

The synopsis of Biological and Pharmacological Events in Saponins

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ABSTRACT - Saponins are subordinate metabolites produced by numerous dissimilar plant species and marine animals. They derive their name from the Latin word "sapo" significance of soap, due to their surfactant properties, which allows fashioning stable soap-like foam when shaken in aqueous solution. They are large molecules and encompass a hydrophobic part, serene of a triterpenoid that is 30 carbon atoms or steroid backbone means 27 carbon atoms with a 6-ringspirostane or a 5-ring furostane skeleton and a hydrophobic part consisting of several saccharide residues linked to the hydrophobic scaffold over glycoside bonds. They have several medical uses with microbial, anti-tumor, anti-insect hepatoprotective, haemolytic and anti-inflammatory activities. They also reduce the blood cholesterol level and may be used as adjuvant in serums. In accumulation, saponins are used in preparation of soaps, detergents, fire extinguishers, shampoos, beer and cosmetic. Lots of saponins that exhibit haemolytic activity has a bitter taste and are toxic to fish. This work provides a summary on the biological and pharmacological activities of saponins with a special focus on their mechanism of action.

Keywords: Saponins, Biological activities, Pharmacological activities.

I. INTRODUCTION

Saponins are a group of subordinate metabolites, nonvolatile surfactants that are widely disseminated in the plant kingdom and marine animal. This group of expected products has the same common characteristic of foaming when shaken with water. The fashioned foam is a result of the establishment of a colloidal solution, having a stable and lasting action of dilute mineral acids, contradictory from ordinary soaps. Another imperative feature of this class of substances is related to the ability of precipitating cholesterol by forming insoluble complexes. Both features are associated to the above amphipathic or amphiphilic nature of these molecules, since they are designed by one hydrophilic and one lipophilic and one lipophilic moiety. Saponins have a range of possessions due to their extensive structural diversity, which includes certain features, bitter sweeteners, detergents and emulsifying properties, in addition to the biological, medical and pharmacological properties, such as haemolytic activity, antimicrobial, insecticides and molluscicides.

Also noteworthy are the submissions in pharmaceutical industries as raw material for the synthesis of steroidal drugs such as birth control, also the intense use in the cosmetic industry. The usage of plants encompassing saponins was accomplished by early civilizations since of their detergents to fish and toxic properties. The early study of biological activities of this class of substance was directed through extracts rich in saponins. Presently, the occurrence in nature, the ethno pharmacological use and the various biological happenings of saponins, scientifically proven, have aroused the interest of mankind and, especially, of the scientists worldwide. Though, the saponins are highly toxic when administered intravenously in higher animals, despite presenting a multitude of biological activities. This toxicity falls to low levels when administered orally and, furthermore, some saponins present in food do not offer oral toxicity significantly.

The amphiphilic performance of saponins and the ability to form complexes with steroids, proteins and membrane phospholipids determined a numeral of altered biological properties for these substances, especially the action on cell membranes, fluctuating their permeability, or causing their destruction. Interrelated to this action on membranes the haemolytic, icthiotoxic, spermicide and molluscicidal activities are frequently perceived. The complexation with cholesterol yielded an important number of studies in order to evaluate the use of saponins in the diet to reduce serum cholesterol levels, antihypercholesterolemic activity. The anti-inflammatory and antiallergic activity of saponins has been known for a long time and is closely related to the core aglycone. Several papers have been published broadcasting the activities of saponins, among the most impressive antidiabetic, antifungal, antitumor activity, antiviral, antiparasitic, immunomodulatory, synthesis of hormones, acting on the cardiovascular system, acting on the central nervous and endocrine systems. Additionally, the saponins are imperative for many actions of drugs derived from plants, such as diuretics, expectorants and components. Though, the mechanism of these activities has not been fully elucidated, it is believed that the irritation caused in the respiratory and renal tract epithelia contribute significantly to the observed activities. Saponins are also widely used in the pharmaceutical industry as adjuvants to enhance the absorption of other drugs by increasing solubility or interfering in the mechanisms of absorption.

II. HAEMOLYTIC ACTIVITY

Chemical studies and scrutinizes of cell casing permeability show that the configuration has lipoprotein or are designed by lipids and proteins. Phospholipids have in their molecules a hydrophobic end with aversion to water and another hydrophilic end with affinity for water. The plasma membrane has a bio-molecular layer of lipids with the hydrophobic portions of molecules facing each other, and opposite internal and external membrane surface hydrophilic moieties. Dipped in "mat fat" are the protein molecules, now exposed on the outer face, in the inner face or sometimes on both sides of the membrane.

The ability to cause perturbation on the casing is the most widely studied effect of saponins, specially the steroidal saponins. This stuff is often associated with haemolytic capacity of saponins to cause lysis of erythrocytes in mammals. The mechanism of action of these subordinate metabolites, that would be the cholesterol target, is essential for the formation of membrane pores.

Since then, many research groups have tried to elucidate the molecular basis of this activity by studying the fragments of saponins. The results established the influence of the chemical composition of the membrane, specifically regarding the concentration and structure of sterols in the permeability change when saponins are added. Consequently, it becomes obvious the haemolytic potential of saponins is affected by its chemical characteristics, including the structure of aglycone, the chain number of sugars, the long chains as well as the types of sugars and incorporated binder units of sugar. Glauert *et al.*, 1962 proposed the first model for the apparatus of action of saponins on the membranes. Conferring to this model, the spontaneous formation of complexes among saponins and cholesterol in the membranes is surveyed by association with a micelle, two-dimensional structure within the membrane. The hydrophilic sugar chains are oriented towards the center of the micelle composite, leading to the formation of an aqueous pore that, in turn, would cause an increase in membrane perviousness allowing the passage of ions and macromolecules across the lipid bilayer (Fig. 1).

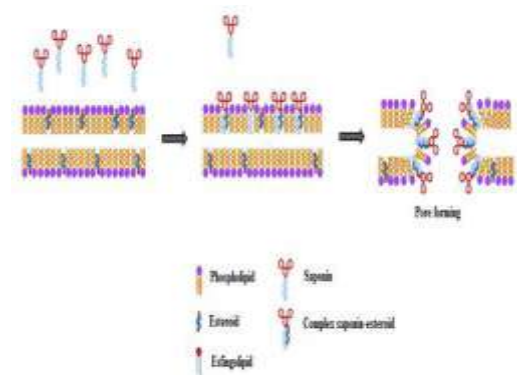


Fig. 1: Model of the mechanism of action of saponins on the Membranes.

2.1 Anti-hypercholesterolemia activity:

Hypercholesterolemia is a risk factor that subsidizes to the expansion and progression of atherosclerosis and subsequent cardiovascular disease. Epidemiological and clinical data have shown that high focusses of LDL cholesterol in the bloodstream are the large pivot of these diseases. Bioactive compounds with hypocholesterolemia activity have been directed, among the most studied are soluble fibers, phytosterols, phospholipids, soy protein, stearic acid and saponins. There are several mechanisms which siphoning may reduce cholesterol levels,

- (1) Formation of an insoluble complex where it is supplementary to the beta-hydroxysteroid, thereby diminishing intestinal cholesterol absorption, constructing an increase of sterols which are excreted along with feces.
- (2) Adsorption of bile acids in the diet of the fibers is augmented in the presence of saponins because they form micelles with large molecular weights, which avoid bile acids that are reabsorbed. Thereby the increase occurs in the liver through the alteration of cholesterol into bile acids.
- (3) Communication with cells of the intestinal mucosa encouraging a higher permeability of these cells and subsequently a rapid loss of cell function by growing proliferation promoting exfoliation and loss of this function. Thus, it donates to a further increase in the excretion of cholesterol.
- (4) The presence of sugars, β -1, 4 coupled enhances the absorption of soluble fiber and promotes the decrease of fatty acids, resulting in a decrease of liver cholesterol.

2.2 Anti-inflammatory and anti-allergic activity:

The evaluation of anti-inflammatory activity of saponins has been accomplished using models of inflammation with carrageenan. In common, the oleanane and ursan saponins are those with higher activity. The mechanisms measured for this activity include corticoid-mimetic activity inhibiting the deprivation of the glucocorticoid or release of mediators of inflammation, inhibition of enzyme formation and inhibition of increased vascular perviousness.

2.3 Cytotoxic and antitumor activity:

There have been numerous reports of scientific papers in relative to the cytotoxic properties of saponins, however saponins do not always have high cytotoxic antitumor properties. The cytotoxic mechanism of saponins occurring via embarrassment of DNA synthesis induces an opposite phenotypic transformation into tumor cells. When the antitumor mechanism occurs through the inhibition of vessels around the tumor, there is a reserve of tumor growth. Inhibition of

metastasis, as well as immunostimulation and experimental chemoprevention mechanisms are imperative in antitumor compounds. As almost all saponins induce apoptosis in tumor cells, they become the favorite drug in treating cancer because they eliminate tumor cells with low side effects for the patient, circumventing mainly necrosis.

2.4 Antiviral activity:

Some saponins may inhibit DNA synthesis of the herpes simplex virus, such as those with saponin of the oleanane type, however saponins type ursane inhibit the synthesis of viral capsid protein of the same virus. Additional saponins may also inhibit virus type II polio over inhibition of the attack of the virus to the host cell. These mixtures have been shown to reduce experimental keratitis caused by herpes simplex virus in rabbits.

2.5 Hormone synthesis:

Steroidal saponins found in the rhizomes of numerous species of the genus *Dioscorea* have a steroidal content around 40% and 50-60% of Diosgenin and other saponin. Diosgenin is frozen with acetic anhydride and ester forms a pseudosaponin. Then when oxidized with chromium trioxide followed by hydrolysis forms two intermediate compounds and finally progesterone (Fig. 2). This work, of crucial reputation for the progress of steroid therapy, contributed expressively to the subsequent development of the female contraceptive pill. From this, many dissimilar classes of ordinary products have been used as raw material for the synthesis of different bioactive substances. The steroidal glycoalkaloids isolated from the leaves of tomato plants, as tomatin is an additional example of usage in the synthesis of steroid hormones.

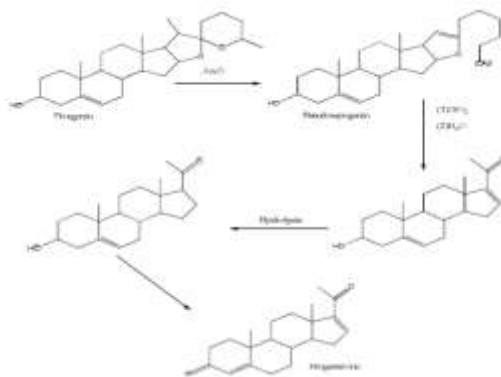


Fig. 2: Synthesis of progesterone from Diosgenin

2.6 Action on blood clotting:

Some saponins inhibit in vitro the accumulation induced by aggregating agents platelets. Some explanations on the mechanism of action have been made, such as increase in cAMP levels in platelets, diminished production and release of thromboxane (TBX) and inhibition of the production of prostacyclin (PGI₂). Ginsenoside R₀ repressed the conversion of fibrinogen into fibrin, induced by thrombin at concentrations of 0.1-1.0 mM, since the R_{b1}, R_{b2}, R_e, R_g and ginsenoside R_{g2} promote the action of urokinase that activates the conversion of plasminogen into plasmin, which, in turn, degrades the fibrin network.

2.7 Action on blood pressure:

In anesthetized rats, ethanolic extract of *Symphytum officinale* and asaponin hederagenin instigated a systolic blood drop and the diastolic blood pressure dose-dependent manner. Though, there is no mechanism established for such hypotensive effects.

2.8 Action on Central Nervous System:

Ginseng saponins have shown bio-modulatory effects on higher centers of the central nervous system, simplifying the physical and mental activities. They also have anti-stress activities and effects on central neurotransmitters in hypobaric hypoxia. The results establish that ginsenosides alter the effects of barbiturates and consultants, signifying that the GABAergic neurotransmitter regulation may have important pharmacological actions of ginsenosides. This has been proven by many studies that have confirmed the simplification of saponins of ginseng on learning and memory. Other saponins have shown sedative and analgesic activity, such as saponins *Aster batangensis*, contrary to amphetamine and synergistic to the chlordiazepoxide effects.

III. CONCLUSION

These papers conclude on the biological and pharmacological happenings of saponins with a special focus on their mechanism of action. They have numerous medical uses with microbial, anti-tumor, anti-insect hepatoprotective, haemolytic and anti-inflammatory activities. They also lessen the blood cholesterol level and may be used as adjuvant in serums. In accretion, saponins are used in preparation of soaps, detergents, fire extinguishers, shampoos, beer and cosmetic. Lots of saponins that exhibit haemolytic activity have a bitter taste and are toxic to fish.

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