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Review

Chemical features of *Ganoderma* polysaccharides with antioxidant, antitumor and antimicrobial activities

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ABSTRACT

Ganoderma genus comprises one of the most commonly studied species worldwide, *Ganoderma lucidum*. However, other *Ganoderma* species have been also reported as important sources of bioactive compounds. Polysaccharides are important contributors to the medicinal properties reported for *Ganoderma* species, as demonstrated by the numerous publications, including reviews, on this matter. Yet, what are the chemical features of *Ganoderma* polysaccharides that have bioactivity? In the present manuscript, the chemical features of *Ganoderma* polysaccharides with reported antioxidant, antitumor and antimicrobial activities (the most studied worldwide) are analyzed in detail. The composition of sugars (homo- *versus* hetero-glucans and other polysaccharides), type of glycosidic linkages, branching patterns, and linkage to proteins are discussed. Methods for extraction, isolation and identification are evaluated and, finally, the bioactivity of polysaccharidic extracts and purified compounds are discussed. The integration of data allows deduction of structure–activity relationships and gives clues to the chemical aspects involved in *Ganoderma* bioactivity.

Contents

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1. Introduction

Ganoderma is a genus of polypore macrofungi growing in decaying logs or tree stumps (Kirk et al., 2011). Commonly known as Lingzhi, *Ganoderma* comprises the most studied species of medicinal mushrooms in the world. In ancient China, Lingzhi was believed to bring longevity, due to its mysterious power of healing the body and calming the mind (Huie and Di, 2004).

1.1. Bioactivity of Ganoderma

The above mentioned genus has been widely studied regarding its bioactive properties (Paterson, 2006; Nie et al., 2013), including antibacterial, antioxidant, antitumor and other effects (Wang et al., 1997; Wasser, 2002; Heleno et al., 2012, 2013; Li et al., 2012; Popović et al., 2013; Zhonghui et al., 2013). The beneficial health properties of *Ganoderma* species are attributed to a wide variety of bioactive components, such as polysaccharides, triterpenes, sterols, lectins and other proteins (Wang et al., 2002; Ferreira et al., 2010).

Different kinds of bioactive polysaccharides have been extracted and isolated from the fruiting bodies of different *Ganoderma* species (Liu et al., 2010; Ma et al., 2013; Shi et al., 2013), and represent a structurally diverse class of biological macromolecules with a wide-range of physiological properties. The major bioactive *Ganoderma* polysaccharides are composed of (1→3), (1→6)-α/β-glucans, glycoproteins and water soluble heteropolysaccharides (Nie et al., 2013) with glucose, mannose, galactose, fucose, xylose and arabinose combined in different proportions and types of glycosidic linkages, as well as peptide bonds (Chen et al., 2008; Wang and Zhang, 2009). As polysaccharides are very complex molecules, their detailed characterization in terms of specific glycosidic linkages, molecular weight and sugars composition is mandatory in order to establish structure-biological activity relationships. Nevertheless most of the articles available in the literature do not report these parameters, which is a drawback in the understanding of the most crucial chemical features for polysaccharides bioactive properties such as antioxidant, antitumor and antimicrobial activities.

1.2. Bioactivity of Ganoderma polysaccharides

Most of the studies on bioactivities of polysaccharides, glycopeptides or polysaccharidic crude extracts have been performed using *Ganoderma lucidum* (Nie et al., 2013). This species has been under special attention because of the potent antioxidant, antitumor and antibacterial activities of the polysaccharides, glycoproteins and polysaccharidic extracts obtained from the fruiting bodies (Jia et al., 2009; XiaoPing et al., 2009; Shi et al., 2013).

Antioxidant properties include free radicals scavenging abilities, reducing power and chelating effects on ferrous ions, among others (Liu et al., 2010; Kozarski et al., 2011). The radicals scavenging activity seems to be related to an increase in the activity of antioxidant enzymes: superoxide dismutase (SOD) which catalyzes dismutation of superoxide anion to hydrogen peroxide; catalase (CAT) which detoxifies hydrogen peroxide and converts lipid hydroperoxides to nontoxic substances; and glutathione peroxidase (GSH-Px) which maintains the levels of reduced glutathione (GSH) (YouGuo et al., 2009; XiaoPing et al., 2009).

Antitumor polysaccharides exert their bioactivity mostly *via* activation of the immune response of the host, enhancing the host's defense system (Mizuno et al., 1995b). The antitumor properties of water-soluble polysaccharide-enriched fractions from the fruiting bodies of *G. lucidum* seem to be related to the production stimulation of interleukin (IL)-1β, tumor necrosis factor (TNF)-α, IL-6 from human monocyte-macrophages, and interferon (IFN)-γ from T lymphocytes (Wang et al., 1997).

There are only a few reports on antimicrobial activities of polysaccharides from *Ganoderma* species. This genus has been widely studied for its therapeutic properties, but less investigated as a source of new antibacterial agents (Gao et al., 2003a). Nevertheless, some polysaccharides from *Ganoderma* species exert antibacterial activity by inhibiting the growth of bacteria and, in some cases, by killing pathogenic bacteria (Skalicka-Woźniak et al., 2012).

Although being very active as antioxidants and antimicrobials, *Ganoderma* polysaccharides are mostly known as antitumor agents; however, the mechanisms of action involved in their bioactivities are not well understood. Furthermore, most of the studies are performed under *in vitro* conditions, with very few experiments using *in vivo* assays.

This review aims to contribute to the knowledge of bioactivity (mainly antioxidant, antitumor and antimicrobial properties) of polysaccharides, glycoproteins and polysaccharidic extracts obtained from *Ganoderma* species. The most common extraction and isolation procedures are presented, including their chemical features. This includes discussion of monosaccharides' composition, type of glycosidic linkages, branching patterns and linkages to proteins, with these features being related to the corresponding bioactivities.

2. Extraction, isolation and identification of *Ganoderma* polysaccharides

2.1. Chemical features of the most common polysaccharides found in Ganoderma

According to different researchers, the polysaccharides isolated from *Ganoderma* are constituted by glucose, mannose, galactose, fucose, xylose and arabinose, with different combinations and different types of glycosidic linkages, and which can be bound to protein or peptide residues (polysaccharide-protein or -peptide complexes) (Sone et al., 1985; Zhang et al., 2007; Chen et al., 2008; Wang and Zhang, 2009; Ferreira et al., 2010; Nie et al., 2013). These carbohydrates are characterized by their molecular weight, degree of branching, and higher (tertiary) structures (Ferreira et al., 2010), and have different compositions, comprising β-glucans, hetero-β-glucans, heteroglycans or α-manno-β-glucan complexes (Moradali et al., 2007).

Homo-glucans are linear or branched biopolymers having a backbone composed of α- or β-linked glucose units (such as (1→3), (1→6)-β-glucans and (1→3)-α-glucans), and might contain