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A Review on Medicinal Applications of Polysaccharides

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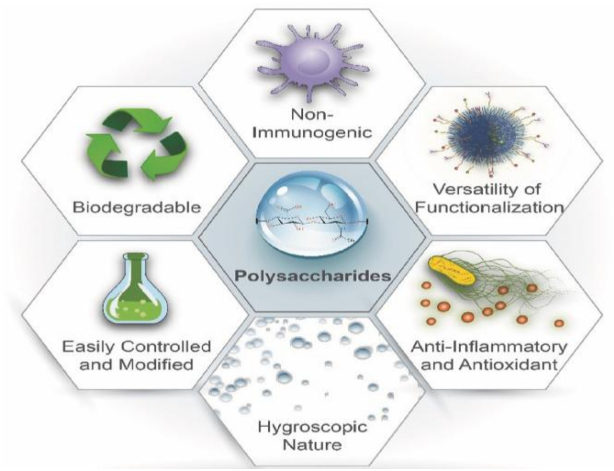
ABSTRACT

Polysaccharides, which are made up of monosaccharide units linked together by glycosidic connections, are the most numerous naturally occurring carbohydrates. They come from plants, algae, and microbes like fungi and bacteria, which are all renewable sources. They're gaining popularity since they have a wide range of biological actions, including anti-tumor, immunomodulatory, antibacterial, antioxidant, anticoagulant, antidiabetic, antiviral, and hypoglycemic, making them one of the most promising biomedical and pharmaceutical options. In this examination, we'll look at some of the most up-to-date polysaccharide applications.



Keywords: Carbohydrates, Polysaccharides, Medicinal Applications, Biological activities.

1. Introduction

Polysaccharides, commonly known as glycans, are common biopolymers found throughout nature [1]. Polysaccharides, along with other biomolecules such as proteins and nucleotides, are vital components of the biological system, performing functions such as cell-cell communication, adhesion, and molecular recognition in the immune system [2]. Polysaccharides, which belong to the third major class of biopolymers (carbohydrates), are important in a variety of physiological processes, including tumor metastasis [3]. They also play important roles in the immune system, blood clotting, fertilization, pathogenesis prevention, and therapeutic efficacy [4]. Natural polysaccharides can be obtained from a variety of sources, including algal origin, e.g., alginate, plant origin, e.g., pectin and gums, microbial origin, e.g., dextran, and animal origin, e.g., chitosan [5], and can be thought of as an essential functional material that plays important roles in a variety of physiological and biological activities, including antioxidant, antitumor, The application of microbial polysaccharides in biotechnology and health sciences has been going on for a long time [7]. Food, energy, wood, paper, textiles, fibers, and oil drilling [9] are just a few of the domains where polysaccharides have been employed as beginning materials to be chemically changed and exploited in different medicinal and non-medical fields [8].

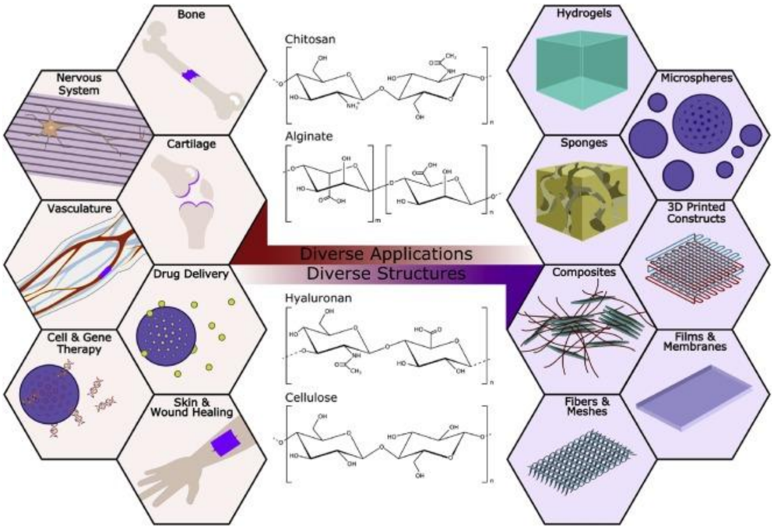


Fig 1: Various Applications of Polysaccharides

2. Applications of Polysaccharides

2.1. Application in Vaccine

When it comes to responding to external exposures such as infectious diseases, inflammatory agents, and even carcinogens, the immune system plays a critical role. Recently, cancer and infectious diseases have become an emerging problem, and pharmaceutical companies are more concerned with the discovery of new safe and effective immune-stimulating alternatives due to drawbacks such as resistance, toxicity, and lack of immune responses of some available drugs. Polysaccharides are one of the best choices in this regard. Polysaccharides derived from traditional Chinese medicine have been shown to activate or regulate T cells and macrophages, improve interleukin activity, increase antibody levels, and regulate the immunological function of the organism [10]. Polysaccharides have also been found to be an essential modulator, since they can boost immunity through a variety of mechanisms, including macrophage, splenocyte, and thymocyte activation [11]. The potential for carbohydrate-based vaccines to become vaccine candidates is being thoroughly investigated. The host immune system can identify tumor-associated carbohydrate antigens and polysaccharides on the surface of pathogenic bacteria [12].which opens a new era in glycobiology and vaccination availability since polysaccharides have a vital role in cell-cell recognition and interaction with the immune system. Many vaccine formulations contain polysaccharides based antigens such as bacterial capsular polysaccharides or tumor-associated carbohydrate antigens which have been used in many vaccines formulations [13]. Since the 80s of the last century, polysaccharides vaccines were available for different infectious diseases like Pneumonia and meningitis. Unfortunately, conventional polysaccharide antigens (mainly high-purified capsular polysaccharides) have disadvantages such as short duration with a poor immunogenic response in infants and young children because of the absence of immunological memory and IgM to IgG class switch. To overcome these shortcomings, new polysaccharides vaccines are conjugated to strongly immunogenic protein carriers like diphtheria and tetanus toxins that induce T cell-dependent response and enhance the immunogenicity through interacting with the immune system [14].

2.2. Biomedical Applications

Polysaccharides have been used in biomedical sectors throughout the last century [15]. Polysaccharides have been evaluated as prospective candidates in various biomedical applications due to a variety of features such as biodegradability, biocompatibility, non-immunogenicity, and increased solubility and stability [16]. Furthermore, due to the abundance of polysaccharide sources and their inexpensive cost, they have been popular in a variety of biological and biotechnological applications [17]. Polysaccharides derived from algae, for example, have been widely used in biomedical applications such as wound treatment, regenerative medicine, and drug delivery control [18]. Another feature of these new developing class of biomaterials is their ability to create hydrogels, such as heparin-loaded hydrogels, which have been effectively employed to distribute bone morphogenetic proteins [19]. The polysaccharide has been shown to increase mechanical properties, which can help synthetic polymers overcome their poor biological performance [20].

2.3. Drugs, Vaccine Delivery and Tissues Engineering

Polysaccharides have recently been widely used as drug carriers, drug delivery building blocks, bioactive materials, and excipients to improve drug delivery. They are also gaining popularity in the domains of tissue engineering [21], cosmetics, and wound healing. Natural polysaccharides' capacity to be molded and changed to achieve specific objectives made them a promising choice for a variety of applications, including medication and vaccine administration. Xanthan gum, gellan gum, and scleroglucan are polysaccharides generated from microorganisms that have been widely researched in drug delivery [22]. By putting the medicine with bioadhesive polysaccharides nanoparticle carriers, the drug's absorption can be enhanced [23]. Pectin, guar gum, amylose, inulin, dextran, chitosan, and chondroitin sulphate are examples of naturally occurring polysaccharides that have been studied for colon-specific drug release and their potential as pharmaceutical excipients [24]. Furthermore, chitin and chitosan are low-immunogenic and tissue compatible polysaccharides that have shown to be beneficial in wound healing, tissue engineering, bone regeneration, and medication and vaccine administration [26]. Chitosan is one of the most widely used biopolymers as a drug and vaccine delivery system in many preparations, owing to its ability to encapsulate a wide range of antigens under mild conditions and without the use of organic solvents, avoiding antigen degradation and denaturation during processing or after loading [27]. Polycations, which are made by reductive amination of primary amines with periodate oxidized polysaccharides, are a new family of nonviral gene delivery vehicles. Cationic polysaccharides are also employed as gene transfection vectors [28]. The hyper-branched polymer is considered a suitable carrier for gene delivery nanoparticles [29]. Hydrogels based on cross-linked polysaccharides are used in essential applications such as medication delivery systems and tissue engineering.

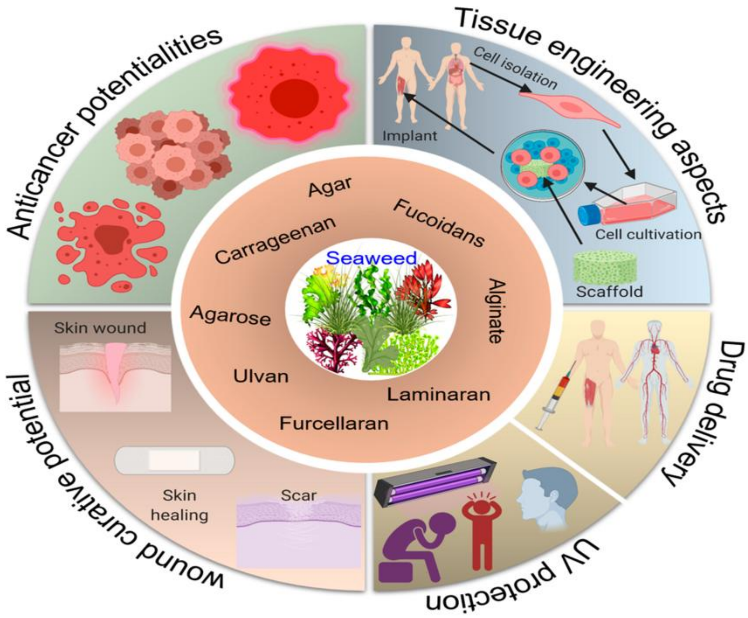


Fig 2: Applications of Polysaccharides in Drugs, Vaccine Delivery and Tissues Engineering

2.4. Antitumor and Immunomodulatory Activities

The tumor is a major health problem, and a leading cause of death worldwide [30]. Antitumor activities can be found in many plants and marine polysaccharides [31]. A wide variety of natural polysaccharides proved to be effective antitumor agents, e.g., lentinan and schizophyllan [32]. It has been indicated that polysaccharide-protein conjugate has antitumor activity and can also enhance the activity of conventional chemotherapeutical drugs [33]. Recently, many researchers have proved the immunosuppressive activity of polysaccharides against tumor growth [34]. Mushrooms are rich sources of many therapeutic agents and have been used for a long time as food and medicinal agents, regardless of the differences in the chemical structures and conjugated parts. It has been established that natural polysaccharides derived from mushrooms have been extensively studied for their potent antitumor and pharmaceutical activities [35]. Examples of polysaccharides from mushrooms include *Ganoderma lucidum* which proved to have potent in vitro immune activation, and antitumor activity on the breast cancer cells [36], and *Lentinus edodes*, which exhibited a marked antitumor effect against subcutaneously transplanted sarcoma. Besides the antitumor activity, mushrooms polysaccharides exhibit a wide range of therapeutic activities and are used in clinical trials to increase the effectiveness of chemotherapeutic agents and minimize their side effects [37]. Algae polysaccharides are also of great importance because they have a diversity of pharmacological activities, including antitumor activity [38].

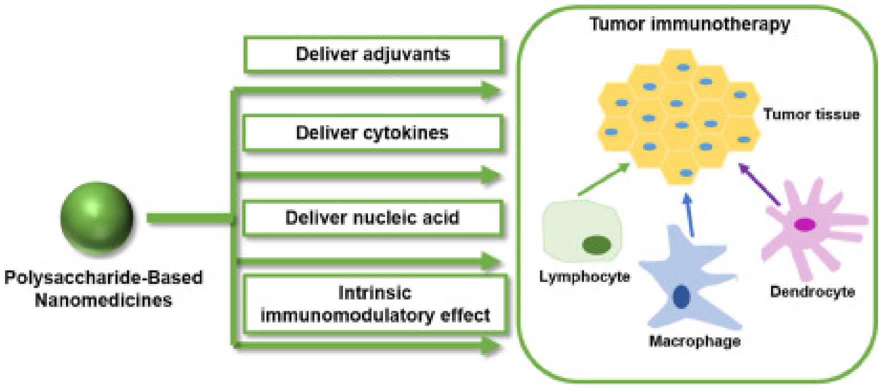


Fig 3: Antitumor Activity of Polysaccahrides

2.5. Antioxidative Applications

Reactive oxygen species (ROS) may cause damages to the human body, they attack different macromolecules such as membrane lipids, proteins, and DNA, leading to many health disorders such as cancer, diabetes mellitus, neurodegenerative and inflammatory diseases with severe tissue injuries. Antioxidative agents are of great benefit in this regard since they can block or reduce the effect of these hazardous agents [39], and improve human health. Antioxidants from scientific resources are bearing many drawbacks like their carcinogenesis and liver damages; for these reasons, an alternative natural substitute will be of great advantage. Polysaccharides derived from plants are promising candidates because they exhibit strong antioxidant activities [40], that could protect the human body against free radicals and decreased the complications of many diseases. Owing to its biological importance, chemical properties of plant polysaccharides have been extensively investigated for their wide range of applications, such as antitumor, immunestimulation, and antioxidant activities [41]. Moreover, the existence of natural antioxidants capable of scavenging these ROS will offer great help in this regard, this is the case with polysaccharides since they possess antioxidant activity which has been proved to protect and inhibit cardio and cerebrovascular disease caused by free radicals [42]. Many of these natural polysaccharides, such as *Hyriopsis cumingii,* were evaluated for their antioxidative ability against different types of free radicals [43]. Another example is the polysaccharides derived from the traditional Chinese medicinal herb *Astragalus,* which showed potent antioxidant and antitumor activity [44]. Sulfated polysaccharides derived from seaweed and red alga also possess many activities like anticoagulant/antithrombotic, antiviral, immuno-inflammatory, antilipidemic, and antioxidant activities [45]. Antioxidative properties of polysaccharides are well proved, different kinds of polysaccharides have been used for this purpose include seaweed polysaccharides, e.g., sulfated polysaccharides, plant polysaccharides, e.g., arabinogalactan, galactomannan, and pectic polysaccharides, and mushroom polysaccharides, e.g., β-glucans and glycoproteins [46].

2.6. Other Applications

2.6.1. Anti‑inflammatory Activity

Natural polysaccharides have been widely used in nanomaterials for controlling inflammatory pathologies [47], and were experimentally tested for their anti-inflammatory activities [48]. The anti-inflammatory effect of polysaccharides could be through one of these mechanisms, e.g., the anti-inflammatory activity of TCM polysaccharides is mainly due to the inhibition of the expression of the chemotactic factor and adherence factor, as well as the activities of key enzymes in the inflammation process [49]. Other polysaccharides have an inhibitory effect on inflammatory-related mediators such as cytokines (IL-1b, IL-6, TNF-a) and NO (nitric oxide), and decreased the infiltration of inflammatory cells [50], sulfated polysaccharides derived from algae exhibit their anti-inflammatory effect through interfering with the migration of leukocytes to sites of inflammation [51]. Hypoglycemic and Hypocholesterolemic Activities Since the 1980s of the last century, polysaccharides have been extensively investigated in clinical trials for their hypoglycemic and hypocholesterolemic effect, *Ganoderma atrum* polysaccharide has potential for the treatment of hyperglycemia, hyperlipidemia, hyperinsulinemia, and insulin resistance, as well as a protective effect on kidney injury in the second type diabetes [52]. Natural polysaccharides can be used as nanocarriers for proteins that enhance the stability of loaded proteins and prolong their therapeutic effect, e.g., the bioavailability of orally administrated Insulin- loaded dextran-chitosan nanoparticulate polyelectrolyte complex is increased with extended hypoglycemic effect [53]. Other examples of polysaccharides with hypoglycemic and hypocholesterolemic effects include sulfated polysaccharides extract from *Bullacta exarate*, chitosan, and Kefiran. Traditional Chinese medicine derived from *Tremella fuciformis* Mushrooms polysaccharides showed a significant dose-dependent hypoglycemic effect and improved insulin sensitivity by regulating PPAR-γ-mediated lipid metabolism when it was administered to mice [54].

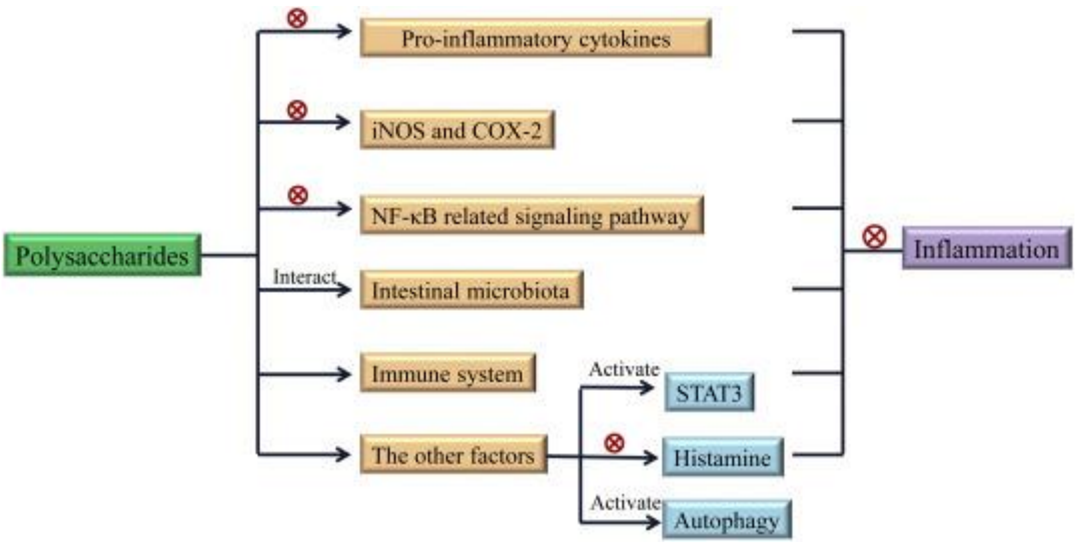


Fig 4: Anti‑inflammatory Activity of Polysaccharides

2.6.2. Anticoagulant Activity

Among the diversity of polysaccharides properties, anticoagulant activity was extensively studied, unfractionated and low molecular weight heparins are sulfated polysaccharides that used as anticoagulant drugs, but unfortunately, they have side effects like bleeding and thrombocytopenia [55]. It was proved that polysaccharides, specially sulfated polysaccharides, have many biological activities like anti-tumor, antioxidant, and anticoagulant activities [56]. The high content of sulfate is a key factor in the anticoagulant activity of these sulfated polysaccharides [57]. Natural polysaccharides obtained from different marine sources like shellfish (shrimp, crab, squilla, lobster, and crayfish, etc.), marine macroalgae (seaweeds), marine fungi, microalgae, and corals [58], and plant-derived polysaccharide, e.g., pectin, could be considered as potential anticoagulant agents [59].

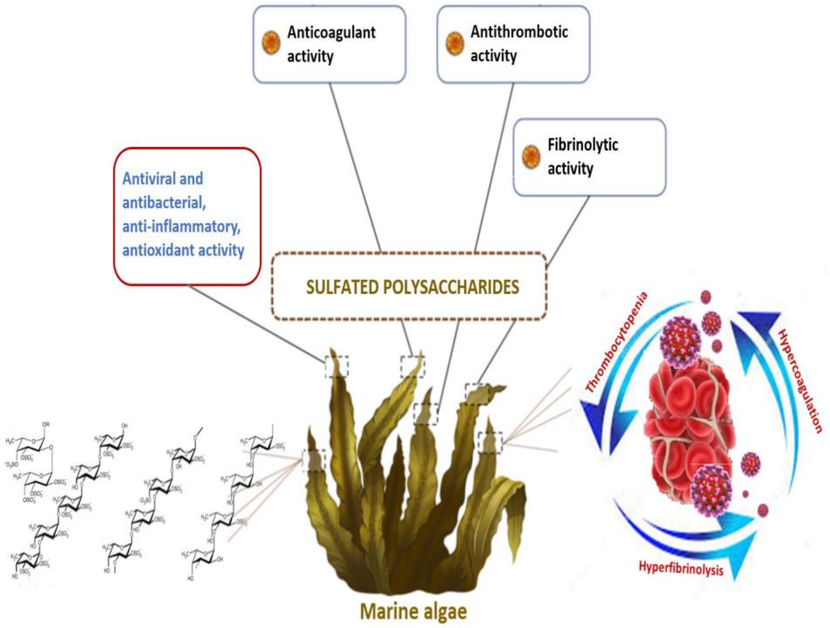


Fig 5: Anticoagulant Activity of Polysacahrides

2.6.3. Antiviral Activity

The antiviral activity of polysaccharides was proved since the 50s of the last century, it has been established that sulfated polysaccharides from seaweeds have an inhibitory effect against the replication of enveloped viruses including herpes simplex virus (HSV), human immunodeficiency virus (HIV), human cytomegalovirus, dengue virus, and respiratory syncytial virus [60]. Different microalgae species can produce sulfated exopolysaccharides which play an important biological role as antiviral agents [61]. Polysaccharides derived from Chinese traditional medicine have also been used for a long time as antiviral agents since they can improve and strengthen the immune system through activating macrophagocytes to promote their phagocytic ability and induce the secretion of IL-2, IFN-γ, and antibodies [62]. Microalgae polysaccharides also possess a lot of biological properties, such as antioxidant, antibacterial, and antiviral activity [63].

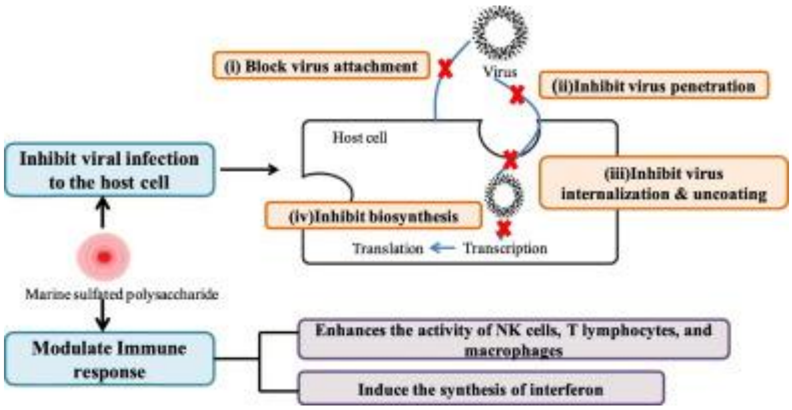


Fig 6: Antiviral Activity of Polysacahrides

2.7. Polysaccharides in Corona Virus Disease (COVID‑19)

Undoubtedly, the Covid-19 outbreak has become a major health challenge, especially with continuous searching for safe and effective therapeutic agents and vaccines [64]. Polysaccharides with their broad antiviral activity are considered one of the promising candidates in COVID-19 prevention and control from both sides as a therapeutic agent and carriers. GAGs, Traditional Chinese Medicine, and marine polysaccharides have shown potent anti-coronavirus activity. The entry of the virus to the host cell can be interfered with by sulfated polysaccharides by blocking the positive charge of the pathogen surface receptors. The cationically modified chitosan shows significant inhibition against the human coronavirus HCoV-229E, HCoV-OC43, HCoV-NL63, and HCoV-HKU1, which indicate its inhibitory effect against low-pathogenic human coronaviruses. Traditional Chinese herbal medicine contains potential anti-SARS-CoV-2 active compounds, especially Hedysarummultijugummaxim, coptidis rhizoma, and forsythiae fructus [65]. In vitro experiments show that sulfated polysaccharides bind tightly to the S-protein of SARS-CoV-2, this interfering of protein binding to the heparan sulfate co-receptors has a potent inhibitory effect on viral infection [66]. Polysaccharides from different origins have also shown anti-pulmonary fibrosis activities, which render them an alternative agent for preventing or treating pulmonary fibrosis in COVID-19 patients [67]. One of the most complications of COVID-19 is the susceptibility of the infected patients to the bacterial secondary infection, polysaccharides can play a major role in this regard such as *Glycyrrhiza* polysaccharide displayed antimicrobial activity, inhibiting the growth of *B. cereus*, *Staphylococcus aureus*, *E. Aerogens*, and *Escherichia coli*. The purified Chinese yam polysaccharide showed inhibitory activity against *E. coli*, with a minimum inhibitory concentration (MIC) of 2.5 mg/mL. A recent study found that *Poria cocos* polysaccharide could inhibit the growth of *S. aureus* and *E. coli*. *Asarum* polysaccharides in the Lung Cleansing and Detoxifying Decoction play an important role in relieving cough symptoms, which are prevalent in COVID-19 patients [68].

3. Conclusion

Polysaccharides are the most available natural biopolymers with diverse physical and chemical properties that render them a promising candidate in many biomedical areas. Polysaccharides have several advantages over other synthetic polymers; they are safe, economical, stable, hydrophilic, biocompatible, biodegradable, and prone to chemical modifications and tailoring for specific purposes in a wide variety of applications, such as preparation of pharmaceutical materials, drug release agent and plasma substitutes. Polysaccharides can be applied biologically in many different therapeutic fields like immune-regulatory, anti-tumor, anti-virus, anti-inflammatory, anti-oxidative, and hypoglycemic activity. Over the past decades, polysaccharides have attracted extensive attention and can be considered as one of the most potent alternatives to conventional therapy. Even though carbohydrate-based pharmaceuticals are proved effective in different areas, they are not gaining as much interest as proteins or nucleic acid-based drugs. At the end of this review, we recommend further studies and investigation because many discoveries still lie ahead and many biological activities of a variety of polysaccharides are still not fully understood. Extensive investigation and elucidation of the structural activity relationship of polysaccharides are crucial to give more insight into the exact mechanisms of their biological activities and fully explore their future applications.

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