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Review Article

In-Situ Gel: A Gastro-retentive Drug Delivery System

S. G. Patil*, S. R. Shahi, J. J. Dandale, R. M. Savakhande

Department of pharmaceutics, Government college of pharmacy, karad.

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ABSTRACT

Conventional oral dosage forms have low bioavailability due to their rapid gastric transition from the stomach, especially for drugs that are less soluble at the alkaline pH of the intestine. Similar to this, medications that have a local effect in the stomach are quickly evacuated and do not have enough time to remain there. To avoid this problem, numerous attempts have been made to prolong the retention duration of the drug delivery method. We will talk about the several methods used to create gastro-retention in drug delivery systems with a focus on the floating in-situ gel system for stomach-specific drug administration. Ionic crosslinking, pH changes, temperature modulation, solvent exchange, and other processes are necessary for the creation of in-situ gels, which allow for the regulated and prolonged release of the medication. The in- situ gelling system uses a variety of polymers, including guar gum, xanthan mucilage, gellan epoxy resin, sodium alginate, pectin, chitosan, sodium citrate, sodium benzoate and polyethylene glycol. The present review briefly addresses the necessity of GRDDS, its pharmaceutical significance, GRDDS methods, variables influencing stomach retention, benefits, drawbacks, Procedure for creating in- situ gelling drug delivery system, the use of polymers in gastro-retentive formulations, assessment of gastro-retentive dosage forms, and comparison of gastro-retentive and conventional drug delivery systems.

INTRODUCTION

Current technological advancements have made feasible dose alternatives available through a variety of administration methods. Nowadays, there are many other ways that can be employed, such as oral, parentral, topical, nasal, rectal, vaginal, ophthalmic, etc. out of these delivery methods the oral route is said to be the most popular and commonly used approach for the reasons that follow [1,2]

- Simple to administer
- Greater adaptability when designing
- Production simplicity
- Inexpensive

The term GRDD refers to dosage forms that are capable of being kept in the stomach. These

***Corresponding Author:** S. G. Patil
Address: Department of pharmaceutics, Government college of pharmacy, karad.
Email ✉: spatil29062001@gmail.com
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dosage forms allow a medication to be released gradually over a long duration until it reaches its absorption site under controlled circumstances. Several factors, including as the feed's volume and content, temperature and viscidity, stomach pH, posture, emotional state of the individual, illness, and the use of medicines that change gastric motility, can affect how fast a given dosage form passes through the stomach [3,4]

Figure 1: Gastro-retentive Drug Delivery

❖ **Rationale For the Use of GRDDS [49]:**

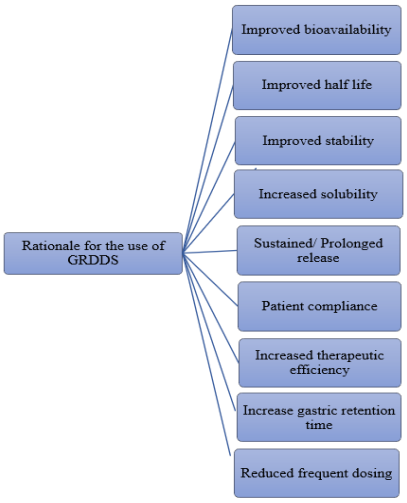


Figure 2: Rationale for the use of GRDDS

❖ **Criteria For the Selection of Drug Candidates For GRDDS: [1,5,6]**

In general, appropriated candidate for GRDDS are molecules that have poor colonic absorption but are characterizes by better absorption properties at upper part of GIT:

Table 1: Suitable drug candidates for GRDDS

Sr. No.	Properties	Examples
1.	Drugs with narrow absorption window in the GIT	Riboflavin, Levodopa
2.	Drugs which are absorbed from stomach and upper part of GIT	Chlordiazepoxide, Cinnarazine
3.	Drugs locally acting in the stomach	Antacids, Misoprostol
4.	Drugs degraded in colon	Ranitidine, Metronidazole
5.	Drugs that disturb normal colonic bacteria	Amoxicilline trihydrate

Table 2: Unsuitable drug candidates for GRDDS

Sr. No.	Properties	Examples
1.	Gastro irritant drugs	Diclofenac, Ibuprofen
2.	For acid labile drugs	Macrolide antibiotics
3.	Drugs which get absorb throughout GIT equally	Phenytoin, Theophylline

❖ **Factors Affecting GRDDS [7,8]:**

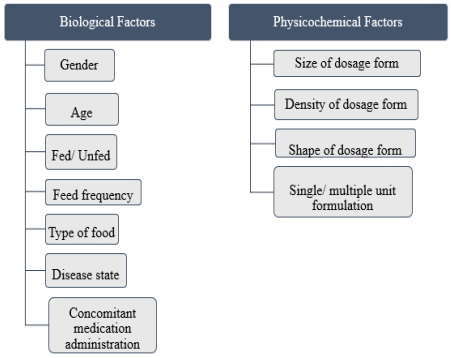


Figure 3: Factors affecting GRDDS

❖ **Advantages and Disadvantages of GRDDS: [9,10]**

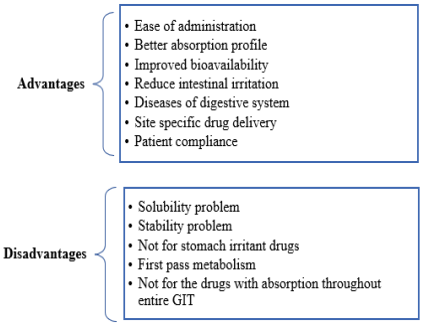


Figure 4: Advantaged and Disadvantages of GRDDS

❖ **Approaches For Gastro-Retentive Drug Delivery System:**

The following are some of the several methods that have been explored for creating dosage forms that results in sufficient gastric retention and release inside the stomach region [1,2,11]:

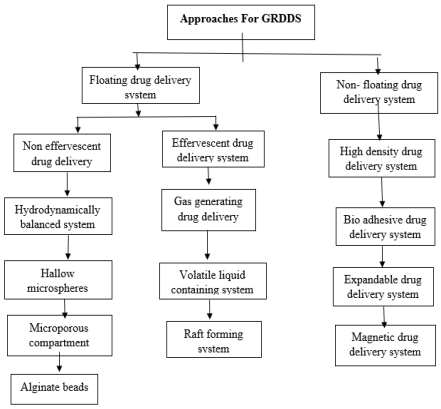


Figure 5: Approaches for GRDDS

A. High Density Drug Delivery System:

Gastric contents have an analogous viscosity as water (1.004 g/ cm3). Sedimentation has been used

as a retention medium. A viscosity lesser than 2.5 g/ cm3 is needed to significantly extend GIT. Excipients that are generally employed include barium sulfate, zinc oxide, titanium dioxide, iron, and so on [12,13].

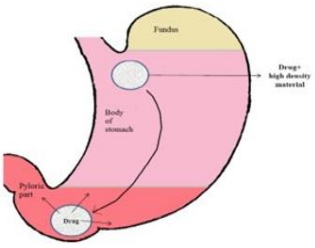


Figure 6: High density drug delivery system

B. Floating Drug Delivery System:

Low-density devices known as floating drug delivery systems (FDDS) can float above stomach contents and stay in the stomach for extended periods of time without slowing down the rate at which the stomach empties. While the system floats above the gastric contents, the medicine is gently released at the desired rate. This leads to enhanced gastric retention time and greater control of changes in plasma medication concentrations [14,15].

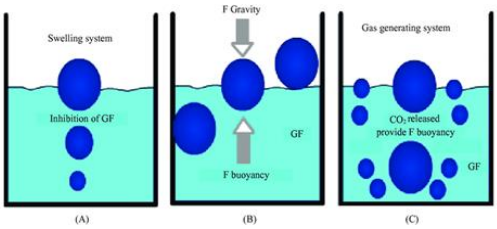


Figure 7: Floating drug delivery system

❖ **Hydro-Dynamically Balanced System:**

These systems are often made up of hydrophilic gel-forming polymers such as HPMC, hydroxy ethyl cellulose, hydroxy propyl cellulose and alginic acid, and are intended for single-unit administration. Hygroscopic gelatin rapidly dissolves in stomach juice, exposing the hydrophilic polymer and medication contents to the bodily fluids. The polymer fraction existing on the surface is then hydrated and swollen, resulting in a floating mass [7,16].

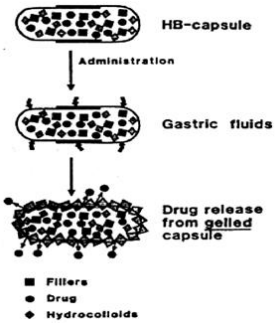


Figure 8: Hydrodynamically balanced system

❖ **Gas Generating System:**

Carbonate/bicarbonate salts and citric/tartaric acid react effervescently to release CO2 in buoyant delivery methods. The CO2 is then trapped in the jellified hydrocolloid layer, lowering its specific gravity and causing it to float above stomach fluid. The dosage forms are designed to create C02 when in contact with acidic gastric contents, which is then encapsulated in swelling hydrocolloids to offer floating properties [17,18].

❖ **Raft Forming System:**

Antacids and drugs for gastrointestinal diseases and infections have been administered using raft-forming systems, which have attracted a lot of interest. This type of GRDDS is induced by the production of a viscous gel in contact with gastric fluids, which forms a continuous layer known as RAFT on top of the fluids due to low bulk density brought on by CO2 formation. Alkaline bicarbonates or carbonates that produce CO2 are typically included in this system's composition, along with a gel-forming substance (such as alginic acid) to help the system float on the stomach juices and become less dense [19-21].

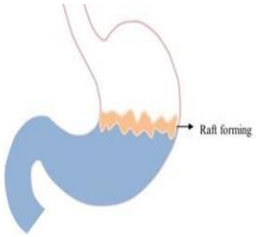


Figure 9: Raft forming system

❖ **Low Density System:**

The time lag before floating on the stomach contents is a major drawback of the effervescent delivery mechanism. Prior to floating and medication release, it is likely that the delivery system will be purged during this time. Hence, low density systems (less than 1000 mg/cm^3) that demonstrate instantaneous drug floating and release on the stomach content surface have been created to get around this restriction. The system is essentially made up of low density materials that trap air or oil [11].

C. Expandable System:

These systems can be mechanically expanded in size in relation to their initial dimensions. They are composed of biodegradable polymers. They come in a variety of geometric shapes, such as tetrahedron, ring, or planner membrane made of bio-erodible polymer that is squeezed inside a stomach-extending capsule. If a dosage form in the stomach is larger than the pyloric sphincter, it will not pass through the stomach [22-24].

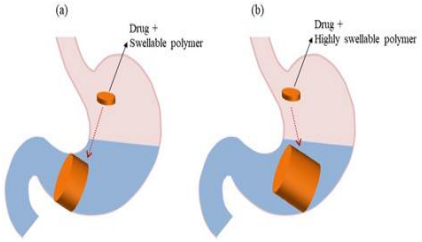


Figure 10: a) Expandable system b) Super porous hydrogel

D. Super Porous Hydrogel:

Conventional hydrogel absorbs water relatively slowly; it may take several hours to achieve an equilibrium condition. Super porous hydrogels (SPH) are porous hydrophilic materials that can absorb aqueous fluids up to a hundred times their own weight. They have a three-dimensional cross-linked, network-like structure. Due to rapid water uptake through multiple linked open pores (average pores of 200 µm), maximum swelling is typically obtained in a fraction of a minute [25,26].

E. Bio-Adhesive System:

By sticking to the gastric mucous membrane of bio-adhesive system, the gastric retention time has increased. The adherence of the delivery system to the stomach wall increases bioavailability by extending residence duration. Nevertheless, the propulsion force of the stomach wall cannot be

resisted by the gastric mucoadhesive force alone [25,26].

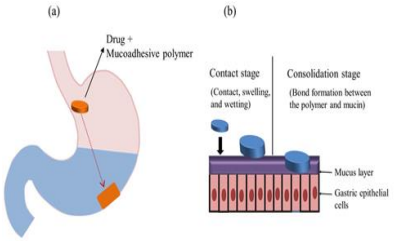


Figure 11: Bioadhesive system

F. Magnetic System:

Using this procedure, a tiny magnet is incorporated into the dose form, and a second magnet is positioned on the abdomen above the stomach. Precise setting of the external magnet may result in less patient cooperation [25].

❖ **Stomach Specific Floating *In-Situ* Gel:**

An applicable system of delivering regulated drug delivery within the stomach has been made possible by gastro-forgetful in- situ gel forming systems, in which an environment-specific gel forming solution floats on the top of the gastric fluids (owing to its lower viscosity than the gastric contents) once it has gelated. This system uses a low density solution, when in contact with the stomach fluids, changes the polymeric conformation to produce a viscid gel with a viscosity that's lower than the gastric fluids. This low density gel conformation produces the continual and phased drug release in addition to the significant desired gastro retention to extend the contact period[6].

❖ **ADVANTAGES:**

- *In-situ* gel offers a greater effective surface area than tablets because it creates a low-density viscous layer on the stomach contents. This increases the drug's release and boosts its bioavailability.
- Compared to floating tablets, floating obtained is faster.

❖ **Limitations**

- *In-situ* gel forming systems are essentially solutions that are more prone to stability issues as a result of microbiological or chemical deterioration (hydrolysis, oxidation, etc.).
- If such a system is not stored correctly, it may experience instability issues as a result of the system's pH changing over time or when it is kept at an improper temperature. Certain polymers may also develop gel inside the packaging in which they are stored if they are exposed to radiations (such as UV, visible, electromagnetic, etc.).

❖ **Approaches To Produce *In-Situ* Gel:**

Various mechanisms have been reported to underlie the formation of *in-situ* gel:

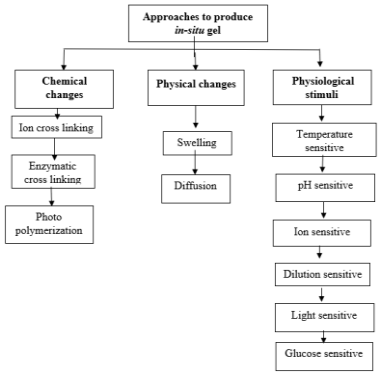


Figure 13: Approaches for *in-situ* gel

❖ **Physical Changes [27]:**

- **Swelling:** Swelling occurs when a polymer in the system, such as glycerol mono-oleate, absorbs water from the surroundings and swells to produce a viscous gel.
- **Diffusion:** Diffusion occurs when a solvent, such as N-methyl pyrrolidone, dissolves or disperses a drug and polymer into the surrounding tissues, precipitating the polymer to form gel.

❖ **Chemical Changes:** Gel formation may result from alterations in the systems chemical environment that create polymeric cross linking.

- **Ionic cross-linking:** When different ions, such as Na^+, K^+, Ca^{2+}, Fe^{2+}, etc., are present in body fluids, ion-sensitive polysaccharides like carrageenan, gellan gum, pectin, etc., experience phase transitions because the polymer cross-linking develop [28].
- **Enzymatic cross-linking:** The most practical method of gel production is thought to be cross-linking, which creates a polymer network through the presence of enzymes in body fluids [27].
- **Photo polymerization:** When a gel producing system is injected into tissues, it can generate gels such as ethyl eosin, 2, 2 dimethoxy-2-phenyl acetophenone, and others within the tissues when exposed to microwave, UV, or electromagnetic radiation [27,29].

❖ **Physiological Stimuli:**

The following physiological triggers can result in the development of gel:

- **Change in temperature:** This method shows a temperature-dependent phase transition from a relatively high viscosity gel to a less viscous solution. A sudden change in temperature causes the solubility of the polymer within the system to alter, and this interaction between the polymers results in the formation of a hydrophobic solvated macromolecule [27,29].
- **Change in pH:** Polymers with different ionizable groups in their chemical structure, such as polymethacrylate, polyacrylic acid, and its derivative carbopol, undergo gel formation in response to pH changes. When the pH rises, polymers containing anionic groups cause swelling to increase, whereas polymers containing cationic groups exhibit decreasing swelling [6].
- **Dilution sensitive:** In the presence of more water, a polymer found in this kind of hydrogel goes through a phase transition. More polymer can be utilized if the system is going through a phase change as a result of being diluted with water. Example, Lutrol F68 [51].
- **Light sensitive:** Light-sensitive hydrogels can be employed as *in-situ* forming gels for cartilage tissue engineering or in the creation of photo-responsive artificial muscle. In order to create a gel by enzymatic processes, polymerizable functional groups and their

initiators, such as ethyl eosin and camphorquinone, can be injected into tissue and electromagnetic radiation applied [51].

- **Glucose sensitive:** Insulin-releasing hydrogels have been used is intelligent stimuli-responsive delivery devices. In reaction to blood glucose levels, cationic pH-sensitive polymers that contain glucose oxidase and immobilized insulin can swell, pulsatively release the trapped insulin [51].

Ideal Characteristics of Polymer [50]:

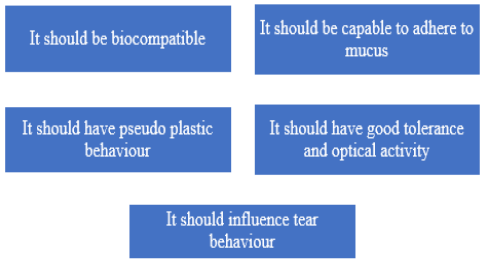


Figure 14: Characteristics of polymers

Polymers Used [51]:

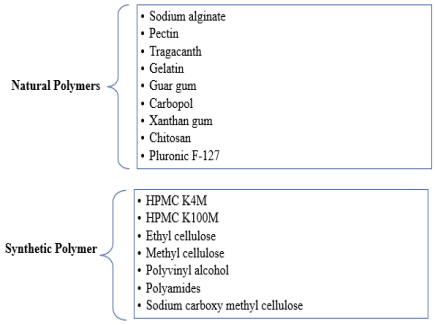


Figure 15: Polymers used for *in-situ* gel

- **Sodium alginate:** One common natural-origin polymer is sodium alginate. The chemical composition of this salt is alginic acid; 1,4-glycosidic linkages bind the residues of -L-glucuronic acid and -D-mannuronic acid together. Alginates dissolved in water can solidify into gels when they come into contact with di- or trivalent ions, such as calcium and magnesium ions [28,30].
- **Gellan gum:** Gellan gum is a chemically anionic deacetylated polysaccharide that is secreted by the pseudomonas elodea (Sphingomonas elodea). A change in temperature or the presence of cations (such as Na^+, K^+, or Ca^{2+}) causes gellan gum to develop [28,29].
- **Pectin:** These are anionic polysaccharides of plant origin. Gel formation occurs in pectin when divalent ions, such as Ca^{2+}, are present. This results in ionic cross linking, which links the galacturonic acid units, and pH dependent gelling, which occurs when H ions are present [27].
- **Xyloglucan:** It is a polysaccharide derived from plants that is extracted from tamarind seeds. While xyloglucan itself does not produce gels, diluted solutions that have been partially broken down by galactosidase when heated up to a certain temperature [27].
- **Xanthan Gum:** Extracting a high molecular weight extracellular polymer, xanthan gum is generated by the bacterium xanthomonas campestris. A powerful gel can be created by

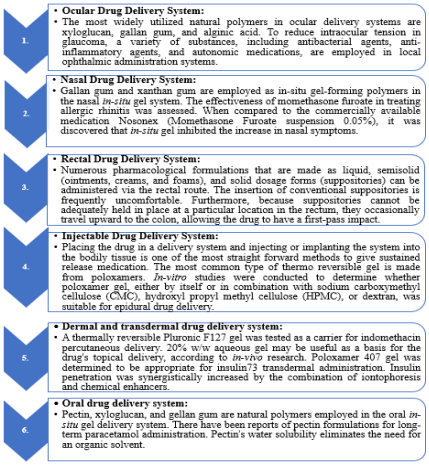
combining positively charged polymers with xanthan gum [31].

- **Chitosan:** By alkaline deacetylating chitin, a natural and adaptable polycationic polymer known as chitosan is produced. It is non-toxic, thermosensitive, and biodegradable. Up to a pH of 6.2, chitosan, a biocompatible pH-dependent cationic polymer, stays dissolved in aqueous solutions [32].
- **Carbopol:** The pH-dependent polymer carbopol remains in solution at an acidic pH but forms a low viscosity gel at an alkaline pH. When used in conjunction with carbapol, HPMC gives the carbopol solution viscosity while lowering its acidity [33].

❖ **Evaluation Of Stomach Specific In -Situ Gel System:**

- **Appearance:** Particulate matter should not be present, and *in-situ* solutions should be transparent. The amount of time needed for a solution to become a gel in a buffer with a pH of 1.2 is monitored, and the gel's visual consistency is examined [34].
- **Viscosity:** Viscosity of solution is measured with a Brookfield viscometer or a cone and plate viscometer at an appropriate temperature (25 ± 1^0 C) using 1 or 2 milliliters of sample aliquots before and after gelling [30,34].
- **pH of *in-situ* gel:** A calibrated pH meter is used to measure the pH of the gel-forming solution at 27^0C [34].
- ***In -vitro* gelation time:** Using a USP (Type II) dissolution device with 500 mL of 0.1N HCl (pH 1.2) at 37±0.5ºC, the *in-vitro* gelation time was ascertained. As the formulation came into contact with 0.1N HCl and the time was recorded, it changed from a sol to a gel. The amount of time needed for an *in-situ* gelling system to gel initially is known as the gelling time. The gel was found to float on the buffer solution in a matter of seconds [33].
- **Buoyant time:** The floating lag time, also known as the buoyant time, is the amount of time it takes the gel to rise to the top from the bottom of the dissolution flask. Visual examination was used to determine the floating lag time of the gel in a USP type II dissolution test device holding 500 ml of 0.1 N HCl (pH 1.2) at 37±0.5ºC [33].
- **Strength of gel:** The gel is made from the sol form in a beaker. A rheometer probe is little by little pushed through the gel by raising the beaker containing the gel at a specific rate. It can be determined by monitoring variations in the probe's loading as a function of the probe's depth of immersion below the gel surface[33].
- ***In-vitro* drug release study:** Using a USP dissolving equipment (type II) at 50 rpm in 900 ml of 0.1N HCl at pH 1.2 at 37 C, *in-vitro* drug release is measured. A Petri plate containing 10 milliliters of the formulation is placed in a dissolving vessel. Subsequently, the dissolve medium is silently added to the dissolution vessel. At every predetermined period, an appropriate sample is taken and replaced with new medium. A minimum of eight hours should be spent conducting the dissolution study [30].

❖ **Applications [50]:**



❖ Recent Research Activities on Stomach Specific *In-Situ* Gel [51]:

Table 2: Recent research activities on *in-situ* gel

Sr. No.	Author	Drugs	Category	Reference No.
1.	Jayswal et al.	Cimetidine	Antihistaminic	61
2.	Patel et al.	Ranitidine HCl	Antihistaminic	62
3.	Jivani et al.	Baclofen	Skeletal muscle relaxant	63
4.	Itoh et al.	Paracetamol	NSAID	64
5.	Wamorkar et al.	Metoclopramide	Anti-emetic	65
6.	Bhimani et al.	Clarithromycin	Antibiotics	66
7.	Patel et al.	Chlordiazapoxide	Antidepressant	67
8.	Rajinikanth et al.	Clarithromycin	Anti-H. pylori	68
9.	Rajlakshmi et al.	Levofloxacin Hemihydrate	Anti-H. pylori	69
10.	Rathod et al.	Ambroxol hydrochloride	Secretolytic agent	70
11.	Patel et al.	Hydrochlorothiazide	Antihypertensive/ Diuretic	71
12.	Patel et al.	Famotidine	Antihistaminic	7
13.	Lahoti et al.	Ofloxacin	Antibiotic	72
14.	Anyanwu et al.	Meloxicam	NSAID	73
15.	Madan et al.	Pregabalin	Anticonvulsant	74

❖ Marketed Formulations Available as GRDDS [52]:

Table 3: GRDDS available in market

Sr. No.	Dosage form	Drugs	Brand name	Company
1.	Colloidal gel forming FDDS	Ferrous sulphate Antianemic	CONVIRON	Ranbaxy, India

2.	Floating Controlled Release Capsule	Levodopa, Benserazide	MODAPAR	Roche Products, USA
3.	Floating Capsule	Diazepam	VALRELEASE	Hoffmann-LaRoche, USA
4.	Effervescent Floating Liquid alginate Preparation	Aluminium hydroxide, Magnesium carbonate	LIQUID GAVISON	Glaxo Smith Kline, INDIA
5.	Floating Liquid alginate Preparation	Aluminum - Magnesium antacid	TOPALKAN	Pierre Fabre Drug, FRANCE
6.	G;2as-generating floating Tablets	Ciprofloxacin	CIFRAN OD	Ranbaxy, INDIA
7.	Bilayer floating Capsule	Misoprostil	CYTOTEC	Pharmacia, USA

❖ ***In-Situ*** **Gelling System Available in Market** [31,51]**:**

Table 4: *In-situ* formulations in market

Sr. No.	Dosage form	Drug/ Polymer	Brand name	Company country
1.	Opthalmic	Timolol maleate	Timoptic- XE	Merk and Co
2.	Regel: depot technology	Paclitaxel	Oncogel	Macromed's drug delivery
3.	Injectable depot formulations	Interleukin- 2	Cytoryn	Macromed's drug delivery
4.	Opthalmic	Lidocaine HCl	Akten	
5.	Opthalmic solution	Azithromycin	Azasite	Insite vision
6.	Opthalmic gel	Pilopine	Pilopine HS	Alcon lab Inc.
7.	Opthalmic	Ganciclovir	Virgan	
8.	Contact lenses	Hydrophilic acrylic acid	Hypan	Hymedix international
9.	Skin adhesive gel	Chitosan	Aquatrix	Hydromere
10.	Topical skincare	Interpolymers of PVP and grafted with urethane	Aquamere	Hydromere
11.	Vaginal insert	Polyethylene oxide and urethane	Cervidil	Controlled therapeutics, UK
12.	Opthalmic, buccal, nasal and vaginal administration	Polyacrylic acid and poly glycol	Smart hydrogel	MedLogic Global Polymouth, UK
13.	Oral administrtion	Chitosan and PEG	SQZ Gel oral controlled	Macromed

❖ **Some Us Patents for In-Situ Gel Drug Delivery System [51]:**

Table 5: Patentable formulations

Sr. No.	US Patent	Formulations
1.	US20120009275	*In-situ* forming hydrogel wound dressing containing antimicrobial agents
2.	US20050063980	Gastric raft composition
3.	US5360793	Rafting antacid formulations
4.	US20110082221	*In- situ* gelling system as sustained delivery for eye
5.	US20020119941	*In-situ* gel formulation of pectin
6.	US20130101656	*In-situ* gelling drug delivery system
7.	US20140221307	*In-situ* gel forming compositions

❖ **Comparison Between Conventional and Gasro-Retentive Drug Delivery System [49]:**

Table 6: Comparison between conventional and GRDDS

Sr. No.	Parameters	Conventional drug delivery	Gastro retentive drug delivery
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.	Drugs having rapid absorption through GIT	Not much advantageous	Very much advantageous
6.	Drugs which degraded into colon	Not much advantageous	Very much advantageous
7.	Drugs which are poorly soluble at an alkaline Ph	Not much advantageous	Very much advantageous
8.	Dose dumping	High risk of dose dumping	No risk of dose dumping

❖ **CONCLUSION:**

It is quite difficult to develop an effective gastro retentive dosage form for stomach-specific medication

delivery. Therefore, a number of strategies have been used to achieve the intended gastro retention, with the floating medication delivery system emerging as the most promising method. One type of floating drug delivery system is the floating *in-situ* gelling system, which transitions from a sol to gel state in an acidic stomach and releases the drug specifically into the stomach for a longer period of time while remaining buoyant on the surface of the gastric fluid. One benefit of these systems is that medications that are absorbed from the upper portion of the stomach absorb them more effectively. The local exertion of the medicine is boosted as the system is in the stomach longer because the gastric mucosa is in contact with it for a longer period of time. This results in fewer dosage adjustments and increased therapeutic effectiveness. Understanding the behavior of polymers that float and gel will help us to increase the stomach retention and, consequently, the bioavailability of a variety of pharmacologically active substances. Similar to this, such a method is more dependable because it has superior stability and drug release compared to other traditional dose forms.

REFERENCES

1. Foda N H and S M: Gastro retentive drug delivery systems as a potential tool for enhancing the efficacy of antibiotics: A Review, International Journal of Pharma and Biosciences (2011), 2(2): 94-104.
2. Nasa P, S Mahant and D Sharma: Floating systems: a novel approach towards gastro retentive drug delivery systems, International Journal of Pharmacy and Pharmaceutical Sciences (2010), 2(3): 2-7.
3. Lahoti SR, Iftequar S, Sabina M, Dehghan MH, Shoaib S, Mohiuddin S: An Overview of Gastro-retentive Drug Delivery System, International Research Journal of Pharmacy (2011), 2: 50-57.
4. Wilding I R, A J Coupe and S S Davis: The role of α-scintigraphy in oral drug delivery, Advance Drug Delivery Review (2001), 46: 103-124.
5. Patil J M, P S Gide and V J Kadam: Trends in floating drug delivery system, Journal of Scientific and Industrial Research (2006), 65: 11-21.
6. Patel J K, J R Chavda and M K Modasiya: Floating in-situ gel based on alginate as carrier for stomach-specific drug delivery of famotidine, International Journal Of Pharmaceutical Sciences And Nanotechnology: (2010), 3(3): 1092-1104.
7. Arunachalam A M, Karthikeyan K, Konam H P Prasad, S. Sethuraman, S. Ashutoshkumar and S. Manidipa: Floating drug delivery systems: A Review, International Journal of Pharmaceutical Science and Research: (2011), 2(1): 76-83.
8. Arora S., J. Ali, A. Ahuja, R.K. Khara and S. Baboota: Floating drug delivery systems: A Review, American Association of Pharmaceutical Scientists Pharmscitech: (2005), 6(3): E372-E390.
9. Shaha, S.H., J.K. Patel, K. Pundarikakshudu and N.V. Patel: An overview of a gastro-retentive floating drug delivery system, Asian Journal of Sciences: (2009), 4(1): 65-80.
10. Khan, A.D. and M. Bajpai: Floating drug delivery system: an overview, International Journal PharmaTech and Research: (2010), 2(4): 2497-2505.
11. Bardonnet, P.L., V. Faivre, W.J. Pugh, J.C. Piffaretti and F. Falson: Gastro retentive dosage forms: overview and special case of Helicobacter pylori, Journal of Controlled Release:(2006), 1(11): 1-18.
12. Hoffman A, Stepensky D, Lavy E, Eyal S, Klausner E, Friedman M: Pharmacokinetic and pharmacodynamic aspects of gastroretentive dosage forms, International Journal of Pharmaceutics: (2004), 277: 141–153.
13. Murphy CS, Pillay V, Choonara YE, Du Toit LC: Gastroretentive drug delivery systems:

Current developments in novel system design and evaluation, Current Drug Delivery: (2009), 6:451– 460.
14. Singh BN, Kim KH: Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention, Journal of Controlled Release: (2000), 63:235–259.
15. Amrutkar PP, Chaudhari PD, Patil SB: Design and in vitro evaluation of multiparticulate floating drug delivery system of zolpidem tartarate, Colloids and Surfaces B: Biointerfaces: (2012),89:182–187.
16. Reddy, L.H. and R.S. Murthy: Floating dosage systems in drug delivery, Critical reviews in therapeutic drug carrier systems: (2002), 19(6): 553-585.
17. Singh BN, Kim KH: Floating drug delivery systems: an approach to oral controlled drug delivery via gastric retention, Journal of Controlled Release: (2000), 63:235–259.
18. Amrutkar PP, Chaudhari PD, Patil SB: Design and in vitro evaluation of multiparticulate floating drug delivery system of zolpidem tartarate, Colloids and Surfaces B: Biointerfaces: (2012), 89:182–187.
19. Johnson FA, Craig DQM, Mercer AD, Chauhan S :The effects of alginate molecular structure and formulation variables on the physical characteristics of alginate raft systems, International Journal of Pharmaceutics: (1997),159:35–42.
20. Hampson FC, Farndale A, Strugala V, Sykes J, Jolliffe IG, Dettmar PW: Alginate rafts and their characterisation, International Journal of Pharmaceutics: (2005), 294:137–147.
21. Kapadia CJ, Mane VB: Raft-forming agents: Antireflux formulations, Drug Development and Industrial Pharmacy: (2007), 33:1350–1361.
22. Streubel A, Siepmann J, Bodmeier R: Drug delivery to the upper small intestine window using gastroretentive technologies, Current Opinion in Pharmacology: (2006), 6:501–518.
23. Darandale SS, Vavia PR: Design of a gastroretentive mucoadhesive dosage form of furosemide for controlled release, Acta Pharmaceutica Sinica B: (2012), 2:509–517.
24. Klausner EA, Lavy E, Friedman M, Hoffman A: Expandable gastroretentive dosage forms, Journal of Controlled Release: (2003), 90:143–162.
25. Omidian H, Rocca JG, Park K: Advances in super porous hydrogels, Journal of Controlled Release: (2005), 102:3–12.
26. Tang C, Yin C, Pei Y, Zhang M, Wu L: New super porous hydrogels composites based on aqueous Carbopol® solution (SPHCs): synthesis, characterization and in vitro bio-adhesive force studies, European Polymer Journal; (2005), 41:557–562.
27. Rathod, H., V. Patel and M. Modasiya: In situ gel as a novel approach of gastro retentive drug delivery, International Journal Of Pharmacy and Life Sciences: (2010), 1(8): 440-447.
28. Nagarwal, R.C., A. Srinatha and J.K. Pandit: In situ forming formulation: development, evaluation and optimization using 3 factorial design, AAPS Pharmscitech: (2009), 10(3): 977-984.
29. Shah, D.P. and G.K. Jani: A newer application of physically modified gellan gum in tablet formulation using factorial design, ARS Pharmaceutica: (2010), 51(1): 28-40.
30. Ganapati, R., K.S. Bhimagoni and S. Anegundha: Floating drug delivery of a locally acting H2-antagonist: an approach using an in situ gelling liquid formulation, Acta Pharmceutica: (2009), 59: 345-354.
31. Nirmal H.B, Bakliwal S.R, Pawar S.P: In-situ gel: New trends in controlled and sustained drug delivery system, International Journal of

Pharmtech Research:(2010), 2(2):1398-1408.
32. S.S Raut and H. A. Shinde: In-situ raft forming system: A review, International Journal of Pharmacognosy: (2018), 5(6): 337-349.
33. Avinash Sharma, Jyoti Sharma, Rupinder Kaur, Vinay Saini: Development and characterization of in situ oral gel of spiramycin, Biomed Res. Int.: (2014), 1-7.
34. Modasiya, M.K., B.G. Prajapati, V.M. Patel and J.K. Patel: Sodium alginate based in-situ gelling system of famotidine: preparation and in-vivo characterizations, e-Journal of Science and Technology: (2010), 5(1): 27-42.
35. Jayswal BD, Yadav VT, Patel KN, Patel BA & Patel PA: Formulation and Evaluation of Floating In-situ Gel Based Gastro Retentive Drug Delivery of Cimetidine, International Journal for Pharmaceutical Research Scholars: (2012), 1(2):327-337.
36. Patel RP, Baria AH, Pandya NB & Tank HM: Formulation Evaluation and optimization of stomach specific in-situ gel of Ranitidine hydrochloride, International journal of Pharmaceutical sciences and Nanotechnology: (2010), 3(1): 834-843.
37. Jivani RR, Patel CN & Jivani NP, The influence of variation of gastric pH on the gelation and release characteristics of in-situ gelling sodium alginate formulations, Acta Pharmaceutica Sciencia: (2010), 52: 365-369.
38. Itoh K, Hatakeyama T, Shimoyama T, Miyazaki S, D'Emanuele A & Attwood D: In-situ gelling formulation based on methylcellulose/pectin system for oral sustained drug delivery to dysphagic patients, Drug Development and Industrial Pharmacy: (2011), 37(7): 790-797.
39. Wamorkar V, Varma MM & Manjunath SY: Formulation and Evaluation of Stomach Specific In-Situ Gel of Metoclopramide Using Natural, Bio Degradable Polymers, International Journal of Research in Pharmaceutical and Biomedical Sciences: (2011), 2(1):193-201.
40. Patel RP, Dadhani B, Ladani R, Baria AH & Patel J: Formulation, evaluation and optimization of stomach specific in-situ gel of clarithromycin and metronidazole benzoate, International Journal of Drug Delivery: (2010), 2: 141-153.
41. Patel RP, Ladani R, Dadhaniya B & Prajapati BG: In-situ gel Delivery systems for Chlordiazapoxide using Artificial Neural Network, International Journal of Pharmaceutics: (2010), 1(1): 10-22.
42. Rajinikanth PS & Mishra B: Floating in-situ gelling system for stomach site-specific delivery of clarithromycin to eradicate H. pylori, Journal of Controlled Release: (2008), 125(1):33-41.
43. Rajalakshmi R, Sireesha A, Subhash KV, Venkata PP, Mahesh K & Naidu KL: Development and Evaluation of a Novel Floating In-situ Gelling System of Levofloxacin Hemihydrate, International Journal of Innovative Pharmaceutical Research: (2011), 2(1):102-108.
44. Rathod H, Patel V & Modasiya M: Development, evaluation, and optimization of gellan gum Based in-situ gel using 32 factorial designs, International Journal of Biomedical Research (2011), 2(4):235-245.
45. Patel RR & Patel JK: Development and evaluation of in-situ novel intragastric controlled release formulation of hydrochlorothiazide, Acta Pharmaceutica:(2011), 61: 73-82.
46. Lahoti SR, Shinde RK, Ali SA & Gulecha B: pH triggered sol-gel transition system of ofloxacin for prolonged gastric retention. Der Pharmacia Sinica, 2011; 2(5): 235-250.

47. Anyanwu NCJ, Adogo LY, Ajide B. Development and evaluation of in situ gelling gastro retentive formulations of Meloxicam, Universal Journal of Pharmaceutical Research: (2017), 2(3): 10-13.
48. Madan JR, Adokar BR, Dua K: Development and evaluation of in situ gel of pregabalin, Int J Pharma Investig: (2015), 5:226-33.
49. Patole R, Chaware B, Mohite V, Redasani VK: A Review for Gastro - Retentive Drug Delivery System, Asian Journal of Pharmaceutical Research and Development: (2023), 11(4):79-94.
50. Sudhi U S, Savitha S, Mathan S: Floating Oral In-Situ Gelling System: A Review, Journal of Pharmaceutical Sciences and Research: (2020), 12(10): 1315-1319.
51. Hemendrasinh JR, Dhruti PM: A Review on Stomach Specific Floating In-Situ Gel, International Journal of Pharmaceutical Research:(2014), 6(4): 19-30.
52. Shivram Shinde, Imran Tadwee, Sadhana Shahi: Gastro retentive Drug Delivery System: A Review, Int. J. of Pharm. Res. & All. Sci.: (2011), 1(1): 01-13.

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