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# The gastrointestinal behavior of saponins and its significance for their bioavailability and bioactivities

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ABSTRACT

Saponins are bioactive compounds of increasing interest. The events that take place during digestion are highly related to their bioactivities, because saponins are poorly absorbed and have a long residence time in the intestinal tract. The poor bioavailability of saponins is explained by a sum of factors, but the more favorable properties of sapogenins result in higher bioavailability and bioactivity. The gastric and colonic transformations of saponins are relevant in the release of sapogenins. Saponins inhibit enzymes and cholesterol absorption, but specific chemical structures of saponins are relevant for an efficient activity. Finally, the recent research has pointed to saponins as "prebiotic-like" compounds. This review summarizes the current knowledge on the events that take place during digestion of saponins and sapogenins related to their bioactivities, with special emphasis on the factors that modulate their bioavailability, bioaccessibility, inhibition of digestive enzymes and cholesterol absorption, and the importance of the microbiota-saponins relationship.

## 1. Introduction

Saponins are a group of natural glycosidic compounds widely distributed in plants, which consist of a hydrophobic aglycone, designated as sapogenin, linked to one or more hydrophilic sugar moieties through an ether or ester glycosidic linkage, at one or two glycosylation sites (Güçlü-Üstündağ & Mazza, 2007). The structural complexity of saponins arises from variability in sapogenin structure, the nature of attached side chains, and the attachment positions of sugar moieties to the sapogenin. According to the chemical structure of the sapogenin, saponins can be classified into steroidal or triterpenoid saponins. Steroidal saponins consist mainly of a C27 spirostane skeleton, generally comprising a six-ring structure, or a furostane skeleton, which is pentacyclic. Triterpenoid saponins consist mainly of a C30 pentacyclic skeleton, commonly as oleanane and ursane structures, or C30 tetracyclic skeleton, as dammarane structure (Sparg, Light, & van Staden, 2004). Furthermore, there are two main types of triterpenoid saponins: neutral, when a typical sugar is attached to sapogenin, and acidic, when the sugar moiety contains uronic acid or one or more carboxylic groups attached to the sapogenin (Lásztity, Hidvégi, & Bata, 1998). Additionally, saponins can be categorized in terms of the number of sugar chains present as monodesmosidic, bidesmosidic, or tridesmosidic (Güçlü-Üstündağ & Mazza, 2007). Monodesmosides are formed by one sugar chain, normally attached through an ether linkage at C-3. In bidesmosides a second sugar chain is attached through an ester linkage at C-28 (in triterpene saponins) or an ether linkage at C-26 (in furastanol saponins). The most common monosaccharides that can be found attached are hexoses (glucose, galactose, fructose), uronic acids (glucuronic acid, galacturonic acid), 6-deoxyhexoses (rhamnose), and pentoses (arabinose, xylose) (Güçlü-Üstündağ & Mazza, 2007; Kharkwal, 2012).

Some examples of saponins and sapogenins that can be frequently found and that will be mentioned in different sections of the current review are illustrated in Fig. 1.

Saponins are ubiquitous phytochemicals widely reported in many species of plants and some marine animals (Sparg et al., 2004; Van Dyck, Gerbaux, & Flammang, 2010; Vincken, Heng, de Groot, & Gruppen, 2007). These compounds have been isolated from different parts of the plants, including the roots, rhizomes, stems, bark, leaves, seeds and fruits. Saponins are plant-derived secondary metabolites found in more than 100 families of both wild and cultivated plants, belonging to the division of Magnoliophyta, in which two major classes

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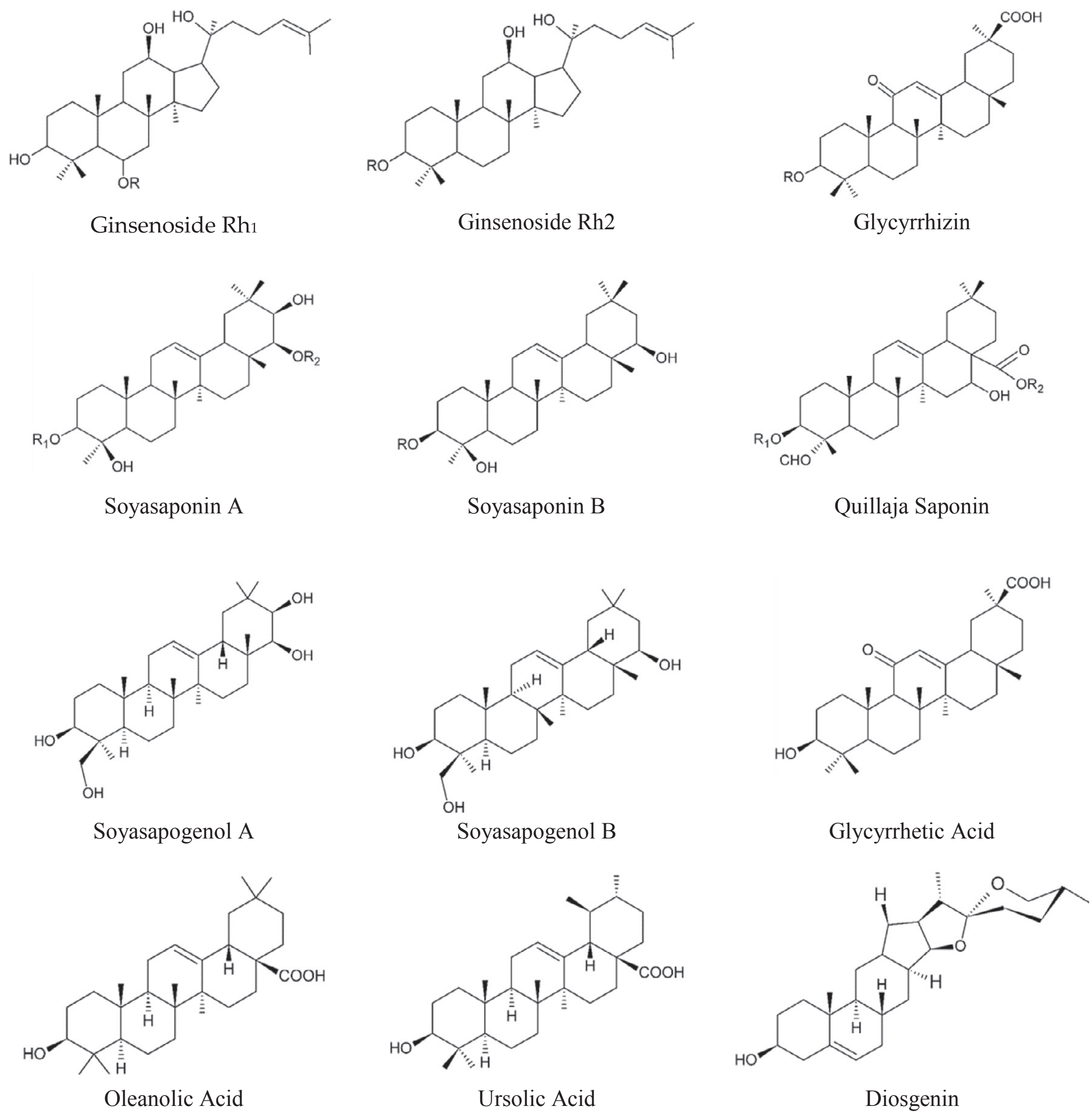


**Fig. 1.** Chemical structure of typical saponins and sapogenins. "R" refers to the glycoside moiety.

can be found: Liliopsida and Magnoliopsida, where the majority of saponins producing species are found (Vincken et al., 2007). In general, the triterpenoid saponins are mostly found in cultivated crops, while steroid saponins are common in medicinal plants (Fenwick, Price, Tsukamoto, & Okubo, 1991; Moses, Papadopoulou, & Osbourn, 2014). Thus, triterpenoid saponins can be found in many legumes (alfalfa, soybean, chickpeas, beans, peanuts, broad beans, kidney beans and lentils), ginseng roots, sunflower seeds, horse chestnut, liquorice roots, spinach leaves, tea leaves, quillaja bark, quinoa seeds, sugar beet or alliums species. Examples of steroidal saponins are those found in oats, yucca, tomato seeds, yam, fenugreek seeds, ginseng roots, asparagus, aubergine or capsicum peppers.

Despite they have traditionally been considered anti-nutrients, there is a current interest on saponins due to the increasing number of studies showing their bioactive properties. In general, saponins have been related to immunostimulatory, hypocholesterolemic, antitumor, anti- inflammatory, antibacterial, antiviral, antifungal, and antiparasitic activities (Francis, Kerem, Makkar, & Becker, 2002; Rao & Gurfinkel, 2000; Sparg et al., 2004). However, although it is clear that saponins have a diverse range of biological activities, very little is known about the mode of action of these compounds. The ability of saponins to complex with sterols and cause membrane permeabilisation is well known and several activities have been attributed to these membrane-permeabilizing properties (Hostettmann & Marston, 1995). However, it is becoming increasingly clear that these molecules can also have other effects on cells that are mediated through specific interactions with metabolic processes, cellular receptors and structural proteins (Siu et al., 2008; Wang et al., 2013; Weng, Bachran, Fuchs, & Melzig, 2008). For more detailed information about the bioactive properties of saponins and suggested mechanisms, the following recent reviews are recommended to the reader (Liu, Yu, Liu, Shu, & Huang, 2015; Marrelli, Conforti, Araniti, & Statti, 2016; Tian et al., 2013; Xu et al., 2016).

Regardless of the specific mechanism, it is important to remark that the events that take place during digestion are highly related to the bioactivities of saponins. This is because most studies have suggested that saponins are poorly absorbed, therefore their residence time within the gastrointestinal lumen causes important bioactive events (Gao, Basu, Yang, Deb, & Hu, 2012; Li, Mu, & Zheng, 2013). One of the most studied activities is the hypocholesterolemic action, and despite several mechanisms have been proposed, the interaction with cholesterol absorption at intestinal lumen is well known (Vinarova, Vinarov, Atanasov, et al., 2015; Zhao, 2016). Additionally, some studies have