JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

# GASTRORETENTIVE DRUG DELIVERY SYSTEMS FOR ORAL ROUTE OPTIMIZATION

**[1]Anushka Ghogare, [2]Ms. Mohini B. Yadav, [3]Dr. Vijaykumar Kale,**
**[4]Dr. Mahesh Thakare, [5]Vaibhav Narwade**

[1]Student, [2]Assistant Professor, [3]Principal, [4]Associate Professor, [5]Assistant Professor
[1]Department of B. Pharmacy,
[1]Kasturi Shikshan Sanstha College of Pharmacy, Shikrapur, India.

***Abstract*:** Oral drug delivery represents the most preferred pharmaceutical route due to its non-invasive nature, patient compliance, and convenience. However, multiple physiological barriers including variable gastric emptying, fluctuating pH levels, limited absorption windows, enzymatic degradation, and transit variability significantly compromise bioavailability and therapeutic effectiveness of many active pharmaceutical ingredients. Gastroretentive drug delivery systems (GRDDS) have emerged as innovative solutions that maintain dosage forms in the gastric region for extended periods, enabling targeted and controlled drug release. The prolonged gastric residence time achieved through GRDDS reduces systemic adverse effects, improves therapeutic outcomes, decreases dosing frequency, and maintains stable plasma drug concentrations. This review comprehensively examines the physiological factors influencing gastric retention, categorizes major GRDDS technologies including floating, mucoadhesive, high-density, swellable, expandable, and magnetic systems, and discusses polymeric materials and excipients essential for formulation development. Additionally, the review addresses advantages, disadvantages, and limitations of GRDDS, evaluates various characterization methodologies, and highlights clinical applications for drugs with absorption windows restricted to the upper gastrointestinal tract. Modern GRDDS technologies employ biodegradable matrices, sophisticated polymers, and innovative design approaches to maximize drug delivery efficacy. This systematic review synthesizes contemporary advances in GRDDS development, establishing GRDDS as a crucial technology for enhancing bioavailability, therapeutic efficacy, and patient compliance in oral pharmaceutical delivery.

**Keywords:** Gastroretentive drug delivery systems, Gastric retention, Floating systems, Mucoadhesive delivery, Prolonged gastric residence time, Controlled drug release, Pharmaceutical formulation.

## I. INTRODUCTION

Oral route represents the most popular and convenient method of pharmaceutical administration, offering multiple advantages including simplicity, high patient compliance, versatility in dosage form design, economic viability, and ease of storage and transportation[1]. Approximately 80% of pharmaceutical products are formulated as oral dosage forms, reflecting the clinical and commercial significance of this delivery route[2]. However, the gastrointestinal tract (GIT) presents substantial physiological challenges that significantly compromise the bioavailability and therapeutic efficacy of numerous active pharmaceutical ingredients (API)[3]. Variable gastric emptying time, fluctuating pH across different gastrointestinal regions, limited absorption windows restricted to specific sites such as the stomach or upper small intestine, enzymatic degradation of acid-labile compounds, and transit variability represent major physiological limitations confronting conventional oral dosage forms[4].

For many pharmaceutical compounds, particularly those exhibiting absorption windows restricted to the upper gastrointestinal tract, narrow absorption zones, or instability in intestinal environments, conventional oral delivery results in suboptimal bioavailability and inadequate therapeutic concentrations. This limitation necessitates frequent dosing regimens, which compromises patient compliance and results in significant fluctuations in plasma drug concentrations with attendant consequences including reduced therapeutic efficacy and increased potential for concentration-dependent adverse effects[5]. Gastroretentive drug delivery systems

(GRDDS) represent an innovative pharmaceutical approach designed to overcome these physiological limitations through prolonged retention of the dosage form in the gastric region[6].

The fundamental principle underlying GRDDS is that extended gastric residence time permits sustained and controlled drug release in the upper gastrointestinal region where absorption is optimized, thereby substantially enhancing bioavailability and therapeutic effectiveness for drugs with absorption windows limited to gastric and upper small intestinal regions[7]. GRDDS technologies have advanced significantly, incorporating sophisticated polymers, biodegradable materials, and innovative design approaches that permit development of robust, efficient systems capable of maintaining therapeutic drug levels while reducing dosing frequency and improving patient compliance[8].

This comprehensive review systematically examines contemporary GRDDS technologies, gastric physiological factors influencing retention, formulation methodologies, polymeric materials and excipients, characterization approaches, and clinical applications[9]. The review synthesizes recent advances demonstrating that GRDDS represent a crucial technological advancement in pharmaceutical oral delivery, particularly for drugs requiring prolonged contact with gastric tissues or upper intestinal regions for optimal therapeutic outcomes[10].

## II. GASTRIC PHYSIOLOGY AND PHYSIOLOGICAL FACTORS INFLUENCING RETENTION

### A. Anatomical and Physiological Characteristics of the Stomach

The stomach represents a dynamic organ with complex physiological functions essential for food processing and initial drug absorption. Anatomically, the stomach comprises four distinct regions: the cardia, fundus, body, and pylorus, with each region possessing specialized functions[5]. The fundus serves as a reservoir for gastric gases, the body secretes digestive enzymes including pepsinogen and hydrochloric acid, while the pylorus functions as a regulatory zone responsible for mucus, gastrin, and pepsinogen secretion. The antral region serves as the primary site for mixing motions and functions as a propulsion pump for gastric emptying through powerful muscular contractions.

Gastric motility patterns exhibit significant differences between fasted and fed states. During the fasted state, an interdigestive series of electrical events termed the migrating myoelectric complex (MMC) occurs at regular intervals of approximately 1.5 to 3 hours, characterized by four distinct phases: Phase I (basal phase) lasting 40-60 minutes with uncommon compressions; Phase II (pre-burst phase) lasting 40-60 minutes with intermittent potential and compressions; Phase III (burst phase) lasting 4-6 minutes featuring strong, regular muscular contractions that propel undigested material into the small intestine; and Phase IV lasting 0-5 minutes occurring between phases III and I[2]. These Phase III contractions, known as "housekeeping waves," effectively clear gastric contents and can prematurely expel gastroretentive dosage forms if their properties do not provide sufficient retention mechanisms.

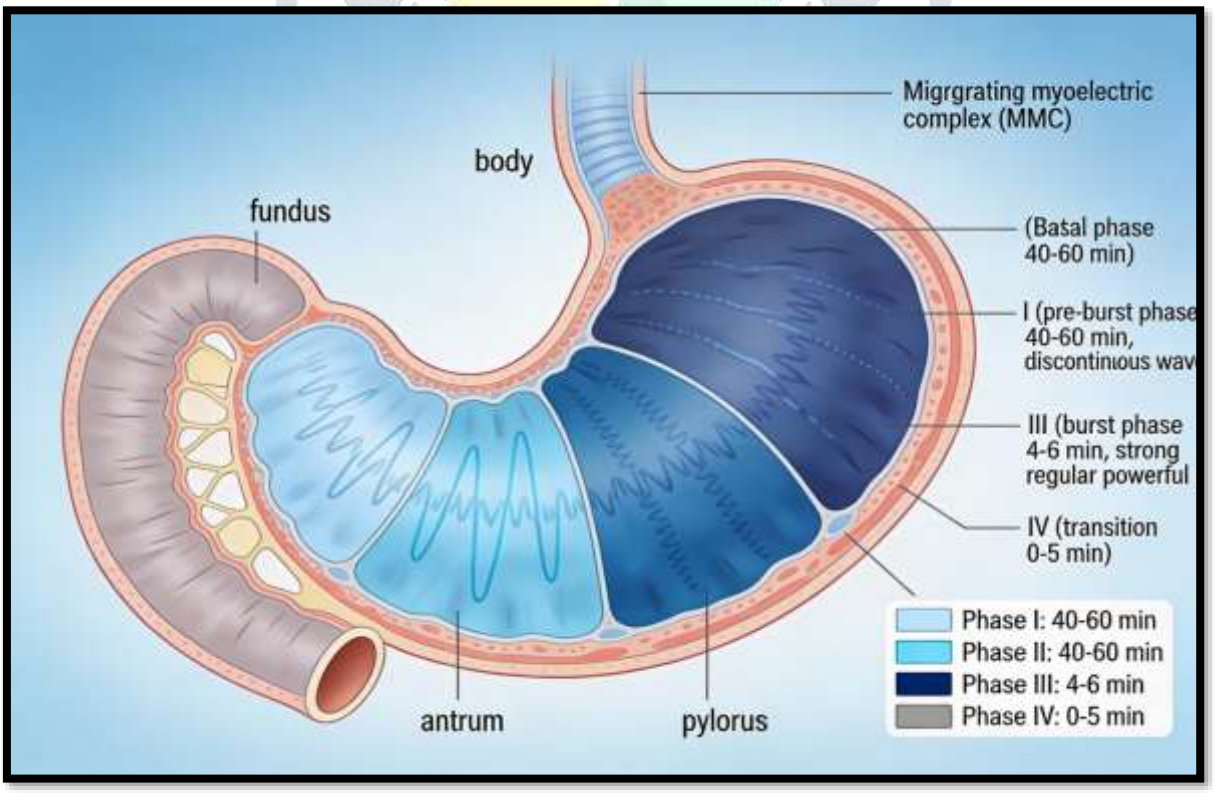



**Fig 1: Anatomy of Stomach and Migrating Myoelectric Complex (MMC) Phases During Fasted State**

Following meal ingestion, gastric motility patterns transition from fasted to fed state, characterized by continuous, irregular contractions that reduce food particles to sizes smaller than 1 mm and propel them toward the pylorus[3]. The transition from fasted

to fed motility patterns represents a critical factor influencing GRDDS performance, as the altered contractile patterns may compromise retention if dosage forms are not specifically designed to resist these powerful peristaltic movements.

### B. Factors Affecting Gastric Retention Time

Gastric retention time (GRT) depends upon multiple physiological, pharmaceutical, and patient-related factors that collectively determine the duration a dosage form remains in the gastric region. The buoyancy characteristics of floating systems fundamentally depend on their density relative to gastric contents, with optimal floating systems maintaining specific gravity less than 1.004 g/mL, the approximate density of gastric fluids[6].

Pharmaceutical factors significantly influencing gastric retention include dosage form size and shape. Dosage forms with unit diameters exceeding 7.5 mm demonstrate enhanced GRT compared to smaller units, while specific geometric configurations such as tetrahedron and ring-shaped devices with specific flexural modulus values demonstrate superior gastric retention compared to conventional cylindrical tablets. Polymer viscosity substantially affects drug release and rafting properties, with lower viscosity polymers demonstrating superior suitability for GRDDS compared to high-viscosity alternatives due to improved rafting characteristics and drug release modulation[7].

Patient-related and physiological factors equally impact GRT. The fed versus fasted state represents a critical determinant, with fasted conditions producing short GRT due to MMC-induced gastric clearance, while fed states substantially prolong GRT by suppressing MMC activity. Meal composition and caloric content exert profound effects, with high-protein and high-fat meals extending GRT by 4-10 hours compared to light meals. Gender differences manifest in GRT, with males demonstrating mean GRT of 3.4±0.4 hours compared to females of similar age exhibiting 4.6±1.2 hours[8]. Advanced age, particularly individuals exceeding 70 years, demonstrates significantly prolonged GRT, while posture influences retention with upright positioning providing superior protection for floating systems against postprandial emptying compared to supine positions. Additional factors including disease states such as diabetes and chronic gastrointestinal diseases, body mass index, physical activity levels, molecular weight and lipophilicity of administered drugs based on their ionization state, and co-administered medications collectively influence gastric retention characteristics.

## III. CLASSIFICATION AND TYPES OF GASTRORETENTIVE DRUG DELIVERY SYSTEMS

### A. Floating Drug Delivery Systems

Floating systems represent one of the most extensively developed and clinically significant GRDDS categories, relying on density characteristics that maintain specific gravity below gastric fluid density (1.004 g/cm³)[9]. This reduced density enables prolonged buoyancy, permitting sustained drug release over extended gastric residence periods. Floating systems are classified into two major categories: effervescent and non-effervescent systems, each employing distinct mechanisms for achieving and maintaining buoyancy.

Effervescent systems incorporate gas-generating substances including sodium bicarbonate, citric acid, and tartaric acid that react with gastric fluid to produce carbon dioxide gas. This generated gas becomes entrapped within hydrocolloid matrix structures, reducing overall system density and enabling flotation. The gas-generating reaction produces consistent $CO_2$ throughout gastric residence, maintaining stable buoyancy characteristics. Non-effervescent systems employ gel-forming or highly swellable cellulose derivatives and hydrocolloid polymers that absorb gastric fluid, form expanding gel matrices, and trap air within polymer networks, achieving and maintaining buoyancy through this mechanism[10].

Specialized floating system designs include volatile liquid systems utilizing inflatable chambers filled with liquids such as ether or cyclopentane that gasify at body temperature, intragastric floating delivery systems incorporating microporous compartments with pharmaceutical reservoirs and flotation chambers, inflatable systems containing bio-erodible polymer filaments that gradually dissolve permitting controlled gas release, and intragastric osmotically controlled systems combining osmotic pressure-driven delivery with flotation mechanisms[11].

### B. Non-Floating Gastroretentive Systems

High-density or sinking systems maintain specific gravity exceeding 2.4 g/cm³ through incorporation of excipients including iron powder, zinc oxide, barium sulfate, and titanium dioxide. These dense pellets resist peristaltic motions and remain within gastric folds proximal to the pyloric region, achieving extended GRT of 5.8 to 25 hours depending primarily on pellet density rather than diameter.

Mucoadhesive or bioadhesive systems utilize polymers with specific surface characteristics that adhere directly to gastric mucosal tissue through multiple mechanisms including wetting interactions, physical and chemical attraction forces, hydrogen bonding, and electrostatic interactions. Chitosan, a positively charged biopolymer derived from chitin, demonstrates particular effectiveness in mucoadhesive applications through ionic interactions with negatively charged gastric mucin, while polymers such as polycarbophil exhibit strong mucoadhesive properties through extensive swelling in gastric fluids[12].

Swellable systems expand to volumes obstructing pyloric passage upon contact with gastric fluids, achieving retention periods of several hours through mechanical obstruction of gastric emptying pathways. These polymeric matrices must balance swelling capacity with structural integrity, requiring careful selection of polymers with appropriate molecular weight and cross-linking density to maintain expanded configuration without loss of mechanical strength through dissolution or erosion[13].

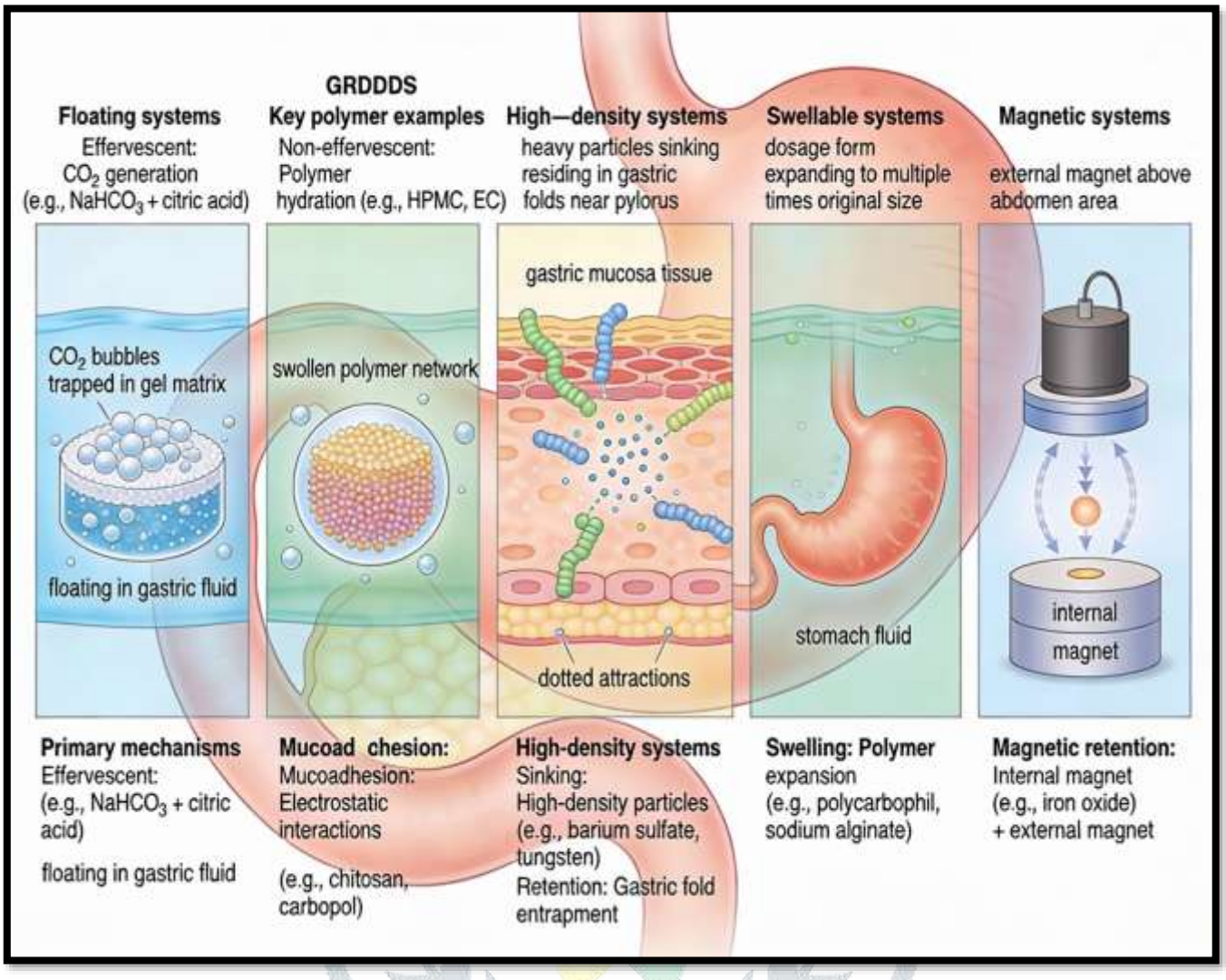



**Fig 2: Classification and Mechanisms of Major Gastroretentive Drug Delivery Systems**

Expandable systems undergo significant volume increases from compact, swallowable configurations to expanded retention-promoting geometries within the gastric environment. These systems typically employ polyethylene oxide and cross-linked polyvinyl alcohol as base polymers, achieving volume increases through hydration of interconnected polymer networks while maintaining structural integrity through appropriate cross-linking strategies[14].

## IV. POLYMERIC MATERIALS IN GRDDS FORMULATION

### A. Hydrophilic Polymers

Hydrophilic polymers form the fundamental structural components of most GRDDS formulations, capable of absorbing substantial water quantities, forming viscous gels, and regulating drug release through diffusion and matrix erosion mechanisms. Hydroxypropyl methylcellulose (HPMC) in various grades (K4M, K15M, K100M) represents the most commonly employed gel-forming polymer in GRDDS, swelling extensively in gastric fluids to form robust gel barriers that provide simultaneous buoyancy and sustained drug release[7]. Higher viscosity HPMC grades produce slower drug release through formation of thicker gel matrices that retard molecular diffusion.

Carbopol (carbomer 934P, 940, 971) comprises highly cross-linked polyacrylic acid polymers demonstrating exceptional swelling capacity and mucoadhesive properties. These polymers swell multiple times their original volume in acidic pH, providing robust gel formation for sustained release while simultaneously exhibiting bioadhesive interactions with gastric mucosa. Sodium alginate, a naturally occurring marine polymer, forms gels in the presence of gastric acid or calcium ions and demonstrates particular utility in raft-forming systems due to its biocompatibility, hydrophilicity, and biodegradability characteristics[8].

Natural polysaccharides including xanthan gum, guar gum, and pectin are increasingly incorporated into GRDDS formulations. Xanthan gum forms strong gels in gastric fluids while contributing to buoyancy through air entrapment mechanisms, guar gum

provides rapid hydration and viscosity modulation, and pectin serves as an anionic polymer suitable for gel formation and raft structure development in antacid and anti-reflux formulations.

### B. Hydrophobic and Swellable Polymers

Ethyl cellulose, a water-insoluble polymer, prevents excessive water penetration while maintaining reduced density, finding particular application in floating microspheres and microballoons where structural integrity must be preserved during extended gastric exposure. Eudragit polymers (RL, RS, NE, NM), comprising methacrylate copolymers with pH-independent swelling and permeability characteristics, provide sustained release capabilities through appropriately selected polymer grades[9]. Polyethylene oxide demonstrates high swelling capacity and elasticity, serving as the primary polymer in expandable tablet systems. Cross-linked polyvinyl alcohol provides structural stability while enabling controlled expansion without premature dissolution.

### C. Mucoadhesive Polymers

Chitosan, derived from chitin through deacetylation, demonstrates pronounced mucoadhesive properties through electrostatic interactions between its positive charges and negative charges on gastric mucin glycoproteins, making it particularly valuable for floating beads, mucoadhesive tablets, and nanoparticulate GRDDS formulations[10]. Polycarbophil exhibits strong mucoadhesive characteristics through extensive swelling in gastric environments combined with physical and chemical interactions with mucosal tissues. Sodium carboxymethyl cellulose contributes mucoadhesive properties through formation of sticky hydrophilic matrices that enhance gastric mucosal adherence.

## V. ADVANTAGES, DISADVANTAGES, AND LIMITATIONS OF GRDDS

### A. Advantages of Gastroretentive Delivery Systems

GRDDS provide substantial therapeutic advantages for pharmaceutical formulation development. Enhanced bioavailability and therapeutic efficacy result from prolonged drug exposure at optimal absorption sites, particularly for compounds with narrow absorption windows restricted to gastric or upper small intestinal regions[11]. Reduced dosing frequency follows from sustained and controlled drug release, improving patient compliance and reducing medication administration burden. Maintenance of stable plasma drug concentrations results in consistent therapeutic effects while minimizing concentration-dependent adverse effects. Local gastric treatment becomes feasible for medications targeting gastric disorders including peptic ulcers, H. pylori infections, and gastric lesions, enabling high local concentrations with minimal systemic side effects. Minimization of first-pass metabolism occurs through prolonged residence in gastric regions before intestinal absorption and hepatic metabolism.

### B. Disadvantages and Limitations

Despite significant advantages, GRDDS present notable limitations. Heavy dependence on variable and unpredictable gastric physiology compromises consistent performance across patient populations and administration circumstances. Fasting state MMC-induced gastric clearance may prematurely expel dosage forms before adequate drug release. Many drugs exhibit instability or degradation in acidic gastric environments, particularly acid-labile compounds susceptible to hydrolysis. Drugs causing gastric irritation, including NSAIDs and corticosteroids, become unsuitable for GRDDS due to enhanced irritation risk from prolonged gastric contact[12]. Floating systems require minimum gastric fluid volumes for proper function, with dehydration or reduced gastric secretion impairing buoyancy mechanisms. Patients with gastrointestinal disorders including gastroparesis, pyloric stenosis, or post-gastric surgery anatomy experience compromised GRDDS performance. Size and shape restrictions impose swallowing difficulties, particularly for elderly patients and individuals with dysphagia. Technological complexity requires advanced formulation expertise and manufacturing capabilities, substantially increasing development costs and timelines compared to conventional oral forms[13].

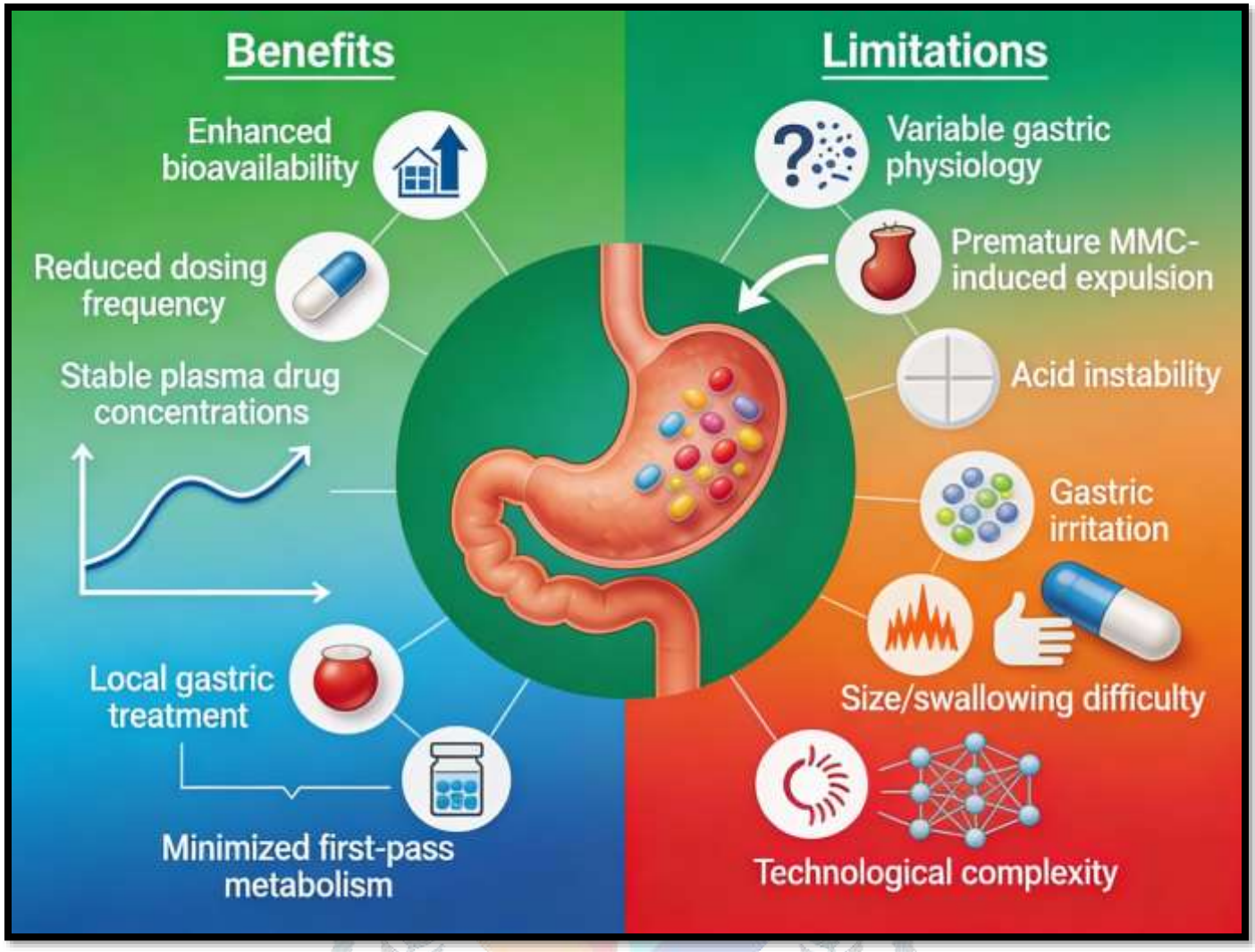



**Fig 3: Advantages and Disadvantages of Gastroretentive Drug Delivery Systems**

## VI. EVALUATION METHODOLOGIES FOR GRDDS

### A. In Vitro Evaluation Techniques

Comprehensive in vitro evaluation protocols establish fundamental GRDDS performance characteristics under simulated gastrointestinal conditions. Drug release studies employ United States Pharmacopeia (USP) dissolution apparatus (Type I or II) in simulated gastric fluid at pH 1.2, quantifying drug release rates and deriving kinetic models including zero-order, first-order, and Higuchi models that predict in vivo release behavior. Swelling studies quantify dimensional and weight changes following immersion in simulated gastric fluid at 37°C, calculating swelling indices that reflect expansion capacity and mucoadhesion characteristics[14]. Floating behavior assessment determines floating lag time (time required for dosage form to float) and total floating duration (continuous buoyancy period), with successful systems demonstrating floating lag times less than 3 minutes and sustained buoyancy exceeding 12 hours.

Bioadhesion testing employs texture analysis equipment and excised gastric tissues to quantify adhesive force between formulation and mucosal surfaces, predicting in vivo mucoadhesive performance. Stability studies subject formulations to various temperature, humidity, and light conditions, assessing physical and chemical stability throughout shelf-life periods. Mechanistic studies utilizing Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) identify drug-excipient interactions that may compromise formulation integrity or drug stability.

### B. In Vivo Evaluation Approaches

In vivo evaluation employs multiple imaging techniques to monitor gastric retention and dosage form behavior. X-ray imaging incorporating radiopaque markers including barium sulfate permits radiographic visualization of dosage form position at predetermined time intervals, correlating gastric retention with drug release characteristics[15]. Gamma-scintigraphy incorporates gamma-emitting isotopes including $^{99}$Tc into dosage forms, enabling external imaging via gamma-cameras to track dosage form movement through the gastrointestinal tract. Gastroscopy utilizing fiber optic endoscopic systems enables direct visual examination of dosage form status and gastric interactions. Magnetic marker monitoring represents a radiation-free alternative incorporating ferrite materials into dosage forms, permitting tracking via sensitive biomagnetism measurement equipment without radiation exposure.

## VII. CLINICAL APPLICATIONS AND PHARMACEUTICAL DEVELOPMENT

GRDDS demonstrate particular utility for pharmaceutical compounds exhibiting specific absorption and physicochemical characteristics. Drugs absorbed primarily in the stomach or upper small intestine (duodenum) including riboflavin, levodopa, amoxicillin, and metformin benefit substantially from enhanced gastric residence time enabling prolonged absorption periods[16]. Local gastric treatment applications include H. pylori eradication utilizing clarithromycin, amoxicillin, and metronidazole through prolonged retention enabling enhanced local antibiotic concentration and superior bacterial eradication. Peptic ulcer management benefits from prolonged gastric retention of agents such as misoprostol, enabling localized tissue protective effects. Drugs exhibiting short half-lives requiring frequent dosing including propranolol, nifedipine, and verapamil achieve superior therapeutic profiles through reduced dosing frequency enabled by sustained gastric release. Pharmaceutical compounds demonstrating poor solubility in alkaline intestinal pH but enhanced solubility in acidic gastric pH including diazepam and chlordiazepoxide maintain therapeutic concentrations through extended gastric residence[17].

## VIII. RECENT TECHNOLOGICAL ADVANCES

Contemporary GRDDS development incorporates sophisticated technologies including three-dimensional printing enabling customizable dosage form geometries precisely engineered for optimal retention characteristics, nanotechnology incorporating nanoparticles within GRDDS matrices for enhanced drug bioavailability, and superporous hydrogels demonstrating instantaneous swelling through interconnected pore networks. These advanced technologies enable development of personalized gastroretentive systems optimized for individual patient physiological characteristics and specific drug requirements.

## IX. CONCLUSION

Gastroretentive drug delivery systems represent a transformative technology in oral pharmaceutical delivery, enabling substantial improvements in bioavailability, therapeutic efficacy, and patient compliance for drugs with absorption windows restricted to the upper gastrointestinal tract. The comprehensive understanding of gastric physiology, availability of sophisticated polymeric materials, and development of multiple GRDDS technologies including floating, mucoadhesive, swellable, expandable, and magnetic systems collectively provide pharmaceutical scientists with diverse options for optimizing oral delivery of therapeutically challenging compounds. Contemporary advances incorporating three-dimensional printing, nanotechnology, and biomimetic design approaches promise continued evolution toward increasingly sophisticated and effective gastroretentive systems. Despite acknowledged limitations including dependence on variable gastric physiology and unsuitability for acid-labile compounds, GRDDS technology continues expanding its clinical applications across diverse therapeutic areas. The convergence of improved formulation technologies, enhanced characterization methodologies, and regulatory acceptance of GRDDS-developed products supports continued expansion of this pharmaceutical technology. Future development should prioritize personalization of GRDDS for individual patient physiological characteristics, integration with targeted release mechanisms for site-specific delivery to lower gastrointestinal regions, and development of alternative retention mechanisms reducing dependence on unpredictable gastric physiology. GRDDS technology will undoubtedly remain central to oral pharmaceutical delivery innovation, contributing substantially to pharmaceutical industry capability to deliver safe, efficacious, and patient-compliant oral medications.

## REFERENCES


**[1]** Shahiwala, A. (2011). Formulation approaches in enhancement of patient compliance to oral drug therapy. Expert Opinion on Drug Delivery, 8(11), 1521-1529.

**[2]** Allen, L., & Ansel, H. C. (2013). Ansel's pharmaceutical dosage forms and drug delivery systems. Lippincott Williams & Wilkins.

**[3]** Soderlind, E., & Dressman, J. B. (2010). Physiological factors affecting drug release and absorption in the gastrointestinal tract. Oral Drug Absorption: Prediction and Assessment, 1-20.

**[4]** Hua, S. (2020). Advances in oral drug delivery for regional targeting in the gastrointestinal tract-influence of physiological, pathophysiological and pharmaceutical factors. Frontiers in Pharmacology, 11, 524.

**[5]** Demeester, C., Robins, D., Edwina, A. E., Tournoy, J., Augustijns, P., Ince, I., & Schlender, J. F. (2023). Physiologically based pharmacokinetic (PBPK) modelling of oral drug absorption in older adults: an AGePOP review. European Journal of Pharmaceutical Sciences, 188, 106496.

**[6]** Tripathi, J., Thapa, P., Maharjan, R., & Jeong, S. H. (2019). Current state and future perspectives on gastroretentive drug delivery systems. Pharmaceutics, 11(4), 193.

**[7]** Gadge, G., Sabale, V., & Khade, A. (2019). Current approaches on gastro retentive drug delivery system: an overview. International Journal of Pharmacy Research & Technology, 9(2), 16-28.

**[8]** Barthe, L., Woodley, J., & Houin, G. (1999). Gastrointestinal absorption of drugs: methods and studies. Fundamental & Clinical Pharmacology, 13(2), 154-168.

**[9]** Gao, L., Zhang, D., & Chen, M. (2008). Drug nanocrystals for the formulation of poorly soluble drugs and its application as a potential drug delivery system. Journal of Nanoparticle Research, 10(5), 845-862.

**[10]** Varum, F. J., Merchant, H. A., & Basit, A. W. (2010). Oral modified-release formulations in motion: the relationship between gastrointestinal transit and drug absorption. International Journal of Pharmaceutics, 395(1-2), 26-36.

**[11]** Razavi, F. S., Kouchak, M., Feizoleslam, F., & Veysi, M. (2021). An overview on floating drug delivery systems (FDDS); conventional and new approaches for preparation and in vitro-in vivo evaluation. FABAD Journal of Pharmaceutical Sciences, 46(3), 345-362.

**[12]** Pawar, V. K., Kansal, S., Garg, G., Awasthi, R., Singodia, D., & Kulkarni, G. T. (2011). Gastroretentive dosage forms: A review with special emphasis on floating drug delivery systems. Drug Delivery, 18(2), 97-110.

**[13]** Taneja, R., Kataria, M. K., Bilandi, A., Gupta, A., & Gedar, S. (2013). Floating microsphere: a potential gastroretentive drug delivery system. Pharmacie Globale, 4(4), 1.

**[14]** Stielow, M., Witczyńska, A., Kubryń, N., Fijałkowski, Ł., Nowaczyk, J., & Nowaczyk, A. (2023). The bioavailability of drugs: the current state of knowledge. Molecules, 28(24), 8038.

**[15]** Narang, A., Chang, R. K., & Hussain, M. A. (2013). Pharmaceutical development and regulatory considerations for nanoparticles and nanoparticulate drug delivery systems. Journal of Pharmaceutical Sciences, 102(11), 3867-3882.

**[16]** Hoffman, A., & Stepensky, D. (1999). Pharmacodynamic aspects of modes of drug administration for optimization of drug therapy. Critical Reviews in Therapeutic Drug Carrier Systems, 16(6), 1-50.

**[17]** Goriacko, P., & Veltri, K. T. (2021). Adverse drug effects involving the gastrointestinal system (pharmacist perspective). In Geriatric Gastroenterology (pp. 297-339). Springer International Publishing.

**[18]** Park, H., Ha, E. S., & Kim, M. S. (2020). Current status of supersaturable self-emulsifying drug delivery systems. Pharmaceutics, 12(4), 365.

**[19]** Gronde, T. V. D., Uyl-de Groot, C. A., & Pieters, T. (2017). Addressing the challenge of high-priced prescription drugs in the era of precision medicine: a systematic review of drug life cycles, therapeutic drug markets and regulatory frameworks. PloS One, 12(8), e0182613.

**[20]** Mahato, R. I., & Narang, A. S. (2017). Pharmaceutical dosage forms and drug delivery: revised and expanded. CRC Press.