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GASTRORETENTIVE DRUG DELIVERY SYSTEMS: CLASSIFICATION, MECHANISMS, FORMULATION STRATEGIES, EVALUATION, THERAPEUTIC APPLICATIONS, AND RECENT ADVANCES

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Abstract:

Gastroretentive drug delivery systems (GRDDS) have surfaced as a viable oral drug administration method to address the challenges posed by fast stomach emptying and inadequate bioavailability of traditional dose forms. By extending stomach retention duration, GRDDS augment medication solubility, promote absorption in the upper gastrointestinal region, and deliver prolonged therapeutic effects. This assessment encapsulates the physiological foundations of gastric retention, biopharmaceutical factors, and the diverse classification methods of gastroretentive systems, such as floating, high-density, mucoadhesive, expandable, swellable, superporous hydrogel, raft-forming, and magnetic systems. The study moreover examines elements influencing gastroretention, frequently utilized polymers and excipients, assessment techniques, therapeutic uses, and current technological innovations. Innovative approaches like nanotechnology and three-dimensional printing have significantly enhanced the capabilities of GRDDS in optimizing oral medication administration. In general, gastroretentive systems serve as a potent framework for improving therapeutic effectiveness, patient adherence, and formulation efficiency, while presenting considerable prospects for the advancement of sophisticated controlled-release pharmaceutical formulations.

Keywords: *Gastroretentive drug delivery systems, Gastric retention, Floating drug delivery system, Controlled drug release, Oral drug delivery, Bioavailability, Mucoadhesive systems, Gastrointestinal tract, Sustained release, Polymers.*

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1. INTRODUCTION:

1.1 Gastric Physiology as a Determinant of Oral Drug Delivery

The efficacy of oral dose forms is intricately linked to the physiological conditions of the stomach. Gastric pH, motility patterns, gastric emptying rate, and the presence or lack of food all affect medication solubility, residence duration, and absorption. Traditional oral formulations aim to release medications post-administration; however, their efficacy is sometimes hindered by fast gastrointestinal transit, leading to inadequate drug breakdown and diminished absorption.[1] These constraints are especially apparent for medications that have pH-sensitive solubility, instability within the intestinal milieu, or preferential uptake from the stomach and upper small intestine. As a result, comprehending stomach physiology is essential for developing oral medication delivery methods that optimize therapeutic efficacy..[2]

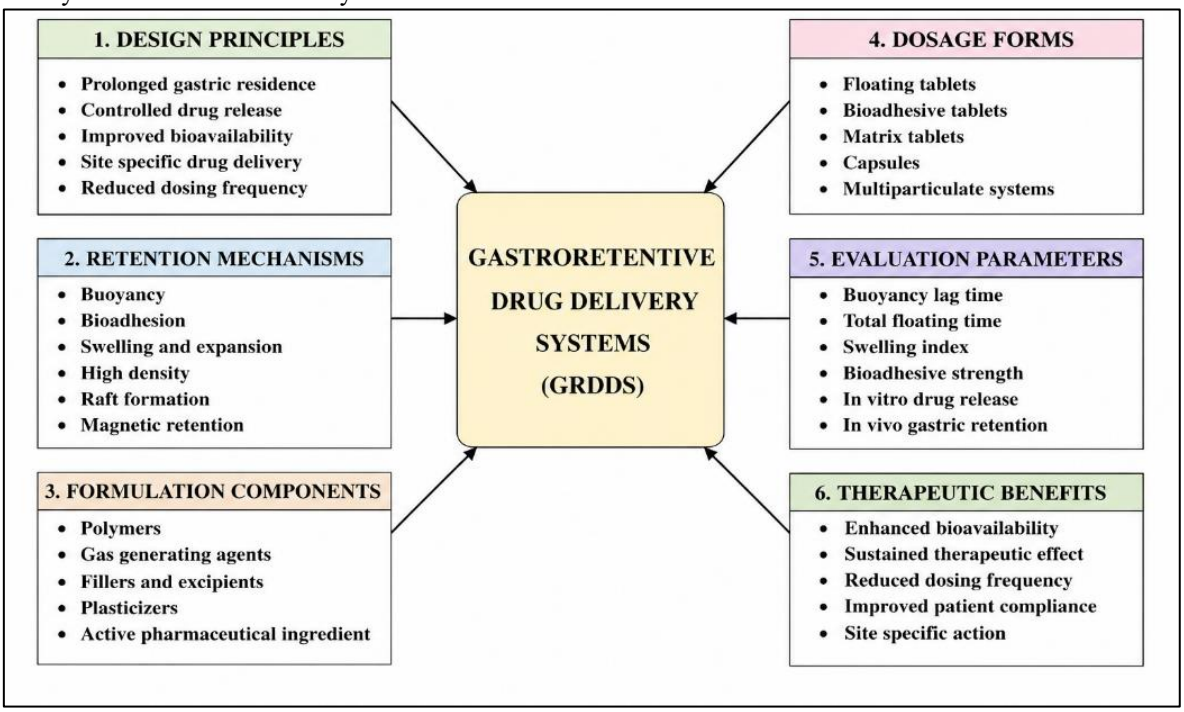

Figure 1. Framework of Gastroretentive Drug Delivery Systems

1.2 Pharmaceutical Strategies for Prolonging Gastric Residence

Progress in pharmaceutical formulation science has resulted in the creation of gastroretentive drug delivery systems (GRDDS), which are engineered to prolong the stomach retention duration of dose forms while maintaining normal gastrointestinal function. These systems utilize formulation techniques such as floating, bioadhesion, swelling, expansion, sedimentation, raft formation, and superporous hydrogels to prevent early gastric emptying.[3] The judicious use of polymers, gas-producing agents, and matrix-forming excipients facilitates prolonged stomach retention while ensuring regulated drug release. The amalgamation of formulation design and physiological principles has markedly enhanced the administration of medications characterized by limited absorption windows, suboptimal intestinal permeability, or localized therapeutic effects in the stomach..[4]

1.3 Emerging Perspectives in Gastroretentive Drug Delivery

Recent advancements in polymer chemistry, materials science, and pharmaceutical engineering have expanded the horizons of gastroretentive technology beyond traditional floating tablets. Contemporary GRDDS utilize multifunctional polymers, hot-melt extrusion, three-dimensional printing, nanotechnology, and Quality by Design (QbD) methodologies to create resilient and consistent formulations with anticipated in vivo efficacy.Five. Moreover, computational modeling and physiologically based formulation design have enhanced comprehension of stomach retention processes and drug release dynamics. These technological innovations have broadened the therapeutic uses of GRDDS for the treatment of gastrointestinal ailments, neurological disorders, diabetes, cardiovascular conditions, and antimicrobial interventions. As investigations progress to connect pharmaceutical technology with clinical necessities, gastroretentive systems are becoming a crucial element of advanced oral controlled drug delivery.[6]

2. Gastric Physiology and Its Influence on Gastroretentive Drug Delivery

The efficacy of gastroretentive drug delivery systems (GRDDS) is primarily influenced by the

physiological attributes of the stomach. In contrast to traditional oral dosage forms that quickly pass into the small intestine, gastroretentive formulations are engineered to stay in the stomach for a prolonged duration to optimize drug absorption and boost therapeutic effectiveness.[7] The ability of these systems to achieve prolonged gastric residence is influenced by several physiological factors, including stomach anatomy, gastric motility, secretion patterns, luminal pH, and the presence or absence of food. A thorough understanding of these physiological characteristics is therefore essential for the rational design and optimization of gastroretentive formulations.[8]

2.1 Anatomical Features of the Stomach

The stomach is a muscular, cavity-like organ located between the esophagus and the duodenum, functioning as a temporary storage for consumed food. It executes various physiological roles, including as nutrient storage, mechanical agitation, enzymatic breakdown, and control of stomach evacuation. The stomach is anatomically segmented into four primary areas: the cardia, fundus, body, and pylorus. Each area has a unique role in stomach physiology and affects the performance of orally ingested dose forms.[9]

The cardia serves as the gateway for ingested food and inhibits reflux into the esophagus. The fundus functions as the primary reservoir for the accumulation of gasses and undigested food. The body represents the predominant section of the stomach, tasked with the release of hydrochloric acid and digesting enzymes, while also enabling the ongoing amalgamation of gastric contents.[10] The pyloric region regulates the controlled transfer of gastric contents into the duodenum through coordinated muscular contractions and relaxation of the pyloric sphincter.

From a pharmaceutical perspective, these anatomical regions provide distinct microenvironments that influence the performance of gastroretentive dosage forms. Floating systems generally remain in the upper gastric region due to their lower density, whereas bioadhesive systems interact with the mucus layer lining the gastric wall. Expandable systems increase their dimensions after administration to resist passage through the pyloric opening, thereby extending gastric residence time.[11]

2.2 Gastric Secretions and Intragastric Environment

The gastric milieu is defined by the incessant release of hydrochloric acid, digesting enzymes, mucus, bicarbonate, electrolytes, and intrinsic factor. Gastric acid sustains an acidic pH typically between 1.0 and 2.5 during periods of fasting, while this measurement initially rises after eating before slowly reverting to baseline levels. Variations in gastric pH directly affect drug solubility, polymer hydration, matrix stability, and drug release rates.[12] For gastroretentive formulations, it is crucial to retain structural integrity in this acidic milieu to ensure prolonged drug release. Hydrophilic polymers frequently employed in buoyant and expandable systems progressively assimilate stomach fluid to create hydrated gel layers that modulate medication transport. In a comparable manner, bioadhesive polymers engage with the gastric mucus layer, thereby enhancing the retention of the dose form in the stomach. Thus, the physicochemical properties of stomach fluid significantly influence the in vivo efficacy of gastroretentive drug delivery devices.[13]

2.3 Physiological Determinants of Gastric Residence

The length of time a dose form stays in the stomach is influenced by a complex interplay of physiological and formulation-related elements. Gastric emptying exhibits specific patterns in fasting and postprandial states. During periods of fasting, the stomach demonstrates rhythmic motor functions referred to as the migrating motor complex (MMC), which intermittently transports undigested substances into the small intestine. This biological mechanism frequently restricts the duration that traditional dose forms remain in the stomach.[14]

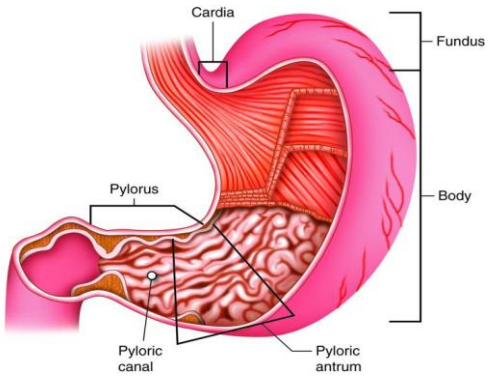

Figure 2. Anatomy of the Human Stomach Relevant to Gastroretentive Drug Delivery

Subsequent to food consumption, gastric motility is modified and the initiation of the migrating motor complex is postponed, permitting dose forms to persist in the stomach for an extended period. Supplementary elements like meal composition, caloric value, patient age, body posture, medical conditions, dosage form dimensions, density, and morphology also have a crucial role in stomach retention. Comprehending these physiological factors allows formulation scientists to create gastroretentive systems that can counteract swift stomach emptying while ensuring consistent and prolonged medication release.[15]

3. Biopharmaceutical Basis of Gastroretentive Drug Delivery

The formulation of gastroretentive drug delivery systems is primarily grounded in the biopharmaceutical properties of medicinal

compounds and their engagement with the gastrointestinal system. While oral administration is the favored method for drug delivery, the efficacy of numerous medications is hindered by quick stomach emptying, inadequate water solubility, enzymatic breakdown, or absorption limited to particular areas of the gastrointestinal system. Traditional oral dose forms often struggle to sustain sufficient drug levels at the targeted absorption location, leading to diminished bioavailability and variable therapeutic results. Gastroretentive drug delivery systems address these constraints by extending the duration of gastric retention and facilitating regulated drug release in the stomach or proximal small intestine. Consequently, comprehending the physicochemical and pharmacokinetic characteristics of pharmacological molecules is crucial for identifying suitable candidates for the development of gastroretentive formulations.[16]

3.1 Drug Candidates Suitable for Gastroretentive Drug Delivery Systems

Not every medication is suitable for gastroretentive administration. GRDDS are especially advantageous for medications that are absorbed mainly in the stomach or upper small intestine, have solubility that depends on pH, or necessitate extended gastric retention for maximum therapeutic efficacy.[17] Pharmaceuticals characterized by a limited absorption window exhibit a substantial enhancement in bioavailability when maintained in the stomach for prolonged durations. In a similar vein, medications designed for localized therapy of gastrointestinal ailments gain from extended interaction with the gastric mucosa, resulting in improved therapeutic effectiveness. Molecules with comparatively brief biological half-lives are also appropriate choices, as prolonged stomach retention can uphold therapeutic plasma levels while minimizing dose frequency. These attributes render gastroretentive systems a compelling framework for enhancing the clinical efficacy of various therapeutic medicines.[18]

3.2 Drug Candidates Unsuitable for Gastroretentive Drug Delivery Systems

Notwithstanding their benefits, gastroretentive systems are not universally suitable. Pharmaceuticals that are unstable in acidic stomach environments, experience significant degradation in gastric fluids, or are primarily absorbed in the distal intestine or colon are typically inappropriate for gastroretentive administration. Drugs that demonstrate inadequate solubility in acidic environments may show restricted dissolution over extended stomach retention, thereby diminishing therapeutic efficacy. Compounds designed for fast action may be unsuitable for controlled gastroretentive formulations, as prolonged stomach retention could hinder drug accessibility. Thorough evaluation of physicochemical attributes, absorption traits, and therapeutic aims is essential prior to choosing a medication candidate for gastroretentive formulation.[19]

3.3 Biopharmaceutical Considerations in GRDDS Design

Effective gastroretentive formulations necessitate a comprehensive comprehension of pharmacological characteristics, gastrointestinal physiology, and formulation science. Factors like water solubility, ionization constant, partition coefficient, molecular weight, permeability, dosage size, elimination half-life, and stability in stomach fluid markedly affect formulation efficacy. Furthermore, physiological factors such as gastric pH, gastric motility, mucus turnover, and gastric emptying dynamics influence the in vivo performance of gastroretentive devices.[20] Enhancing these characteristics by suitable polymer selection, formulation design, and release kinetics facilitates the creation of formulations that can attain extended stomach retention and consistent drug release. Thus, the biopharmaceutical principles behind GRDDS provide the groundwork for creating efficient gastroretentive formulations that enhance therapeutic efficacy.[21]

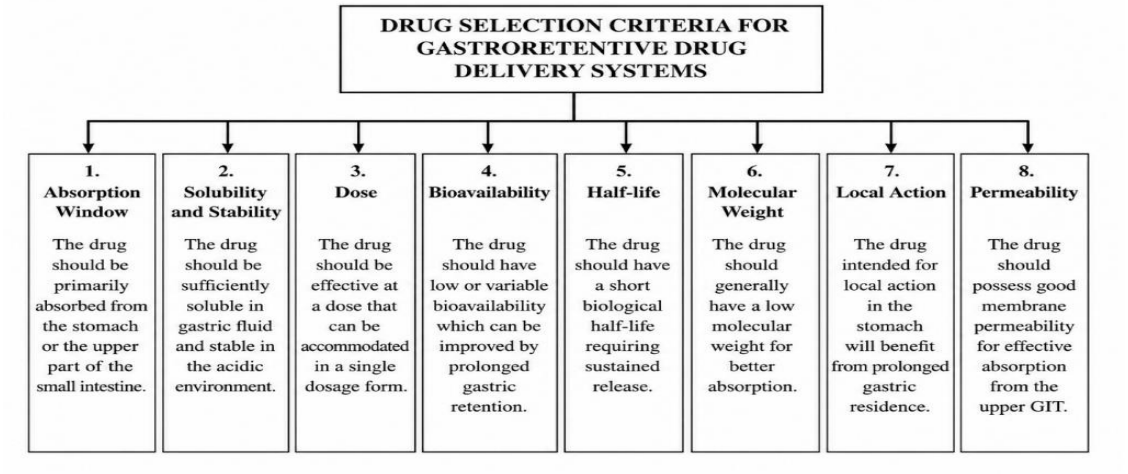

Figure 3. Drug Selection Criteria for Gastroretentive Drug Delivery Systems

4. Classification of Gastroretentive Drug Delivery Systems

Gastroretentive drug delivery systems (GRDDS) are engineered using various formulation strategies to extend the duration of dose forms in the stomach. These systems augment drug absorption, elevate oral bioavailability, facilitate prolonged drug release, and boost therapeutic effectiveness by postponing stomach emptying. The choice of an appropriate gastroretentive approach is contingent upon the drug's physicochemical characteristics, absorption location, therapeutic goals, and the physiological state of the gastrointestinal system. GRDDS are categorized into various types according to the technique utilized for gastric retention.[22]

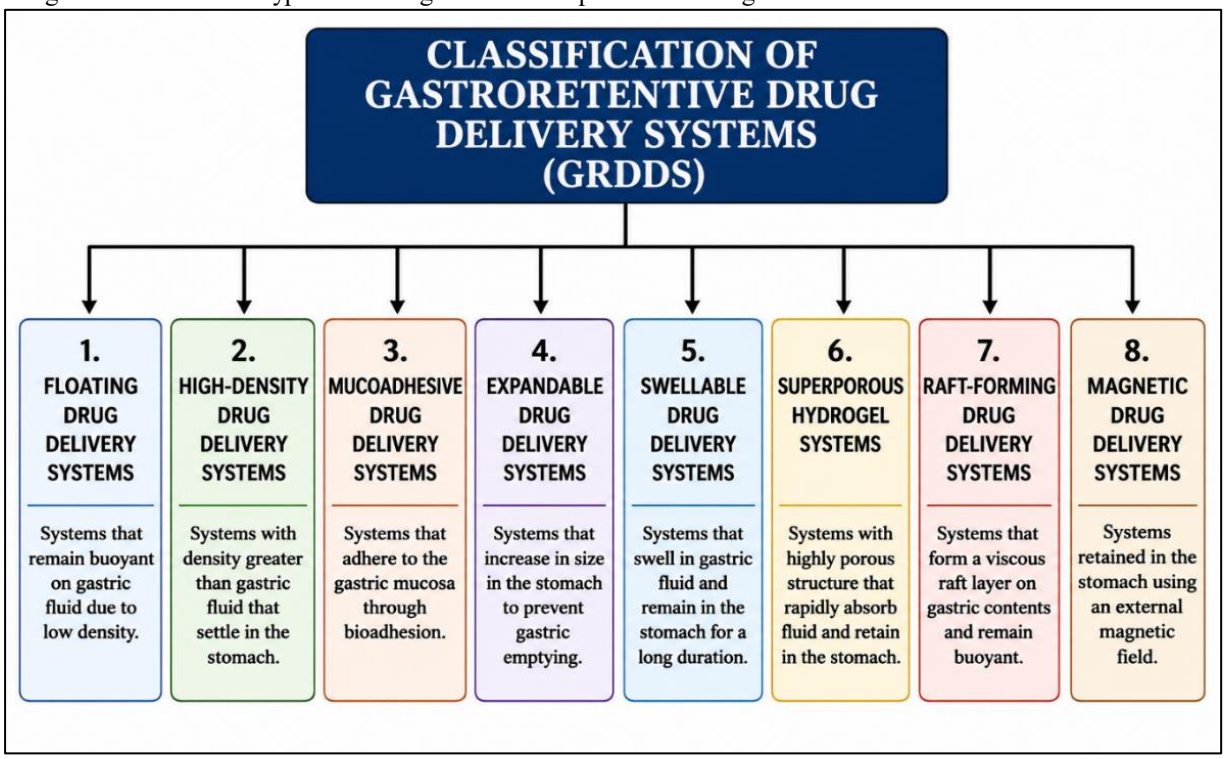

Figure 4. Classification of Gastroretentive Drug Delivery Systems

4.1 Floating Drug Delivery Systems

Floating drug delivery systems (FDDS) are engineered to possess a density that is less than that of gastric fluid, allowing them to remain buoyant on the contents of the stomach for extended durations. This buoyancy postpones stomach emptying while facilitating ongoing and regulated medication release. Buoyant systems are among the most extensively studied gastroretentive methods due to their straightforward formulation, high patient adherence, and efficacy in enhancing the bioavailability of medicines with limited absorption capacity.

4.2 High-Density Drug Delivery Systems

High-density systems remain in the stomach by possessing a density considerably greater than that of gastric fluid. Their increased weight allows them to settle in the lower portion of the stomach, thereby resisting gastric emptying. Although this approach offers prolonged gastric retention, formulation difficulties and limited clinical success have restricted its widespread pharmaceutical application.[23]

4.3 Mucoadhesive (Bioadhesive) Drug Delivery Systems

Mucoadhesive systems prolong gastric residence by adhering to the mucus layer covering the gastric epithelium. The use of bioadhesive polymers enables the dosage form to maintain close contact with the gastric mucosa, resulting in prolonged drug release and enhanced absorption. These systems are particularly useful for drugs intended for local gastric action or those absorbed primarily from the upper gastrointestinal tract.[24]

4.4 Expandable Drug Delivery Systems

Expandable systems are formulated to increase their size after reaching the stomach through unfolding or structural expansion. The enlarged dosage form becomes too large to pass through the pyloric sphincter, thereby remaining in the stomach for an extended period. After complete drug release, the system either degrades or returns to its original dimensions, allowing safe elimination from the gastrointestinal tract.[25]

4.5 Swellable Drug Delivery Systems

Swellable systems contain hydrophilic polymers that rapidly absorb gastric fluid and undergo substantial swelling. The increase in volume prevents the dosage form from passing through the pylorus while simultaneously providing sustained drug release. Their simple manufacturing process and reliable gastric retention make them attractive for controlled-release formulations.[26]

4.6 Superporous Hydrogel Systems

Superporous hydrogel systems consist of highly porous polymeric matrices capable of absorbing large amounts of gastric fluid within a short period. Rapid swelling combined with high mechanical strength allows these systems to withstand gastric contractions while maintaining prolonged gastric retention. They are particularly suitable for drugs requiring rapid expansion immediately after administration.[27]

4.7 Raft-Forming Drug Delivery Systems

Raft-forming systems produce a viscous, floating gel layer upon contact with gastric fluid. This gel forms a protective barrier over the stomach contents, reducing gastroesophageal reflux while providing localized and sustained drug release. These formulations are widely employed in the treatment of gastroesophageal reflux disease (GERD), gastric ulcers, and other acid-related disorders.[28]

4.8 Magnetic Drug Delivery Systems

Magnetic drug delivery systems incorporate magnetic materials into the dosage form, allowing gastric retention through the application of an external magnetic field. This strategy enables site-specific localization of the formulation and prolonged residence within the stomach. Although magnetic systems offer precise control over gastric retention, their clinical application remains limited due to the need for external magnetic devices and practical concerns regarding patient convenience.[29]

5. Factors Affecting Gastroretentive Drug Delivery Systems

The performance of gastroretentive drug delivery systems (GRDDS) is influenced by numerous physiological, formulation-related, and drug-specific factors. These factors determine the gastric residence time, drug release pattern, and overall therapeutic effectiveness of the dosage form. A comprehensive understanding of these variables is essential for designing gastroretentive formulations with predictable in vivo performance.[30]

5.1 Physiological Factors

Physiological conditions of the gastrointestinal tract play a major role in determining the effectiveness of GRDDS. Gastric emptying rate is one of the most critical factors because it directly influences the duration for which the dosage form remains in the stomach. The presence of food, particularly meals rich in fats and proteins, significantly delays gastric emptying and promotes prolonged gastric retention. In contrast, fasting conditions accelerate gastric emptying due to the migrating motor complex (MMC), reducing the retention time of gastroretentive formulations.[31]

The volume and composition of gastric fluid also affect the performance of floating and swellable systems. Adequate gastric fluid facilitates polymer hydration, swelling, and buoyancy, whereas insufficient fluid may compromise these mechanisms. Furthermore, gastric pH influences the solubility and stability of pH-dependent drugs and polymers, thereby affecting drug release and absorption.[32]

5.2 Drug-Related Factors

The physicochemical properties of the drug significantly influence the suitability of GRDDS. Drugs with a narrow absorption window in the upper gastrointestinal tract, high solubility in acidic media, or local action within the stomach are considered ideal candidates. Drug dose, aqueous solubility, stability in gastric fluid, molecular weight, and elimination half-life should also be carefully evaluated during formulation development. Highly acid-labile drugs or drugs absorbed primarily from the distal intestine are generally unsuitable for gastroretentive delivery.[33]

5.3 Formulation Factors

The design of the dosage form greatly affects gastric retention and drug release. Polymer type and concentration determine the swelling behavior, gel strength, and sustained-release characteristics of the formulation. The density and size of the dosage form are equally important, as floating systems require densities lower than gastric fluid, whereas high-density systems depend on increased density for retention. The shape, mechanical strength, and integrity of the dosage form must be optimized to withstand gastric motility while maintaining controlled drug release throughout the desired period.[34]

5.4 Patient-Related Factors

Individual patient characteristics also influence the performance of GRDDS. Age, gender, body posture, physical activity, disease conditions, and concomitant medications may alter gastric motility and gastric emptying rate. Disorders such as diabetes mellitus, gastroparesis, or gastrointestinal surgeries can significantly modify gastric physiology, thereby affecting the in vivo behavior of gastroretentive formulations. Consequently, these patient-related variables should be considered during dosage form design and clinical evaluation.[35]

6. Polymers and Excipients Used in Gastroretentive Drug Delivery Systems

The successful formulation of gastroretentive drug delivery systems largely depends on the appropriate selection of polymers and pharmaceutical excipients. These ingredients govern buoyancy, swelling, mucoadhesion, matrix formation, drug release kinetics, and mechanical stability. An ideal polymer should exhibit excellent biocompatibility, controlled hydration, adequate gel strength, chemical stability, and compatibility with both the drug and other formulation components.[36]

6.1 Natural Polymers

Natural polymers are widely utilized because of their biodegradability, biocompatibility, and low toxicity. They readily hydrate in gastric fluid to form viscous gels that prolong gastric retention and sustain drug release. Common natural polymers

include sodium alginate, xanthan gum, guar gum, pectin, chitosan, carrageenan, locust bean gum, and gellan gum. Their natural origin and favorable safety profile make them suitable for various gastroretentive formulations.[37]

6.2 Semi-Synthetic Polymers

Semi-synthetic cellulose derivatives are among the most frequently employed polymers in GRDDS because they provide predictable swelling behavior and excellent matrix-forming properties. Hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), hydroxyethyl cellulose (HEC), methylcellulose (MC), and sodium carboxymethyl cellulose (NaCMC) are commonly used to regulate hydration, buoyancy, and sustained drug release. These polymers also improve the mechanical integrity of gastroretentive formulations.[38]

6.3 Synthetic Polymers

Synthetic polymers offer superior control over drug release and formulation stability. Carbopol, polyethylene oxide (PEO), polyvinyl alcohol (PVA), polymethacrylates (Eudragit®), and polyvinylpyrrolidone (PVP) are extensively employed in floating, swellable, and mucoadhesive systems. Their reproducible physicochemical properties facilitate the development of controlled-release gastroretentive dosage forms with consistent performance.[39]

Gas-generating agents are essential components of effervescent floating systems. Sodium bicarbonate, calcium carbonate, and citric acid react with gastric acid to produce carbon dioxide, which becomes entrapped within the hydrated polymer matrix. This decreases the density of the dosage form, enabling it to float on gastric fluid while maintaining prolonged gastric residence and sustained drug release.[40]

6.5 Other Functional Excipients

In addition to polymers, several excipients are incorporated to improve formulation performance. Lubricants such as magnesium stearate facilitate tablet compression, while glidants like talc enhance powder flow. Fillers including lactose and microcrystalline cellulose provide bulk to the formulation. Release modifiers, plasticizers, binders, surfactants, and coating agents are also employed to optimize drug release, improve mechanical strength, and enhance formulation stability.[41]

7. Evaluation Parameters of Gastroretentive Drug Delivery Systems

Evaluation of gastroretentive formulations is essential to ensure their quality, performance, and therapeutic efficacy. Both pre-compression and post-compression parameters are assessed to determine the physical characteristics, gastric retention ability, and drug release behavior of the dosage form.[42]

7.1 Pre-Compression Evaluation

Before tablet compression or capsule filling, powder blends are evaluated for flowability and compressibility. Parameters such as angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner ratio provide information regarding powder flow properties and suitability for large-scale manufacturing.

7.2 Physical Evaluation

Finished gastroretentive dosage forms are examined for appearance, hardness, friability, thickness, diameter, weight variation, and drug content uniformity. These quality control tests ensure uniformity, adequate mechanical strength, and compliance with pharmacopeial standards.[43]

7.3 Floating and Swelling Studies

Floating lag time and total floating duration are important evaluation parameters for floating formulations. Floating lag time represents the time required for the dosage form to begin floating after contact with gastric fluid, whereas floating duration indicates the period during which buoyancy is maintained. Swelling studies determine the extent of polymer hydration by measuring the swelling index at predetermined time intervals.[44]

7.4 In Vitro Drug Release Studies

Drug release is commonly evaluated using USP dissolution apparatus under simulated gastric conditions. Dissolution studies determine the rate and extent of drug release and help establish the sustained-release characteristics of the formulation. Mathematical models such as zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell equations are frequently applied to understand drug release kinetics and release mechanisms.[45]

7.5 In Vivo Gastric Retention Studies

The gastric retention capability of GRDDS is evaluated using imaging techniques such as gamma scintigraphy, X-ray radiography, magnetic resonance imaging (MRI), or ultrasonography. These studies provide direct evidence of gastric residence time and confirm the effectiveness of the gastroretentive formulation under physiological conditions.[46]

7.6 Stability Studies

Stability studies are conducted according to the International Council for Harmonisation (ICH) guidelines to evaluate the physical, chemical, and microbiological stability of gastroretentive formulations during storage. Parameters including drug content, dissolution profile, floating behavior, moisture uptake, appearance, and mechanical strength are monitored under accelerated and long-term storage conditions to ensure product quality throughout its shelf life.[47]

8. Therapeutic Applications of Gastroretentive Drug Delivery Systems

Gastroretentive drug delivery systems (GRDDS) have gained considerable attention because of their ability to improve therapeutic outcomes through prolonged gastric residence and controlled drug

release. By maintaining the dosage form in the stomach for an extended duration, GRDDS enhance drug absorption, increase oral bioavailability, minimize dosing frequency, and improve patient compliance. These systems are particularly beneficial for drugs exhibiting narrow absorption windows, poor intestinal stability, or localized action within the stomach.[48]

8.1 Drugs with Narrow Absorption Window

Many drugs are absorbed predominantly from the stomach or the upper part of the small intestine. Rapid gastric emptying may reduce their absorption, leading to poor therapeutic efficacy. Gastroretentive formulations prolong drug residence in the absorption region, thereby improving bioavailability and maintaining consistent plasma drug concentrations. Examples include levodopa, riboflavin, metformin hydrochloride, ciprofloxacin hydrochloride, and furosemide.[49]

8.2 Local Treatment of Gastric Disorders

GRDDS are highly effective for drugs intended to exert their action locally within the stomach. Prolonged gastric retention ensures continuous drug exposure at the site of action, thereby improving therapeutic effectiveness. This approach is particularly useful in the treatment of gastric ulcers, gastritis, gastroesophageal reflux disease (GERD), and *Helicobacter pylori* infections. Sustained local drug delivery also reduces systemic exposure and minimizes adverse effects.[50]

8.3 Controlled Drug Delivery for Chronic Diseases

Patients with chronic diseases often require long-term medication, making frequent dosing a challenge. Gastroretentive formulations provide sustained and controlled drug release, reducing dosing frequency while maintaining therapeutic plasma concentrations over extended periods. This improves medication adherence and enhances treatment outcomes in chronic conditions such as diabetes mellitus, hypertension, Parkinson's disease, and cardiovascular disorders.[51]

8.4 Improvement of Oral Bioavailability

Several drugs exhibit poor oral bioavailability due to rapid gastrointestinal transit or limited absorption in the distal intestine. Gastroretentive systems increase the time available for dissolution and absorption in the upper gastrointestinal tract, resulting in enhanced bioavailability and reduced interpatient variability. This strategy is particularly advantageous for poorly soluble and pH-dependent drugs.[52]

8.5 Future Clinical Potential

Recent developments in polymer science, nanotechnology, and advanced pharmaceutical manufacturing have expanded the clinical applications of GRDDS. Emerging formulations such as gastroretentive nanoparticles, three-dimensional (3D) printed dosage forms, multiparticulate floating systems, and intelligent polymeric carriers are being investigated to achieve personalized drug delivery, improved therapeutic efficacy, and enhanced patient convenience.[53]

9. Recent Advances and Future Perspectives in Gastroretentive Drug Delivery Systems

Continuous progress in pharmaceutical technology has significantly improved the design and performance of gastroretentive drug delivery systems. Modern formulation approaches focus on achieving prolonged gastric residence, predictable drug release, enhanced patient compliance, and improved therapeutic outcomes while overcoming the limitations associated with conventional gastroretentive formulations.[54]

9.1 Advanced Formulation Technologies

Novel formulation strategies such as multiparticulate floating systems, expandable capsules, superporous hydrogels, floating microspheres, and floating beads have demonstrated improved gastric retention compared with conventional single-unit dosage forms. These advanced systems provide more uniform drug distribution, reduced risk of dose dumping, and better reproducibility of therapeutic response.[55]

9.2 Nanotechnology-Based Gastroretentive Systems

Nanotechnology has introduced new possibilities for gastroretentive drug delivery through the development of nanoparticles, nanosponges, liposomes, solid lipid nanoparticles, and polymeric nanocarriers. These nanoscale systems improve drug solubility, enhance mucosal adhesion, facilitate controlled drug release, and increase oral bioavailability, making them promising candidates for future gastroretentive formulations.

9.3 Three-Dimensional Printing

Three-dimensional (3D) printing has emerged as an innovative manufacturing technology for producing personalized gastroretentive dosage forms. This technique enables precise control over tablet geometry, internal architecture, drug loading, and release characteristics, allowing the development of patient-specific formulations with optimized floating or swelling properties.[56]

9.4 Current Challenges

Notwithstanding significant progress, various obstacles persist in hindering the extensive clinical utilization of GRDDS. Disparities in gastric physiology among individuals, erratic stomach emptying, reliance on dietary consumption, intricate formulations, challenges in scaling up, and restricted in vivo–in vitro correlation continue to pose significant challenges in the effective advancement of gastroretentive systems.[57]

9.5 Future Perspectives

Anticipated future investigations will concentrate on the creation of intelligent gastroretentive systems that can react to physiological cues, amalgamating nanotechnology with biodegradable polymers, and employing artificial intelligence for the

enhancement of formulations. The integration of sophisticated biomaterials, tailored medicine, and precise drug administration is expected to significantly improve the safety, effectiveness, and market viability of gastroretentive drug delivery systems, establishing them as a crucial foundation for future oral controlled-release formulations.[58]

10. CONCLUSION:

Gastroretentive drug delivery systems (GRDDS) have surfaced as a potent method for addressing the shortcomings of traditional oral drug delivery by extending stomach retention duration and enhancing drug absorption. These systems are especially advantageous for medications characterized by a limited absorption window, pH-sensitive solubility, localized gastrointestinal effects, and brief biological half-lives. Diverse gastroretentive methodologies, such as floating, mucoadhesive, swellable, expandable, high-density, raft-forming, superporous hydrogel, and magnetic systems, have shown considerable promise in improving bioavailability and therapeutic effectiveness. The effective creation of GRDDS relies on suitable drug choice, polymer properties, formulation architecture, and physiological elements affecting gastric retention. Recent progress in polymer science, nanotechnology, and three-dimensional printing has broadened the possibilities for gastroretentive formulations, facilitating the creation of more effective and patient-oriented medication delivery systems. Ongoing investigation and technical advancement are anticipated to surmount current obstacles and enable the conversion of sophisticated gastroretentive systems into secure, efficient, and marketable pharmaceutical offerings.

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