# THE BIOACTIVITY OF SAPONINS: TRITERPENOID AND STEROIDAL GLYCOSIDES

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**SUMMARY**

Triterpenoid and steroidal glycosides, referred to collectively as saponins, are bioactive compounds present naturally in many plants. They have considerable potential as pharmaceutical and/or nutraceutical agents in natural or synthetic form. Saponins, from a variety of sources, have been shown to have hypocholesterolemic, anti-coagulant, anticarcinogenic, hepatoprotective, hypoglycemic, immunomodulatory, neuroprotective, anti-inflammatory and anti-oxidant activity. This paper reviews saponin research of the last decade, focussing on developments in understanding their mechanism of action and structure-activity relationships. Virtually all of this work has used animal and *in vitro* models. To date there are very few human data.

**KEY WORDS**

saponins, triterpenoid glycosides, steroidal glycosides, hypocholesterolemic activity, anti-coagulation, anticarcinogen, hepatoprotection, hypoglycemic activity, immunomodulation, neuroprotection, anti-inflammatory activity, anti-oxidant activity

## 1. INTRODUCTION

Triterpenoid and steroidal glycosides, referred to collectively as saponins, are bioactive compounds. Saponins are found in many plant-derived foods, the most concentrated source being legumes /1/. The dietary intake for saponins has been estimated at 15 to 240 mg daily, depending on the amount and type of legumes consumed /2/. Saponins are also present in many medicinal plants, such as ginseng, and likely play a role in their bioactivity. The potential of saponins as pharmaceutical and/or nutraceutical agents, in natural or synthetic form, has stimulated much of the research described below. Saponins have been shown to have hypocholesterolemic, anti-coagulant, anticarcinogenic, hepatoprotective, hypoglycemic, immunomodulatory, neuroprotective, anti-inflammatory and anti-oxidant activity, in animal and *in vitro* models. To date there are very few human data. This paper reviews saponin research of the last decade, focussing on developments in understanding their mechanism of action and structure-activity relationships.

## 2. CHEMISTRY OF SAPONINS

Saponins are triterpenoid or steroidal glycosides. A detailed treatment of the chemistry of saponins is beyond the scope of this review and the reader is directed to the excellent work by Hostettman and Marston for more information /3/. Saponins are generally named after the plant from which they were first isolated, e.g. ginsenosides from ginseng; soyasaponins from soybeans. Saponins contain both lipophilic and hydrophilic groups. The lipophilic group is either a triterpenoid or steroidal moiety, referred to as the aglycone or sapogenin. Attached to the sapogenin are hydrophilic sugars. There are many variations in the nature of the sapogenin. Ginseng saponins, for example, are derived from two steroidal sapogenins, one diol, protopanaxadiol, and, one triol, protopanaxatriol. There is also considerable variation in the number and type of sugars present and the manner in which they are attached to the sapogenin. The triterpenoid soyasaponins, for example, are divided into two groups, one in which sugars are attached only to carbon 3 of the triterpenoid moiety and one in which sugars are attached at both carbon 3 and carbon 22. Saponins with sugars attached to only one carbon are referred to as monodesmosides, while bisdesmosides have attachment at two carbons.

## 3. METABOLISM OF SAPONINS

Some work has been done on the metabolism of orally-ingested saponins /4-6/. The saponins are modified by gut microflora. Sugars are hydrolyzed, leaving, as the major metabolites, the sapogenin or a saponin with fewer sugars than the original material. In many animal studies, saponins were administered by intravenous, subcutaneous, or intraperitoneal injection rather than orally. The biological significance of saponin metabolites is poorly understood.

## 4. SAPONINS AND CARDIOVASCULAR DISEASE

The role of saponins in the prevention of cardiovascular disease has been recently reviewed. Saponins decreased blood cholesterol levels /7-9/, decreased blood coagulation /7/ and reduced lipid peroxide formation in cardiac muscle and liver /7/.

**Hypocholesterolemic effects**

The steroidal saponins from fenugreek /10/ and alfalfa /11/ lowered serum cholesterol levels in animals. Several studies suggested this effect was due to decreased absorption of cholesterol, observed as increased fecal neutral steroids /11-13/. Increased excretion of bile acids was also observed in some studies /11,13/.

Synthetic saponins have also been investigated. Tiqueside, the synthetic saponin beta-tigogenin cellobioside, reduced non-HDL cholesterol levels in various animal species /14/. This effect was linked to a decrease in intestinal cholesterol absorption, and a reduction in hepatic cholesterol levels with compensating increases in hepatic HMG-CoA reductase activity and hepatic LDL-receptor levels. No effect on bile acid metabolism was observed.

Similar effects occurred in human studies of hypercholesterolemic patients treated with tiqueside /15/. Decreased serum LDL cholesterol levels, linked to decreased cholesterol absorption and increased fecal neutral sterol excretion, were observed. Fecal fat, bile acid excretion and fat-soluble vitamin absorption were unchanged.

Modification of the steroid portion of tiqueside, i.e. the conversion of tigogenin cellobioside to 11-ketotigogenin cellobioside (pamaqueside) enhanced potency by a factor of ten. The further modification of the hydroxyl groups on the cellobiose, to form a 4",6"-bis[(2-fluorophenyl)carbamoyl] derivative resulted in a compound that increased the cholesterol absorption inhibitory effect by a factor of over 2000 /16/.

A detailed investigation of the mechanism by which pamaqueside and tiqueside inhibited cholesterol absorption suggested a non-stoichiometric mechanism, i.e. a mechanism other than the formation of a 1:1 cholesterol:saponin complex observed experimentally *in vitro*. Ratios of neutral sterol excreted to pamaqueside administered averaged approximately 5:1, while ratios in tiqueside-treated rabbits were less than 1, consistent with its 1/10 potency relative to pamaqueside. Other mechanisms, such as interaction with cholesterol in the cell membrane, micellar exclusion of cholesterol, or inhibition of enzymes involved in lipid absorption, are inconsistent with available data. It was suggested that these saponins acted by a novel mechanism possibly involving a putative cholesterol transporter /17/.

**Anti-coagulant activity**

Saponins from *Acanthopanax gracilistylus var. pubescens* Li /18/, steroidal saponins from several *Allium* plants /19/, and various ginsenosides /21,22/ inhibited blood coagulability. Possible mechanisms included increased synthesis of urinary-type and tissue-type plasminogen activator /20/ and increased platelet activating factor antagonist activity /21/.

**Other effects**

Studies suggested that tenuifolic saponin /22/ and tea-leaf saponins /23/ reduced hypertension. Ginsenosides from the protopanaxatriol group, but not from the protopanaxadiol group, enhanced the release of nitric oxide from endothelial cells, possibly via activation of tetraethylammonium-sensitive $K^+$-channels /24,25/. Both groups of saponins protected myocardial cells from oxidative damage /26/. *Panax notoginseng* saponins suppressed the hypocholesterolemic serum-induced cell proliferation of arterial smooth muscles *in vitro* /27/ and enhanced the electrophysiological properties of cardiac muscles /28,29/. Saponins from American ginseng, *Panax quinquefolium*, improved serum lipid profiles and reduced LDL oxidation /30/.

## 5. SAPONINS AND CANCER

Many saponins display anti-carcinogenic activity and research in this area has been recently reviewed /31/.

**Anticarcinogenic activity of triterpenoid saponins**

Antiprofilerative triterpene saponins were isolated from *Treveria palmata* /32/. Majonoside R2 from Vietnamese ginseng inhibited the growth of chemically-induced skin cancer in mice /33/. Anti-tumour promoting activity was observed by soyasaponin I, afromosin, gleditsiasaponin C and gymnocladussaponin G /34/. Soyasaponins inhibited the growth and viability of colon carcinoma cells in culture /35/. Electron micrographs revealed that cells treated with 600 ppm or more of soybean saponins developed numerous cytoplasmic vesicles, had decreased density of cytoplasmic material and had deformed plasma and nuclear membranes /36/. Soyasaponins also inhibited the

development of aberrant crypt foci, precursor lesions of colon cancer, in azoxymethane-treated mice /37/.

Structure-activity relationship studies suggested that the nature of the sugar moiety was very important to cytotoxic activity. One survey of 16 triterpenoid saponins found monodesmosides more active than bisdesmosides in killing cancer cells /38/, while another report noted that different sugar moieties influenced the rate of cytotoxic effects /39/. The licorice root saponin, glycyrrhizin, suppressed liver and lung tumours, while its sapogenin, glycyrrhetinic acid, suppressed mouse skin tumour formation in animal models /40/.

**Anticarcinogenic activity of steroidal saponins**

Many steroidal saponins have been shown to suppress the growth of cancer cells *in vitro*. Furcreastatin, isolated from the leaves of *Furcraea foetida,* decreased the viability of mutant p53 over-expressing mouse fibroblasts /41/. Steroidal saponins from *Diocorea coiletti* were cytotoxic against the cancer cell line K52 /42/. Cytostatic activity of saponins from several sources in leukemia HL-60 cells has also been reported /43-45/. Tubeimoside 1 induced differentiation of HL-60 cells to more mature cells with the functional characteristics of granulocytes /46/. A primary screening test for anti-tumor-promoter compounds measured the ability of saponins to inhibit the incorporation of $^{32}P$ into the phospholipids of HeLa cells, a reaction stimulated by tumour-promoter 12-O-tetradecanoylphorbor-13 acetate. Saponins from several sources demonstrated this activity /47-52/.

The most thoroughly studied of the anticarcinogenic saponins are the ginsenosides and most mechanistic studies involved these saponins. Ginsenosides Rh2 inhibited the growth of human ovarian cancer in nude mice /53/, and antitumour activity of ginseng intestinal metabolites in mouse melanoma cells /54/ and in four other cancer cell lines was reported /55/.

Ginsenosides Rh1 and Rh2 inhibited cellular proliferation in NIH 3T3 fibroblasts. This was due to the inhibitory effects of the saponins on phospholipase C which in turn reduced intracellular protein kinase C activity /56/. Ginsenosides induced differentiation in F9 terato-carcinoma cells by increasing the nuclear translocation of gluco-corticoid receptor /57/, the ginsenosides being structurally similar to glucocorticoid hormone. The differentiation of HL-60 cells into granulocytes by ginsenosides Rh2 and Rh3 was linked to modulation

of PKC isoform levels, specifically increased beta and gamma isoform levels with prolonged treatment /58/.

Ginsenoside treatment, specifically ginsenoside-Rg5 /59/ and ginsenoside-Rh2 /60-62/, induced the cell cycle arrest of B16 melanoma cells, BALB/c 3T3, A31-1-1 and A31-1-13 murine cell lines /62/, MCF-7 human breast cancer cells /61/, and SK-HEP-1 cells /59,60/. This arrest was reported in G1 /61,62/ or at the G1/S transition phase /59,60/ and was linked to down-regulation of cyclin D3 and upregulation of cyclin-dependent kinase inhibitor $p21^{WAF1/CIP1}$ /61/, down-regulation of cyclin-dependent kinase-2 activity /62/, and upregulation of $p27^{Kip1}$ and down-regulation of cyclin E-dependent kinase activity /59,60/. This cell cycle arrest was found in some studies to ultimately lead to induction of apoptosis. Ginsenoside Rs4 initiated cell cycle arrest at the G1/S boundary and consequently induced apoptosis by upregulation of protein levels of p53 and $p21^{WAF1}$ in SK-HEP-1 cells /63/. Ginsenoside-Rs3 was found to induce cell cycle arrest at low concentrations and to induce apoptosis at higher doses /64/. Ginsenoside-Rh2 induced apoptosis in SK-HEP-1 cells /65/ and C6 gliomal cell line /66/, in both cases by a capase-dependent but Bcl-2 /65/ and Bcl-$X_L$ /66/ insensitive mechanism.

**Anti-metastatic activity**

*In vitro* studies of tumour metastasis demonstrated 20(R)- and 20(S)-ginsenoside-Rg 3 inhibited adhesion of B-16-BL6 melanoma fibronectin and laminin and inhibited invasion of B16-BL6 cells into a reconstituted basement membrane /67/. In a similar cell monolayer model, 20(R)-ginsenoside-Rg suppressed the invasion of cells induced by 1-oleoyl-lysophosphatidic acid (LPA) by inhibiting the LPA-triggered rise of intracellular calcium /68/.

Intravenous injection of ginsenosides inhibited lung metastasis in mice by B16-BL6 melanoma and colon 26-M3 tumour cells, linked to inhibition of adhesion and invasion of tumour cells and to anti-angiogenic activity /67/. Bombesin-enhanced peritoneal metastasis by AOM-induced intestinal adenocarcinomas in rats was inhibited by subcutaneous injections of ginsenoside Rg2 /69/. Orally administered ginsenoside Rb1, Rb2, and Rc also inhibited metastasis in animal models /54,70/ but these ginsenosides were ineffective *in vitro*. This suggested that the bioactive component was the intestinal metabolite 20-O-beta-D-glucopyranosyl 20-(S)-protopanaxadiol to which all

orally-ingested ginsenosides were converted. Subsequent studies demonstrated that animals that lacked the ability to convert ginsenoside Rb1 into its metabolite had the least anti-metastatic protection /70/.

**Anti-mutagenic activity**

Several studies indicated that saponins ameliorate the deleterious effects of toxic substances. Alpha-hederin induced metabolic enzymes which inactivated doxorubicin /71/. Ginseng intestinal metabolites reduced the frequency of chromosome aberration induced by benzo[a] pyrene /72/. Saikosaponin a and ginsenoside Rb1 reduced the mutagenicity of 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide in a *Salmonella* mutagenicity assay, by enhancing DNA repair /73/. Soyasaponins suppressed the genotoxic activity of 2-acetoxyacetyl-aminofluorene /74/.

## 6. SAPONINS AND LIVER FUNCTION

Many saponins exerted hepatoprotective effects in both *in vitro* models using cultured rat hepatocytes and animal models, using rats or mice. Liver injury was typically induced with agents such as carbon tetrachloride or galactosamine and the activity of enzymes such as glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), or alanine aminotransferase (ALT) was measured. The activity of these enzymes increased during injury. When their activity was reduced in the presence of saponins, hepatoprotection was indicated.

Using this experimental approach, the following saponins showed hepatoprotective effects: total red ginseng saponins /75/, ginsenoside Ro /76/, kudzusaponin SA3 /77/, soyasaponin I /77,78/, kaikasaponin III /78/, saponins from notoginseng /79/, saponins from American ginseng /80/, and oleanene-glucuronides from various sources /81-85/.

Alpha-hederin injected subcutaneously was shown to have hepatoprotective effects in mice by increasing the levels of nonenzymatic antioxidant components in the liver, such as glutathione, metallothionein, zinc and copper /86/.

Several studies have linked the hepatoprotective effects of alpha-hederin to suppression of the activity of cytochrome P450 enzymes

/87-90/. Sapindoside B also suppressed cytochrome P450 levels /90/. Ginsenoside Rd had a very weak inhibitory effect on the activity of CYP3A4, CYP2D6, CYP2C19, and CYP2C9, while ginsenoside Rc increased the activity of CYP2C9 and ginsenoside Rf produced an increase in CYP3A4 activity /91/. Total saponins from Vietnamese ginseng increased the content of cytochrome P450 isoforms with $M_r$ of 57 kDa and 54 kDa in rat liver microsomes/92/.

**Structure-activity relationships**

Hepatoprotective effects were observed for several oleanene-glucuronides /81,82/. Studies of these oleanene glucuronides suggested that the presence of the hydroxymethyl group on galactose units /81/, the presence of an hydroxyl group at C-5" of the sugar moiety, and beta orientation of the hydroxyl group at C-21 of the sapogenin enhanced hepatoprotection, while a hydroxyl group at C-30 of the sapogenin reduced hepatoprotection /82/. The presence of a carbonyl group was equivalent to a hydroxyl group at C-22 of the sapogenin in terms of hepatoprotective action /83/. Sugar moieties were important for the hepatoprotective effects of soyasaponins. Disaccharide groups showed greater protective action than trisaccharide groups and saponins with hexosyl units were more active the pentosyl units /84/. The linkage between sapogenin and glucuronic acid also enhanced hepatoprotection /85/.

## 7. SAPONINS AND HYPOGLYCEMIC ACTIVITY

Several saponins have hypoglycemic activity. This activity was generally measured in animal models by an oral glucose tolerance test. Often hyperglycemia or diabetes was chemically induced in the animals. *In vitro*, typical analysis involved measuring the uptake of tritiated deoxy-2-glucose by cells in culture. Using these experimental approaches, saponins from the following sources have demonstrated hypoglycemic activity: *Kalopanax pictus* /93/, Tonburi, the fruit of Japanese *Kochia scoparia* (L) Scchrad /94/, the leaves of *Gymnema sylvestre* /95,96/ and *Gymnema inodorum* /97/, sugar beet /98/, Senegae Radix /99,100/; Taranome, the young shoot of *Aralia elata* Seem /101/, the root cortex of *Aralia elata* Seem /102,103/ and the leaves of *Acanthopanax senticosus* /104/. Two steroidal glycosides

from *Polygonati rhizoma,* PO-1 and PO-2, /105/, triterpenoids escins la, lb, IIa, IIb /106,107/, christinin A isolated from the Egyptian folk medicine Zizphus /108/, and pseudoprototimosaponin AIII and prototimosaponin AIII from rhizomes of *Anemarrhena asphodeloides* also had similar activity /109/.

A ginseng extract containing saponins stimulated glucose uptake in sheep erythrocytes, *in vitro*, while ginsenoside Rg3, chikusetsusaponin la and glycyrrhetic acid inhibited glucose uptake /110/. It was suggested that this inhibition may play a mechanistic role in the cytotoxic and antiviral activity of some saponins /111/. Studies on escins /112/ and saponins from *Gymnema inodorum* /97/ suggested that the saponins' hypoglycemic activity was due to inhibition of glucose absorption from the gut. Escin also slowed gastric emptying and accelerated gastrointestinal transit /113/. Hypoglycemic pseudoprototimosaponin AIII and prototimosaponin AIII appeared to have no effect on glucose uptake or insulin release and the authors suggested that inhibition of hepatic gluconeogenesis and/or glycogenolysis may play a role /109/. Investigation of christinin A in diabetic rats suggested a similar mechanism. The saponin reduced liver phosphorylase and glucose-6-phosphatase activity and increased liver glycogen levels. This saponin also appeared to have a stimulatory effect on the pancreas, increasing pancreatic cAMP and serum insulin levels /108/. Platycodin D, a saponin from the root of *Platycodon grandiflorum*, stimulated pancreatic exocrine secretion /114/.

Several structure-activity relationships have been studied. Saponins from *Kalopanax pictus*, kalopanaxsaponin B and H, showed no antidiabetic activity, while their metabolites, partially-hydrolyzed kalopanaxsaponin A and sapogenin hederagenin, demonstrated hypoglycemic effects in animal studies /93/. On the other hand, glucose-containing steroidal saponins PO-1 and PO-2 were more potent than the steroid sapogenin diosgenin /105/. Desacylescin I and II were inactive while escin la, lb, IIa, and IIb had hypoglycemic activity /106/.

## 8. SAPONINS AND THE IMMUNE SYSTEM

Saponins have immunomodulatory activity.

### Saponins and ISCOMs

Saponins from quillaja have been incorporated into immuno-stimulating complexes (ISCOMs), open cage structures with a 40 nm diameter, built up by cholesterol, lipid, immunogen and quillaja saponins. These ISCOMs promoted antibody responses, induced T helper cells, and cytotoxic T lymphocyte responses /115/. Structure activity studies suggested that more lipophilic saponins (i.e. less glycosylation and longer fatty acyl units) enhance adjuvant activity /116/. Different quillaja saponin fractions, obtained by reverse-phase HPLC, differed in their responses. The QH-A fraction, for example, stimulated proinflammatory cytokines and primary antibody and T-cell responses, while QH-C mediated a potent booster effect, causing a high secondary antibody response /117/.

### Saponins and anti-viral activity

Several saponins have been shown to have antiviral activity. *In vitro* studies demonstrated that soyasaponin II inhibited the replication of several viruses including HIV type I /118/. Tubeimoside 1, a triterpenoid saponin, also had inhibitory action on the infection of HIV-1 isolates /119/. Gleditsia saponin C and gymnocladus saponin G also inhibited HIV replication. Structure-activity studies suggest that the monoterpenyl moieties present in these saponins are essential to their anti-viral activity /120/. Triterpenoid saponins from *Calendula arvensis* inhibited the replication of vesicular stomatitis virus and rhinovirus *in vitro* /121/. Tea-seed saponins inactivated several human type A and B influenza viruses /122/.

### Other effects

Tea-leaf saponins, tea-seed saponins, ginsenosides, soyasaponins and saikosaponins activated neutrophils *in vitro*, by a protein kinase C-mediated mechanism /123/. Timosaponin E1 and E2, two steroidal saponins, also activated superoxide generation in neutrophils /124/. Several triterpenoid saponins inhibited histamine release *in vitro* /125-

127/. Tea-leaf saponins suppressed experimentally-induced asthma in guinea-pigs and rats /128/.

## 9. SAPONINS AND THE CENTRAL NERVOUS SYSTEM

Ginseng saponins have demonstrated neuroprotective effects against many neurotoxic agents. In rats scopolamine-induced cognitive impairment was ameliorated by ginsenosides Rg1 and Re through an increase in choline acetyltransferase activity /129/. Similar effects of ginsenosides on acetyl choline metabolism were found using mice /130/ and in *in vitro* models /131/. Majonosides R2, a major constituent of Vietnamese ginseng, attenuated the effects of morphine /132/ and psychological stress /133/ in animal studies. Ginsenoside Rg1 also inhibited the effects of morphine on mice /134/. Both ginsenosides Rb1 and Rg1 inhibited methamphetamine-induced hyperactivity in mice, by reducing dopamine receptor supersensitivity /135/. A similar mechanism accounted for inhibitory effects of total ginseng saponins on nicotine-induced hyperactivity /136/. Ginsenoside Rb1 reduced the impact of cerebral ischemia induced in rats /137/ and gerbils /138/. It also prevented apoptosis induced by serum-deprivation, in cultured cortical neurons /139/. Ginseng saponins also ameliorated ethanol-induced reduction of brain growth in neonatal rat pups /140/.

## 10. SAPONINS AND ANTIOXIDANT ACTIVITY

Saponins from several sources have demonstrated antioxidant activity. Soyasaponins with a 2,3-dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one (DDMP) moiety have antioxidant activity /141/. These soyasaponins, as well as soyasaponins I and soyasaponin Ab, inhibited damage to mouse fibroblasts by hydrogen peroxide /142/. Soyasaponin I decreased the free radical content of rat myocardiocytes induced by xanthine and xanthine oxidase /143/. Alpha-hederin protected against hydrogen peroxide-mediated DNA damage in HepG2 cells in culture. Free-radical scavenging and enhancement of catalase activity were two identified mechanisms /144/. Ginsenosides exerted protective effects against induced free radical damage in cultured endothelial cells /145/. Several animal studies demonstrated that

ginsenosides reduced oxidative damage to heart muscle /146-148/. Panaxadiol ginsenosides enhanced superoxide dismutase (SOD) activity /147/. Ginsenoside Rb2 was also a major inducer of SOD1 and catalase /149/. Ginsenoside Rb2 induced SOD1 through induction of transcription factor AP2 binding sites /150/. Ginsenosides Rb1 and Rg1 were also found to inhibit lipid peroxidation in rats, by increasing catalase and glutathione peroxidase activity. They, however, had no effect on superoxide dismutase /151/.

## 11. SAPONINS AND ANTI-INFLAMMATORY ACTIVITY

Several studies have demonstrated the anti-inflammatory activity of triterpenoid saponins /152,153/ and steroidal saponins /153/. The anti-inflammatory activity of escins Ia, Ib, IIa, IIb were investigated using carrageenan paw-induced edema. Acyl groups were essential to their activity. Escins Ib, IIa and IIb with either a 21-angeloyl group or a 2′O-xylopyranosyl moiety showed more potency than escin Ia which had both moieties /154/. The anti-inflammatory activity of saponins of *Argania spinosa* /155/ and saikosaponins /156/ was explained by their inhibitory effect on leukotriene activity. Tea-leaf saponin also antagonized the action of leukotriene D4 and inhibited the activity of hyaluronidase, an enzyme involved in inflammatory reactions /157/. Anti-inflammatory activity of saponins from *Panax notoginseng* was linked to decreased intracellular levels of free calcium in neutrophils, decreased dinoprostone, and decreased phospholipase $A_2$ activity /158/. Two oleanolic acid glucuronides with $C_6H_9O_5$ and $C_9H_{15}O_2$ substituents at the C-3 position of glucuronic acids exhibited a sialyl mimetic structure and inhibited excess neutrophil recruitment to injured tissue a thousand times more potently than sialyl Lewis X /159/. Korean red ginseng saponins and oleanolic acid bisdesmosides had anti-complement activity which can suppress the inflammatory response /160,161/. Structure-activity comparisons of ginsenosides showed that the anti-complement activity varied with the sugar moiety at C-6, i.e. glucosyl ≅ glucosyl-glucosyl > glucosyl-rhamnosyl, and at C-20, hydroxyl > glucosyl ≅ glucosyl-arabinosyl > glucosyl-glucosyl /160/.

## 12. CONCLUDING REMARKS

As the above survey indicates, saponins are bioactive compounds of considerable potential. Much, however, remains to be learned about their mechanism of action and structure-activity relationships. Research to date has used predominantly animal or *in vitro* models. There remains a dearth of human data, due, in part, to the difficulty of isolating large quantities of relatively pure saponin preparations. Nonetheless, as promising data continue to be assembled from both *in vitro* and animal models, clinical trials will hopefully be undertaken, enhancing our understanding of the role of saponins in human health.

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