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Polysaccharides from Natural Sources: Chemical Structures And Some Pharmacological Activities

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Abstract: *Recently, many compounds having potent antiviral activity in cell culture have been detected and some of these compounds are currently undergoing either preclinical or clinical evaluation. Among these antiviral substances, naturally occurring sulfated polysaccharides are noteworthy. Several controversies over the molecular structures of sulfated polysaccharides, viral glycoproteins, and cell-surface receptors have been resolved, and many aspects of their antiviral activity have been elucidated. It has become clear that the antiviral properties of sulfated polysaccharides are not only a simple function of their charge density and chain length but also their detailed structural features. The in vivo efficacy of these compounds mostly corresponds to their ability to inhibit the attachment of the virion to the host cell surface although in some cases virucidal activity plays an additional role. This review summarizes experimental evidence indicating that sulfated polysaccharides might become increasingly important in drug development for the prevention of sexually transmitted diseases in the near future.*

Keywords: *antiviral activity, mechanisms, sulfated polysaccharides, structural diversity, structure–function relationship*

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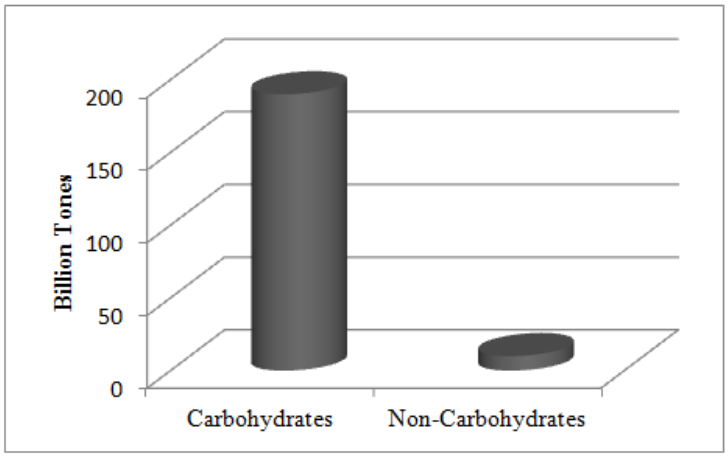
I. Introduction

Carbohydrates are the fuel of life, being the main source of energy for living organisms and the central pathway of energy storage and supply for most cells. They are the major products through which the energy of the sun is harnessed and converted into a form that can be utilized by living organisms. According to rough estimates, carbohydrate represent roughly 95% of the annually regrowing biomass of about 200 billion tons (Fig. 1); of these only 3% are used by man, the rest decays and recycles along natural pathways [1] .



Polysaccharides proposed as the first biopolymers to have formed on Earth [2], are a major group in carbohydrate chemistry. These natural macromolecules occur in almost all living organisms and serve diverse functions of the living material in which they are endogenous. The function of cellulose, the most abundant naturally occurring substance, as structural support in plant is well established. But, in animals, they rarely serve such purposes as structural support. However, the special physical texture and the hydrophilic character are responsible for their multi-various roles.

Fig.1 *Carbohydrate a renewable biomass: 200 billion tons/year.*

Cell-walls of many bacteria contain polysaccharides, which are responsible for their protective coatings and serologic specificity [3]. Some bacterial polysaccharides are highly antigenic having endotoxin properties. Other natural macromolecules, which are not composed entirely of sugar units, contain blocks of monosaccharide units as part of their molecular structure, and contribute extensively to the production and maintenance of living tissues of animals. The blood-group polysaccharide constitutes a group of glycoproteins in which arrangement of monosaccharide residues in carbohydrate subunits controls the blood-group specificity to the overall molecule [4]. Immunoglobulins are a group of glycoprotein that has antibody activity [5]. Transferrin is a glycoprotein, which forms complexes with iron and is responsible for transporting iron from the storage form in tissues, especially in liver to the metabolically functioning iron in hemoglobin [6]. Glycosaminoglycans are amongst the essential building blocks of the macromolecular framework of connective and other tissues [7]. Hyaluronic acid appears to act, on account of its viscosity in solution, as a lubricant, shock-absorbing gel in limb joints [8]. In the presence of appropriate enzyme it serves as 'spreading factor' of skin [9] and its role in the advancement of sperm in the cervical canal for fertilisation is well accepted. Giving salutation to those life building and nurturing activities of polysaccharides, this review is dedicated to describe briefly the pharmacological activities of plant polysaccharides.

1. PHARMACOLOGICAL ACTIVITIES OF POLYSACCHARIDES

In traditional medicine, the use of plants against wounds, both externally and internally can be found as part of the customs from all continents; these plants are still used even in European countries as so-called "traditional" remedies [10]. Often the extracts of the plants appear to have one thing in common: they were sticky and contained material forming mucilages or gels when extracted with water, and this was an indication that they were rich in polysaccharide materials. Recent developments show that polysaccharides exhibit many beneficial pharmacological effects such as anticoagulant, antiviral, antioxidative, anticancer and immunomodulating activities [11, 12]. The next part of this chapter, which summarizes experimental evidences indicating that polysaccharides might play increasingly important roles in the management of diseases in the near future, is divided into three parts according to their pharmacological activities. Further classification within each activity is made by structural type.

1.1. Antioxidative activity

In the mid-1950s, Denham Harman articulated a 'free-radical theory' of ageing, speculating that the endogenous oxygen radicals were generated in cells and resulted in a pattern of cumulative damage [13]. Reactive oxygen species (ROS) are recently evidenced to be closely linked to degenerative diseases such as Alzheimer's disease, neuronal death including ischemic and hemorrhagic stroke, and acute and chronic degenerative cardiac myocyte death [14]. Although many drugs are proved to be successful in the management of these diseases, their use is often limited because of toxic side-effects, and the development of drug resistance. Thus, there is a need to develop new compounds with strong anti-oxidative activity accompanied by favourable clinical properties. Natural products have been invaluable as biologically validated platforms for drug development [15]. In a series of review articles, Newman and colleagues have analyzed the sources of drugs in the last 30 years. The analysis demonstrated the continuing and valuable contributions of nature as a source of lead compounds that have provided the basis and inspiration for the synthesis of new drugs [16].

In recent years, a number of polysaccharides containing fractions isolated from various sources as for example, marine algae [17], plants [18], fungi, bacteria, and animal possess antioxidative activity [19]. Some of them, in particular the sulfated polysaccharides from marine algae such as fucoidan [17], sulfated galactan [20], sulfated polysaccharide fractions containing galactose and xylose residues as constituent sugar, and rhamnose-rich polysaccharide fractions showed considerable antioxidative properties [21]. Many of the studied antioxidative polysaccharides from higher plants had arabinogalactan structure. In some cases these highly branched polymers contained esterified phenolic acid [18]. In addition, chemically modified macromolecules such as acetylated and benzoylated ulvans also possess antioxidative property [22]. Potency of some of these compounds is higher than the native polymer.

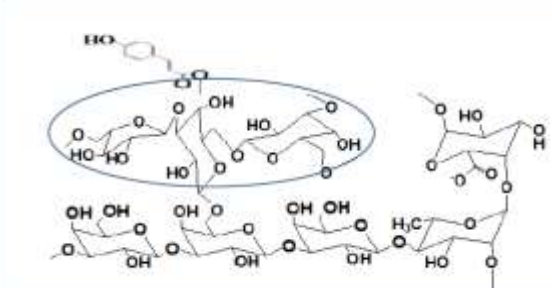


Fig.2. *The structure of the arabinogalactan from the Enhydra fluctuans. This polymer contained esterified phenolic acid.*

Structure-activity relationships

The antioxidative property of polysaccharides depends upon a number of parameters including molecular mass. In case of sulfated polysaccharides, potency depends upon their sulfate content [23]. For example, sulfated polysaccharides from *Undaria pinnitafida* had stronger antioxidant abilities than their de-sulfated derivatives [19] . The increased hydrophobic character of the macromolecule also leads to higher potency [22]. Publications linking biological activities and structures of arabinogalactan have emphasized the importance of highly branched side chains for activity [18]. It has been shown that high activity correlates to large neutral side chains with high amounts of (1→6)- and (1→3,6)-linked Galactose [24]. The arabinogalactan from medicinal plants possesses highly branched side chains containing variously linked galactosyl and arabinosyl units and this might possibly be linked to their anti-oxidative activity [18,25]. Moreover, carbohydrate polymers from several medicial plants including *Enhydra fluctuans* also contained ester linked phenolic acids, (**Fig.2**) which can prevent oxidative stress by direct scavenging of free radicals. In this way, phenolic acid became oxidized and formed a more stable and less reactive radical. Therefore, esterified phenolic acid moieties, if any, are important functional sites [18, 25].

Biocompatibility is an important parameter in medical science as failures in compatibility may cause severe clinical complications. Incidentally, the distribution and metabolism of many biologically active compounds (drugs, natural products, etc) in the body are correlated with their affinities toward serum albumin. Thus the investigation of pharmacologically active molecules with respect to albumin binding is of imperative and fundamental importance [26].

Mechanism of action

Antioxidant enzymes are considered to be a primary defense that prevents biological macromolecules from undergoing oxidative damages [27]. For example, superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) are two important endogenous enzymes related to antioxidant defense mechanisms [28]. The intracellular antioxidant enzyme, SOD protects against oxidative processes initiated by the superoxide anion, while GSH-Px reduces lipid hydroperoxides to their corresponding alcohols and free hydrogen peroxide to water [29]. Now polysaccharides have been reported to stimulate the production of both SOD and GSH-Px. Thus, enhanced SOD and GSH-Px activity along with increased total antioxidant capacity can be effective in scavenging the various types of oxygen free radicals and their byproducts in aging animals [29].

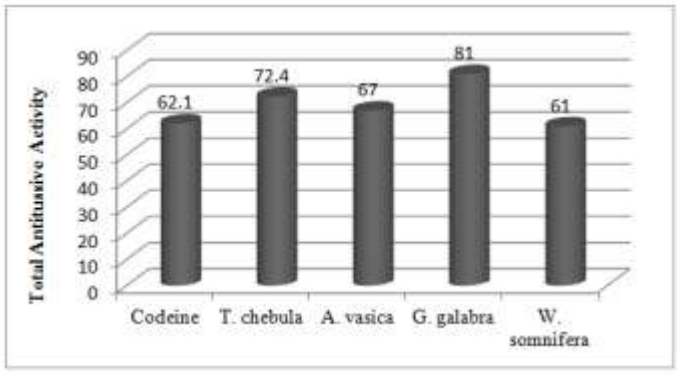


Fig.3 ***T****otal antitussive activity on guinea pigs of the carbohydrate polymer (CP) from Terminalia chebula, Adhatoda vasica, Withania somnifera, and Glycyrrhiza glabra along with standard antitussive compound codeine.*

1.2. Antitussive activity

The cough reflex represents the most important defensive reflex of the airways, which together with mucociliary transport system forms the main mechanism for the cleaning of respiratory tract [30]. Coughing protects the breathing passages from blocking, thereby preventing the infected mucus from falling into lungs and bronchial

tubes, which could be very dangerous. The cough reflex belongs to the most frequent symptoms of respiratory system diseases and is the most common reason why sick patients visit physicians [31]. Pathological cough has significant impact on patient's quality of life observed either in physical activity or psychosocial domain. Conventional therapies are often limited for the lack of effective medications. Moreover, most of the existed medicines could bring about inevitable side effects. Thus, there is a need to develop new compounds with strong antitussive activity accompanied by favourable pharmacological and clinical properties. Growing evidences showed that several families of polysaccharides from medicinal plants have effects on citric acid-induced cough reflex and reactivity of airways smooth muscle *in vivo* conditions [32]. Indeed, the total antitussive activity of some of these polymers is either higher or similar to the clinically approved drug codeine (**Fig.3**). Such carbohydrate polymers include arabinogalactan, rhamnogalacturonan, glucuronoxylan and other acidic heteroglycans (**Table 1**). Other natural macromolecules, which are not composed entirely of sugar units, contain blocks of monosaccharide units as part of the molecular structure, and contribute extensively to their antitussive activities. For example, a low molecular mass arabinogalactan-protein (AGP) from the instant coffee powder of *Coffea arabica* beans, possess prominent antitussive (*in vivo*) activity in a dose dependant way [33]. The mucilagineous extracellular proteoglycan (EPG) from culture medium of red alga *Rhodella grisea,* which contained xylose, its 3-*O*-and 4-*O*-methyl-derivates (55%), glucuronic acids (17%), rhamnose (14%), galactose (8%), glucose (4%), minor amounts of other sugars (~2%) & protein (13%) also showed a cough suppressing effect on laryngopharyngeal type of cough [34]. The high molecular mass polysaccharide-polyphenolic conjugate (74% carbohydrates and 17% phenolics) from flowering parts of *Lythrum salicaria* [35] and the polyphenolic–polysaccharide–protein complex (molar mass 11.2 kDa) from flowers of *Solidago canadensis* L. [36] also showed antitussive activities.

Table 1. Types of carbohydrate polymers from medicinal plants possessing antitussive activity

Types of carbohydrate polymer	Source	Testing systems	Reference
Arabinogalactan & rhamnogalacturonan	*Trichilia emetica*	Guinea pigs	[35]
Arabinogalactan, rhamnogalacturonan and Glucuronoxylan	*Opilia celtidifolia*	Guinea pigs	[35]
Pectin & Arabinogalactan	*Crossopteryx febrifuga*	Guinea pigs	[35]
Rhamnogalacturonan	*Althaea officinalis L.*	Guinea pigs	[36]
Pectin material with high arabinose and galacturonic acid	*Opilia celtidifolia*	Guinea pigs	[36]
Polysaccharide-polyphenolic conjugate	*Lythrum salicaria*		[36]
Arabinogalactan	*Adhatoda vasica*	Guinea pigs	[50]
Arabinogalactan	*Withania somnifera*	Guinea pigs	[51]
Arabinogalactan	*Glycyrrhiza glabra*	Guinea pigs	[52]
Pectic polysaccharides	pumpkin fruit biomass	Guinea pigs	[33]
Extracellular proteoglycan	*Rhodella grisea*	Cats	[34]

Structure-activity relationships

The antitussive properties of polysaccharides from various sources as high highlighted in Fig.3. Their chemical structures are also different. Because of limited data available the relationship between the structure of polysaccharides and their antitussive activity has not yet been established [32, 36]. Growing evidences suggest that arabinogalactan structures have been associated with various biological activities [11]. Investigations of biological activities of arabinogalactan isolated from various medicinal plants emphasized the importance of highly branched side chains for the expression of the observed activities [11]. Samuelsen and coworker [24] employing multivariate statistical analysis suggested that the magnitude of the biological activity of arabinogalactan is influenced by the content of certain side chains in the polymer. It has been shown that high activity correlates to large neutral side chains with high amounts of (1 → 6)- and (1 → 3,6)-linked Galactose and low amounts of (1 → 4)-linked Galacturonic acid. The arabinogalactan of various plant sources often contains side chains possessing such distinctive features. Hence, these portions might be considered to be important as functional sites.

Mechanism of action

The mechanism behind the antitussive activity of the carbohydrate polymers is poorly understood, although it has been reported that many antitussive herbs work by an antispasmodic action or bronchodilator action [37]. They cause bronchial muscle relaxation *in vitro*, or decrease airways resistance *in vivo*. [38] reported that broncho constriction causes or enhances the sensitivity of cough, while bronchodilation does the opposite. However, possible role of other type of mechanisms including bioadhesive effect of the polysaccharide to the epithelial mucosa cannot be ruled out. Further research should be directed in this area.

1.3. Antiviral activity

Many viruses display affinity for cell surface proteoglycans, especially heparan sulfate proteoglycans, with high biological relevance to virus entry. This raises the possibility of the application of sulfated polysaccharides in antiviral therapy. In recent years, screening assays of the antiviral activity of extracts from a number of marine algae and cyano bacteria have led to the identification of carbohydrate polymers with potent inhibitory effects against several human and animal viruses, including Herpes simplex virus [39]. These polysaccharides include carrageenans, fucoidans, mannans, rhamnan sulfates, sulfated galactans and others (**Table 2**). In addition, semisynthetic sulfated carbohydrate polymers from dextran, cellulose and glucan also possess promosing antiviral activity.

Structure-activity relationships

Publications relating to antiviral activity of sulfated polysaccharide demonstrate that the potency of these macromolecules depends upon a number of factors [12]. For example, degree of sulfation has a major impact on the antiviral activity of polysaccharides [40]. Specific position of sulfate groups might be important for antiviral activity [41]. Molecular weight contributes to antiviral activity [40]. Antiviral potency also depends upon the molecular structure of the polysaccharide [12]. Low-molecular weight compounds inhibit cell-to-cell spread of viruses more efficiently than high molecular weight compounds [42].

Table 2. Carbohydrate polymers and their antiviral activities

Families of polysaccharide	Source	Molecular weight	Virus[a]	CC_{50}[b] (µg/ml)	IC_{50}[c] (µg/ml)	Reference
Fucan	*Padina tetrastromatica*	50 kDa	HSV-1 & HSV-2	1000	0.30-1.05	[53]
Fucan	*Sargassum tenerrimum*	30 ± 5 & 26 ± 5 kDa	HSV-1	1000	0.5-15	[54]
Xylogalactofucan and Alginic acid	*Sphacelaria indica*	26 ± 5 & 21 ± 5 kDa	HSV-1	200	0.6-10	[25]
Xylogalactofucan and Alginic acid	*Laminaria angustata*	56 ± 5 & 32 ± 5 kDa	HSV-1	1000	0.2-25	[55]
Arabinogalactan	*Azadirachta indica*	80 kDa	BoHV-1	>1600–1440	31.12 to 105.25	[56]
Galactan	*Gracilaria corticata*	30 kDa	HSV-1 & HSV-2	> 1000	1.1-27.4	[57]
Xylan	*Scinaia hatei*	120 kDa	HSV-2	> 1000	0.22-1.37	[58]
Xylomannan	*Scinaia hatei*	160 kDa	HSV-1	> 1000	0.5-4.6	[59]
Xylomannan	*Sebdenia polydactyla*	150 kDa	HSV-1	1000	0.35-2.8	[12]
Glucan	*Oryza sativa*	1-30 kDa	HCMV	270	3.46±0.63	[18]

Virus[a] : HSV = Herpes Simplex Virus; BoHV = Bovine Herpes Virus; HCMV = Human Cytomegalo Virus.
CC_{50} [b] = 50% cytotoxic concentration; defined as compound concentration required to reduce cell viability by 50%
IC_{50}[c] = 50% inhibitory concentration; defined as compound concentration required to reduce virus plaques by 50%

Mechanism of action

The entry of Herpes Simplex Virus (HSV) into host cells is a complex process initiated by the specific interaction between host-cell-surface receptors and viral envelope glycoproteins [43]. In the case of HSV type-1 and HSV type-2, attachment to Heparan Sulfate (HS) seems to be primarily mediated through glycoprotein C (gC) although glycoprotein B (gB) may contribute to this function [44]. Clusters of basic and hydrophobic amino acids located between residues 129 and 160 of gC1 [45] as well as the mucin-like region (amino acids

33–123) of this protein were identified as important for HSV type-1 attachment to cell-surface Heparan Sulfate/Chondroitin Sulfate. HSV type-1 gB1 consists of 904 amino acids and approximately 85% of the sequence is homologous to its HSV type-2 counterpart [46]. Most of the variability between gB1 and gB2 is seen in a lysine-rich region (amino acids 68–76), which is also responsible for binding to HS. As shown in **Fig. 4.** gB1 occurs as a trimer with each of the monomers divided in five distinctive domains: I-base, II-middle, III-core, IV-crown, and V-arm [46]. The results from a more recent study suggest that specific hydrophobic/aromatic amino acids from domain I are important for the fusogenic activity of gB [47]. In this context, an attractive concept is that sulfated polysaccharides act as antiviral agents in cell culture because that these charged polymers may mimic HS chains on cell-surface proteoglycans and thus they block viral attachment by competitive inhibition.

A novel approach to inhibit HSV-1 infection by targeting the gD-mediated membrane fusion step has been described by [48]. Notably, the anti-herpetic properties of sulfated polysaccharides may depend not only on their charge density but also on the characteristics of their uncharged portions which may be involved in hydrophobic and hydrogen bonding interactions. [49] reported that hydrophobic interactions, in addition to electrostatic forces, are decisive for the CS as well as HS binding to viral glycoprotein gC. In present case, the interaction of the methyl groups of fucoidan with the hydrophobic pocket of HSV-1 gC seems to be important in the binding of the polysaccharide to the viral glycoprotein. Finally, in addition to the polysaccharide-mediated antiviral effects directed to the cell surface (viral receptor binding, entry, fusion); a second type of effects may also play a role, i.e., the induction of intracellular events contributing to the antiviral activity of sulfated polysaccharides. To make it simple, as the binding of a number of known polysaccharides to cell-surface receptors can induce intracellular signaling pathways, this second type of effects should be additionally taken into consideration. For example, the anticytomegalo viral effect of spirulan-like polysaccharides was demonstrated to be composed of these two antiviral activities, i.e., (1) an inhibition of human cytomegalo virus (HCMV) entry on the one side (2) the induction of intracellular anti HCMV effects on the other side. The replication efficiency of most viruses is dependent on specific intracellular signaling pathways, the inhibition or the induction of particular signaling by surface-binding polysaccharides can provide a significant part of the overall antiviral activity. One explanation for such intracellularly produced activity is the stimulatory effect of sulfated polysaccharides onto interferon production with the consequence of a broad antiviral effect [12].

II. Conclusions

In conclusion, study of the chemistry of polysaccharides from natural origin has many practical applications. Each polysaccharide has special properties that are a result of its individual unique molecular structure. These properties can be altered to suit marketing requirements by various processes including chemical treatment of the isolated polysaccharides. It will be a continuous challenge to select the most promising drug candidates among the wide array of available polysaccharide compounds. The numerous advantages over other classes of antiviral drugs, such as relatively low production costs, broad spectrum of antiviral properties, low cytotoxicity, low induction of viral drug resistance, high lyophilicity, safety, wide acceptability, and novel modes of action, suggest sulfated polysaccharides as promising drug candidates in the near future.

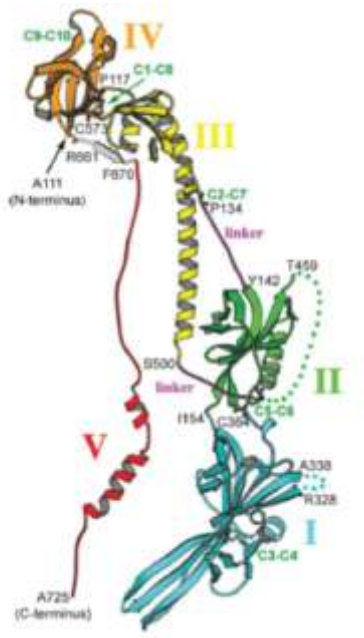


Fig. 4 Ribbon diagram of a single gB1 protomer.

References

[1] Lichtenthaler, F., & Mondel, S. (1997). Pure and Applied Chemistry, 69, 1853-1866.
[2] Tolstoguzov, V., (2004). Food Hydrocolloids, 18, 873-877.
[3] Holst, O. (1999). In Endotoxin in Health and Disease, eds, Brade H., Morrison D. C., Opal S., Vogel S., Marcel Dekker, Inc., New York, 115.
[4] Feizi, T. (2000). Immunological Reviews, 173, 79-88.
[5] Van de Perre, P. (2003). Vaccine, 21, 3374-3376.
[6] Hiroshi, K., Rasha, S. G., Peter, T. V., Tsuyoshi, N., Jonathan, W. S. H., & Phillip, K. (2000). Journal of Biological Chemistry, 275, 16618-16625.
[7] Taylor, K. R., & Gallo, R. L. (2006). The FASEB Journal, 20, 9-22.
[8] Grigorij, K., Ladislav, S., Robert, S., & Peter, G. (2007). Biotechnology Letters, 29, 17-25.
[9] Lokeshwar, V. B., & Selzer M. G. (2008). Seminars in Cancer Biology, 18, 281-287.
[10] Paulsen, B., & Samuelsen, A. B. (2001). Plantago Species. Harwood Academic Publishers GmBH, Amsterdam.
[11] Baek, S. H., Lee, J. G., Park, S. Y., Bae, O. N., Kim, D. H., & Park, J. H. (2010). Biomacromolecules, 11, 2044–2052.
[12] Ghosh, T., Chattopadhyay, K., Marschall, M., Karmakar, P., Mandal, P., & Ray, B. (2009). Focus on anti-virally active sulfated polysaccharides: From structure–activity analysis to clinical evaluation. Glycobiology, 19, 2-15.
[13] Harman, D. (1956). Journal of Gerontology, 11, 298–300.
[14] Mucke, L. (2009). Nature, 461, 495-497.
[15] Newman, D. J., & Cragg, G. M. (2012). Journal of Natural Products, 75, 311–335.
[16] Cragg, G. M., Grothaus, P. G., & Newman, D. J. (2009). Chemical Review, 109, 3012–3043.
[17] Chattopadhyay, N., Ghosh, T., Sinha, S., Chattopadhyay, K., Karmakar, P., & Ray, B. (2010). Food Chemistry, 118, 823–829.
[18] Ghosh, D., Ray, S., Ghosh, K., Micard, V., Chatterjee, U. R., Ghosal, P. K., & Ray, B. (2013). Biomacromolecules, 14, 1761–1768.
[19] Wang H., Liu Y. M., Qi Z. M., Wang, S. Y., Liu, S. X., Li, X., Wang, H. J., & Xia, X.C. (2013). Current Medicinal Chemistry. 20, 2899-913.
[20] Barahona, T., Chandía, N. P., Encinas, M. V., Matsuhiro, B., & Zúñiga, E. A. (2011). Food Hydrocolloids, 25, 529-535.
[21] Yang, Y., Liu, D., Wu, J., Chen, Y., & Wang, S. (2011). International Journal of Biological Macromolecules, 49, 1031-1037.
[22] Qi, H., Zhang, Q., Zhao, T., Hu, R., Zhang, K., & Li, Z. (2006). Bioorganic & medicinal chemistry letters, 16, 2441-2445.
[23] Hu, T., Liu, D., Chen, Y., Wu, J., & Wang, S. (2010). 46, 193-198.
[24] Samuelsen, A. B., Westereng, B., Yousif, O., Holtekjølen, A. K., Michaelsen, T. E., & Knutsen, S. H. (2007),Biomacromolecules, 8, 644-649.
[25] Bandyopadhyay, S. S., Ghosh, D., Micard, V., Sinha, S., Chatterjee, U. R., & Ray, B. (2012). International Journal of Biological Macromolecules, 51, 158-164.
[26] Kokkonen, H. E., Ilvesaro, J. M., Morra, M., Schols, H. A., & Tuukkanen, J. (2007). Biomacromolecules, 8, 509-515.
[27] Xu, C.L., Wang,Y.Z., Guo, J., Liu, J.X., & Feng, J. (2007). Comparative Biochemistry and Physiology Part B: Biochemistry and Molecular Biology, 147, 445-451.
[28] Johnson, P. (2002). Toxicology & Pharmacology,133, 493-505.
[29] Kodali, V. P., Perali, R. S., & Sen, R. (2011). Journal of Natural Products, 74, 1692-1697.
[30] Nasra, J., & Belvisi, M. G. (2009). Pharmacology & Therapeutics, 124, 354-375.
[31] Schappert, S. M., & Burt, C.W. (2006). Vital and Health Statistics, 13, 1−66.
[32] Nosalova, G., Fleskovaa, D., Jureceka, L., Sadlonovaa, V., & Ray, B. (2013). Respiratory Physiology & Neurobiology, 187, 47– 51.
[33] Nosáľová, G., Prisenžňáková, Ľ., Košťálová, Z., Ebringerová, A., & Hromádková. Z., (2011). Fitoterapia, 82, 357-364.
[34] Nosáľová, G., Capek, P., Matáková, T., Nosáľ, S., Flešková, D., & Jureček, Ľ. (2012). Carbohydrate Polymers, 87, 752-756.
[35] Sutovska, M., Capek, P., Fraňová, S., Pawlaczyk, I., & Gancarz, R. (2012). International Journal of Biological Macromolecules, 51, 794-799.
[36] Sutovska, M., Capek, P., Kocmálová, M., Fraňová, S., Pawlaczyk, I., & Gancarz, R. (2013). International Journal of Biological Macromolecules, 52, 192-197.
[37] Ernst, E. (1998). The Journal of Asthma: Official Journal of the Association for the Care of Asthma, 35, 667–671.
[38] Pavord, I. M., & Chung, K. F. (2008). The Lancet, 371, 1375–1384.
[39] Balzarini, J., & Van Damme, L. (2007). Lancet, 369, 787-797.
[40] Witvrouw, M., & De Clercq, E. (1997). General Pharmacology, 29, 497–511.
[41] Marchetti, M., Trybala, E., Superti, F., Johansson, M., & Bergstorm, T. (2004). Virology, 318, 405–413.
[42] Ekblad, M., Adamiak, B., Bergstrom, T., Johnstone, K. D., Karoli, T., Liu, L., et al. (2010). Antiviral Research, 86, 196–203.
[43] Kleymann, G. (2005). Expert Opinion on Investigational Drugs, 14, 135–161.
[44] Cheshenko, N., & Herold, B. C. (2002). Journal of General Virology, 83, 2247–2255.
[45] Mardberg, K., Trybala, E., Tufaro, F., & Bergstr¨om, T. (2002). Journal of General Virology, 83, 291–300.
[46] Heldwein, E. E., Lou, H., Bender, F. C., Cohen, G. H., Eisenberg, R. J., & Harrison, S. C. (2006). Crystal structure of glycoprotein B from herpes simplex virus 1. Science, 313, 217–220.
[47] Hannah, B. P, Heldwein, E. E., Bender, F. C., Cohen, G. H., & Eisenberg, R. J. (2007). Journal of Virology, 81, 4858–4865.
[48] Copeland, R., Balasubramaniam, A., Tiwari, V., Zhang, F., Bridges, A., Linhardt, R. J., Shukla, D., & Liu, J. (2008). Biochemistry. 47, 5774–5783.
[49] Mardberg, K., Trybala, E., Glorioso, J. C., & Bergstr¨om, T. (2001). Journal of General Virology, 82, 1941–1950.
[50] Chatterjee, U. R., Bandyopadhyay, S. S., Ghosh, D., Ghosal, P. K., & Ray, B. (2011). International Journal of Biological Macromolecules, 49, 637– 642.
[51] Sinha, S., Nosál'ová, G., Bandyopadhyay, S. S., Flešková, D., & Ray, B. (2011). Journal of Ethnopharmacology, 134, 510-513.

[52] Saha, S., Nosál'ová, G., Ghosh, D., Flešková, D., Capek, P., & Ray, B. **(2011).** International Journal of Biological Macromolecules, 48, 634-638.
[53] Karmakar, P., Pujol, C.A., Damonte, E.B., Ghosh, T., & Ray, B. (2010). Carbohydrate Polymers, 80, 514–521.
[54] Sinha, S., Astani, A., Ghosh, T., Schnitzler, P., & Ray, B. (2010). Phytochemistry, 71, 235–242.
[55] Saha, S., Navid, M. H., Bandyopadhyay, S. S., Schnitzler, P., & Ray, B. (2012). Carbohydrate polymers, 87, 123-130.
[56] Saha, S., Galhardi, L. C. F., Yamamoto, K. A., Linhares, R. E. C., Bandyopadhyay, S. S., Sinha, S., Nozawa, C., & Ray, B. (2010). International Journal of Biological Macromolecules, 47, 640–645.
[57] Chattopadhyay, K., Ghosh, T., Pujol, C. A., Carlucci, M. J., Damonte, E. B., & Ray, B. (2008). International Journal of Biological Macromolecules, 43, 346–351.
[58] Mandal, P., Pujol C. A., Damonte, E. B., Ghosh, T., & Ray, B. (2010). International Journal of Biological Macromolecules, 46, 173-178.
[59] Mandal, P., Pujol, C. A., Carlucci, M. J., Chattopadhyay,K., Damonte, E. B., & Ray, B. (2008). Phytochemistry, 69, 2193–2199.

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