phyto therapy®

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PHYTOTHERAPY

- **Phytotherapy** is the **study of the use of extracts of natural origin as medicines or health-promoting agents**.
- Traditional phytotherapy is a synonym for **herbalism** and regarded as **alternative medicine** by much of Western medicine.

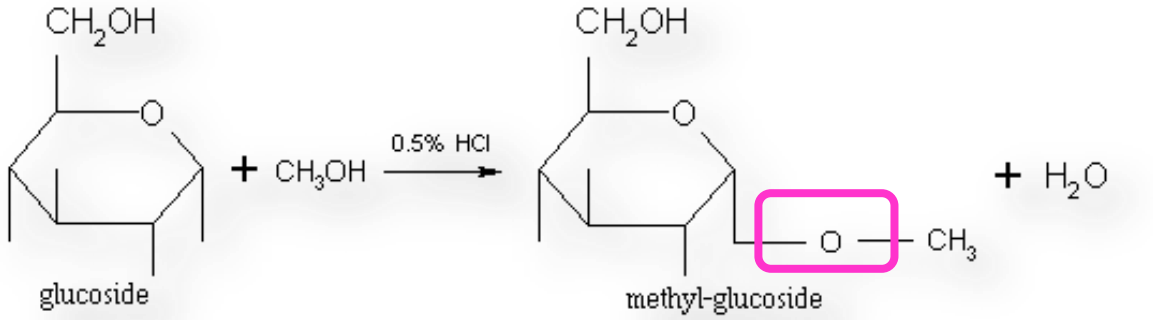
PART – 1

Menu

- Glycosides
- Saponin glycosides
- Flavonoid glycosides
- Anthocyanidin
- Cyanogenic glycosides
- Isothiocyanate glycosides
- Phenolic & Aldehyde glycosides
- Coumarins - Bitter principles
- Terpenes and Terpenoids
- Tannins

Glycosides

- They are compounds containing a **carbohydrate (sugar)** and a **noncarbohydrate** residue in the same molecule.
- The **carbohydrate** residue is **attached by an acetal linkage at carbon atom 1** to a **noncarbohydrate** residue.
- The **carbohydrate (sugar) component** is called the **GLYCONE**.
- The **noncarbohydrate component** is known as the **AGLYCONE**.

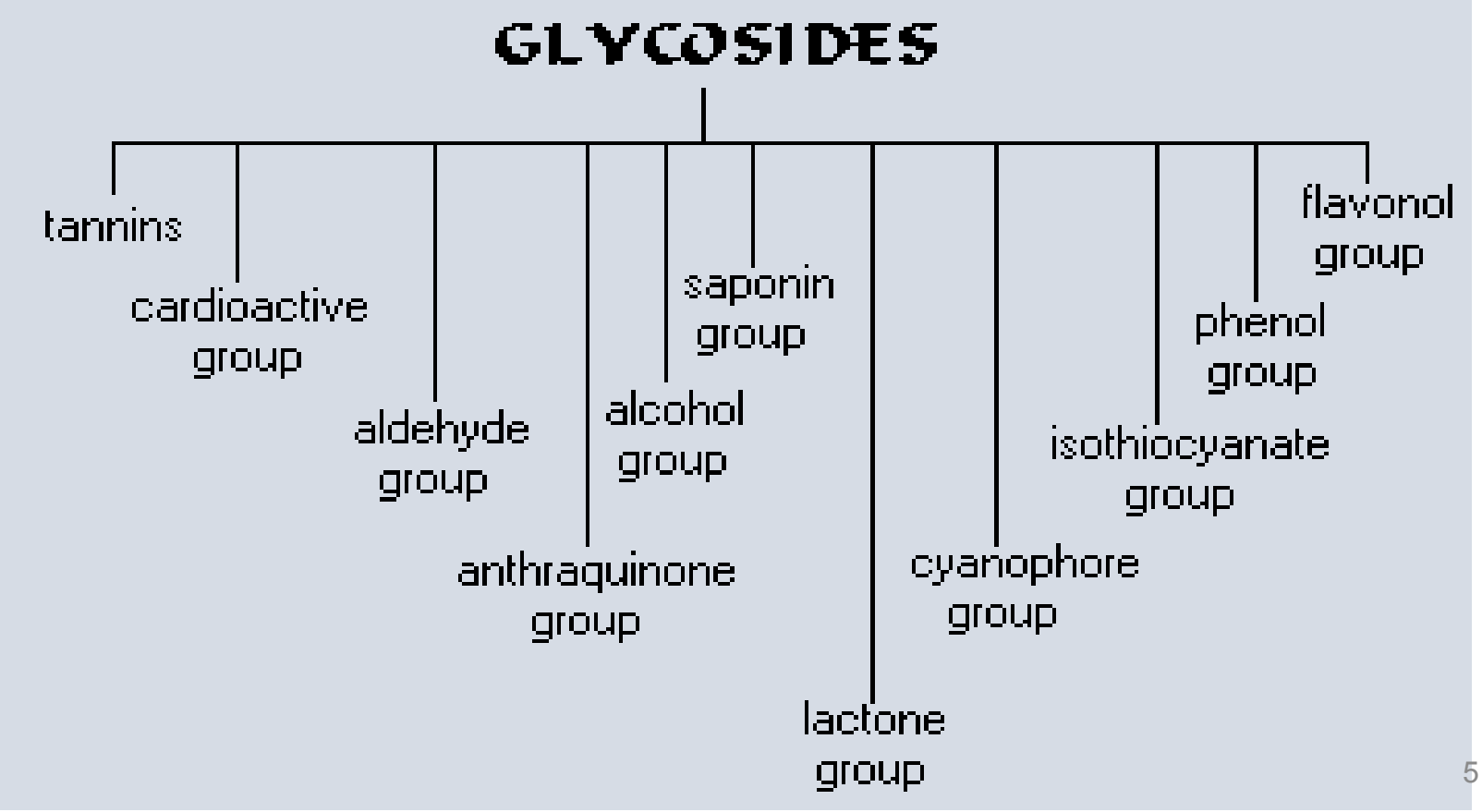


- The sugar moiety can be joined to the aglycone in various ways:
  1. **Oxygen *(O-glycoside)***
  2. **Sulphur *(S-glycoside)***
  3. **Nitrogen *(N-glycoside)***
  4. **Carbon (*C-glycoside)***

Classification of Glycosides

- The aglycone may be methyl alcohol, glycerol, a sterol, a phenol, etc.

- Based on the chemical nature of the aglycone group, glycosides can be classified as follows:




SAPONIN GLYCOSIDES

SAPONIN GLYCOSIDES

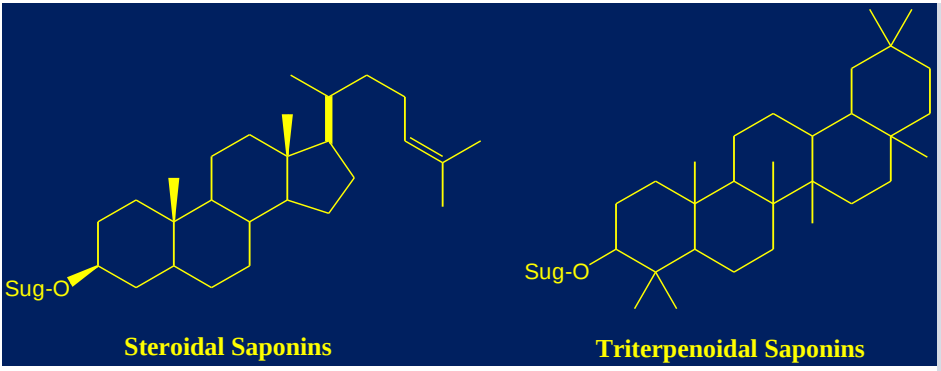
- Saponins on hydrolysis yield an **aglycone known as** "**sapogenin**".
- Saponin glycosides are divided into 2 types based on the chemical structure of their aglycones (**sapogenins**).

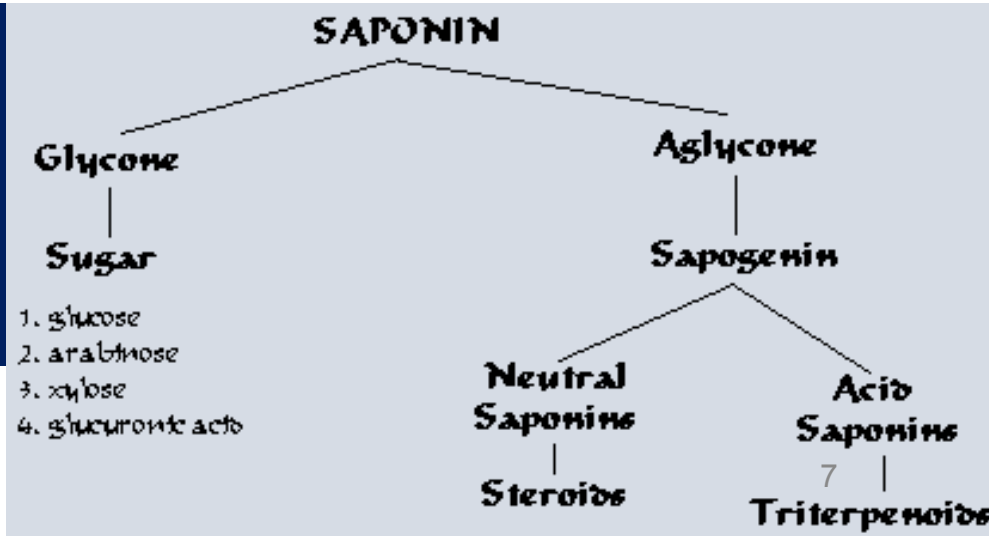
SAPONIN = SUGAR + SAPOGENIN

glycone	aglycone

Classification of Saponins: According to the nature of the aglycone:

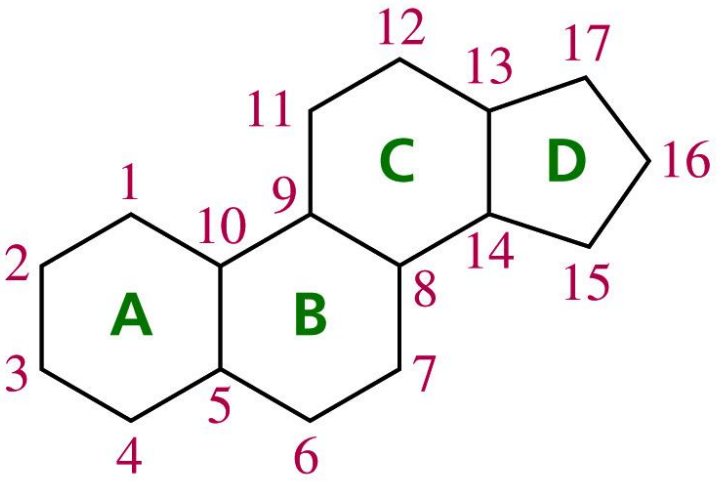
1. **Neutral saponins** or **Steroidal saponins** with **spiroketal** side chains.
2. **Acid saponins** or **Triterpenoidal saponins**



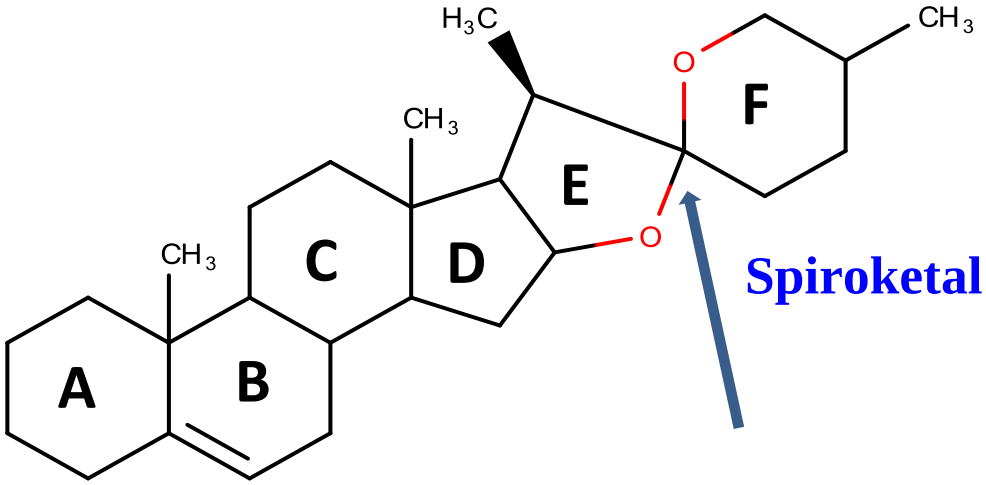


Steroidal Saponins

- **Neutral steroidal glycosides** which contain **spiroketal side chain**.
- Two rings **E** and **F** called **ketal** because they are attached through **two oxygen atoms** and called **spiral** because they are **not on the same level.**
- Less distributed in nature comparing to Triterpenoidal saponins.
- **Used mainly as precursors** for the **partial synthesis of sex hormones and corticosteroids**.
- Drugs containing Steroidal saponins such as:
  - *Discoria* species Diosgenin
  - *Sarsaparilla* Roots Sarsapogenin



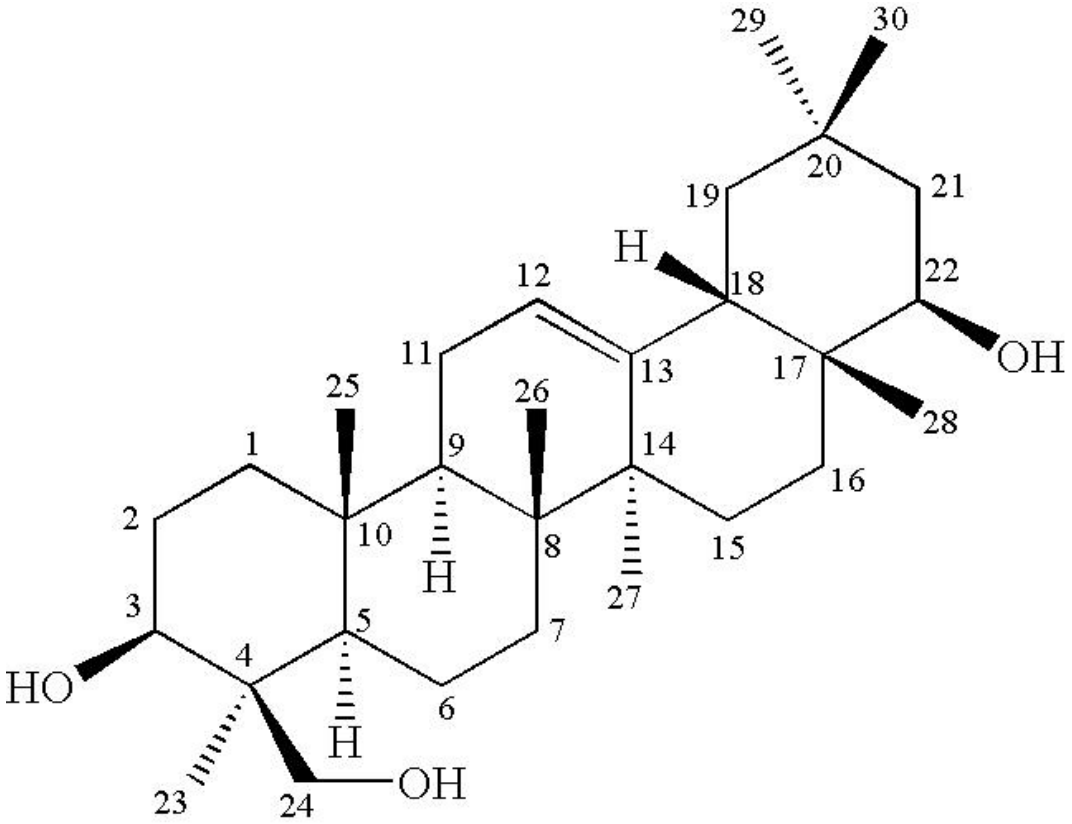
the steroid ring system



Spiroketal steroid nucleus (Diosgenin)

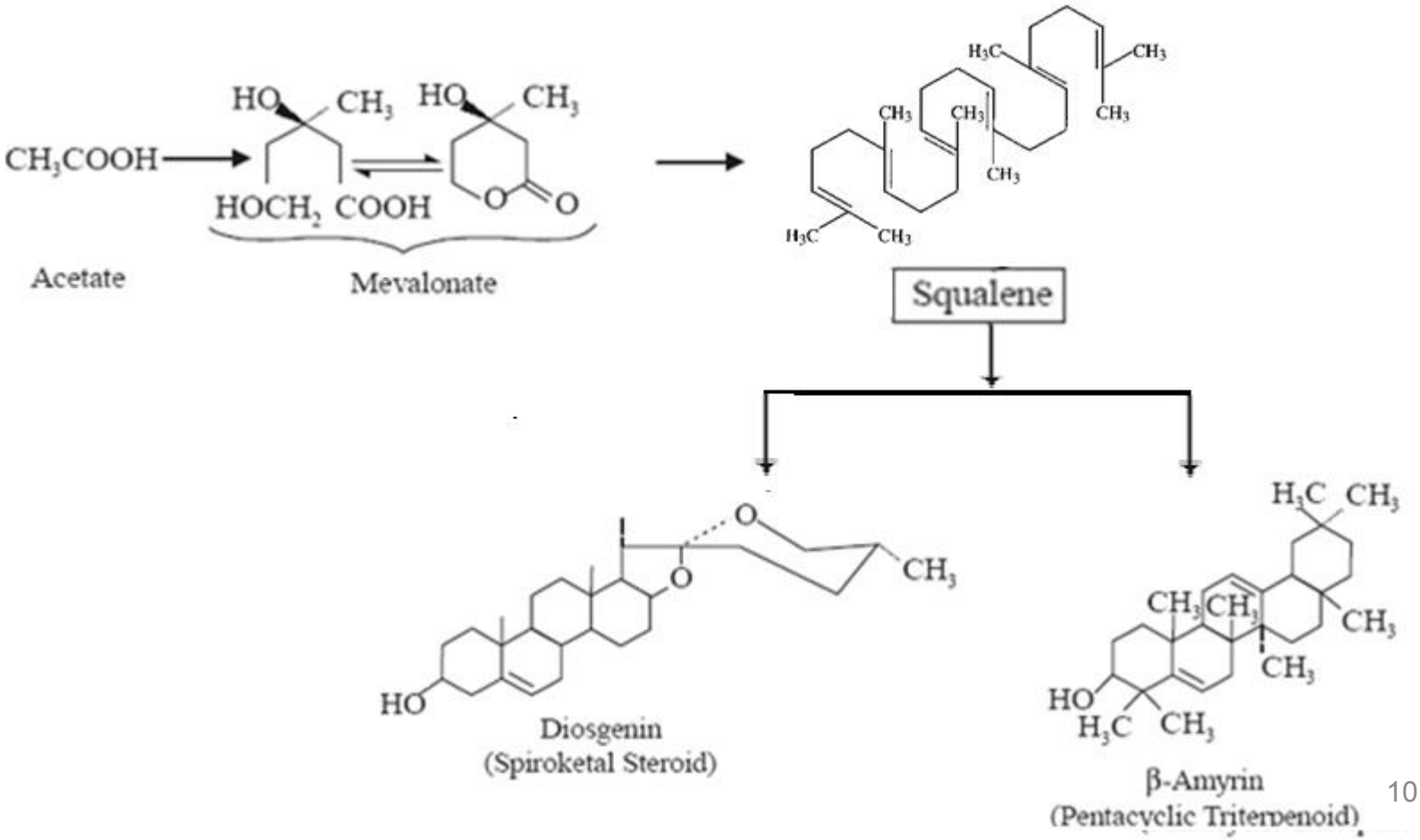
Triterpenoidal Saponins

- They are **triterpene structure** which contains **30 C-atoms**.
- They have **pentacyclic skeleton** with 5 rings.
- Much **more distributed in nature**.



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 **triterpenoid** or **spiroketal** steroids.



SAPONINS

❖This group of glycosides is widely distributed in the higher plants.

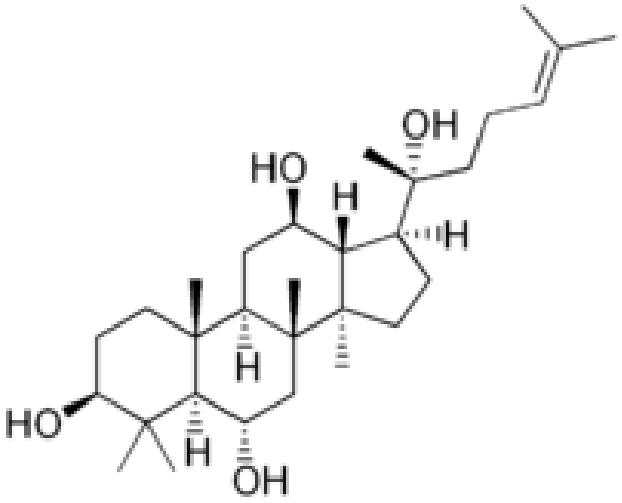
❖Saponins are characterized by two or three common characters:

- Forms **colloidal solutions in water** which yields **foam upon shaking** or **produce froth of aqueous solutions**, and that is why they have been used for long time in different parts of the world as **detergents**.
- These substances **modify and lower the surface tension** and therefore produce 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.**

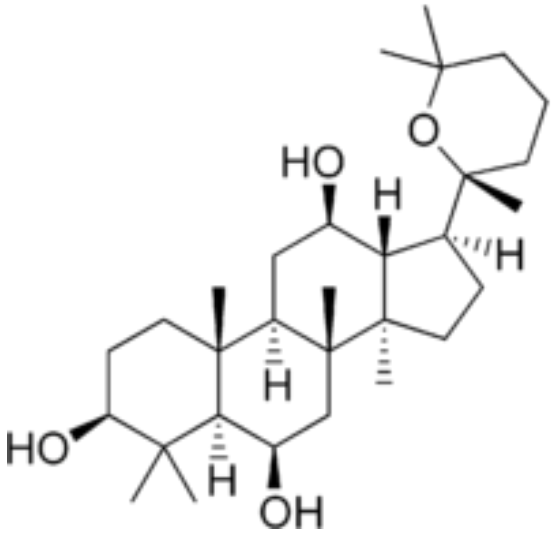
- All saponins can cause **hemolysis of red blood corpuscles (RBC)** and destroy them.
- They are **highly toxic when injected** into the blood stream.
- **BUT** when **taken by mouth**, **saponins are harmless**, because they cannot be absorbed from the intestinal tract.
- **Note -** if a plant contains hemolytic substances, it is not a proof that it contains saponins, the action could be due to other plant constituents.
- Saponins are **toxic especially to cold-blooded animals** e.g. frogs
- Used as **fish poisons** as they accumulates in gills preventing O_2 transfer
- They are used in **synthesis of corticosteroids like cortisone**.
- **Sarsaparilla** (is a soft drink, originally made from the *Smilax regelii* plant, but now sometimes made with artificial flavours) is rich in saponins and is widely used in the preparation of non-alcoholic beverages.

Ginseng Saponins

- It is obtained from the **root** of the perennial herbs:
  - ***Panax quinquefolius*** Linne (Family: Araliaceae)
  - ***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 (ginsenosides / panaxosides).**
- **Ginsenosides** can be broadly divided into two groups based on the carbon skeletons of their aglycones**:**
  - **Four-ring dammarane family:** Dammarane is a tetracyclic triterpene
    - protopanaxadiols and protopanaxatriols
  - **Oleanane family:** natural triterpene

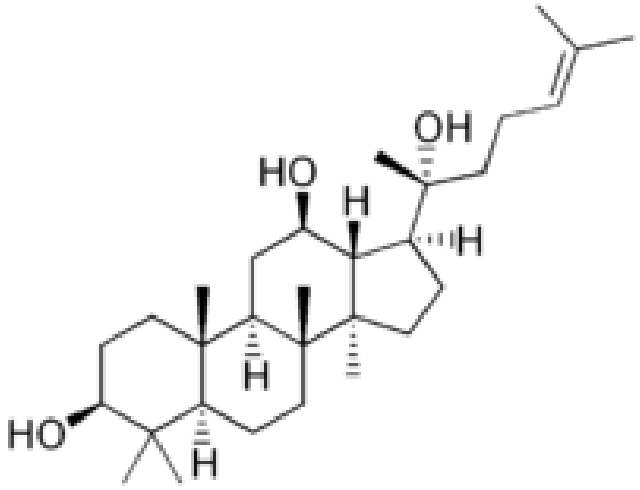


Protopanaxatriol

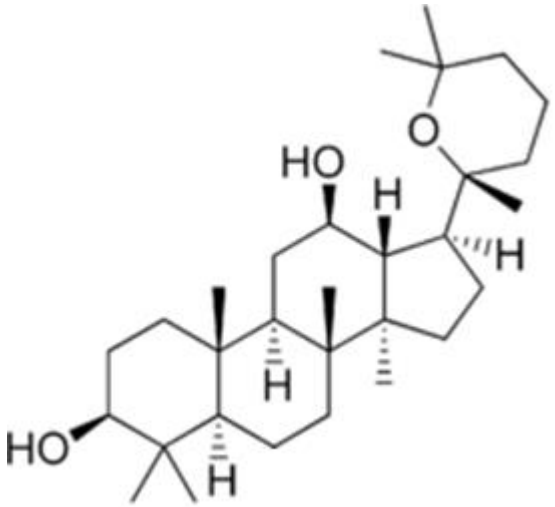


Panaxatriol

Panaxatriol is formed by the dehydration of protopanaxatriol.



Protopanaxadiol



Panaxadiol

Ginseng Saponins

Uses

- It has an adaptogenic (antistress, anti-fatigue) effect.
- It improves both physical and mental performance including learning, memory and physical capabilities.
- It improves the immune function and metabolism.
- It improves liver functions.
- It stabilizes blood glucose and blood pressure.

Ginseng abuse syndrome:

a. Hypertension

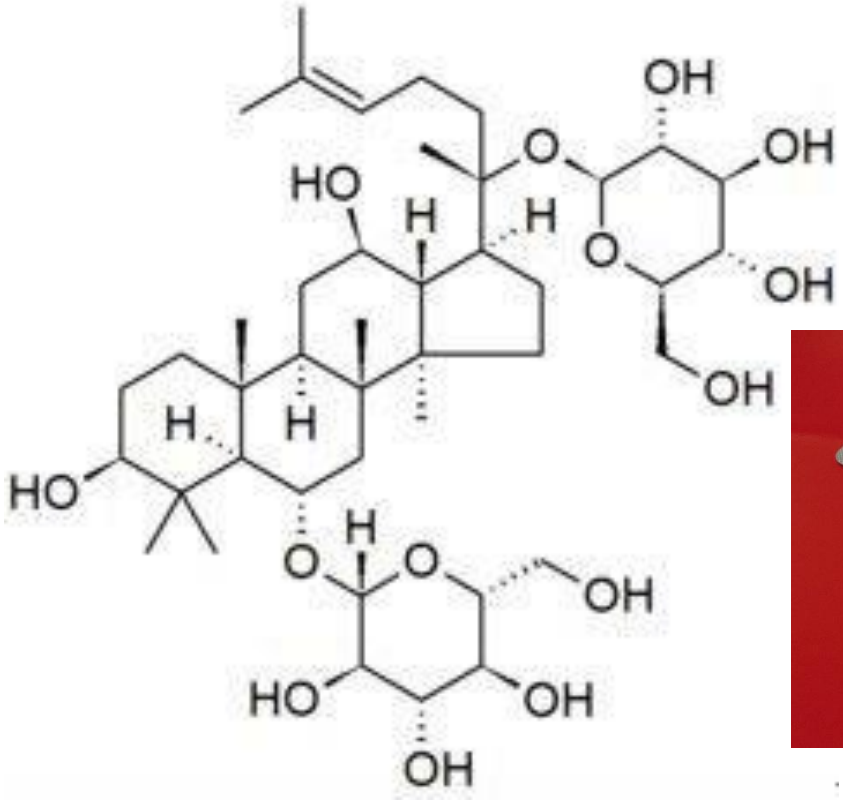
b. Skin eruption

c. Edema

d. Diarrhea

e. Mastalgia in females (mastalgia: breast pain).

Panaxoside A = Ginsenoside Rb_1



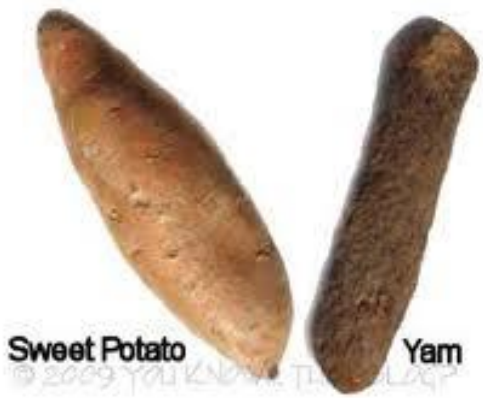
Eleutherococcus senticosus

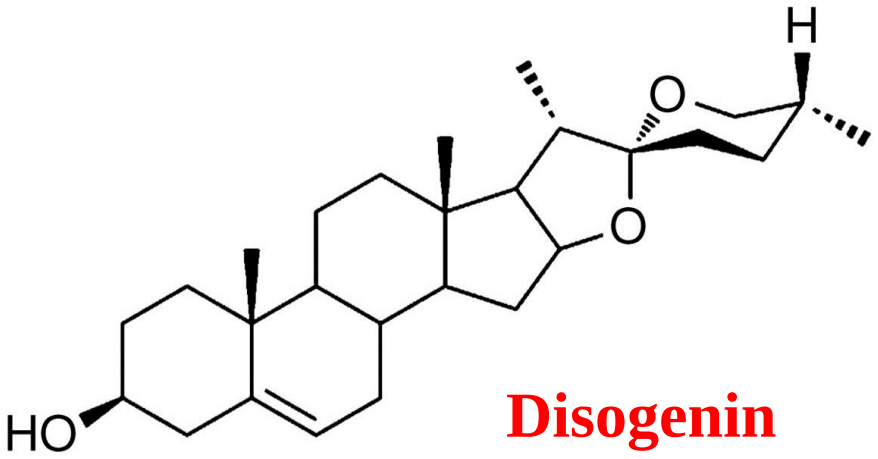
(Siberian ginseng, Acanthopanax senticosus)

- 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 the treatment of **rheumatoid arthrities.**

Dioscorea species (Neutral saponins)

- **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.
- The tubers of this species **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**.
- The main constituent is **disogenin**.



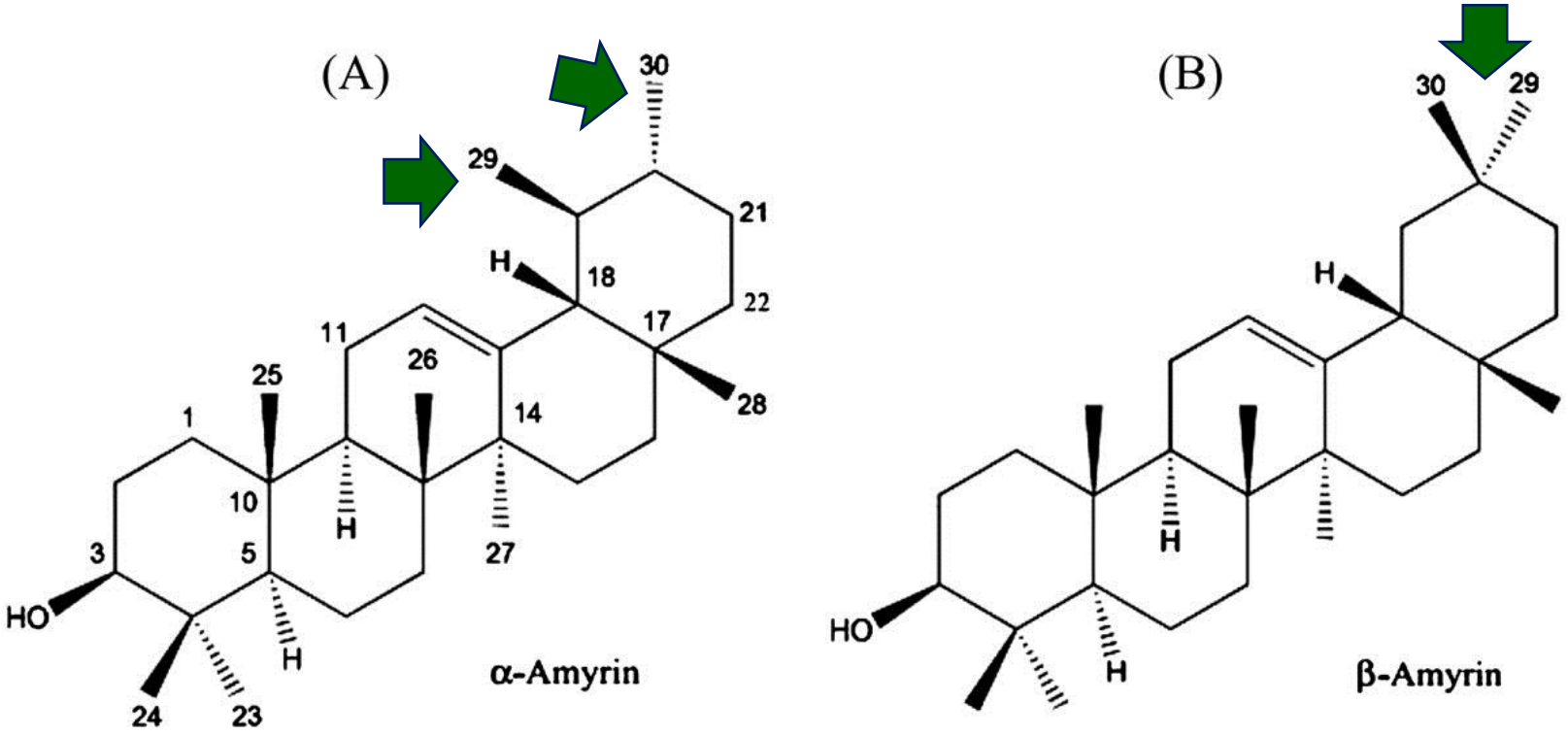


Disogenin

Acidic Saponins

- The are either derivatives of **α and β-amyrin.**

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



Glycyrrhiza (Licorice)

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

a) ***Glycyrrihiza glabra*** variety ***typica*** : known as Spanish Licorice.
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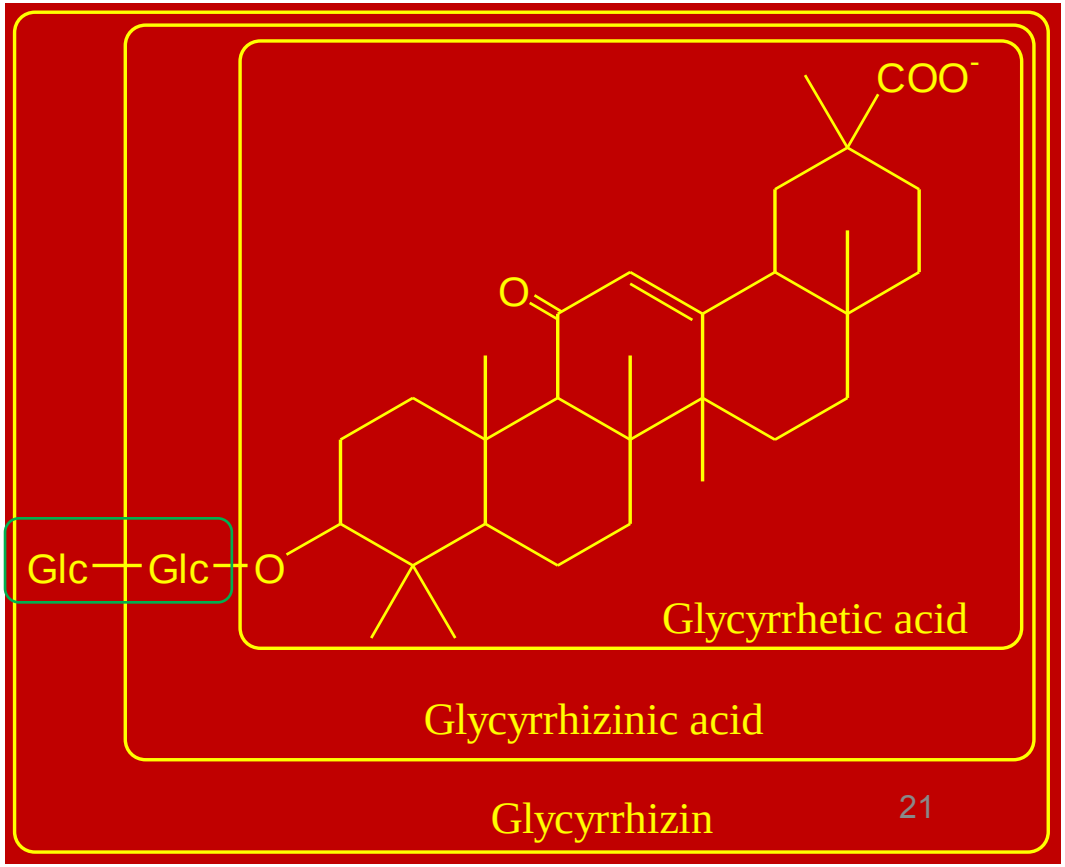
b) ***Glycyrrhiza glabra*** variety ***glandulifera:*** known as Russian Licorice.

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

Constituents of Glycyrrhiza:

- The main constituents of glycyrrihiza is the saponin glycosides **glycyrrhizin** or **glycyrrhizinic acid** which on hydrolysis yields **glycyrrhetic acid** (glycyrrhetinic acid) and 2 molecules of **glucuronic acid**. Glucuronic acid is a sugar acid derived from glucose
- The yellow colour of licorice root is due to **flavonoid** and **coumarin** glycoside constituents.

Two molecules of glycon

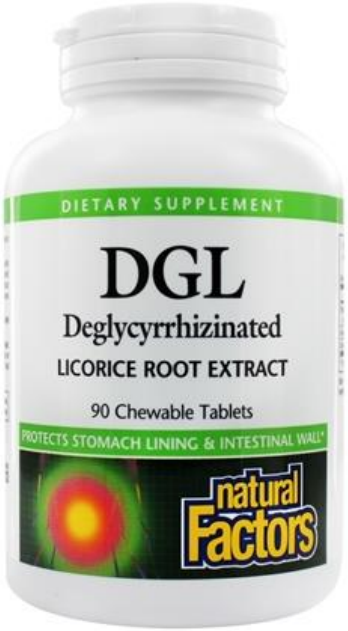


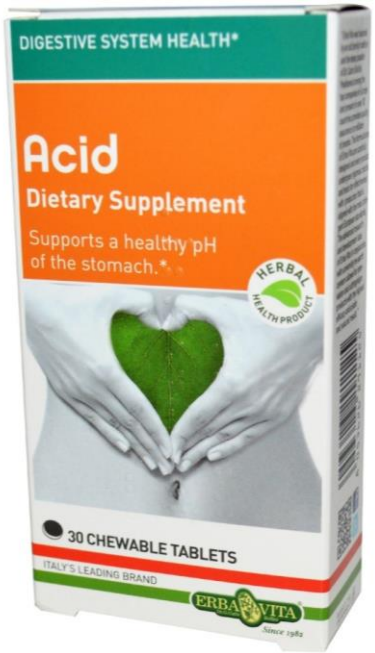
Uses of licorice

1. Glycyrrhiza is used as flavoring agent, demulcent 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. Treatment of **peptic ulcer**.
4. Recently, it has shown antiviral and anti-tumor effect in mice.
5. Treatment of liver diseases and liver protection.

Uses of licorice

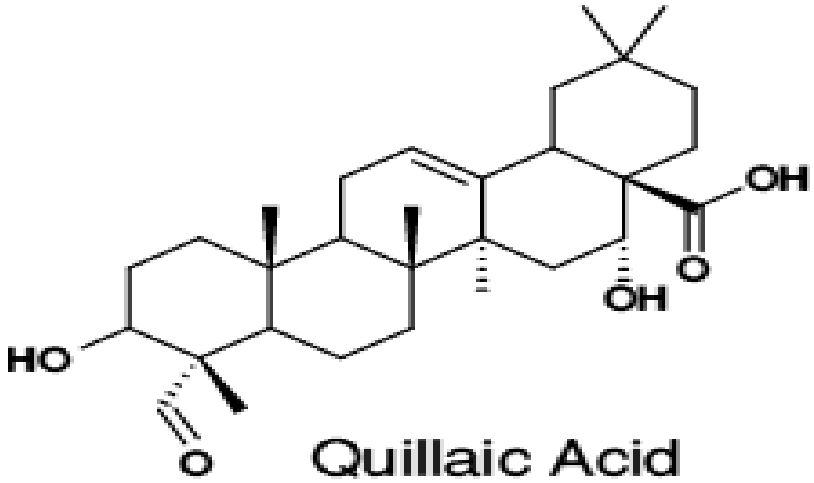
- The dried licorice roots and underground stems are used in herbal remedies.
- In China, licorice root is used for stomach ulcers, dry cough and to detoxify other herbs and drugs.
- **Glycyrrhizinic** and **glycyrrhetinic acids**, substances in licorice root **associated with high blood pressure**, have been removed.
- **Side effect:** licorice root extract can **raise blood pressure** (can cause hypertension).





Quillaja Bark (Soapbark tree)

- It is the dried inner **bark** of ***Quillaja saponaria*** and other species of Quillaia.
- Family: **Quillajaceae**
- The glycoside constituents are **quillaic acid (**aglycone**)** and **glucuronic acid**.
- Other constituents include tannins, polyphenols, and calcium oxalate.



Quillaic Acid

Uses of Soapbark

- Soapbark is famous for the medicinal and commercial use of its **inner bark,** an abundant source of saponins (distinguished as **quillaia** saponin).
- The inner bark is dried, powdered, and used as an emulsifier and foaming agent in cosmetics, shampoos, cream, beer, soft drinks, and even fire extinguishers.
- Soapbark saponins are supposedly **poisonous when consumed at greater concentrations** than the amount added to commercial products.
- Despite safety concerns, people take quillaia for **cough, bronchitis**, and **other breathing problems**.
- Quillaia extract is also **applied directly to the skin** to treat **skin sores, athlete's foot,** and **itchy scalp**. It is sometimes included in **shampoos for dandruff**, in hair tonic preparations for thinning hair, and in douches for vaginal discharges.
- It is also used in veterinary vaccines as adjuvant (e.g., foot-and-mouth disease vaccines)
- In foods, quillaia is used in frozen dairy desserts, candy, baked goods, gelatins, and puddings.
- In South America, quillaia bark is used to wash clothes.

QUILLAIA Side Effects & Safety

- Quillaia contains high amounts of **tannins** which can cause **stomach and intestinal disturbances**. Don't use in stomach or intestinal disorder.
- It can also irritate and damage the lining of the mouth and throat.
- Quillaia also contains chemicals called **oxalates** that **can lower blood calcium levels** and **cause kidney stones**.
- Quillaia use can also cause diarrhea, serious breathing problems, convulsions, coma, red blood cell destruction, liver and kidney failure.
- **Pregnancy and breast-feeding:** Quillaia might be UNSAFE for both mother and infant. Avoid use.

QUILLAIA - Drug Interactions

- Medications taken by mouth (Oral drugs) interacts with QUILLAIA.
- Quillaia contains **tannins** which can absorb substances in the stomach and intestines. If quillaia is taken along with oral medications, it can decrease absorption and effectiveness of medicine. To prevent this interaction, take quillaia at least one hour after medications you take by mouth.
- **Example**: Taking quillaia along with metformin (orally) **decreases the absorption and effectiveness of metformin for lowering blood sugar**.

Ivy

(Hedera helix; Common ivy; English ivy)

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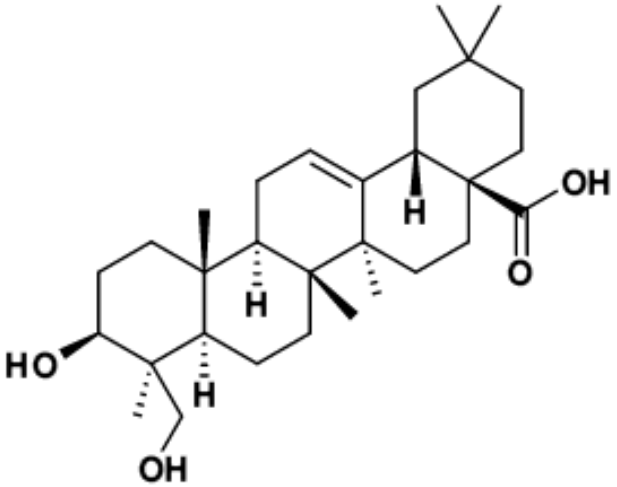
- It is a climbing and widely distributed plant throughout Europe and Asia.
- The used part of plant is the **leaves** and it belongs to family **Araliaceae**.
- The important constituent are **saponins** involving triterpene genins **hederagenin**, **bayogenin**.
- Other constituents are flavonoids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



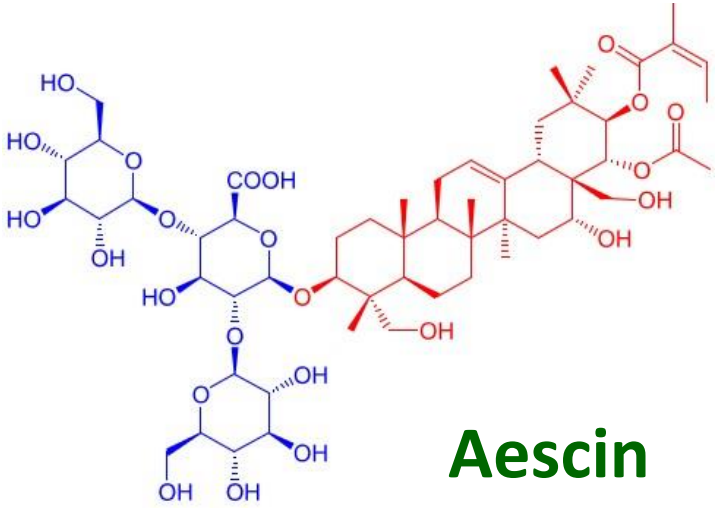
Hederagenin

- 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.

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 **coumarins** and **tannins**.

- **USES**: The plant is traditionally used for **peripheral vascular disorders** including **haemorrhoids, varicose veins, leg ulcers**.
- It is also 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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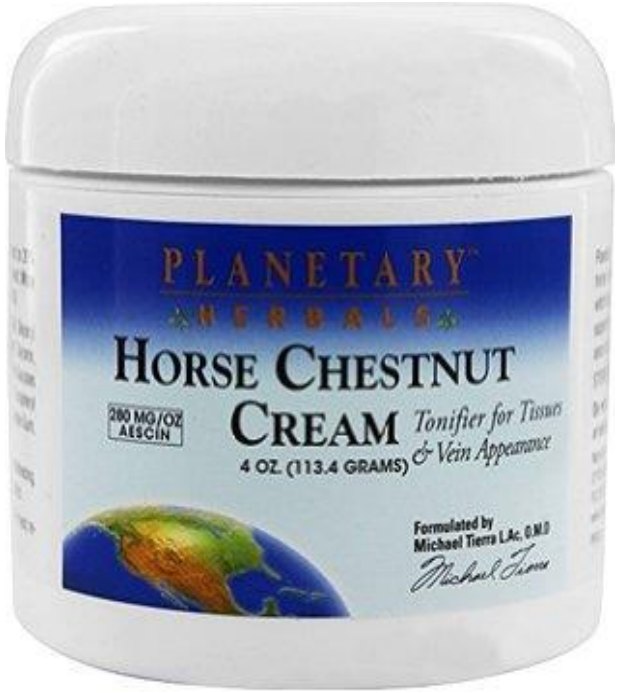
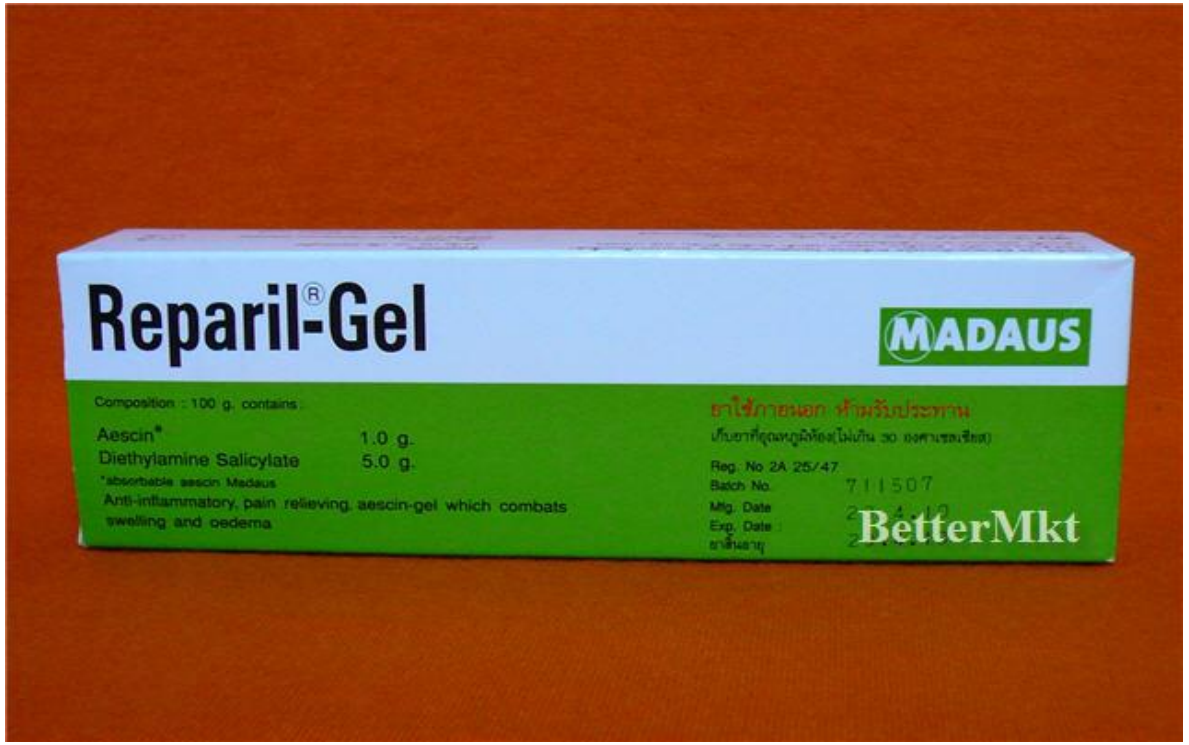

PLANETARY
HERBALS
HORSE CHESTNUT
CREAM
Tonifier for Tissues & Vein Appearance
280 MG/OZ AESCIN
4 OZ. (113.4 GRAMS)
Formulated by Michael Tierra L.Ac. O.M.D


Reparil®-Gel
MADAUS
Composition : 100 g. contains
Aescin* 1.0 g.
Diethylamine Salicylate 5.0 g.
*absorbable aescin Madaus
Anti-inflammatory, pain relieving, aescin-gel which combats swelling and oedema
Reg. No 2A 25/47
Batch No.
Mfg. Date
Exp. Date
BetterMkt

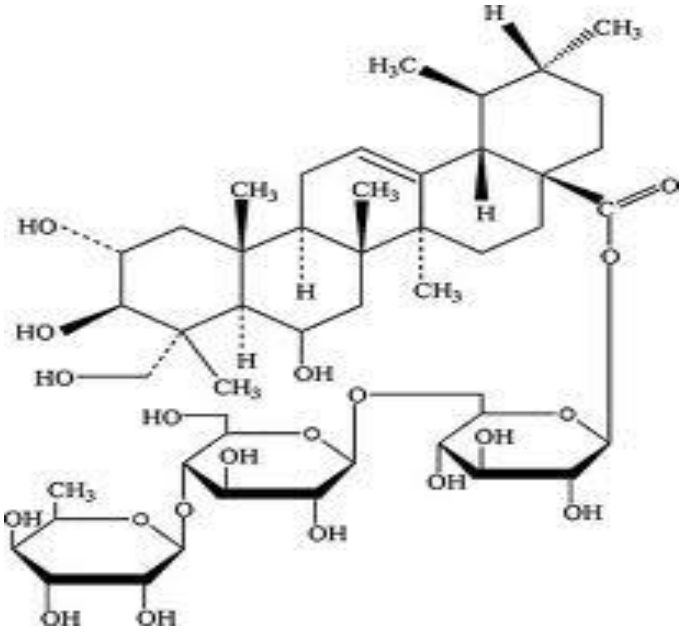
Centella: سرة الأرض (Gotu Kola)

- Grows in tropical swampy areas and wetlands in Asia.
- It is found in India, Pakistan and Africa.
- The **aerial parts** of ***Centella asiatica***
- **Family**: Umbelliferae or **Apiaceae**
- The main constituents are **triterpenoid saponins asicoside** (**asiaticoside, centelloside, madecassoside**).
- Also, it contains small amounts of **volatile oil** (chiefly **α-humulene**) which has **antibacterial activity**.
- In addition, it contains **flavonoids** like **quercetin**, and **phytosterols**.

Main uses:

1. **Anti-rheumatic** and lowers back pain.
2. Dermatological agent for **wound-healing** and cosmetic preparations.
3. Asitic and madecassic acids and asiaticoside and madecassoside **stimulate and regulate the production of collagen**, **essential for wound healing**.
4. It also has the ability to facilitate the **regeneration of axons of the nerves** that border the wound. Aqueous extract (infusion) of eaves can **increase cognitive abilities**, learning, memory while **alleviating anxiety**.
5. It protects the stomach wall (ulcer) **by increasing the secretion of mucus.**
6. Peripheral vasodilator.

Centella
سرة الأرض



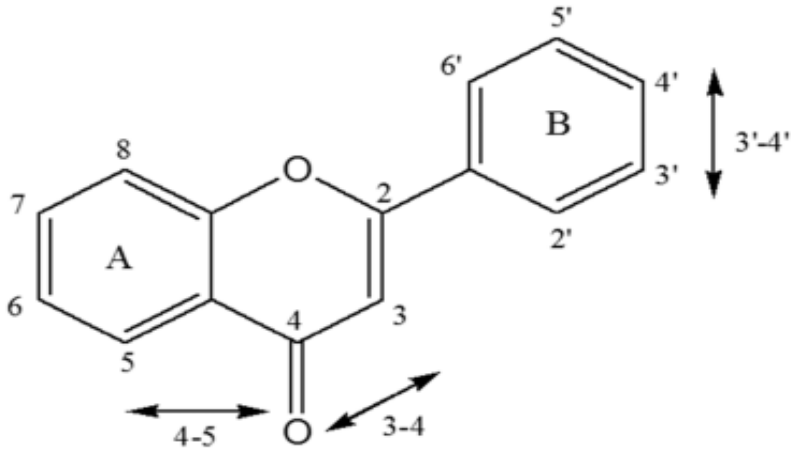
Asiaticoside
(Centelloside)
A triterpenoid


Flavonoid
Glycosides

Flavonoid Glycosides

- Flavonoids are the **largest group of naturally occurring phenols** and **found either in free form or as glycosides**.
- **Flavonoids** (from the Latin word *flavus* meaning **YELLOW**, their color in nature) are a class of plant and fungus secondary metabolites.
- The flavonoids **contribute to many other colours found in nature**, particularly the **yellow and orange of petals**; even the **colourless flavonoids absorb light in the UV spectrum** (due to their extensive chromophores) and **are visible to many insects**. [A chromophore is the part (or moiety) of a molecule responsible for its color].
- It is likely that these compounds have **high ecological importance** in nature **as colour attractants to insects and birds as an aid to plant pollination.**
- Certain flavonoids also markedly **affect the taste of foods**: for example, some are very **bitter** and **astringent** such as the flavonone glycoside **naringin**, which occurs **in the peel of grapefruit** (Citrus paradisi).
- Interestingly, the closely related compound **naringin dihydrochalcone**, which lacks the pyranone ring of naringin, is **exceptionally sweet**, being some **1000 times sweeter than table sugar** (sucrose).

- Chemically, they have the general structure of a **15-carbon skeleton**, which consists of **two phenyl rings (A and B)** and **heterocyclic ring (C)**. This carbon structure can be abbreviated **C6-C3-C6**.
- Flavonoid glycosides are mainly **O-linked glycosides**

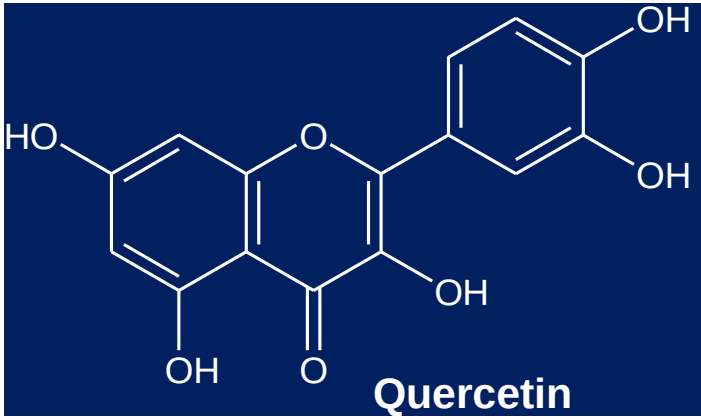


Basic flavonoid structure

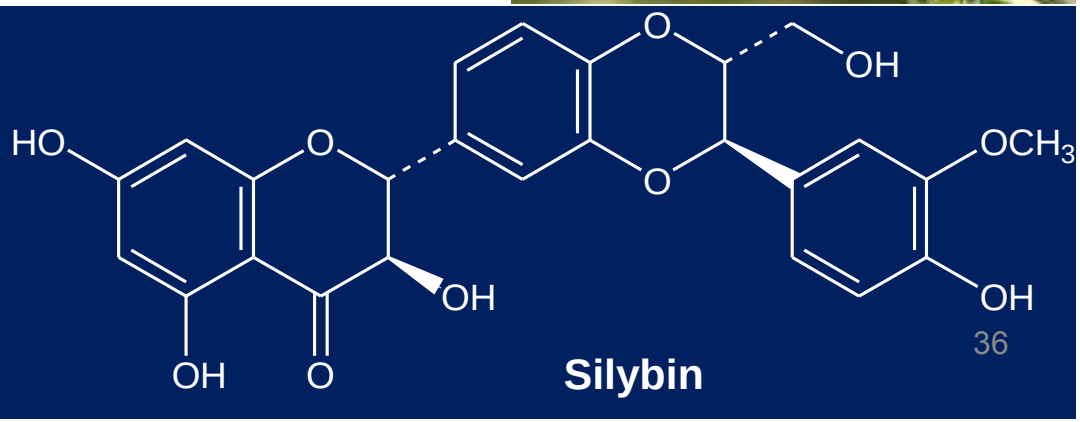
- Flavonoids have important dietary significance because, being phenolic compounds, they are **strongly antioxidant**.
- Many disease states are known to be exacerbated by the presence of *free radicals* such as superoxide and hydroxyl, and flavonoids have the ability to scavenge and effectively 'mop up' these damaging oxidizing species.

- Foods rich in this group have therefore been proposed to be important in ameliorating diseases such as **cancer** and **heart disease** (which can be worsened by oxidation of low-density lipoprotein).
- **Quercetin**, a flavonoid present in many foodstuffs, is a **strong antioxidant.**

- Components of milk thistle *(Silybum marianum),* in particular **silybin**, are **anti-hepatotoxins**; extracts of milk thistle are generally known as **silymarin.**

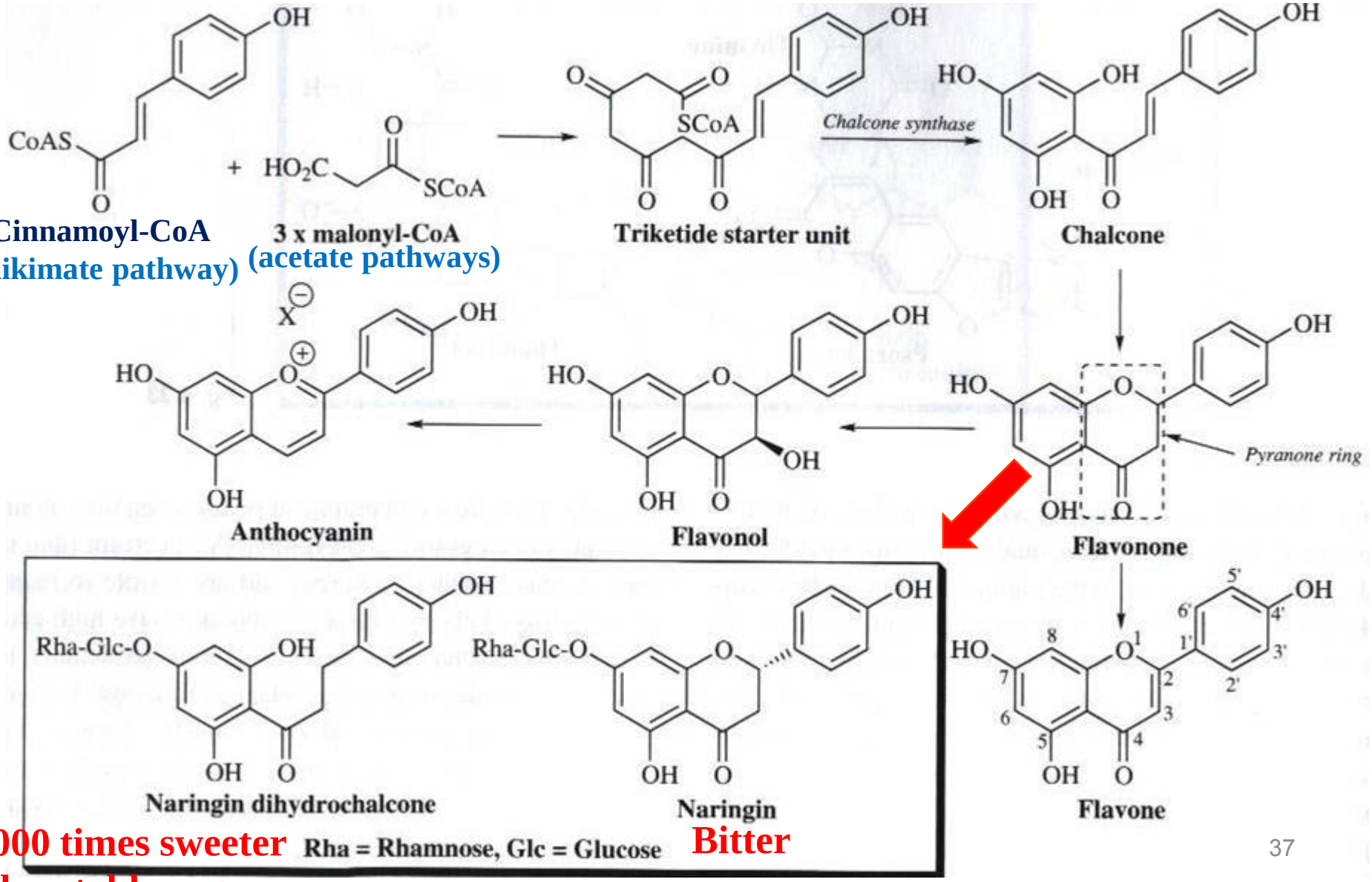


Quercetin



Silybin

Biosynthesis of Flavonoids

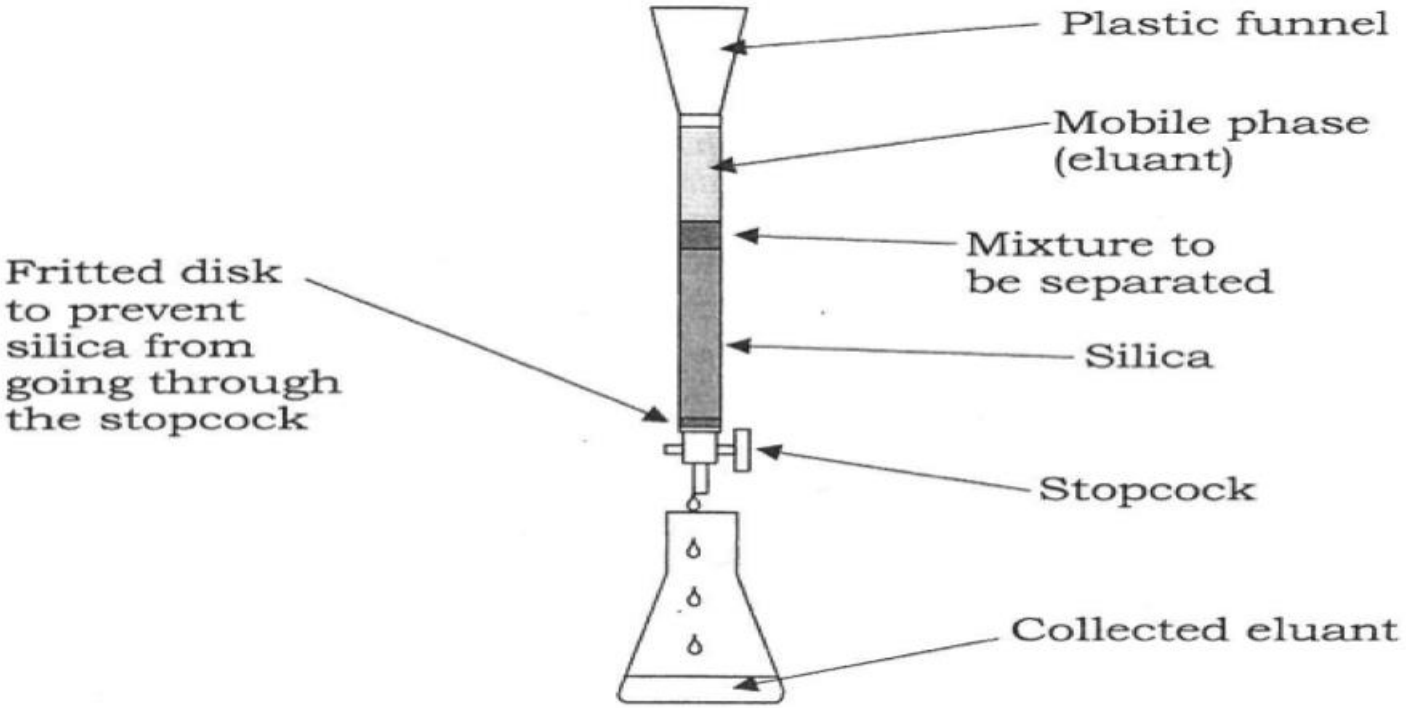


Biosynthesis of Flavonoids

- Flavonoids are products from a **cinnamoyl-CoA** (C_6C_3, precursor from the **shikimate pathway**) starter unit, with chain extension using **three (3) molecules of malonyl-CoA (**from **acetate pathways)**.
- Flavonoids are therefore of **mixed biosynthesis**, consisting of units derived from both **shikimate** and **acetate pathways.**
- The **triketide starter unit** undergoes cyclization by the enzyme **chalcone synthase** to generate the **chalcone** group of flavonoids.
- Cyclization of chalcone then occur to give a **pyranone ring** containing **flavonone** nucleus.
- Flavonone can either have the **C2-C3 bond oxidized (unsaturated)** to give the **flavones** or be **hydroxylated at position C3** of the pyranone ring to give the **flavonol** group of flavonoids.
- The flavonols may then be further oxidized to yield the **anthocyanidins,** which contribute to the **brilliant blues of flowers** and the dark colour of red wine.
- The **formation of the glycosides (eg Naringin) occurs through introduction of sugar unit/s** (glucose, rhamnose, arabinose, xylose) to the **hydroxyl groups of flavonoids (flavonone/flavone/flavonolol).**
- **Flavonoids are the aglycone part of glycosides.**

Isolation and Extraction of Flavonoids:

- Since they are **highly hydroxylated** and as glycosides, usually they are extracted from plants with ethanol, methanol or water.
- Sometimes, purifying is done with alkaline solution or precipitation with lead acetate.
- The different **classes** can generally be separated by **column chromatography**.

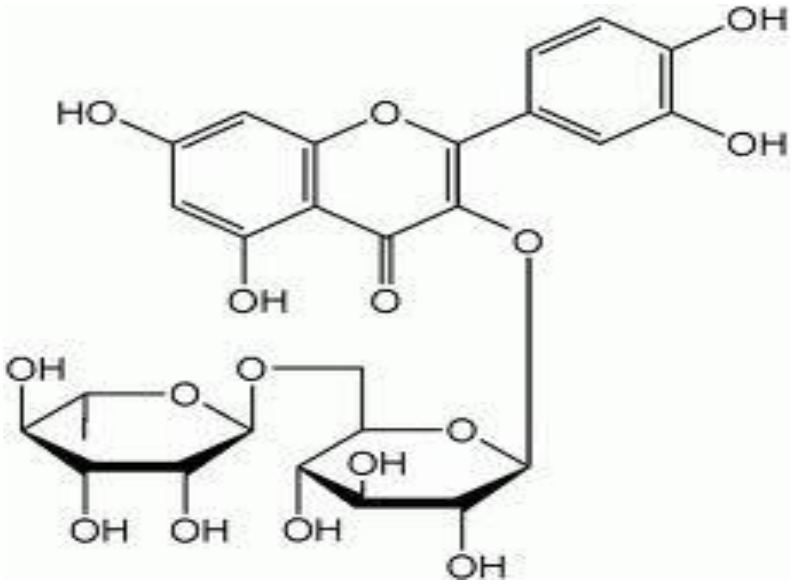


Flavonoid Glycosides

Rutin

- Chemically rutin is 5,7,3’,4’-tetrahydroxy flavonol 3-rhamnoglucoside.

- On hydrolysis, it gives **quercetin** and the **two sugar varieties** which are called **Rutinose** (Rutinose is the disaccharide also known as 6-O-α-L-rhamnosyl-D-glucose ($C_{12}H_{22}O_{10}$) that is present in some flavonoid glycoside. It is prepared from rutin by hydrolysis with the enzyme **rhamnodiastase**.



- Rutin is usually isolated from ***Fagopyrum esculentum*** ***الحنطة السوداء*** or **Buckwheat** (Family **Polygonaceae** **البَطْبَاطِيَّة أو الرَأوَنْدِيَّة**).

- Rutin was first isolated from the **leaves** of ***Ruta graveolens*** **سذاب شديد الرائحة** (**Rutaceae** **الفصيلة السذابية**).

Fagopyrum esculentum

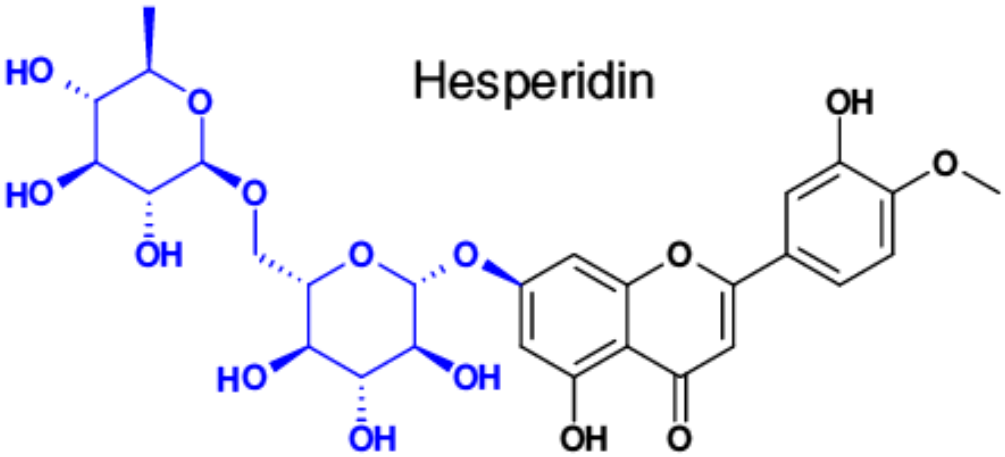
Ruta graveolens

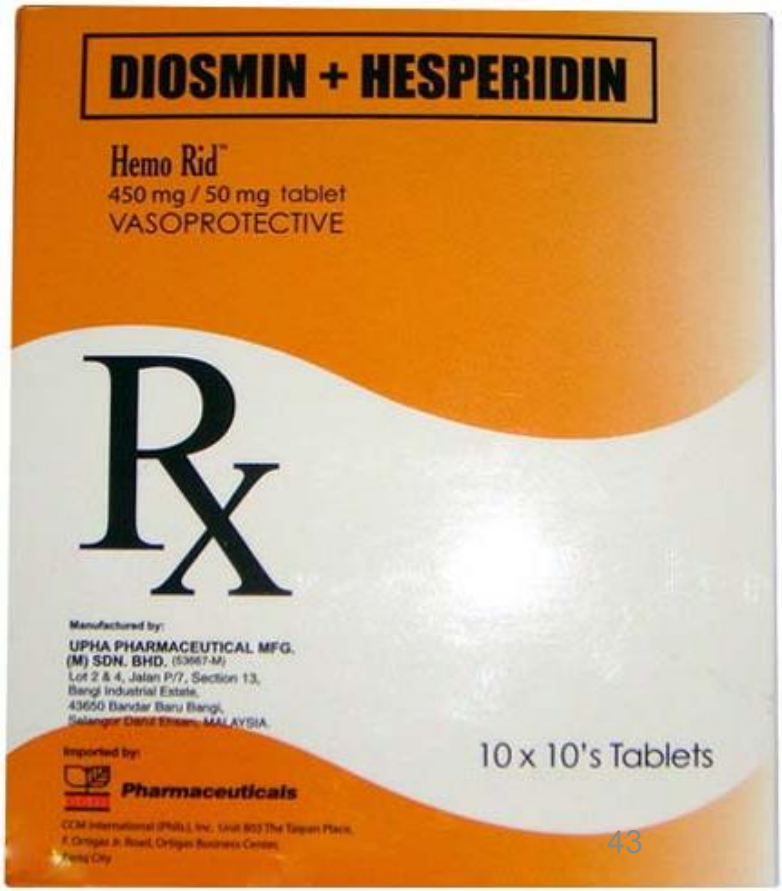
Uses

1. Rutin has been used to **decrease** capillary fragility and permeability in cases of hypertension and radiation injuries.
2. Anti-inflammatory properties that may be beneficial for various types of **dermatitis**, an itchy skin inflammation.
3. According to the University of Maryland Medical Center, **taking 50 to 250 mg of a rutin supplement two or three times a day** may **help relieve symptoms of allergic contact skin reactions, as well as eczema and seborrheic dermatitis** التهاب الجلد الدهنيwhich causes dandruff.
4. Rutin also may be helpful for treating various types of **erythema**, a condition involving skin redness or rash caused by health conditions.

Hesperidin

- It is also called **citrin** or **Vitamin P** or **permeability vitamin.**
- Chemically it is **hesperitin-7-rutinoside** (a flavan-on glycoside).





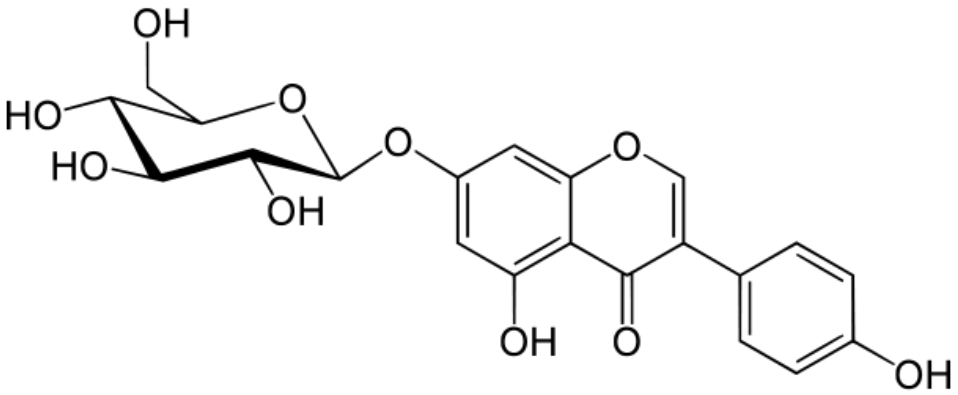
- Usually, it is found in the **peels** of **species of citrus fruits** like ***Citrus aurantium*** **Bitter Orange** **نارنج** and ***Citrus sinensis*** **البُرتُقال**
- **Family:** **Rutaceae** **تشمل مجموعة الحمضيات السذابية**).

Citrus aurantium

Citrus sinensis

Genistin:

- It is an **isoflavon** found in some plants such as ***Genista*** species (**BROOMS**) and **Glycine max, soya (Soybean** in USA and Europe**). Family: Fabaceae or leguminosae.**
- **Genistin** is a **phytoestrogen** which is indicated as a **diet supplement** to contrast the **side effect caused by lack of estrogen** specially in women **during the menopause.**
- It **prevents osteoporosis** and estrogen dependent cancer like **breast cancer.**



Genistin (an Isoflavone)

Anti-cancer,
Estrogenic,
Anti-atherosclerotic
Anti-viral

Daidzein:

- An isoflavone.
- The same effect as the previous.