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Review Article
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Polysaccharides Obtained from Vegetables: an effective source of alternative excipient

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Polymers are the major constructive material of pharmaceutical formulations that play a prime role in designing effective drug-delivery systems and releasing drugs at their sites of application. Polymers are composed of multiple repeating units of high molecular mass components with attendant properties. Most synthetic polymers are non-biocompatible, expensive, and extremely inclined to deliver adverse impacts. Meanwhile, edible polymers obtained from natural sources have gained remarkable recognition for their promising use in modern medicine. Moreover, polymers derived from natural sources are generally preferred due to certain of their unique features such as abundant availability, biocompatibility, nontoxicity, economical, safe, and effective functions that fit the purpose. Polysaccharides including starch, cellulose, hemicellulose, pectin, and mucilage are identified as a major class of naturally obtained molecules that have a substantial role as functional polymers. This review summarizes the potential role of polysaccharides derived from vegetable sources such as adhesives, anticaking agents, binders, disintegrants, emulsifiers, film-framing agents, and thickeners. This is simply an opportunity to abandon synthetic excipients that hurt our bodies and think back to nature from where we originate.

Keywords: excipients, natural polymers, polysaccharides, pharmaceutical excipients, vegetable polysaccharides

INTRODUCTION

Excipients are characterized as "the substance utilized as a vehicle for giving a medicament"; these substances make a medication suitable for patient administration. Natural excipients are effectively exceeding the requirement and utilization of synthetic excipients in the pharmaceutical industry, because of their lesser toxicity, easy availability, and low expense. Consumers accept that natural substances are more secure in contrast to synthetic ones [1]. In pharmaceutical industries, natural excipients are very popular as they enhance the rate of absorption and permeability of formulation. Excipients influence the organoleptic properties of formulations wherever applicable to enhance patient acceptance and optimize the performance of formulations [2].

Polysaccharides are the most common biopolymers available in abundance in natural resources. About 99% of all natural polysaccharides are obtained from plants and vegetables that have various utility in different sectors [3].

As formulation development is a concern, natural polysaccharides have certain unique advantages including enhanced stability, bioavailability, patient acceptability, safety, efficacy during storage, or use and ease of processing during manufacture [4]. Polysaccharides of vegetable origin including starch, carrageenan, gelatin, and pectin are the key components of the modern pharmaceutical industry. Considering the above facts, the present study has been designed to summarize the key role of polysaccharides of vegetable origin as pharmaceutical excipients in the field of formulation development and manufacturing [5].

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FUNDAMENTALS OF NATURAL POLYSACCHARIDES

Natural polysaccharides are extensively utilized for the advancement of solid dosage forms. They are inexpensive and readily obtainable from various sources such as plants, animals, microorganisms, and marine organisms. Polysaccharides show a range of versatile properties and offer high stability, safety, lesser toxicity, and a wide range of solubility features [6]. In living organisms, polysaccharides provide the necessary energy for cell activities and act as structural elements that are generally hydrophilic in nature and enzyme-degradable. Polysaccharides show an extraordinarily decent variety of features due to the unique variation in their structural design like monosaccharide unit composition, chain links, chain length, and shapes, which influence their properties such as solubility, gelling ability, flow behavior, and surface characteristics [7]. Polysaccharides are usually known as the Cinderella of biopolymers due to their wide scope of applications. Polysaccharides obtained from vegetables can be broadly categorized into two types: structural polysaccharides (cellulose, hemicellulose, and pectin) and storage polysaccharides (starch).

POLYSACCHARIDES COMMONLY OBTAINED FROM VEGETABLE SOURCES

About 99% of all natural polysaccharides are located in plants and vegetables. Table 1 presents the polysaccharides that are mostly derived from vegetable sources.

Polysaccharides such as starch, cellulose, pectin, hemicellulose, mucopolysaccharides like gum and mucilage, xyloglucan, and inulin are abundantly found in natural sources and highly used as excipients.

1. Starch

Starch is the most utilized polysaccharide obtained from plants and vegetables and is often composed of repeating α-d-glucose units connected via α-(1,4)-glycosidic bonds and comprises two structurally distinct polysaccharides, namely amylose and amylopectin (Fig. 1a) [8].

Starch is primarily acquired from grains such as corn, wheat, potato, cassava (or custard), and different varieties of yams such as *Dioscorea rotundata* and *Dioscorea deltoidea* [9]. The application of starch in the pharmaceutical industry includes as a bulking agent, binder, disintegrant, aiding agent for drug delivery, and film-forming agent [10].

2. Structural polysaccharides

The polysaccharides found in plant cell walls are called structural polysaccharides; they participate in shaping the structural framework of cell walls in plants and animal skeletons [11]. The most commonly used structural polysaccharides in pharmaceutical industries are discussed below:

3. Cellulose

In higher plants (such as wood, cotton, and vegetables) with a linear unbranched structure, cellulose is an important structural component of the cell wall. A cellulose molecule is formed by the attachment of β-1,4-1 connected D-glucose units, and many of these molecules then assemble in parallel to form a crystalline microfibril (Fig. 1b).

Cellulose is mainly found in four different pomaces from apple (*Malus domestica Borkh*.), tomato (*Solanum lycopersicum L*.), cucumber (*Cucumis L*.), and carrot (*Daucus cabrota L*) [12]. When treated with hydrochloric acid, high-quality powdered cellulose used as a filler in tablet formulation yields more rheo-

Table 1. Natural polysaccharides and their vegetable sources

Constituents	Vegetable	Ref.
Starch	Potato, corn and wheat, tubers and roots of potato,cassava Yum verities	[3, 4, 11]
Cellulose	Potato, pea, beans, lady's finger, green leafy vegetables	[10-13]
Pectins	Potato, carrots, sweet potato, lady's finger, onion, cabbage, banana peels, tomato, papaya, orange, lemons	[18, 19]
Hemicellulose	Potato, lady's finger, cauliflower	[15, 16]
Mucilage	Potato, lady's finger	[22]
Polymers (xylogucan)	Tamarind seeds (*Tamarindus indica*)	[24]

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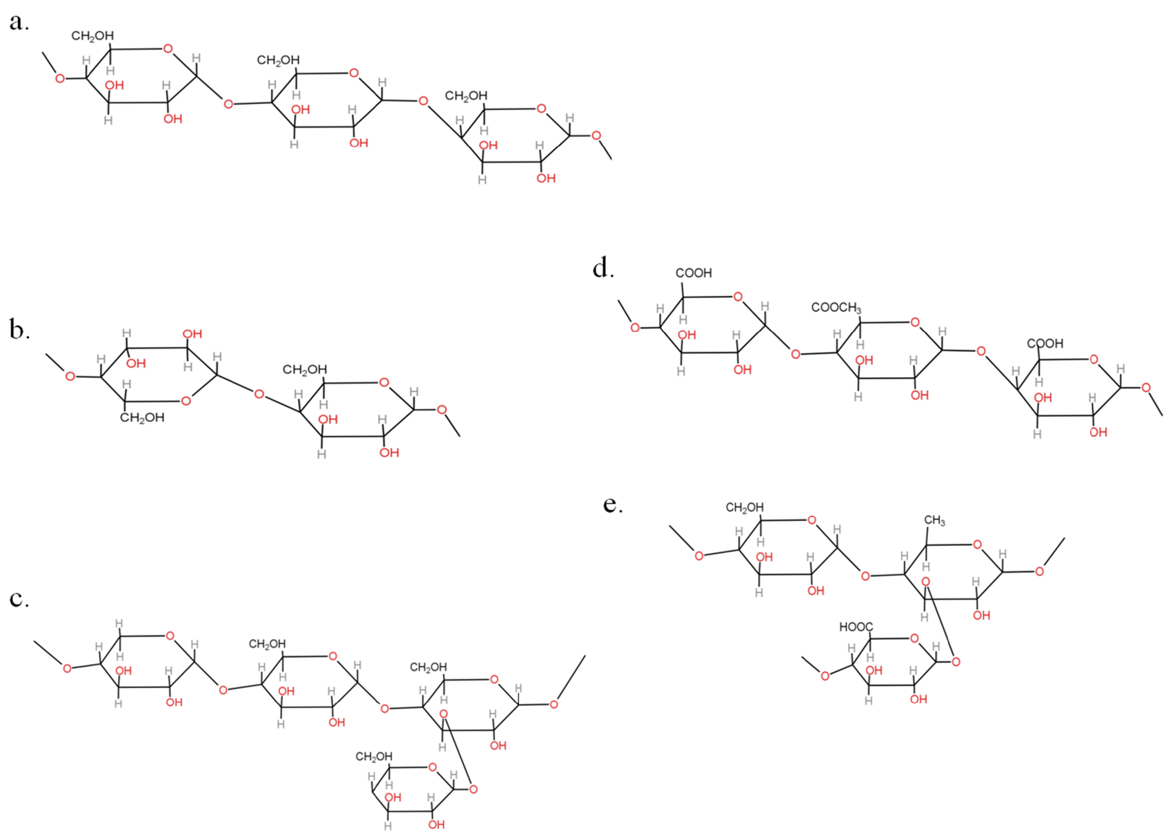

Figure 1. Structure of (a) starch, (b) cellulose, (c) hemicellulose, (d) pectin, (e) mucilage.

logically superior and freely flowing microcrystalline cellulose particles. Cellulose derivatives play a vital role in the formulation of enteric-coated dosage forms and serve as semipermeable membranes in osmotic pump delivery systems [13]. Most popular cellulose derivatives like hydroxypropyl methylcellulose, carboxy methyl cellulose, and sodium carboxy methyl cellulose effectively serve as gel-forming agents and have proven roles as promising polymeric carrier materials for release control in drug-delivery systems [14].

4. 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 (Fig. 1c) [15].

Hemicelluloses consist of β-(1→4)-linked backbones of glucose, mannose, or xylose; they are soluble in alkali and hydrolyze easily in acids and may be classified into two groups: cellulosans and polyuronides. Cellulosans are hemicelluloses framed by sugar units, hexosans (for example, mannan, galactan, and glucan), and pentosans, including xylan and arabinan. Hemicellulose is mainly used as a hydrogel-forming agent, viscosity modifier, gelling agent, tablet binder, or wet strength additive [16]. Konjac glucomannan, which is most commonly extracted from *Amorphophallus konjac* tubers, is an excipient mostly used in the fabrication of controlled-release drug delivery devices. Further, in matrix tablets, the combination of konjac glucomannan and xanthan gum substantially creates a network of intermolecular hydrogen bonds between the two polymers that stabilizes the gel phase and exhibits changes in the drug release characteristics [17].

5. Pectin

Pectins are hydrophilic polysaccharides obtained from maximum plant cell walls comprising of a linear chain predominantly comprised of α-(1→4)-linked D-galacturonic acid (Fig. 1d) [18].

Citrus fruits such as oranges, lemons, limes, grapefruit, and passionfruit, green beans, carrots, tomatoes, and potatoes all have peels that are excellent sources of pectin. The degradability of pectin by colonic enzymes is an advantage for its use in colon-targeted drug formulations. Pectin is used in the formulation of microparticulate delivery systems for ophthalmic preparations and the preparation of matrix-type transdermal patches. Blends of pectin with chitosan have been studied for use in nasal and oral drug-delivery systems; crosslinked mixtures of pectin with high amylose starch exhibit suitable performance in retarding release rates [19]. Pectin has high potential as a hydrophilic polymeric material for controlled-release-matrix drug-delivery systems, but its aqueous solubility contributes to the premature and fast release of the drug from these matrices [20].

6. Mucopolysaccharides

Mucopolysaccharides are slimy substances or mucilages that possess acidic or aminated polysaccharides formed from galactose, mannose, sugar derivatives, and uronic acids. Mucopolysaccharides or mucilages are quite commonly found in both plants and animals; they are mostly harvested from unripe okra fruits (*Abelmoschus esculentus*) or by soaking the husks or seeds of *Plantago ovata* (Plantain, Vern. Isabgol) [21].

7. Gum and Mucilage

Gums and mucilage (Fig. 1e) are produced and stored in various parts of plants and organisms, including the plant epidermis, special secretory cells are found in squills (*Scilla sibirica*), schizogenous sacs found in the young stems of *Frangula purshiana* and *Artocarpus heterophyllus*.

To some extent, they are also found in the stem of *Abelmoschus esculentus* (Okra) [22]. After hydrolysis, the gum and mucilage both produce sugars and uronic acids. They are nonionic, hydrophilic in nature, and form a viscous solution upon contact with water. They are formed by condensations of pentoses and or hexoses. Gums including tragacanth, acacia, and sterculia have been used for pharmaceutical purposes since the early 1800s; they are mostly used as suspending agents, emulsifying agents, adhesives, binders, and disintegrating agents. The chain structure of gums and mucilages affect important characteristics, including the viscosity, gelling ability, and water-holding capacity [23].

8. Xyloglucan

Xyloglucan is a natural polymer derived from tamarind seeds (*Tamarindus indica*), tomato, cabbage, lettuce, and eggplant (*Solanum melongena*). It has a “mucin-like” molecular structure, shows mucoadhesive properties, and is innocuous, biodegradable, and biocompatible in nature. The FDA has approved its usage as a food additive, stabilizer, thickening agent, and gelling agent [24].

9. Inulin

Inulin (Fructan) is a type of oligosaccharide mostly found in dandelion greens, Jerusalem artichoke, onion, garlic, chicory roots, and bitter gourd. Its main purposes include substituting fat, sweeteners, and thickeners in food and serving as a diagnostic tool for glomerular filtration rates [25].

ROLE OF POLYSACCHARIDES AS PHARMACEUTICAL EXCIPIENTS

Natural polysaccharides have been used for a long time in the pharmaceutical industry as excipients. This is particularly because they are natural byproducts and show very minimal side effects. Synthetic excipients are comparatively easy to synthesize for pharmaceutical productions but they have certain drawbacks, so finding an alternative is a pressing need. Natural polysaccharides are an enormous and plentiful wellspring of pharmaceutical excipients. In our work, we have concentrated on natural polysaccharides that are being used traditionally and that can be used as excipients (Table 2).

1. Adhesives

Natural polysaccharides such as hemicellulose and mucilage obtained from potato, lady’s finger, etc. have successfully been used as adhesives in different pharmaceutical formulations. Further, modified potato starch with citric acid and glutaraldehyde show wonderful binding ability. Again, mucilage derived from lady’s finger shows effective binding properties and serves a vital role in the design of controlled-release dosage form [26].

2. Anticaking agent

Cellulose obtained from vegetables such as potato, pea, bean,

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Table 2. Pharmaceutical uses of various polysaccharides

Pharmaceutical use	Constituents	Ref.
Adhesive	Hemicellulose, mucilage	[26]
Anticaking agent	Cellulose	[27]
Binder	Starch, pectin, cellulose	[28]
Coating material	Pectin	[29]
Diluent	Starch	[30]
Disintegrant	Starch	[31]
Dispersing agent	Cellulose	[32]
Drug release modifier	Pectin	[33]
Emollient	Mucilage	[34]
Emulsifier	Cellulose, mucilage, hemicellulose	[35, 36]
Film-forming agent	Cellulose, hemicellulose	[37]
Polymer	Cellulose, pectin, xylogucan	[39]
Stabilizer	Starch, cellulose, pectin	[41]
Suspending agent	Mucilage	[42]
Thickener	Starch, cellulose, hemicellulose, pectin	[43]

lady's finger, and green leafy vegetables can be effectively used as proficient anti-caking agents. These vegetable sources contain around 40-67% cellulose in their composition. Apart from this, the hydrolyzed form of cellulose that is microcrystalline cellulose serves as a binder and super-disintegrating agent in various pharmaceutical dosage forms [27].

3. Binder

Starch, pectins, and cellulose derived from various vegetable sources such as potato, carrots, sweet potato, lady's finger, onion, pea, beans, green leafy vegetables, and cabbage are effective binders when designing different pharmaceutical dosage forms (Fig. 2) [28].

4. Coating material

Natural polysaccharides such as pectins obtained from vegetables like potato, carrot, sweet potato, lady's finger, onion, cabbage, banana peel, tomato, and papaya work effectively as coating materials. Furthermore, they can serve effective roles in colon-targeting and as preservatives in different food preparations [29].

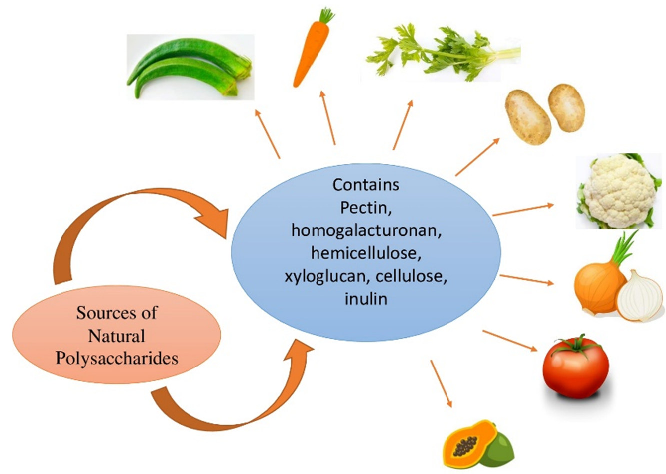

Figure 2. Natural polysaccarides obtained from various vegitables.

5. Diluent

Starch and microcrystaline cellulose mostly obtained from vegetables like potato and corn are very common diluents used in pharmaceutical preparations [30].

6. Disintegrant

Disintegrants are substances that help tablet matrixes break up into small particles in the presence of an aqueous medium. Starch and its derivatives are recognized as tablet disintegrants. Physically and chemically modified starches show enhanced disintegrant activity. Further, sodium starch glycolate is used as a super disintegrant [31]. Again, microcrystaline cellulose is also recognized as an effective super disintegrant.

7. Dispersing agent

Dispersed systems consist of at least two phases: the substance that is dispersed—known as the dispersed or internal phase—and a continuous or external phase. Dispersing agents allow the formation of a dispersed system. Cellulose can be used as an efficient dispersing agent. Recently, a nanocomposite hydrogel has been formulated using nanofibrillated cellulose (prepared by means of microfibrillated cellulose treated with 2, 2, 6, 6-tetramethyl-1-piperidinyloxy, and sonication thereafter) as a dispersing agent [32].

8. Drug release modifier

The polymer hydrates and swells on contact with aqueous media used in the formulation of modified release dosage form. Hydroxypropyl methylcellulose, corboxymethyl cellulose, and pectin are examples that are used to design matrix-forming materials for controlled-release drug-delivery system [33].

9. Emollient

Emollients like sweet almond oil, avocado oil, and olive oil are mainly used in skincare for maintaining the skin's moisture level. Natural polysaccharides like different mucilages can be used as emollients due their unique moisture preservation ability [34]. The added advantages of natural mucilages like non-toxic, gell-forming capacity, and effective moisture retention capacity made them a good choice for a pharmaceutical emollient.

10. Emulsifier

Cellulose, mucilage, and hemicellulose are well absorbed in an oil-in-water emulsion interface and stabilize the system. Hence, they may act as an effective emulsifying agent [35]. Mucilage obtained from mutamba seed has been utilized in the development of thoroughly stable orange peel oil-in-water emulsion. This experiment demonstrates that the mucilages can be used effectively as emulsifiers. Further, mucilage obtained from lady's finger varieties have proven utility as emulsifiers [36].

11. Film-forming agents

Film-forming agents are polymers capable of hardening into coherent films. After applying to the dosage forms, they become dried and form films. Cellulose and hemicellulose are both useful as efficient film formers [37]. In recent research, a carboxymethylcellulose bio-nano composite film with starch has been developed that shows a reasonably higher degree of elasticity and water-vapor resistance. In that experiment, the lignin–hemicellulose combination has shown extraordinary results, which may be applicable in tablet coatings and transdermal patch formation [38].

12. Polymer

Polymers play an integral role in the advancement of drug delivery technology; these regulate the release of therapeutic agents in a controlled release manner and are well capable of maintaining cyclic dosage and the tunable release of both hydrophilic and hydrophobic drugs. Cellulose derivatives and pectins obtained from vegetable sources play a remarkable role as polymers [39]. Hydroxypropyl methylcellulose (HPMC) is one of the most utilized cellulose derivatives used as a polymer; pectin plays a crucial role in designing colon-targeted sustained-release drug-delivery systems. Recently, cellulose nanocrystals and cellulose nanofibrils have been tested to check their polymeric nanocomposite activity; the reported results were satisfactory [40].

13. Stabilizer

In many pharmaceutical formulations, drugs or excipients do not remain stable in solvents or matrixes. Stabilizers are agents that stabilize drug particles by forming a stabilizer layer around them. The natural-origin polymers cellulose, starch, and pectin are used as stabilizers. Stabilizers play a key role in maintaining the bioavailability of drugs. A comparative study on HPMC, CMC, and bacterial cellulose reveals that bacterial cellulose as a stabilizing agent shows the most promising result among all. Furthermore, a study suggests that pectin extracted from beet plays an important role as a stabilizer in an oil–water emulsion system [41].

14. Suspending agent

Suspending agents increase the viscosity of a formulation so that the particles show slower settling velocity and remain dispersed for longer. Mucilage is a water-soluble, sticky, and gummy polysaccharide that helps increase the viscosity. Hence, it can be used as a suspending agent. Reported research suggests that lady's finger mucilage has been successfully used as a suspending agent to stabilize a paracetamol emulsion and is found to be effective at a very low concentration, i.e., 4% w/v [42].

15. Thickening agent

Thickening agents are used to increase the viscosity of a solution. The effectiveness of a polymer as a thickening agent depends on its molecular structure and the effective volume depends on the three-dimensional structural arrangement represented in the solution. The formation of rod-like structures means that their effective volume increases beyond their actual volume. Starch, pectin, cellulose, and hemicellulose are some examples of effective thickening agents [43].

FUTURE PROSPECTS OF NATURAL POLYSACCHARIDES

Polysaccharides have gained in popularity in recent years due to their dynamic structural variability and functionality. Furthermore, the introduction of various polysaccharide modifications through homogeneous and heterogeneous reactions enrich their versatile utilization in the field of formulation development. The design of various stimuli-responsive controlled release systems, including transdermal films, buccal tablets, matrix tablets, microsphere/hydrogel bead systems, and nanoparticulate systems could make meaningful use of these modified polysaccharides. To develop new drug-delivery methods, biotechnological applications, and other delivery systems, this contribution aims to both establish new and modify existing natural sources.

CONCLUSION

Polysaccharides, irrespective of their source availability, play an important role in the development of modern pharmaceutical dosage forms. The application of natural excipients is an emerging and preferred trend in pharma industries. The natural polysaccharides obtained from vegetable sources have gained huge popularity and acceptability as excipients due to their versatile features like abundance, low cost, unique chemical structures, versatile features, and added advantages like their lesser toxicity profile. Natural polysaccharides as excipients surely have a promising future and great roles to play in the domain of dosage form development in the near future.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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