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## Review Article

# Polymers And Techniques Used in The Development of Gastro Retentive Drug Delivery System

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## ABSTRACT

Oral drug delivery: This system enables dosage forms to remain in the stomach for a longer duration, allowing for a slow release of the drug. This approach addresses several drawbacks of traditional oral delivery methods, particularly the issue of poor bioavailability. These dosage forms are designed to release drugs in the upper part of the gastrointestinal tract, especially in the stomach, in a controlled manner, which can provide sustained release without significantly compromising overall bioavailability. A polymer is a large molecular compound characterized by long repeating chains and can be either natural or synthetic, each with unique advantages. Polymers are valued for their ability to control drug release, their favourable flow properties, and their potential to enhance drug dissolution, ultimately improving bioavailability and stability during bodily processing. Often, a combination of natural and synthetic polymers is utilized to take advantage of their strengths and mitigate the weaknesses of existing polymers. This review discusses various polymers and other substances used in the formulation of gastro retentive drug delivery systems, including hydrodynamically balanced systems, raft systems, muco-adhesive systems, floating systems, high-density systems, and magnetic systems. Additionally, it presents an overview of various gastro retentive dosage forms along with the different drugs and polymers that have been employed in these formulations.

## INTRODUCTION

**Definition:** A dose form that can remain in the stomach for a long period of time is known as a gastro retentive drug delivery mechanism [1].

Targeting site-specific medication release in the upper gastrointestinal tract for both local and systemic effects, it is a strategy for prolonging the stomach residence duration [2]. There are many therapeutic advantages of GRDDS that are not as great with oral standard systems. They show local

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drug activity, improve bioavailability and patient compliance, and lessen fluctuations in plasma drug concentration levels [3]. By prolonging the stomach residence time, gastro-retentive drug delivery aims to target site-specific medication release in the upper gastrointestinal tract for both local and systemic effects. Compared to oral standard systems, GRDDS delivers more therapeutic benefits. They improve bioavailability and patient compliance, reduce fluctuations in plasma drug concentration levels, and demonstrate local drug activity [4]. Creating controlled release gastro-retentive forms can improve the solubility of drugs in high pH conditions and extend their gastrointestinal residence time for several hours. This would also help reduce drug waste. GRDDS can improve the regulated administration of drugs with a narrow absorption window by releasing them continuously [5].

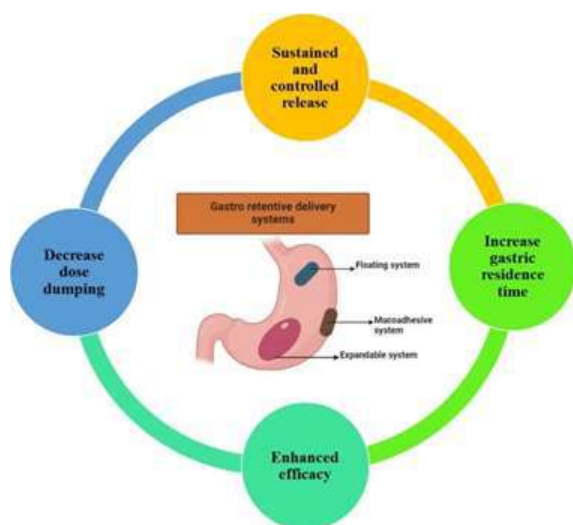


FIGURE NO:1

### INTRODUCTION OF POLYMER:

The term "polymer" originates from the Greek roots "Poly" signifying many and "meros" signifying parts. Polymer chains possess extremely high molecular weights because of the repeating units (monomers) they consist of. A category of macromolecules is presumed to consist of polymers. To create a polymer, a small

molecule called a monomer combines with other molecules of the same or different types. Dimer, trimer, tetramer, or pentamer describes the compound formed when two, three, four, or five monomers are connected together. Here are two components of drug release. The first component is polymer studies, while the second [6].

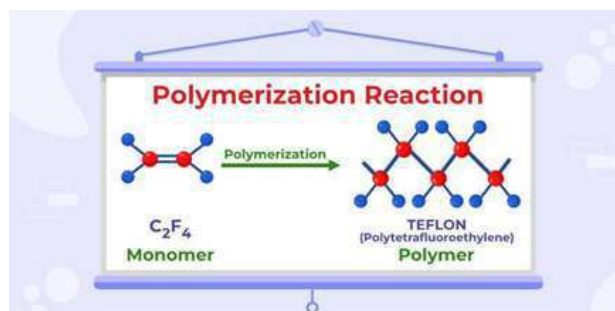


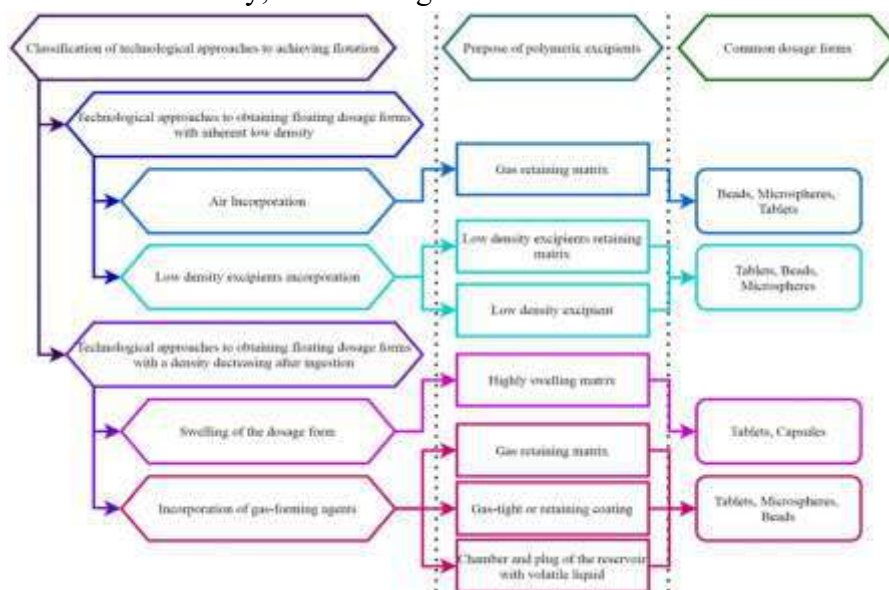
FIGURE NO:2

### NATURAL POLYMERS:

In the pharmaceutical industry, polymers are utilized as solubilizers, stabilizers, mechanical supports, flow control agents for liquids, suspensions, and emulsions, tablet binder, film coating agents to mask drug taste, and protective and stable. In the pharmaceutical industry, polymers are employed as mechanical supports, solvents, stabilizers, tablet binders, flow control agents for liquids, suspensions, and emulsions, film coating agents to cover the taste of medications, and stabilizing and protective compounds [7]. Pharmaceutical polymers are frequently used to increase stability, improve bioavailability, and provide controlled release (such as prolonged, pulsed, and targeted). The pace at which a drug is released from a matrix product, which contains a sustained release characteristic agent, depends on the initial drug concentration and polymer chain relaxation [8]. Depending on the technological methods that have historically underpinned the FDF classification, targeted medication delivery in this instance takes the shape of a buoyant feature that can be attained in a number of ways. Currently, they can be

divided into two primary directions: creating systems with a low starting density by adding air or explosives with a low bulk density, and creating

systems whose density drops after ingestion as a result of gas production or swelling [9].



**FIGURE NO3: Classification of technological approaches to achieve flotation, the purpose of polymers in these approaches, and the most common dosage forms.**

**SYNTHETIC POLYMER:**

Medications frequently contain synthetic polymers. Synthetic polymers are frequently employed as film coating agents and binders.

Large macromolecules with many functional groups are called polymers. Synthetic polymers can be fully synthetic or semi-synthetics, which are altered forms of natural polymers [10].

**TABLE :1 Advantages and Disadvantages of Natural and Synthetic polymers[11].**

Natural polymers		Synthetic polymers
<ul style="list-style-type: none"> <li>• Less toxic</li> <li>• Biodegradable</li> <li>• Biocompatibility</li> <li>• Easily available</li> </ul>	Advantages	<ul style="list-style-type: none"> <li>• Biocompatibility</li> </ul>
<ul style="list-style-type: none"> <li>• High degree of variability in natural materials derived from animal sources</li> <li>• Structurally more complex</li> <li>• Extraction process very complicated and high cost</li> </ul>	Disadvantages	<ul style="list-style-type: none"> <li>• Toxic</li> <li>• Non degradable</li> <li>• Synthetic process is very complicated and high cost</li> </ul>

**NATURAL POLYMERS:**

**GUAR GUM :**

Cyamopsis tetragonolobus seeds are the source of this plant, which is a member of the Leguminosae family. A number of aliases are used to describe guar gum, including Cluster bean, Guaran, Calcutta lucerne, Cyamopsis, and Guarini. This

powder has a whitish-yellow appearance and has no flavor or smell. While guar gum dissolves in water, it does not dissolve in organic solvents. It is used as a binder and dissolving agent in pharmaceutical tablets and can increase viscosity [12]. In the presence of a transparent water suspension, it grows quickly. Guar gum's constituents can be divided into two groups: water-

soluble and non-water-soluble. Guarana, a hydrocolloid polysaccharide with a high molecular weight, accounts for around 85% of the soluble fraction. The hydrolysis of guarana results in the formation of 65% galactose and 35% mannose, which are connected by glycosidic linkages [13].

#### **XANTHAN GUM:**

It is a well-known biopolymer made of glucose, mannose, and glucuronic acid that is edible, natural, and biosynthetic. It has several uses, including thickening, suspending, emulsifying, gelling, stabilizing, and raising viscosity. Compared to HPMC, xanthan gum has zero-order drug release kinetics, which means that with greater electrolyte concentrations (potassium chloride or sodium chloride), drug release occurs more quickly. When it comes to controlled release formulations, particularly when included into tablets, xanthan gum is a fitting candidate. Because of its natural origin, biocompatibility, safety, and affordability of production, it is utilized as a pharmaceutical excipient [14].

#### **CHITOSAN:**

Chitosan is a linear amino polysaccharide that is produced when glucosamine and Acetylglucosamine copolymerize. Chitosan is a naturally occurring polymer that is produced when chitin undergoes deacetylation. It has beneficial biological properties such as biodegradability, biocompatibility, and non-toxicity. This polymer is appropriate for site specific delivery applications since it has antibacterial and bio adhesive qualities. Chitosan has a pKa value between 6.2 and 7, making it a polycationic weak base with a high molecular weight. It experiences buoyancy in neutral or acidic pH conditions (around 1.2), which makes controlled release methods easier. A chitosan film's thickness can

slow down the release process by decreasing the pace at which chemicals are released [15].

#### **CARRAGEENAN:**

The marine red algae *Chondrus crispus* or *Gigartina stellata*, which belong to the Rhodophyceae class, are the source of carrageenan, which are high molecular weight sulphated polysaccharides. There are three primary types of carrageenan from a functional perspective: lambda, kappa, and iota. Specific carrageenan types differ structurally in relation to their water absorption and gel forming characteristics. For instance, iota (~-carrageenan) and kappa (ˆ carrageenan) create hydrogels with varying rigidities when in contact with water, whereas lambda type ({} -carrageenan) forms viscous solutions [16]. The two primary natural gelling polysaccharides that are isolated from plants or seaweeds (apart from starch) and utilized as high-value food ingredients are carrageenan and pectin; in 1997, their projected global sales were US\$263 million. the three commercially used carbohydrate polymers from marine organisms are: (1) alginates, which are polymers from brown seaweeds that contain mannuronic and guluronic acids; (2) agar, which is a polymer from red seaweeds that contains o-galactose and anhydro-L-galactose; and (3) carrageenan [17].

#### **SYNTHETIC POLYMER:**

##### **HYDROXY METHOXY PROPYL CELLOUSE:**

Methoxy and hydroxy propyl, which have molecular weights ranging from 10,000 to 1,500,000 Dalton, are present in HPMC. HPMC has the ability to create colloids and dissolve in water. As a bio-adhesive polymer, HPMC can thicken preparations, improve coating activity, regulate media release, and function as an



emulsion agent. HPMC is frequently utilized in topical, ophthalmic, nasal, and oral therapies. HPMC polymers are used as bonding ingredients in tablets, coating solutions, and controlled and delayed release [18]. To design new controlled drug delivery systems based on HPMC that are meant to provide specific, pre-determined release profiles, it is highly desirable to (i) comprehend the precise mass transport mechanisms involved in drug release and (ii) be able to quantitatively predict the resulting drug release kinetics. One practical benefit of having an adequate mathematical model is the ability to simulate the effects of design parameters on release profiles of HPMC-based drug delivery systems [5]. The ideal controlled drug delivery system would have the required geometry (size and shape) and composition (drug type and quantity, polymer, and additives) predicted theoretically in order to generate a certain drug release profile [19].

### EUDRAGIT:

Eudragit is amorphous in nature. It comes from acrylic acid and polymerization of mainly used for coating materials and taste-masking substances in oral methacrylic acids dosage forms via spray atomization methods. Its glass transition temperature spans from ninety to one hundred fifty degrees Celsius. This substance is unbiodegradable, non-absorbent and non-toxic. This polymer comes in two grades, L and S. L grade dissolves at pH 6 and finds usage for applied in colon-targeted systems; S grade dissolves at pH 7. Sustained release uses the RS and RL grades, which have a quaternary amino group. At pH 5, Eudragit E prevents medication release in saliva by not dissolving. Find Eudragit in different forms including powders, granules, organic solutions, and dispersions. Based on the We have gone over their solubility, traits, and uses in grade. Ranitidine HCL was the active ingredient in developed

floating microspheres made with two polymers; HPMC and Eudragit grade E-100 in varying proportions. This mix produced long release inside the digestive tract, which improved absorption and increased Eudragit RL100 had quicker floating characteristics than Eudragit Refresher 100 [20].

**Table 2: Various grade of Eudragit**

Immediate Release	Colon Targeting	Delayed Release
E 100	FS 100	L 100
E P0	S 100	L 100-55
E 12,5	-	L 12,5

### POLY VINYL PYRROLIDINE:

Polyvinylpyrrolidone (PVP), often known as polyvidone or povidone, is a biodegradable and water-soluble polymer derived from N-vinylpyrrolidone. PVP, a hydrophilic polymer, is highly soluble in various solvents, has strong binding characteristics, and may stabilize suspensions and emulsions. The FDA has recognized this biocompatible and nontoxic polymer as safe. As a result, PVP finds widespread application in the pharmaceutical and biomedical industries as well as in the food sector, medicine, and cosmetics. PVP has special physical and chemical properties, including chemical inertness, colorlessness, temperature resistance, and pH stability. Different molecular weights of six PVP are differentiated by different K-values, e.g. K12.K17 (7900–10,800 Daltons), K25 (23,000–32,000 Daltons), K30K90 (900,000–1,300,000 Daltons) and K35 (35,000–51,000 Daltons). PVP is finding uses in the biomedical and pharmaceutical industries for the creation of various drug delivery oral, topical, transdermal, and ocular approaches among systems. Moreover, PVP is other useful in gene delivery or can be coupled with metal particles for application in regenerative targeted delivery and medicine. PVP's versatility makes it a very flexible plastic. Proposed for drug delivery systems are



morphologies of PVP as the polymeric carrier. PVP helps poorly soluble medications' bioavailability by enabling regulated drug release. guards operating chemicals against pH, temperature, and oxygen among other environmental elements. and assists to cover bad scents and tastes. Many active chemicals over

several PVP microparticles and nanoparticles provide merged categories. Using a variety of processes, from conventional approaches like spray, these PVP-based particles have been created drying to more sophisticated methods using supercritical fluids [21].

**TABLE 3: VARIOUS POLYMERS USED IN GRDDS**

Approaches	Description	Polymers used	Evaluation tests	References
Hydro dynamic balanced system (HBS)	In these system Hydrocolloids and medications are combined to create a formulation that floats on the stomach contents. These come in dose forms that are one unit in size. HBS system comprise one more hydrophilic gel-forming polymers.	Polycarbophil, Alginate, Sodium carboxymethyl cellulose, HPMC, Polyacrylate, Hydroxy ethyl cellulose (HEC), Carrageenan's Hydroxypropyl cellulose (HPC), Polystyrene, or Agar etc	Floating lag time, Total floating time, Invitro drug release studies, Swelling Index, Density measurement, Stability studies, Hardness, Content uniformity	22
Raft systems integrating alginate gels	The dose form can float over stomach fluid because these contain a carbonate component that reacts with gastric acid to produce bubbles in the gel.	Sodium alginate, Sodium bicarbonate, Acid neutralizer.	Viscosity and Rheology, Floating lagtime and Duration, Gel strength/Raft strength, Invitro Drug Release Study	23,24, 25
Bio adhesive system	Bio adhesive polymer included in these devices can adhere to the GIT's epithelial layers. Electrostatic bonding and the stomach interface's edge are how bio adhesive systems function.	Sucralfate, HPMC, Cholestyramin Dextrin, Sodium Alginate, Tragacanth Gliadin, Sodium , CMC ,Poly acrylic acid, Chitosan, polylactic acids, Lectin etc.	Mucoadhesive strength, Cohesion time Swelling index, Surface pH, Drug content uniformity, Invitro drug release, Stability studies, FTIR/DSC studies.	26
High density system	Pallets coated in these systems have a density of 1.004gm/cm <sup>3</sup>	Zinc oxide, Barium	Apparent Density	27,28, 29.

	which is higher than the stomach's contents. The high-density pellet used to prepare these kinds of pellets is based on the idea that thick pellets will remain in the stomach longer.	sulphate, Iron powder, Titanium dioxide	Measurement, Invitro Buoyancy test, Invitro drug release studies, Matrix Integrity, Hardness test, Surface morphology, Swelling studies, Drug Content uniformity	
Swelling type system	Ingredients with swelling properties are found in swelling type systems. and they enlarge so much that they are unable to flow out through the pylorus from the stomach. They can also be referred to as the "Plug type system," which keeps them in the pyloric sphincters for longer	Biodegradable polymers are used, Swelling agents (risperidone, sodium starch glycolate)	Gravimetric method, Dimensional change measurement, Water uptake, Visual observation and photographic documentation	30,31, 32
Magnetic system	These systems use external stimuli as a magnetic field to deliver drugs precisely; compounds with magnetic activity are added to these systems to achieve the desired drug delivery.	-	Magnetic field calibration test, Magnetic Retention test, Electromagnetic interference test Ect.	33,34
Hollow Micro spheres	Hollow microsphere drug delivery systems use formulations with the captured air in them that are sustained or prolonged released. Microspheres or hollow microspheres offer significant advantages for achieving gastroprotective medication delivery; these hollow microspheres also possess the ability to float over the stomach contents to have a therapeutic effect.	Poly Vinyl Alcohol (PVA), Poly D, L-lactic glycolic acid.	Particle size and shape Analysis, Surface morphology, Floating test, Density measurement, Drug loading and entrapment efficiency, Invitro drug release Stability studies, Thermal and crystallinity Analysis.	35,36
Floating micro sphere	Floating microspheres are in the form of powders that are free flowing. These are composed of synthetic polymers and proteins. Ideally Size of these floating microspheres should be less than two hundred micro meter.	DEAE cellulose, Poly(acryl) dextran and Poly(acryl) starch	Floating strength, Floating lag time, Total floating time, Zeta potential, surface charge, Stability studies, Invitro drug release study	37,38

	Drug is uniformly dissolved in these microspheres. On interaction of these microspheres with the fluid in the stomach, they form the colloidal gel barrier that controls the water intake in the microsphere and the release of drug from microspheres. Swollen polymer has air entrapped in them that gives floating property to the microspheres, thus GRT is increased.			
Micro porous compartment system	In these systems the drug pool is enclosed in a compartment having pores all around the membrane. The trapped air in the chamber of floatation that produce buoyancy in the gastric fluid in the stomach enters by the hole into the system then drug is dissolved into it, so in this way drug depot provides the constant drug transport	For instant cellulose ether polymer, Poly vinyl pyrrolidine, methylcellulose polymer and Poly vinyl alcohol and HPMC etc.	Buoyancy test, Drug release study, Swelling index, Water uptake and porosity measurement, Membrane integrity and morphology, Drug content uniformity, In vivo gastric retention.	39,40
Alginate beads	Floating alginate dosage forms were announced in the 1980s. Alginates are made up of linear anionic block copolymer hetero polysaccharides that are extracted from various species of cell walls of brown algae The formation of the hydrogel is carried out by inotropic gelation by reaction with the bivalent alkaline earth metals. For example: calcium alginate form has no solubility and has resistance in acidic environment. The beads	Sodium alginate, Low Methoxylated pectin, Calcium alginate, Ca <sup>2+</sup>	Particle size and shape analysis, Swelling index, Floating. Behaviour, Mechanical strength, Zeta potential, Stability studies, Invitro drug release studies.	27,30, 34

## CONCLUSION:

Drug delivery through various gastro-retentive methods has opened a new opportunity for effective approaches to enhance patient compliance and the bioavailability of numerous medications administered orally. Numerous techniques utilizing different polymers and

additional components can generate a broad array of gastro-retentive systems. The floating drug delivery method is the most widely used among gastro-retentive dosage forms. Nevertheless, significantly more research is necessary to address the numerous physiological and pharmacological challenges and to create more effective gastro-retentive dosage forms. Polymers are utilized in



conventional dosage forms, such as binders for enteric-coated tablets to conceal unpleasant tastes, viscosity modifiers to regulate flow in liquids, gel formulations for semisolids, and the production of transdermal patches. Ultimately, polymers possess a vast range of uses within drug delivery systems, even though their functions have been examined. The role of polymers in delivery is continuously advancing. Polymers are often extensively utilized in the pharmaceutical sector due to their wide array of applications.

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