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# EXPLORING THE ROLE OF POLYMERS IN SUSTAINED GASTRORETENTIVE DRUG DELIVERY SYSTEMS

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## Abstract

Gastroretentive Drug Delivery Systems (GRDDS) are designed to prolong the residence time of dosage forms in the stomach, thereby enhancing the bioavailability of drugs that are primarily absorbed in the upper gastrointestinal tract or have a narrow absorption window. One of the key components determining the performance of these systems is the use of suitable polymers. Both natural and synthetic polymers have been widely explored for their ability to provide buoyancy, mucoadhesion, swelling, and gel formation. Natural polymers like chitosan, gellan gum, xanthan gum, pectin, and guar gum are favored for their biodegradability and biocompatibility. In contrast, synthetic and semi-synthetic polymers such as Hydroxypropyl Methylcellulose (HPMC), Carbopol, Polyox WSR, and Ethyl Cellulose offer predictable behavior and consistent drug release profiles. This review article explores the types, roles, mechanisms, advantages, and limitations of various polymers used in GRDDS, with an emphasis on their formulation potential and future prospects.

**Keywords**:

Gastroretentive Drug Delivery Systems (GRDDS), Natural Polymers, Synthetic Polymers, Floating Systems, Mucoadhesive Systems, Controlled Drug Release, Chitosan, HPMC, Xanthan Gum, Carbopol, Drug Bioavailability.

## Introduction

Oral drug delivery is the most convenient and widely accepted route of drug administration, offering benefits such as ease of administration, patient compliance, and cost-effectiveness [1].

However, certain drugs face challenges in oral bioavailability due to their short gastric residence time, poor solubility in the intestinal environment, or instability in alkaline pH [2].

To overcome these limitations, gastroretentive drug delivery systems (GRDDS) have been developed, which prolong the gastric retention time of dosage forms and enhance drug absorption in the upper gastrointestinal (GI) tract [3].

One of the significant components in GRDDS is the use of polymers both natural and synthetic which provide the matrix structure necessary for buoyancy, swelling,

mucoadhesion, and controlled release. Natural polymers such as xanthan gum, guar gum, and chitosan are biocompatible, biodegradable, and widely accessible [4].

On the other hand, synthetic polymers like hydroxypropyl methylcellulose (HPMC), carbopol, and polyvinyl alcohol (PVA) offer reproducible physicochemical properties and predictable behavior [5].

This review aims to explore the role of both natural and synthetic polymers in gastroretentive formulations, their mechanisms, advantages, limitations, and recent advances in polymer-based GRDDS, supported by various formulation examples and case studies.

Mechanisms of Gastroretention

Gastroretentive drug delivery systems (GRDDS) are specially designed to retain the dosage form in the stomach for an extended period, thereby enhancing the absorption of drugs that are preferentially absorbed from the upper part of the gastrointestinal tract. The success of gastroretention relies on various physiological and physicochemical factors such as gastric emptying rate, formulation density, and interactions with the gastric mucosa. The major mechanisms used in GRDDS are as follows [6]:

Floating Drug Delivery Systems (FDDS)

These systems are based on the principle of buoyancy. They have a lower density than gastric fluids and hence remain buoyant in the stomach for a prolonged period without affecting the gastric emptying rate. As the system floats on the gastric contents, the drug is released gradually, enhancing bioavailability. FDDS can be further classified into:

- **Effervescent systems**, which generate gas ($CO_2$) by reaction with gastric acid (using agents like sodium bicarbonate), creating a floating effect.
- **Non-effervescent systems**, which incorporate low-density polymers (e.g., HPMC, ethyl cellulose) to maintain buoyancy [7].

Mucoadhesive or Bioadhesive Systems

These systems adhere to the gastric mucosal lining through interactions between the mucin layer and the formulation's polymers. Natural and synthetic mucoadhesive polymers such as chitosan, carbopol, and pectin are used to increase the residence time of the dosage form. The adhesion prevents the formulation from being rapidly emptied with gastric contents, allowing for prolonged and localized drug release at the absorption site [8].

Swelling and Expanding Systems

Swelling systems are composed of hydrophilic polymers that absorb water and swell in the gastric environment. The expanded size prevents the dosage form from passing through the pyloric sphincter, thus prolonging its stay in the stomach. Polymers like HPMC, carbopol, and xanthan gum are commonly used. Once the drug is released, the swollen system gradually erodes or disintegrates and exits the stomach [9].

High-Density Systems

Unlike floating systems, high-density systems are designed to sink and remain at the bottom of the stomach. These formulations are prepared using excipients with a density

greater than that of the gastric contents (usually >1.5 g/cm$^3$), such as barium sulfate, zinc oxide, or titanium dioxide. The increased weight ensures that the system resists gastric emptying and remains in the antrum or lower stomach for an extended period [10].

Natural Polymers in Gastroretentive Drug Delivery Systems (GRDDS)

Natural polymers have gained substantial attention in the development of gastroretentive drug delivery systems due to their biodegradability, biocompatibility, non-toxicity, and widespread availability. These polymers are generally regarded as safe (GRAS) by regulatory agencies and are often preferred in pharmaceutical formulations. They exhibit various functionalities such as swelling, mucoadhesion, gel formation, and film-forming properties, making them ideal candidates for GRDDS. Below are some commonly used natural polymers and their roles in gastroretentive systems [11]:

*Gellan Gum*

Gellan gum is an anionic polysaccharide produced by *Sphingomonas elodea*. It forms a strong gel in the presence of mono- or divalent cations (such as calcium or sodium ions), making it suitable for in situ gelling and floating systems. Its gelation capability allows for the formation of a floating matrix that can prolong gastric residence time. Gellan gum is also used in combination with other polymers to control the drug release rate.

*Xanthan Gum*

Xanthan gum is a high-molecular-weight extracellular polysaccharide obtained from *Xanthomonas campestris*. It has a high viscosity even at low concentrations and exhibits excellent swelling behavior in aqueous media. In GRDDS, xanthan gum acts as a hydrophilic matrix former that can swell upon contact with gastric fluids, allowing for sustained drug release and extended gastric retention.

*Guar Gum*

Derived from the endosperm of the guar plant (*Cyamopsis tetragonoloba*), guar gum is a galactomannan polysaccharide that swells significantly in the presence of gastric fluid. Due to its hydrophilic nature and gelling ability, it is often used in matrix tablets. It is commonly blended with synthetic or other natural polymers to modulate drug release profiles and enhance mucoadhesive strength.

*Pectin*

Pectin is a complex polysaccharide found in the cell walls of citrus fruits and apples. It possesses mucoadhesive properties and can form gels under acidic conditions (such as gastric pH), which makes it suitable for GRDDS. It helps in maintaining the drug at the absorption site and provides controlled drug release. Pectin also contributes to bioadhesion and gastric retention through its carboxylic acid groups.

*Chitosan*

Chitosan is a cationic polysaccharide obtained by the deacetylation of chitin, which is found in the shells of crustaceans. It has excellent mucoadhesive and film-forming properties due to its positive charge, which allows interaction with the negatively charged mucosal lining of the stomach. In GRDDS, chitosan enhances gastric retention, forms gels at low pH, and supports sustained drug release through matrix formation or coating systems.

*Tragacanth Gum*

Tragacanth is a natural gum exuded from the dried sap of *Astragalus* species. It forms highly viscous colloidal solutions in water and is used as a binder and suspending agent in pharmaceutical formulations. In GRDDS, tragacanth gum forms viscous gels that swell in gastric fluids, thereby enhancing gastric retention and providing a sustained drug release matrix.

*Maize and Jowar Stem Pith*

Maize and Jowar stem piths are relatively novel natural swelling agents obtained from agricultural sources. These lignocellulosic materials exhibit significant water uptake and swelling characteristics, which make them suitable for use in gastroretentive formulations. Their abundant availability and natural origin add to their appeal as cost-effective and eco-friendly alternatives in controlled drug delivery systems.

Synthetic and Semi-Synthetic Polymers in Gastroretentive Drug Delivery Systems (GRDDS)

Synthetic and semi-synthetic polymers play a critical role in the design of gastroretentive drug delivery systems due to their consistency, stability, and ability to provide controlled and reproducible drug release profiles. These polymers are often used to engineer various types of GRDDS such as floating, mucoadhesive, swelling, and high-density systems. Their physicochemical properties can be precisely tailored, allowing better control over drug release kinetics, mechanical strength, and bioadhesion. Below is a discussion of some commonly used synthetic and semi-synthetic polymers in GRDDS [12]:

*Carbopol (Carbomer)*

Carbopol is a synthetic high molecular weight, cross-linked polyacrylic acid polymer that swells extensively in aqueous environments. It possesses strong mucoadhesive properties due to its ability to form hydrogen bonds with mucin. In acidic gastric conditions, Carbopol swells to form a gel-like matrix, thereby increasing the residence time of the dosage form. It is commonly employed in floating tablets and mucoadhesive systems, where it helps to prolong drug retention and release.

*HPMC (Hydroxypropyl Methylcellulose)*

HPMC is a widely used semi-synthetic, non-ionic cellulose ether derivative known for its biocompatibility, non-toxicity, and ability to form hydrophilic matrices. It is available in various viscosity grades and serves as a key matrix-forming agent in sustained-release formulations. In GRDDS, HPMC swells upon contact with gastric fluids, forming a gel barrier that controls the diffusion of the drug and slows gastric emptying. Its versatility makes it suitable for floating tablets, matrix tablets, and film-coated systems.

*Polyox WSR (Polyethylene Oxide)*

Polyox water-soluble resins (WSRs) are non-ionic, hydrophilic polymers known for their high swelling capacity and viscosity. They are used in controlled-release dosage forms due to their ability to rapidly hydrate and expand, forming a robust gel matrix. In GRDDS, Polyox helps in the design of expandable or swelling-type systems that resist gastric transit by increasing the size of the dosage form, thereby enhancing gastric retention and providing sustained drug delivery.

*Ethyl Cellulose*

Ethyl cellulose is a water-insoluble, semi-synthetic derivative of cellulose commonly used as a film-forming and matrix-forming agent in sustained-release formulations. In GRDDS, it serves as a rate-controlling membrane or coating material that slows down the release of the drug by acting as a barrier to water penetration and drug diffusion. Ethyl cellulose is especially useful in floating systems where it contributes to the buoyancy of the dosage form and maintains its integrity in gastric fluids.

*Sodium Alginate*

Sodium alginate is a naturally derived but often chemically modified polymer that forms strong gels in the presence of divalent cations (such as calcium) and under acidic conditions. It is particularly suited for forming floating beads and in-situ gel systems. Upon contact with the acidic gastric environment, sodium alginate gels instantly, forming a stable matrix that floats and gradually releases the drug. Its biocompatibility and gel-forming ability make it a key component in floating and swelling GRDDS.

## Advantages and Limitations of Polymers in GRDDS

### Advantages

Polymers both natural and synthetic play a pivotal role in the formulation and performance of gastroretentive drug delivery systems (GRDDS). Their use imparts multiple advantages that enhance drug bioavailability, patient compliance, and therapeutic effectiveness. One of the primary advantages of using polymers in GRDDS is their ability to control the release rate of the drug over an extended period, thus maintaining therapeutic drug levels and reducing dosing frequency. Natural polymers like xanthan gum, guar gum, chitosan, and pectin offer biocompatibility, biodegradability, and minimal toxicity, which makes them ideal for safe long-term use. Meanwhile, synthetic and semi-synthetic polymers such as HPMC, carbopol, polyox, and ethyl cellulose provide consistent performance, better mechanical properties, and reproducible drug release kinetics.

Polymers also enable the design of diverse GRDDS mechanisms such as floating, swelling, mucoadhesive, and high-density systems. Mucoadhesive polymers prolong gastric retention by adhering to the mucosal lining, while swelling polymers increase in size to prevent early passage through the pylorus. Floating systems benefit from low-density polymers that keep the formulation buoyant in gastric fluids. In addition, polymers can be modified chemically or physically to tailor the drug release profile according to the specific therapeutic needs.

Despite these advantages, the use of polymers in GRDDS is not without limitations. Natural polymers often suffer from batch-to-batch variability, poor mechanical strength, and slower gelation rates, which can affect the reliability and scalability of formulations. They may also be sensitive to environmental conditions like pH and temperature, which could compromise the stability of the dosage form. On the other hand, synthetic polymers, although consistent and customizable, may pose biocompatibility issues in some cases and require regulatory scrutiny. High viscosity of some polymers may lead to processing difficulties, while others may show poor swelling or gelling in acidic environments, limiting their effectiveness in gastric conditions [13].

## Limitations

Although polymers play a key role in enhancing the performance of gastroretentive drug delivery systems (GRDDS), they also present several limitations that must be addressed during formulation development. Natural polymers such as guar gum, xanthan gum, and pectin often suffer from batch-to-batch variability, which can result in inconsistent drug release profiles and mechanical properties. These polymers may also exhibit low mechanical strength, making the dosage forms prone to deformation or disintegration under gastric motility. Additionally, many natural polymers are sensitive to environmental conditions like humidity, temperature, and pH, affecting their swelling, gelling, or mucoadhesive behavior. On the other hand, synthetic and semi-synthetic polymers such as HPMC, Carbopol, and ethyl cellulose, while more consistent in performance, may raise concerns regarding long-term safety and biocompatibility. Processing challenges can also arise due to the high viscosity of some polymers, which may complicate manufacturing. Moreover, certain polymers may not function efficiently in the acidic gastric environment, limiting their utility in specific GRDDS approaches. Therefore, the appropriate selection and combination of polymers are essential to ensure formulation stability, desired drug release, and effective gastric retention [14].

**Table 1: Application of Polymers in GRDDS Formulations**

| S. No. | Drug | Polymers Used | Reference |
|---|---|---|---|
| 1 | Gemfibrozil | Gellan gum, Gum Arabic | Pranita et al., (2025) [15] |
| 2 | Gemfibrozil | Carbopol, Sodium alginate, Xanthan gum, HPMC K4M | Janaki and Sathyaraj, (2024) [16] |
| 3 | Propranolol HCl | Guar gum, Pectin | Wakde et al., (2013) [17] |
| 4 | Lansoprazole | Xanthan gum, Gellan gum, Carbopol 940P, Chitosan | Sonam and Banveer, (2021) [18] |
| 5 | Nateglinide, Gemfibrozil | HPMC K4M, Polyox WSR 303, Carbopol 971P | Wajid et al., (2022) [18] |
| 6 | Glimepiride | Chitosan, Xanthan gum, Gum Tragacanth | Vikas and Ashutosh, (2021) [19] |
| 7 | Cefixime Trihydrate | HPMC K100M, Carbopol 934P, Ethyl cellulose | Jadhao et al., (2021) [20] |
| 8 | Captopril | Maize Stem Pith, Jowar Stem Pith | Bhushan et al., (2023) [21] |
| 9 | Celiprolol | HPMC, Sodium alginate | Shahid et al., (2023) 22] |
| 10 | Cinnarizine | HPMC, Ethyl cellulose | Himanshu et al., (2024) [23] |

## Conclusion

Gastroretentive drug delivery systems (GRDDS) represent a promising approach to enhance the bioavailability and therapeutic efficacy of drugs with narrow absorption windows, poor solubility in intestinal fluids, or local action in the stomach. The selection and application of suitable natural, synthetic, or semi-synthetic polymers play a vital role in achieving prolonged gastric retention, controlled drug release, and improved patient compliance. Natural polymers like gellan gum, xanthan gum, chitosan, and pectin offer biocompatibility and biodegradability, whereas synthetic polymers such as HPMC, Carbopol, and ethyl cellulose provide consistency, mechanical strength, and controlled release characteristics. However, each class of polymer comes with its own advantages and formulation challenges. A rational combination of these polymers, tailored to the drug's properties and therapeutic needs, is essential for the successful design of GRDDS. Ongoing research and development in polymer science continue to expand the possibilities for innovative gastroretentive systems, paving the way for more effective and patient-friendly oral drug delivery solutions.

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