
- Typhoid

Adverse effects :

- Nausea
- Vomiting
- Dizziness
- Headach
- Rash

IV. CONCLUSION

Based on the reviewed literature, it is possible to draw the conclusion that gastroretentive drug delivery offers a number of potential benefits for medications with low bioavailability because these medications' absorption is limited to the upper gastrointestinal tract (GIT) and because they can be efficiently delivered, maximising absorption and improving absolute bioavailability. Current methods for improving the bioavailability and regulated distribution of medications that have an absorption window are gastriretentive drug delivery systems. The basic methods used for gastroretentive drug administration are floating, bioadhesive, swelling, magnetic, and high density systems. These technologies offer the medication in an absorbable form in the absorption-optimal locations while also allowing for regulated drug release. Each of these medication delivery methods has benefits and downsides of its own. The physicochemical qualities of the drug, physiological processes in the GIT, formulation techniques, and the right mix of the drug and excipients must all be taken into account when designing a successful GRDDS.

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REFERENCES

[1]. Gastroretentive drug delivery system(grdds), Article in Indian journal of pharmaceutical and biological research: march2015

[2]. Streubel A, Siepmann J, Bodmeier R. Gastroretentive drug delivery system.

[3]. Garg R, Gupta GD. Progress in controlled gastroretentive delivery systems. Trop. JPharm Res 2008;

[4]. Shrma S, Pawar A. Low density multiparticulate system for pulsatile release of meloxicam. Int J Pharm 2006; 313: 150-58.

[5]. Deshpande AA, Shah N, Rhodes CT, Malik W. Development of a novel controlled-release system for gastric retention. Pharm Res 1997

[6]. Park K. Enzyme-digestible swelling as platforms for longterm oral drug delivery:synthesis and characterization. Biomaterials 1988; 9: 435.

[7]. Ali J, Arora S, Khar RK. ; Floating Drug Delivery System: A Review; AAPSPharm Sci Tech. 2005;06(03): E372-E390.

[8]. Yie W, Chein; Novel Drug Delivery System 2nd ed. Marcel dekker ;Inc. NewYork. 1992; 1-3.

[9]. Sanjay Garg, Shringi Sharma; Gastroretentive Drug Delivery Systems; Pharmatech.2003; 160-166., A. Badoni , A. Ojha, G. Gnanarajani, P. Kothiyali; Review on Gastro RetentiveDrug Delivery System; The Pharma Innovation, 2012;1(8): 32-42.

[10]. Devkant Sharma, Anjali Sharma; Gastroretentive Drug Delivery System- a minireview; Asian pacific Journal of Health Sciences, 2014; 1(2): 8089.

[11]. Robinson J, Lee R. Controlled Drug Delivery, 2nd edition , 1987

[12]. Vyas SP, Khar RK. Gastroretentive systems. In: Controlled drug Delivery. Vallabh Prakashan, Delhi, India. 2006. p. 197-217.

[13]. Singh B and Kim KH; Floating drug delivery system: an approach to oral controlled drug delivery system via Gastric Retention; Journal of Controlled Release,2000;63:235-259.

[14]. Groning R, Heun; Oral Dosage forms with Controlled Gastrointestinal TransitDrug Delivery;1984;10(4):527-539.

[15]. Agyilirah GA, Green M, Ducret R; Evaluationof Gastric Retention Properties ofCross linked Polymercoated tablet versus those of non Disintegrating Tablets; Int JPharma;1991;75:241-247

[16]. Talukder R, Fassihi R. Gastroretentive Delivery Systems;Drug Development andIndustrial Pharmacy;2004;3

[17]. Huang Y, Leobandung W, Foss A, Peppas NA. Molecular aspects of muco- and bioadhesion: tethered structures and site-specific surfaces.

[18]. Arrora S, Ali J, Khar RK, Baboota S. Floatng drug delivery systems: A review. AAPS Pharm Sci Tech 2005; 6(3):

[19]. Khosla R, Feely LC, Davis SS. Gastrointestinal transit of non-disintegratingtablets in fed subjects. The treatment of gastrointestinal infections with ciprofloxacin a lppolito et al. Minerva Med.1991