WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Role of Herbal Excipients in Novel Drug Delivery System

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ABSTRACT :-

Herbal excipients have garnered significant attention in recent years for their potential applications in novel drug delivery systems (NDDS). This review explores the evolving landscape of herbal excipients, emphasizing their roles and advantages in enhancing drug delivery efficiency and therapeutic outcomes. The integration of herbal excipients in NDDS offers several benefits, including biocompatibility, biodegradability, sustainability, and often, inherent therapeutic properties. Moreover, herbal excipients contribute to formulation stability, controlled drug release, and improved bioavailability through synergistic interactions with active pharmaceutical ingredients. This abstract provides an overview of current research trends, challenges, and future prospects in leveraging herbal excipients for advancing NDDS, highlighting their promising role in pharmaceutical sciences.

Smart drug delivery systems (DDSs) with stimuli-responsive features have been included into traditional DDSs. Many smart DDSs have been extensively proven in the academic sector for a number of fascinating systems, including liposomes, metals/metal oxides, exosomes, and stimuli-responsive polymeric nanoparticles.

Herbal excipients

Introduction :-

The word "excipient" comes from the Latin word excipients, which means to receive, gather, or take out. The quality of a formulation is influenced by the excipients used, manufacturing processes, and active pharmaceutical ingredient (API). These excipients maintain the product's efficacy and safety while greatly enhancing the API's performance [(1)]. There are three main reasons why using herbal medicines is common:-

1. There is an increasing number of concerns about the safety and dependence of drugs and surgery.

2. Modern medicine does not adequately treat a large number of the most common health problems.

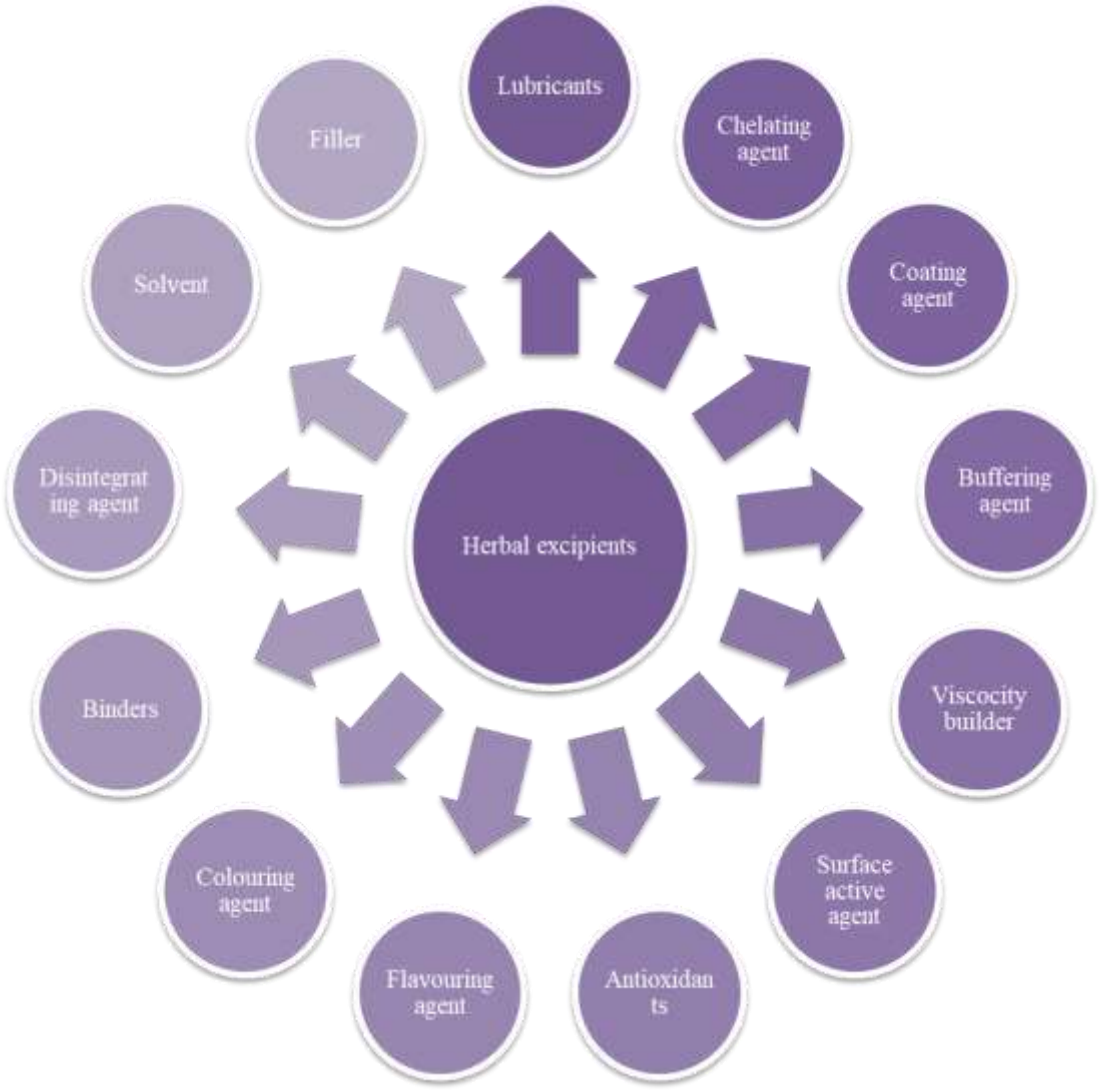
3. Research shows that a lot of natural treatments have greater beneficial effects than prescription drugs or surgery without the drawbacks [(2)].

The systemic side effects of conventional medication delivery are linked to non-specific biodistribution and unpredictable drug release qualities. Consequently, these limitations are addressed by a new delivery method that enables the controlled release of payloads at the designated site. Compared to the conventional delivery method, the innovative drug delivery system has the benefit of reducing dosing frequency while maintaining the drug concentration in the targeted organs and tissues for an extended amount of time [(3)]. Excipients are mostly utilized in conventional dosage forms such tablets and capsules as diluents, binders, disintegrants, adhesives, glidants, and sweeteners[(4)]. To control the medication's dispersion in innovative drug delivery, the drug is either integrated into a carrier system or its molecular structure is changed. Increased bioavailability, stability, improved solubility, toxicity protection, sustained delivery, and protection against chemical and physical degradation are all made possible by the innovative drug delivery [(5)].

The disadvantage of heavy metal contamination that is frequently linked to herbal excipients is outweighed by their relative non-toxicity, ease of availability, and financial benefits in the pharmaceutical sector when compared to synthetic alternatives. Consumers today search for natural substances in food, medications, and cosmetics because they think that natural products are safer and have fewer adverse effects. It is now acknowledged that excipients may have an impact on the rate and/or degree of drug absorption, contrary to the conventional belief that they are inert and have no therapeutic or biological effect or alter the biological activity of the medicinal component. Herbal excipients are important in pharmaceutical formulation since they are compatible and non-toxic. Therefore, this paper provides an overview of natural excipients that are utilized in both innovative and conventional drug delivery systems [6,7,8]

Classification

Based on the application



Classification of Excipients

Excipients are commonly classified according to their application and function in the drug products-

a. Binder and Diluent

b. Lubricants, Glidants, Disintegrants

c. Polishing film former, Coating Agents

d. Plasticizer, Colouring

e. Suspending Agent, Preservatives

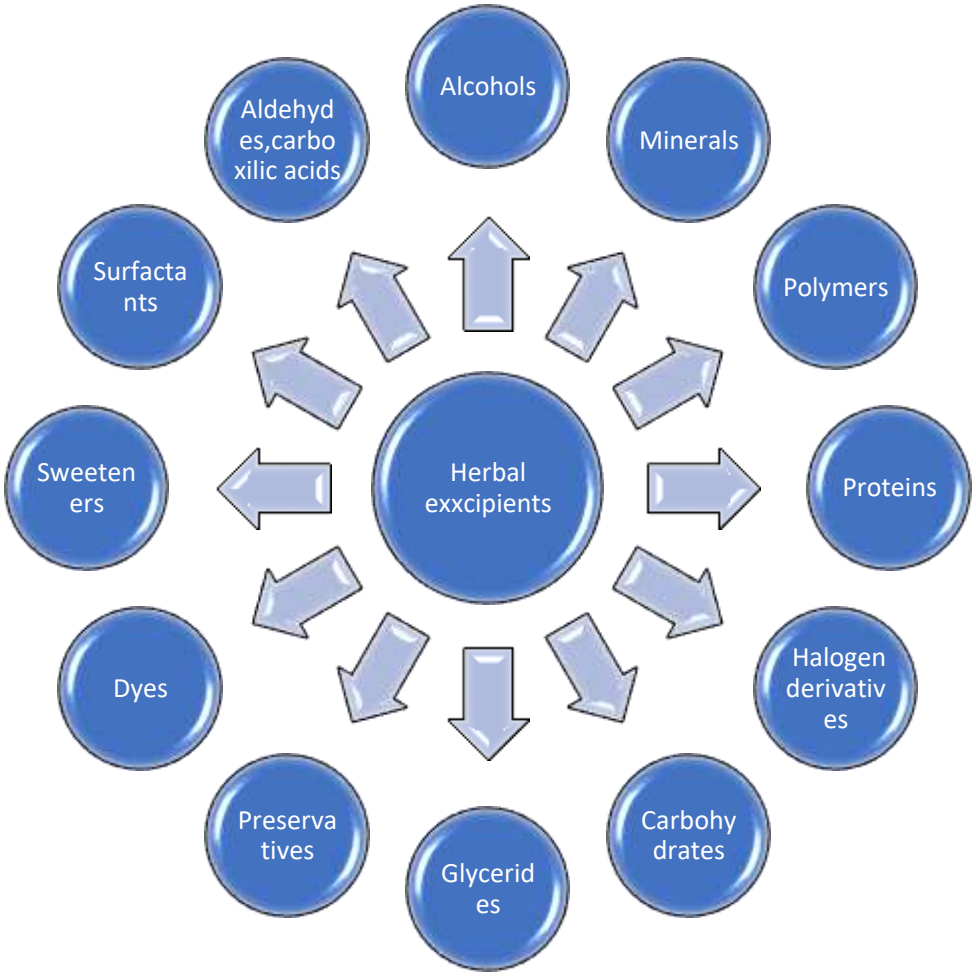
f. Flavourig, Sweeteners, Taste Improving Agent

g. Printing Ink, Dispersing Agent Gum

h. Antioxidant [9]

Classification

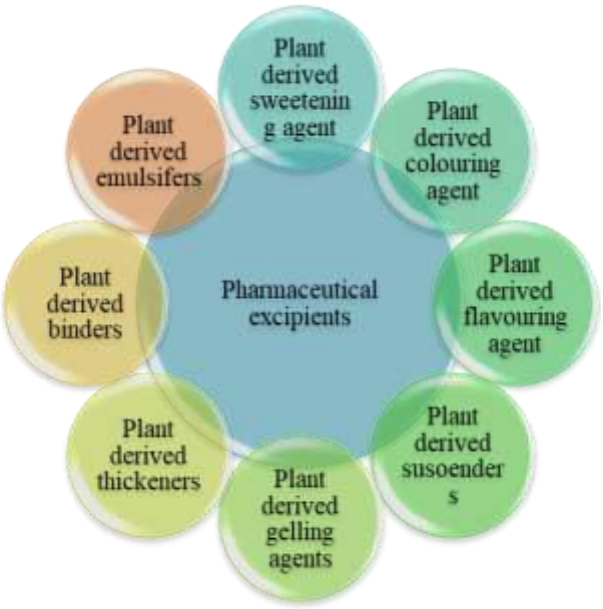
Based on chemical nature



Difference between Herbal excipients and Synthetic excipients [10] :-

GUM ACACIA	**GUAR GUM**	**KARAYA GUM**
1) The dried gummy exudate from the leaves and branches of Acacia Senegal (Linne) Willdenow and other related Acacia species (Family Leguminosae) is known as gum Arabic or gum acacia. 2) It has been established that gum is an acidic polysaccharide that contains D-glucuronic acid, L-arabinose, L-rhamnose, and D-galactose. 3) The primary function of acacia is as an emulsifying and suspending ingredient in oral and topical medicinal formulations; it is frequently used in conjunction with tragacanth. It's also utilized as a tablet binder and to make pastilles and lozenges. 4) By making gum Arabic pellets, ferrous	1)Gaur gum is a naturally occurring polysaccharide composed of galactomannan that is obtained from the seeds of Leguminosae family plant,Cyamopsis teragonolobus. 2) It is composed of D-mannopyranose linked in linear chain by (1-4) linkages and D-galactopyranosyl units connected by 1,6-links in a 1:2 ratio. 3) Because guar gum slows down the release of drugs and is easily broken down by microbes in the large intestine, it is utilized in colon delivery systems. Five-aminosalisylic acid (5-ASA) core tablets were made by wet granulating starch paste, and they were then	1) Karaya gum is a partly acetylated polymer of galactose, rhamnose, and glucuronic acid 26 that is derived from sterculiau urens (Family sterculiaceae). 2) In order to produce directly compressed matrices, sweaallable hydrophilic natural gums such as xanthan gum and karaya gum were utilized as release regulating agents. 3) Diclofenac sodium and caffeine were chosen as the model drugs despite their differing solubilities in aqueous media.

sulfate was released continuously for seven hours. By applying polyvinyl and ethylene vinyl acetate coatings to the pellets, respectively, release was further maintained for over 12 hours.	compression coated with a coating mixture that included varying amounts of guar gum. 4) To be used in the chemoprevention of colorectal cancer, rofecoxib matrix tablets based on guar gum were produced.	4) Gum erosion, both significantly impacted by the rate of agitation. Therefore, it was determined that the speed, solubility, and percentage of the drug all affected the release of the drug from the xanthan and karaya gum matrices.



Functions of Excipients [10] :-

• Give the formulation more body.

• It facilitates handling active pharmaceutical ingredients during manufacture.

• Help with the administration of drugs.

• Strengthen adherence from patients.

• Improve the bioavailability and drug solubility of active pharmaceutical ingredients. Prevent the deterioration of drugs.

• Provide a reliable and repeatable formulation outcome.

• Alter the liquid dose forms' osmolarity and pH.

• Aids in the dispersion of drug particles and inhibits drug agglomeration.

• Aids in hiding offensive smell, color, and taste.

• Contributes to stability maintenance.

Ideal Properties of Excipients [11] :-

• They have practical applications.

• They ought to be innocuous and non-irritating by nature.

• Their nature need to be stable.

• Hydrolysis, light, and temperature shouldn't have an impact on them.

• They ought to be affordable and conveniently accessible.

• They shouldn't have a particular taste, color, or smell.

• They should be compatible with the active ingredient in the formulation and not interfere with its function.

• They should have good solubility in water and lipids.

• They ought to be inert pharmacologically.

POLYSACCHARIDES IN PHARMACEUTICALS

For the creation of solid dosage forms, natural polysaccharides are widely utilized. These low-cost polymers of monosaccharides come in a range of forms and attributes. Being hydrophilic and gel-forming by nature, they are extremely safe, non-toxic, and stable. Among the polysaccharides frequently found in dosage forms are pectins, starch, guar gum, amylase, and karaya gum. The bacterial occupants of the human colon break down non-starch, linear polysaccharides, which makes them potentially helpful in targeted delivery systems to the colon. However, they remain intact in the physiological milieu of the stomach and small intestine [(12)].

Pectins:

Pectins are linear polysaccharides derived from plant cell walls that do not contain starch. They are primarily linear polymers with a few hundred to a few thousand building units per molecule, corresponding to an average molecular weight of roughly 50 000 to about 1 80 0002. They are primarily composed of (1–4)-linked D-galacturonic acid residues interrupted by 1,2-linked L-rhamnose residues. Due to its water solubility, pectin cannot adequately protect the medication load when it passes through the small intestine and stomach. It was discovered that, in simulated in vivo settings, a layer of significant thickness was necessary to protect the drug core [(13)] Controlled-release matrix tablets are a common application for polymeric hydrogels.[(14)]

Alginates:

Natural polysaccharide polymers called alginates were extracted from brown seaweed (Phaeophyceae). Alginate is a salt that can be made from alginic acid; the most common form that is used today is sodium alginate. A linear polymer with blocks of D-mannuronic acid and L-guluronic acid residues arranged in the polymer chain; blocks of random or alternating mannuronic and guluronic acid units separate these homogeneous blocks (composed of either acid residue alone). Alginates have several uses in drug delivery, including local applications, delivering biomolecules for tissue engineering applications, modifying gastrointestinal transit time, and forming matrix type alginate gel beads [(15)].

Starches:

It is the main source of carbohydrate reserve in green plants, with seeds and subterranean organs containing the most of it. As granules, or starch grains, starch is found in various forms. The size, shape, and ratio of the primary ingredients, amylose and amylopectin, are unique to the species. It is known that certain starches have use in medicine. like potatoes (Solanum tuberosum), rice (Oryza sativa), wheat (Triticum aestivum), and maize (Zea mays) [(16)]. In immediately compressible controlled-release matrix systems, modified starch was tested to determine its broad application as a new pregelatinized starch product. It was made by enzymatically breaking down potato starch, which was then precipitated (retrogradated), filtered, and washed with ethanol[(17)].

Gums :

The clear, amorphous materials that plants create are called gums. Gums are often pathological compounds that plants make when they are harmed or grow in poor conditions. Anionic or non-ionic polysaccharides make up gums, which are hydrocolloids derived from plants. Sugar and uronic acid salts are produced during the hydrolysis of gums [(18)].

Guar gum :

Cyamopsis tetragonolobus (Family Leguminosae) seeds are the source of guar gum, a naturally occurring polysaccharide known as galactomannan. It consists of β-D-mannopyranose linked in a linear chain by β-(1-4) linkage and α-D-galactopyranosyl units connected by 1, 6-links in a 1:2 ratio [(19)].

Gum acacia :

Gum arabic, often known as gum acacia, is a dried sticky substance that is extracted from the branches and stem of Acacia senegal (Linne) Willdenow and other closely related trees.

Leguminosae family. D-galactose, L-arabinose, L-rhamnose, and D-glucuronic acid are among the acidic polysaccharides that have been identified in the gum. In oral and topical medicinal formulations, particularly in conjunction with tragacanth, as a suspending and emulsifying ingredient, is the primary usage of mica. Along with being a tablet binder, it is also utilized in the making of pastilles and lozenges.[(20)]

Tragacanth :

The branches of the Leguminosae family plant Astragalus gummifer are the source of this gum [(21)]. Tragacanth, either by itself or in conjunction with other polymers, provided a suitable release prolongation when utilized as the carrier in the development of 1- and 3-layermatrices[(22)].

VOLATILE OILS

In general, combinations of hydrocarbons and oxygenated molecules produced from these hydrocarbons make up volatile oils. Terpenoids are the source of several oils, some of which are aromatic derivatives combined with terpenes (e.g., clove and cinnamon). Despite having an aromatic structure, certain chemicals (such thymol and carvacrol) are actually terpenoid in origin [23]

Menthol :

The botanical family Labiatae's Mentha piperita is used to make menthol through steam distillation of its flowering tips. 2%w/w hydroxypropylmethylcellulose (HPMC) gel was created as the reservoir system for a membrane-moderated transdermal therapeutic system (TTS) of nimodipine. The solvent system used was 60%v/v ethanol-water, with menthol serving as a penetration enhancer. In order to evaluate if the manufactured menthol-based TTS patch could provide the prescribed plasma concentration of the medication in human volunteers, an in vivo study of the nimodipine TTS patch was conducted. [24]

Caraway :

The ripe, dried fruits of Carum carvi (Umbelliferae) are what make up caraway fruit. The terpene limonene with the ketone carvone make up the volatile oil [26]

Vegetable oil :

Cellulose :

For higher plants with a linear, unbranched structure (vegetables, cotton, wood), cellulose plays a crucial role in the cell wall's structural integrity. β-1,4-1 linked D-glucose units join to create a cellulose molecule, and several of these molecules assemble in parallel to form a crystalline microfibril [27]

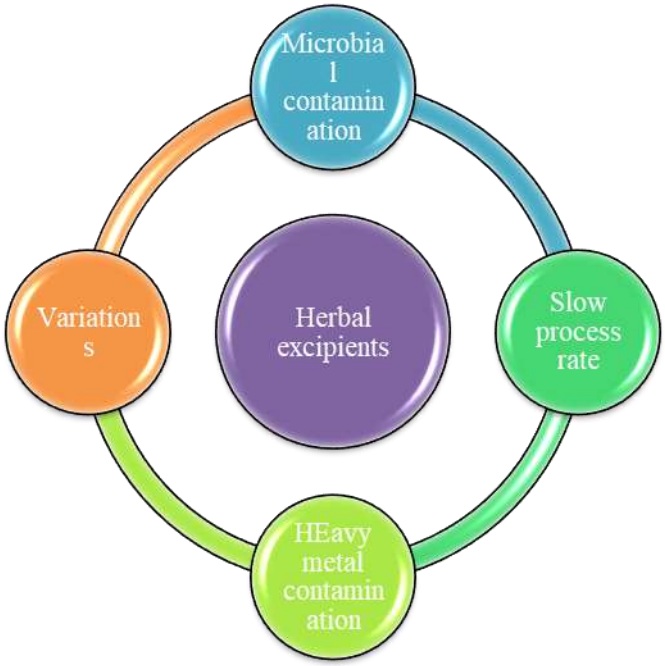
Hemicellulose :

Hemicellulose is mainly obtained from several cereal grains including rice, wheat, rye, barley, millet, maize, and vegetables like olive, carrot, potato pulp, and cabbage. Hemicellulose is a heteropolymer that plays a great role in the formation of cell walls alongside cellulose [28]

ADVENTAGES OF HERBAL EXCIPIENT [29,30,31,32] :

1. Biodegradable polymers are naturally occurring substances that are generated by all living things. They don't seem to have any negative consequences on people or the environment.
2. Non-toxic and biocompatible – Nearly all of these plant components are carbohydrates by nature, consisting of repeating monosaccharide units. They are hence non-toxic.
3. Economical - Compared to synthetic materials, they are less expensive and require less production.
4. Safe and without negative effects – Since they come from a natural source, they are safe and have no negative consequences.

5. Easy availability: Because they are used in so many different industries, they are produced in many different nations.



DISADVANTAGES OF HERBAL EXCIPIENTS [33,34,35,36] :

1. During the production process, there is a possibility of microbial contamination due to their exposure to the external environment.
2. Variation: While the creation of natural polymers is influenced by the environment and other physical elements, the manufacturing of synthetic polymers follows a regulated process with predetermined ingredient quantities.
3. The unregulated pace of hydration: This is caused by variations in the timing of natural material collection, as well as variations in the species' climatic circumstances and the percentage of chemical constituents contained in the material.
4. Slow Process: There is no way to alter the production pace because it is determined by the environment and numerous other factors. Thus, the pace of creation of natural polymers is slower.

APPLICATIONS OF HERBAL EXCIPIENTS :-

• Guar gum: The endosperm of the seeds of the legume plant Cymopsis tetragonolob us is the source of guar gum. Once the husk is removed and polished away from the endosperm halves, refined guar splits are produced. Viscosity is lost and hydrolysis is brought on by strong acid. Furthermore, alkalis in high concentrations are also known to lower viscosity. Most hydrocarbon solvents do not dissolve it.[37]
• Tamarind gum: the endosperm of tamarind tree seeds contains xyloglucan and tamarind.One of the 21 evergreen families is Tamrondous indica. Tamrind kernels are another name for tamrind gum.

The extracted powder (TKP) from the seed microsphere ranges in size from 230 to 460µm.[38,39]

• Locust bean gum: Also referred to as carob gum, locust bean gum (LBG) is made from the refined endosperm of seeds from the ceretonia siliqua L carobe tree.It belongs to the family of legume trees and is evergreen. The endosperm from the seeds of the carob tree is extracted and processed to produce carob bean gum. [40]

• Sweet Sweet Locust gum Its botanical name is Gleditsia triacanthos, and it is a member of the Leguminosea group. The gum is extracted from the seeds. [41,42]

• Khaya gum comes from the incised trunk of the Khaya grandifoliola tree, which is a member of the Meliaceae family. Khaya gum is composed of polysaccharides. The interest in creating gum for pharmaceutical application has also been sparked by the gum's affordable, non-toxic, and naturally occurring nature.[43]

• Aloe mucilage: Aloe barbadensies Miller leaves are used to make it. It has been demonstrated that, in addition to various carbohydrates, aloe parenchyama tissue or pulp also contains proteins, lipids, amino acids, vitamins, enzymes, and tiny chemical compounds. Some researchers have

determined that the main polysaccharide in the gel is partly acetylated mannan, while others have determined that the principal polysaccharide is pectic substance. [44]

• Pectins: A non-starch linear polysaccharide obtained from plant cell walls for use in the food sector, pectins and alginate were combined to create folic acid encapsulated microcapsules that enhanced the stability of folic acid.[45]

Alginate: Alginate is a naturally occurring polymer composed of polysaccharides that are isolated from brown seaweed. It can be converted into its sodium salt, which is the main form that is currently in use. Alginate has several uses in drug delivery, including matrix-type alginate gel beads, liposomes, modulating gastrointestinal transit time for local applications, and delivering biomolecules for tissue engineering applications. [46]

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