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Pharmaceutical, nutritional, and cosmetic potentials of saponins and their derivatives

Maral Maghsoudloo[1*], Razieh Bagheri Shahzadeh Aliakbari[2], Zeinab Jabbari Velisdeh[3]

[1]*Institute for Micromanufacturing, Louisiana Tech University, Ruston, Louisiana, 71272, USA*

[2]*College of Applied and Natural Sciences, Louisiana Tech University, Ruston, Louisiana, 71272, USA*

[3]*College of Applied and Natural Sciences, Louisiana, Tech University, Ruston, Louisiana, 71272, USA*

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ABSTRACT

Saponins as glycoside type of pentacyclic triterpenoids comprising an aglycone (triterpenoid component) and glycone (sugar moiety) are acknowledged phytochemicals with various pharmaceutical and nutritional activities as natural additives in food and cosmetic sections. These amphiphilic molecules and their derivatives have shown numerous therapeutic and nutritional benefits. Antioxidant, anticancer, hypoglycaemic, hypolipidemic, anti-asthmatic, and antimicrobial effects have been found for saponins and their derivatives such as furostanol saponin as the main therapeutic potential along with low cytotoxicity. In the case of the nanotechnology aspect, these emulsifiers are significantly employed to stabilize and produce nanoemulsions. However, the bioavailability and stability of these glycoside metabolites are affected by the processing method owing to the changes between the linkages of glycone chains and aglycones. Organic nanomaterials such as lipidic and polymeric nanomaterials may be promising nanocarriers for increasing the bioavailability and stability of saponins, we have reviewed recent findings about this issue focusing on cosmetic, nutritional, and pharmaceutical potentials.

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1.Introduction

There are three main types of pentacyclic triterpenoids including lupine, oleanane, and ursane [1, 2]. Saponins ($C_{27}H_{42}O_3$) as a glycoside type of pentacyclic triterpenoids (Figure 1) are acknowledged phytochemicals with various pharmaceutical, nutritional, and cosmetic potentials [3]. Saponins or glycoconjugates are plant triterpenoid metabolites with amphiphilic molecules having carbohydrate and either steroid aglycone or triterpenoid components with several multiple biological activities [4]. In this regard, synthetic saponin production is indispensable because of the augmented demand for more saponins in three sections of pharmaceutical, nutritional, and cosmetic products [5, 6]. In the nanotechnology field, saponins are significantly employed to stabilize and produce nanoemulsions (kinetically stable colloidal system of immiscible liquid-liquid dispersion with droplet sizes of about 100 nm). The electronegativity and interfacial tension of the nanoemulsions are augmented and decreased, respectively by saponins [7]. As the main limitations, the bioavailability and stability of saponins and their derivatives are reduced via the processing method due to the changes between the linkages of glycone chains and aglycones [3, 8]. In some marine and about 100 families of plant sources, saponins can be extracted for industrial production. Quillaja, yucca, ginseng, tea, glycyrrhizin, red beet, and oat bran have been found as natural sources of saponins [7]. According to their carbon skeletons, 11 main classes of saponins including steroids, cucurbitanes, lanostanes, cycloartanes, ursanes, oleananes, hopanes, lupanes, tirucallanes, dammaranes, and taraxasteranes [9]. Suitable micro and nanoformulations are needed to reduce the low absorption and bitter taste as the main limitations for the clinical and nutraceutical applications of saponins [3, 10]. In the present mini-review, the major pharmaceutical, nutritional, and cosmetic potential of saponins and their derivatives have been addressed by considering both micro and nano aspects.

*Corresponding author. E-mail: mma079@email.latech.edu

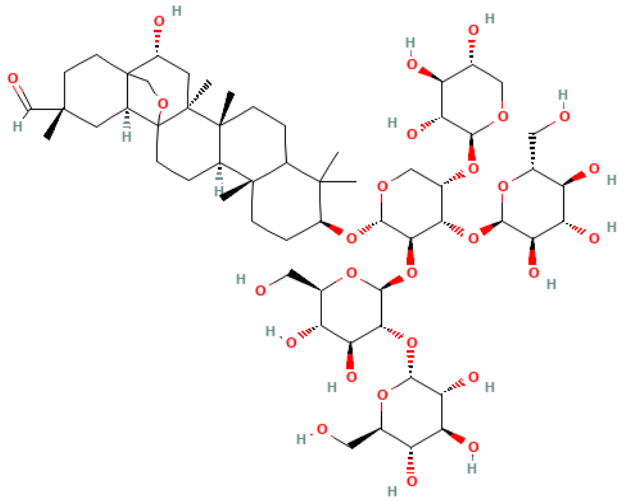

Fig. 1. Chemical structure of saponin (Source: PubChem database).

2. Pharmaceutical potentials

Multiple therapeutic effects comprising anti-inflammatory, antioxidant, anti-neurodegenerative, anticancer, immunomodulatory, antibacterial, antileishmanial, antiviral effects, and the capacity to hinder α-glucosidase have been reported for saponins [11].

2.1. Antioxidant activity

Antioxidant activity holds a pivotal role in safeguarding our cells and tissues against the deleterious effects of free radicals, which are harmful molecules that can cause cellular damage. By counteracting these free radicals, antioxidants assume a crucial function in preserving our overall well-being and mitigating the risk of various chronic diseases. The broader literature has extensively explored the impact of different antioxidants, with notable investigations highlighting the potential of herbal compounds as antioxidant agents. Antioxidant activity is crucial because it helps protect our cells and tissues from damage caused by harmful molecules called free radicals [12-14]. By neutralizing these free radicals, antioxidants play a vital role in maintaining our overall health and reducing the risk of various chronic diseases [15]. Saponins, a diverse group of plant secondary metabolites, have emerged as promising candidates for pharmaceutical development due to their multifaceted bioactivities. Among their noteworthy attributes, their potent antioxidant activity stands out prominently. Saponins possess significant free radical scavenging capabilities, which can help mitigate oxidative stress and its associated pathologies. Oxidative stress is a key factor in the development of numerous chronic diseases, including cancer, cardiovascular diseases, and neurodegenerative disorders. Saponins, through their antioxidant properties, can neutralize reactive oxygen species (ROS) and prevent cellular damage. For instance, Total saponin and crude extracts of *Chlorophytum borivilianum* were found to have the chelating activities as values of 36.5% and 2.4% at 0.5 mg/mL concentration and 72.2% and 30% at a concentration of 2.5 mg/mL, respectively [16]. These findings highlight the potential of saponins in effectively combating oxidative stress by chelating metal ions that contribute to ROS formation. Moreover, recent studies have elucidated the mechanisms behind saponin-mediated antioxidant effects, including the activation of endogenous antioxidant enzymes and modulation of intracellular signaling pathways. These findings underscore the potential of saponins as valuable agents in the prevention and treatment of oxidative stress-related diseases.

2.2. Anticancer activity

Saponins have exhibited notable anticancer activity, making them an intriguing focus in pharmaceutical research. Their multifaceted mechanisms of action include inducing apoptosis, halting cell cycle progression, inhibiting angiogenesis, and modulating various signaling pathways crucial for cancer cell growth and survival. Additionally, their low toxicity to normal cells and ability to enhance the efficacy of conventional cancer therapies, such as chemotherapy, make them promising candidates for further exploration in the quest to combat cancer. The development of a point-of-care microfluidic device for acoustic blood cell separation can enhance the delivery and precision of potential anticancer therapies by ensuring efficient isolation of therapeutic agents and cancer cells from blood samples [17, 18], further emphasizing the evolving role of saponins in advancing cancer treatment strategies. Lutein's potent antioxidant properties and its ability to modulate critical signaling pathways, when combined with saponins, offer a promising synergy in suppressing cancer cell growth and survival [19]. Many signaling pathways such as protein kinase B (PKB or AKT) /mitogen-activated protein kinase (MAPK), phosphatidylinositol 3-kinase (PI3K)/AKT, PI3K/AKT/mammalian target of rapamycin (mTOR), ring finger protein 6 (RNF6)/AKT/mTOR, and the epidermal growth factor receptor (EGFR)/PI3K/AKT pathways are inhibited by these amphipathic glycosides [20]. According to *in vitro* results, the isolation of the novel furostanol saponins from the roots of *Asparagus cochinchinensis* inhibited the proliferation of lung adenocarcinoma (H1299) and human liver (MHCC97H) cancer cells [21].

2.3. Antimicrobial activity

Saponins with detergent-like features can augment the permeability of bacterial cell membranes and influx antibiotics through the bacterial cell wall membrane [22]. The isolation of several furostanol saponins from the roots of *A. cochinchinensis* had antifungal and antibacterial activities against *Candida albicans* (ATCC 2091), *Bacillus subtilis* (ATCC 6633), and *Staphylococcus aureus* (ATCC 4330) strains [21]. In a comparative study, the antimicrobial of *Catharanthus roseus* root extract was evaluated compared to aqueous and saponin-enriched fractions. In a concentration of 4 mg/mL, *Escherichia coli* showed 7 and 8.5 mm diameter of inhibition zone under root extract and saponin-enriched fraction, respectively. Moreover, minimum inhibitory concentrations (MICs) for *Candida albicans* were >10, 2.125, and >10 upon the effect of root extract, saponin-enriched extract, and aqueous extract, sequentially [23]. Six different saponins have been isolated and identified from *Chenopodium quinoa* Willd. (Quinoa) by column chromatography and high-performance liquid chromatography (HPLC)/mass spectrometry (MS)/nuclear magnetic resonance (NMR), respectively. The MIC and minimum bactericidal concentration (MBC) values of 0.125 and 0.25 mg/mL were found for these quinoa saponins compared to penicillin antibiotic with 0.0625 and 0.125 mg/mL, respectively. The major antibacterial mechanisms for these saponins were damage of the bacterial cell wall, and disruption of the cytoplasmic membrane followed by leakage of the bacterial macromolecules [24].

3. Nutritional potentials

Saponin, specifically Quillaja saponins and saponin glycyrrhizic acid, as bio-surfactants have obtained great interest because of their appropriate interfacial properties for the formation and stabilization of multiphase systems such as foams and emulsions [25]. Development of obesity is one the main causes of cardiovascular diseases and chronic metabolic diseases such as type 2 diabetes (Figure 2) [26]. Dietary saponins are regarded as anti-nutrients. However, according to *in vitro* results, dietary saponins can hinder the function of pancreatic lipase and fatty liver formation. In addition, dietary saponins can significantly influence the synthesis of lipids by accelerating the fecal excretion of triglycerides and bile acids, blocking intestinal absorption of lipids, and hindering adipogenesis [27].

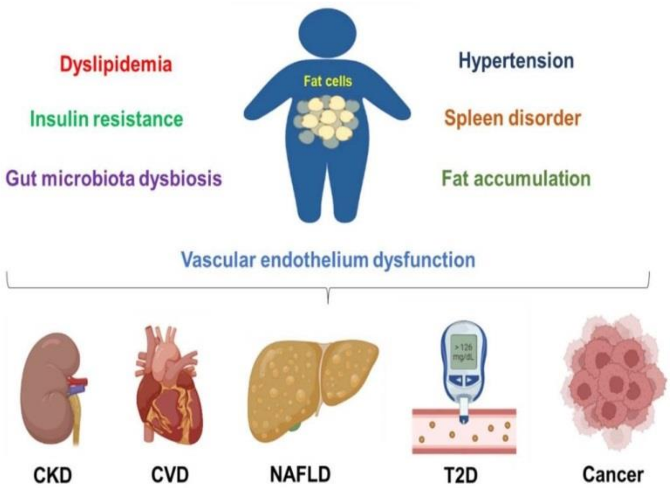

Fig. 2. Obesity can cause chronic diseases including cancers, type 2 diabetes (T2D), non-alcoholic fatty liver disease (NAFLD), cardiovascular diseases (CVDs), and chronic kidney disease (CKD) (Adapted and modified from [26]).

4. Cosmetic potentials

Saponins, natural compounds found in various plant sources, are increasingly gaining recognition for their substantial cosmetic potential. These versatile molecules possess a range of properties that can benefit skincare and cosmetic formulations. Saponins have been found to exhibit gentle cleansing properties, making them suitable as natural surfactants in cleansers, shampoos, and body washes. Their ability to create a rich, stable foam without causing skin irritation or stripping natural oils is particularly appealing for mild yet effective cleansing [28]. Additionally, saponins have demonstrated anti-inflammatory and antioxidant properties, which can help soothe and protect the skin from environmental stressors, potentially reducing signs of premature aging. Moreover, their natural emulsifying capabilities can aid in stabilizing and improving the texture of cosmetic products, such as creams and lotions. As the demand for natural and sustainable cosmetic ingredients grows, glycyrrhizic acid as a triterpenoid saponin glycoside has been employed in the formulations of skincare and beauty products, offering consumers effective and eco-friendly alternatives for maintaining healthy and radiant skin. In this regard, inhibition of MMP1 activation via regulation NF-κB signaling has been reported as the main therapeutic activity of glycyrrhizic acid [29]. Acne vulgaris is a chronic skin disorder that can result from an overload of *Propionibacterium acnes* that resides at the surface and within hair follicles of the skin is the leading cause of inflamed lesions such as papules, nodules, and pustules on the skin [30]. The saponin fraction and the fermentation liquid-based water extract of *Sapindus mukorossi Gaertn* exhibited a prominent antibacterial effect on *P. acnes* ATCC 6919 with the MIC of 0.06 mg/mL and 2.0 mg/mL, respectively [31].

5. Conclusions

The bioavailability and stability of saponins depend on the structures of glycone and aglycone molecules, which can be affected via the processing methods. Many singling pathways such as PKB/MAPK, PI3K/AKT, PI3K/AKT/mTOR, RNF6/AKT/mTOR, and EGFR/PI3K/AKT pathways are blocked by saponins. The permeability of bacterial cell membranes and influx the antibiotics through the bacterial cell wall and membrane may be increased by saponins. Damaging of the bacterial cell wall and disruption of the cytoplasmic membrane followed by leakage of the bacterial macromolecules were the main antibacterial mechanisms for quinoa saponins. As the anti-obesity functions, dietary saponins can hinder the function of pancreatic lipase, and fatty liver formation, accelerate fecal excretion of triglycerides and bile acids, block intestinal absorption of lipids, and suppress adipogenesis. As a cosmetic application, the growth of *P. acnes* bacteria is inhibited by the saponin fraction in lower concentration compared to the fermentation liquid-based water extract of *Sapindus mukorossi* Gaertn.

Study Highlights

- Many singling pathways such as PKB/MAPK, PI3K/AKT, PI3K/AKT/mTOR, RNF6/AKT/mTOR, and EGFR/PI3K/AKT pathways are blocked by saponins.
- The permeability of bacterial cell membranes and influx the antibiotics through the bacterial membrane can be enhanced by saponins.
- Dietary saponins can hinder the function of pancreatic lipase and fatty liver formation.
- The growth of *P. acnes* bacteria is inhibited by the saponins.

Abbreviations

CKD: Chronic kidney disease
CVDs: Cardiovascular diseases
EGFR: Epidermal growth factor receptor
HPLC: High-performance liquid chromatography
MAPK: Mitogen-activated protein kinase
MBC: Minimum bactericidal concentration
MIC: Minimum inhibitory concentration
MS: Mass spectrometry
mTOR: Mammalian target of rapamycin
NAFLD: Non-alcoholic fatty liver disease
NMR: Nuclear magnetic resonance
PI3K: Phosphatidylinositol 3-kinase
PKB: Protein kinase B
RNF6: Ring finger protein 6
T2D: Type 2 diabetes

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Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with animals or human participants performed by any of the authors.

Author contributions

All authors: conceptualization, writing the first draft, and revising the manuscript.

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