Article

BIOLOGICAL ACTIVITY OF NATURALLY OCCURRING PHARMACEUTICAL EXCIPIENTS: A REVIEW ON RESINS, GUMS AND MUCILAGES

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ABSTRACT

Biologically active natural pharmaceutical excipients and their substructures have long been valuable in drug development and formulation strategies. The article explores biologically active gums, resins and mucilage used as pharmaceutical excipients and their applications in phytopharmaceuticals drug development. Being natural products with therapeutic activities, these compounds present a broad scope in their refinement and applications in today's pharmaceuticals. The article casts light on pharmaco-therapeutically active excipients that give an insight into medications today and their practical implementation in pharmacotherapy.

INTRODUCTION

Polysaccharide hydrocolloids are abundantly available in nature, especially in higher plants. It is underlined that among various polysaccharides, gums, resins, and mucilage are of utmost importance as pharmaceutical excipients. They owe their roles for different purposes, such as improving the manufacturing process and/or facilitating drug delivery. Recent trends incline towards the use of natural products derived from plant materials and minimise and restrict the use of synthetic additives because the former is biodegradable, found in abundance in nature, non-toxic, and provides ease in working and low cost. These polysaccharides are structurally diverse macromolecules with a comprehensive array of physicochemical characteristics and biological activities that render them useful for broad applications in medicines. Mucilages are commonly employed as adjuvants such as thickening, binding, suspending, disintegrating, emulsifying, gelling, stabilising agents etc., in various pharmaceutical preparations. These are generally natural products of metabolism formed intracellularly. Gums are the products of pathological reactions and mechanisms in plants formed due to their protection mechanism following any injury, unfavourable conditions or stress such as drought or breakdown of cell walls. Upon hydrolysis, these macromolecules yield simpler sugar units (e.g.,arabinose, galactose, glucose, mannose etc.) Resins are the

amorphous mixtures of essential oils obtained as exudates from trunks of various trees. These are mainly hydrocarbon secretion of higher plants, particularly coniferous trees. Despite their pharmaceutical applications being employed as excipients in drug delivery systems, the niche lies in their untapped potential as biologically active compounds. The work is contemplation to specify the biological activity of various naturally occurring compounds used as pharmaceutical excipients.

CLASSIFICATION OF NATURAL GUMS AND RESINS

There happens to be no straightforward or singular classification of gums and resins, and thus different authors have put effort into classifying them in different ways. One such classification is based on their source. The listed sources are weeds, higher plants, various micro-organisms or derivatives of other complex polysaccharides such as cellulose, as shown in Table 1 [1]. Another utile manner of classifying them is based on charge, shape & chemical structures. This is shown in Table 2 [2].

Table 1: Classification of gums based on their source.

SOURCE	GUMS
Marine Algae	Agars, Alginic acid, Laminarin, Carrageenans
Shrub/ Tree	Gum arabica, Gum ghatti, Gum karaya, Gum tragacanth
Plants Extracts	Larch gums, Pectins
SeedGum	Guar gum, Locust bean gum, Tara gum, Amylose, Starch, Cellulose
Tubers and roots	Inulin, Konjac glucomannans, potato starch
Microorganisms	Curdlans, Dextran, Gellans, Curdian, Lentinan, Scleroglucan
Cellulose derived (by Chemical Modifications)	Carboxymethyl Hydroxyethylcellulose, Cetyl Hydroxyethylcellulose S, Ethyl Hydroxyethyl Celluloses, Hydroxyethyl Celluloses, Hydroxypropyl Cellulose, Hydroxypropylmethylcellulose, Hydroxyethyl Methylcellulose S, Methyl Cellulose.

Table 2: Classification of gums based on charge, shape and monomeric units.

BASIS OF CLASSIFICATION	CLASS	EXAMPLES
Charge	Non-Ionic	Guar gum, Locust Bean Gum, Tamarind gum, Xanthan gum, amylase, Arabinans,
	Anionic	Gum arabic, Gum karaya, Carrageenans, Gellan gum,

		Agar, Algin, Pectic acid
Shape	Short Chain	Xanthan gum, Guar gum
	Branched Chains / Branch on branch	Gum Arabic, Tragacanth gum
Monomeric Units or Chemical structures		
	Homoglycans	Amylose, Arabinose, Cellulose
	Di-heteroglycans	Algins, Carrageenans
	Galactomannans	Fenugreek gum, Alfalfa, Guar gum, Locust bean gum, Tara gum, Cassia gum
	Glucomannans	Salep, Konjac
	Gums containing Uronic acid	Xanthan gum, Pectin, Ulvan, Gellan gum
	Tri-heteroglycans	Arabinoxylans, Gellan gum, Xanthan gums
	Tetra-heteroglycans	Gum arabic, Psyllium seed gum
	Penta-heteroglycans	Gum ghatti, Gum tragacanth

Biological activities of some naturally obtained gums, mucilage and resins generally employed as pharmaceutical excipients:

1. Okra gum

Okra gum is a naturally obtained Polysaccharide from the Okra plant (pods), commonly known by its trivial name, Lady's Finger (*Abelmoschus esculentus* L.), and belonging to the Malvaceae family [3]. This plant is mainly found near tropical and subtropical regions [3]. Isolation and purification of okra polysaccharides depend upon the method of extraction and purification solutions involved. Liu et al. employed the hot water method to extract and isolate okra polysaccharides. It showed its composition of four main monosaccharides, i.e. arabinose, galactose, rhamnose and galacturonic acid. Liu et al. found that polysaccharides isolated from the plant showed good hyperglycaemia activity [3]. Kunli et al. performed the extraction of okra polysaccharides by ultrasound-assisted extraction method. The extracted okra polysaccharides constituted mainly seven monosaccharides, i.e. glucose, galactose, mannose, arabinose, fructose, xylose and rhamnose. They reported that the extracted polysaccharides exhibited high antioxidant activity [4].

Further several studies were performed on the polysaccharide constituents. It was found that the

determined antioxidant activity of the okra chemical constituents is specifically related to the contents present in the okra seeds, flowers and fruits, i.e. phenolic and flavonoid constituents. Gemede et al. too reported with their studies that mucilage from the okra pods possesses high antioxidant activity [5]. Huricha et al. employed the maceration method to extract and isolate okra polysaccharides and identified three fractions with different molecular weights (600,900 and 1300 kDa) and two distinct groups of monosaccharides composition. Group 1 consisted of monosaccharides – galactose, rhamnose, galacturonic acid & glucuronic acid. Group 2 monosaccharides were galactose, rhamnose, galacturonic acid, glucuronic acid & glucose. Their studies on these monosaccharides reported that they could be potentially utilised as novel immunomodulators [6]. Gao et al. used fractions of okra polysaccharides and reported their anti-fatigue activity [7]. Wahyuningsih et al. carried out their studies for the immunomodulating properties of the okra polysaccharides. They reported that crude polysaccharides could act as immunomodulators by enhancing and controlling the immune response by phagocytic activity, spleen index, splenocyte proliferation and cytokine production [8]. Liu et al. reported the hypoglycemic activity of okra polysaccharides by studying hypoglycaemia function in OP [9]. Ortaçetal (2018) demonstrated via in vivo research to report that okra mucilage showed a gastro-protective effect and is capable of significantly lowering the occurrence of gastric ulcers. They concluded that the gastro-protective activity of okra mucilage is due to its alkaline nature, which neutralises the gastric acid and provides a protective coating within the gut wall and digestive tract, which aids in the faster healing of peptic ulcers [10].

2. Albizia gum

Albizia is a genus of about 150 species belonging to Leguminosae and the subfamily Mimosoideae[11]. The gum essentially comprises a leading chain of β (1-3) D galactose units with some β (1-6) linked D galactose units & α (1-3) L arabinose units [11]. The gum exudates from the plant show dark colouration and are imperfectly soluble (in water). Thanzami et al. found that the gum exudates from A. stipulate exhibit specific anti-radical activity. They carried out a reducing power assay and studied that a concentration increment enhanced the reducing capacity of the gum. This indicates the capacity of the albizia gum to terminate the free radical chain reaction. Furthermore, antioxidant activity of albizia gum was confirmed in the form of DPPH activity, test for reducing capacity, hydroxyl scavenging tests & total phenolic content [12].

3. Cashew Gum

The cashew tree (*Anacardium occidentale*), from the family Anacardiaceae, is a source of cashew gum obtained in the form of exudates. The tree is native to tropical America. Cashew gum holds its usefulness from a bygone age in treating various gastrointestinal diseases, including diarrhoea. Cashew gum is obtained as a complex heter-polysaccharide. Previously performed studies have reported that the gum essentially comprises galactose (72-73%), arabinose (4.6-5%), glucose (11-14%), rhamnose (3.2-4%) and glucuronic acid (4.7-6.3%) in weight % [13]. The structural studies reveal that cashew gum mainly comprises 3 types of galactan units in its core, joined by C-1 & C-3, C-1 & C-6 & C-1, C-3 & C-6. Side chain in the structure is constituted of five units long glucose units [14]. Cashew gum has been reported to

have antimicrobial [15], anti-inflammatory [16], antiulcerogenic [17] and antidiarrheal activity. The model used for assessing antidiarrheal activity was the castor oil-induced model of acute diarrhoea for both acute diarrhoea & intestinal motility. The study results demonstrated cashew gum tested significantly well for inhibiting the total quantity of stool (frequency of diarrhoea) [18]. Marques et al. (1992) noted that the cashew gum polysaccharide showed potential inhibitory effects upon the growth of certain bacteria and fungi.

4. Cordia mucilage

Cordia gum is an anionic polysaccharide obtained from the *Cordia myxa* plant belonging to the family Boraginaceae. The genus comprises trees and shrubs that are distributed mainly in warmer regions [19]. There are about 300 species identified worldwide, mainly in the warmer regions. The gum is an arabinogalactan polysaccharide with a backbone of (1/6) – linked D-glucopyranosyl & (1/2) – linked L – arabinofuranosyl residues. Determination of the antibacterial effect of mucilage of *Cordia myxa* was carried out by a suitable diffusion method. They found that the mucilage extract from the fruit part was effective as an antibacterial against gram-negative bacteria isolated from urine samples. The microorganisms used for the experiment were E Coli, Klebsiella pneumoniae and Staphylococcus aureus (urine) [20].

5. Fenugreek mucilage

Fenugreek mucilage is obtained from *Trigonella foenum*, a herbaceous plant belonging to the family Leguminosae. The fenugreek seeds serve as the source containing a high percentage of mucilage. The mucilage forms 28% of the seed constituents [21]. The main component extracted from the seed albumen (endosperm) is a galactomannan. Galactomannans are found to be heterogeneous polysaccharides composed of β- (1-4) D-mannan backbone with a single D-galactose branch linking α-(1-6) units. Boban et al. reported activity of fenugreek mucilage in arthritic conditions. They reported that the polysaccharide mucilage reportedly decreased cell influx, suppresses the release of mediators and reduces oxidative stress related to arthritis [22,23]. Sindhu et al. researched on different doses of mucilage to report its effect on paw oedema formation, on inflammatory mediators and oxidative stress. For this purpose, they utilised the carrageenan-induced arthritic condition in albino rats. Their study revealed the inhibition of oedema formation in a dose-dependent mode. A significant reduction in paw swelling was observed. In a further study, a decrease in 5-lipoxygenase activity upon administration of fenugreek mucilage suggested pronounced inhibition of leukotriene synthesis mediating its anti-inflammatory action. The induced arthritis rats showed a subsequent decrease in total erythrocytes count and haemoglobin concentration but an increase in ESR, which typify anaemic condition representing a classical feature of chronic arthritis patients. They additionally reported that treating with fenugreek mucilage to increase the erythrocyte count, raise the haemoglobin concentration and maintain the Erythrocyte Sedimentation Rate level to almost a near-average value that signifies therapeutic improvement from anaemic condition of chronic arthritis [24].

6. Guar Gum

Guar gum is a dietary fibre extracted from the endosperm of the seeds of Cyamopsis tetragonolobus[25], commonly known as the Indian cluster bean belonging to the family Leguminosae.

When exposed to water, the gum forms a viscous gel and undergoes colonic fermentation to yield short-chain fatty acids. The structural studies reveal that the gum is a galactomannan with a backbone of (1-4),β-D-mannopyranosyl units with every 2nd unit bearing a (1-6), β-D-galactopyranosyl units. Prashant et al. reported in an in vitro study the result of inhibition of α-amylase activity by Guar gum. The study revealed the activity of Guar gum towards amylase inhibition marking its potential as an active antidiabetic agent. Halter of the α-amylase enzyme is appropriate for anti-hyperglycemic activity (for oral administration), interfering with the absorption of glucose and controlling diabetes. Their inhibition assay showed that the action of α-amylase was delayed to digest the carbohydrate and sustained the overall digestion time of carbohydrate, which resulted in a decrease in the postprandial plasma glucose level by reducing the glucose absorption [25]. Guar gum has also been reported to lower the total serum cholesterol by 10-15% and LDL cholesterol by 15-25% without producing any significant change in serum HDL in hypercholesterolaemic animals, diabetic patients and healthy subjects [26]. The ability of Guar gum to affect serum lipids has been reported in animals [27], healthy human subjects [28] and patients with diabetes [29]. The more well-studied hypothesis regarding this study is that Guar gum increases bile acid excretion, thereby diverting cholesterol away from the systemic circulation to the liver [30]. Another report suggests that guar gum may decrease appetite and body weight; therefore, products containing guar gum have been marketed as slimming aids.[31]

7. Locust Bean Gum

Carob tree, *Ceratonia siliqua*, is a flowering tree or shrub of legume family, found abundantly in the Mediterranean regions. The seeds serve as the source of the locust bean gum, which is chemically neutral polysaccharide mainly composed of mannose and galactose monomer units. Several names are also known in the literature, such as Gum carob, Carob bean gum, Carob seed gum, Carob flour, and Ceratonia [32]. Several studies and works have been reported to describe the bioactive potential of the gum. In 1983, the locust bean gum was first reported to possess a hypolipidemic effect, decreasing LDL cholesterol.

Further subsequent studies also confirmed the ability of LBG to be used to control hypercholesterolemia[33-35]. Additionally, it was also shown that gum polymers could significantly decrease the hepatic synthesis of lipids [33]. Some other studies reveal the gum can be potentially used in the treatment of diabetes [36,37].

8. Moi gum

Moi gum is an exudate from the wounds & cracks of *Lannea coromandelica* (Houtt) bark, belonging to family Anacardiaceae. The deciduous tree is known to be common in tropical regions. Moi gum is commonly Jhingan gum or Joel gum, Wodier and Indian ash tree gum. The gum shows yellowish white incision but quickly oxidises to brown colouration & is teared-off from the trees in a round shape. The gum exudates from the plant are reported to be used to treat sprains [38].

9. Moringa gum

Moringa gum is obtained from *Moringa oleifera*, which the mono-generic family, Moringaceae, characterises. The plant is majorly located in tropical and arid countries. It is well known by other names such as Horseradish tree, Ben oil and Drumstick. The

gum is used essentially to treat dental caries and shows astringent, abortifacient and rubefacient properties. The gum as a mixture with sesame oil relieves headaches, fever, intestinal complaints, asthma, syphilis and rheumatism [39].

10. Tamarind seed polysaccharide

Tamarind Seed Polysaccharide is derived from the plant's seeds, *Tamarindus indica*, usually known as the Indian date. The tree is a large evergreen species from the family Fabaceae. It is abundantly found in the dry tracks of central and south Asian states of India and other south Asian countries. Structural findings have revealed that tamarind seed polysaccharide is a non-ionic, neutral, hydrophilic, mucoadhesive and highly branched polysaccharide polymer composed of cellulose like backbone consisting of xylose and galactose substitution at the glucan chain (80%) [40]. Sreelekha et al. reported in their study that tamarind seed polysaccharides possess immunomodulatory activities indicated by phagocytic enhancement and inhibition of cell proliferation effects. When the polysaccharide was added at the time of cell culture initiation, the absence of dividing cells indicates that the polysaccharide has an inhibiting effect on the mitotic activity on phytohemagglutinin-stimulated lymphocytes. They also suggested that the phagocytic enhancement obtained from the polysaccharide from T. indica may be due to the activation of the complement (C3) and initiation of the complement cascade, indicating that the polysaccharide may have properties of zymosan or the lipopolysaccharides and may activate the depressed functions of phagocytes in malignancies, suggesting anti-tumour activity of Tamarind seed polysaccharide. [41].

11. Xanthan gum

Xanthan is an exo-polymer obtained from a gram-negative bacteria, *Xanthomonas campestris*. Xanthan polysaccharide comprises glucose, mannose and glucuronic acid units in a molar ratio of 2:2:1 and contains variable ratios of O-acetyl and pyruvic acid residues responsible for its anionic charge. The xanthan trisaccharides consist of (β-1,4) glucuronic acid and, in the backbone, an attachment between alternative glucose and mannose by linkage of α-1,3. The glucuronic and pyruvic acids inside chains give it an anionic charge. Munir et al. reported that xanthan gum oligosaccharides, which were produced by using enzymes of xanthan degradation, showed hydroxyl radical scavenging ability suggesting that xanthan gum could be a potential natural antioxidant. Their other study showed the biofilm inhibition activity of xanthan gum against E. coli and B. Subtilis. The gum showed high biofilm inhibition activity suggesting its potential to be used as a preservative in the food industry [42]. Xiaolong Hu et al. performed their studies on low molecular weight xanthan gum (LW-XG). They reported that the LW-XG exhibits potentially good free radical scavenging activity & excellent protective effect on the Caco-2 cells injured by H_2O_2, thereby indicating its antioxidant bioactive property[43].

12. Lac

Lac is a protean naturally obtained resin excreted by a scale insect species Laccifer lacca that belongs to the family Laccifer Ideas. The insect essentially sucks on the sap of several plants, majorly thriving on tropical plants widely distributed in South East Asian countries and secrete Lac as their protective covering. The chemical and structural investigations unveiled that the backbone of lac resin is composed of a polyester complex of hydroxy fatty acids in a straight chain unit of the C14-C18 carbon chain, mainly aleuritic acid,

butanoic and threo aleuritic acid. Aisha et al. reported the antifertility activity of lac which they tested in female Wistar rats. They analysed the anti-ovulatory activity on mature female Wistar rats separated into two distinct groups by cyclic administration of lac in a fixed dose of 470 and 800 mg/kg. A significant Lac mediated estrogenic activity was seen to be confirmed by the immature vaginal opening as compared to the control group (received 1 ml of 0.5% CMC), suggesting that lac possesses antifertility activity due to its estrogenic nature [44].

Table 4: Reported pharmaceutical applications of aforementioned gums, mucilages and resins

S. No.	Common Name	Biological Source	Family	Pharmaceutical application	Reference
1	Okra gum	Abelmoschus esculentus L.	Malvaceae	Binder, as hydrophilic matrix for CDDS	Mo. Emeje et al. (2007)
2	Albizia gum	Albizia stipulata	Mimoseae	As tablet binder	Oluwatoyin (2005)
3	Cashew gum	Anacardium occidentale L.	Anacardiaceae	As suspending agent	Pontes (1971), Zakaria and Zainiah (1996)
4	Cordia mucilage	Cordia myxa	Boraginaceae	As enteric resistant and sustained release material	Subas and Biswajit (2009), Mukherjee et al. (2008)
5	Fenugreek Mucilage	Trigonella foenum graecum	Leguminosae	As an emulsifying agent, binder, suspending agent, mucoadhesive preparations.	Garti et al. (1997), Senthil et al. (2011), Nayaka et al. (2013)
6	Guar gum	Cyamopsis tetragonolobus	Leguminosae	As a binder, disintegrant, thickening agent, emulsifying agent, sustained-release agent, and colon targeted drug delivery.	Krishnaiah (2011,2013), Chourasia and Jain (2004), Saleh et al. (2005)
7	Locust Bean Gum	Ceratonia siliqua	Leguminosae	As a thickening agent, stabiliser and controlled release agent.	Xiaohong et al. (2003), Deshmukh et al. (2009)

8	Moi gum	Lannea coromandelica	Anacardiaceae	As a microencapsulating agent, release rate control material.	Amelia et al. (2011)
9	Moringa gum	Moringa oleifera	Moringaceae	As a mucoadhesive agent, binder, disintegrant	Mitul et al. (2012)
10	Tamarind seed polysaccharide	Tamarindus indica	Fabaceae	As a binding agent, emulsifying agent, suspending agent, sustaining agent, mucoadhesive agent and in nasal drug delivery	Kulkarni et al. (1997), Datta and Bandyopadhyay (2006)
11	Xanthan gum	Xanthomonas campestris	Xanthomonadacae	As a suspending agent, emulsifying agent, stabilising agent in toothpaste and ointments, sustaining agent, and buccal drug delivery system.	Dhopeshwar and Zatz (1993), Santos et al. (2005), Vendruscolo et al. (2005), Ganesh et al. (2011)
12	Lac	Laccifer lacca	Laccifer Ideas	Coating tablets and confection sustained-release formulations.	Parimal et al. (2011)

CONCLUSION

Natural products and their structural analogues have historically proven to be a significant contributor to pharmacotherapy. They are being used as excipients; they offer certain advantages over their synthetic analogues in possessing biodegradability, ease of availability, non-toxicity and cost-effectiveness. Advancement in isolation, characterisation and optimisation technologies have inclined more towards using natural products, especially gums, resins, and mucilage, as potent bioactive compounds leading to intensive research in phytopharmaceuticals, consequently revitalising their use as drug leads.

Further research in their phytochemical analysis, characterisation and pharmacological investigations can focus on the success of these naturally available resources to aid in drug discovery and develop comparatively more robust methods of identifying viable lead compounds. A better knowledge of physicochemical characteristics & establishing detailed safety profile data can attract pharmaceutical companies to unveil the concealed therapeutic potential of these compounds for novel pharmaceutical applications.

CONFLICT OF INTEREST

Authors don't have any conflict of interest

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