ADITUM

Aditum Journal of Clinical and Biomedical Research

Open Access Review Article

Natural Gums Used in The Preparation of Floating Drug Delivery System

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Article Info

Received: September 16, 2022
Accepted: December 22, 2022
Published: February 22, 2023

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Citation: Uma Rani, Asma Begum and M. Sumakanth. (2023) "Natural Gums Used in The Preparation of Floating Drug Delivery System.", Aditum Journal of Clinical and Biomedical Research, 6(1); DOI: http;//doi.org/02.2023/1.1096.

Abstract:

The purpose of this review on floating drug delivery systems is to compile current research with a specific focus on polymers used in floating drug delivery systems, which are mostly of natural origin. Because the floating drug delivery system is less dense than stomach fluids, it can float in the upper gastrointestinal tract for an extended period of time, releasing the medicine at the appropriate rate. This is possible by using a variety of polymeric materials, including natural polymers. Despite the introduction of synthetic biodegradable polymers, a variety of polymeric materials are available to serve as release retarding floating matrices; however, the use of natural polymers to delay drug delivery is an ongoing research topic. Natural polymers are appealing because they are abundant in nature, are inexpensive, are made by living creatures, degrade easily in vivo, and are non-toxic.

Keywords: floating drug delivery system; natural polymers.

Introduction:

Gastric emptying of dosage forms is a highly variable process, and the ability to extend and control the emptying time is a crucial asset for dosage forms that stay in the stomach for longer than conventional dosage form. Designing controlled release systems for improved absorption and bioavailability presents a number of challenges. [1,2,3] Drug absorption from the gastrointestinal system is a complicated process that is influenced by a number of factors. It is well accepted that the amount of medication absorption in the gastrointestinal tract is proportional to the amount of time the drug spends in touch with the small intestine mucosa. As a result, for medications that are only partially absorbed, small intestinal transit time is an essential metric. [4] Gastro retentive systems can stay in the gastric region for several hours, significantly extending the time drugs spend in the stomach. Prolonged stomach retention improves bioavailability, minimises drug waste, and improves solubility for medicines that are less soluble at high pH. It can also be used to deliver drugs to the stomach and proximal small intestines. Gastro retention aids in the provision of innovative drugs with novel treatment possibilities and significant patient advantages. [5]

Fdds [Floating Drug Delivery System]:

These are low-density systems with a lower density than gastric fluid, allowing them to float in the stomach for longer periods of time without affecting the gastric emptying rate.
The FDDS are classified into two groups: [3-9].
A. Effervescent system.
B. Non effervescent system.

A. Effervescent system:

Effervescent systems release carbon dioxide when they come into touch with stomach juices. Inside the inflated hydrocolloids, the carbon dioxide is trapped. This gives the dose form buoyancy, which allows it to float. Volatile liquids that gasify at body temperature may also be present in these systems.

Non effervescent system:

This type of system swells after ingesting gastric fluid to the point where it prevents them from exiting the stomach. Because they tend to stay close to the pyloric sphincter, these systems are also known as "plug type systems." Combining the drug with a gel-forming polymer, which swells in contact after oral administration while maintaining relative shape integrity and a bulk density of less than one, is one method for creating such dosage forms. Excipients that form gels, such as polycarbonate, polyacrylate, and polystyrene, are the most commonly used. This hydrocolloid begins to hydrate by first forming a gel on the dosage form's surface.

Natural Polymers Used in The Preparation of Floating Drug Delivery Systems:

Hydrocolloids:

Hydrocolloids are gel-forming agents that swell when in contact with gastric fluid while maintaining relative shape integrity and bulk density less than the gastric content. For Eg: Acacia, pectin, agar, alginates, gellan gum, guar gum, okra gum, cashew gum, xanthan gum, gelatin, and casein are a few examples.[12]

Chitosan:

Chitosan is a straight chain homopolymer composed of (1, 4 -2-acetamido-2deoxy D-glucose) units that is commercially obtained by hydrolysis of the amino acyl groups of chitins. Chitosan contains one primary amino acid and two free hydroxyl groups or glucose units. Hydrogels are formed when cationic amino groups react with a variety of multivalent anions. Increased deacetylation improves chitosan biocompatibility. The modification of chitosan was central to the preparation of hydrogels. [26-28]

Hascicek C et al. used direct compression to prepare gastric floating bi-layer tablets containing acetyl salicylic acid. Tablets, such as the HPMC K100M, had the slowest release pattern. The release rate was effectively modified for up to 8 hours by combining HPMC K100M and chitosan. The drug release was discovered to be governed by the Higuchi diffusion mechanism. [26]

H. M. El-Nahas et al prepared Chitosan microspheres containing TMZ by a capillary extrusion procedure.

Xanthan gum (XG):

Is a polysaccharide with a high molecular weight that is derived from specific species of bacteria. It is made by fermenting glucose with the gram-negative bacteria Xanthomonas campestris. It is naturally nontoxic and nonpathogenic. Xanthan gum is soluble in both cold and hot water, resulting in a highly viscous solution that is resistant to heat and pH changes. Xanthan gum is also used as an excipient for drug sustained release and has time independent release kinetics. Each xanthan gum repeat unit has five sugar residues, including two molecules of glucose, two molecules of mannose, and one molecule of glucuronic acid. At C-6, the mannose closest to the main chain carries a single group. Xanthan gum has also been combined with guar gum to create floating drug delivery systems. It has also been derivatised to sodium carboxymethyl xanthan gum and cross-linked with aluminium ions to prepare microparticles as a protein delivery carrier. [13-24]
S Venkata et al. prepared non-effervescent floating drug delivery systems of the poorly soluble drug carvedilol phosphate using solvent evaporation and melt granulation techniques with release retarding polymers/swellable polymers such as xanthan gum and poly ethylene oxide. [25]

A. Kulkarni et al. used a direct compression technique to prepare a region selective bilayer tablet of atenolol and lovastatin using sodium starch glycolate as a super disintegrant, HPMC K100M and xanthan gum as release controlling polymers, and sodium bicarbonate as a gas generating agent. [13]

Okra gum:

Okra gum is a natural polymer derived from the pods of the okra plant (Abelmoschusesculentus). It's been used as a binder, a hydrophilic polymer matrix, a suspending agent, and a bioadhesive agent. It has been reported that okra gum, obtained through traditional extraction, has the potential to be used as a film coating agent. At gastric pH, it remains insoluble. It swells dramatically and aids in the delay of drug release. [38]

Rajamma AJ et al. prepared gastro-retentive ziprasidone HCl tablets using natural gums as sustained release carriers. The floating lag time was found to be longer at higher levels of okra gum and shorter at higher levels of HPMC K4M. [38]

Gellan gum:

Gellan gum is a polysaccharide with a high molecular weight derived from pseudomonas species. It is a byproduct of the fermentation of the microbe Sphingomonas elodea and nontoxic gram-negative bacteria. Gellan gum is a deacetylated anionic extracellular linear polysaccharide composed of glucuronic acid, rhamnose, and glucose. Its structure is made up of four linked monosaccharides, including one glucuronic acid molecule and two glucose molecules. This gum has excellent gel strength, exceptional stability, flexibility, high clarity, good film forming ability, and thermally reversible gel characteristics. Gellan gum easily dissolves and hydrates in hot or cold water, forming a viscous solution. Various researchers have considered this gum as a potential carrier for various floating dosage forms. [48]
Navjot Kanwar et. al prepared Pregabalin floating tablets by varying the concentrations of the gums (xanthan gum and guar gum), Carbopol 974P NF, and HPMC K100.

Starch:

Starch is a natural polysaccharide composed of amylose that represents the linear fraction of this macromolecule. A modified starch containing a high percentage of amylose (70%) has been successfully used in the research and development of swellable hydrophilic matrices. Some of the properties of high amylose starch can be changed by esterifying, etherifying, and oxidising its hydroxyl groups, or by cross-linking with chemicals such as epichlorohydrin, sodium trimetaphosphate, and others. The lowest drug release rates demonstrated that cross linking reactions introduced interchain ester linkages into polymer structures. [42,44-46]

Saritha M et al. prepared pioglitazone floating matrix tablets with Olibanum, starch acetate, and HPMC K15M and compared them to one another. The floating lag time of the starch-containing formulation was 4-7 minutes, and the floating duration was 44-48 hours. Olibanum>starch acetate>HPMC K15M.47 were the release retardant characters.

Sodium alginate:

Sodium alginate is a nontoxic, biodegradable copolymer composed of L-glucuronic acid and D-mannuronic sea weed species extracted via ion exchange. In aqueous media, it hydrates and swells. In an acidic medium, however, it swells and remains insoluble, contributing to the buoyancy and controlled release properties. [30-32]

Patel N et al. prepared a gastro retentive drug delivery system for glipizide tablets. In vitro drug release studies revealed that increasing the concentration of polymer (sodium alginate) in the formulation resulted in a lower rate of drug release and a longer total floating time. [33]

LG (Locust Bean Gum):

It is a natural polysaccharide that is translucent white at the edges and contains approximately 88% D-galacto-D-mannoglycan, 4% pentan, 6% protein, 1% cellulose, and 1% ash. The D-galactose to D-mannose ratio is roughly 20:80. [37,38]

Salve PS et al. prepared gas-generating floating metformin hydrochloride tablets. The tablet formulation containing metformin hydrochloride, locust bean gum in a 1:1 ratio, and 10% sodium bicarbonate demonstrated 90% drug release in 8 hours. Due to the weak matrix forming tendency of locust bean gum, a faster drug release was observed in the formulation batch containing locust bean gum alone compared to xanthan gumalone.

Guar gum:

Guar gum is a polysaccharide found in the seeds of the Cymopsis tetragonolobus plant (family Leguminosae). Guar gum has been used by researchers to create sustained release dosage forms, either alone or in combination. In the presence of water, it swells rapidly and forms a translucent suspension. Guar gum's contents are separated into water soluble and insoluble components. The water-soluble fraction contains approximately 85 percent Guaran gum, a high molecular weight hydrocolloid polysaccharide. Guaran hydrolysis yields 65 percent galactose and 35 percent mannose, both of which are linked together via glycosidic linkages. Guar gum mucilage has a viscosity similar to that of acacia mucilage and a viscosity similar to that of tragacanth mucilage. It has a thickness that is 5-8 times that of starch. It functions as a protective colloid, binding agent, disintegrant, emulsifier, and so on. Guar gum is compatible with the majority of other plant hydrocolloids, including tragacanth. It is incompatible with acetone, ethanol (95 percent), tannins, strong acids, and alkalis. [14, 17,22]

Navneeth K et al. prepared Atorvastatin calcium floating tablets with guar gum as a release retardant. The formulated batches were able to stay in the stomach for approximately 12 hours, resulting in improved drug solubility and bioavailability. [17]

Pectin:

Pectin is a carbohydrate-like plant constituent with a high molecular weight that is made up primarily of chains of galacturonic acid units linked as 1,4-a-glucosides. Pectin is defined in the USP 32 as a purified carbohydrate product derived from a dilute acid extract of the inner portion of the rind of citrus fruits or apple pomace. It is primarily composed of partially methoxylated polygalacturonic acids. There are two types of pectin gelation characteristics. There are two types of gelation: high-methoxy and low-methoxy. Pectin is a complex polysaccharide that primarily consists of esterified D-galacturonic acid residues in a 1, 4glucoside chain. Pectin gel beads have been demonstrated to be an effective medium for controlling drug release in the gastrointestinal tract. Pectin has been used as a component in the preparation of mixed polymer microsphere systems in order to achieve controlled drug release. [35]

Navneeth K et al. created Atorvastatin calcium floating tablets with guar gum as a release retardant. The formulated batches were able to stay in the stomach for approximately 12 hours, resulting in improved drug solubility and bioavailability. When compared to synthetic polymers, formulations containing natural polymers demonstrated a greater release retardant effect and more predictable drug release profiles. [17]

Casein:

Casein can enclose bioactive molecules, modifying their release and/or improving their bioavailability. It has the ability to alter the dissolution of drugs from compacts. Because casein films have a high tensile strength, they are an acceptable film-coating for tablets. As cross linkers, natural genipin and a natural tissue enzyme, transglutaminase, were used to create novel casein-based hydrogels for the controlled release of bioactives. [55-56]

Based on its emulsifying and bubble-forming properties, Elzoghby AO et al. created casein floating beads to increase the residence time of drugs in the stomach. Casein-based micro particles entrapping bioactive molecules were created using emulsification-chemical cross linking with glutaraldehyde, enzymatic cross linking with transglutaminase, simple co-acervation, and electrostatic complexation.

Olibanum:

Olibanum is an oleo gum resin extracted from the incised trunk of the tree Boswelliaserrata of the Burseraceae family, also known as Sallakiguggul, Salai gum, and Indian Olibanum. Boswellia species are found in tropical parts of Asia and Africa. Olibanum is primarily composed of an acid resin (56-60%), gum (30-36%), and volatile oil (3- 8 percent). Gum is primarily composed of arabinose, with a trace of xylose and galactose. It works well as a matrix former and micro encapsulating agent for controlled release. [38,40,41]

Devi C et al. created pioglitazone sustained release floating matrix tablets using Olibanum gum and HPMC. Olibanum was used as a matrix former, and sodium bicarbonate was used as a gas generating agent. As floating enhancers, bee's wax and ethyl alcohol were also used.

Cashew gum (CG):

Cashew gum is an exudate derived from AnacardiumoccidentaleLinnstem bark (family, Anarcardiaceae). Cashew gum is composed of 61 percent galactose, 14 percent arabinose, 7% rhamnose, 8% glucose, 5% glucuronic acid, and less than 2% other sugar residues. Larabinose, Lrhamnose, Dgalactose, and glucuronic acid are produced when the gum is hydrolyzed. The gum is made up of a highly branched galactan framework made up of chains of (13) linked –D-galactopyranosyl units interspersed with (1 6) linkages. Because of its low cost, nontoxicity, biodegradability, and appropriate physicochemical properties, cashew gum has been extensively researched for a variety of pharmaceutical applications. [42]

Sterculia gum:

Gum sterculia is a dried exudation obtained from the stems and branches of "Sterculia Urens," an Indian tree in the Sterculiaceae family. Gum sterculia belongs to the class of gums that have galactouronan or galacturonorhamnan basal chains with D-galacturonic acid (or its 4methyl) ether residues in the interior chain (as terminal units in side chain attached to a variety of different sugar residue). Gum sterculia contains approximately 43% D-galacturonic acid, 13% Dgalactose, and 15% L-rhamnose. Gum Karaya is a negatively charged colloid and a complex acidic polysaccharide with a high molecular weight. It was found to be suitable for the preparation of hydrophilic matrices, minimatrices, and microcapsules, among other things. [49,50]

Singh B et al., prepared a gastro-retentive floating drug delivery system of pantoprazole by simultaneous ionotropic gelation of alginate and sterculia gum using BaCl2 as a cross linker.

Conclusion:

Because of their biodegradability, biocompatibility, Eco friendliness, and widespread availability, natural polymers have been widely used in the design and synthesis of novel drug delivery systems. As a result, these natural polymers will broaden the scope of future drug delivery systems. According to our discussions, sodium alginate and xanthan gum have recently become popular for the development of floating drug delivery systems. There are several expensive synthetic polymers available, but sodium alginate and xanthan gum may be the best alternatives. Better floating dosage forms with improved floating lag time, floating duration, and drug release can be achieved with proper selection of natural polymers and their blending with other polymers. Plant-based materials can be modified to meet the requirements of drug delivery systems, making them a viable alternative to synthetic polymers in the development of controlled release floating dosage forms. Formulations made from such renewable and environmentally friendly plant resources can be regarded as promising floating matrix forming agents for achieving sustained release action with site specific delivery for improved bioavailability, as supported by further research in this area. Despite its numerous advantages, this drug delivery system has seen very few industrial applications to date. With a decrease in dosing frequency, this delivery system may aid in the absorption of acidic active pharmaceutical ingredients.

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