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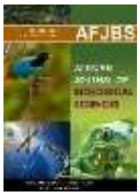

Stability and Utilization of Biopolymer in Formulation Development: A Review

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Abstract
Enzymes supported by biopolymers can be used for continuous biocatalytic reactions because they are more durable, resilient, and recoverable than enzymes in their free form. Due to their natural abundance and availability over the years, all over the world, naturally-derived biopolymers such as alginate, chitosan, cellulose, agarose, guar gum/guaran, agar, carrageenan, gelatin, dextran, xanthan, and pectins, etc. have drawn significant attention. Additionally, they have a variety of adaptable qualities like non-toxicity, biocompatibility, biodegradability, flexibility, renewability, and the presence of multiple reactive sites that provide substantial capabilities with multipurpose applications. For various applications in the medicinal, environmental, pharmaceutical, culinary, and biofuel/energy sectors, intense research has been concentrated on designing enzymes using natural biopolymers as innovative supports or composite materials. To increase the stability and physicochemical characteristics of food emulsions, biopolymers are frequently utilized as emulsifiers in the food business. Materials called biopolymers are created with the aid of many living creatures, including plants. Biopolymers are polymeric compounds made from biological sources. Because of their renewability, abundance, biodegradability, and other specific properties including high adsorption capacities and simplicity of functionalization, they have been studied for a variety of industrial applications. The application of biopolymers in agriculture and green technologies is the main focus, with other elements of biopolymers also being discussed. The use of biopolymers and their improved composites as support carriers for the immobilization of a number of different enzymes to create biocatalysts with desired catalytic activity and stability is highlighted in the review as current advancements.

Keywords: Biopolymer, Renewability, Immobilisation, biodegradability.

INTRODUCTION:

Worldwide, million tonnes of Biopolymers is created each year. Biopolymers are incredibly very stable and can undergo an endless number of cycles of degradation in the biosphere. Water-soluble polymers in wastewater and waste plastics have been identified as great source of synthetic polymer contamination of the environment. Polymers and plastics are used often in our daily lives. However, because to their stability and resistance to degradation, these are accumulating in the environment at a rate of around 8% per weight and 20% per volume of the landfills [1]. An example of a "giant" molecule is a biopolymer, which is composed of distinct building components that are joined to create lengthy chains. Repeat units are more sophisticated building components than monomers, which are simpler building blocks. All organisms naturally produce biopolymers as part of the growth cycles. Also referred as natural polymers as a result. Biopolymers are synthetic materials made by living things. A biodegradable polymer is referred to as a "biopolymer." Biopolymers are older than manmade polymers like plastic and have been existing for billions of years[2]. Cells create them through intricate metabolic processes. Applications for cellulose and starch-based materials are the most fascinating. Though attention is being drawn to more complex hydrocarbon polymers produced by bacteria and fungus, particularly polysaccharides such as xanthan, curdlan, lectin, chitin, chitosan & hyaluronic acid [2]. The importance of biodegradable polymers is rising, and current research efforts are concentrated on creating newer biodegradable polymers. Numerous biodegradable polymers have been created artificially or arise spontaneously during the growth cycles of all creatures. For instance, several enzymes and microbes that can break them down have been discovered. Several kinds of biodegradable polymers have been proposed based on the progress of the synthesis[3].

Biopolymers are biodegradable materials made from biological things. Biopolymers are older than manmade polymers like plastic and have been existing for billions of years. These polymers play an important role in nature. They are incredibly helpful for tasks including cellular building, genetic information transmission, and energy storage. Sugar-based polymers, like polylactide, naturally break down in the body without posing any risks, which makes them useful in medicine. Starch-based biopolymers can be utilized to make conventional plastic through extrusion and injection moulding techniques. Mats are made using biopolymers that are synthetic polymers. As packaging materials, cellophane and other cellulose-based biopolymers are used. The Classification of Biopolymers is highlighted here. There seem to be 4 categories total, the first 3 of which are made from sustainable sources. -

- Biomass-derived polymers, such as those produced from agricultural sources (e.g.- cellulose).
- Polymers produced by microorganisms, such as polyhydroxyalkanoates.
- Polymers created conventionally and chemically whose monomers come from agricultural resources.
- Polymers whose monomers are produced chemically in a typical manner, such as polycaprolactones. **[4-7]**

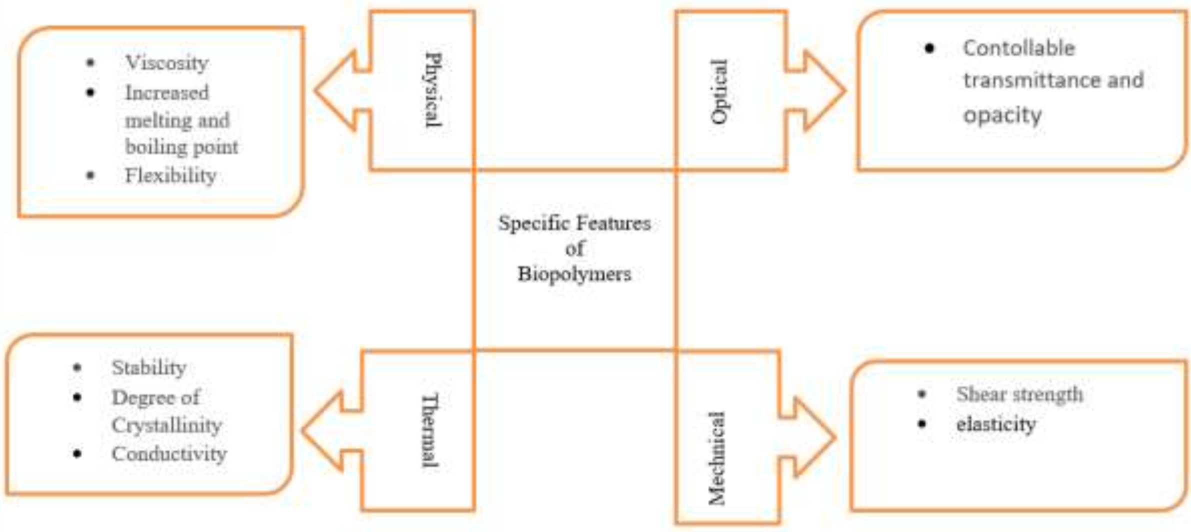

Figure 1 Features of biopolymers

Biopolymers, also known as biologically degradable polymers, are produced by living things[8-12]. offer potential alternatives to synthetic plastics in light of growing environmental sustainability concerns[13]. Biopolymers are biodegradable because of their structural backbone, which is composed of atoms of carbon, oxygen, and nitrogen. After biodegradation converts these materials into carbon dioxide, water, humic matter (organic macromolecular material), biomass, and other natural components, they are naturally recycled through biological processes. Diverse biodegradable polymers have different classification systems based on their sources, processes, and methods of production[14-18] is presented in Figure 1 shows the features of Biopolymers. Medical community microorganisms, and biotechnological, medical, and petrochemical products are the three main divisions of biopolymers. In biomass products, biopolymers come in a variety of forms, including polysaccharides (celluloses, starches, gums, and chitosan, alginates, among others)[19], proteins of both animal and plant origin (gelatine), and zein, wheat gluten, and soya [20,21]. Plus lipids (beeswax, free fatty acids carnauba wax) [22,23]. Algae, agricultural waste, and other natural sources of plants, microbes, and animals can all be used to extract biopolymers [24]. Biopolymers can be found in a variety of agricultural products, such as corn, potatoes, bananas, tapioca, sweet potatoes, wheat, rice, wool, and barley[25, 26], whereas animal sources include cattle, pigs, and other items. The origins of agricultural waste include things like apple pomace, pineapple tomato pomace, orange, wheat straw, lemon peels, rice husks, crops, timber, and green trash, whereas marine sources include things like sponges, corals, fish, lobsters, and shrimp. Stretchy, squishy, gel-like biomaterials created from these substances are defined as having both solid and fluid qualities. It is well recognized that biopolymers, which constantly change in response to both external and internal stimuli, can function as intelligent and adaptable materials even in living creatures[27,28,39].

Currently, the manufactured design of biopolymers with mathematical model optimization shows benefits as they improve the physical, thermal, chemical, and mechanical characteristics to increase resistance in moist, chilly, and warm storage conditions, as well as for applications requiring some specific features. [30,31,32]. However, because polysaccharides have better qualities than other categories of biopolymers, like lipids or proteins, significant research performed on the types and uses of the wide range of biopolymers. The review's emphasis is on the stability and application of biopolymers for them to be employed successfully outside of the pharmaceutical business. Here we further discuss the various structures of alginate, starch, agar, chitosan & cellulose in particular, mentioning their qualities and behaviors which further makes them favorable candidates to be employed in product distribution and that provide advantages over chemically generated polymers. There are many restrictions and difficulties in the production of biopolymers, such as the encapsulating process, controlled release for embedded pharmaceuticals, shelf life, protection, viability in living strains, and the release rate for various GI fluid pH levels. Biopolymer composites can be made using a variety of techniques, including electrospinning, extrusion, grafting, moulding of different sorts, solvent casting, intercalation, melt mixing, filament winding, laser printing, and phase separation film stacking. Despite the fact that there has been a lot of study on the usage of numerous biopolymers, the majority of it is based on polysaccharides because of their superior qualities when compared to other categories, such as lipids or proteins. Excipient production has several effects on formulation development and the medication delivery mechanism, it has lately become recognized as a crucial field for research in pharmaceutical drug delivery. Researchers interested in controlled delivery have been interested in polymeric drug delivery systems due to its superior drug loading and releasing characteristics.[33,34,35]

1. Conventional Synthetic Materials vs Biopolymers:

There have already been various studies on the creation of biopolymer-based sustainable packaging materials. Despite significant developments, there is still a great deal of dispute on economic, environmental, and packaging performance issues [36]. Living creatures' morphology, cellularity, and dry matter are all significantly influenced by polymers. The retention and expression of genetic material, reaction catalysis [37], the detection of energy or other nutrients, defense against other cell attacks, carbon storage, and negotiating adherence to organisms' surfaces are all significant aspects of the life cycles of these biopolymers. Biodegradability [38, 39], sustainability [41], antibacterial activity [44], biocompatibility [40], bio resorbability [42], flexibility [43], and stability are important properties of biopolymers. They are less toxic [45, 46], easier to extract, non-immunogenic [47], non-carcinogenic, carbon-neutral, and non-thrombogenic. The type of material which is used for the structural matrix (charge that is distributed, conformation, and molecular mass), the environment in which the films are developed (pH, concentration, solvent, temperature, among others), and the type and concentrations of the additives (antimicrobials, cross-linking agents, plasticizers, antioxidants, and so forth) all have a direct impact on these properties [48]. Until recently, typical synthetic materials were used in almost every area of our life, including food and drink, clothing, baby toys, common household items, and biomedical applications such as surgical instruments, medicine delivery systems, cosmetics, and personal care items. These materials may pose health concerns, particularly to developing youngsters and pregnant women, according to some research. A group of polymeric molecules known as hormonally active substances in this context has been linked to serious health issues like cancer, congenital disability, with other disorders. Additionally, because chemically produced compounds are used in traditional synthesis and have detrimental effects on both human health and the environment, people are becoming more aware of their effects. The traditions of today are quite refined and informed [49]. Biopolymers are complex molecular assemblies with exact 3D arrangements and structures, in contrast to regular manufactured materials, which have a more simple and random structure [50]. In terms of composition and chemical makeup, biopolymers resemble macromolecules found in the extracellular environment quite closely [51]. Due to their extraordinary hydrophilicity, sustainability, low to no toxicity, and biocompatibility, the two types of materials can be distinguished by a number of factors, which all is listed below (Table 1).

Biopolymers have many benefits over synthetic polymers. Additionally, changes in its biodegradation rate due to chemicals can have a substantial impact on its shape [52], which is also a crucial element in the creation of novel applications for the food, pharmaceutical, and biomedical industries. Contrarily, synthetic polymers are more useful since they are more affordable and have better thermal and mechanical properties as compared with biopolymers. Many applications of biopolymers has combined them with other synthetic polymers (such as polyethylene or polyvinyl).

Table 1. Characteristics behavior of synthetic polymers vs Biopolymer.

Characteristic of Materials	Biopolymers	Synthetic Polymers	References
Sustainability and biodegradability	YES	NO or slow	[49,50]
Structure	Defined	Stochastic	[48]
Chemical backbone structure	Carbon, oxygen, nitrogen	Mostly carbon	[48]
Dispersity	Unity	˃1	[51]
Chemical and physical resistance	Less	High	[52]
Toxicity	Less	High	[41]
Thermal stability	Less	High	[52]
Mechanical properties	Less	High	[53]
Sustainability	High	Less	[52,53]
Availability	High	Decrease	[54,55]
Cost	High (depends on the type)	Less	[56]

The below figure shows the major classification of biopolymers: in which is Proteins, Polysaccharides, Special Polymers, and Polyphenols that is further pre-classified as[57]:

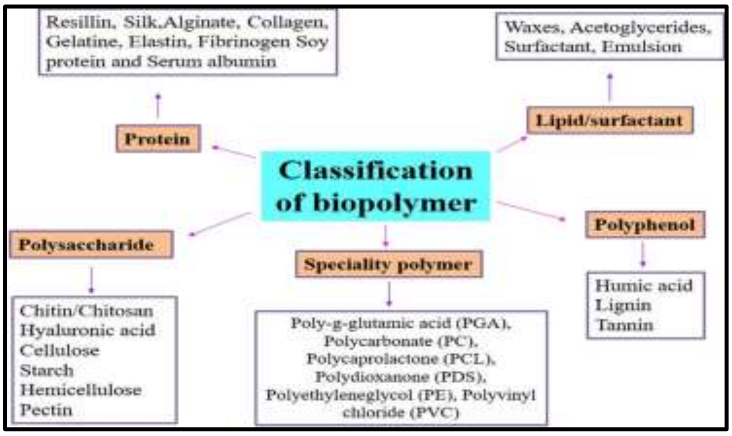

Fig 2: Shows major classification of biopolymer

2. Synthesis & Function biopolymers

Living beings are capable of producing a wide range of polymers, and in the majority of species, these biopolymers account for the vast bulk of the dry matter in cells. Bio-based polymer functions are frequently as diverse as cell shapes and are essential for cells. [58,59]. Such biopolymers carry out a number of essential tasks for living things, including –

- Genetic information preservation and expression.
- Catalysis reactions, energy, carbon or other nutrient storage.
- Protecting and defending against attacks from other cells, dangerous environmental variables, and biotic and abiotic factor sensing.
- Environment and other species are involved in the interaction.

• Among other things, mediating adherence to non-living or surfaces of other creatures.

All biomaterials are created by enzymatic processes that take place in the cytoplasm, distinct cell compartments or organelles, the cytoplasmic membrane or cell wall components, the cell surface, or even extracellularly. A biopolymer's synthesis could start in one area of a cell and progress to another as it happens. [60,61]

3. Biopolymer Production

Biopolymers can be produced using a variety of techniques to make them suitable for a range of uses [62] :-

- The origins of agar and alginates include various brown algae, sometimes known as seaweeds, or red algae of the species Gelidium.
- From very natural sources, only a few biopolymers have been extracted. Hyaluronic acid, which is taken from newborns' umbilical cords, is one such exception.
- Another method for creating biodegradable polymers is in vitro synthesis, which uses isolated enzymes in cell-free environments. One example is the PCR reaction, which is used as heat-stable DNA polymerases to create mono disperse specified DNA components. Another illustration is dextran, which may be manufactured on a large scale utilising isolated dextran sucrose.

Biopolymers produced through fermentation, like polysaccharides, are employed in industry. Production of biopolymers by biotechnological methods can occur either intracellularly or extracellularly. Due to the shortcomings of the upstream and downstream processes for obtaining pure biopolymers, this has a number of grave repercussions.

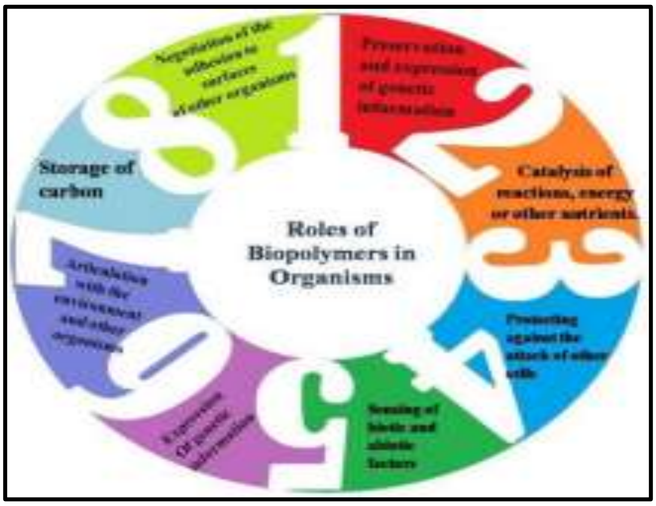

Fig 3: Biological role of biopolymers in living organisms

The availability, compatibility, photodegradation stability, mechanical behaviour, cost, and moisture absorption of biopolymers used in construction are all crucial factors. The two most common biopolymers that are in terms of manufacture and application is poly lactic acid (PLA) and poly hydroxyalkane (PHA).but they are primarily used for short-term applications.[63,64]

Below is the Table showing the Mechanical Properties of biopolymer with Tensile Strength,Tensile Modulus, Elongation at break[65]

Table 3: Biopolymer mechanical properties

Biopolymer	**(MPa)**	**(MPa)**	**Elongation break (%)**
SPC	50	2000	12
PHB	24-40	1700-4000	5-9
PHBV	25	1000	25
PLA	21-60	350-3800	2.5-6
Cellulose acetate	30-40 (flexural strength)	1000-2000	-
Starch	5-6	130-850	31-44

Below attached Figure shows the Dual-Role of biopolymers and osmolytes in the different formulations [66]-

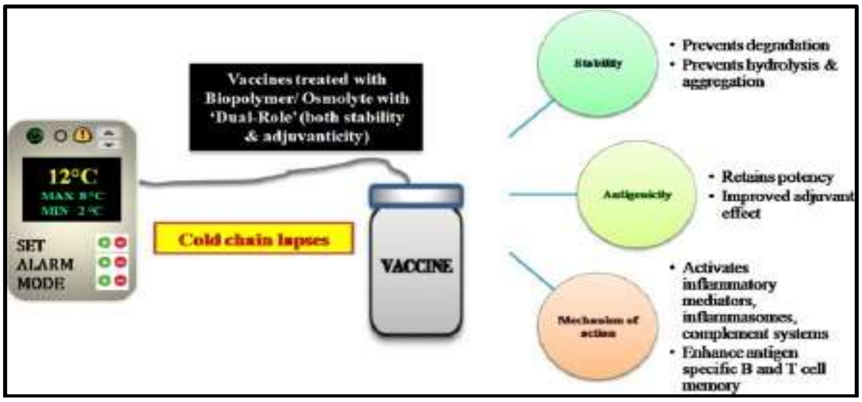

Fig 4: Shows the stability of biopolymer

Over the last three decades, environmental pollution has piqued researcher's enthusiasm for creating fresh health and hygiene goods for people. Large-scale development of bioactive textiles is presented by the application of sustainable biopolymers-based low-impact technologies in the textile industry. The purpose here is to give a broad picture of how proteinic biopolymers have influenced the growth of the textile industry [67,68]. The unconventional nom-textile applications of these biopolymers are also discussed. Proteinic biopolymer extraction methods from renewable natural resources were discussed in order to determine the best extraction method. Biodegradable-based polymers are being employed in the oil field as scale inhibitors for various scale kinds. The idea of scale, methods for handling scale, and the application of synthetic polymer-based scale inhibitors.[68]

4. Biopolymers in Drug Development

The majority of Polymers or polymer matrix composites are materials created naturally during life cycle of animals, green plants, bacteria, and fungus. Examples of biopolymers include starch, bacterial and fungal carbohydrate polymers, and animal protein-based polysaccharides like cellulose. An example of a biopolymer is collagen, gelatin, gelatinized wool, and silk. Biopolymers, especially those derived from carbohydrates, have a wide range of industrial uses. The following list of polysaccharides gives a brief description of each compound's biological makeup, potential uses in medicine, and other factors.[69] Among the most prevalent organic substances in the kingdom of plants are polysaccharides. They are typically made of biopolymers of complicated carbohydrates. Monosaccharide units are divided into three categories based on their basic building blocks: monosaccharide components, linkage type, and anomeric configuration of glycosidic bonds. These monosaccharide units can be joined together in linear or branching chains by glycosidic bonds of variable lengths[70]. All aspects of plant life depend on polysaccharides. Structured Depending on their functions, they are categorised into three major groups: , protective polysaccharides (pectin and hemicelluloses),polymers (cellulose) and reserve polysaccharides (starch). In cell wall & cell wall membrane, poly saccharides may also form glycol conjugates with different proteins and lipids to produce biological macromolecule that are crucial to a number of physiological and biochemical activities. One of the most significant polysaccharides in the industrial world which is starch.[71]

Clear starch also its major derivatives are largely employed in food sector (as an essential human nutrient), pharmaceutical and medical industries and pulp industries & textile industries, and so forth. A ideal raw material, starch is inexpensive, biodegradable, and has a simple chemical structure. [72,73]

Some of the Basic chemical structures of natural biopolymers are shown below[74]:

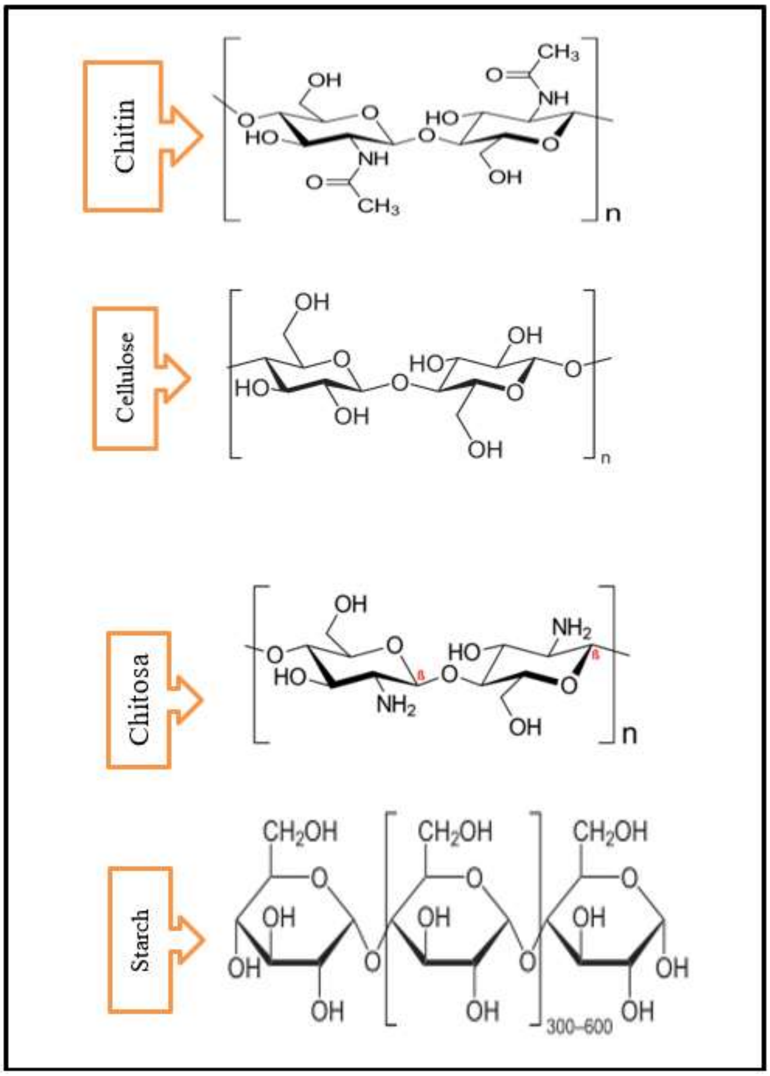

Fig 5: Basic chemical structures of natural biopolymers are shown below[74]:

Table 2: Biopolymers of different origin source with their applications

Biopolymer	Origin Source	Physical appearance	Application	References
Cellulose	Plant tissue (cotton etc) and Bacteria (Acetobacter)	Solvents that are hydrophilic, chemical-free, odourless, and environment-friendly are insoluble in water.	Scaffolds for regenerative medicine, Wound dressings, cellophane films, thickeners, adhesives, wrappers, coatings, ligatures, preservers, dispersion agents, flow controllers, tile sealants, board fixatives, indelible inks, and cosmetics are examples of controlled drug delivery devices.	[79,80,81]
Pectin	Plant cell walls, citrus peels, apple pomace.	Yellowish-white, coarse or fine-powder, odourless, with a mucilaginous flavour, and completely soluble in 20 parts of water.	Gastrointestinal diseases, lead and mercury removal from the lungs and intestines, haemorrhage management, antibacterial action in tablet form, improved coagulation, treatment of overeating, and anti- inflammatory.	[80,82,83]
Carrageenan	Cell wall matrix of red seaweeds.	At normal temperature, large, flexible molecules form helical shapes and solidify.	Antiviral activity, anticoagulant and antithrombotic activity, and textural functioning, especially in dairy products.	[84]
Xylan	Hardwood (eg- Eucalyptus globule etc), almond shell, rice husk, corn cobs.	Highly complicated yellow gummy pentosan.	Low-calorie sweetener, preventative measure, textile printing, paper manufacturing, and medicine delivery system.	[85,86,90]
Guar Gum	Cyamopsis tetragonolobus or Cyamopsis psoraloides.	90% of this granule, which is white to off-white in colour and odourless, dissolves in water.	Disintegrating, binding, thickening, gelling, film-forming, stabilising, emulsifying, bio adhesive, bulk-forming laxative, and non-toxic properties.	[87,91]
Alginate	Brown algae of the Genera:'Nacrocystis, Laminaria, Ascophyllum, Alario, Ecklonia, Eisenia, nercocystis,sargassum,cystoseria,focus	Fibrous powder. White to yellow	diffusion-set gel, Fruit texturization protein ejection, prolonged potato shelf life, enzyme inhibition in bananas, crumbled fish patties, goods made from animal flesh, water-holding properties, and dispersive capabilities.	[88]
Gum Arabic	From Stems, branches (Acacia) Seyal, Acacia Senegal tree.	yellowish white to white, almost without flavour or odour. Dried, gummy.	Fabric, ceramics, photolithography prints, beauty products, pharmaceutical, stabilizer, thickening agent, emulsifier, and manufacturing industries Antioxidant, nephroprotective, and therapy of internal and exterior inflammation.	[89]

The above Table shows the origin source, Physical appearance, and applications of different Biopolymers such as; Gum, Alginate, Gur Gum, Xylan, Carrageenan, Pectin, and Cellulose.

Two criteria for stability are molecular weight and conformation, and a variety of techniques, from simple viscometry measurements to sophisticated analytical ultracentrifuge, multi-angle light scattering, size exclusion chromatography, and precision viscometry measurements, have been found to be useful.[92,93] To improve stability and successfully create high-performance composite materials that can compete with their conventional petrochemical-based polymer counterparts by interfacial bonding with biopolymers, natural fibre modification or functionalization is necessary. Combining various fiber types into a single matrix is another extensively utilised technique for developing composites that results in highly prized hybrid composites.[94,95] Million tonnes of natural fibres are generated each year and used as acceptable raw materials in a variety of industries, including textiles, paper production, packaging, sports equipment, vehicles, and building materials.[96,97] To ensure that neither the chemical nor physical properties of the biopolymer composite change, the heat stability of the components must be understood and monitored. As a result, the thermal activity of the composite is determined by the thermal stability of the natural fibre and biopolymer. It is common practise to evaluate the thermal stability of biopolymer composites utilising DSC, DMTA & TGA.·TGA is used in composite production and fire exposure to analyse the degradation of composite materials at high temperature. While comparing thermal stability over various service range useful deterioration takes place at lower temperatures [98]

5. Future developments and biopolymer composites' Limitations

Biopolymer composites offer several significant disadvantages in addition to their advantages. The range of potential applications for biopolymer composites is constrained by poor thermal decomposition temperature, low moisture resistance, dimensional stability, fire, Ultraviolet, and biological rigidity[99,100]. Another significant barrier to the use due to the poor compatibility of natural fibres and biopolymers, biopolymer composites in highly loaded, interior, and non-structural applications are not recommended[101]. There is a lot of uncertainty regarding the long-term properties of biopolymer composites, including their durability and lifespan prediction [102]. To evaluate the effectiveness of biopolymers composites over their lifespan, new approaches and experimental procedures need be created. Additionally, it should be mentioned that biopolymer composites are developed for industrial production by fibre treatment, plasticizer and biopolymer blending with some filler addition, coating, and sophisticated processing techniques [103].

6. Conclusion

Biopolymers are natural macromolecules produced by animals and plants, making them readily available and renewable resources. Biopolymers' due to biodegradability and tunable properties make them ideal candidates for research and development in many fields. biopolymer-based materials can be easily processed and are frequently biocompatible. The higher surface-to-volume ratio of these biopolymers offers a great potential for macromolecule interaction. They offer encapsulated pharmaceuticals with a regulated release and a protracted residence period at drug absorption sites. From last some decades, there has been an increase in the amount of research done on biodegradable polymers. Because they offer a wider variety of disposal options with less negative effects on the environment, these polymers greatly contribute to sustainable development. To maximise the environmental, social, and economic benefits, it is now necessary to move forward with the creation of biodegradable products. The success of such highly creative items depends on meeting high quality (environmental quality) criteria. Advanced, original, and effective medication delivery systems have previously been developed with the help of biodegradable polymers. They have capacity to deliver the wide variety of bio active substances. Biopolymers are plastics that degrade naturally. These polymers could take the place of an equivalent volume of polymers derived from fossil fuels saves roughly 192 trillion gallons of fossil fuel annually and reducing CO2 emissions by 10 million tonne. Process followed must be cyclic and devoid of biological or chemically imbalances to prevent ecological disruption. Biodegradable polymers have emerged as a major topic of discussion and are regarded scholars in the contemporary world as the most practical substitute for conventional plastic materials. To address environmental concerns, the development of environmentally friendly products for everyday use, as well as the use of biodegradable materials, is accelerating. Natural sources are being used by the medical and pharmaceutical industries to improve because they are cheap, readily available, biodegradable and absorbable, abundant, and biocompatible with modern medical and pharmaceutical specimens. Several active pharmaceutical components and biopolymers originating from various sources are used in the development of the medical and pharmaceutical domains. Different effects of these biopolymers on formulation creation and medication delivery can be observed. Biopolymers have gained popularity because of their diverse compositions, low toxicity, degradability, organic product, stability, renewable nature, and a host of other advantages. High-value businesses like pharmaceuticals and medical find these compounds particularly alluring. This review's objective is to explain how diverse biopolymers can be used in pharmaceutical and medical applications.

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