



FLAVONOIDS

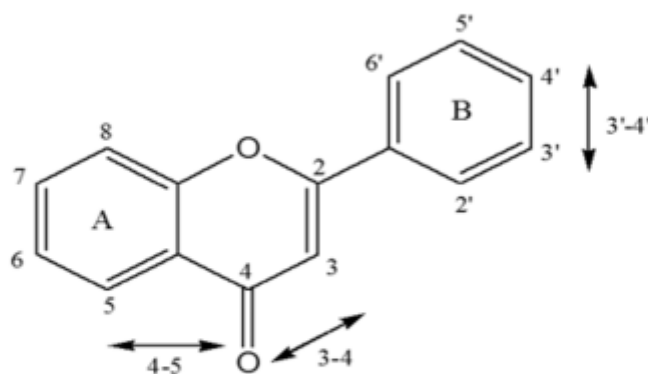
Phytotherapy

FACULTY OF PHARMACY

Dr. Yousef Abusamra

Flavonoid Glycosides

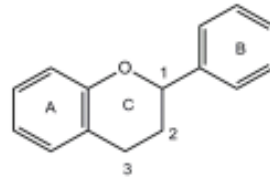
- ❖ Flavonoids are the largest group of naturally occurring phenols and found either in free form or as glycosides. The flavonoid group may be described as a series of $C_6 - C_3 - C_6$ compounds.
 - ❖ Flavonoids (or bioflavonoids) (from the Latin word *flavus* meaning yellow, their color in nature) are a class of plant and fungus secondary metabolites.
 - ❖ 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. According to the IUPAC nomenclature.
- ❖ **Flavonoid Skeleton:**
- The different classes within this group are distinguished by additional oxygen heterocyclic rings and by hydroxyl groups distributed in different patterns.
 - Therefore the flavonoid glycosides are substitutions of flavone, isoflavone, flavanol and flavanone.



Basic flavonoid structure

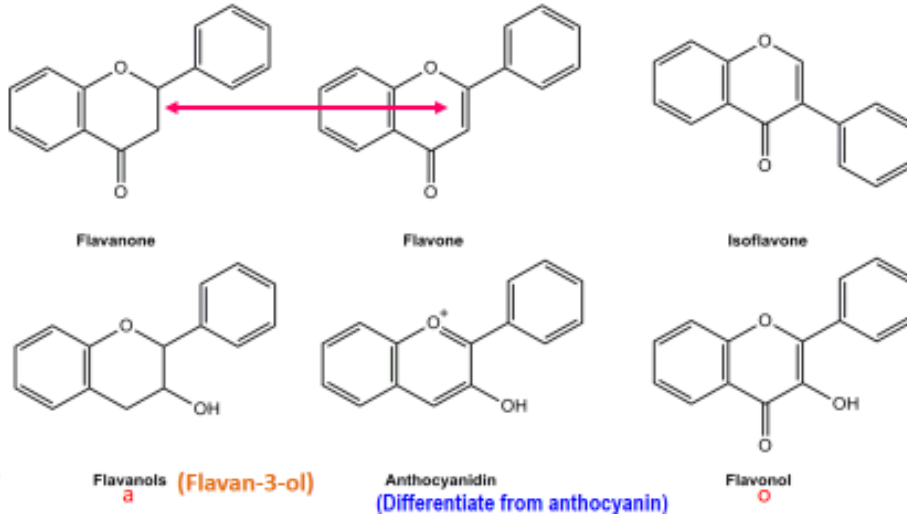
(a)

(A)



Flavonoid

(B)



Flavanone

Flavone

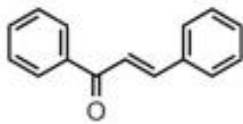
Isoflavone

Flavanols (Flavan-3-ol)

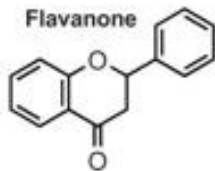
Anthocyanidin (Differentiate from anthocyanin)

Flavonol

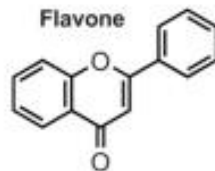
Chalcone



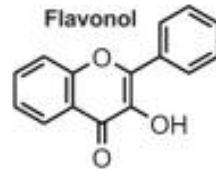
Flavanone



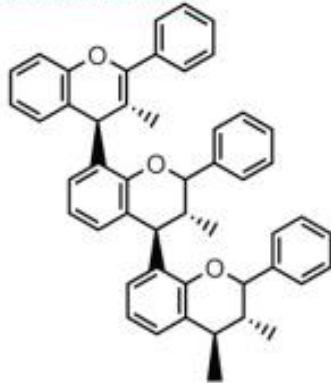
Flavone



Flavonol



Proanthocyanidin (Condensed tannins)



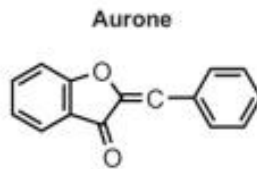
Anthocyanidin



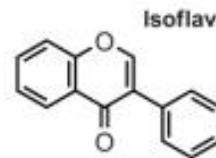
Flavandiols



Aurone

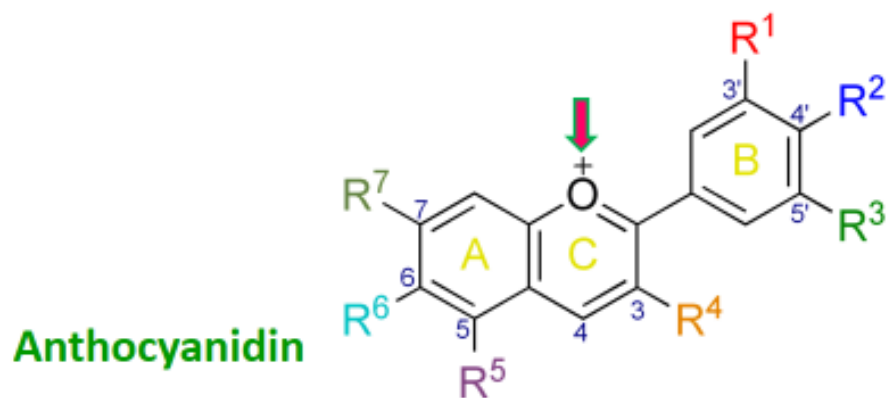
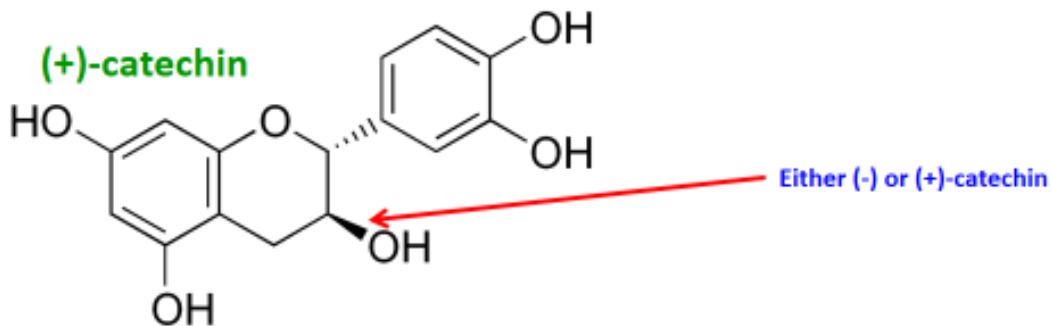
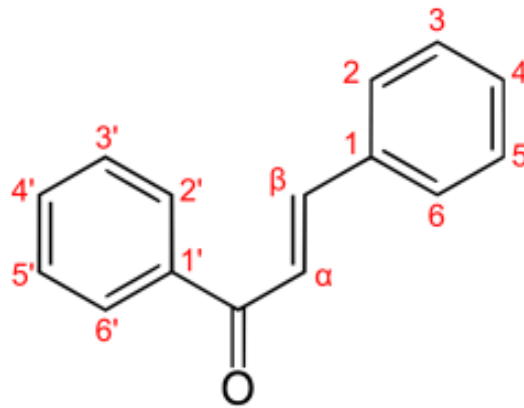


Isoflavone



Chalcone

- Chalcone is an aromatic ketone and an enone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones or chalconoids.



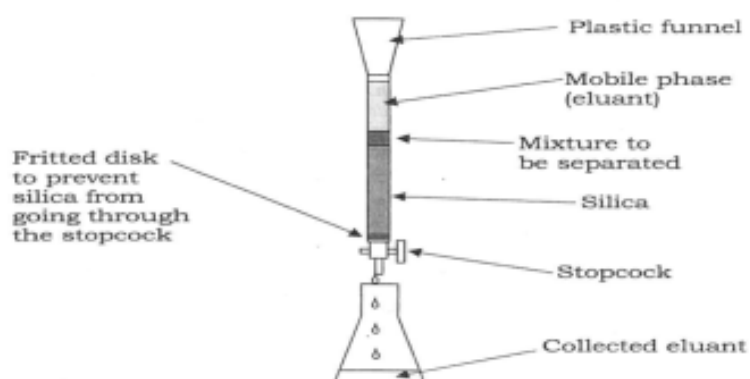
Anthocyanidin:

- ❖ The hydroxyl groups are usually found on positions 5, 7 of ring **A** or at 4⁻, (3⁻, 4⁻), on ring **B** and sometimes they maybe in the form of methoxy or alkoxy, **and the sugar is usually attached to the OH groups to form the glycosides.**
- ❖ They could be found in different parts of the plant specially in cell sap (**the watery fluid within the central vacuole of a plant cell**).
- ❖ Many of them are **diuretic**, **diaphoretic** معرق, and **some have the ability to decrease the bleeding tendency of blood vessels and to affect the permeability of the capillaries** like **Rutin** and **Hesperidin** which decrease the capillary fragility.
- ❖ In plants, in addition to being **flower pigments** and **attracting pollinating birds and insects**, other suggested roles e.g. **control of plant growth, inhibiting and activating plants enzymes**, some have **fungicidal effect** and **protect plant against attack by parasites.**

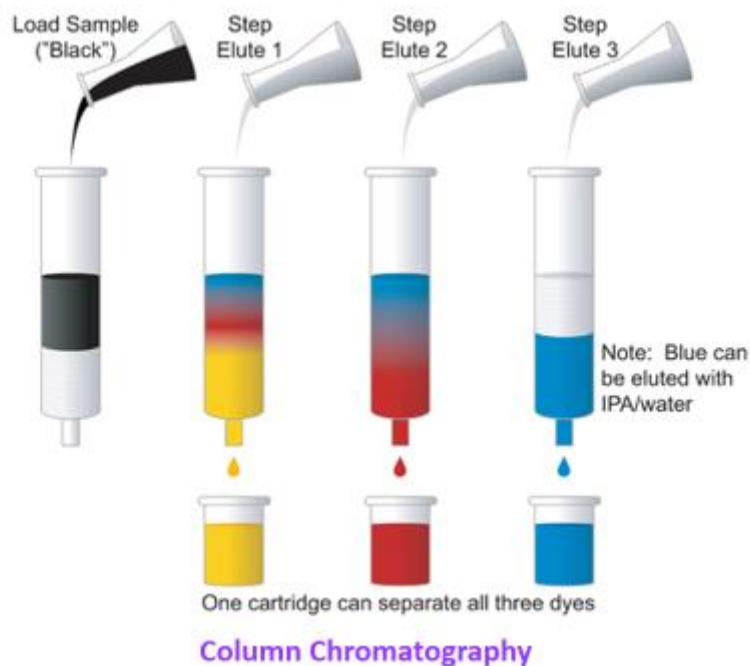
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• Isolation and Extraction of Flavonoids:

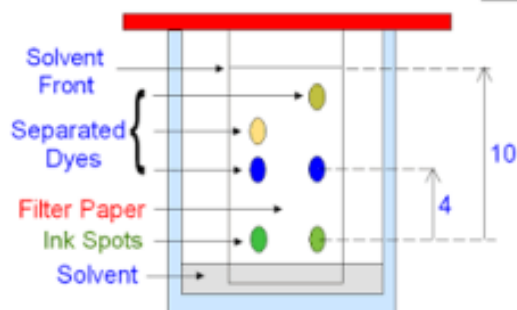
- ❖ Since they are highly hydroxylated and as glycosides, usually they are extracted from plants with **ethanol**, **methanol** or **water**.
- ❖ Sometimes, purifying is done with **alkaline solution** or precipitation with **lead acetate**.
- ❖ The different **classes** can generally be separated by **column chromatography**, but it is more difficult to separate **individual** members of one class of flavonoid by this technique.



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- ❖ **Paper chromatography** has been developed for **identification** and **separation** of flavonoids.
- ❖ **BAW** solvent system (Butanol - Glacial Acid - Water) is one of the best developing solvents.
- ❖ The detection is relatively easy since :
 - a. They form occasionally visible colored spots.
 - b. All spots are visible in U.V. light.
 - c. Spots can be seen after fuming with **ammonia** either as such or under U.V. light.
 - d. By use of **aluminium chloride** to increase the intensity of color.



- Alkaline degradation of flavonoids with **alcoholic potassium hydroxide** produces a **phenol** from ring A and a **substituted benzoic acid** from ring B, although acetophenones and cinnamic acids may be isolated.

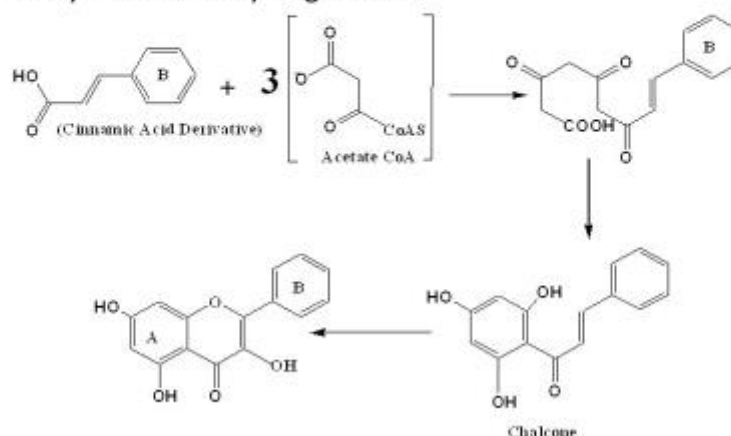
Biosynthesis of Flavonoid Glycosides:

- ❖ Radio-labelled C atoms study has proven that the flavonoids are derived from **mixed** pathways:
 - The benzene ring A is formed from **three acetate units**.
 - The remainder of the molecule which is $C_6 - C_3$ (which is called phenylpropanoid) is usually formed from **shikimic acid**, most probably **cinnamic acid**.
 - Both of the above units unite together to form first **chalcone** which is converted to **flavanone**.

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Flavonoids Biosynthesis

- Biosynthesized from shikimate (cinnamic acid part) forming starting molc. & acylpolymalonate (3 acetate residues) pathways. Followed by ring closure.

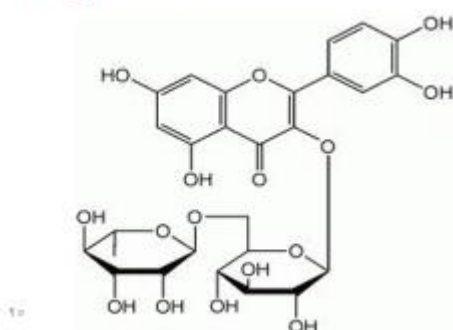


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- The formation of the glycosides occurs at the later stages through introduction of sugar unit/s with the hydroxyl groups.
- The evidence of that is the occurrence of aglycones (free aglycones) with the glycosides in the same plant.

Drugs Containing Flavonoid Glycosides:

I. Rutin: chemically rutin is 5, 7, 3', 4'-tetrahydroxy flavonol 3-rhamnoglucoside.



- ❖ Rutin is usually isolated from *Fagopyrum esculentum* الحنطة السوداء or Buckwheat (Family Polygonaceae البطباطيية أو الراوندية).
- ❖ Rutin was first isolated from the leaves of *Ruta graveolens* سذاب (الفصيلة السذابية Rutaceae شديد الراححة).

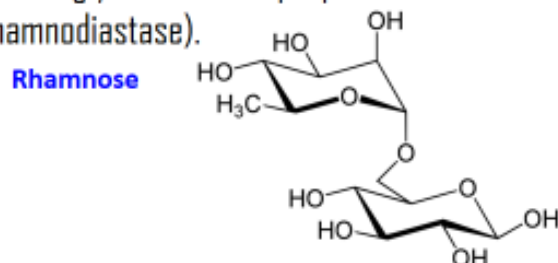
Fagopyrum esculentum



Ruta graveolens



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

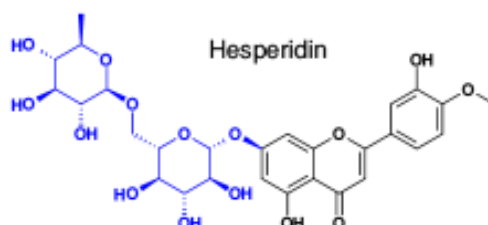


Uses:

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.
- 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 الدهني which causes **dandruff**.
 - 3. Rutin also may be helpful for treating various types of **erythema**, a condition involving skin redness or rash caused by health conditions.

2. Hesperidin:

- ❖ It is also called **citrin** or **Vitamin P** or **permeability vitamin**.
- ❖ chemically it is **hesperitin-7-rutinoside**.



- ❖ Usually, it is found in the peels of species of citrus like *Citrus aurantium* Bitter Orange نارنج and *Citrus sinensis* البرتقال (F. Rutaceae تشمل مجموعة الحمضيات السذابية).



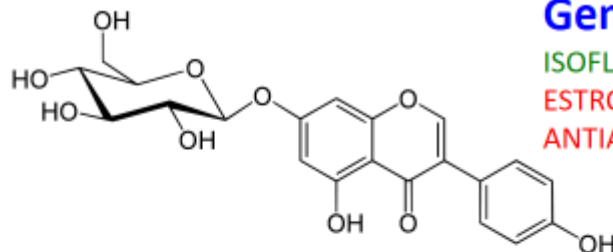
Citrus aurantium

Citrus sinensis



3-Genistin:

- ❖ It is an isoflavone 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 estrogen lack specially in women during the menopause, it prevents osteoporosis and estrogen dependent cancer like breast cancer.



Genistin

ISOFLAVONE (ANTI-CANCER,
ESTROGENIC,
ANTIATHEROSCLEROTIC
ANTI-VIRAL

4-Daidzein:

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



3-Genistin:

❖ Also, it occurs in considerable amounts in red clover flower
(*Trifolium pratense*) نفل المروج أو النفل الأحمر أو برسيم المروج - القرطاة

➤ Benefits or red clover:

1. Cancer, whooping cough, respiratory problems, skin inflammation such as psoriasis and eczema.
 2. Diuretic, expectorant, improves circulation and cleans liver.
 3. Owing to the isoflavone-content, red clover has a great beneficial effect in the treatment of severe conditions associated with menopause such as hot flashes, cardiovascular health and osteoporosis.
- ❖ Also, it occurs in *Cytisus scoparius* اللزان المكنسي: one of the brooms.



Red clover (*Trifolium pratense*)
Leguminosae = Fabaceae



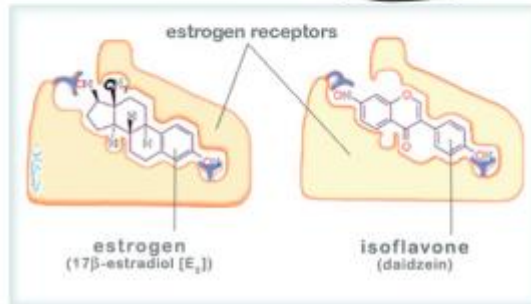
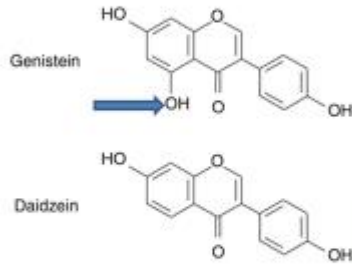
BROOM (*Cytisus scoparius*)
Leguminosae = Fabaceae



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4-Daidzein:

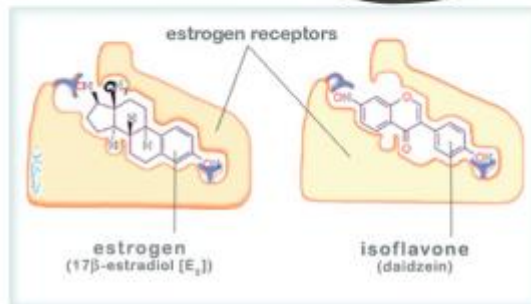
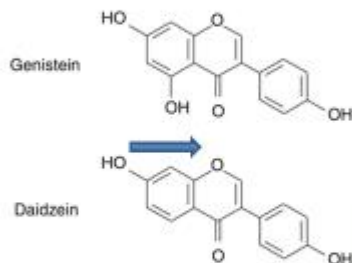
- ❖ An isoflavone.
- ❖ The same structure as genistin, but it lacks a hydroxyl group on position 5.
- ❖ The same effect as the previous.



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4-Daidzein:

- ❖ An isoflavone.
- ❖ The same structure as genistin, but it lacks a hydroxyl group on position 5.
- ❖ The same effect as the previous.



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