Faculty of Pharmacy

Saponins

Phytotherapy

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Saponins

- This group of glycosides is widely distributed in the higher plants.
- Saponins are characterized by two or three common characters:

1. Forming colloidal solutions in water which foam upon shaking or producing froth of aqueous solutions, and that is why they have been used for long time in different parts of the world as detergents.
2. These substances modify and lower the surface tension and therefore foam when shaken. This has led to their use to increase the foaming of beer.

- Practical industrial applications of saponins is in cleaning industrial equipment and emulsifier of certain resins, fats and fixed oils.

- A characteristic for all saponins is their ability to cause hemolysis of red blood corpuscles (small cells) and to destroy them. When injected into the blood stream, they are highly toxic. However the fact that a plant contains **hemolytic** substances is not a proof that it contains saponins, the action could be due to other plant constituents.
- When taken by mouth, saponins are harmless, being not absorbed from the intestinal tract. Sarsaparilla (**is a soft drink, originally made from the *Smilax regelii* plant, but now sometimes made with artificial flavors**) for example, is rich in saponins but is widely used in the preparation of non-alcoholic beverages.

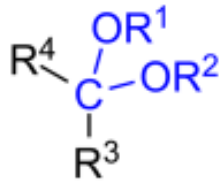
- Saponins are **toxic** especially to cold-blooded animals e.g. frogs, many are used as **fish poisons**.

❖ They are used in synthesis of **corticosteroids** like cortisone.

- We have two main groups of saponins:

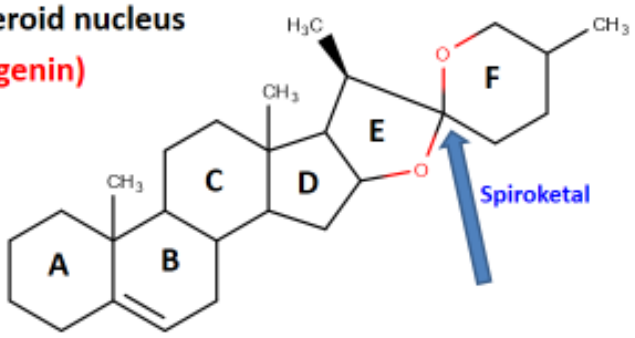
1. **Neutral steroidal glycosides** which contain spiroketal side chain. (Spiroketal: Ketal: **acetal** derived from a **ketone** --- **acetal**: **is a functional group with the following connectivity $R_2C(OR')_2$, where both R' groups are organic fragments. The central carbon atom has four bonds to it, and is therefore saturated and has tetrahedral geometry. The two R'O groups may be equivalent to each other or not. The two R groups can be equivalent to each other (a "symmetric acetal") or not (a "mixed acetal")**)

R' or (R^1 and R^2) is not H



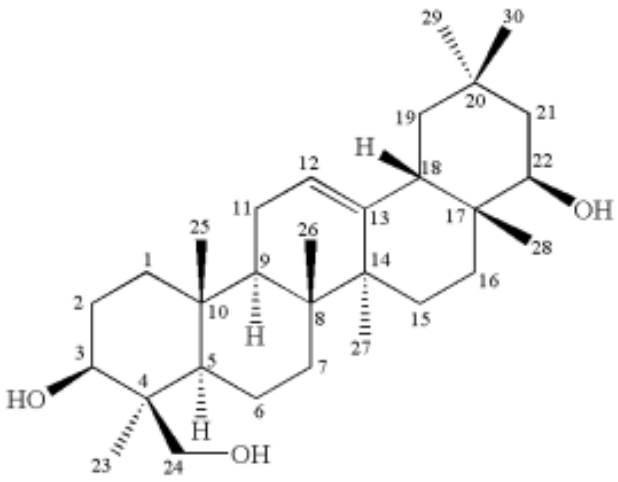
Spiroketal steroid nucleus

(Diosgenin)



❖ two rings E and F called **ketal** because are attached through **two oxygen atoms** and are called **spiral** because they are not on the same level.

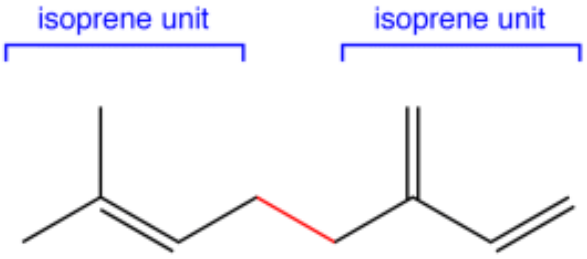
2) Acidic-pentacyclic (triterpenoid structure): They are triterpene structure which contains 30 C-atoms, and pentacyclic as they are 5 rings.

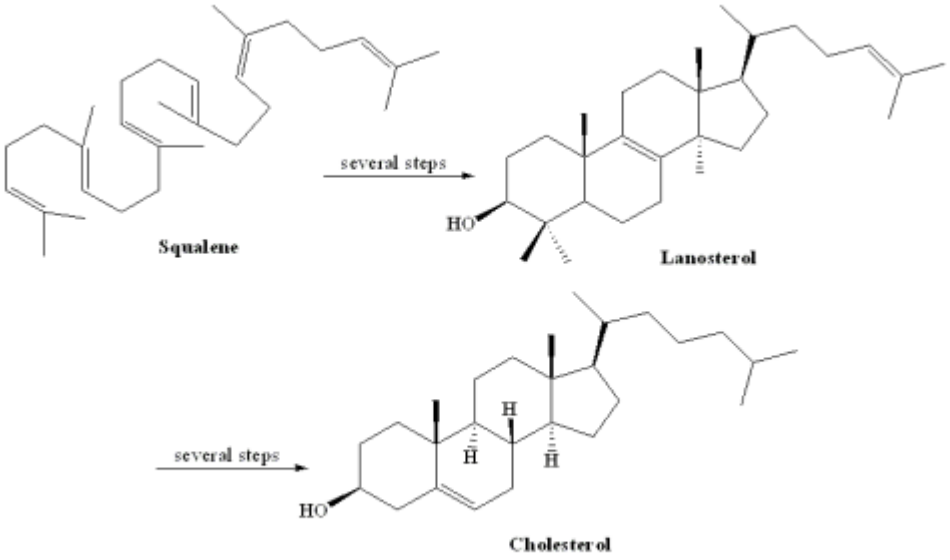


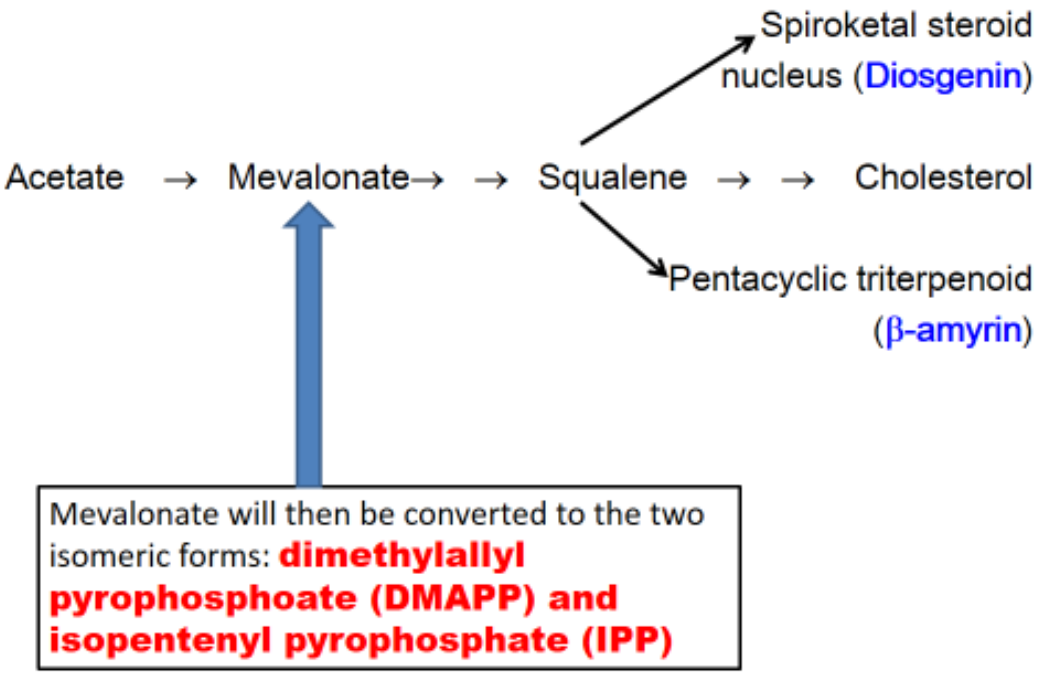
- It is found that the saponins, which are desired to be used as starting material for corticosteroid, must have OH group at C-3 and 11, so as to be converted to corticosteroids.

Biosynthesis of saponin glycosides:

- The biosynthesis of saponin glycosides is the same as that of cardiac glycosides which is started from **acetate** through **mevalonic acid** to **squalene**, which is usually formed by head-to-tail conjugation fashion of isoprene units, the squalene is then converted to either triterpenes or spiroketal steroids.




several steps
HO
Squalene
Lanosterol
several steps
H
H
H
HO
Cholesterol


Spiroketal steroid
nucleus (Diosgenin)
Acetate → Mevalonate→ → Squalene → → Cholesterol
Pentacyclic triterpenoid
(β-amyrin)
Mevalonate will then be converted to the two isomeric forms: dimethylallyl pyrophosphoate (DMAPP) and isopentenyl pyrophosphate (IPP)

Isolation of sapogenins

- Yams contain in addition to starch saponins and alkaloids.
- The material is fermented for 4-10 days.
- The sapogenin is isolated by acid hydrolysis from saponins.
- The water-insoluble sapogenin is then extracted by an organic solvent.
- Both wild and cultivated plants are used.

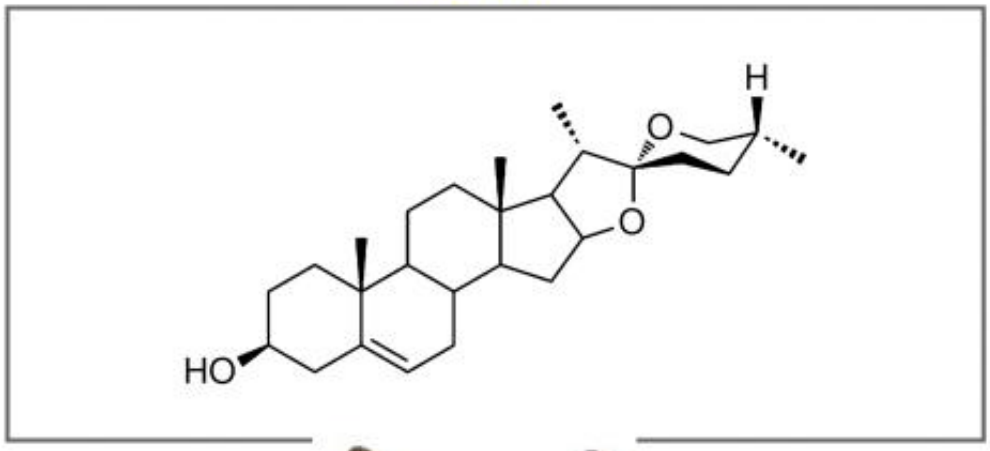
I. Neutral saponins:

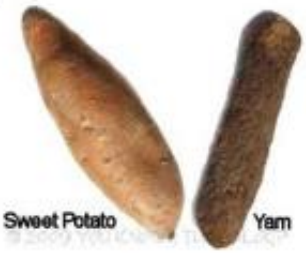
1. Discorea species:

- Tubers of Dioscoreas (Yams = plants with tubers containing a high content of starch, water and some sugars) have long been used as food for their starch content.
- According to the species, the tubers reach maturity in 3-5 years.
- On average yams yield 1-8% of total sapogenin according to the species of the families **Liliaceae** and **Dioscoraceae**.

Chinese Yam

- The main constituent is **disogenin**.





2. Sisal (*Agave sisalana*) السيزال:

- A plant prefers warm humid areas such as East Africa and the Caribbean countries.
- The leaves are used to produce **hecogenin** and other sapogenins that are used in cortisone manufacture.

3. Fenugreek (*Trigonella foenum-graecum*, Leguminosae) الحلبة:

- The seeds are a good source of diosgenin.
- As with dicoreas, the yield of diosgenin is increased by fermentation of the seed prior to acid hydrolysis.
- The seed yield of sapogenins is lower than that of discoreas.
- The seeds are source of fixed oil, mucilage, flavoring extracts and high protein-fodder (علف).

4. *Smilax* spp. (Family: Lilaceae) الفشاغ:

- Roots and sometimes rhizomes are the source of sapogenins such as the isomers **smilagenin** and **sarsasapogenin** (differ from each other in the configuration at C-25).
- Dried in the sun and packed into large bales.

USES:

- High reputation in the treatment of syphilis, rheumatism and certain Skin diseases.
- Treatment of psoriasis and eczema.
- As a vehicle in non-alcoholic drinks.

- For partial synthesis of cortisone and other steroids.

5. Butcher's Broom (*Ruscus aculeatus* Family: Lilaceae) السفندر المدبب:

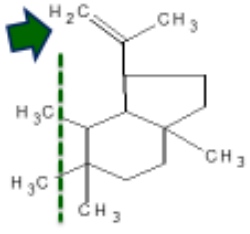
- A perennial dark green highly branched plant.
- The roots and rhizome are dried as source of saponins.
- Contain sapogenins related to those of discorea, and thus one of them is ruscogenin (1β-hydroxydiosgenin).

II. Acidic saponins:

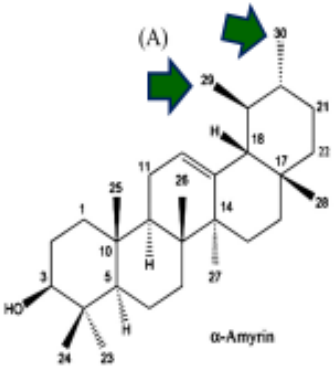
- Rare in monocotyledons (e.g. Liliaceae), but found in consdierable amounts in dicotyledons.
- The are either derivatives of α and β-amyrin or lupeol.

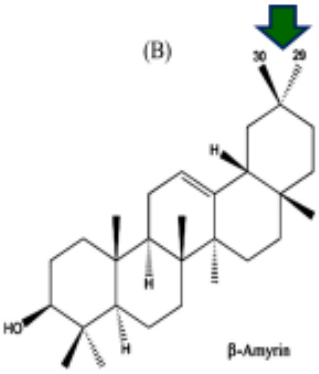
Amyrin is (organic compound) either of two isomeric triterpenoids found in some vegetable oils and resins.

The derivatives of amyrin have a carboxyl group replacing the methyl group on C-3, 17 or 20.



Lupeol





1. Glycyrrhiza: is the dried **rhizome** and **roots** of:

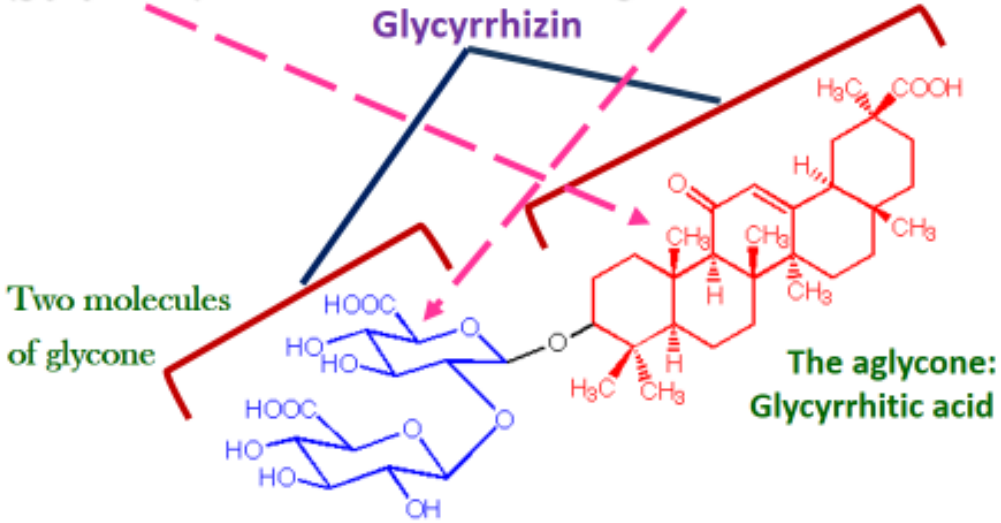
   a) *Glycyrrihiza glabra* variety *typica* : known in commerce as Spanish Licorice.العرقسوس أو نبات السوس

   b) *Glycyrrhiza glabra* variety *glandulifera:* known as Russian Licorice.

   c) *Glycerrhiza glabra* variety *violacea* : known as Persian Licorice.

Family: Leguminoseae.

- **Constituents:** The main constituents of glycyrrihiza is the saponin glycosides glycyrrhizin= a mixture of K and Ca glycyrrhizinic acid which on hydrolysis yields glycyrrhetinic (glycyrrhitic) acid and 2 molecules of glucuronic acid.



Glucuronic acid is a sugar acid derived from glucose,

- The yellow color of licorice root is due to flavonoid and coumarin glycoside constituents, while, the sweet taste is due to glycyrrhizin which is a mixture of K- and Ca- salts of glycyrrhizinic acid.

Uses of licorice:

1. Glycyrrhiza is used as flavoring agent, demulcent ملطف and mild expectorant.
2. Because of its deoxycorticosteroidal effect, it is used for the treatment of rheumatoid arthritis, Addison's disease (**is a rare, chronic endocrine system disorder in which the adrenal glands do not produce sufficient steroid hormones (glucocorticoids and mineralocorticoids)**) and various inflammatory conditions.
3. In confectionary industry.
4. Recently, they have found that it has antiviral and anti-tumor effect in mice.

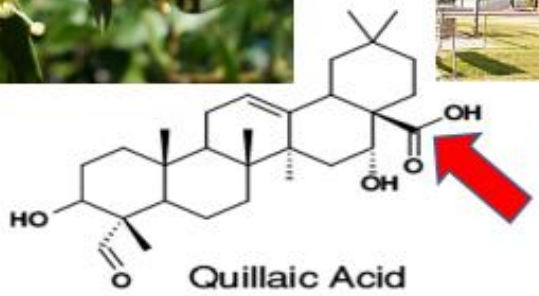
- Licorice root supplement extract health benefit by Ray Sahelian, M.D.

Licorice is a plant that grows in southern Europe, Asia, and the Mediterranean. The dried licorice roots and underground stems are used in herbal remedies. In China, licorice root is used for stomach ulcers, dry cough and to detoxify other herbs and drugs (Cont. The **Uses** of licorice or liquorice).

- Research has shown that deglycyrrhizinated licorice root supports and promotes healthy stomach lining and intestinal flora.
- One important side effect: licorice root extract can raise blood pressure (can cause hypertention).
- Deglycyrrhizintaed licorice (DGL), where glycyrrhizin was removed, can be used for long periods of time without any worry of hypertention.

2. Quillaja Bark: is the dried inner bark of *Quillaja saponaria* القلاجة الصابونية and other species of Quillaja. (Fam. Quillajaceae, was ranked under Rosaceae). The glycoside constituents is **quillaic acid** and **glucuronic acid**.

Soap tree



Quillaic Acid

3. Ivy (Hedera helix; Common ivy; English ivy):
اللبلاب السام

- It is a climbing and widely distributed plant throughout Europe and Asia.
- The used part of plant is the leaves and it belong to family **Araliaceae**.
- The important constituent are **saponins** involving triterpene genins hederagenin, bayogenin. Other constituents are flavonoids like **rutin**, **quercetin**.

Hederagenin

There is OH group on this carbon in quillaic acid

- The leaf extracts have been used traditionally as an expectorant for chest conditions such as bronchitis and whooping cough, also for gout and rheumatic pain.
- Externally, ivy is used cosmetically and for variety of skin conditions.
- Antibacterial, anti-leishmanial (protozoan disease transmitted by sand fly) and molluciscidal (a type of snails) effect (reported for the saponins).

4. Horse chestnut :

- The seeds are used part of the plant, *Aesculus hippocastanum* (family **Hippocastanaceae**), native to **western Asia** and **Balkan** and now widely distributed all over the world as ornamental plant.
- The seeds have long been used for their **saponin content** like aescin. It also contains **flavonoids** like quercetin, kaempferol, and also it contains **coumarins** and **tannins**.

The plant is traditionally used for **peripheral vascular disorders** including haemorrhoids, varicose veins, leg ulcers.
Also, it is used as anti-inflammatory due to its content of flavonoides, coumarins.
Coumarins cause a thinning of the blood, so should not be taken with anticoagulants.

Aescin

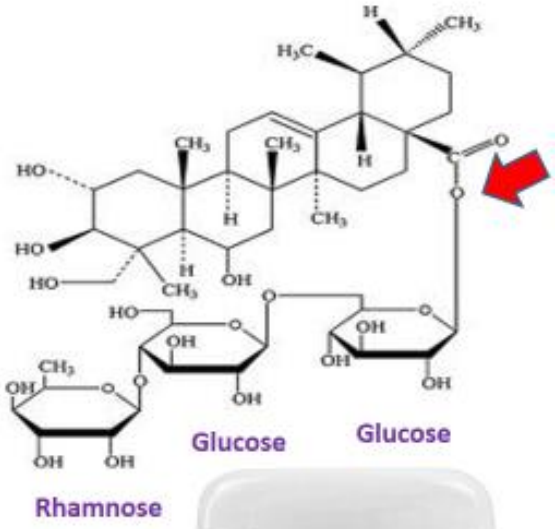
5. Centella: سرة الأرض

- Grows in tropical swampy areas and wetlands in Asia.
- The **aerial parts** of *Centella asiatica* (family: Umbelliferae or **Apiaceae** : الفَصيلَة الخَيْمِيّة).
- **Most famous plants belonging to Apiaceae or Umbelliferae:**
- البقدونس و الكزبرة و الشبت و الجزر و الكمون و اليانسون و الكرفس والكراويا و القزع
- It is found in Pakistan, India and Africa.
- The main constituents are **triterpene saponins asicoside** = (centilloside = asciaticoside the main constituent).
- Also, it contains small amounts of **v.oil** (chiefly **α-humulene**) which have **antibacterial activity.**
- In addition, contains **flavonoids** like **quercetin,** and **phytosterols**.
- **Main uses:**

1. Anti-rheumatic. **2.** dermatological agent for wound-healing and cosmetic preparations. **3.** peripheral vasodilator.

Asiaticoside = Centelloside

A triterpenoid



7. **Ginseng:** is the **root** of the perennial herbs:

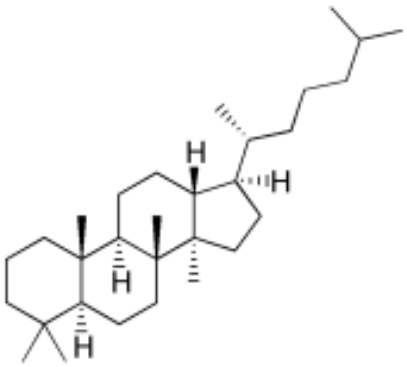
a. *Panax quinquefolius* Linne (Family: Araliaceae).

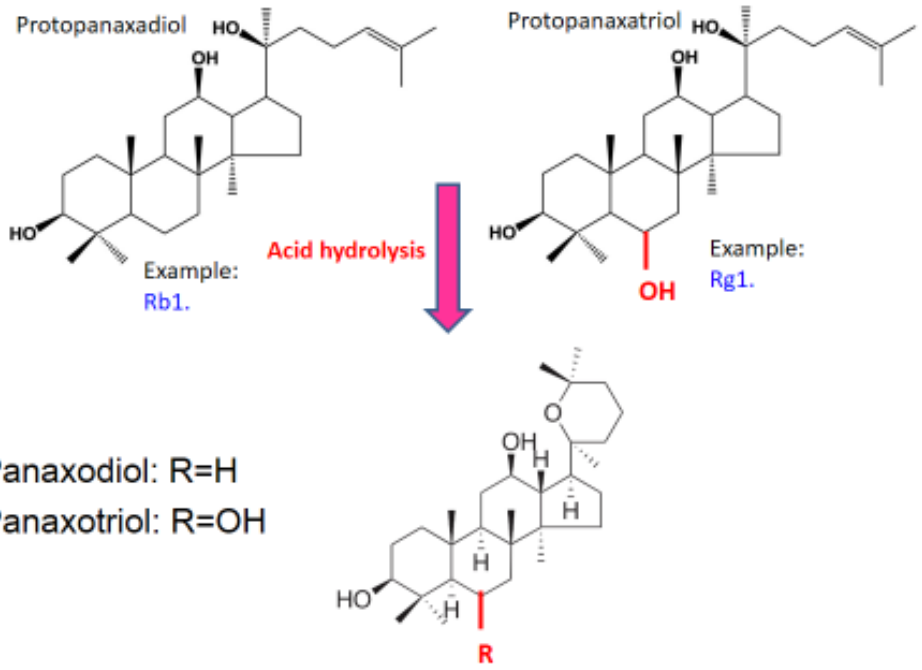
b. *Panax pseudoginseng* Wallich (Family: Araliaceae).

- The former grows in eastern **United States** and **Canada**, while the latter is indigenous to the mountainous areas of **Asia**.
- The roots are collected at the age of **3-6** years.
- Ginseng contains up to **3%** of **saponins** which is a complex mixture of triterpenoid saponins.
- Constituents: mainly dammarane-type saponins: ginsenosides (Japanese researchers) and panaxosides (Russian researchers).
- Generally, these two categories are called ginsenosides (panaxosides).
- Ginsenosides or panaxosides can be obtained by acid hydrolysis of protopanaxodiols and protopanaxotriols, where ring closure occurs (next slide).

i.e.:

- Protopanaxadiol(has a drammarane structure) gives ginsenoside (acid hydrolysis and ring closure).
- Protopanaxadiol (has a drammarane structure) gives panaxosides (acid hydrolysis and ring closure).
- Drammarane structure: **is a tetracyclic triterpene found in sapogenins like those of ginseng.**



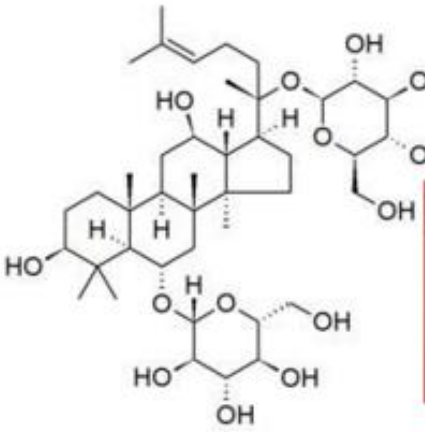


Uses and pharmacological effects

- One or more of these glycosides appear to account for the biological properties of ginseng which is:
  - Tonic (modulates life and improves the feeling to happiness; improves mode).
  - Stimulant.
  - Diuretic.
  - Carminative.

- It also reduces blood glucose and acts on metabolism, central nervous system and endocrine secretions, it is used in Orient in treatment of anemia, diabetes, insomnia, neurasthenia (a condition with symptoms of fatigue, anxiety, headache, heart palpitations, high blood pressure, neuralgia and depressed mood), gastritis and sexual impotence.





Panaxoside A = Ginsenoside Rb_1

Ginseng abuse syndrome:

a. Hypertension
b. Skin eruption
c. Edema
d. Diarrhea
e. Mastalgia in females (mastalgia: breast pain).

8. *Eleutherococcus senticosus* (Siberian ginseng, Acanthopanax senticosus):

- The rhizomes are used for their medicinal effect as it contains constituents termed *Eleutheroside glycosides* (A-G, M).
- Also, it has coumarins, and a group of compounds which are called heteroglycans (eleutherans A-G), which have hypoglycemic effect.

- The plant has been used in China for many centuries for rheumatoid complaint.