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**Review Article**

# Natural, Semisynthetic, and Synthetic Polymers in Floating Drug Delivery Systems: A Comparative Review

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## ABSTRACT

Oral drug delivery systems are widely preferred because of their convenience, cost-effectiveness, and better patient compliance. However, conventional oral dosage forms often have limitations such as short gastric residence time and variable drug absorption. Gastro-retentive Drug Delivery Systems (GRDDS), particularly Floating Drug Delivery Systems (FDDS), have emerged as an effective approach to overcoming these limitations by prolonging gastric retention and providing controlled drug release. FDDS remain buoyant in gastric fluid for a prolonged period, which can improve bioavailability, therapeutic efficacy, and patient compliance. Polymers play a central role in FDDS by promoting gel formation, swelling, buoyancy, and controlled drug release, and are broadly classified as natural, semisynthetic, or synthetic depending on their origin. Natural polymers such as xanthan gum, guar gum, sodium alginate, chitosan, pectin, and gum karaya are widely used because of their biodegradability, biocompatibility, safety, and eco-friendly nature. Semisynthetic polymers, including HPMC, HPC, CMC, and ethyl cellulose, are chemically modified derivatives of natural cellulose that combine reasonable biocompatibility with more consistent film- and matrix-forming behavior than unmodified natural gums. Fully synthetic polymers such as Eudragit, PVA, PVP, and Carbopol are produced entirely from petrochemical monomers and generally offer the greatest formulation stability, mechanical strength, and reproducibility of drug release, though usually at higher cost and with a greater likelihood of irritation or limited biodegradability. This review examines the properties, advantages, and limitations of natural, semisynthetic, and synthetic polymers used in FDDS, and considers the circumstances under which each category or a combination of

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categories may be preferred. Natural polymers are generally safer and more environmentally friendly, semisynthetic polymers offer a practical middle ground between biocompatibility and formulation control, and synthetic polymers usually provide the most precise control over release; appropriate polymer selection, or combination, therefore depends on the specific requirements of the drug and the formulation.

## INTRODUCTION

Oral drug delivery is one of the most convenient and widely preferred routes of drug administration for systemic effect, mainly because of its simplicity, affordability, ease of administration, and better patient compliance compared with parenteral routes.[1] Reducing dosing frequency, simplifying administration, and minimizing infection risk associated with invasive routes are all recognized ways of improving medication compliance. Drug release from oral dosage forms usually occurs through diffusion, dissolution, or a combination of both, and the drug must be adequately absorbed across the gastrointestinal mucosa to produce its intended effect.[2] Oral administration is widely regarded as the most common and most preferred route of drug delivery, largely because of its convenience, cost-effectiveness, and ease of large-scale manufacture[3,68], and this route is nonetheless associated with several limitations, including short residence time of the dosage form within the gastrointestinal tract, variability in gastric emptying, and possible degradation of the drug in the reactive gastrointestinal environment.[4]

Most orally administered drugs are absorbed predominantly in the small intestine, with only a minor contribution from the large intestine. If gastric emptying is too fast or too slow, the amount of drug reaching its main absorption site and the time taken to reach that site can vary considerably, which can lead to irregular absorption and unpredictable time to maximum plasma concentration. Some drugs are not fully absorbed simply because the dosage form leaves the stomach, and consequently the upper small intestine, too quickly; this is a particular problem for drugs absorbed only from a specific “absorption window” in the upper gastrointestinal tract. Conventional oral dosage forms can therefore suffer from variable gastric emptying, incomplete drug release, and short gastric residence time, all of which can cause part of the dose to pass beyond its main absorption site without being absorbed. An ideal oral drug delivery system would remain in the stomach and release the drug gradually into the upper small intestine, allowing more complete and predictable absorption.[5,6,7] The general aim in designing such controlled oral drug delivery systems is to maximize the pharmacological effect of the drug at its intended site of action.[8]

Controlling gastric residence time (GRT) using gastro-retentive dosage forms (GRDFs) is one of the more practical approaches available for achieving a prolonged and predictable pattern of drug release in the gastrointestinal tract.[9] A range of synthetic, natural, and semi-synthetic polymers is used in the development of GRDDS, and polymer characteristics such as molecular weight, viscosity, and other physicochemical properties strongly influence the performance of the resulting formulation.

## 2. GASTRO-RETENTIVE DRUG DELIVERY SYSTEMS (GRDDS):

Gastro-retentive drug delivery systems (GRDDS) are a family of sustained-release approaches designed to retain the dosage form in the stomach for an extended period. Prolonging gastric residence can improve drug bioavailability by allowing more complete dissolution under acidic conditions, promoting better absorption, enabling sustained local action in the stomach, and

maintaining more even plasma drug levels with reduced dosing frequency.[10,11] GRDDS can provide both local and systemic effects within the gastrointestinal tract.[12] Drugs that irritate the stomach, are unstable at gastric pH, or undergo extensive first-pass metabolism are generally poor candidates for GRDDS, whereas drugs with poor solubility at intestinal (alkaline) pH, instability in intestinal fluids, or a narrow absorption window in the upper gastrointestinal tract are often better suited to this approach. GRDDS are broadly classified into floating, high-density, expandable, mucoadhesive, and magnetic systems.[13] Among these, floating systems are the most extensively studied and form the focus of the remainder of this review.

### *2.1 Floating Drug Delivery Systems:*

Floating drug delivery systems (FDDS) are a low-density type of GRDDS that remain buoyant over the gastric contents for a prolonged period without affecting the normal rate of gastric emptying; they are also known as hydrodynamically balanced systems. Because their bulk density is lower than that of gastric fluid, these dosage forms float on the stomach contents rather than being emptied along with the rest of the gastric contents. Many floating systems form a gel-like barrier at their outer surface on contact with gastric fluid and behave largely as hydrophilic matrices. The exact duration for which a given formulation remains buoyant depends on the polymer system and formulation design used and is normally established experimentally for each formulation rather than assumed.[14,15]

The concept of FDDS was first described by Davis in 1968 as a way of overcoming the difficulty some patients experience in swallowing conventional dosage forms. Davis proposed that this could be addressed by formulating dosage forms with a bulk density lower than that of gastric fluid (approximately 1.004 g/cm³), so that the dosage form floats on the surface of the gastric contents rather than sinking.[16] FDDS provide prolonged drug release and improved local gastric action, which makes them well suited to antibiotics used to treat *Helicobacter pylori* infection and other localized gastric conditions.[17]

## 3. POLYMERS USED IN FLOATING DRUG DELIVERY SYSTEMS:

Polymers used in FDDS are broadly classified into three categories based on their origin: natural, semisynthetic, and synthetic.[19] Semisynthetic polymers are chemically modified derivatives of natural polymers most commonly cellulose and are often grouped separately from both their natural precursors and from fully synthetic, petrochemical-derived polymers because chemical modification changes their solubility, viscosity, and film-forming behavior in ways that are relevant to FDDS formulation.

### *3.1 Natural Polymers:*

Natural polymers are widely used in FDDS because of their biodegradability, biocompatibility, and generally low toxicity. By promoting gel formation and swelling at the surface of the dosage form, they help lower the bulk density of the formulation and support buoyancy, while also contributing to muco-adhesion in some systems. Because prolonging the presence of the drug in the stomach can improve its dissolution and absorption, these swelling and gel-forming properties are directly relevant to the therapeutic performance of the formulation.[20] The natural polymers most commonly used in FDDS are summarized in Table 1.

**Table 1: Natural polymers used in FDDS**

| Sr. No | Polymer | Synonym | Biological Source | Properties | Merits | Demerits | Ref |
|---|---|---|---|---|---|---|---|
| 1. | Guar Gum | Guaran | Obtained from the endosperm of Cyamopsis tetragonolobus, Family: Leguminosae | Gelling property, emulsifying ability, thickening effect, binding capacity, excellent biocompatibility, biodegradability | Low cost, enhances buoyancy, good matrix former | Viscosity variation | [20, 21] |
| 2. | Xanthan Gum | Corn sugar gum, Polysaccharide B-1459 | Fermentation by Xanthomonas campestris | Stable over wide pH range, gel-forming ability | High solubility, gastric stability, good sustained-release property | High viscosity may slow drug release | [22, 23] |
| 3. | Sodium Alginate | Algin | Derived from the cell walls of brown algae (Phaeophyceae), Family: Laminariaceae | Forms ion-sensitive gel, swelling ability | Good gelling agent, prolonged release, improved gastric retention | pH-dependent gel formation | [24, 25] |
| 4. | Chitosan | Polyglucosamine, Poly-(D-glucosamine) | Derived from chitin (crustacean shells) | Biodegradable, permeation enhancer, mucoadhesive | Increases bioavailability | Solubility depends on acidic pH | [26, 27] |
| 5. | Pectin | Polygalacturonic acid | Extracted from citrus peel, apple pomace | Biodegradable, mucoadhesion and swelling property | Biocompatible, improved buoyancy | Low mechanical strength, pH-dependent solubility | [28 - 30] |
| 6. | Gum Karaya | Indian Tragacanth | Exudate of Sterculia urens, Family: Sterculiaceae | High swelling capacity, viscosity enhancer | Good thickening agent | Slow hydration rate | [31, 32] |
| 7. | Carrageenan | Irish moss extract, red seaweed gum | Originated from red seaweeds | Gel-forming ability, swelling ability | Suitable for sustained-release systems | Possible gel instability in some formulations | [33 - 35] |
| 8. | Psyllium Husk (Isabgol) | Isabgol, Ashwagolan, Aspaghol, Aspagol, Bazarqutuna, Blond Psyllium | Obtained from Plantago psyllium and from the seeds and husk of Plantago ovata, Family: Plantaginaceae | Mucilage formation, biodegradability, swelling property | Improves buoyancy, cost-effective natural polymer | High swelling may affect tablet hardness | [36, 37] |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 9. | Gellan Gum | Kelcogel, microbial gum | Produced by fermentation using Sphingomonas elodea | Strong gel formation, high mechanical strength | Stable gel formation, excellent sustained release | Requires proper concentration for gel formation | [38, 39] |

### *3.2 Semisynthetic Polymers:*

Semisynthetic polymers used in FDDS are chemically modified derivatives of natural cellulose. Modification of the cellulose backbone typically by etherification, as in HPMC, HPC, and CMC, or by partial ethylation, as in ethyl cellulose improves aqueous solubility, viscosity control, and film- or gel-forming consistency relative to unmodified natural gums, while the polymers generally retain good biocompatibility because they are still cellulose-derived.[43] This combination of modifiable performance and established biocompatibility is part of why cellulose-derivative polymers are among the most widely used gel-forming excipients in commercial floating tablets. The semisynthetic polymers most commonly used in FDDS are summarized in Table 2.

**Table 2: Semisynthetic polymers used in FDDS**

| Sr. No. | Polymer | Properties | Merits | Demerits | Ref. |
|---|---|---|---|---|---|
| 1. | HPMC (Hydroxypropyl Methylcellulose) | Gel-forming ability, non-ionic polymer, high viscosity | Sustained drug-release profile | Burst release at low concentration | [40-42] |
| 2. | HPC (Hydroxypropyl Cellulose) | Water-soluble, thermoplastic polymer | Enhanced controlled release | High concentration required | [43] |
| 3. | CMC (Carboxymethyl Cellulose) | Hydrophilic polymer, high viscosity, strong gel formation, swelling ability | Good matrix former, improved sustained drug release | Hygroscopic nature, possible burst release | [44] |
| 4. | Ethyl Cellulose | Hydrophobic polymer, water-insoluble, permeable to fluids | Sustained drug release | Limited swelling capacity | [45, 46] |

### *3.3 Synthetic Polymers:*

Fully synthetic polymers are produced entirely from petrochemical-derived monomers under controlled manufacturing conditions; catalysts and initiators are used during manufacture to start and control the polymerization reaction, and the resulting materials are broadly classified as thermoplastics, elastomers, or thermosets. Commonly used examples in FDDS include Eudragit, PVA, PVP, polystyrene, and Carbopol[56]. Because their molecular weight, substitution pattern, and cross-linking can be controlled precisely during synthesis, and because they contain no natural starting material, fully synthetic polymers generally offer the most consistent film-forming and matrix-forming behavior of the three polymer categories. The synthetic polymers most commonly used in FDDS are summarized in Table 3.

**Table 3: Synthetic polymers used in FDDS**

| Sr. No. | Polymer | Properties | Merits | Demerits | Ref. |
|---|---|---|---|---|---|
| 1. | Eudragit | Acrylic copolymer, pH-dependent permeability | Excellent film-forming polymer, controlled and targeted drug release | Expensive, polymer combination often required | [47, 48] |
| 2. | PVA (Polyvinyl Alcohol) | Water-soluble polymer, strong film-forming ability, mechanical strength | Improved tablet strength, enhanced swelling and controlled drug release | Moisture sensitivity | [49, 50] |
| 3. | PVP (Polyvinylpyrrolidone) | Water-soluble polymer, binding property, solubilizing ability | Improved drug dispersion, enhanced solubility | Hygroscopic nature, stability issues | [51] |
| 4. | Carbopol (Carbomer) | High swelling capacity, gel-forming polymer | Sustained drug release | High viscosity may slow drug release | [52] |

### *3.4 Comparative Evaluation:*

Natural, semisynthetic, and synthetic polymers all contribute to gastric retention in FDDS, but they tend to do so through different mechanisms and with different trade-offs. Natural polymers such as guar gum, xanthan gum, sodium alginate, and pectin are polysaccharides that swell and form physically cross-linked gel networks on contact with gastric fluid; this is what gives them their favorable biocompatibility, biodegradability, and low cost, but it also makes their swelling and gelling behavior more sensitive to factors such as pH, ionic strength, and microbial or enzymatic degradation, which can translate into batch-to-batch variability in floating performance.[20]

Semisynthetic polymers such as HPMC, HPC, CMC, and ethyl cellulose sit between these two extremes: because they are chemically modified cellulose, they retain much of the biocompatibility associated with natural polymers while their degree of substitution can be controlled during manufacture to give more consistent gel- and film-forming behavior than unmodified natural gums.[43] Fully synthetic polymers such as Eudragit, PVA, PVP, and Carbopol generally form the most chemically stable and reproducible gel or matrix structures of the three categories, which is why they tend to give the most predictable and sustained drug-release profiles. This greater control comes at the cost of higher raw-material and processing cost, and some synthetic polymers can cause gastrointestinal irritation or allergic reactions in sensitive individuals; several are also poorly biodegradable, which raises environmental concerns over their disposal.[53-55]

In practical terms, natural polymers may be preferable when low cost, biocompatibility, and biodegradability are the priority, or when some batch-to-batch variability in release can be tolerated. Semisynthetic polymers are often a practical default choice when a reasonable balance of biocompatibility and reproducibility is needed without the higher cost of fully synthetic materials. Fully synthetic polymers are usually favored when precise, reproducible control over drug release is essential for example, for drugs with a narrow therapeutic index or when formulation stability under varied storage conditions is a priority. Because the three categories address different aspects of formulation performance, a number of recent studies combine polymers from more than

one category in the same formulation, for example using a natural or semisynthetic polymer for buoyancy and biocompatibility alongside a synthetic polymer to control the rate of drug release; this combination approach is a recurring theme in the more recent floating-tablet literature.[53-55] Table 4 summarizes the key differences between natural, semisynthetic, and synthetic polymers relevant to FDDS.

**Table 4: Comparison of natural, semisynthetic, and synthetic polymers used in FDDS**

| Parameter | Natural Polymer | Semisynthetic Polymer | Synthetic Polymer | Ref. |
|---|---|---|---|---|
| Source | Obtained directly from plants, animals, or microorganisms (e.g., guar gum, pectin, chitosan) | Chemically modified natural polymers, mainly cellulose derivatives (e.g., HPMC, HPC, CMC) | Produced entirely from petrochemical-derived monomers (e.g., Eudragit, PVA, PVP, Carbopol) | [56] |
| Biodegradability | Highly biodegradable and environmentally friendly | Generally biodegradable, though modification can slow degradation somewhat | Variable; many are poorly biodegradable | [57] |
| Biocompatibility | Excellent biocompatibility, low toxicity | Good biocompatibility; long history of pharmaceutical use | Generally safe, but may cause irritation in some cases | [58] |
| Cost | Low cost | Moderate cost | Usually the most expensive of the three categories | [59] |
| Stability | Sensitive to microbial contamination and environmental conditions | More stable than unmodified natural polymers | Highest chemical and physical stability | [60] |
| Availability | Easily available | Widely available through industrial cellulose processing | Depends on industrial synthesis | [61] |
| Environmental impact | Eco-friendly | Generally low impact, though chemical modification is involved | May raise environmental concerns | [62] |
| Swelling capacity | Good | Good and controllable via degree of substitution | Controlled swelling | [63] |
| Gel-forming ability | Forms naturally in gastric fluid | Forms consistent gels; behavior tunable through modification | May require formulation aids to gel | [64] |
| Side effects | Minimal | Minimal; well-tolerated pharmaceutical excipients | May cause gastrointestinal irritation or allergy | [65] |
| Examples | Guar gum, xanthan gum, sodium alginate, chitosan, pectin, gum karaya, carrageenan | HPMC, HPC, CMC, ethyl cellulose | Eudragit, PVA, PVP, Carbopol | [66,67] |

## 4. DISCUSSION:

The comparison above shows that the choice among natural, semisynthetic, and synthetic polymers in FDDS is rarely a matter of one category simply being “better” than the others; it depends on which formulation properties matter most for a given drug and patient population.

Cost, biodegradability, and biocompatibility consistently favor natural polymers. Because they are derived from plant, algal, or microbial sources, natural polymers are generally inexpensive and are broken down by normal physiological or environmental processes, which is attractive from both a patient-safety and a sustainability standpoint. Their main limitation is variability: because their gelling and swelling behavior depends on physical entanglement and ionic interactions rather than covalent cross-linking, natural polymers are more sensitive to differences in raw-material quality, storage conditions, and gastric pH, which can make floating lag time and drug-release rate less predictable from batch to batch.

Semisynthetic polymers such as HPMC, HPC, CMC, and ethyl cellulose occupy a practical middle ground. Because they are chemically modified natural polymers, they retain much of the biocompatibility of natural gums, while modification of the cellulose backbone gives more consistent, controllable gel- and film-forming behavior than unmodified natural gums typically provide. This is part of why cellulose-derivative polymers such as HPMC are among the most widely used gel-forming polymers in commercial floating tablets they offer a reasonable balance of biocompatibility and reproducibility without the full cost and processing complexity of fully synthetic polymers.

Fully synthetic polymers address reproducibility most directly, by offering the most precisely controllable molecular weight, substitution, and cross-linking of the three categories, which generally translates into the most reproducible floating behavior and drug-release kinetics. This makes them particularly useful for drugs with a narrow therapeutic index, where consistent release is clinically important. The trade-off is higher cost, a greater likelihood of side effects such as gastrointestinal irritation in some patients, and, for several synthetic polymers, limited biodegradability.

These differences suggest that the three polymer categories are often more complementary than competing. Several of the reviewed studies describe combining polymers from different categories for example, a natural or semisynthetic polymer for buoyancy and biocompatibility together with a synthetic polymer for controlled release and this hybrid approach appears to be an increasingly common formulation strategy for floating tablets.[53-55] The literature reviewed here, however, is largely composed of narrative or property-focused reviews and individual formulation studies rather than systematic head-to-head comparisons; direct comparative data on floating duration, drug-release kinetics, and in vivo gastric retention time for matched natural-, semisynthetic-, and synthetic-polymer formulations of the same drug remain limited. This is a genuine gap that future formulation studies could usefully address.

Overall, all three categories of polymer have a legitimate and largely complementary role in FDDS. The appropriate choice, or combination, depends on the specific drug's stability and release requirements, the target patient population, cost constraints, and the desired balance between formulation reproducibility and environmental or biocompatibility considerations.

## 5. CONCLUSION:

Floating drug delivery systems remain a practical way of prolonging gastric residence time and improving the bioavailability of drugs that are poorly absorbed lower in the gastrointestinal tract or that act locally in the stomach. Natural, semisynthetic, and synthetic polymers each play

essential, largely complementary roles in these systems: natural polymers contribute biocompatibility, biodegradability, and low cost; semisynthetic cellulose derivatives offer a practical balance between biocompatibility and formulation control; and fully synthetic polymers contribute the most precise and reproducible control over drug release and formulation stability. Rather than favoring one category outright, polymer selection in FDDS should be guided by the specific requirements of the drug and the intended patient population, with combination approaches across categories offering a practical way to draw on the strengths of each polymer type. Further comparative studies particularly head-to-head evaluations of natural, semisynthetic, synthetic, and combined polymer systems under standardized conditions would help clarify when each approach offers the greatest clinical benefit.

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