Saponins and their biological activities

Article *in* Pharma Times · March 2009

3 authors, including:

Sapna Desai
Pioneer Pharmacy Degree College, Vadodara, India

Harmeet Kaur
Maharshi Dayanand University

Article

Saponins and their Biological Activities

Sapna D. Desai*[a], Dhruv G. Desai[b], Harmeet Kaur[c]

[a] Department of Pharmacology, Pioneer Pharmacy Degree College, Vadodara- 390019, Gujarat, India.
[b] Sun Pharmaceutical Industries Ltd. Vadodara, Gujarat.
[c] Department of Pharmaceutical Chemistry, PDM College of Pharmacy, Bahadurgarh- 124507, Haryana.

Abstract

Saponins are steroid or triterpenoid glycosides, common in a large number of plants and plant products that are important in human and animal nutrition. Several biological effects have been ascribed to saponins. Extensive research has been carried out in the membrane-permeabilising, immunostimulant, hypocholesterolaemic and anticarcinogenic properties of saponins and they have also been found to significantly affect reproduction in animals. These structurally diverse compounds have also been observed to kill protozoans and molluscs, to have an effect on cold blooded animals, also to have the analgesic, anti-nociceptive, antioxidant activity, to impair the digestion of protein, to cause hypoglycemia and to act as antifungal and antiviral agents.

Introduction

Saponins are naturally occurring surface-active glycosides with a distinctive foaming characteristic. They are mainly produced by plants but also by lower marine animals and some bacteria,[1,2] but get their name from the soapwort plant *(Saponaria)*[3], the root of which was used historically as a soap (Latin *sapo* means soap). The combination of hydrophobic or fat-soluble sapogenin and hydrophilic or water-soluble sugar part enhances the foaming ability of saponins.

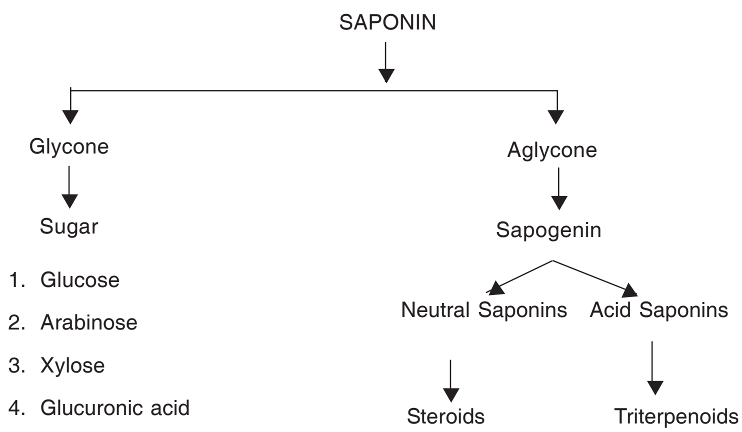


Fig. 1 Classification of Saponins

Classification

Saponins on hydrolysis yielde glycon (sugar) and aglycone (sapogenin). According to the structure of the aglycone or sapogenin, saponins are classified as neutral and acid type, the so-called neutral saponins are derivatives of steroids with spiroketal side chains which are almost exclusively present in the monocotyledonous angiosperms and the acid saponins that possess triterpenoid structure type, which is the most common and occur mainly in the dicotyledonous angiosperms.[4]

Sapogenins consist of a polycyclic aglycone i.e. either a choline steroid or triterpenoid. The aglycone may contain one or more unsaturated C-C bonds. The oligosaccharide chain is normally attached at the C^3 position (monodesmosidic), but many saponins have an additional sugar moiety at the C_{26} or C_{28} position (bidesmosidic). The great complexity of saponin structure arises from the variability of the aglycone structure, the nature of the side chains and the position of attachment of these moieties on the aglycone. The third classified group is steroidal amines, which is also known as steroidal alkaloids.[3]

Saponins consist of a sugar moiety usually containing glucose, galactose, glucuronic acid, xylose, rhamnose or methylpentose, glycosidically linked to a hydrophobic aglycone (sapogenin) which may be triterpenoid or steroid in nature. The ability of a saponin to foam is caused by the combination of the nonpolar sapogenin and the water-soluble side chain. Saponins are bitter and reduce the palatability of livestock feeds.[5]

The main pathway leading to both types of sapogenins is similar and involves the head-to-tail coupling of acetate units. However, a branch occurs, after the formation of the triterpenoid hydrocarbon, squalene, that leads to steroids in one

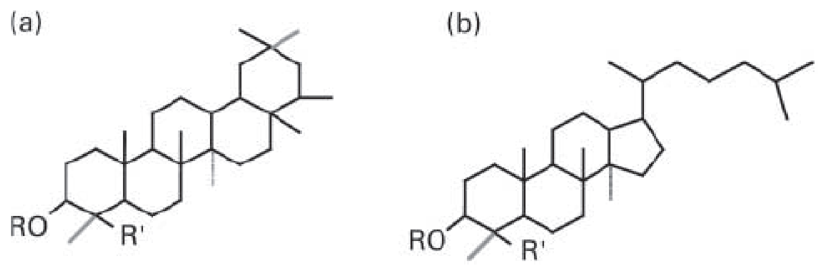
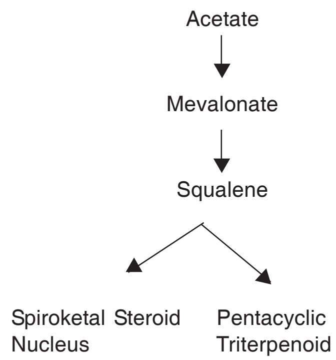


Fig. 2 Basic structures of sapogenins: (a) a triterpenoid and (b) a steroid

Contact details:* **Mrs. Sapna D. Desai**
Pioneer Pharmacy Degree College, N.H-8, Near Ajwa Nimeta Road, Vadodara-390019, Gujarat
E mail: sapna_peer@rediffmail.com Mobile: 09377896196

direction and to cyclic triterpenoids in the other.



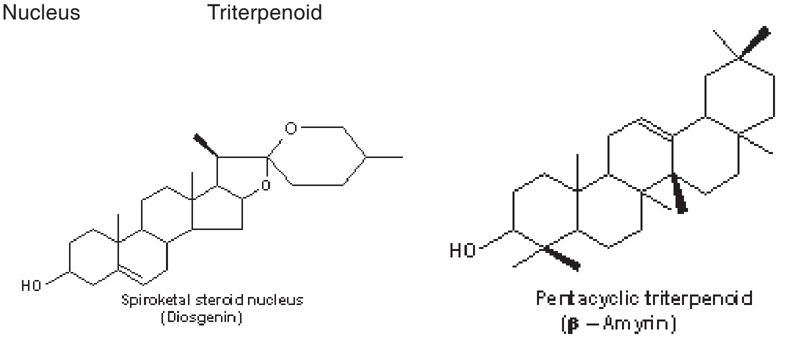


Fig. 3 Conversion of acetate to spiroketal steroid nucleus and pentacyclic triterpenoid

Occurrence

Saponins are an important group of plant secondary metabolites that are widespread throughout the plant kingdom. Saponins are basically phyto-chemicals which are found in most of the vegetables, beans and herbs. Saponins occur constitutively in a great many plant species, in both wild plants and cultivated crops. In cultivated crops the triterpenoid saponins are generally predominant, while steroidal saponins are common in plants used as herbs or for their health-promoting properties. Triterpenoid saponins have been detected in many legumes. The well known sources of saponins are soybeans, peas, and some herbs with the names that indicate foaming properties such as soapwort, soapberry, soapbark and soap root. Commercial saponins are mainly extracted from Quillaja saponaria and Yucca schidigera.[5, 6]

Role Of Saponins In Plant

The saponins have multiple effects on animal cells and on fungi and bacteria, only a few have addressed their function in plant cells. Many saponins are known to be antimicrobial, to inhibit mould, and to protect plants from insect attack. Saponins may be considered a part of plants' defense systems, and as such have been included in a large group of protective molecules found in plants named 'phytoanticipins' or 'phyto-protectants'[7]. The first term describes those saponins, such as A and B avenacosides in oat, that are activated by the plant's enzymes in response to tissue damage or pathogen attack. The second describes those saponins that have a general anti-microbial or anti-insect activity. A glycosylated triterpenoid saponin from peas (Pisum sativum) was purified and characterized as a specific inhibitor of diguanylate cyclase, a key regulatory enzyme in the synthesis of cellulose.[5,8] It has also been suggested that saponins could be a source of monosaccharides.

Biological Effects

The term saponin has become accepted to define a group of structurally diverse molecules.

These secondary metabolites often occur in plants as complex mixtures, and saponin content and composition may vary markedly depending on the genetic background of the plant material, the tissue type, the age and physiological state of the plant and environmental factors. Saponins have been variously attributed with a diverse range of properties, some of which include both beneficial and detrimental effects on human health, pesticidal, insecticidal and molluscicidal activity, allelopathic action, antinutritional effects, sweetness and bitterness, and as phyto-protectants that defend plants against attack by microbes and herbivores.[6]

1. **Effects on cell membrane permeability**

   The large number of the biological effects of saponins has been associated to their action on permeability of cell membranes. They have a specific ability to form pores in membranes. Saponins have a lytic action on erythrocyte membranes. The hemolytic action of saponins is believed to be the result of the affinity of the aglycone moiety for the phospholipids present in the cell membrane with which they form insoluble complexes.9,10 The amount of glycosides required for permeabilisation is much lower for cholesterol-rich lipid layers than cholesterol-free membranes.[11]

2. **Effect on cold blooded animal**

   Saponins have been reported toxic to cold-blooded creatures like snake and/ or fish because of their damaging effect on the respiratory epithelia. They are also considered to be the active components of many traditionally used fish poisons, like mahua oil cake. Fish also exhibits stress reactions to the presence of saponins in water. It was reported that as the perch (Anabas testudineus) was exposed to 5mg Quillaja saponin/l for 24 h there was a concomitant increase in the erythrocyte, haemoglobin, packed cell volume levels, increase in O2 uptake and NH4 excretion. The Quillaja saponins was also responsible for damaging the intestinal mucosa in rainbow trout.[12]

3. **Hypoglycemic activity**

   The saponins present in fenugreek are responsible for hypoglycemic activity either by stimulating the ?- cells or by suppressing the transfer of glucose from the stomach to the small intestine and the inhibition of glucose transport across the brush border of the small intestine.[13]

   The saponin momordin Ic was found to significantly and dose-dependently inhibit gastric emptying.[14] .The inhibition of gastric emptying may be inhibited by the release and/or production of dopamine to act through D2 receptors, which in turn causes the release of prostaglandins.[15]

4. **Effect on cholesterol metabolism**

   The saponins from different sources lower serum cholesterol levels in a variety of animals including human subjects. Large mixed micelles formed by the interaction of saponins with bile acids account for their increased excretion when saponin-rich foods such as soyabean, lucerne and chickpea are consumed. The resulting accelerated metabolism of cholesterol in the liver causes its serum levels to go down.[16]

5. **Effects on animal reproduction**

   The negative effects of saponins on animal reproduction have long been known and have been ascribed to their abortifacient, antizygotic and anti-implantation properties. Saponins are found to be extremely strong stimulators of luteinising hormone release from cultured hypophysial cells[17]. However, saponin-rich extracts from Combretodendron africanum injected into female rats, stimulated uterine growth, lowered luteinizing hormone release and blocked the oestrous cycle.

The steroid saponin was found to directly inhibit the genes responsible for steroidogenesis, and also suppress the proliferation of follicle-stimulating hormone-modulated granulosa cells in the ovarian follicle. The mechanism of suppression of cell proliferation might be through a similar mechanism as saponin-induced proliferation of tumor cells. Saponins have been shown to have both positive and negative effects on the viability of human sperm cells in vitro with some ginseng saponins increasing motility as well as progression of sperm.[18]

6. **Virucidal activity**

Some saponins and sapogenins are capable of deactivating viruses, for example, purified saponin mixture from Maesa lanceolata .The triterpenoid sapogenin oleanolic acid inhibits HIV-1 virus replication probably by inhibiting HIV-1 protease activity.[19,20]

7. **Effect as an anti-inflammatory**

The significant ameliorative activity of the saponins may be due to inhibition of the mediators of inflammation such as histamine, serotonin and prostaglandin along with its antioxidant property which inhibits the formation of ROS which also plays a major role in inflammation.[21,22]

8. **Hypolipidaemic activity**

The mechanism involved in the hypolipidemic activity is, saponins and high fiber content in the different plant extracts. The fiber significantly binds to cholesterol hence aiding its excretion. Saponins have also been shown to posses' high degree of hypolipidaemic activity. The combine activity of saponins and fiber content of the plant extract brings about the reduction in plasma concentration of cholesterol and the lipids. Thus reducing the possible occurrence of coronary heart disease such as atherosclerosis.[23]

9. **Effects on protein digestion**

Saponins reduce protein digestibility probably by the formation of sparingly digestible saponin-protein complexes[24]. Endogenous saponins affected the chymotrypsic hydrolysis of soyabean protein, particularly glycinin[25]. The heat stability of bovine serum albumin was increased by the addition of soyasaponin due to electrostatic and hydrophobic interactions. The digestibility of the bovine serum albumin- soyasaponin complex is much lower than that of free bovine serum albumin indicating that complexing with saponin had an obstructing effect.

10. **Antifungal activity**

The antifungal activity of the steroidal saponin is associated with their aglycone moieties and the number and structure of monosaccharide units in their sugar chains.[26]

11. **Antimicrobial activity**

The saponins show the antimicrobial activity by inhibiting the growth of Gram +ve or Gram -ve microorganism. Some saponins are not effective against Gram -ve microorganisms because of the reason that they are not able to penetrate into the cell membranes of the microorganisms. [27,28]

12. **Effect on the transverse-tubular system and sarcoplasmic reticulum membranes**

At low concentrations, saponin increases Ca^{2+} loss from the sarcoplasmic reticulum (SR) of mammalian cardiac and also mammalian and crustacean skeletal muscle. The increased Ca^{2+} leak from mammalian skeletal SR after saponin treatment does not depend upon concentration but specifically act through the ryanodine receptor. [29]

13. **Other Biological activities**

The saponins are also responsible for lowering cancer risks by lowering the blood cholesterol levels. A high saponin diet can be used in the inhibition of dental caries and platelet aggregation, in the treatment of hypercalciuria in humans, and as an antidote against acute lead poisoning. In epidemiological studies, saponins have shown to have an inverse relationship with the incidence of renal stones.[18] Saponins are also responsible for many other important activities Molluscidal, Anthelmintic, Antiulcerogenic, Anticancer, Antioxidant, Immuno-modulatory, Anti-malarial, Anti-bacterial, Eczema, Analgesic, Anti-nociceptive, hepatoprotective.[30,31,32]

Poisoning Symptoms Of Some Saponins

Along with the beneficial effects, saponins are also responsible for certain adverse activities in animals. Some of the poisoning symptoms of saponins are:

Alfalfa *(Medicago sativa)* poisoning in poultry and swine:

- irritated mucous membranes of the mouth and digestive tract
- reduced feed intake,
- low dietary protein quality.
- the above factors lead to decreased performance and growth rate.
- increased excretion of cholesterol.

Corn cockle *(Agrostemma githago),* soapwort *(Saponaria officinalis),* cow cockle(Saponaria vaccaria) and broomweed *(Gutierrezia sarothrae)* poisoning

- listlessness
- anorexia
- weight loss
- rough hair coat
- gastroenteritis and diarrhea
- in the case of broomweed, possibly abortion.

Alfombrilla *(Drymaria arenaroides)*

- symptoms are same but more progressive
- arched back
- coma
- death

Saponins are also responsible for irritating the membranes of the respiratory and digestive tract, the aglycones in certain saponins increase the permeability of the membranes of red blood cells. In severe cases, the membranes are destroyed and their hemoglobin escapes into the bloodstream.

Conclusion

Saponins are a diverse family of secondary metabolites. Many plants used in traditional medicines worldwide contain saponins, which can often account for their therapeutic action. It is believed that the natural role of these compounds in plants is to protect against attack by potential pathogens, which would account for their antimicrobial activity. Although saponins are extremely toxic to cold-blooded animals, their oral toxicity to mammals is low. Due to their toxicity to various organisms, saponins can be utilized for their insecticidal, antibiotic, fungicidal, and other pharmacological properties. The wide chemical diversity of saponins has resulted in renewed interest. This review provides a summary of saponin research.

References

1. Riguera R. Isolating bioactive compounds from marine organisms. Journal of Marine Biotechnology. 1997, 5: 187-193
2. Yoshiki Y., Kudou S & Okubo K. Relationship between chemical structures and biological activities of triterpenoid saponins from soybean. Bioscience Biotechnology and Biochemistry. 1998, 62: 2291-2299
3. Sparg S.G., Light M.E & Van Staden J. Biological activities and distribution of plant saponins. Journal of

Ethnopharmacology. 94, 2004: 219-243
4. www.friedli.com/herbs/phytochem/saponin
5. Francis G., Zohar Kerem., Harinder P. S., Makkar & Klaus Becker. The biological action of saponins in animal systems. British Journal of Nutrition. 2002, 88:587-605
6. Haralampidis K., Trojanowska M & Osbourn A.E. Biosynthesis of triterpenoid saponins in plants. Advances in Biochemical Engineering/ Biotechnology. 2002,75: 31-49
7. Morrissey J.P & Osbourn A.E. Fungal resistance to plant antibiotics as a mechanism of pathogenesis. Microbiological and Molecular Biological Reviews. 1999, 63: 708-724
8. Ohana P., Delmer D.P., Carlson R.W., Glushka J., Azadi P., Bacic T & Benziman M. Identification of a novel triterpenoid saponin from Pisum sativum as a specific inhibitor of the diguanylate cyclase of Acetobacter xylinum. Plant and Cell Physiolology. 1998, 39: 144-152
9. Bangham A.D & Horne R.W. Action of saponins on biological cell membranes. Nature. 1962,196: 952-953
10. Surana S.J., Tatiya A.U., Jain A.S., Desai D.G., Shastri K.V & Katariya M.V. Pharmacognostical and physio-chemical standardization of root of *Eranthemum roseum* (Vahl) R. Br. Phcognosy Magazine. 2008, 4: 75-79
11. Gogelein H & Huby A. Interaction of saponin and digitonin with black lipid membranes and lipid monolayers. Biochimica et Biophysica Acta. 1984, 773: 32-38
12. Francis G., Makkar H.P.S & Becker K. Antinutritional factors present in plant-derived alternate fish feed ingredients and their effects in fish. Aquaculture. 2001, 199: 197-227
13. Petit P.R., Sauvaire Y., Ponsin G., Manteghetti M., Fave A & Ribes G. Effects of a fenugreek seed extract on feeding behaviour in the rat: metabolic endocrine correlates. Pharmacology Biochemistry and Behaviour. 1993, 45: 369-374
14. Matsuda H., Li Y.H., Murakami T., Yamahara J & Yoshikawa M. Structure-related inhibitory activity of oleanolic acid glycosides on gastric emptying in mice. Bioorganic and Medicinal Chemistry. 1999, 7: 323-327
15. Matsuda H., Morikawa T & Yoshikawa M. Antidiabetogenic constituents from several natural medicines. Pure Appl. Chem. 2002, 74 (7): 1301-1308
16. Oakenfull D.G. Aggregation of bile acids and saponins in aqueous solution. Australian Journal of Chemistry. 1986, 39: 1671-1683
17. Benie T., El-Izzi A., Tahiri C., Duval J & Thieulant M.L.T. Combretodendron africanum bark extract as an antifertility agent : Estrogenic effects in vivo and LH release by cultured gonadotrope cells. Journal of Ethnopharmacology. 1990, 29: 13-23
18. Chen J.C., Xu M.X., Chen L.D., Chen Y.N & Chiu T.H Effect of Panax notoginseng saponins on sperm motility and progression in vitro. Phytomedicine 1998, 5: 289-292
19. Sindambiwe J.B., Calomme M., Geerts S., Pieters L., Vlietinck A.J & Vanden Berghe D.A. Evaluation of biological activities of triterpenoid saponins from Maesa lanceolata. Journal of Natural Products. 1998, 61: 585-590
20. Mengoni F., Lichtner M., Battinelli L., Marzi M., Mastroianni C.M., Vullo V & Mazzanti G. In vitro anti-HIV activity of oleanolic acid on infected human mononuclear cells. Planta Medica. 2002, 68: 111-114
21. Sayyah M., Hadidi N & Kamalinejad M. Analgesic and anti-inflammatory activity of *Lactuca sativa* seed extract in rats. Journal of Ethnopharmacology. 2004, 92: 325-329
22. Tatiya A.U., Desai D.G., Surana S.J., Patil P.H. Anti-inflammatory and nitric oxide scavenging activity of roots of *Eranthemum roseum.* Indian Drugs. 2007, 44(11): 815-818
23. Raju J., Gupta D., Rao A., Yadava P & Baquer N. *Trigonella foenum graecum* (fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. Molecular and Cellular Biochemistry, 2001; 224, 45-51
24. Potter S.M., Jimenez-Flores R., Pollack J., Lone T.A & Berber-Jimenez M.D. Protein saponin interaction and its influence on blood lipids. Journal of Agricultural and Food Chemistry. 1993, 41: 1287-1291
25. Shimoyamada M., Ikedo S., Ootsubo R & Watanabe K. Effects of soybean saponins on chymotryptic hydrolyses of soybean proteins. Journal of Agricultural and Food Chemistry. 1998, 46: 4793-4797
26. Chong-Ren Yang., Ying Zhang., Melissa R. Jacob., Shabana I. Khan., Ying-Jun Zhang and Xing-Cong Li. Antifungal Activity of C-27 Steroidal Saponins. Antimicrobial Agents and Chemotherapy. 2006, 50(5): 1710-1714
27. Jain A.S., Surana S.J., Gokhale S.B., Tatiya A.U & Bothara R.C. Antimicrobial properties of *Eranthemum roseum* (Vahl) R. Br. Iranian Journal of Pharmaceutical Research. 2007, 6(2): 131-133
28. Soetan k. O., Oyekunle M. A., Aiyelaagbe O.O & Fafunso M. A. Evaluation of the antimicrobial activity of saponins extract of *Sorghum Bicolor* L. Moench. African Journal of Biotechnology. 2006, 5(23): 2405-2407
29. Bradley S., Launikonis D & George Stephenson. Effects of ß-escin and saponin on the transverse-tubular system and sarcoplasmic reticulum membranes of rat and toad skeletal muscle. Eur J Physiol.1999, 437: 955-965
30. Shi J., Arunasalam K., Yeung D., Kakuda Y., Mittal G & Jiang Y. Guelph. Saponins from edible legumes: chemistry, processing, and health benefits. J Med Food. 2004, 7(1):67-78
31. www.herbs2000.com
32. Tadros M.M., Ghaly N.S & Moharib M.N. Molluscicidal and schistosomicidal activities of a steroidal saponin containing fraction from Dracaena fragrans (L.). J Egypt Soc Parasitol. 2008, 38(2): 585-98

Forthcoming Events

Pharmaceutical Leadership Summit

Date : **3rd April, 2009**
Venue : Renaissance Mumbai Hotel and Convention Centre, Mumbai
Organized by : Akshay Patra Foundation

Workshop on 'Dissolution'

Date : **15th - 16th May, 2009**
Organized by : IPA Regulatory Division / AAPS / IPA Karnataka State Branch
Venue : Bangalore
Contact : Dr. Premnath Shenoy -krpshenoy@yahoo.com
Mob No. 9845175011

Indian Pharmaceutical Association - Students' Congress

Date : **10th - 12th July, 2009**
Venue : DM Acharya College of Pharmacy, Bangalore
Organized by : Indian Pharmaceutical Association - Students' Forum
Contact Person / details: ipasf@ipapharma.org