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Potential for Biomedical Applications of Galactomannans and Xyloglucans from Seeds: An Overview

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Abstract

Galactomannans and xyloglucans can be isolated from seeds with relatively high purity and yield; they are water soluble, non-toxic, and biocompatible. These polymers have broad spectra of potential use in medicine, from drug delivery systems to biological response modifiers. The biological activity of polysaccharides is intrinsically linked to their structural aspects. In general the chemical modification of galactomannans and xyloglucans, e.g., sulfation and complexation with oxovanadium, potentiate effects such as cytotoxicity against tumor cells, leishmanicidal activity, and activation of macrophages to release proinflammatory mediators. The wide range of seeds and structural variety favor the isolation of galactomannans and xyloglucans. This allows derivatives to be obtained with targeted properties and activity enabling their use in new applications in the biomedical area.

Keywords: Galactomannans; Xyloglucans; Seeds

Introduction

Seeds play a central role in plant reproduction and human nutrition. A seed contains all the genetic material and nutrients required for the successful propagation of the species. After germination, the reserve material is mobilized to sustain the plantlet before it becomes a self-sufficient autotrophic organism [1,2].

Storage compounds can account for up to 90% of the seed's dry weight and they are usually responsible for the economic value of seeds [1,2]. The main storage compounds accumulated in seeds consist of starch, triacylglycerols, and proteins [1]. Although starch is the most abundant storage carbohydrate, some seeds produce other polysaccharides, which are categorized as reserve compounds [3]. The best studied polysaccharides of this group are galactomannans and xyloglucans. The main reason is the interest due to the economic importance of these polymers, which can be used as thickening and stabilizing agents in the industry [3,4]. In addition, as galactomannans and xyloglucans can be isolated from seeds with relatively high purity and yield, are water soluble, non-toxic, and biocompatible, they are also suited for biological applications [5-10].

Galactomannans

Galactomannans are linear chains of β(1→4) D-mannosyl units, which are substituted by single α(1→6) linked D-galactopyranosyl residues as side chains. They are usually found in the endosperm of leguminous seeds and the Man/Gal ratio is species specific, typically ranging from 1.1 to 5.0 [3,4,11]. The yield of galactomannan can reach up to 38% of the seed weight [11]. It has been pointed out that more than 70 species of the family *Leguminosae* have been identified storing galactomannans [11]. The Man/Gal ratio and the distribution of the galactose units along the main chain strongly affect the functionalities of galactomannans [4]. On the other hand, the relation between Man/Gal ratio and the biological function of galactomannans has not been established yet [4]. Guar (*Cyamopsis tetragonolobus*) and locust bean (*Ceratonia siliqua*) are the main sources of commercial galactomannans, which have Man/Gal ratios of 4:1 and 2:1, respectively. However, several other species have been described to contain galactomannans [11]. Among the alternative sources of galactomannans, *Schizolobium amazonicum* and *Mimosa scabrella* seeds have been investigated [3,12].

Regarding the biomedical area, galactomannans have broad spectra of applications, from potential drug delivery systems to biological response modifiers (BRMs) [7,13-18]. The latter ability enables some galactomannans to be used as immunomodulators [17,18]. Since galactomannans are heterogeneous and polydisperse polymers [19-21], several studies indicate that applications and effects of galactomannans are intrinsically linked to structural features of the polymers [4]. For example, matrix tablets of galactomannan from *Senna tora* seeds showed better ability for sustained release potential of losartan potassium when compared to the matrix tablets from other galactomannans, such as that prepared with guar gum [4]. In this regard, chemical modification of galactomannans can be used to improve specific applications [22-27]. Galactomannans extracted from *Mimosa scabrella* and *Leucaena leucocephala* seeds, after sulfation protected against infection by flavivirus [23]. Chrestaniet al. [28] also observed antiviral (antiherpectic and antirotavirus) effects by sulfated galactomannan from *M. scabrella*. Galactomannans from *L. leucacephala* seeds and their chemically sulfated derivative, both at the same concentration, were cytotoxic to HepG2 cells and decreased their viability by ~30% and 50%, respectively [24]. Chemically sulfated galactomannan from *Dimorphandra gardneriana* seed was cytotoxic to Vero cells while its unmodified form did not exhibit any effect [25] and the galactomannan from *Senna macranthera* showed strong anticoagulant activity after sulfation [26].

Galactomannans and their derivatives oxovanadium (IV/V)-complexes were evaluated for cytotoxicity against tumor cell lines [29], immunomodulation, and leishmanicidal activities [26]. Native galactomannans (GALMAN-A) isolated from seeds of *M. scabrella* and its enzymatically hydrolyzed form (GALMAN-B), as well as their oxovanadium(IV/V) complexes designated GALMAN-A:VO^{2+}/VO^{3+} and GALMANB:VO^{2+}/VO^{3+}, respectively, were evaluated in HeLa

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cells [29]. Only the complexed forms promoted cytotoxicity against this cell line and GALMAN-B:VO^{2+}/VO^{3+} was ~3-fold more potent than GALMAN-A:VO^{2+}/VO^{3+}. In another study, GALMAN-A and GALMAN-A:VO^{2+}/VO^{3+} preparations modulated macrophages at different intensities to produce pro-inflammatory mediators [27]. The uncomplexed form increased nitric oxide production by ~33% compared to control, while GALMAN-A:VO^{2+}/VO^{3+} inhibited it. On the other hand, the complexed form increased interleukin-1 beta (IL-1β) and interleukin-6 (IL-6) by 45% and 139%, respectively, compared to GALMAN-A. Both preparations, i.e., GALMAN-A and GALMAN-A:VO^{2+}/VO^{3+}, exhibited leishmanicidal activity against amastigotes of *Leishmania (L.) amazonensis* and reached ~60% toxicity. However, GALMAN-A:VO^{2+}/VO^{3+} promoted this effect at a four-fold lower concentration than the uncomplexed form. In addition, GALMAN-A and its oxovanadium were three and 12 times more potent, respectively, than Glucantime (300 μg/mL), the main drug used in leishmaniasis treatment. Together, these data indicate that the suitable chemical modification contributes to potentiate the effect of galactomannans.

Xyloglucans

Storage xyloglucans consist of a cellulose-like backbone carrying single α-D-xylopyranosyl units attached to *O*-6, while some xylosyl residues were further substituted at O-2 by β-D-galactopyranosyl units. They are found in the cotyledons of some leguminous seeds [4]. The content of xyloglucan can reach up to 45% of the seed [6]. The only commercial source is *Tamarindus indica* (tamarind). Other leguminous seeds which were described to contain xyloglucans include *Copaifera langsdorffii*, *Hymenaea courbaril*, and *Mucuna sloanei* [6,30]. Xyloglucans from different sources can differ regarding side chain distribution patterns [6].

Xyloglucans possess broad spectra of application in textile, cosmetic, nutritional, and pharmaceutical industries [31]. Regarding the biomedical area, the main use of xyloglucans is in the preparation of formulations for drug delivery system [32-34] due to their capacity to form thermoreversible gels. When galactose units from xyloglucan are partially removed by enzymatic treatment, the modified polymer exhibits thermoreversible gelation in dilute aqueous solutions [35-37]. Due to the relatively low transition temperature of the gels, it is also used in formulations to sustain viscosity and improve application [38]. Tamarind xyloglucan hydrogel scaffolds have also been investigated for neural tissue engineering of the spinal cord [39]. The xyloglucan from *T. indica* seeds is the best studied [40], either in its native or chemically modified forms [41]. As observed for galactomannan, different biological effects of xyloglucans can be achieved by chemical or enzymatic modification of the native polymers. Some biochemical parameters, such as reduction of plasma lipids [42] and inhibition of D-glucose absorption in rats [43], have been observed for oligosaccharides obtained by partial hydrolysis of tamarind xyloglucan. These findings favor their use in formulations as antiobesity agents [31]. Xyloglucan from *T. indica* with different degrees of sulfation exhibited antiviral activity [44].

Tamarind xyloglucan was used by Bodin et al. [45] to modify cellulose to increase the adhesion of human endothelial cells to tissue while engineering blood vessels. Cao and Ikeda [46] observed that xyloglucan selenious ester and sulfated xyloglucan from *Tamarindus indica* were active against oxidative damage and tumors. According to those authors, the selenious derivative was more potent than the sulfated one.

Studies with xyloglucans from other seeds have been reported. Xyloglucan from *Tropaeolum majus* seeds inhibited the effect of the carcinogen 1-nitropyrene [47]. This effect opens possibilities to add the polymer to food as an antimutagenic agent. Xyloglucans from *C. langsdorffii* (XGC), *H. courbaril* (XGJ), and *M. sloanei* (XGM) seeds were evaluated for their biological response modifier capacity [48]. All three xyloglucans increased the number of macrophages in the peritoneal cavity and XGC was 3.3-fold more potent than XGJ to activate macrophages for nitric oxide production. In another study, XGC, XGJ, and xyloglucans from *Tamarindus indica* (XGT) stimulated mouse peritoneal macrophages to produce IL-1β, IL-6, and tumor necrosis factor alpha (TNF-α), except for XGC, which did not stimulate IL-6 production [49].

Amaral et al. [27] showed that XGJ, as well as its oxovanadium (IV/V) complex (XGJ:VO), exhibits important leishmanicidal effects. XGJ reduced growth of *Leishmania (L.) amazonensis* by 59% compared to the control, while XGJ:VO had a similar effect at 5-fold lower concentration. Additionally, XGJ:VO also increased IL-1β and IL-6 levels by macrophages after the incubation of cells with the complex. Those studies clearly show that the intensity of effects is different for each polymer preparation.

Data from the literature demonstrates that xyloglucans from different seeds can exhibit different biological effects due to differences in the fine structure of polymers. In addition, new biological effects can be achieved by xyloglucan modifications.

Conclusions and Perspectives

This minireview shows that galactomannans and xyloglucans from seeds can be readily obtained and possess a wide variety of characteristics, from proper physical chemistry properties that enable them to be used as vehicle to drugs to the ability to modify biological responses. Given the broad range of seeds, these polymers can be obtained at higher amounts to be used in broad spectra of applications.

Immunomodulation is used to improve health by preventing and treating many diseases. In recent years, it has been demonstrated that the cure of leishmaniasis can be reached by activating the immune system. Thus, it can be suggested that many activities exhibited by galactomannans and xyloglucans from seeds, such as ability to form gels and their immunomodulating potential, enable them to be used in formulations for topical use in the treatment of diseases such as cutaneous leishmaniasis since local applications can contribute to treatment efficacy. This possibility is in progress in our group.

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