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Novel Approach in Floating Drug Delivery System: Raft Forming System

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ABSTRACT
A raft forming system is a promising approach for GRDDS of medicament with stable plasma profiles and an extended-release mechanism. It is superior to other floating systems in terms of its enhanced capacity to float and bioavailability. Nevertheless, it has certain drawbacks, including the inability to administer drugs which are poorly soluble in acid, drugs that are unstable in gastric media, and medications that are intended for selective release in the colon but have stability issues. The present review systematically assembles the results of multiple experiments carried out on this novel methodology. This comprehensive review aims to discuss drug selection criteria's, Preformulation studies, strategies for formulation of raft system, evaluation parameters, different packaging systems, advantages and limitations along with details of marketed and patented formulations.
Keywords: Raft systems, GRDDS (Gastroretentive drug delivery system), various approaches to raft systems, Oral dosage forms.

I. INTRODUCTION

Oral sustained release dosage forms offer several advantages such as simplicity in dosage administration thereby enhancing patient compliance and offering extended release of the drug by maintaining an effective concentration in systemic circulation. Furthermore, there are drawbacks to using typical oral dosing forms, including an increased chance of gastrointestinal adverse effects and the possibility of dose dumping [1]. This was particularly significant for medications that break down in the colon or are poorly soluble in alkaline ph. To improve the performance of oral dose forms in response to these barriers, researchers have been investigating novel approaches[2].To improve drug absorption and therapeutic efficacy, one of the most effective approaches is to develop Gastroretentive drug delivery systems, which extend the duration of a drug's residence in the stomach. In general, even though oral dosage forms have long been the preferred method of drug administration, new developments in drug delivery technology are constantly expanding the limits of what is achievable. Researchers have overcome the difficulties associated with traditional oral formulations indicating the future of safer, more efficient drug delivery with creative solutions like the raft system.Several studies investigated ways to improve the distribution of medications throughout the stomach. The aim is to minimize variations in drug concentrations in the bloodstream and increase the half-life of the drug, which will result in more effective therapy with fewer side effects and lower dosage frequency[3]. GRDDS represent a potentially effective strategy in this attempt.In order to increase a drug's bioavailability, GRDDS are made to keep it in the stomach for longer. They provide a solution for different issues related to specific medications. Drugs like
Albuterol that needs special absorption from the stomach, or those that break down rapidly in the intestine, can be treated with their assistance. Furthermore, drugs with poor absorption and low solubility might perform better because GRDDS reduces the duration of time that a drug passes through the gastrointestinal tract.Compared to traditional dosage forms, GRDDS have several advantages[4]. First of all, they increase the bioavailability of drugs that are difficult for the upper gastrointestinal tract (GIT) to adequately absorb. It suggests that the body can now use these

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medications more efficiently.Secondly, by lowering the frequency at which dosages must be given, GRDDS can enhance patient compliance as patients find it simpler to follow their prescription regimen. Additionally, GRDDS minimize variations in drug plasma levels, which can improve the medications' overall bioavailability. Though they have many benefits, not all drugs are suitable for Gastroretentive drug delivery systems (GRDDS)[5]. Acidic drugs, for example, are not good candidates for GRDDS because they disintegrate poorly in the stomach's acidic environment. Furthermore, drugs that can irritate or harm the lining of the stomach, as well as those that are absorbed mostly in the colon, like corticosteroids, could not work well with this delivery mechanism.Other concerns about GRDDS included formula size and how it will impact stomach emptying Furthermore, the formula's structure plays an important role in achieving gastric retention. Ring- and tetrahedron-shaped ones have demonstrated longer residence times[6]. Furthermore, when taken orally, one unit formulation may have certain difficulties such as sticking to one another or being clogged in the GIT, which may have a strong potential to cause irritation. They may also be unpredictable and non-reproducible in their ability for extending the stomach's residence period. For this reason, several unit formulations have been developed, offering a greater chance to reduce the chance of dose dumping and shorten the absorption inter-subject variability. It was discovered that a minimally fed stomach improved residence time[2].

I] APPROACHES OF GRDDS

A] Floating drug delivery systems (low density)

These systems can be identified by a density of less than 1.004 g/cm^3, which allows them to float in the stomach for an extended amount of time while the drug is released gradually and raising GRT. This lower density prevented the systems from affecting the gastric emptying rate. There are two types of floating systems: effervescent and non-effervescent. Gel-forming polymers or highly swellable cellulose derivatives are utilized to embed drugs into non-effervescent systems. On the other hand, hydrophilic polymers are combined with agents like sodium bicarbonate, calcium carbonate, tartaric acid, and citric acid to create effervescent solutions in order to affect medication release by releasing CO_2 when they come into contact with stomach juice and trapping it in a hydro-colloid matrix[7] .

B] Non-floating systems (high density)

High-density systems are larger in density than gastric fluids (1.004 g/cm^3), which causes them to be retained in the stomach's rugae. Gastric Retention time (GRT) will be significantly prolonged when the density is closer to 2.5 g/ml. Excipients such as barium sulphate, zinc oxide, iron powder, titanium dioxide, etc. can be used to achieve this. The gastro-intestinal transit time can be increased from an average of 5.8 to 25 hours by changing the density of these systems[8].

C] Ion-exchange resin systems

A lipid-soluble cross-linked polymer, which may be cationic or anionic, makes up these systems. Their purpose is to raise GRT, particularly for medications with limited bioavailability. They are created by combining several suitable excipients with medication and ion exchange resin in a polymeric matrix[9] .

D] Swelling/Expandable systems

These systems grow after consumption by absorbing gastric fluid to obstruct the pyloric sphincter. This allows the medicine to be released gradually and remain in the stomach for an extended period of time. As an example, hydroxypropyl methylcellulose (HPMC), polyethylene oxide, and Carbopol are hydrophilic polymers that may be employed because they form a network of physicochemical crosslinks that allow the polymer to swell extensively. However, intestine blockage, intestinal adhesion, and gastropathy are potential side effects of expandable systems. They also face some limitations and challenges when it comes to storing rapidly hydrolyzable and biodegradable polymers, which are difficult to produce and may not be economically viable due to issues with preserving their strength[10].

E] Mucoadhesive/Bio-adhesive systems

The contact that takes place between the polymer compound and the mucus layer is known as Mucoadhesion. Adhesion of the dose form to mucus and/or mucosal surface is known as bio-adhesion. In order for the formula to adhere to the intestinal mucosa and cause an interaction, bio adhesive agents, either synthetic or natural, are needed. In these systems, bio adhesive compounds such as pectin’s, chitosan, Carbopol, and others are typically included. Better medication absorption is possible as a result of these polymers' ability to

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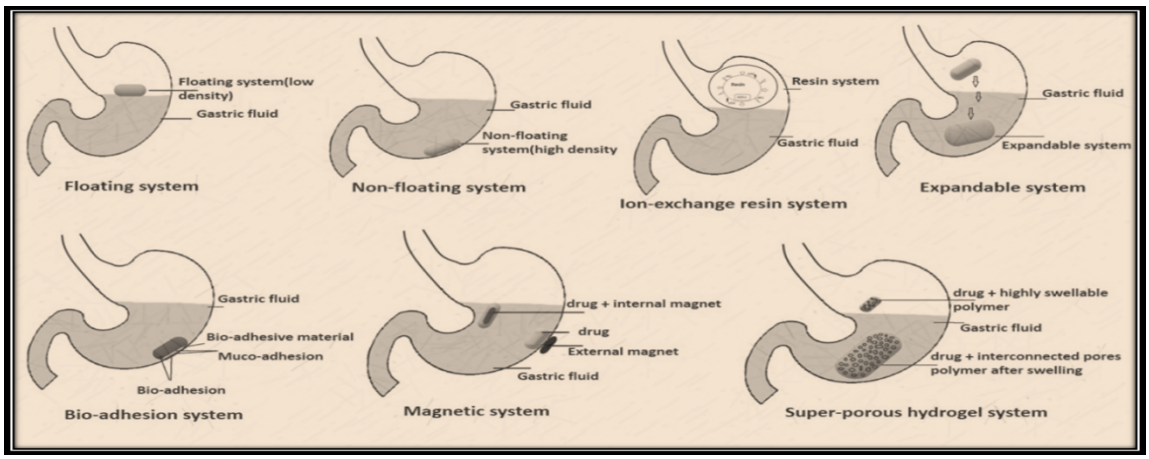
extend the drug residence period at the site of application[11].

F] Magnetic systems

These systems consist of the medication, excipients, and a little quantity of an intramural magnet. Additionally, there is an extramural magnet that may be applied to the stomach. It is possible to locate the formula containing the internal magnet with the help of this extramural magnet. The extramural magnet's location and strength of the magnetic field can affect the GRT. In the event that the extramural magnet's location is not precisely stated, the intended results will not be achieved. The proper use of these systems is thus questionable[12].

G] Super-porous hydrogel systems

Water-absorbent polymer systems include those that are super-porous hydrogel systems. These networks are made up of countless unbound linked holes that have an average size of more than 100 µm. As a result, they quickly swell to their equilibrium size as a result of water absorption by capillary wetting. As a result, these devices get sufficient mechanical strength to sustain the pressure associated with stomach contraction and raise GRT. Its strong mechanical strength and elastic qualities resulted in the wide acceptability of this method in the controlled-release formulation. However, these systems may have limited mechanical strength in their structure and their swelling capability may be impacted by pH changes. Croscarmellose sodium and sodium alginate are two examples of highly swellablepolymers[13].



H] Raft-forming system

It is one of the important approaches in the floating drug delivery system. In-situ gel-forming polymers, such as alginate salts, gellan gum, pectin, chitosan, and others, gas-forming agents, such as carbonates or bicarbonates, are the main

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components of raft-forming systems. In order to stop stomach contents from refluxing into the oesophagus, the theory suggests acting as a blocker between the oesophagus and stomach. They enlarge and condense into a viscous cohesive gel, which results in the creation of a continuous layer called a raft. Due to the bio adhesive properties of the polymers utilized, this gel can floats remain adhere to the gastric mucosa and remain on the surface of the stomach, even though it is heavier than stomach fluids[14]. The presence of the gel-forming ingredient causes the residence duration to increase. Because of their low bulk density, they can release the drug molecule steadily and with comparatively stable plasma profiles. Furthermore, these in-situ gels maintain their integrity for over 48 hours, facilitating the continuous release of medication. Because of this, they float in the stomach for an extended amount of time without changing the rate at which they are cleared[15].The capacity of the medication to be released gradually from the formulation is one of the many challenges that the raft system must overcome in order to achieve the necessary retention period of the dosage. For the formulation's capacity to withstand the force of the stomach's peristaltic movement, systems should keep their specific gravity (1.004–1.01 g/cm^3) below that of the contents of the stomach.Alkaline bicarbonates or carbonates, (which affect the production of a low-density system that floats on the stomach juices), and a gel-forming agent are ingredients employed in the preparation of this system. Acid-soluble medications that are insoluble or unstable in intestinal fluids match the Raft system excellently[16].The creation of raft systems involves the usage of many polymers. There is a significant variation in the availability of various polymers, both synthetic and natural .These characteristics include the following: first, it should be biocompatible; second, it should exhibit pseudoplasticbehavior; and third, it should be able to increase viscosity as shear rate increases Natural polymers such as alginic acid, guar gum, gellan gum, xyloglucan, pectin, chitosan, etc. and synthetic polymers such as poly(DL lactic acid), poly(DL-lactide-co- glycolide) and poly-caprolactone, HPMC, etc. can be applied . Because of these advantages, raft systems are the best in the controlled release system category. Because they have a low-density viscous coating over the stomach contents, they increase the drug's release and bioavailability and offer a larger surface area. They also offer consistent drug delivery. enhancing the drug's prolonged release mechanism and effectiveness. Compared to other floating systems, their floating capabilities are more sophisticated. Additionally, because of the convenience of administration and decrease in dosage frequency, patient compliance is significantly improved. They also have an easy production method.The raft systems do have certain drawbacks, though; for example, they are rapidly degraded by chemicals or microbes. To prevent stability issues, careful storage requirements are necessary. The formula may get destroyed due to the formation of the gel within the package caused by exposure to various radiations such as UV, visible light, electromagnetic waves, and so on. The mechanical strength is readily disruptible and insufficient to withstand the migrating impulses. Medications with limited acid solubility, medications that are unstable in gastric media, and medications intended for selective release in the colon cannot be utilized with raft systems[17].

II] STRATEGIES USED TO FORMULATE RAFT FORMING SYSTEM

I. Physical based raft system

There are two mechanisms that make up these physically designed structures. The **first is swelling**, which occurs when the polymer absorbs water and grows to form gel. Thus, when the liquid effervescent structure comes into contact with the stomach fluid, the gel forms. Additionally, materials that absorb water from their surroundings and expand at the intended site of action are considered to create gel in situ. A polar Lyotropic liquid crystalline phase formation is produced by the swelling of a lipid known as glycerol monooleate. It is a biodegradable lipid with certain bio adhesive qualities that can be broken into smaller components in vivo by an enzyme. The **second method is Diffusion,** which produces consolidation by allowing the solvent to permeate neighbouring tissues from the polymer solution[18].

ii. Chemical-based raft system

Various ions cause a phase change in a variety of polysaccharides. Researchers refer to this chemical process as ionic cross-linking. For example, the most often employed polysaccharides are those that belong to the class of ion-sensitive ones. When K+, Ca+, Mg+, and Na+ are present, ion-sensitive polysaccharides such as gellan gum, pectin, and sodium alginate go through a phase shift. In the presence of other monovalent and divalent cations, such as low-methoxyl pectin and alginic acid, other polysaccharides also gel. In

addition, gellan gum is an anionic polymer that gels in situ when it comes into contact with divalent and monovalent cations[2].

iii. Physiological stimuli-based raft system

First, there is a pH-sensitive gelling process that allows gel formation based on the pH of the medium. Numerous pH-dependent polymers exist that can form in situ gel inside the system. pH changes can cause poly (acrylic acid) (Carbopol®, carbomer) or its derivatives, polyvinyl acetal diethyl amino acetate, and mixes of poly (ethylene glycol) and poly (methacrylic acid), to transition from sol to gel. Negatively charged moieties are found in anionic networks, positively charged moieties are found in cationic networks, and both positive and negatively charged moieties are found in neutral networks.

Second, systems showed gelling that was responsive to temperature. Hydrogels of this sort are liquid at room temperature (20–25 °C), but they gel when they come into contact with bodily fluids (35–37 °C) as the temperature rises. In drug delivery research, these hydrogels are arguably the most frequently researched type of environment-sensitive polymer systems. For the creation of temperature-sensitive hydrogels, polymers including Pluronic, polymer networks of poly (acrylic acid), polyacrylamide, and poly (acrylamide-co-butyl methacrylate) are frequently utilized. The swelling of polymer networks including poly(acrylic acid), polyacrylamide, or poly(acrylamide-co-butyl methacrylate) is temperature dependent[2].

III] PREFORMULATION STUDIES FOR FORMULATING RAFT SYSTEM[19][20][21]

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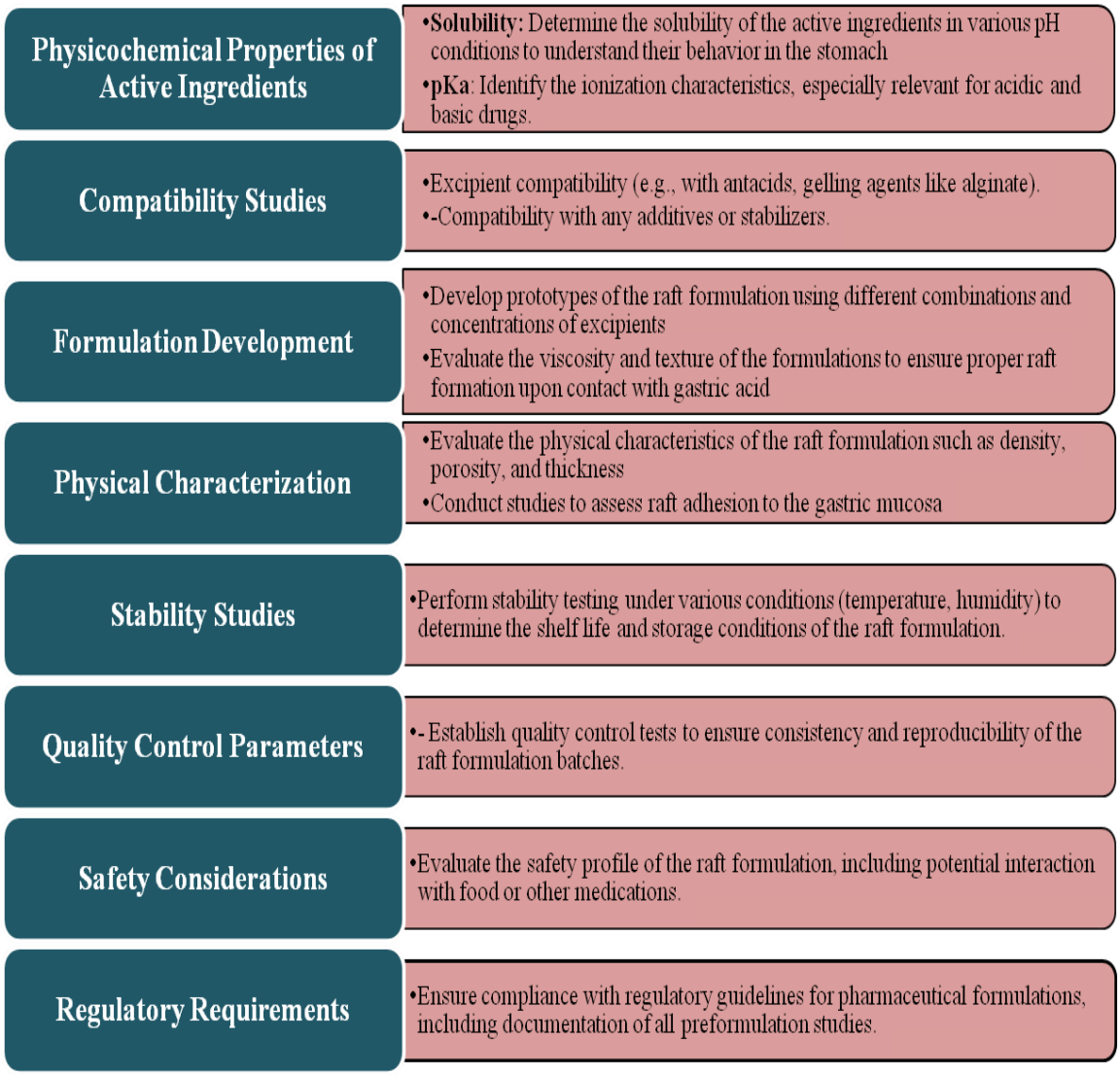

Fig No :2. Preformulation studies Of Raft Systems

IV] DRUG SELECTION CRITERIA ;

Table No.1.Drugs Profile

DRUG NAME	HALF LIFE	ACID STABILITY	BID / TID
Ranitidine[22]	2.5 - 3 hrs	Stable in acidic conditions (pH 1- 3)	It is usually taken once a day at bedtime or two to four times a day. Over-the-counter ranitidine comes as a tablet to take by mouth. It is usually taken once or twice a day.
Cimetidine[23]	2 hrs	Stable in acidic conditions (pH 1- 3)	300 mg 4 times daily with meals and at bedtime; max 2.4g/day. GERD: 800mg 2 times daily or 400mg 4 times daily for max 12 weeks

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

Metoclopramide[24]	4 - 6 hrs	Stable in acidic conditions (pH 1- 3)	The usual adult dose is 10mg, taken up to 3 times a day.
Famotidine[25]	2.5 - 3.5 hrs	Stable in acidic conditions (pH 1- 3)	Adults and children weighing 40 kilograms (kg) or more—20 milligrams (mg) 1 or 2 times per day, in the morning and at bedtime, or 40 mg once a day at bedtime for up to 12 weeks.
Nizatidine[26]	1-2 hrs	Stable in acidic conditions (pH 1- 3)	Adults—300 milligrams (mg) once a day at bedtime or 150 mg 2 times a day
Erythromycin[27]	1.5 - 2 hrs	Degrades in acidic conditions it requires protection from stomach acid , often in the form of enteric coated tablet	The usual dose of erythromycin is 250mg to 1,000mg, taken 4 times a day. Sometimes it's taken twice a day.
Levodopa[28]	1 - 3 hrs	Stable in acidic conditions	2 tablets in the morning, 2 tablets in the afternoon, and 1 tablet in the evening.
Tizanidinehcl[29]	2.5 hrs	Stable in acidic environments.	starting dose is 2 mg up to three times daily
Baclofen hcl[30]	3 - 4 hrs	Baclofen HCl is generally stable in acidic environments, which is essential for its efficacy when administered orally, as it needs to pass through the stomach without significant degradation.	Typically starts at 5 mg taken three times daily, with gradual increases to a maximum of 80 mg per day.
Methocarbamol[31]	1.14 hrs	Methocarbamol is relatively stable in acidic environments. This stability is crucial for its oral bioavailability, ensuring that the drug remains effective as it passes through the stomach.	Starting dose is 1500 mg four times daily for the first 48 to 72 hours. Maintenance Dose: After the initial period, the dose is usually reduced to 750 mg every 4 hours, 1500 mg three times daily, or 1000 mg four times daily, as needed. but it is a class 2 drug but also stable at acidic environment.
Guaifenesin[32]	1 hrs	Stable in acidic condition	200 to 400 milligrams (mg) every four hours

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

Cefuroxime sodium[33]	70 min	The optimum pH range of stability was determined to be approximately 4.5-7.3	250 to 500 milligrams (mg) two times a day for 10 days.but it is class 2 drug.
Tranexamic[34]	2- 11 hrs	Generally stable in acidic environments	Adults—Two tablets (650 milligrams per tablet) three times a day

V] UNSUITABLE DRUG CANDIDATE FOR RAFT FORMULATION [35][36][37][38][39][40][41][42][43][44]

Drug candidate	Reason for instability	Examples
• Acidic drugs	• Acidic drugs may interact negatively with antacids, leading to reduced efficacy or altered drug release profiles.	• Aspirin, Indomethacin
• Drugs requiring precise pH control	• Raft formulations can alter the local pH, which may affect drugs that need specific pH conditions for stability or absorption.	• Omeprazole, Lansoprazole
• Hydrophobic drugs	• Hydrophobic drugs may have poor solubility in the aqueous medium of raft formulations, leading to inconsistent drug release.	• Ibuprofen, Naproxen
• Drugs with narrow therapeutic index	• Raft formulations may cause variable release rates, which can be problematic for drugs with narrow therapeutic windows.	• Digoxin, Warfarin
• Proteins and peptides	• The acidic environment of the stomach and the presence of proteolytic enzymes may degrade proteins and peptis before they ↓ can exert their effects.	• Insulin, Enoxaparin
• Drugs Prone to Gelation-Induced Precipitation	• Drugs that precipitate in the presence of gelling agents can lose bioavailability and efficacy	• Amoxicillin, Tetracycline

VI] LIST OF MATERIALS USED FOR FORMULATION OF RAFT SYSTEMS

Table No .2. Components of Raft Systems.

Component	Role	Example
Antacids[45]	Neutralizes stomach acid, reducing reflux and discomfort.	Calcium carbonate Sodium bicarbonate
Carbonates Bicarbonates[46]	Reacts with gastric acid to release CO_2, which helps the raft to float.	Sodium bicarbonate Potassium bicarbonate
Gelling agents[47]	Enhance the viscosity of the raft and its stability. Forms a viscous gel when in contact with gastric acid. Creating the “raft”.	Xanthan gum, hydroxypropyl Methylcellulose, Sodium alginate, Potassium alginate
Flavors sweeteners [48]	Improve palatability and patient compliance	Sorbitol, Aspartame

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

Preservatives[49]	Prevent microbial growth in liquid formulation	Sodium benzoate, Potassium sorbate

ANTACIDS :

1, Sodium bicarbonate (NaHCO3)

It is also known as baking soda a white crystalline solid that appears as a fine powder. It is a bit salty and alkaline in taste .In effervescent tablets and granules, it is used as a gas-forming agent. Maintenance or production of basic pH in various preparations As a buffer in tablet formulations wherein its role is to buffer weak acidic drugs aiding in their dissolution and reducing irritation of the stomach[50].

2.Calcium carbonate (CaCO3)

It is available as a powder that is essentially composed of precipitated calcium carbonate. Employed as an antacid for managing heartburn Prevention of treatment of calcium deficiency[50].

VII] BIOCOMPATIBLE POLYMERS :

Table No : 3

Material	Function
Sodium alginate[51]	Forms a gel like raft upon contact with gastric acid , creating a barrier to prevent reflux .
Pectin	Acts as a gelling agent , enhancing the viscosity and stability of the raft .
Chitosan	Enhances the mucoadhesion , prolonging the retention time of the raft in the stomach .
Xanthan gum[51]	Increases the viscosity , providing structure and stability to the raft .
Hydroxypropyl methylcellulose[51]	Serves as a thickening agent , contributing to the raft's consistency and stability .

VIII] Polymer Used for raft Formulation:

A floating drug delivery system utilizes a variety of polymers to carry the medication to the stomach, which is part of the gastrointestinal tract. When the raft-forming drug system forms Several synthetic and natural polymers are employed. Natural polymers include guar gum, gellan gum, and alginic gum. Synthetic polymers include poly (DLlactide-co-glycolide), HPMC, and poly-caprolactone.

The polymers used in in situ gels must possess the following qualities:

1. It needs to be biocompatible.
2. There needs to be pseudoplasticbehavior.
3. The polymer should have the ability to enhance viscosity when combined with an increase in shear rate[52].

Several polymers utilized in the raft-forming mechanism include:

1.Sodium alginate: This naturally occurring substance is commonly used.

Polymer in the system of Raft Forming. Chemically speaking, it is an alginic acid salt made

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Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

up of 1,4-glycosylated linkages between the residues of D mannuronic and L glucuronic acids. When di- or trivalent ions, such as magnesium ions, are present, the alginates solution gels firmly. Gel-forming solution is made with sodium alginate salt, which is made from alginate salt. Alginate salts are most often thought of since they are naturally harmless and biodegradable. They also possess bioadhesivequalities[52].

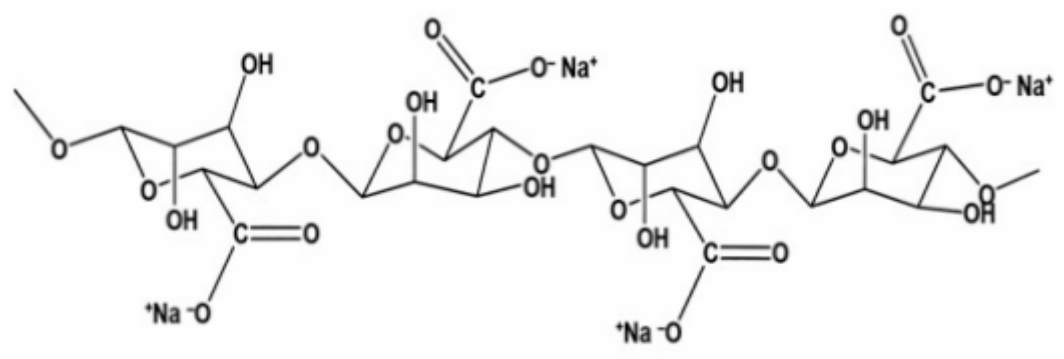

Fig. 2 Chemical structure of Sodium Alginate

2. Pectin:

They originate from plants that are anionic in nature, are classified into two types of polysaccharides, and have residues of -(1-4) -D-galacturonic acid. It can gel in the presence of a medium and continue to do so until gel formation is achievable. Pectin is a complex polysaccharide that is often formed at pH values below 3.5. It is made up of D-galacturonic acid residues arranged in an a-(1-4) chain[52].

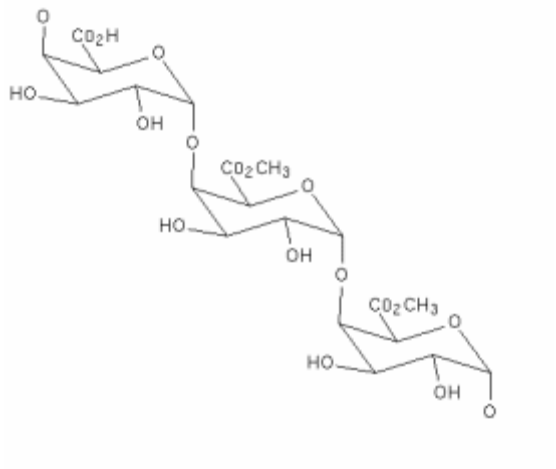

Fig. 3 Chemical structure of pectin

3.Hydroxy propyl methylcellulose:

Hydroxypropyl methylcellulose is a granular or fibrous white odorless and tasteless powder.As a binder (2-5%w/w) in tablets and HPMC of higher viscosity grades in matrix composition for extended-release tablets and

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Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

capsules in the concentration range of 10-80% w/w.Used in film-forming solutions in concentrations of 2-20%w/w according to the HPMC viscosity grade used with lower viscous ones in solutions and higher viscous ones with organic solvents. Used in topical preparations as suspender and thickener.In ophthalmic preparations like artificial tear solutions and eye drops, HPMC is employed as a thickening agent in 0.45-1.0% w/w concentration and is preferred over methylcellulose owing to its clarity with fewer UN dispersed fiberspresence.In ointments and topical gels, hypromellose is employed as a stabilizer, emulsifier, and suspending agent[52].

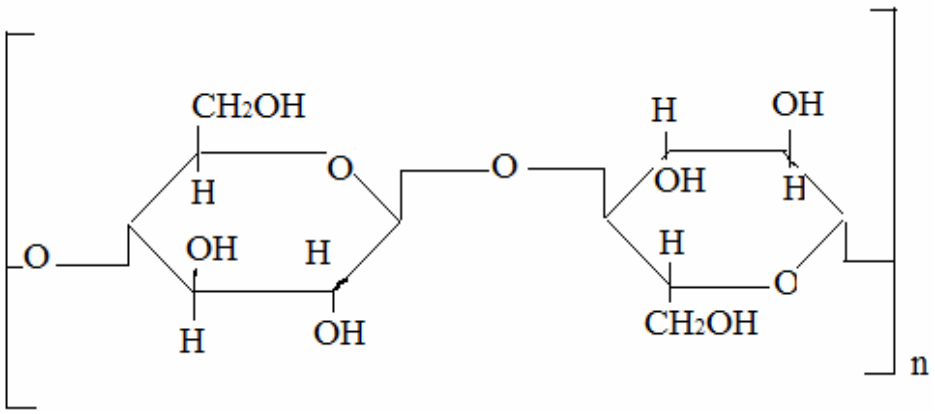

Fig. 4 Chemical structure of Hydroxypropyl methyl cellulose

4.Xanthan Gum:

Xanthan gum is a naturally available creamy white-coloredodorless gum. The powder form of gum is free flowing.It is also used as a thickener and emulsifier. Its compatibility with other excipients, non-toxicity, and stability make it a widely used excipient in pharmaceutical formulations.It is also used in Ophthalmic to prolong retention of dosage form by interacting with mucin.Enhancement of strength of bioadhesive formulations and as a binder in colon specific drug delivery systems.As a hydrocolloid in the food industry, and as a thickener in shampoo[52].

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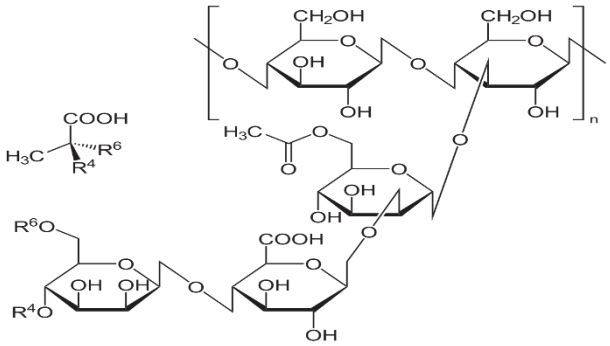

Fig. 4 Chemical structure of Xanthan gum

IX] EVALUATION PARAMETERS OF RAFT SYSTEMS[1]:

A] In vitro evaluation parameters

1.Texture analysis

The purpose of texture analysis is to determine the consistency and robustness, and consistency of the formulation. The primary indication of this analysis is the sol's syringeability, which allows the formulation to be conveniently given in vivo. Gels must have a higher adhesiveness value to keep close contact with surfaces like tissues.

2.Gelling time and the sol-gel transition

An effervescent liquid called a "raft forming system" generates a cohesive, viscous gel since it comes into contact with gastrointestinal liquids. The temperature at which the phase transition of the sol meniscus is first seen when it is maintained at a particular temperature in a sample tube and subsequently heated at a particular pace is known as the sol–gel transition temperature. When the tube is tilted, the meniscus should not move, which indicates the development of gel. The above-described "gelling time" is a time at which gelation is first detected.

3.Gel strength

This is employed to determine the pre-prepared formulation's gelling property. A rheometer can be used to evaluate this parameter. In this experiment, a predetermined volume of gel is made from the sol form in a beaker. A beaker filled with gel gets raised at a certain pace, and a rheometer probe is then gradually fed through the gel. As the probe is submerged below the gel surface, the variations in the load on the probe may be quantified .

4.Rheology and viscosity

It is crucial to evaluate this parameter in relation to the raft forming system. Using a different viscometer, the viscosity and rheological properties of the polymeric formulations were measured, either in solution or in gel formed with counterfeit tissue fluid (depending on the administration method). The viscosity may be measured with an Ostwald viscometer or a Brookfield rheometer, among other types of viscometers. Formulations should have a viscosity that is unlikely to give the patient difficulties while administering them.

5.Fourier transform infrared investigation of drug-excipient interaction/ Thermal analysis / Spectroscopy

Infrared spectroscopy using Fourier transform is used to investigate component compatibility. While this technique may be used for determining the nature of interacting forces and the gelation process, this method employs potassium bromide pellet technique. The proportion of water in hydrogel may also be detected via thermogravimetric analysis, which is applicable to in situ forming polymeric systems. Furthermore, differential scanning calorimetry can be utilized to monitor any variations in thermograms as compared to the pure chemicals utilized, hence revealing the interactions.

6.Floating/buoyancy test

After the dosage form has been introduced into the dissolving medium, it is investigated to see how long it takes for it to float on top of the medium. Measured were the floating lag time (the amount of time that elapses before the dosage form becomes buoyant on the simulated gastric fluid) and the floating time (the amount of time that the dosage form stays buoyant).

7.In vitro release studies

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Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

The USP type-II equipment performs at 50 rpm in order to carry out the in vitro drug release of the raft forming system in 0.1 N HCl for a duration of 0 to 8 hours. The temperature is maintained at 37±0.2 °C and the dissolving media is 900 ml of simulated gastric fluid (0.1N HCl, pH 1.2). A precisely taken sample of the dissolving media is pipetted out and replaced with a new medium at each time interval. Spectrophotometric analysis can be used to determine the drug concentration in the aliquot.

B] In-vivo evaluation test

1.Radiology and scintigraphy

This involves the use of radio-opaque markers When a dosage form is located in the GIT, scintigraphy can be utilized to predict when the stomach will empty and how long the dosage form will take for it to move through the GIT. Barium sulphate is a commonly used radio-opaque marker. When it is included into a solid dose form, it may be seen on X-rays at various intervals to assess stomach retention. Comparably, adding radioactive γ-emission to a formulation permits indirect external observation with a scintiscanner. in which the dose form housed in the GIT may be monitored by focusing the γ-rays that the radionuclide emits on a camera. One common transmitting substance is 99Tc.

2.Gastroscopy

Per-oral endoscopy using fibre optics or video technologies is called gastroscopy. It can be used for visually evaluating the dose form's prolonging impact in the stomach. Additionally, it can provide a thorough assessment of the Gastroretentive medication delivery mechanism.

3.Magnetic marker monitoring

The iron powder inside the dose form is magnetically labelled to indicate its contents. Using extremely sensitive bio-magnetic measuring equipment, the dose form image may be captured. There is no radiation and this method is less hazardous.

4.^{13}C octanoic acid breath test

^{13}C octanoic acid and the Gastroretentive drug delivery system are injected into the stomach, where octanoic acid undergoes a chemical reaction to release CO_2 gas. The ^{13}C isotope takes the place of the crucial carbon atom that will be found in CO_2. Therefore, the stomach retention time of the dose form might be defined as the amount of time that $^{13}CO_2$ gas is detected in the breath. There isn't a response or CO_2 emission when the dose form enters the colon.[1]

X] Floating Raft Forming System-Advantages[53]**:**

1. **Enhanced Therapeutic effectiveness:** It is well known that floating raft producing devices increase the therapeutic effectiveness of drugs. Through extended contact with the gastrointestinal mucosa, these devices provide a more uniform and controlled release of the medication, therefore enhancing its overall efficacy.
2. **Rapid Floating Mechanism:** One of these systems' most important qualities is its ability to float rapidly after administration. This quick buoyancy makes sure the medication stays in the stomach for an extended period of time, which improves absorption and prolongs the effects of the medication.
3. **Ease of Administration:** Using floating raft forming systems to administer medications is a simple and patient-friendly method. Promoting patient compliance and convenience, the dose forms are made to be simple to use and swallow.
4. **Formation of Low-Density Viscous Layer:** Floating raft producing systems induce the formation of a low-density viscous layer when they come into contact with the stomach contents. This layer helps to keep the dosage form floating and allows the medication to discharge gradually and continuously, improving the efficacy of the treatment.
5. **Decreased Plasma Level Fluctuations:** As reducing fluctuations that may cause unfavourable side effects or less than ideal therapeutic results, these systems improve in the maintenance of steady plasma medication levels. A constant medication concentration in the bloodstream is ensured by the controlled release method
6. **Targeted Drug Absorption:** Approaches that create floating rafts are especially helpful for medications that have limited windows of absorption in the small intestine. The effectiveness of such drugs' absorption is improved by these systems, which assure the drug stays in the stomach and is delivered steadily.[2]

XI] Disadvantages of Raft Systems in Drug Delivery[1]**:**

1.Restricted Application to Specific Compounds: Not all medication may be

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

appropriate for raft systems. It is possible that some drugs have particular physicochemical characteristics that make them incompatible with the formulation specifications of raft systems, which would restrict their use in particular therapeutic contexts.

2.Variable Gastric Emptying Time: The duration of time it takes for the stomach to empty can vary greatly between individuals as well as between physiological situations. The performance of raft systems may be impacted by this variability, which might result in uneven rates of medication release and absorption and compromise the effectiveness of treatment.

Limitation of floating raft forming gastroretentive drug delivery system[54]

1. These systems are developed as solutions, which are more prone to issues with stability. These result from either microbial or chemical deterioration (oxidation, hydrolysis, etc.).
2. The formulation needs to be maintained correctly since improper storage might lead to stability issues. This results from the system's pH changing after extended storage or from improper temperature storage.
3. When certain polymers are exposed to radiations (such as ultraviolet, visible, electromagnetic, etc.), gel is created inside the package.

XII] LIST OF PACKAGING MATERIALS FOR RAFT SYSTEMS [55]**:**

Usually Raft formulations are packed in bottle containers made up of different materials . Unit doses packed in sachets.

Table No :4

Name of material	Types
A] Glass	**Type I Borosilicate Glass** : Highly resistant to thermal shock and chemical interactions. It is the preferred choice for storing sensitive formulations, including raft-forming suspensions, due to its inert nature. **Type II Soda-Lime Glass**: Used for less sensitive formulations but typically coated to improve chemical resistance and prevent interaction with the suspension.
B]Plastic	**Polyethylene Terephthalate (PET)**: Offers good barrier properties against oxygen and moisture, making it suitable for oral suspensions. It's commonly used due to its clarity and lightweight nature. **High-Density Polyethylene (HDPE)**: Provides excellent moisture barrier properties and chemical resistance, often used for bulkier packaging of oral suspensions. **Low-Density Polyethylene (LDPE)**: More flexible and often used for squeezable

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

	bottles or unit-dose applications, providing ease of administration. **Polypropylene (PP)**: Often used for caps and closures due to its strength and resistance to high temperatures, ensuring a tight seal and protection against contamination.
Closures and Liners	**Polypropylene (PP) Caps**: Used with plastic bottles to provide a secure seal, preventing leakage and contamination. **Aluminum Seals:** Sometimes used for sealing glass containers, providing an additional layer of protection. **Child-Resistant and Tamper-Evident Closures**: Essential for ensuring safety, particularly with suspensions used in pediatric settings
Laminated Tubes	**Aluminum Barrier Laminates (ABL)**: Used for packaging unit doses or small volumes of raft-forming suspensions. It provides an excellent barrier against oxygen and moisture, ensuring the formulation's stability. **Plastic Barrier Laminates (PBL)**: Used for more flexible packaging solutions, offering protection while being easy to handle and use.
Secondary Packaging	**Cartons:** Often used to house primary containers, providing additional protection from light, mechanical stress, and other environmental factors. **Foil Pouches:** Used for unit-dose packaging, offering excellent barrier properties against moisture and oxygen
Sachet Packaging	**Multi-layer Sachets (e.g., aluminum foil, polyethylene)**: Used for single-dose applications, providing protection against moisture, oxygen, and light, while being convenient for patient use.

XIII] Gastro-retentive Drug Delivery Systems Market Outlook (2023 to 2033)[56]

Newly-released Gastro-retentive Drug Delivery Systems industry analysis report by Future Market Insights reveals that global sales of Gastro-retentive Drug Delivery Systems in 2022 were held at US$ 13.3 Billion. With a CAGR of 10.1% from 2023 to 2033, the market is expected to reach US$ 24.8 Billion by 2033. Floating Drug Delivery System is expected to be the highest revenue generating type, with a CAGR of 5% from 2023 to 2033.

Table No :5

Attribute	Details
Global Gastro-retentive Drug Delivery Systems Market (2023)	US$ 14 Billion
Global Gastro-retentive Drug Delivery Systems Market (2033	US$ 24.8 Billion

XIV] Marketed formulation of the raft forming system

Various marketed formulations of the raft forming system are stated in the table below-

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 2098-2114 www.ijprajournal.com ISSN: 2456-4494

Table No : 6

Brand name	Active ingredient	Company	Delivery system
Liquid Gaviscon®[1]	Aluminum hydroxide (95 mg) and magnesium carbonate (358 mg).	GlaxosMithKline, India.	Effervescent floating liquid alginate preparations.
Topalkan®[1]	Aluminum and magnesium mixture.	Pierre fabre drug, France.	Effervescent floating liquid alginate preparation.
Almagate Float-Coat®[1]	Aluminum and magnesium mixture.	Pierre fabre drug, France.	Floating dosage form.
Madopar®[57]	Levodopa (100 mg) Benserazide (25 mg)	Roche products , USA	Floating CR capsule (Hydrodynamically balanced system) .
Valrelease®[58]	Diazepam (15 mg)	Hoffmann La Roche , USA	Floating capsule
Conviron®[59]	Ferrous sulfate	Ranbaxy , India	Colloidal gel forming floating system .
Cytotec®[60]	Misoprostot	Pharmacia , USA	Bilayer floating capsule .

XV] Patented preparations[1]
Various patents on the preparation of the raft forming system.

Table No :6

Sr. no.	US patent	Formulations
1.	US20050063980	Gastric raft composition
2.	US5360793	Rafting antacid formulation
3.	US20020119941	In situ gel formation of pectin

XVI]Future perspectives[7]

Although drug delivery methods have advanced significantly in recent years, they may

yet be made better. Raft systems provide a potential route with their numerous advantages and controlled release capabilities. These systems may be modified to satisfy specific requirements, such as the duration of therapy or the speed at which a medicine is delivered. Particularly helpful when it's difficult to maintain a consistent dosage regimen over an extended period of time.

Raft systems are beneficial because they improve the way drugs perform and maintain consistent blood levels of the drugs. Strong medications like sedatives and painkillers, as well as the treatment of grave illnesses like cancer, are two areas in which they perform. Patients can get pain relief using raft systems throughout the entire day with just one dose, which is very helpful and reduces pain. More research can be done to improve raft systems so that they may be applied to more emergency situations.

II. CONCLUSION

The raft system has demonstrated significant promise for regulated medication release. It has many benefits and few disadvantages, is simple to create, and uses common components. It is simple and cost-effective to test in the laboratory and on living things. Studies and patents demonstrate that the raft system is capable of releasing medications gradually and maintaining consistent blood levels, which is very beneficial to patients. Because it increases the amount of medicine that the body can utilize and decreases adverse effects, it is even more effective than previous comparable systems. Modifying the raft system has been the main focus of recent work, and it appears that this improvement trajectory will continue.

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