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

GASTRO RETENTIVE DRUG DELIVERY SYSTEM(GRDDS)

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Abstract: -

Gastroretentive Drug Delivery Systems (GRDDS) present a promising approach to enhance the bioavailability and therapeutic efficacy of orally administered drugs, particularly those with narrow absorption windows or low solubility. This innovative drug delivery system aims to prolong gastric residence time, thereby optimizing drug release and absorption. By leveraging various formulation strategies such as floating systems, mucoadhesive systems, and expandable systems, GRDDS ensures sustained drug release and improved patient compliance. This abstract provides an overview of GRDDS, including its rationale, design principles, formulation approaches, and potential applications in pharmaceutical research and development. Furthermore, it discusses the advantages, challenges, and future perspectives of GRDDS, highlighting its significant impact on the advancement of oral drug delivery technology.

Key Eelments:
Introduction, Importance, Floating Systems, Bioadhesive Systems, Swelling and Expanding Systems, High-Density Systems, Drug Release Kinetics, Mucoadhesive Systems, Expandable Systems, Treatment of Gastric Ulcers, Controlled Release of Drugs, Safety and Tolerability,
Patient Compliance, Regulatory Perspectives.

1. *Introduction to Gastroretentive Drug Delivery Systems:-*

a) . Definition and Importance

Define what gastroretentive drug delivery systems are (systems designed to prolong the residence time of drugs in the stomach). Explain the significance of gastroretentive systems in pharmaceuticals, especially for drugs with absorption or degradation issues in the lower gastrointestinal tract. The most convenient and recognised approach for the administration of drugs was the oral route. During oral controlled release, huge curative advantages prefer to the advantage of therapeutic advantages, as an attractive issue in the pharmaceutical sector. Gastro-resistant medicines are new systems in delivery that are of upper hand because of their capacity to maintain their stomach for longer periods. The non-site special release of medication is also a drawback to conventional rapid release tablets. [1,2] On the other hand, certain medicinal products are absorbed from specific places and must be released at this spot solely for maximum absorption. It depends on variables such as the emptying process, dosage form transit length through the digestive system, the release of medication from the dosage form and the site of the absorption. The oral routes remain the most popular way of drug delivery to systemic circulation, due to their simplicity of administration, low drug costs, patient compliance and flexibility in formulation. Estimated 90% of all systemic drugs are administered orally in drugs administered orally; solid oral dosage forms are preferable over liquid oral dosage forms. [3] Tablets are now the most prevalent type of solid dose. Depending on drug release patterns, they might be categorised in two groups, namely immediate release and delayed release. Drug having short halves that are quickly absorbed and eliminated from the gastrointestinal tract quickly eliminates systemic circulation. In order to be successful, these medications must be taken regularly. In addition, medications with a low absorption fencing in the upper portion of the GIT are not suitable for oral, sustained release systems due to the short gastric emptying time of 2.7±1.5 hours (h) and 3.1±0.4 hour of intestinal transit. [6] One method to extend gastric residency is to employ gastroretentive medicines for local or systemic effects. These types of dosage may remain long in the stomach and increase the period of stomach retention. The medicine is therefore given continually to the absorption point in the gut, i.e. the gastric stomach. [7] In 1968, after observing several patients chocked after eating pills, David explained the floating drug distribution process for the first time. Its solution consisted of using tablets of less than 1 g / ml to float on the surface of the water. Since then several approaches for optimum floating supply systems have been developed. [8] Increased interest in novel dosage formulations which remain in the stomach for a lengthy and predictable period of time is manifested in the industry and academic. [9]

1. Challenges in Gastrointestinal Drug Delivery

Discuss the physiological factors affecting drug absorption in the gastrointestinal tract (e.g., gastric emptying rate, pH variability, enzymatic degradation). Highlight challenges faced in traditional oral drug delivery systems, such as poor bioavailability and inconsistent drug release.[2]

3. Advantages of Gastroretentive Systems

Enumerate the benefits of gastroretentive drug delivery systems over conventional delivery methods.
Emphasize improved bioavailability, enhanced therapeutic efficacy, reduced dosing frequency, and better patient compliance.

Mention specific patient populations that may benefit from gastroretentive systems (e.g., geriatric patients, patients with gastrointestinal motility disorders).[2]

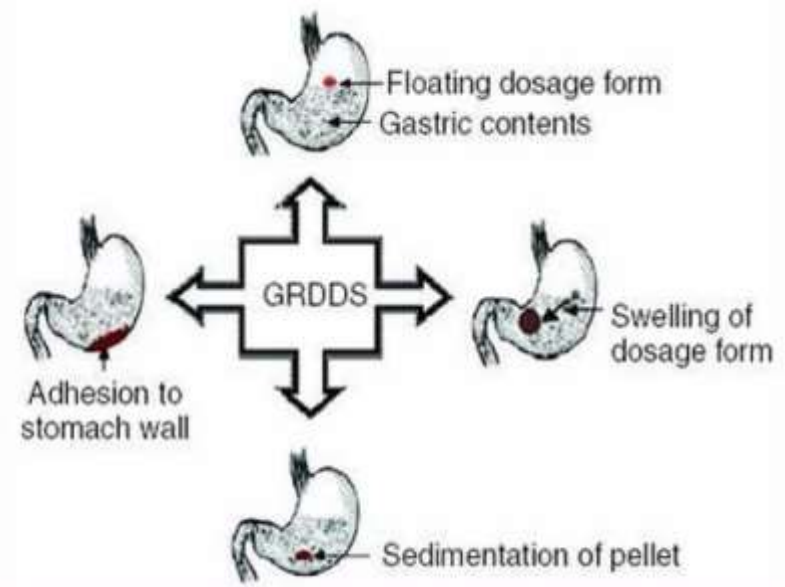

Fig.1

2. Mechanisms of Gastroretention

1. Floating Systems

Explain how floating systems work: these formulations contain buoyant materials that decrease the density of the dosage form, allowing it to float on the gastric contents. Achieved through the incorporation of gas-generating agents or low-density materials. Highlight examples of commonly used floating systems, such as floating tablets, capsules, or multiparticulate formulations.

Describe the advantages of floating systems, including prolonged gastric residence time, improved drug absorption, and enhanced therapeutic efficacy for drugs with absorption site specificity in the stomach.[9]

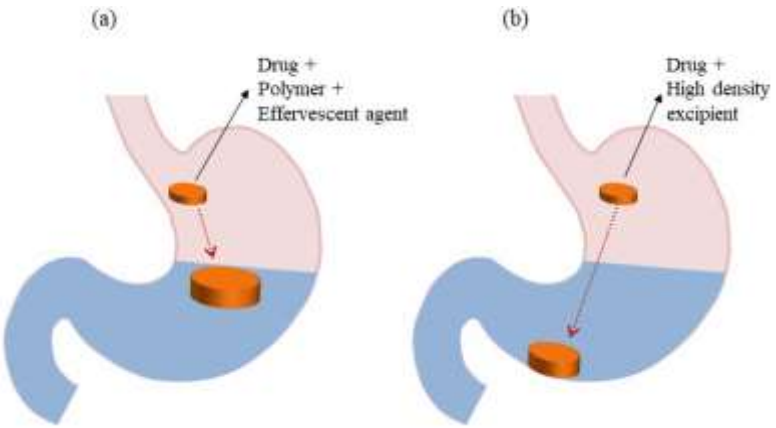

Fig.2

2. Bioadhesive Systems

Define bioadhesive systems: these formulations adhere to the gastric mucosa upon contact, prolonging the residence time in the stomach. Explain the mechanisms of bioadhesion, which involve interactions between adhesive polymers in the formulation and mucin glycoproteins on the mucosal surface.

Discuss various bioadhesive polymers commonly used in gastroretentive formulations, such as carbomers, cellulose derivatives, and chitosan.

Highlight the advantages of bioadhesive systems, including localized drug delivery, improved bioavailability, and reduced dosing frequency.[9]

3. Swelling and Expanding Systems

Describe swelling and expanding systems: these formulations undergo swelling or expansion upon contact with gastric fluids, leading to increased size and retention in the stomach. Explain the mechanisms of swelling, which typically involve the uptake of water by hydrophilic polymers in the formulation.

Discuss examples of polymers used in swelling and expanding systems, such as hydroxypropyl methylcellulose (HPMC) and sodium alginate. Highlight the benefits of swelling and expanding systems, including prolonged gastric retention, controlled drug release, and reduced variability in drug absorption.[25]

4. High-Density Systems

Define high-density systems: these formulations have densities higher than gastric fluids, enabling them to sink and remain in the stomach for an extended period. Explain the principle behind their high density, often achieved through the incorporation of heavy metals, salts, or inert materials.

Discuss examples of high-density formulations, such as pellets or tablets containing barium sulfate or other heavy materia

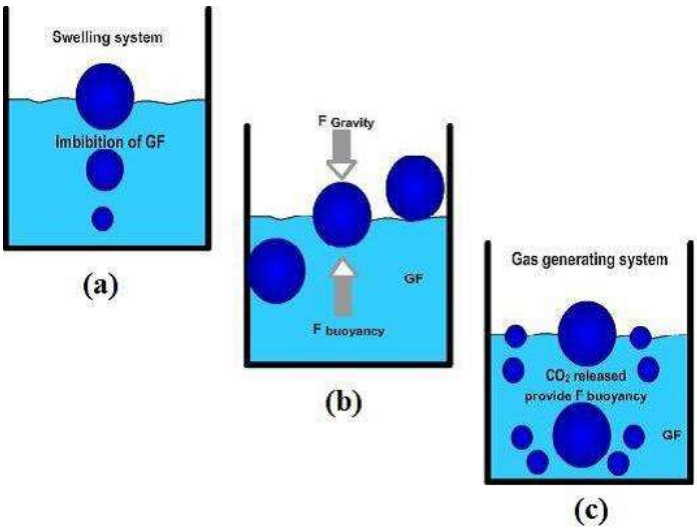

Fig.3

Highlight the advantages of high-density systems, including prolonged gastric retention, controlled drug release, and suitability for drugs requiring targeted delivery to specific regions of the stomach.

3. Formulation Consideration:-

1. Selection of Polymers

Discuss the importance of polymers in gastroretentive formulations, as they play a critical role in determining drug release kinetics, buoyancy, bioadhesion, and swelling properties. The criteria for selecting polymers, including biocompatibility, mucoadhesive properties, swelling capacity, and mechanical strength.

Describe commonly used polymers in gastroretentive systems, such as cellulose derivatives (e.g., hydroxypropyl methylcellulose, hydroxyethyl cellulose), carbomers, chitosan, and alginate. Highlight the impact of polymer properties (e.g., molecular weight, degree of cross-linking, charge) on the performance of gastroretentive formulations.[15]

2. Drug Release Kinetics

Explain the importance of drug release kinetics in gastroretentive systems, as it influences the rate and extent of drug release in the gastrointestinal tract. Discuss different mechanisms of drug release, including diffusion, erosion, swelling, and osmosis, and how they are modulated in gastroretentive formulations.

Describe mathematical models used to characterize drug release kinetics, such as zero-order, first-order, Higuchi, and Korsmeyer-Peppas models.

Highlight factors influencing drug release kinetics, including polymer characteristics, drug properties, formulation design, and environmental conditions.[15]

3. Stability Issues

Address stability concerns associated with gastroretentive drug delivery systems, such as physical and chemical degradation of active pharmaceutical ingredients (APIs) and excipients.

Discuss strategies to enhance the stability of formulations, including the selection of stable polymers and excipients, optimization of formulation parameters, and incorporation of antioxidants or stabilizing agents.

Highlight the importance of stability testing during formulation development, including studies on physical stability (e.g., particle size, aggregation) and chemical stability (e.g., degradation kinetics, drug-excipient interactions).

Emphasize the need for proper packaging and storage conditions to maintain the stability of gastroretentive formulations throughout their shelf life.[19]

4. ***Factors Influencing Gastric Retention***

1. Gastric Emptying Process

Describe the gastric emptying process, wherein ingested food and fluids are emptied from the stomach into the small intestine.

Explain the factors affecting gastric emptying, including the volume and composition of the meal, gastric motility, gastric pH, and the presence of drugs or other substances.

Discuss the implications of gastric emptying on drug absorption and bioavailability, particularly for drugs susceptible to degradation or absorption in the stomach.

Highlight strategies to modulate gastric emptying, such as formulation design (e.g., delaying gastric emptying with viscous or fatty meals) or administration timing (e.g., administering drugs before or after meals).[22]

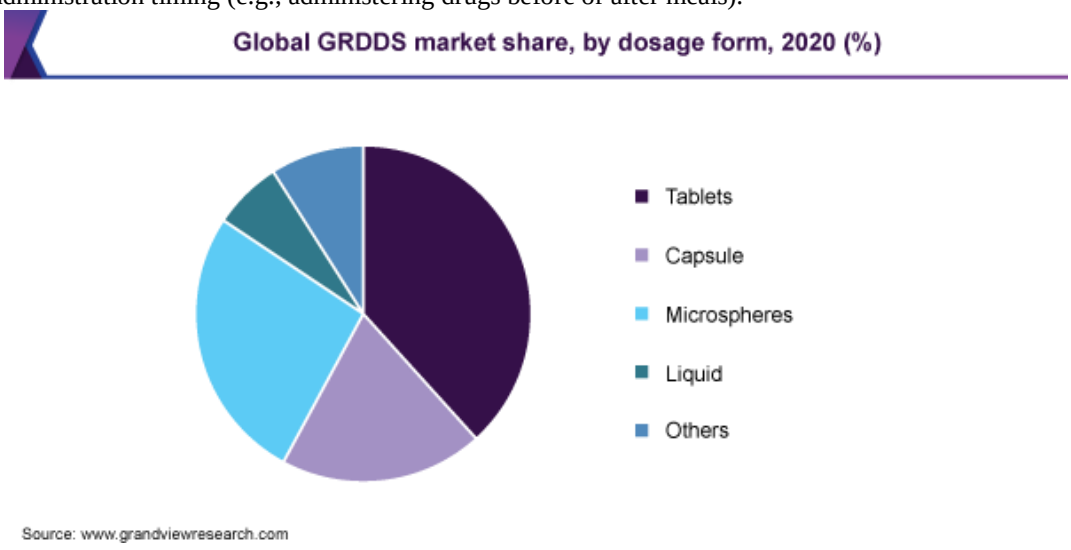

Fig.4

2. Gastrointestinal Transit

Explain the concept of gastrointestinal transit, which refers to the movement of ingested materials through the gastrointestinal tract, including the stomach, small intestine, and large intestine.

Discuss the factors influencing gastrointestinal transit time, such as the physicochemical properties of ingested materials (e.g., size, density, solubility), gastrointestinal motility, and the presence of food or other substances.

Describe how variations in gastrointestinal transit time can impact drug absorption and release kinetics, as well as the overall efficacy of gastroretentive drug delivery systems.

Highlight methods for assessing gastrointestinal transit time, including scintigraphy, magnetic resonance imaging (MRI), and capsule endoscopy.[21]

3. Physiological Factors

Discuss physiological factors that influence gastric retention, including age, gender, gastric motility disorders, and concomitant medical conditions (e.g., diabetes, gastroparesis).

Explain how age-related changes in gastrointestinal physiology (e.g., decreased gastric motility, altered gastric pH) can affect drug absorption and gastric retention.

Address gender differences in gastrointestinal physiology and drug pharmacokinetics, highlighting potential implications for gastroretentive drug delivery.

Consider the impact of physiological variability among patient populations on the design and optimization of gastroretentive formulations.[16]

5. *Types of Gastroretentive Drug Delivery Systems*

1.**Floating Systems**

Describe floating systems, which are designed to float on the gastric contents, prolonging their residence time in the stomach the principle behind their buoyancy, often achieved through the incorporation of low-density materials or gas-generating agents. Discuss examples of floating dosage forms, including floating tablets, capsules, and multiparticulate formulations. Highlight the advantages of floating systems, such as enhanced gastric retention, improved drug absorption, and reduced dosing frequency.[9]

2. Mucoadhesive Systems

Define mucoadhesive systems, which adhere to the gastric mucosa upon contact, prolonging their residence time in the stomach.

Explain the mechanisms of mucoadhesion, which involve interactions between adhesive polymers in the formulation and mucin glycoproteins on the mucosal surface.

Discuss commonly used mucoadhesive polymers, such as carbomers, chitosan, and cellulose derivatives.

Highlight the benefits of mucoadhesive systems, including localized drug delivery, improved bioavailability, and reduced dosing frequency.

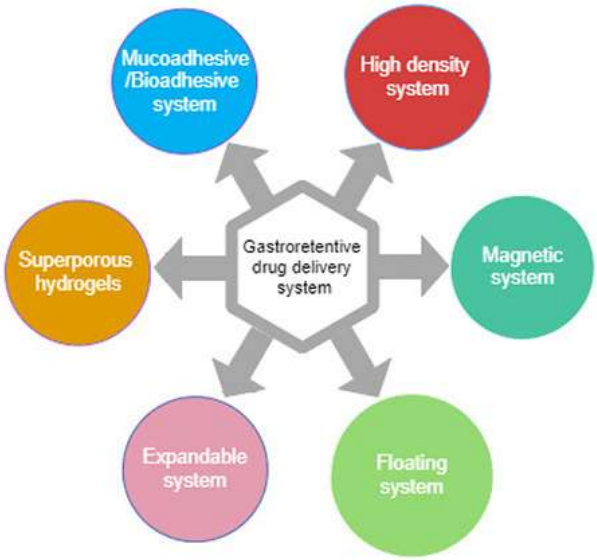

Fig.5

3. Expandable Systems

Describe expandable systems, which undergo swelling or expansion upon contact with gastric fluids, leading to increased size and retention in the stomach. Explain the mechanisms of expansion, typically involving the uptake of water by hydrophilic polymers in the formulation.

Discuss examples of polymers used in expandable systems, such as hydroxypropyl methylcellulose (HPMC) and sodium alginate.

Highlight the advantages of expandable systems, including prolonged gastric retention, controlled drug release, and reduced variability in drug absorption.[7]

4. Magnetic Systems

Define magnetic systems, which utilize magnetic forces to retain dosage forms in the stomach.

Explain how magnetic systems work, involving the incorporation of magnetic materials (e.g., iron oxides) into the formulation and the application of external magnets to retain the dosage form in the desired location.
Discuss the advantages of magnetic systems, such as precise control over gastric retention and targeted drug delivery to specific regions of the stomach.

Highlight potential applications of magnetic systems in gastroretentive drug delivery, including the treatment of gastric disorders and localized drug therapy.[7]

6. *Applications of Gastroretentive Drug Delivery:-*

Treatment of Gastric Ulcers

Discuss the application of gastroretentive drug delivery systems in the treatment of gastric ulcers, which are open sores that develop on the lining of the stomach.

Explain how prolonged gastric retention of anti-ulcer medications, such as proton pump inhibitors (PPIs) or histamine H2-receptor antagonists, can enhance their efficacy in healing gastric ulcers.

Highlight the benefits of gastroretentive formulations for the treatment of gastric ulcers, including improved drug bioavailability, enhanced therapeutic efficacy, and reduced dosing frequency.

Discuss specific examples of gastroretentive formulations used in the management of gastric ulcers and their clinical effectiveness. [22]

2. Controlled Release of Drugs

Explain how gastroretentive drug delivery systems can be utilized for controlled release of drugs, allowing for sustained and consistent drug release over an extended period.

Discuss the advantages of controlled-release formulations, including improved patient compliance, reduced side effects, and optimized pharmacokinetics.

Highlight examples of drugs that benefit from controlled release in the stomach, such as pain medications, antiemetics, and antibiotics.

Describe various approaches to achieve controlled release in gastroretentive formulations, such as matrix systems, coated pellets, or osmotic pumps.[19]

3. Targeted Drug Delivery to the Stomach

Discuss the potential of gastroretentive drug delivery systems for targeted drug delivery to the stomach, allowing for localized therapy and minimizing systemic exposure.

Explain how targeted delivery to the stomach can be advantageous for the treatment of gastric disorders, such as Helicobacter pylori infections, gastritis, or gastric cancer.

Highlight the importance of site-specific drug delivery in minimizing adverse effects and maximizing therapeutic outcomes.

Discuss examples of targeted gastroretentive formulations designed for specific indications, including gastric mucosal protection, eradication of pathogens, or treatment of gastric motility disorders.[14]

7. *Recent Advances and Innovations:-*

1. Novel Technologies

Discuss recent advancements in gastroretentive drug delivery technologies, including innovative formulation approaches and delivery systems.

Highlight the development of novel polymers, excipients, and manufacturing techniques aimed at improving gastric retention and drug release kinetics.

Explore emerging trends such as 3D printing, microfabrication, and nanotechnology in the development of gastroretentive formulations.

Provide examples of cutting-edge technologies and their potential applications in gastroretentive drug delivery, such as microneedle patches, gastro-floating microcapsules, or gastric resident devices.[12]

2. Nanotechnology in Gastroretentive Systems

Explore the role of nanotechnology in the development of gastroretentive drug delivery systems, leveraging the unique properties of nanomaterials for enhanced drug delivery.

Discuss the application of nanoparticulate systems, such as liposomes, polymeric nanoparticles, or solid lipid nanoparticles, in prolonging gastric retention and improving drug bioavailability.

Highlight the benefits of nanotechnology-based gastroretentive systems, including increased drug solubility, improved cellular uptake, and targeted delivery to specific regions of the gastrointestinal tract.
Address challenges and considerations associated with the translation of nanotechnology-based gastroretentive formulations from the lab to clinical practice, including safety, scalability, and regulatory approval.[12]

3. Combination Therapies

Discuss the growing interest in combination therapies using gastroretentive drug delivery systems, which involve the co-delivery of multiple drugs or therapeutic agents in a single dosage form.

Explain how combination therapies can offer synergistic effects, improved therapeutic outcomes, and simplified treatment regimens for patients.

Explore examples of combination gastroretentive formulations, such as fixed-dose combinations of anti-ulcer medications, pain relievers, or antimicrobial agents.

Highlight strategies for optimizing combination therapies in gastroretentive drug delivery, including dose optimization, drug compatibility, and release kinetics modulation.[10]

8. *Clinical Considerations and Challenges:-*

1. Safety and Tolerability

Discuss the importance of safety and tolerability in the clinical development and use of gastroretentive drug delivery systems, Address potential safety concerns associated with gastroretentive formulations, such as gastrointestinal irritation, mucosal damage, or allergic reactions to excipients. Highlight strategies for assessing the safety and tolerability of gastroretentive formulations in preclinical studies and clinical trials, including toxicity testing, pharmacokinetic studies, and adverse event monitoring.

Discuss approaches for minimizing safety risks and optimizing tolerability, such as selecting biocompatible polymers, optimizing formulation parameters, and conducting thorough risk assessments.[16]

2. Patient Compliance

Explore the role of patient compliance in the success of gastroretentive drug delivery systems, particularly for chronic or long-term therapies.

Discuss factors influencing patient compliance with gastroretentive formulations, including dosing frequency, ease of administration, taste, and side effects.

Highlight strategies for improving patient compliance with gastroretentive drug delivery, such as patient education, dose simplification, and the development of patient-friendly dosage forms.

Address challenges in assessing and monitoring patient compliance with gastroretentive formulations in clinical practice, including reliance on self-reporting, pill counts, or electronic monitoring devices.[16]

3. Regulatory Perspectives

Provide an overview of regulatory considerations for the development and approval of gastroretentive drug delivery systems, including regulatory pathways, guidelines, and requirements.

Discuss regulatory requirements for demonstrating the safety, efficacy, and quality of gastroretentive formulations, including preclinical testing, clinical trials, and manufacturing standards.

Explore challenges and considerations specific to regulatory approval of gastroretentive formulations, such as demonstrating equivalence to conventional dosage forms, addressing variability in gastric physiology, and ensuring product stability.

Highlight the importance of collaboration between pharmaceutical companies, regulatory agencies, and academic researchers in addressing regulatory challenges and advancing the field of gastroretentive drug delivery.[16]

9 . Case Stu*dies and Success Stories*

1.Examples of Commercially Available Products

Provide examples of commercially available gastroretentive drug delivery products across various therapeutic areas.

Discuss the formulation characteristics, mechanism of action, and clinical indications of each product.

Highlight key success factors contributing to the commercialization and market acceptance of these products, such as improved efficacy, safety, and patient convenience.

Explore case studies of successful gastroretentive formulations, including drug delivery platforms, dosage forms, and market penetration strategies.[20]

2. Clinical Trials and Research Findings

Summarize key findings from clinical trials and research studies evaluating gastroretentive drug delivery systems.

Discuss the design, methodology, and outcomes of relevant clinical trials, including efficacy, safety, pharmacokinetics, and patient-reported outcomes.

Highlight notable research findings supporting the effectiveness of gastroretentive formulations in specific therapeutic areas or patient populations.

Explore case studies of successful clinical development programs for gastroretentive formulations, including regulatory approvals, market access, and post-marketing surveillance. [20,21]

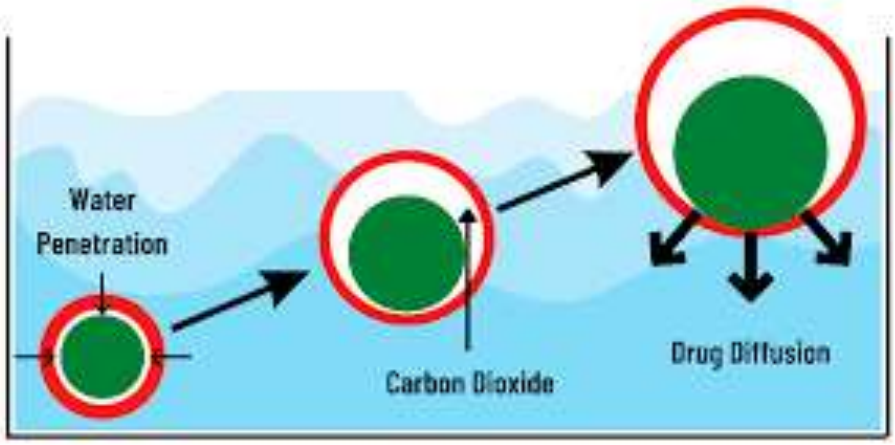

Fig.6

10. *Future Directions and Opportunities*

1,Emerging Trends

Discuss emerging trends in gastroretentive drug delivery, such as the integration of advanced technologies (e.g., nanotechnology, 3D printing, microfluidics) to enhance formulation design and drug delivery efficiency.

Explore the development of novel biomaterials, stimuli-responsive systems, and targeted delivery approaches for gastroretentive formulations.

Highlight emerging research areas, such as personalized medicine, combination therapies, and precision gastroretentive drug delivery, driven by advances in pharmacogenomics and biomarker identification.[19]

2. Potential Applications in Different Disease Areas

Explore the potential applications of gastroretentive drug delivery systems in different disease areas, beyond traditional indications like gastric ulcers and gastrointestinal disorders.

Discuss the role of gastroretentive formulations in targeted therapy for diseases of the gastrointestinal tract (e.g., Crohn's disease, colorectal cancer) and systemic conditions (e.g., cardiovascular diseases, diabetes).

Highlight opportunities for repurposing existing drugs or developing novel therapeutics using gastroretentive delivery platforms to address unmet medical needs in diverse patient populations.[17]

3. Market Growth Prospects

Assess the market growth prospects for gastroretentive drug delivery systems, driven by increasing demand for innovative drug delivery technologies, rising prevalence of chronic diseases, and growing geriatric population.

Discuss market drivers, including favorable regulatory policies, advancements in formulation science, and partnerships between pharmaceutical companies and research institutions.

Explore potential barriers to market adoption, such as manufacturing challenges, regulatory hurdles, reimbursement issues, and competition from existing dosage forms.

Provide insights into market dynamics, including key players, market segmentation, geographic trends, and growth projections for gastroretentive drug delivery systems.[14]

11. *Conclusion*

In conclusion, gastroretentive drug delivery systems offer promising solutions to overcome the challenges associated with conventional oral drug delivery. Throughout this presentation, we have explored various aspects of gastroretentive formulations, from their mechanisms of action to their clinical applications and future prospects. Let's recap the key points discussed:

Gastroretentive drug delivery systems utilize different mechanisms, including floating, mucoadhesion, expansion, and magnetic forces, to prolong gastric residence time and enhance drug absorption.

These systems have shown potential applications in the treatment of gastric ulcers, controlled release of drugs, and targeted delivery to the stomach, offering benefits such as improved bioavailability, reduced dosing frequency, and enhanced therapeutic efficacy.[17]

Recent advances in gastroretentive technology, including novel formulations, nanotechnology, and combination therapies, present exciting opportunities for innovation and personalized medicine.

However, challenges remain in ensuring the safety, tolerability, and regulatory approval of gastroretentive formulations, as well as addressing market barriers and optimizing market access.[19]**Implications for Drug Delivery and Healthcare**

The development and adoption of gastroretentive drug delivery systems have significant implications for drug delivery and healthcare. By improving drug bioavailability, enhancing therapeutic efficacy, and increasing patient compliance, these systems have the potential to revolutionize treatment outcomes and patient care across various disease areas. Furthermore, advancements in gastroretentive technology pave the way for personalized medicine, targeted therapy, and precision drug delivery, ultimately improving the quality of life for patients worldwide.

As we continue to explore new avenues in gastroretentive drug delivery, collaboration between researchers, pharmaceutical companies, regulatory agencies, and healthcare providers will be crucial to translating innovation into tangible clinical benefits. Together, we can harness the full potential of gastroretentive drug delivery systems to address unmet medical needs, optimize drug therapy, and shape the future of healthcare delivery.[21,22.24]

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