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A Comprehensive Review on Natural polymers used for the formulation Pharmaceutical dosage forms

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Abstract

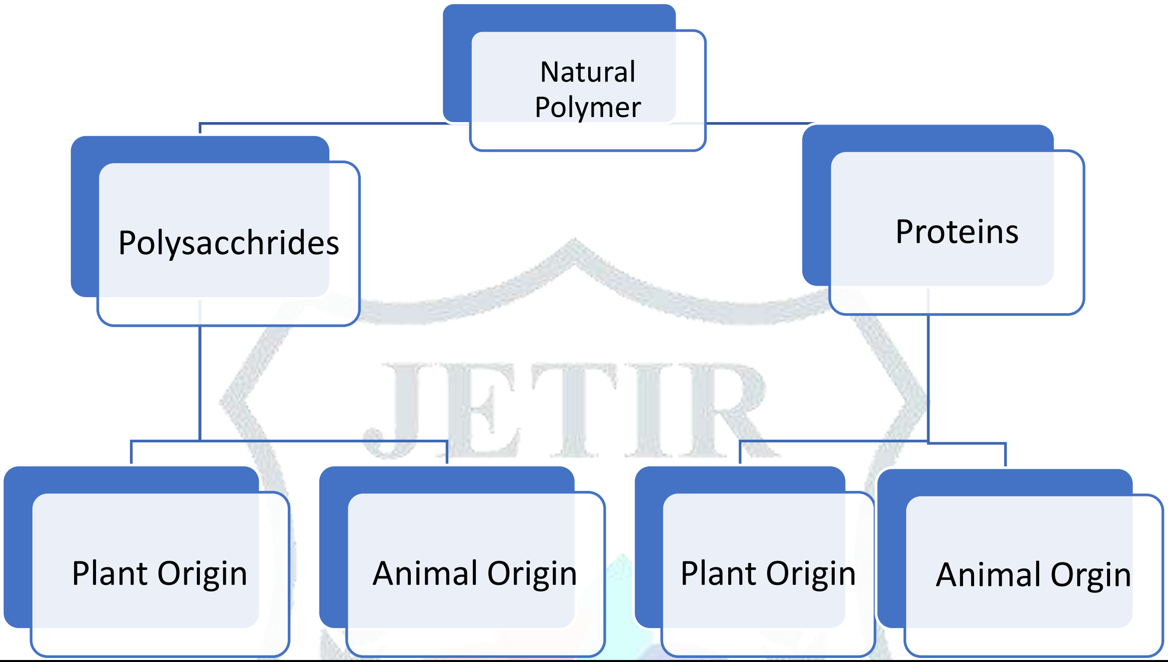
One of the main instruments for managing the frequency of drug liberation from formulations has been polymers. Numerous uses of polymers in pharmaceuticals the delivery has been made possible by their special qualities, which no other material has yet to provide. The natural polymer family contains polymers with many derivates able group a broad variety of molecular mass, different chemical formulas, minimal toxicity, biodegradability, along with substantial stability, making it very appealing for drug delivery.In recent decades, numerous natural gums and mucilages have been investigated as macromolecules for prolonged medication delivery and control. The two main elements of any pharmaceutical formulation are the active ingredientaid in the manufacturing of dosage forms and improve their physicochemical properties.Polymers play a crucial role as excipients in every type of dosage form.The ability of polymers to influence the release of the drug should be stable, safe to use, and economically compatible etc. They can be categorized generally divided into three categories: synthetic, semi-synthetic, and natural, in oral drug delivery systems, natural polymers are generally used as stabilizing agentsprotective, taste-mapping, and rate-controlling agents. Certain polymers are utilised to provide consistent drug delivery, lower dosage frequency, and boostthe efficacy of the drug by targeting the specific area of action. Natural polymers are increasingly used by manufacturers due to the numerous short comings in the drug release as well as toxic effects of synthetic polymers. As they are polysaccharides, natural polymers do not have adverse side effects and are biocompatible. There are several applications for natural polymers in pharmacy. They find larger applications when compared to synthetic polymers, as they have common applications in food and cosmetology industries.

Key Words: Polymers, toxicity, biodegradability, macromolecules, polysaccharides,

Introduction

Every molecule is made up of an incredibly vast number of distinct structural elementspolymers are units that are connected in an organized manner through covalent bonds, high molecular weight massive compounds known as macromolecules that are produced by the combination of a significant quantity of tiny molecules known as building blocks the procedure through which building blocks are theprocess of joining together to form a polymer is known as polymerization. The term "polymer" is a term that originates from the Greek word "poly," which translates to "many" and the Greek term "meros" meaning "parts or units of high molecular mass." A chemical reaction known as polymerization occurs when two or more substances join forces, either with or without the addition of heat, water, or other solventscreate a high molecular weight molecule. [1] The final product is referred to as a polymer, and the raw material used to create the polymers is known as a monomer.A polymer is a large molecule, also known as a macromolecule, composed of repeating structural units. Covalent bonds are typically employed to connect these subunits. Overall, polymers can be classified into three types: natural, synthetic, and semi-synthetic.Componentswith high molecular weights that come from natural sources, like plants, microbes, and animals, are known as natural polymers.Natural polymers remain favored compared to synthetic and semi-synthetic alternatives primarily due to their cost-effectiveness, availability, capacity for various chemical transformations, and potential for biodegradability and compatibility based on their origin. Natural Polymers find extensive application in the food, cosmetic, and pharmaceutical sectors.They preferred materials for drug delivery are natural polymers because they are biogenic and have biological characteristics like cell reorganization and interaction, enzymatic degradability, extra cellular matrix similarity, and chemical flexibility. Organic polymers are generally present in nature through sources like proteins, cellulose, starch, and resins found in plants and animals.Unquestionably, one factor contributing to the increased interest in natural polymers is their easy accessibility and abundance in renewable natural sources.In nature, polysaccharides are abundant and easily obtained from an assortment ofsources, encompassing microorganisms (such as dextran and xanthan gum), botanical sources (like pectin, guar gum, and mannan), animal derivatives (including chitosan and chondroitin), and algal substances (e.g., alginates) through the use of recombinant DNA methods. Among the many advantageous characteristics of monosaccharide polymers are their high stability, nontoxicity, the properties of hydrophilicity, biodegradability, gel-forming capacity, and ease of chemical alteration are significant.[2] Plant polysaccharides exhibit a wide variety in their structural makeup, which is associated with specific plants and the different plant parts they come from, such as leaves, seeds, roots, and tubers. Two unique structural features can help elucidate the complexity and variety of polysaccharides: Firstly, monosaccharides can be linked in multiple configurations, such as α- or β-forms; secondly, due to their branching side chains, nature's polymer can be subdivided.[3] There are three primary categories into which natural polymers fall Origin of plants, microbes and animals.

Classification of Polymers



Plant-Based Polysaccharides

Cellulose

Composition

It is an organic polymer with the formula (C6H10O5) n3 composed of a straighta series of several hundred to over ten thousand β (1→4) connected D-glucose units. The cell wall mainly consists of plant cellulose, hemicelluloses, and pectin. [4]

Application

The pharmaceutical industry primarily uses microcrystalline cellulose as asequence of several hundred to more than ten thousand β (1→4) linked D-glucose units forms the structure.[5] The primary components of the cell wall include plant cellulose, hemicelluloses, and pectin. [6,7,8] Cellulose acetate fibers are utilized in dressings for wounds. [9,10]

Starch

All plants rely on this polymer as their food source. D-glucose is the monomer of starch. Glycosidic linkage is the process by which numerous D-glucose units are linked together to create a starch polymer. This polymer is primarily sourced from grains such as rice (Oryza sativa), corn (Zea mays), and wheat (Triticum aestivum). Additionally, it can be extracted from tropical root vegetables. [11] Its main functions include serving as a binder, disintegrant, drug delivery enhancer, and coating agent.in the pharmaceutical industry.Acetylation significantly reduces the swelling and enzymatic breakdown of starch. There have been reports of controlled drug delivery systems based on starch-acetate (SA). [12] According to these researchers,acetylated potato starch significantly slows down drug release when compared to natural potato starch. It has been studied to coat tablets with amylose-rich maize starch. [13]

Acacia

The dried gummy material called "Indian gum" is takenfrom the stem and branches of the Leguminoseae species Acacia arabica. The primary component is arabin, which consists of a blend of calcium, magnesium, and potassium salts derived from Arabic acid. It can be employed in the osmotic drug delivery system, as well as a binder, emulsifier, suspending agent, demulcent, and emollient. [14–15]

Tragacanth Gum

It is the secretion from the Astragalus plant, which features a long, deep root and typically grows close to the ground. It consists of various compounds. The soluble polysaccharide tragacanthin appears to be the active ingredient. Methyl ether groups are present in the main fraction, bassorin (60–70%), whichonly expands in water to create gel-like particles. The exudate also contains protein and cellulose fibers. Emollient, demulcent, emulsifier, suspending agent, and sustained release agent are among its pharmacological uses. [16]

Animal-Based Polysaccharides

Chitin

First discovered in 1884, chitin, which is also referred to as poly (β-(1→4)-N-acetyl-D-glucosamine), is an important natural polysaccharide.(Figure 1) After cellulose, this biopolymer is one of the most prevalent natural polymers and is generated by a large variety of organisms [17]. In its place of origin, chitin exists as structured crystalline microfibrils, which serve as structural components in the cell walls of fungi and yeasts, as well as in the exoskeletons of arthropods. Is frequently added to get rid of pigments and create colorless, pure chitin.Because of differences in the ultrastructure of the original material, all treatment methods must be adjusted for the chitin source (various extraction and pre-treatment processes for chitin will be examined later). To initially obtain high-quality chitin and, after that, partially deacetylated chitosan.[18] When undergoing conformational changes, chitin is sparingly soluble and infusible. One of the main issues with the development of chitin's processing, use, and characterization is the question of its solubility. [19] There are additional uses for chitin when it is converted to chitosan is produced through the process of partial deacetylation under alkaline conditions. It is a random copolymer composed of a fraction (1-DA) of β-(1→4)-D-glucosamine and a molar fraction DA (degree of acetylation) of β-(1→4)-N-acetyl-D-glucosamine. The degree of acetylation in chitosan is described using the molar fraction of N-acetylated units (DA) or the percentage of acetylation (DA%). [20]

Xanthan gum

The plant bacterium Xanthomonas campestrispv. Campestris ferments glucose to produce xanthan gum, a complex microbialexopolysaccharide. It weighs roughly two million molecules [21]. The components of the gum include D-glucosyl, D-mannosyl, and D-glucuronyl acid components are present in a molar ratio of 2:2:1. Additionally, it contains different quantities of pyruvyl and O-acetyl residues [22]. Penta-saccharide subunits make up the acidic polysaccharide gum known as xanthan gum. Tri saccharide side-chains join the penta saccharide components combine to create a cellulose structure. The applications of xanthan gum have been thoroughly researched. The Food and Drug Administration (FDA) has authorized its safe use as a food additive without any limitation on amount. Various fields, such as food, oil extraction, cosmetics, and pharmaceuticals, utilize it extensively [23], have made use of xanthan gum. Its exceptional rheological qualities account for its broad use. It serves as a stabilizer for suspensions and emulsions. Gum produces extremely viscous solutions with pseudoplasmic flow characteristics [24]. There are numerous examples of xanthan being used as a pharmaceutical material in the literature [25,26,27].

Proteins from Vegetal Sources

Wheat Gluten

It is a protein by-product created during the starch manufacturing process. Its molecular weight is at least ten times greater than that of gliadins. Research has shown that it is an excellent agent for film formation.28Gliadin and glutenin are the two primary protein groups found in wheat gluten. Gliadins are low molecular weight, disulfide-bonded protein molecules with a low concentration of charged side groups in amino acids,wheat glutenhas been shown to be an outstanding agent for film formation. [28]

Soy Protein

These include textured soy protein, soy protein isolate, and soy protein concentrates. Because of its useful qualities, which include texturizing and emulsifying, it has been a component of many foods since 1959. [29]

Proteins Derived from Animal Sources

Collagen

Collagen is the primary protein present in the connective tissues of animals. Collagen is most abundant in pig skin, cow hide, and the bones of cattle and pigs.Collagen comes in 27 varieties and is made up of various polypeptides, the majority of which includeflexibility is its glycine content. Collagen films have been usedfor applications in tissue engineering, such as skin replacements, bone alternatives, and synthetic blood vessels and valves. They are additionally utilized in ophthalmology as delivery systems for medications that allow for the gradual release of incorporated drugs. [30,31]

Gelatin

By hydrolyzing nonsoluble Col, gelatin, a naturally occurring polymer, can be produced 33.Gelatin has nearly the same properties as Col because it is a derivative of Col.Gelatin has demonstrated stability, flexibility, and compatibility with human tissues. It can also be altered to serve as a scaffold base34. Gelatin mimics the extracellular matrix by having a similar amino acid composition to Col and contains proline, glycine, and hydroxyproline [32,33,34]. The adherence of cells is caused by the glycine amino acid content of the gelatin35the process of extraction mainly dictates gelatin's shape. However, it is made up of heterogeneous, randomized macromolecular forms with low melting points. [35] The main reason behind the usage of gelatin in the pharmaceutical industry is its ability to be metabolized by human tissue. Its application is always adjustable, and it does not make the body respond immunologically [36]. Pig skin is used to produce gelatin mainly for extraction, and owing to its distinctive properties, gelatin is highly sought after in the global market, reaching around 412.7 kilotons in 2015. Gelatin can be classified into two categories based onthe extraction method: type A and type B. [37] Alkaline extraction is referred to as type B (negatively charged), whereas acid extraction is referred to as type A (positively charged) [38,39]. The isoelectric point and variation produced during extraction improve the gelatin's ability to bind to the charged medicinal substances [40]. Type A and type B gelatins typically have isoelectric points of pH 9 and pH 5, respectively. Gelatin has a wide range of biodegradability and is obtainable from a very inexpensive commercial source [41]. Gelatincan create flawless films, and its characteristics are affected by the temperature at which it dries. This qualifies gelatin for widespread use as a drug delivery agent. Furthermore, despite its low mechanical strength, gelatin is recognized for its ability to act as a barrier against gas and hydrophilicity [42].

Moringa oleifera

The Moringaceae family contains roughly thirteen species of Moringa trees. The most well-known species is Moringa oleifera Lam. (also known as Moringa pterygosperma Gaertn.), but other species merit more investigation into their potential applications [43].The most extensively grown member the only member of the Moringaceae family, Moringa oleifera, is native to the Sub-Himalayan areas of Bangladesh, India, Pakistan, and Afghanistan. This rapidly growing tree is known by various names, including the horseradish tree, drumstick tree, benzolive tree, kelor, marango, mlonge, moonga, and mulangay. Historically, the ancient Romans, Greeks, and Egyptians referred to it as nébéday, saijhan, or sajna, and it is now widely cultivated and has become naturalized in numerous tropical areas. This softwood perennial tree has been utilized for centuries for various traditional industrial and medicinal applications, despite its timber being of low quality. Apart from being cultivated in West, East, and South Africa, Tropical Asia, Latin America, the Caribbean, Florida, and the Pacific Islands, it has become an important crop in countries like Ethiopia, India, the Philippines, and Sudan. Humans have consumed all parts of the Moringa tree throughout history as they are all edible. The oil extracted from moringa seeds (which yield 30–40% by weight), commonly known as Ben oil, is a sweet, non-drying oil that does not spoil. It has been utilized in salads, fine machinery lubrication, as well as in the manufacture of hair care and fragrance products [44]. One of Moringa's most well-known applications in the West is the flocculation of impurities and purification of drinking water using powdered seeds [45, 46, 47].

Pharmacological significance

Analgesic action

Research employing the heated surface and tail submersionmethods has demonstrated an alcoholic extract of the leaves and seeds of Moringa oleiferaexhibits strong analgesic activity [48] and is comparable to a standard medication (Aspirin 25 mg/kg).

Anti-inflammatory properties

Leaf poultice has anti-inflammatory properties and helps reduce glandular swellings. In rats with paw oedema caused by carrageen, the root extract demonstrated strong anti-inflammatory properties [49].

Antipyretic action: -

Using the yeast-induced hyperpyrexia method,the antipyretic effects of seed extracts from ethanol, petroleum ether, solvent ether, and ethyl acetate were assessed. For comparison purposes, paracetamol I.P. at a dosage of 200 mg/kg was used as the reference standard. Seed extracts in ethanol and ethyl acetate demonstrated strong antipyretic properties. Rat activity.

Wound healing properties

To assess the wound healing properties of ethanolic and ethyl acetate extracts of leaves, three different wound models were utilized: excision, incision, and dead space wounds. The extracts dissolved in ointment form at a concentration of 10% w/w demonstrated considerable wound healing effects comparable to those of the standard Vicco turmeric cream from Vicco Laboratories. The presence of phytosterols and phenolic compounds in these extracts plays a role in promoting wound healing [50].

Asthma-relieving effects

A research investigation was carried out to examine the safety and efficacy of Moringa oleifera seed kernels in treating bronchial asthma. The findings demonstrated both a concurrent improvement in respiratory tract functions and a notable reduction in the intensity of asthma symptoms [51].

Antitumor and anticancer activity

Utilising 7, 12-dimethylbenzanthracene (DMBA) as an initiator and 12-O-tetra-decanoyl-phorbol-13-acetate (TPA) as a tumour promoter, several bioactive compounds that were isolated from Moringa oleifera seeds were examined for antitumor promoting activity. In chemical carcinogenesis, niazimicin, a thiocarbamate derived from Moringa oleifera leaves, was discovered to be a strong chemopreventive agent [52]. The seed extracts have also been shown to have an impact on antioxidant parameters, skin papilloma genesis in mice, and hepatic carcinogen metabolising enzymes. When it came to Staphylococcus aureus pyoderma in mice, a seed ointment and neomycin had comparable effects. Niazimicin has been shown to inhibit Epstein-Barr virus activation induced by tumour promoters [53, 54]. It has been reported that every part of the tree can be employed as a stimulant for the heart and circulation.Moringinineis a cardiac stimulant that affects the sympathetic nervous system [55].

Pharmaceutical applications

Gelling agent

A study was carried out to assessthe ability of gum exudates derived from the stems to gel. Mucilage concentrations ranging from 5.5 to 8.5%w/w were used to prepare gels containing diclofenac sodium. At theBetter gel qualities were observed at a concentration of 8%w/w. The formulation's viscosity (8.5% w/w) is 4.6x10^6 cps, and the gum's pH is below 5.77, making it perfect for topical application. [56].

Agent in stasis

A research paper was published that analyzed the gums from tragacanth and Moringa oleifera. Gums from Moringa oleifera and tragacanth were utilized to create zinc oxide suspensions. We analyzed their flow properties, level of flocculation, sedimentation characteristics, and ability to be redispersed. The results indicated that gum tragacanth [57] and Moringa oleifera gum have similar suspending qualities.

Stabilizer

Due to their possible ability to combat food-related microbes, plant phenolics have attracted a lot of attention lately. Stabilising activity was demonstrated by phenolic extract derived from M. oleifera and M. orusindica leaves. The impact of adding phenolic extract derived from M. oleifera and M. leaves was used in this study. The impact of indica on the shelf life of pineapple juice stored at 4.0 °C was investigated by monitoring the variations in titrable acidity and sensory attributes over an eight-week period.Quality and safety of foods can be enhanced by using natural phenolic extracts, according to the results [58].

Conclusion

The biocompatibility, biodegradability, non-toxic nature, and versatility of natural polymers are crucial for creating and formulating drug delivery systems, starch, chitin, xanthan gum, and different proteins, are derived from plant, microbial, and animal sources and have shown promise in boosting drug stability, regulating release rates, and boosting therapeutic efficacy. Particularly noteworthy are the many pharmacological and pharmaceutical uses of Moringa oleifera, including its usefulness as a gelling, suspending, and stabilising agent as well as its analgesic, anti-inflammatory, antipyretic, antitumor, and wound-healing qualities. Natural polymers provide a sustainable, secure, and efficient substitute for synthetic polymers in contemporary pharmaceutical applications, as worries about their effects on the environment and human health continue to grow. Alongside their role in traditional medicine, their versatile properties lay the groundwork for the future creation of innovative drug delivery systems.

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