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COMPREHENSIVE REVIEW ON RECENTLY INVESTIGATED NOVEL NATURAL POLYMERS IN HYDRODYNAMICALLY BALANCED DRUG DELIVERY

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ABSTRACT

The rationale of writing this review on Hydrodynamically Balanced drug delivery system (FDDS) was to assemble current literature with unique center of attention on the role of Natural Polymers in flotation to attain gastric retardation. Mouth drug delivery system is the majority preferential Course of management for drug delivery system of several components participate crucial function. In current existence, diverse scientists were put their efforts to found more advancements in their investigation and develop a release restricted oral drug delivery system to conquer the difficulties such as low gastric residence time, impulsive gastric emptying time. To conquer these difficulties gastroretentive drug delivery system was established which has the capability to hold the drug release in stomach in favor of larger time and there by enhances the availability of drug in plasma, conceivably it provides therapeutically efficient plasma drug concentration for longer period of time, in so reducing doing frequency and increasing the bioavailability. In current scenario major researchers will focuses on applications of natural gums. Natural polymers and their compounds are frequently utilized to create different dosage forms for pharmaceuticals than synthetic polymers because they are readily available, inexpensive, biodegradable, and non-toxic. By extending the dose form's retention period in the stomach, the gastric floating drug delivery

method increases the medicine's oral bioavailability. This review has talk about applications of some recently investigated gums in FDDS approaches such as low-density system, high density system, mucoadhesive system, swellable system.

Keywords: FDDS, Natural gums, SiteSpecific Drug Delivery, Gastric Retention, Hydrodynamically balanced systems

INTRODUCTION

The most practical and recommended method of delivering any medication to the systemic circulation is oral administration. Recently, the pharmaceutical industry has become more interested in oral controlled release drug delivery in an effort to improve therapeutic advantages such patient compliance, dose administration convenience, and formulation flexibility **[1]**. Deceitful controlled release methods for improved absorption and bioavailability encounter a number of challenges **[2]**. To target the site-specific release of pharmaceuticals in the upper gastrointestinal tract to produce a local (or systemic) effect, the gastro retentive drug delivery system (GRDDS) is a method for extending the length of gastrointestinal residency **[3]**. Drug bioavailability, side effect elimination, dosage frequency reduction, drug preservation due to prior benefit, improved solubility for medications that are less soluble in high pH environments, optimal therapy, and finally simple patient compliance **[3, 4]**. Numerous methods for delivering gastroretentive drugs have been developed over the past few decades, such as high density (sinking) systems that are kept at the stomach's bottom **[5]**, low density (floating) systems that give stomach fluid its buoyancy Mucoadhesive systems **[6-7, 8]** that induce stomach mucosa bioadhesion **[9]**, expandable, unfoldable, or swellable systems that restrict the amount of dose forms that can be emptied beyond the stomach's pyloric sphincter **[10, 11]**, super porous hydrogel systems, magnetic systems, etc. It is commonly known that contact time with the small intestinal mucosa influences the amount of medication absorption in the gastrointestinal tract **[12–13]**. Therefore, for medications that are not fully absorbed, the small intestine transit time is a crucial component.

DRUG DELIVERY SYSTEM THAT FLOATS

Hydrodynamically balanced system (HBS) is another name for floating medication delivery system. The medication is gradually removed from the system at the desired rate while it is floating on the contents of the stomach. The stomach is cleared of the drug's

leftover system once it has been released. As a result, the variations in plasma drug concentration are better controlled and the GRT is raised.

Floating drug delivery system uses

The limited absorption window in the upper gastrointestinal system of medications with low bioavailability can be addressed by floating drug delivery in a number of ways. By keeping the dosage form where it is absorbed, it increases the bioavailability. Here is a summary of them.

1. Long-Term Medication Delivery
2. Specific to the site Dispensing of Medicines
3. Improvement of the absorption

Categorization of Floated Drug Distribution Network

1. Float dosages system with a single unit

(a) Systems that produce gas and are effervescent

(b) Non-effervescent

2. Multiple Unit Floating Dosage Systems

a) Absent flowing system

b) System that produce gas, or exuberant systems

c) Empty microspore

d) Algorithms for the raft Formation.

MECHANISM OF FLOATS DRUG DELIVERY SYSTEM

Because floating drug delivery systems (FDDS) have a lower bulk density than gastric fluids, they float in the stomach for extended periods of time without slowing down the rate at which the stomach empties. The medicine is released from the system gradually and at the desired rate while it is floating on the stomach contents **(Figure 1)**. The stomach is cleared of any leftover medication after the substance has been released. As a result, the variations in plasma drug concentration are better controlled and the GRT is raised. To maintain the dose form consistently buoyant on the meal's surface, however, a minimum level of floating force (F) is also necessary in addition to the minimal stomach content necessary to permit the correct realization of the buoyancy retention principle. A unique apparatus for determining the resultant weight has been disclosed in the literature in order to measure the kinetics of the floating force. The device works by continually measuring the force (as a function of time) equal to F needed to keep the submerged object stable. If F is higher on the positive side, the object floats more easily. This device assists in maximizing FDDS in terms of stability and longevity of generated floating forces to avoid the negative effects of unpredictable intra-gastric buoyancy capacity fluctuations. 25. (Df - Ds) gV = F = F buoyancy - F gravity where g is the acceleration caused by gravity, V is

volume, Ds is object density, F is the total vertical force, and Df is fluid density.

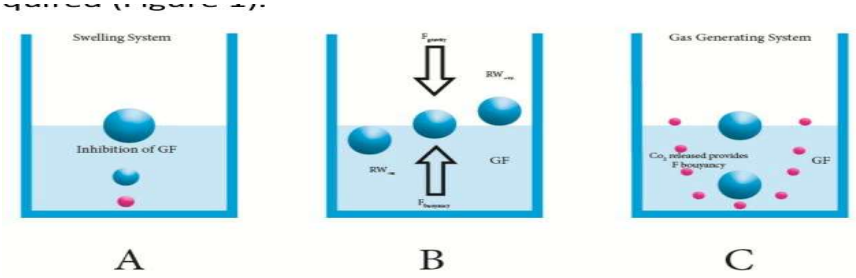

Figure 1: Mechanism of Floating Systems

Natural Gums

Plant-based polymers can be produced into natural polymers and are readily available in nature. Natural gums are high molecular weight hydrophilic carbohydrate polymers **[6]**. Because these plant components are high in carbohydrates, the majority of these natural gums are found to be biocompatible, nontoxic, and non-irritable. In organic solvents, they are insoluble. Gum can either dissolve in water or overlap.

Compared to artificial polymers,

Natural polymers have benefits. They are:

- Non-toxic,
- Biocompatible,
- Environmentally friendly.
- Low cost
- Eco-friendly
- Readily available locally.

Natural polymers has few drawbacks. These include:

- Microbiological contamination
- Batch-to-batch fluctuation.
- Unchecked rate of hydration
- Compact gumminess during storage.

Recently Investigated Natural Gums in Floated Drugs Transport System:

In literature some review papers already gave information regarding the usage of some natural gums in floating drug delivery system. Here we go with some recently investigated natural gums. Those are given below:

Moringagum

Biological source: *Moringa oleifera* (munga) plant

Dried moringa powder is utilized as a medicinal excipient in a variety of compositions. Moringa gum is used to treat rheumatism, gastrointestinal issues, and syphilis. It also contains antipyretic, antioxidant, anti-asthmatic, astringent, and rubefacient qualities.

7Swapna Vellivela *et al*. used moringa gum as

a functional polymer to create a gastro-retentive drug delivery system for ranitidine HCl. In order to extend the drug's gastrointestinal residence time and improve absorption, floating matrix tablets containing ranitidine HCl were created, thereby boosting the drug's bioavailability. The functioning of moringa gum powder was investigated in this study, and the findings suggested that the system would be beneficial in terms of enhanced bioavailability.

Figure 2

GrewiaGum

Biological source: *Grewia Mollis*

Grewia gum is a polymeric pharmaceutical excipient that has gained attention recently. It is used as a binding agent, mucoadhesive, and suspending film coating. Grewiagum was analyzed for micrometric properties and the drug excipients compatibility study was done using FT IR spectroscopy. The low aqueous solubility is also stabilizer, suspending agent in food, cosmetics and in pharmaceuticals.

Uhumwangho uwumagbe Michael *et al*. used Grewia gum as a functional polymer to create a gastro-retentive drug delivery system for metformin. Metformin floating matrix pills were created to extend the duration of gastric residency. Grewia gum has been used to create metformin gastro floating matrix tablets, which may be helpful for medications with a limited window of absorption in the upper gastrointestinal tract **[8]**.

Cordia Gum

Biological source: Cordia dichotomy

Natural gums are used in a variety of therapeutic preparations like cordia gum. The gum used in this investigation is an extract from Cordia dichotomy (Lasunda) berries. The gum is initially white, but when exposed, it turns reddish brown and then brownish black. It dissolves very slowly in water but becomes very viscous when it comes into touch with it. An anionic polysaccharide with high adhesive qualities, cordia gum is utilized as a tablet binder and emulsifier.

V.M. Darvhekar *et al*., developed a gastro retentive drug delivery system for losartan with Cordia gum as functional polymer. Floating matrix tablets of losartan were developed to prolong gastric residence time and increase drug absorption further increasing the bioavailability. In this study the functionality of Cordia gum powder was studied, and the results showed that the system could be possibly advantageous in terms of increased bioavailability. The results suggested that sulfated Cordia gum as polymer can be successfully employed for formulation of mucoadhesive drug delivery system **[9]**.

Bhara gum

Biological source: Terminalia Billerica

Dried powdered bhara gum is utilized as a medicinal excipient in a variety of compositions. The usage of nontoxic products and vegetables has been more popular recently, which calls for the substitution of natural additives for synthetic ones. Its primary uses have been as purgatives and demulcents. It is also used as an emulsion in cosmetic industries. Bhara gum has number of therapeutic properties, peptic ulcers, diarrhea, dizziness, headache and anorexia etc.

Bhara gum is used to formulate microcapsule for sustained delivery of famotidine. Using bhara gum as a functional polymer, Nayak Bhabani Shankar *et al*. created a gastro-retentive drug delivery system for famotidine. Famotidine floating matrix pills were created to increase the duration of gastrointestinal residency. The gum was found to have significant release-controlling qualities that might be applied to long-term medication administration **[10]**.

Kondagogu Gums

Biological resource: The bark of the Cochlospermum Gossypium species is the natural source of kondagogu gum, a polysaccharide.

Konda, gogu gum is used as a matrix polymer carrier or matrix floating tablet. Its properties are uniform smoothness and texture. Its therapeutic uses are stomach problems, dental problems, menstruation problems, skin problems, smallpox and chickenpox.

Valluru Ravi *et al*.'s current study used kondagogu gum as a matrix-forming carrier to create floating tablets of diltiazem HCL. Diltiazem HCL, which has a roughly 3.5-hour elimination half-life. It was discovered that the medicine released from manufactured tablets varied according to the polymer, kondagogu gum, content. The study's findings indicated that kondagogu gum, which acts as a carrier, can be used to create a floating drug delivery system **[11]**.

Figure 3

Albizia Gum

Biological source: The incised trunk of the Albizia zygia tree is the source of albizia gum.

Since albizia gum is a naturally occurring emulsifier for food and medicine, it has being looked into as a potential gum Arabic replacement. Thisgumswastriedhas an coating material in atablet with compression coating, it was diminished by colonic micro flora, there by releasing the drug. Albizia gum has atherapeutic uses cough, diarrhea, insomnia, rheumatism, stomachache, tuberculosis.

Using albizia gum as a functional polymer, Kunal Pal *et al*. created a gastro-retentive drug delivery system for pioglitazone. Pioglitazone floating matrix tablets were created to extend the duration of gastric residency. The created floating tablets released pioglitazone gradually over the course of 24 hours, depending on the polymer and tablet composition **[12]**.

Khaya Gum

Biological source: This hydrophilic polysaccharide occurs naturally and is derived from the Khaya Grandi Fiola tree.

Dried powdered kaya gum is utilized as a medicinal excipient in a variety of compositions. Additionally, some investigations assessed Khaya Scnegalensis gum's suspending qualities in relation to Acacia Siberians' and Acacia Senegal's gums. The use of Khaya gum has matrix formed in the formulation of gastroretentive floating formulation. Its therapeutic uses are Antidiabetes, hypoglycemic, immunomodulatory, anti-ulcer, chronic renal failure.

Using Khaya gum as a functional polymer, Clifford Orakwe *et al*. created a gastro-retentive drug delivery system for metronidazole. The purpose of this study is to manufacture and assess metronidazole gastro retentive floating matrix tablets utilizing Khaya gum. The development of metronidazole, which can maintain medication formulation for up to 10 hours, is the conclusion drawn from the use of Khaya gum **[13]**.

Figure 4

Copal Gum

Biological source: Copal gum is natural resinous materials of plant Burscra Bipinnate. Dried powdered copal gum is utilized as a medicinal excipient in a variety of compositions. This substance has been utilized as a raw material for varnishers because it creates glossy films that have strong resistance to weathering. Because of its superior binding qualities, varnishers have utilized it as a pigment binder. Mostly, it has been utilized as a stabilizer and emulsifier for color production, paints, printings, and meal preservatives. Copal gum is used medicinally for a number of conditions, including burns, headaches, nosebleeds, fevers, stomachaches, and the creation of dental treatments that treat dysentery and loose teeth.

The evaluation of natural gums, such as Copal and Gum Damar, is covered in a study by D.M. Morkahade *et al*. Gum Damar is a unique sustain release matrix forming substance used in tablet manufacturing. The conclusion is that copal gum has the ability to create a matrix over time, which may be exploited for long-term medication administration. Gum damar (10&20% w/w) and gum copal matrix drug release followed zero order kinetics. It is determined that both gums have significant matrix formation that may be applied to long-term medication administration **[14]**.

Gellan Gums

Biological source: The bacteria Auromonas elodea produces gellan gum, which is the extracellular polysaccharide in a deacetylated form.

The most practical and often utilized method of administering medication is orally. With the advancement of the Controle drug release delivery system, the route dosage forms have

grown more complex over time. In order to provide adequate medication bioavailability, the most popular method for extending the GRT is the floating drug delivery system. Gellan gum's medicinal uses include controlled release beads, hydrogels, sustaining agents, floating in-situ gelling, and ophthalmic medication delivery. Gellan gum is used in dentistry, bone restoration, allergy treatment, tissue regeneration, and medication production.

DS Using gellan gum as a functional polymer, Goswami *et al*. created a gastro-retentive drug delivery system for pioglitazone. Pioglitazone floating matrix tablets were created to extend the drug's gastrointestinal residence time and improve absorption, hence raising its bioavailability. The study's goal is to create and assess floating pioglitazone tablets using Guar gum, a natural gum, as opposed to Gellan gum, another natural polymer. Studies on the drug's release in vitro revealed that an optimal formulation may release the medication (98%) for longer than 12 hours **[15]**.

Abelmoschus Gum

Biological source: Fresh fruits of the Abelmoschus esculentus plant are used to make Abelmoschus gum.

At low concentrations (4%), the gum of Abelmoschus esculentus mucilage powder proved to be an excellent disintegrant. Abelmoschus esculentus gum is utilized as a polymer in the creation of gastric floating dosage forms. The gum has a therapeutic uses gonorrhea and urinary tract infections, anti-cancer and fungicidal properties.

Ordu John *et al*. created a medication administration method that is gastro-retentive. For the floating matrix tablets of cotrimoxazole with Abelmoschus gum as a functional polymer. The observation derives from the conclusion that the Abelmoschus esculentus, the polysaccharide under study may be able to transport the medication to the target location nearly intact. Where in presence of anaerobic microorganisms which causes it to degrade **[16]**.

Mimosa seeds mucilage

Biological source: Mimosa pudica is a creeping annual flowering plant of the pea.

Mimosaseedmucilagederivativesareextensively utilized in the food and pharmaceutical industries since they are usually regarded as safe and non-toxic for consumption by humans and animals. In an earlier study, the mucilage of mimosa pudica seeds was assessed as a sustained release application, employing diclofenac sodium as the reference medication. It has several therapeutical uses anti-fungal agents, oral candidiasis, piles,

dysentery, sinus.

Munish Ahuja *et al*. investigated the mimosa pudica seed mucilage's prolonged release characteristics on diclofenac sodium floating matrix tablets. By using the wet granulation process, tablets were made. The findings indicated that the release of medication from tablets reduces as the concentration of mucilage in the formulation increases. The polymer demonstrated a bio adhesion time of 10 hours and a medication release of over 85% in 10 hours, according to the results **[17]**.

Figure 5

Locustbean gum

Biological source: The polysaccharide locust bean gum, which is derived from the seeds of the carob tree (Ceratonia siliqua), is a member of the galactomannan group.

Due to its beneficial effects on hardness and floatability, locust bean gum makes up the majority of the formulation. The floating tablets were assessed for dissolving studies, in vitro buoyancy, hardness, friability, drug content, and uniformity of weight. Because of its high fiber content, locust bean gum may help lower blood fat and sugar levels. It lessens reflux and is also added to baby formulae.

Acyclovir's gastro-retentive floating tablet was created by Pritam Dinesh Chowdary and colleagues utilizing natural gums like locust bean gum. This formulation included a variety of floating polymer combinations. Studies on the release of drugs in vitro demonstrated that an improved formulation could maintain drug release for sixteen hours and maintain buoyancy for twenty-four hours. According to the study's findings, a pill formulation with 10% locust bean gum disintegrated in 13 seconds **[18]**.

Figure 6

Katira Gum

Biological source: The roots of the **Astragalus plant** are tapped for the Gond Katira gum. The gum is drained out of the roots in the form of thin sheets like flakes or twisted ribbons. This is allowed to dry and powdered into the commercial Gond Katira powder available in the markets.

The non-toxic and biocompatible katira polysaccharide possesses antimicrobial, antioxidant, and immune-modulating qualities. It is an organic polysaccharide and exudate that is obtained from *Cochlospermum reliogosum* Linn's stem bark. Traditionally, katira gum was used as a sedative and to treat a variety of illnesses, including syphilis, jaundice, gonorrhea, and stomach problems **[19]**.

Using Tramadol as a model drug, Yakujaku Zasshi *et al*. developed the drug release retardant property of Katira gum in floating matrix tablets. Three characteristics of katira gum were measured: pH, viscosity, and swelling index. The tablets underwent a battery of physical tests, including those for drug content, tensile strength, friability, and hardness. The functioning of Katira gum powder was investigated in this study, and the findings suggested that the system would be beneficial in terms of enhanced bioavailability **[20]**.

Figure 7

Leucaena Gum

Biological source: Leucaena gum derived from seeds of Leucaena leucocephalas

Polysaccharide from Leucaena leucocephala seeds for long-term medication release. This maintained the seed gum's release behavior in both water soluble and water insoluble forms of Leucaena leucocephala. This gum has a few therapeutic uses such as anti-diabetic, anti-cancer, anti metastatic, antibacterial and anti helminthic.

Deborah Bera *et al*. investigated the long-term release characteristics of Leucaena gum on floating matrix tablets of Ibuprofen.Ibuprofen floating matrix tablets were created to extend the drug's stomach residence time and improve absorption, hence boosting the drug's bioavailability. It is possible to draw the conclusion that Leucaena gum might be utilized successfully in the formulation of matrix tablets as a drug release retardant based on the findings of this investigation **[21]**.

Flaxseed Mucilage

Biological source: This is a natural polymer-based plant polysaccharide material from *LinumusitatissimumL.*

Flaxseed mucilage contains a polysaccharide. The main polysaccharide of flaxseed mucilage Is a neutral polymer. The mucilage found in flax seed is mostly found in the outermost layer of the seed hull and has been linked to a number of health advantages, including a delayed stomach emptying, lowered blood cholesterol, and better glycemic management. Applications for flaxseed mucilage include encapsulating, stabilizing, gelling, and prebiotic purposes. Ramteke *et al*; developed gastroretentive floating tablet of Metformin hydrochloric acid developedby using natural gums like Flaxseed mucilage. The bulk of the polymeric compounds originating from plants (mucilage and gums) are covered in this review. Recent studies have found that their source usage are excipients in floating medication delivery systems **[22]**.

Moi Gum

Biological source: The stem Lannea Coromandelica's leaves, stems, fruits, and bark are used to make moi gum.

When this gum is new, it is yellowish white; when it dries, it turns dark. Gum ducts are found in leaves, stems, and fruits; the stem's bark has the greatest concentration of gum ducts. Moi gum was assessed as a material for regulating release rate and as a micro-encapsulating agent. Through the process of solvent evaporation, microspheres were created. Moi gum is non-toxic, can be used as an emulsifier in food, and is safe for human consumption.

Figure 8

Using natural gums like locust bean gum, Harshal Ashok Pawar *et al*. created a gastro-retentive floating tablet of bata-sitosterol. The bulk of the polymeric compounds originating from plants (mucilage and gums) are covered in this review. Recent studies have found that their source usage are excipients in floating medication delivery systems **[23]**.

PhoenixMucilage

Biological source: The dried fruit of Phoenix dactylifera is used to make phoenix mucilage. 44–88% of the fruit is composed of carbohydrates, which are primarily reduced sugars including fructose, sucrose, mannose, glucose, and maltose. There are also trace amounts of polysaccharides such pectin (0.5–3.9%), starch, and cellulose. Mucilage's binding qualities were effectively assessed. The concentration of the increases increased the binding ability, resulting in good tablet hardness and weight uniformity. Medical uses are to treat pain, inflammation, swelling which are associated with rheumatoid arthritis, headache, toothache.

Pritam Dinesh Chowdary *et al*; develop gastroretentive floating matrix tablet of Aceclofenac produced with phoenix mucilage were discovered to be less friable than those made with tragacanth and Acacia. This outcome demonstrates their original applications, and some current studies have used excipients in floating medication delivery systems **[24]**.

Dendrophthoe Mucilage

Biological source: The dried and fresh stem parasite of Dendrophthoe falcate on Mangifera indica is used to make dendrophthoe mucilage. In the traditional medical systems of India and Indonesia, Dendrophthoe Falcata and Dandrophthoe were used to cure a wide range of illnesses, including cancer, ulcers, asthma, paralysis, skin conditions, TB, and menstruation problems.

Dendrophthoe Falcata mucilage was assessed

by Harshal Ashok Pawar *et al*. as a binder for pharmaceutical dosage of floating medication dosage form. Dendrophthoe Falcata mucilage was made into tablets using wet granulation. Various mucilage concentrations were employed in the formulation; nevertheless, it was found that 6% w/w binder concentration produced the best tablet binder outcomes **[25]**.

Tara Gum

Biological source One can extract tara gum from the endosperm of Caesalpinia Spinosa seed. This gum mainly contains galactomannans.

Because Tara gum swells, it is used as a controlled release carrier in the formulation of gastroretentive controlled release tablets. Another name for tara gum is Peruvian carob. Tara gum is necessary in foods and beverages because it acts as a stabilizing, thickening and jelling agent in food, which affects the viscosity and texture of products.

Kunal Paletal; develop gastroretentive floating matrix tablet of manufactured Tramadol HCL using Tara gums. Combining Tara gum with other medications lengthens the dosage's floating period for patients with strong gastroretentive properties. Emulsions were also made with tara gum. Combining Tara gum with medications that have excellent gastroretentive properties to lengthen the floating time of the dosage **[26]**.

CassiaTora

Biological source: Mucilage from the seeds of the Cassia torta plant.

Among its other ingredients were sugars, resins, and mucilage. The binding property of Cassia Tora mucilage was investigated. It has been noted that mucilage concentrations that are higher result in tablets that are harder and dissolve more quickly than those that have varying amounts of Cassia Tora gum in them. No – based on the above, I confirmthat I do not have a potential conflict of interest. Cassia Tora gum hastherapeutic uses such as skin diseases such as ringworms, itching of the body, scratches, and management of skin allergies.

Using Cassia Tora gum, Harshal Ashok Pawar *et al*. create a gastro-retentive floating matrix tablet containing zidovudine. Zidovudine floating matrix tablets were created to increase the duration of gastric residency. When choosing which ingredients to use for immediate, controlled, or sustained release formulations, Casia Tora is a key factor **[26]**.

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