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Isolation and Structural Analysis of Water-Soluble Polysaccharides for Antiviral Drug Delivery: A Review

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Abstract

SARS-CoV-2 is a new strain of coronavirus that ravaged humanity in the last three years, requiring new and effective drug delivery systems to deliver the novel antivirals. Water-soluble polysaccharides are considered to be important in different pharmaceutical activities especially in drug delivery. The isolation, purification and structural properties directly affect their usage. With recent advantages in drug delivery, excipients and adjuvants fulfill specific functions where they directly or indirectly influence the rate or extent of drug delivery. Recent trends towards use of natural water-soluble polysaccharides as excipients demand the replacement of synthetic additive due to the advantages of being chemically inert, nontoxic in nature, low cost, biodegradable, and wide availability. This review not only provides ideas for optimization of the isolation, purification and structural analysis of natural water-soluble polysaccharides but also provides a theoretical basis for their uses as an adjuvant in different antiviral drug delivery.

Key words: Water-soluble polysaccharides, Isolation, Purification, Physicochemical properties, Methylation, Antiviral drug delivery

The global pandemic of COVID 19 produced by the virus SARS-CoV-2 has triggered a catastrophic public health disaster around the world. As a result, new antiviral active pharmaceutical components as well as safe excipients are needed for targeted drug delivery formulations to battle this global pandemic [1]. Polysaccharides are biopolymers comprised of long-chain monosaccharides linked by glycosidic bonds, can be good option for its usage as excipients. Structurally these biopolymers are generally comprised of branched or linear side chains with molecular weights ranging between thousands to millions Dalton. Polysaccharides could be sourced from diverse sources including most plants, animals, microorganisms and marine organisms as well as can be manufactured synthetically. Some of the functions of polysaccharides include nutrient carrier, soil conditioners, tissue engineering, drug delivery, wound dressing, antibacterial material, food packaging. So, more attention needed to be paid to the research of polysaccharides [2].

Recently, various research has contributed to the progress in exploitation of the pharmacological properties and drug delivery potentials for natural biopolymers, as well as polysaccharides-based biomaterials for various applications such as regenerative medicine and tissue engineering. Nonetheless, polysaccharides are still an enigmatic material where more explorations are required. Firstly, the structure–activity relationship is still unexplored and nextly, detection and quantification of polysaccharides are yet to be standardized. Although in last two decades, there has been a significant development in synthesis of polysaccharides but further researches have been limited by their complexity in structure and also the synthetic process challenging and time consuming due to the lack of commercial instruments like automated synthesizers and difficulties in controlling the stereochemical properties of the glycosidic linkages in the long chain of polysaccharides [3]. Compared to synthetic polymers, the extraction and purification methods of natural polysaccharides are still preferred to obtaining polysaccharides. Over the years, certain successful polysaccharide separation and purification methods have been outlined. Moreover, these methods act as pre-conditions for structural characterization and study of the structure–activity relationship [4]. This study outlines the comprehensive methods of isolation, purification and structural analysis of various natural polysaccharides and their potential usage in antiviral drug delivery.

Isolation of polysaccharide

Various methods for extracting and isolating water-soluble polysaccharides from various sources have been published in recent decades. Table 1 summarizes the extraction methods of various selected sources that can preserve polysaccharide's intrinsic features [5]. In general, water is the most common solvent used extraction and isolation of polysaccharides, due to their higher solubility in hot water and receive minimum damage in it. The usual practice is to heat the plant parts for 2-6 h and if it is found that the extract has low viscosity it can be easily isolated by filtration while the viscous extract was isolated by centrifugation usually in the range of 3500-8000 RPM [6]. Carlotto et al, found the optimum

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condition for extraction of polysaccharide from *Handroanthus heptaphyllus* bark. The polysaccharide was extracted in 500 ml hot water for 6h and centrifuged at 8000 rpm. The yield was found to be at 1.43% w/w [7]. However, this method of extraction had some disadvantages like higher time consumption, inconsistent yield and possibilities of polysaccharide degradation. So, in order to combat these problems, other methods such as ultrasonic, microwave assisted and infrared methods are also used, which work by promoting breakdown of cells. For example, Wang et al, demonstrated a polysaccharide extracted from *Artemisia selengensis* using ultrasound extraction. The optimum power used was 150-200 W with time of 15-20 min. Under this condition the yield increased to 8.9% w/w [8]. Microwave assisted extraction has also been explored to maximize the yield of polysaccharide from Yupingfeng. The most favorable conditions were found to be the following: microwave power 560 W; extraction time 5 min. A considerable improvement of the extraction yield has been realized. An extraction yield of 21.33% w/w was achieved using an extraction temperature of 75°C, and an extraction time of 2 h [9]. Farhadi et al., reported a low moisture polysaccharide from balangu shirazu found Iran with a short aqueous extraction process of 40 min. The polysaccharide finds its usage in transdermal antiviral drug delivery saving from stratum corneum [11]. Various other examples of traditional aqueous isolation performed between 2-6h showed yield of 2.6-6% which was much lower as compared some modern methods like infrared extraction of *Bletilla striata* which had an yield of 43.95% which can find its usage in microneedle drug delivery specific to virus [11-14, 17]. In summary, we could find that each of these assisted extraction methods could contribute to shorten the processing time, reduce solvent consumption, and further decrease the economic cost while improving the extraction efficiency of polysaccharides as well as they can be used novel controlled release drug delivery of antiviral drugs [10].

Table 1 A summary of the extraction of polysaccharides from different sources

Source of polysaccharide	Time	Temp. (°C)	Yield (%)	References
		Aqueous extraction		
Handroanthus heptaphyllus	6h	100	1.43	[7]
Lallematia royelana	40 min	60	8.2	[11]
Dioscorea alata	2h	80	5.62	[12]
Dioscorea opposita	3h	60	6.0	[13]
Calocybe indica	6h	50	2.7	[14]
		Ultra sound extraction		
Artemisia selengensis	15min	Room temperature	8.9	[8]
Agaricus bisporus	15min	Room temperature	14.7	[15]
		Microwave extraction		
Yupinpeng	5 min	75	21.33	[9]
Mullberry leaf	10 min	50	9.44	[16]
		Infrared extraction		
Bletilla striata	150 min	75	43.95	[17]

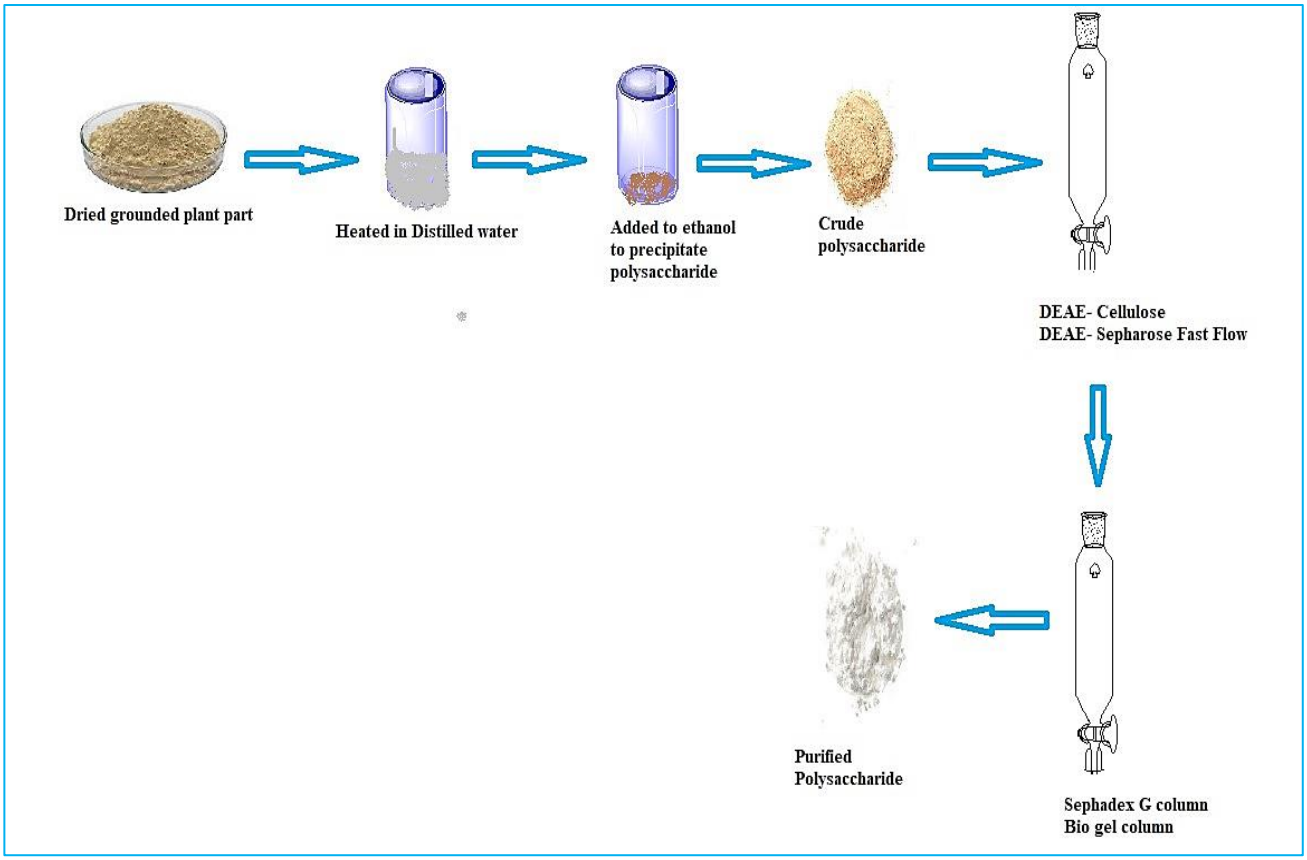

Fig 1 Schematic representation of the extraction, and purification of natural polysaccharides

Purification of polysaccharides

Purification of crude polysaccharides is required in order to verify the content and molecular weight of the isolated polysaccharides. The polysaccharides were lyophilized and the separation procedure was carried out utilizing chromatography. For the purification process, two types of chromatography are used: gel permeation chromatography (Sephadex G and Bio-gel columns) can be used to separate polysaccharides based on molecular weight differences, and ion exchange chromatography (DEAE-cellulose and DEAE-Sepharose Fast Flow) can be used to separate neutral polysaccharides from acidic polysaccharides [5]. Zhang et al., for example, isolated and purified a new polysaccharide from *Anredera cordifolia*. DEAE-cellulose A52 and Sephadex G-100 gel-filtration columns were used to purify the polysaccharide. The samples from both columns were collected, lyophilized, for further structural characterization. From gel filtration analysis four fractions of molecular weight between 52.8 kDa to 355.6 kDa were observed [18]. In similar way Tang et al., performed purification of sweet potato polysaccharide with DEAEcellulose A52 column while molecular weight was detected using Sepharose G 100 column. The standard curve prepared using T5, T40 and T70 standard dextrans and the resulting molecular weights were found to be 109 kDa and 127 kDa [19]. The neutral polysaccharide separated from these polysaccharides using DEAE columns finds immense potential for its usage in targeted drug delivery of antiviral drugs [20].

Physicochemical iroperties

Swelling and solubility

Excipient swelling properties refer to the volumetric expansion of excipient particles due to water adsorption, while excipient shape recovery refers to excipient deformation upon contact with water. Excipient solubility refers to the amount of excipient that passes into solution when equilibrium is established between the solute in solution and any excess, un-dissolved excipients to produce a saturated solution at a specified temperature [21-22]. Some findings suggest that swelling properties of polysaccharides obtained from the polysaccharide of Dandelion observed against different solvents where the highest swelling capacity was seen in distilled water followed by phosphate buffer and lowest against 0.1mol/L HCl [23]. Swelling property of the polysaccharide increases the floating ability of the formulation thereby potentially increasing the drug release of antibacterial like ciprofloxacin and antivirals in the site of stomach [22]. Swelling and solubility of hibiscus leaf mucilage were determined in different solvents under neutral acidic and alkaline conditions. The mucilage was found to be hot water-soluble with gel formation in cold water. The swelling ratio was also found be highest (5.13) in distilled water compared to HCl and NaOH [24]. Due to these properties, the mucilage can find its usage in sustained release of antivirals like Acyclovir [25].

Morphological properties

Morphological research reveals the physical correlations between the size, crystallinity, and juxtaposition of the phases. Morphological properties of the polysaccharides are determined by SEM. For instance, the process of SEM determination the dried polysaccharide sample was mounted on a metal stub. It was then sputtered with gold to make the sample conductive, and at 230 magnifications, the images were taken voltage of 15 kV. The particle was seen mostly in aggregates of irregular shapes [26]. In another instance, the shape and surface characteristics of the polysaccharides extracted from *Actinidia chinensis* roots were determined by fixed on the silicon wafer at a 10 KV acceleration voltage under a high vacuum condition, as well as image magnification of 100×,500× and 800×. The micrograph of all sample showed cloud like rough surfaces with large wrinkles [27]. Thus, this rough irregular surface can help in entrapment of drug thereby inducing sustained and targeted release in encapsulated delivery of antiviral drugs [28,29]. Sardaf et al., reported a polysaccharide from flaxseed gum which under SEM (JSM-5800LV) at 2000X magnification showed smooth surface with multiple flaky morphologies. This flaky morphological nature induces drug entrapment which promote delayed release of drug. Morphology of almond gum exudate was analyzed by SEM with acceleration potential of 15 kV. The shapes of the particles were irregular and diverse in their forms [30]. The drug entrapment increases due to irregular shape which sustains the release of antiviral drugs as excipient [25].

Thermal properties

For thermal analysis of the water-soluble polysaccharide, differential scanning calorimetry was performed, in a temperature range of 50-220 ^{o}C, the polysaccharide was scanned. The rate of heating was 30 ^{o}C/min and the cooling back cycle was 30 ^{o}C at the same rate. The glass transition of temperature was found to be 40.8 ^{o}C without any melting peak [31]. Hence targeted delivery of antivirals could be achieved as glass transition temperature is near to body temperature thereby promoting burst of drugs at the target [32]. Differential scanning calorimetry of okra gum was performed in temperature range of 25-600 ℃ at 20 ℃/min under a nitrogenous atmosphere. In the first stage, temperature between 25-208 ℃ there was mass reduction of 15.45% which increases to 49.99% in 208-600 [33]. This mass reducing temperature properties can be used for potential colon targeted drug delivery of natural antiviral drugs like quercetin [34]. Thermal analysis carried out on the polysaccharide derived from Chinese quince showed two stages of weight loss over a wide temperature range (30-700 ^{o}C). The polysaccharide lost 12.3% of its weight in the first stage over a broad temperature range (30-203^{o} C), which was mostly caused by the bond water in the purified polysaccharide evaporating and losing its weight. The main reduction in weight happened between 260 and 600 degrees Celsius. The weight of the polysaccharide decreased by about 60.3%, which could be related to chemical reactions and modifications in the function groups. The polysaccharide broke down into its constituent parts quite quickly, as evidenced by the comparatively narrow breakdown peak [35]. This narrow breakdown point can lead to formulation of temperature dependent drug delivery targeting viruses. Hence from this information, it can be observed that thermal properties with low glass temperature, narrow breakdown point can lead to temperature dependent drug delivery targeting multiple viruses.

Crystalline properties

Polysaccharide displays wide range of crystalline properties. The way tiny crystalline molecules dissolve differs from the dissolution of polysaccharides. The dissolution of most crystalline small molecules involved the process crystal structure disintegration and followed by the release of the separate atoms, ions while polysaccharides dissolution is a continuous hydration process with the conversion of inter-polysaccharide binding to polysaccharide-water binding, and most of the non-starch polysaccharides are in amorphous or semi crystalline state. X- ray diffraction is a usual method to obtain the crystallinity of any compound [36]. In case of polysaccharide, it can be used to estimate the symmetry and

spiral structure along with crystallinity[3]. As reported by Suvakanta et al, in a rectangular aluminum stud the powder sample of *Musa sapientum* polysaccharide was packed and illumination was done using CuKa radiation (k = 1.54056 Å) at 45 kV and 40 mA. Between the diffraction angles of 5 °C to 40 °C the sample was scanned. The sample had four small peaks at 25°, 32°, 40°, 43° indicating semi-crystallinity of the polysaccharides [26]. The X-ray powder diffraction of the polysaccharide obtained from *Glycyrrhiza glabra* was observed from 5 to 80 °C. From the analysis it was observed that there was a single prominent peak at 18° indicating semi-crystallinity of polysaccharide [37]. The XRD pattern of *Ganoderma leucocontextum* was scanned at 40 kV and 40 mA. The 2θ angle was recorded between 5–90° at a rate of 10°/min. Analysis of the polysaccharide showed one wide peak at 21° which indicate the semi-crystalline of drugs [38]. The common semi crystalline nature of these polysaccharides can be useful in antiviral therapeutics and vaccines [39-41].

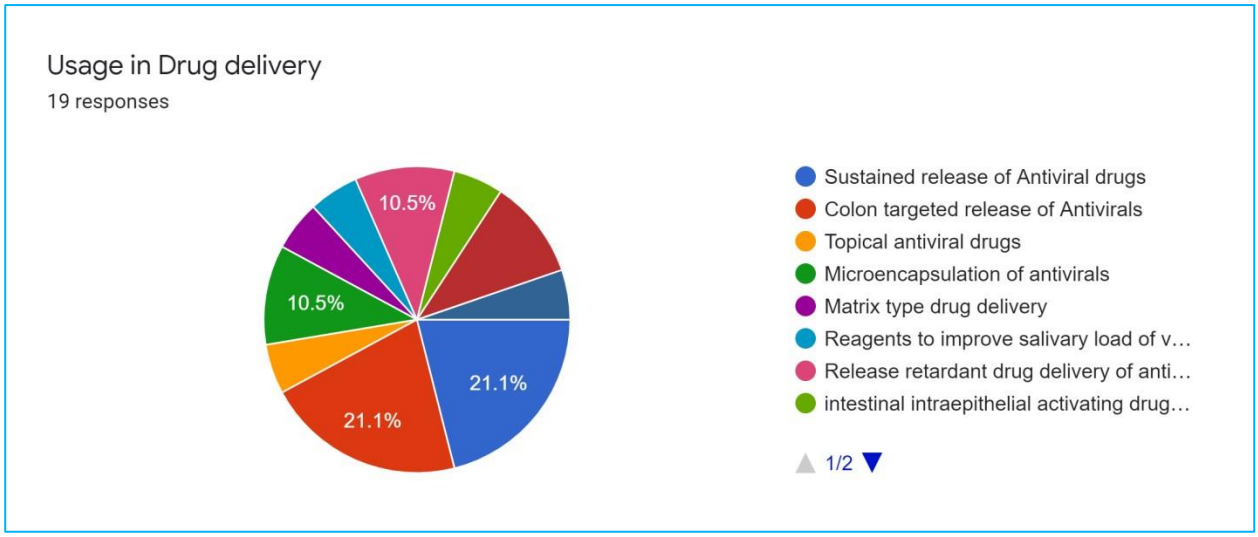

Fig 2 Potential antiviral drug deliveries for water soluble polysaccharides

Structural analysis of water-soluble polysaccharides

Methylation analysis

Monosaccharide analysis is a critical way to profile the composition of complex carbohydrates while methylation analysis which is also known as linkage analysis, has been in use for decades to determine the linkage of polysaccharides. It involves the preparation of partially methylated alditol acetates (PMAAs) from a glycan sample, followed by GC/MS analysis [42]. Zhang et al. investigated monosaccharide analysis of okra flower mucilage using modified 1-phenyl-3methyl-5-pyrazolone (PMP)-HPLC-UV method, where 10 mg of the sample was hydrolyzed using 2M TFA and then labeled with PMP and 0.3M NaOH. The sample was neutralized with 0.3M HCl and HPLC was performed Shimadzu VP-ODS column (4.6 × 250 mm) with phosphate buffer and acetonitrile as mobile phase. There was identification of three prominent peaks indicating presence of three monosaccharide units (Rha, GalA and Gal) when compared with standard chromatogram. For the glycosidic linkage analysis, sample was acetylated by acetic anhydride and was analyzed by GCMS. The data of GC-MS indicated that the sample showed four separate glycosidic linkages in the form of (1→2)-D-Rha, (1→)-D-Gal, (1→2,4)-DRha and (1→4)-linked-D-GalA in the approximate ratio of 1: 6.71: 6.52: 7.65. The ratio of these residues showed consistency with the monosaccharide content present in the sample [43]. The okra gum have been traditionally used in colon targeted drug delivery, thereby finding potential as adjuvant in colorectal targeted antiviral drugs against overexpressing retroviral elements [44]. Further, another method was used for monosaccharide linkage composition analysis of Moringa gum. The gum sample is hydrolyzed with 1M H_2SO_4, then reduced with $NaBH_4$ and acetylated with Ac_2O and analyzed as their alditol acetate using GC-MS. The polysaccharide was also degraded using Smith degradation with 200 mL of $NaIO_4$. The results indicated presence of highly branched chain composed of 2,3,5-Me_3-Ara, 2,3,4-Me_3-Ara, 2,3,4,6-Me_4-Gal, 2,3,4-Me_3Xyl and 2,3,4-Me_3-Rha units. The moringa gum have been reported to be used in colon specific drug delivery and can be useful in delivery of natural antivirals like curcumin [45-47]. Jeong et al., explored the monosaccharide composition of *Terminalia chebula* mucilage using HPLC methods. The purified mucilage sample was subjected to tagging using 1-phenyl-3-methyl-5pyrazolone. The glycosidic linkage of the sample was determined by GC-MS of partially methylated alditol acetates of the sample from procedure including carboxyl reduction, permethylation, acidhydrolysis, and acetylation [48]. From the result, it could be observed that ratio between 1→4-α-Glc and 1→4,6-α-Glc was 18.2, indicating the sample might be amylopectin. This gum finds its potential as adjuvant in formulation of in situ gel system with prolonged time for ophthalmic drug delivery of antivirals like ganciclovir [49,50]. Varshney et al., suggested a process of acetylation and hydrolysis for structural analysis of *Cassia tora* gum. The acetylation was performed by sodium acetate and acetic anhydride and then the polysaccharide was hydrolyzed using 2M sulfuric acid. The result of methanolysis, followed by acid hydrolysis of the methylated product, yielded 2,3,4,6-Me_4-Glc, 2,3,4-Me_3- Xyl, 2,3,4,6-Me_4-Gal, 2,3,4-Me_3Glc, 2,3,6-Me_3-Man, 2,3-Me_2 - Man, and 2,3-Me_2 -Glc in the approximate molar ratio of 1:4:8:1:1:20:8:5 [51]. This chemical nature of gum can find its potential usage in formulation of interpenetrating polymer network microspheres for controlled release of antivirals like acyclovir [52-53]. A process of complete methylation analysis was studies for Cashew gum. The methylation was performed with sodium hydroxide and dimethyl sulfate in presence of dimethyl sulfoxide and finally treated with Purdee's reagent. The methylated product was hydrolyzed using 12.5% sulfuric acid. The hydrolyzed product was quantitatively measured by partition chromatography yielded four monosaccharide unit namely 2,3,4,6- tetramethyl Gal, 2,3,4- trimethyl Gal, 2,4,6trimethyl Gal, 2,4-dimethyl Gal

[54]. This property of cashew gum can find its potential usage in formulation of matrix type sustained delivery for several antiviral drugs [55, 56]. Analysis of these polysaccharides (Fig 2) from different literature sources revealed that, there is a high monosaccharide concentration of Glc, Gal and Xyl in cases of polysaccharides used in colon specific drug delivery while for sustained release of drugs, concentration of Glc, Gal and Man were found to be higher. Monosaccharides, Glc and Ara were mostly seen on the biopolymers used in microencapsulation. In case of linkage analysis, colon specific drug deliveries have highest presence of t-Glc, t-Xyl and (1→4,6)-Glc linkages of polysaccharides, while for microencapsulation process (1→6)-Glc and (1→4)-Glc are observed much more than other linkages.

NMR analysis

Nagel *et al*. [57] studied the structure of arabinogalactan obtained from Mango gum using NMR analysis. The NMR spectra was recorded in D_2O and detected in 500MHz. NMRanalyses of the purified mango fruit polymers polymer revealed 11 components, including the (1→3)- linked and the (1→6)-linked β-galactopyranose residues of hairy-arabinogalactans. α-Arabinofuranose moieties, along with terminal moieties of, a-L-rhamnopyranoseβ-glucopyranuronic acid, and 4O-methyl-β-glucopyranuronic acid. The arabinogalactan-based mango gum can find its potential as an adjuvant to the reagents which would likely improve salivary viral load status of viruses like SARS CoV-2 [58]. In the same way galactomannan were detected in Fenugreek mucilage using 1D and 2D NMR operating at 600 MHz. Assignment of NMR using DQF-COSY, TOCSY, HSQC and HMBC experiments showed (1→4) linked mannan back bone with (1→6) attachment of galactopyranosyl [59]. This galactomannan type gum can be very useful for antiretroviral release retardant drug delivery systems [44]. Gidley et al., studied the structure of tamarind seed mucilage using NMR for its potential uses. The ^{1}H- (200.13 MHz) and ^{13}C-N.M.R. (50.32 MHz) spectra were recorded for solutions in D_2O at 85-90^{o} with a Bruker AM 200 spectrometer. The result showed two residues from the mucilage, a minor polysaccharide (2-3%) contains unbranched (1→5)-α-L-arabinofuranosyl and branched (1→4)-β-D-galactopyranosyl with branched chains of terminal xylose and glucose [60]. The use of tamarind gum as gastroprotective intestine targeted excipient can be very useful in formulation of intestinal intraepithelial activating drug delivery for innate antiviral resistance [61]. Singh and Bothara described structural properties of *Diospyros melonoxylon* gum using 1D NMR spectra recorded in an NMR (400 MHz) spectrometer. The sample was dissolved in D_2O with internal standard being TSP. From the study, it can be observed that the gum was chemically consisted of arabinofuranosyl, fructopyranosyl, glucopyranosyl, mannopyranosyl, rhamnopyranosyl, and xylofuranosyl [62]. The gum can find its potential as adjuvant in encapsulation of antiviral analogues for polymeric nanocapsules for poorly soluble drugs. Another mucilage derived from *Anredera cordifolia* using NMR showed two major polysaccharide residues. The main backbone chain of the first polysaccharide was determined to be composed of (1→3,6) galacturonopyranosyl residues distributed with (1→4)-residues and (1→3)-mannopyranosyl residues while for second polysaccharide was composed of (1→3)-galacturonopyranosyl residues distributesd with (1→4)-glucopyranosyl residues [18]. Thus, these two polysaccharides enables its potential usage as excipient for sustained release delivery for anti-HIV drugs [63]. Arab et al., reported a polysaccharide from *Ocimum album* with a backbone consisting of →3)-β-D-Man*p*-(1→, →3,4)-β-D-Man*p*-(1→, →3,6)-β-D-Man*p*-(1→, →3)-α-D-Glc*p*-(1→, →6)-β-D-Gal*p*-(1→, →4)-α-L-Rha*p*-(1→ and α-D-Glc*p*-(1→ detected by ^{1}H and ^{13}C NMR, having gelling property which can be useful for targeted drug delivery of antivirals [64]. Various reports on the polysaccharide of zedo gum to be an arabinogalactan possessing a backbone of →3,6)-β-D-Galp-(1→, →3)-β-D-Galp-(1→, and →3)-α-L-Araf-(1→ residues with side chains attached to O-3 and O-6 positions of 1,3,6-linked β-D-Galp. The side chains are consisted of β-D-Xylp-(1→3)-α-L-Araf-(1→3)-α-L-Araf-(1→), α-L-Rhap-(1→6)-β-D-Galp-(1→), and β-D-GlcAp-(1→6)-β-D-Galp-(1→) with high viscosity indicating its usage in matrix forming release retardant gel formulation which can find its use in antiviral drug delivery [65]. Wang et al., reported a polysaccharide from Chinese quince (*Chaenomeles sinensis*), using both 1D (^{1}H and ^{13}C) and 2D NMR (COSY, NOESY, HSQC, HMBC) yielded a polysaccharide consisting of Ara, Glu, Xyl, Galacturonic acid and Glucoronic acid. It was found to be highly branched heteropolysaccharide with backbone (α → 4)- β -D-Xyl*p*-(1→ 2, 4)- β D-Xyl*p* with side chains of 1, 2- α -D-Glc*p*A, 1, 2, 3, 5-L-Ara*f* or 1, 4- β -D-Glc*p* attached to O-2, which can be useful in designing pH sensitive drug delivery for antiviral drug [66]. A polysaccharide from African Grewia gum detected by ^{1}H and ^{13}C NMR studies indicated that the backbone is composed of six membered β Galacturonic acid. The gum polysaccharide can find its usage as aqueous film coating agent for delayed release drug delivery [67]. Thus, from the analysis of NMR studies from different literature, it is revealed that mannose and galactose of different linkages were useful in release retardant delivery of antiviral drugs while, nanocapsular drug delivery of different antiviral drugs were performed in presence of heteropolysaccharides like arabinofuranosyl, fructopyranosyl, glucopyranosyl, galactopyranosyl, mannopyranosyl, rhamnopyranosyl, and xylofuranosyl.

FT-IR analysis

Liang *et al*. [68] reported a FTIR spectra of *Lycium barbarum* polysaccharide collected on a Nicolet Magna 750 FT-IR spectrometer with a DTGS detector. The samples pressed into KBr pellets (2mg of sample per 200mg of KBr) showed bands at 3400.38, 2930.49, 1629.66, 1411.40 cm^{-1} might correspond to the bending vibration of C–H, C-C bonds with 920 cm^{-1} indicating β glycosidic linkages. In drug-carbohydrate coupled nanoparticles for targeted delivery of cancer drugs, the polysaccharide was utilized. Because of their nanometric size and variable hydrophobicity and lipophilicity, nanoparticles can be employed to deliver tailored antiviral drugs to certain biological locations. Therefore, the administration of specifically designed antiviral medications in a systematic manner leads to a decrease in side effects in healthy, uninfected cells [69]. Samajdar et al., reported a polysaccharide from *Buchanania lanzan* comprised of glucose, galactose, rhamnose and arabinose in equal proportion, had FTIR bands of O–H stretching, C–H stretching, as well as both α and β glycosidic bonds, was useful in designing of delayed drug releasing nanoemulsion for antiviral drug delivery by diffusion of the hydrophilic co-solvent or co-surfactant from the organic phase into the formulation's aqueous phase, which results in the creation of negative free energy at extremely low interfacial tension and makes it easier for the virus to pass through its nanocapsule [70]. Three fractions (crude, water soluble, water insoluble) of a polysaccharide sourced from gums of *Prunus domestica* were subjected to FTIR studies showed O–H stretching peaks at around 3400 cm^{-1} with glycosidic bond peaks especially β glycosidic peaks at 720 cm^{-1} which finds its usage in formulation of nanoparticles, which

has potent usage against cancer and multiple microbes. [71] Another report by Malviya et al., about a polysaccharide from tamarind gum, shows multiple peaks, including 3209.93 cm^{-1} (O–H stretching), 2873.42 cm^{-1} (C–H stretching), 1491.67 cm^{-1} (C=C stretching), 1349.93 cm^{-1} (C–N stretching), and 1141.67 cm^{-1} (C–O stretching) as well as visible small peaks around 930 indicate peaks for both α and β glycosidic bonds [72-73]. A polysaccharide from flaxseed gum was subjected to IR spectroscopy using FTIR spectrophotometer (Thermo-Fisher, USA) showed a broad and strong peak observed at 3,400 cm^{-1} demonstrated the presence of stretching vibration of OH group, existence of a weak stretching vibration at 2,934 cm^{-1} was ascribed to the presence of saturated bonds of C–H. Further peaks at 1,145 cm^{-1} recommended the existence of the glycosidic linkages β C–O–C and C–OH, with peaks at 826 cm^{-1} specified the existence of mannose and the bands in the range of 839–810 cm^{-1} were assigned to α-d-Galactose. It finds its usage in metal binding nano materials for targeted drug delivery due to its favourable properties such as being a biopolymer, low solubility, high metal binding ability, and the ability to spontaneously form nanoparticles [74-75]. Thus, from all these instances it can be observed that a typical polysaccharide, with β glycosidic bonds can find their usage in novel drug delivery.

CONCLUSION

To combat life threatening viral diseases like COVID 19 (SARS CoV 2), several studies are ongoing for the delivery of the active molecules. The use of natural polysaccharides for pharmaceutical applications especially in drug delivery, is highly sought after due to their economical, easily availability, non-toxic, capable of chemical modification, biocompatible and biodegradable. In recent years, many water-soluble polysaccharides have become important majorly due to their investigation for usage in drug delivery of antiviral drugs. In this study, the extraction, separation, physicochemical studies and structural characterization of polysaccharides were reviewed, and their antiviral activity as well potential usage in delivery of antiviral drugs were discussed. In the future research, we can further expand the source of polysaccharides to find new potential adjuvant for delivery of SARS CoV 2 targeted drugs.

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