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POLYMERIC FRONTIERS IN GASTRORETENTIVE DRUG DELIVERY: FROM BENCHSIDE INNOVATION TO CLINICAL REALITY

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Abstract
This review evaluates recent advancements in floating Gastro-retentive drug delivery systems, or GRDDS and emphasises the importance of polymers in enhancing buoyancy, gastric retention, and controlled drug release. . The literature was reviewed using a focused narrative approach covering peer-reviewed research articles published between 2015 and 2025, selected from major scientific databases based on relevance to polymer-based GRDDS design and performance. It emphasises the need for a cogent understanding that links the properties of polymers in GRDDS to their functionality. Examined are the effects of various synthetic and natural polymers on swelling behaviour, mucoadhesiveness, and matrix integrity, such as xanthan gum, polyethylene oxide (PEO), and hypromellose (HPMC). By identifying relationships between polymer characteristics and drug retention capacities, the review offers a methodology for optimising polymer selection to improve bioavailability and therapeutic outcomes for drugs requiring prolonged stomach residence. Enhancing patient compliance and medication delivery effectiveness is the ultimate objective of this polymer-driven approach.
Keywords: *Buoyancy control, Patient-focused design, Polymer functionality and gastro-retention mixing polymers, Regulated release*

INTRODUCTION

This study examines the effects of polymer physicochemical properties on buoyancy, gastric residence time, matrix stability, and drug release kinetics in floating gastro-retentive drug delivery systems (GRDDS). Using both synthetic and natural polymers as design tools, it describes the evolution of GRDDS from the perspective of structure-function polymer science. This framework serves to reinforce the concept of "buoyancy by design" throughout the discussion. Even though the oral route is still the recommended method of medication administration, gastrointestinal tract problems like pH fluctuations and gastric emptying have a significant impact on medication bioavailability (1).

Despite extensive research in this area, many published studies focus predominantly on formulation outcomes without sufficiently correlating polymer physicochemical properties with functional performance in gastric retention systems. Conventional drug delivery techniques often fail to regulate gastric emptying, resulting in insufficient drug release for medications that are primarily absorbed in the upper digestive tract (2).Conventional drug delivery techniques often fail to regulate gastric emptying, resulting in insufficient drug release for medications that are primarily absorbed in the upper digestive tract (3).

Some of the primary benefits of GRDDS include extended delivery of drugs that target the stomach or upper intestine, such as amoxicillin for the treatment of Helicobacter pylori; slower release rates for acidic-soluble drugs, such as ranitidine; prolonged release for drugs with limited absorption in

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the lower gastrointestinal tract, such as levodopa and carbidopa for Parkinson's disease; and low bioavailability drugs, such as metformin (4).

Being responsible for buoyancy, swelling property, matrix stability, muco-adhesion, and drug release rate, etc., the use of the polymer is essential for GRDDS formulations. Natural as well as synthetic polymers like xanthan gum, guar gum, and sodium alginate and hypromellose, polyethylene oxide, and carbomers, etc., have been well explored. Still, the literature lacks ample investigation regarding the structured system establishing the correlation between the gastro-retentive mechanism and the polymer characteristics like molecular weight, viscosity, swelling ratio, and gel strength, etc. Originality of this review lies in the conceptual outlook based upon the polymer aspect emphasizing the correlation between structure and function rather than formulation-wise analysis.Among the techniques to improve gastric retention are floating systems, bioadhesive systems, expandable systems, high-density systems, super-porous hydrogel systems, and magnetic systems; floating systems are especially effective at prolonging the duration of drug residence in the stomach (5).

FLOATING GASTRO-RETENTIVE DRUG DELIVERY SYSTEMS

Floating dosage forms (FDDS) improve drug absorption by remaining buoyant in gastrointestinal juices due to their reduced density. This allows for controlled medication release and lessens disruption of stomach emptying. Clearing the system after the drug has been completely discharged ensures stable plasma medication concentrations and prolonged stomach retention (6).

One of the primary requirements for floating drug delivery systems is a delayed release of the medication that serves as a reservoir. A slow release of the drug, functioning as a reservoir.

- A specific gravity that is lower than stomach contents, ranging from 1.004 to 1.01 gm/cm^3.
- The formation of a cohesive gel barrier.
- The formation of a cohesive gel barrier (7).

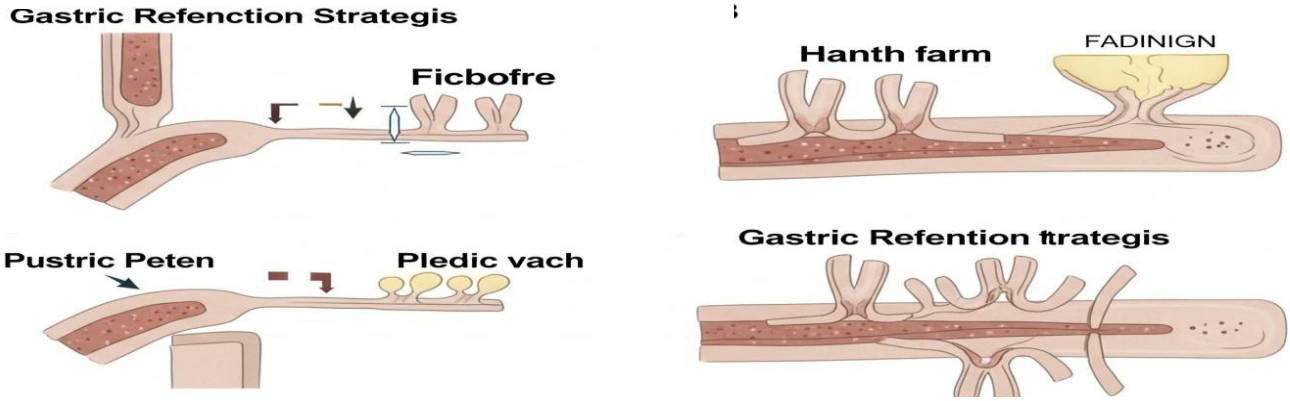

Fig. 1. Illustration of various gastric retention strategies, demonstrating various methods for extending the duration of drug residence in the stomach

TWO MAIN TYPES OF TECHNOLOGIES HAVE BEEN DEVELOPED TO ACHIEVE FLOATING OF A DOSAGE FORM

Effervescent Floating Dosage Forms: These systems consist of matrix forms that combine swellable polymers like methylcellulose and chitosan with effervescent agents like citric acid, tartaric acid, and sodium bicarbonate. When they come into contact with the acidic stomach contents, they release carbon dioxide, which causes gas bubbles to form and aid in the system's ability to float (8).

Non-Effervescent Floating Dosage Forms: These technologies prolong the gastric stay by using polymers that expand in stomach fluids, increasing their volume and buoyancy without generating gas (9).

CLASSIFICATION OF FLOATING SYSTEM

Systems for Single Unit Floating Dosage: Systems those are effervescent or non-effervescent. Floating Dosage Systems with Several Units: Systems that are effervescent or non-effervescent (10).

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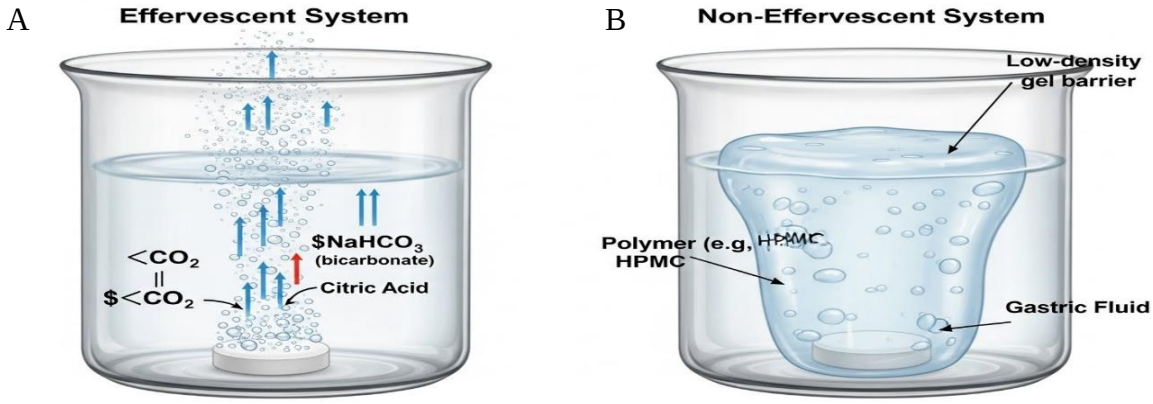

Fig. 2. Comparison of effervescent and non-effervescent gastro-retentive systems, showing CO_2 generation and polymer gel formation in gastric fluid

Table I. A thorough description of medications in all therapeutic classes, including manufacturers, brand and generic names, and the reasons behind gastric retention

Drug indication	Brand name	Generic name	Manufacturer	Reason for gastric retention	Ref.
Anti-Histamine	Zantac	Ranitidine	GlaxoSmithKline	Prolonged inhibition of gastric acid secretion for heartburn and GERD relief	(6)
Anti-Ulcer	Tagamet	Cimetidine	GlaxoSmithKline	Sustained reduction in acid production for ulcer healing and GERD relief	(6)
	Pepcid	Famotidine	Merck & Co.	Prolonged acid suppression for ulcer healing and GERD relief	(11)
Anti-Hypertension	Calan SR	Verapamil	Abbot Laboratories	Sustained blood pressure reduction and angina prevention	(11, 12)
Anti-Diabetic	Glucotrol	Glipizide	Pfizer	Consistent glycemic control through prolonged insulin stimulation	(13)
Anti- Anxiety	Xanax	Alprazolam	Pfizer	Sustained anxiolytic effect and prevention of withdrawal symptoms	(13, 14)
Anti-inflammatory	Diclofenac Sodium	Voltaren	Novartis	Prolonged local action for stomach inflammation and pain relief	(15)
Anti-Biotic	Clarithromycin	Biaxin	Abbot Laboratories	Long-term dosages of antibiotics to get rid of H. pylori	(16)
Proton Pump Inhibitor	Omeprazole	Prilosec	AstraZeneca	GERD and ulcers can be treated with long-term suppression of stomach acid production.	(16, 17)
Anti- Epileptic	Valproate Sodium	Depakene	Abbot Laboratories	Sustained therapeutic levels for seizure control	(15)
Anti-Hypertension	Atenolol	Tenormin	AstraZeneca	Sustained blood pressure reduction	(15)
Anti-Inflammatory	Ibuprofen	Motrin	Upsher-Smith Laboratories	Prolonged local anti-inflammatory action in the stomach	(15, 18)
Anti-Depressant	Venlafaxine	Effexor	Wyeth	Sustained antidepressant effect and prevention of withdrawal symptoms	(15, 19)
Anti-	Loratidine		Merck & Co.	Sustained antihistaminic effect for relief of	(13)

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Histamine		Claritin		allergies	(13, 16)
Anti-Inflammatory	Misoprostol	Cytotec	Searle	Prolonged gastric cyto-protection and ulcer prevention	
Anti-Biotic	Metronidazole	Flagyl	Pfizer	Sustained antibacterial levels for treatment of H. pylori infection	(13, 20)

The purpose of this introduction is to present the concept of "buoyancy by design," in which polymers are regarded as active functional components rather than passive excipients in gastro-retentive drug delivery systems (GRDDS). Accordingly, this review primarily focuses on a critical evaluation of recent scientific advances in the design of floating GRDDS, with particular emphasis on the role of polymer properties in governing buoyancy, gastric retention, swelling behavior, mucoadhesive characteristics, and sustained drug release. Furthermore, this discussion aims to guide formulation scientists toward rational polymer selection and design strategies to enhance drug biocompatibility, therapeutic efficacy, and patient compliance.

METHODOLOGY

This paper was thus conducted to ensure reproducibility, rigour, and comprehensive coverage of relevant research works in polymer-based floating GRDDS using an organized and transparent literature review approach. Google Scholar, PubMed, and Science Direct were searched for articles about "Polymers used in floating gastro-retentive drug delivery systems" to carry out a systematic review. A PRISMA flow diagram illustrates how the studies were chosen and filtered according to PRISMA guidelines with set inclusion and exclusion criteria.

METHOD FOR SEARCHING LITERATURE

The major scientific databases like Google Scholar, PubMed, Science Direct, and Research Gate were searched thoroughly for the relevant literature. Peer-reviewed publications between the years 2015 and 2025 were included in the search. The major keywords and Boolean operators used were "floating gastro-retentive drug delivery systems," "GRDDS," "floating drug delivery," "gastro-retentive polymers," "natural polymers," "synthetic polymers," "buoyancy mechanisms," and "controlled drug release."

CRITERIA FOR INCLUSION AND EXCLUSION

Studies that (i) focused on floating or gastro-retentive drug delivery systems, (ii) addressed the role of polymers in buoyancy, swelling, mucoadhesion, or drug release, (iii) were original research articles or relevant review papers, and (iv) were published in English were included. Those excluded were studies that (i) did not pertain to gastro-retentive or floating systems, (ii) provided insufficient detail regarding experiments or mechanisms, (iii) represented conference papers, editorials, or patents, or (iv) provided duplicate or outdated information.

EXAMINE THE SELECTION AND SCREENING PROCEDURE

The PRISMA guidelines were followed when selecting the study for the review. The procedure entailed the removal of duplicate articles, as well as the importation of all study entries that were obtained from the databases. The process further entailed the review of the titles as well as the abstracts separately to avoid duplication, ensuring that they were relevant to the objective of carrying out the review. The full-text articles that were selected for evaluation used the criteria set for exclusion and inclusion criteria for evaluation by the authors, who reached a consensus on any disagreements that may have arisen, particularly concerning the selection of studies for review.

DATA EXTRACTION AND SYNTHESIS

The polymer used, formulation method, floating mechanism, swelling properties, gastric residence time, drug release rate, and significant findings regarding bioavailability, therapeutic effects, et cetera, were

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systematically extracted from the trials. In order to provide an assessment that was not merely for description but for comparison, the extracted information was qualitatively synthesized based on the type of polymer used (natural/synthetic) in GRDDS. The quality of the studies in terms of methodological quality, relative to the robustness of in vitro and in vivo testing, the importance of the characterization of the polymers and the quality of the study design, though without the use of a risk of bias assessment tool, has been assessed.

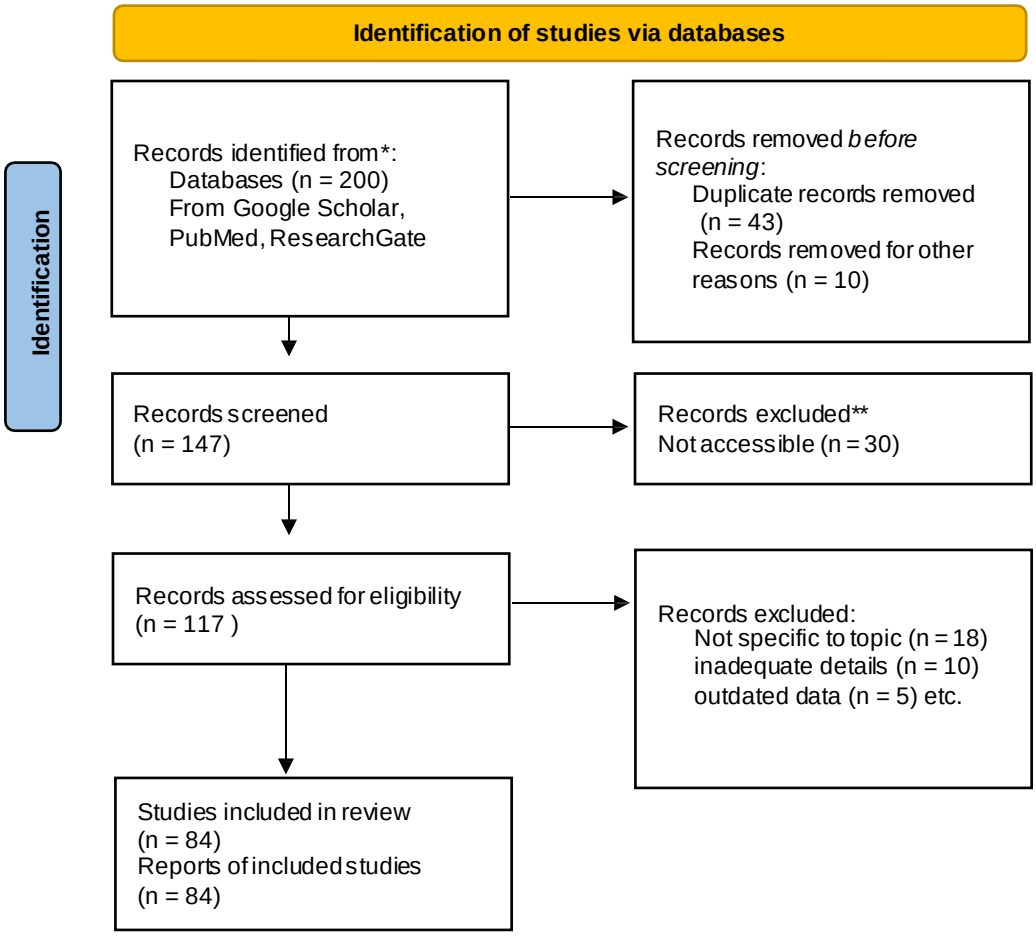

Fig. 3. Flow diagram showing the steps involved in choosing a study, such as searching databases, eliminating duplicate and ineligible records, determining eligibility, and finally adding the studies to the systematic review

POLYETHYLENE OXIDE (PEO)

Water and organic solvent-soluble polymers that melt between 65 and 70 °C are known as non-ionic ethylene oxide homopolymers, or PEOs (21). Elevated molecular weight Because of their exceptional mucoadhesive properties and significant swelling capacity, which increases size, PEO grades are used as matrix formers in floating delivery systems (22). PEO to create bisoprolol pulsatile release tablets In order to create the moulded coating that was applied to the previously formed core, these polymers were blended with blowing agents (23).

Drug tablets that produce gas and float showed a flotation period of 90 to 640 minutes and an ascent delay of 90 to 150 seconds. They delayed the pulsatile release of the active medicinal ingredient by up to four hours, took three minutes to manifest, and stayed buoyant for nine hours (24).

High molecular weight polyethylene oxide (PEO) is used in controlled release formulations due to its swelling and erosion rates, which allow the continuous release of active pharmaceutical ingredients (APIs). PEO's viscoelastic behaviour when swollen, which creates dense polymer networks in aqueous environments, enhances the mechanical properties of robust and swellable matrix tablets (25, 26).

CARBOMERS

The allyl esters of pentaerythritol (or allyl sucrose) are used for the cross-linking of acrylic acid (high

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molecular weight) to create synthetic polymers (carbomers) (27). They can create a three-dimensional, cross-linked micro-gel structure when combined with glycerin or water (swelling, but not dissolved). The bulk density of these carbomers is generally low (0.2–0.4 g/cm³) and the compaction density is low (0.3–0.4 g/cm³) (28). Floating drug delivery systems are other type of matrix tablets that increase dosage form dimension, enhance mucoadhesion and act as matrix former. Using Carbopol 934, Ma et al. prepared gabapentin microspheres with immediate flotation and controlled release, which maintained its buoyancy for nine hours with drug sustaining release of twelve hours (29). Wani et al. prepared a floating gel with carbomer and HPMC K4M for filling capsules with losartan. The gel was held afloat in dissolution for more than 12 h and then slowly released the active ingredient (30). To prepare the floating tablets of calcium disodium salt which were obtained into 24 hrs and remain in stomach for 6 hrs, Kumar et al. used Carbopol 934 and HPMC. Fernandes and Rathnanand developed gassing tablets containing carvedilol that floated for 14 hours with a 12-hour API release delay using Carbopol 934P and HPMC E50 (31).

HPMC

Hypromellose (HPMC) is a cellulose derivative powdered extremely fine which has the ability to form different viscosity (thick) and solubilized (soluble) colloidal suspensions; upon dissolution in water,(32) the apparent density of HPMC is 0.341 g · cm -3 while it's actual density is 1.326 g · cm -3 . HPMC finds use in gastro-retentive forms of drug dosage to produce prolonged release formulations of losartan in the gastro-intestinal tract and through the gastro-intestinal tract;(33) in addition HPMC has matrix forming and bioadhesion characteristics allows HPMC to maintain gas retention and thus achieve drug delivery for a period greater than 12 hours (34, 35). The amount of HPMC present in a dosage form will define the degree of effectiveness and furthermore combining HPMC with other polymers increases the rate of release of drugs and their floating ability (36-38).

PEG

PEG is a water-soluble polymer with molecular weights. between 200 and 35,000 and is used as a matrix agent and to enhance adhesion to mucosal membranes in formulation design. Vasvari (39), invented delivery system for metronidazole by using melt foaming to prepare a buoyant matrix that provided release of the API without ascent delay and conformed to the Korsmeyer-Peppas model over ten hours. Similarly, Haimhofer prepared a gastro-retentive system for acyclovir by utilizing ultrasonic foaming to create a mucoadhesive foam from stearic acid and PEG 4000 that exhibited zero-order release kinetics over the same period (40).

By increasing mechanical strength and flexibility of plastics (Polymeric Materials), PEG allows for safer operation of the floating apparatus at higher CO2 (41), pressures than other plastics. The PEG polymer has an adjustable molecular weight and structure, allowing it to be customised for many different types of medications and their corresponding requirements for therapeutic effectiveness (42). Additionally, PEG increases the solubility of a number of poorly soluble drugs, increasing their bioavailability and therapeutic efficacy (43).

XANTHAN GUM

With its exceptional solubility and stability, xanthan gum, which is a high molecular weight polysaccharide produced from Xanthomonas campestris, is ideally suited for floating drug delivery devices (44). Hydroxypropyl methyl cellulose (HPMC) and xanthan gum are combined to create modified release systems for diltiazem HCl that conform to Hixson-Crowell ecuations for predicting dissolved drug concentration and provide sustained drug delivery for a minimum of 12 hours. Xanthan gum is an ingredient of sustained release tablets used to deliver metoprolol tartrate. xanthan gum continues to be investigated as possible ingredients in new sustained release formulations of metoprolol tartrate. Studies have shown that tablets with xanthan gum and citric acid will maintain floatation properties for over 24 hours. Increasing the amount of xanthan gum in metoprolol tartrate sustained release tablets has been shown to enhance the release of the drug from the tablet (45). Xanthan gum was employed as a matrix

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formation for gas-forming propranolol floating tablets in order to create a gastro-retentive system with an ascent delay of approximately 150 seconds and enable a controlled API release over 12 hours while maintaining buoyancy (42).

SODIUM ALGINATE

While sodium alginate is not soluble in 95% ethanol or acidic conditions, sodium alginate is soluble in water and forms gels, suitable for GDDS. Sodium alginate viscosity increases with increased concentration and ionic composition (46). Alginate beads with mucoadhesive, floating properties coated with chitosan have been shown to effectively deliver amoxicillin to Helicobacter pylori by achieving drug encapsulation efficiency of greater than 90% and sustaining the release of the drug in simulated stomach fluids for > 6 hours (47). Therefore, additional studies focus on improving the buoyancy and drug release characteristics of sodium alginate-based systems for GDDS. In addition, sodium alginate has also displayed immunomodulatory and anticancer effects and has been shown to increase the activity of vascular endothelial growth factor (46).

GUAR GUM

Guar gum, obtained from Cyamopsis tetragonolobus seeds, is a high molecular weight natural polysaccharide that is used in the pharmaceutical industry for its ability to act as a binder and disintegrator (48). Glorax not only has this property but also creates a gel-like consistency when mixed together with water, allowing for slower dissolution time for dosage forms such as floatable drug delivery systems and also allowing for the delivery of medication via slow release over time (49). The only materials that are incompatible with guar gum are acetone and strong acids, while it can be mixed with many different hydrocolloids (50). Several studies indicate that adding other polymer materials, such as hydroxypropyl methyl cellulose (HPMC), will enhance drug absorption and influence ring dissolution rate (51). An example of this is with floating matrix-type tablets where blending of polymers will play a key role in drug release rate adjustment and ultimately therapeutic effect (52, 53).

ETHYLCELLULOSE

Ethylcellulose, commonly known as Ethocel, is a cellulose derivative used in the pharmaceutical industry as a coating agent, binder and viscosity enhancer (47). It is used for the development of extended-release coatings, stabilisation of formulations, masking of undesirable flavours as well as providing moisture protection. When ethylcellulose is ingested, it swells within the stomach, providing a sustained-release mechanism rather than dissolving immediately in either water or stomach acid (54). There are several different grades of ethylcellulose available for various pharmaceutical applications, such as wet granulation and the manufacture of extended-release dosage forms (55). Ethylcellulose technology has led to advances in solubility of clarithromycin floating microspheres and gastro-retentive systems for cefditoren pivoxil (CP) and provided the benefits of prolonged release (56). The different forms of ethylcellulose vary widely in terms of viscosity and polymer chain length (57).

STARCH

The carbohydrate starch is made up of amylose and amylopectin; amylose is a polymer of glucose and amylopectin is a polymer containing both glucose and some other sugars. Regardless, both starches have potential for the creation of drug carriers with good selectivity to hydrophilic drugs (58). On the other hand, starch is a very high molecular weight polysaccharide; however amylose dissolves only in boiling water. A number of studies of starches from different plant sources (potatoes, rice, wheat, maize) have displayed the ability of starch to create floating dosage forms (59). Several studies of pioglitazone matrix tablets have shown effective floating times, and formulations of rosiglitazone maleate with starch have been shown to have improved dissolving and floating properties (60, 61). Therefore, it appears that starches enhance the release of drugs from dosage forms in the stomach, and thus enhance the localized delivery of drugs to their intended sites of action (62).

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CHITOSAN

Chitosan, which is formed from Glucosamine and N-acetylglucosamine,(47) is a linear amino polysaccharide that is soluble in an acidic medium but partially soluble in both an aqueous and alkaline medium. Chitosan can be used as a film and matrix-forming material for floating mucoadhesive drug delivery systems. The density of Chitosan is between 1.35 to 1.40 g/cm3 (63). The process of deacidification of Chitosan produces buoyant granules that are able to control the release of drugs. Chitosan also increases the viscosity, delivery of drugs, and decreases the gastrointestinal transit time of laminated drug delivery systems made with Chitosan membranes by slowing the release rate of drugs (64).

Ibrahim El-Gibaly created a series of floating chitosan microcapsules with prolonged drug entrapment properties by utilizing the buoyancy of Biofluids over 12 hours and varying the concentration of chitosan and drug-to-polymer ratios (65). Svirskis and others created hollow floating mucoadhesive granules containing Acyclovir that could maintain buoyancy for over three hours in vitro using ionotropic gelation (66). Conversely, Hascicek C *et al*., developed bi-layer tablets utilizing direct compression methods, which contained acetylsalicylic acid and were designed to offer delayed release (up to eight hours), particularly when combined with HPMC K100M (67).

PECTINS

Pectins are linear polysaccharides found in plant cell walls and consist mostly of α-(1,4)-linked D-galacturonic acid and L-rhamnose. Citrus peels and apple pomace are the most common sources of pectin, and they are often used as gellifying and stabilizing agents. In terms of solubility, pectins dissolve readily in aqueous solutions (68). Many researchers are interested in designing pectin systems as drug carriers. For example, Badve et al. designed hollow calcium-pectinate beads for pulsatile delivery of diclofenac sodium, which is active for five hours in the stomach after administration (69). Abouelatta et al. demonstrated that ionotropic gelation could create an eight-hour float with a zero-order release profile from a bead formulation of cinnarizine, while Sriamornsak *et al*., (70) used metronidazole to create buoyant beads (69, 71).

Table I. Overview of research on synthetic and natural polymers in gastroretentive and floating drug delivery systems, including publication years, journal details, study focus, and polymer types

Type of polymers	Crucial utilization in GRDDS	References
Pectin	Floating beads and microspheres are used to extend the stomach residence period and boost the bioavailability of drugs with short absorption windows.	(4, 70)
Xanthan Gum	Utilised as a naturally occurring hydrophilic polymer to make floating matrices and environmentally friendly gastroretentive dosage forms.	(72)
Guar Gum	Acts as a swellable matrix that forms in floating tablets to provide regulated and extended drug release.	(73, 74)
Chitosan	Because of its mucoadhesive and floating properties, it is used to improve stomach retention and localised drug distribution.	(75)
Polyethylene Oxide (PEO)	Provides viscosity and matrix integrity for floating and controlled-release gastroretentive systems.	(42, 76, 77)
Polyethylene Glycol (PEG)	Utilised in foam-based systems and polymer blends to increase buoyancy and mechanical strength.	(78-80)
Ethylcellulose	Utilised in foam-based systems and polymer blends to increase buoyancy and mechanical strength.	(57, 81)
Carbomers / Carbopol	Utilised in gastroretentive tablets to regulate drug release kinetics, swelling, and floating behaviour.	(21, 76, 82)
Sodium Alginate	Develops matrices and gel-based floating microspheres to treat stomach retention and ulcers.	(83, 84)
Starch and Derivatives	Utilised as matrix formers and excipients in bilayer and floating tablet systems.	(85, 86)

POLYVINYL ALCOHOL

Polyvinyl Alcohol (PVA) is a man-made thermoplastic polymer with a molecular weight range of

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26,300-30,000 that dissolves in water. Its solution concentration can vary based on its degree of hydrolysis (86.5-89%) and pH level (5.0-6.5) (87). PVA is used widely in drug delivery systems for various types of administration, including ocular, colon, rectum, buccal and transdermal delivery. Due to its ability to create films, emulsify and adhere, Polyvinyl Alcohol is particularly useful in creating products that can control the extent to which drugs are released. An example being the floating tablets created with 3D-printed casing made from metronidazole which allows for an extended release period of over 8 hours (88). Similarly, floating microspheres containing ofloxacin (1% PVA concentration) also exhibited excellent floating characteristics and have shown varying drug release profiles (89, 90).

XANTHAN GUM

Xanthan gum is a naturally derived polysaccharide that enhances drug retention in pharmaceutical floating drug delivery systems (FDDS), thereby increasing both bioavailability and therapeutic effectiveness (53).When combined with other polymers such as guar gum or HPMC, xanthan gum increases drug buoyancy and helps to support sustained drug release from 12 to 24 hours (91). Xanthan gum is chemically modified in ratio with other polymers depending on the desired release kinetics; higher xanthan gum-to-polymer ratios are associated with a more consistent, regulated release profile (92). Xanthan gum itself is biodegradable and biocompatible and can be modified chemically for improved properties to ensure the safe delivery of drugs and a consistent, reliable time delay in the delivery of the drug, as well as improved buoyancy properties when suspended in gastric fluid (93-95)

CELLULOSE ACETATE

The Polymer cellulose acetate is a major contributor to floating drug delivery systems (FDDS) as a polymeric material that improves medication bioavailability and retention in the stomach by controlling the rate of drug release (96). The floating microspheres in the FDDS are extremely buoyant and exhibit zero-order kinetics, which allows the prolonged release of medications for greater than 10 hours (97, 98) addition, floating microcapsules made of cellulose acetate butyrate possess greater mucoadhesive characteristics and an extended floating time than traditional formulations, making them suitable for delivery of medications requiring prolonged residence time in the stomach (99). Additionally, starch/microcrystalline cellulose hybrid gels combined with cellulose acetate exhibit superior gastric-holding capabilities with the ability to remain buoyant for as long as 24 hours while releasing medication for more than 10 hours (100).

GUAR GUM

Guar gum, a galactomannan polysaccharide, can swell in cold water to produce viscous solutions. These properties make guar gum suitable as a flexible carrier of pharmaceutical formulations for controlled release; acting as both a polymer and disintegrant in floating delivery systems (101). Guar gum is an effective agent for controlling the rheology, hydrogen bonding, thickening, forming emulsions and films, and has high levels of solubility in water. The behaviour of guar gum when used in drug delivery significantly impacts the patterns of drug release; formulations of drugs using guar show no dependence on the speed of rotation in the in vitro test for dissolving drugs (102).

ETHYL CELLULOSE

This study's purpose was to formulate microparticles created from "slowly dissolved" ethyl cellulose and HPMC K100M for pioglitazone hydrochloride by using an emulsion solvent diffusion-evaporation approach, combined with the full factorial design to optimise the particle formulation. The formulations were developed using a full factorial design.

According to the study findings, the variables that significantly impacted the properties of the microparticles, including surface smoothness, flow ability, as well as maximum floating time (greater than 10 h) and high compatibility percentage(i.e., drug entrapment) 97% w/w, were stirring speed and polymer concentration in the preparation of the formulations. Scanning electron microscopy indicated that the microparticles had a hollow shape and a size of 190 μm.

Furthermore, increasing the concentration of the hydrophilic polymer led to higher release rates from the

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microparticles. Thus, the effects of increasing the concentration of ethyl cellulose and decreasing the stirring speed, respectively, were observed on the entrapment percentage and the release rates after 8 h of release time (81).

DISCUSSION

This review highlights how the functionality of floating gastro-retentive drug delivery systems (GRDDS) depends on the interrelationship of polymer structure and function (for instance, how they affect gastric retention, buoyancy, swelling, mucoadhesion and drug release).

This time, the debate is intertwined with the chemistry of polymers and the gastroretentive properties of the formulation and the possible mechanistic interpretation of formulation behavior over and above the descriptive comparisons made between different formulations in previous reviews. Parameters such as molecular weight, viscosity grade, extent of swelling, and gel strength have been consistently demonstrated to be influential in determining the lag time to floating and the total stomach retention time. For the purposes of the sustained-release formulation, synthetic polymers such as hypromellose (HPMC), polyethylene oxide (PEO), and carbomers can be used.

On the other hand, there are natural polymers such as sodium alginate, xanthan gum, and guar gum, giving better biocompatibility and biodegradable properties but with probable lower mechanical strength and batch variation. The use of blends often gives better performance than stand-alone polymers, and this has been an important finding from most studies. The hydrophilic and hydrophobic polymers have been found to act together for enhanced matrix strength, facilitating carbon dioxide entrapment within effervescent matrices, as well as minimizing initial erosion. The concept of smart polymer selection gets reinforced by these combined systems, permitting optimization of kinetic release with sustained buoyancy maintenance. However, the prevailing literature base suffers from some drawbacks despite all these advances. There has been a weak link between laboratory performance and clinical outcomes since most studies only show performance based on buoyancy testing and dissolution performance studies with insufficient testing based on clinical properties. Lack of inter-study comparability due to differences in experimental conditions, including composition of dissolving media, rate of agitation, and methods of buoyancy analysis, further restricts inter-study comparability. Lack of standard parameters describing polymer characterization in the GRDDS studies also remains another major weakness. Lack of reproducibility and inter-formulation comparability due to inadequate characterization of the grade and rheological properties further underscores the inadequacies and opens the way for future studies on gastro-retentive medication delivery with much stricter guidelines. Construction of the polymer-by-design frameworks, which classify polymers on the basis of function rather than basic chemical names, should remain one of the highest priorities in future studies. To translate GRDDS from the laboratory bench to the bedside, the application of quality by design (QbD) principles and advanced polymer characterization, as well as IVIVC modeling, should all be brought together. It is now possible to make floating systems for shape, porosity, and drug release profiles precisely controlled due to advancements in manufacturing techniques available to utilize foam-based processing, hot-melt extrusion, and three-dimensional printing. Furthermore, intelligent gastro-retentive systems that could respond to changes in pH and stomach motility could potentially become reality due to research being pursued regarding intelligent polymers. Indeed, as shown by the work done here, there is a focus that should be placed upon shifting from formulation approaches to a polymer-based approach. This could bring about faster translation of floating gastro-retentive drug delivery systems to the clinic.While synthetic polymers provide predictable mechanical performance, natural polymers allow for better patient compatibility but are more fragile to formulate. Furthermore, when considering gastro-retentive qualities, polymer blend systems commonly offer superior performance compared to single-polymer systems. New manufacturing processes have enabled further refinement of the concept of 'buoyancy by design' as well as providing data to further support this concept. However, with respect to the continued development of GRDDS systems for patient use, one must also consider challenges associated with a low degree of correlation between in vivo and in vitro studies and the

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fact that clinical testing has not fully validated the use of these systems.

CONCLUSION

The work above makes it clear that the solution to efficient floating gastroretentive drug delivery systems (GRDDS) depends on the appropriate selection of polymers, thereby enabling better bioavailability of the orally administered medication, especially those with narrow absorption windows or those that require prolonged stomach dwell time. This new research treats polymers not just as passive drug carriers, but also considers their role in the following phenomena: buoyancy, stomach retention, matrix integrity, swelling ratios, or controlled drug release by applying the concept of "buoyancy by design". Through the provision of formulation scientists with a rational framework of thoughtful polymer choice and optimization, this polymer-centric approach, therefore, signifies an unprecedented conceptual leap over and above the existing formulation-centric assessments.

Finally, this approach paves the way for the design and development of patient-centric and more successful gastroretentive delivery systems with excellent clinical translation and therapeutic effects.In future studies aimed at promoting the bench-to-bedside transition, the current work should form the basis of adding quite sophisticated polymer characterization expertise, quality-by-design methodologies, in vivo in vitro correlation model development, and sophisticated manufacturing technologies such as 3D printing and hot melt extrusion.

Future Directions:

Future studies of floating gastroretentive drug delivery systems (GRDDS) should not rely on empirical methods, but should introduce a polymer-by-design approach, classifying polymers based on their functional characteristics. Improved characterisation methods and the development of smart polymers that are responsive to physiological conditions have improved patient-specific gastric residence time. Moreover, increasing emphasis on in vivo–in vitro correlation models has provided enhanced control of the parameters affecting drug release using 3D printing and hot-melt extrusion technology. The use of sustainable polymers will support clinical acceptance and regulatory compliance. Overall, GRDDS must evolve into patient-centric, efficient therapies through the combination of polymer chemistry, cutting-edge manufacturing, and biopharmaceutical evaluation methodologies.

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There are no conflicts of interest for the authors.

Authors' contribution:

ZB & MN Conceived the idea & designed the structure of the review; AN Analyzed recent literature; SS, SA, AA & SAS Data compilation, referencing, and critical revision of the draft; AAl Literature review, language editing.

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While the article was being prepared, the authors used Chat GPT to make it easier to read. The authors accepted full responsibility for the publication's content after using this tool or service, reviewed it, and made any necessary revisions.

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