Lignans and Flavonoids

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ALL THE CONTENT MATERIAL PROVIDED HERE IS ONLY FOR TEACHING PURPOSE.

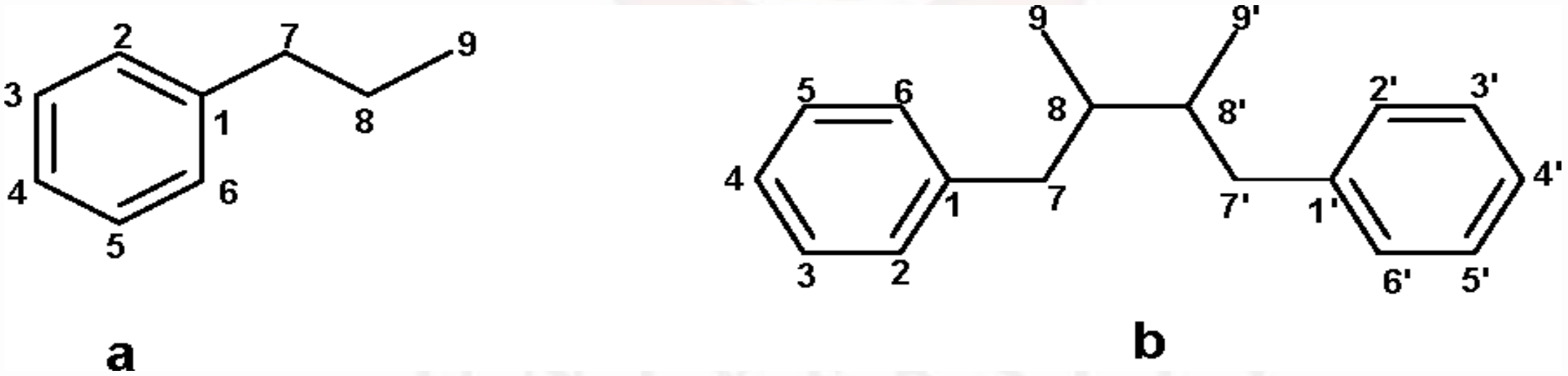
Introduction Lignans

The term “Lignan” was first introduced by Haworth (1948) to describe a group of dimeric phenylpropanoids where two phenylpropanoid molecules are attached by its central carbon (C8). **Lignans** are a subgroup of **non-flavonoid polyphenols**.

They are widely distributed in the plant kingdom, being present in more than 55 plant families, where they act as **antioxidants** and **defence** molecules against **pathogenic fungi** and **bacteria.**

Flowing structure contains

a) Phenylpropanoid and b) Lignan



a) Phenylpropanoid unit; b) Lignan structure

Chemical structure of lignans

Their basic chemical structure consists of **two phenylpropane units**linked by a C-C bond between the central atoms of the respective side chains (position 8 or β), also called β-β' bond; in these cases the dimers are called **neolignans**.

Hence, their chemical structure is referred to as $(C6\text{-}C3)_2$, and they are included in the **phenylpropanoids group**, as well as their precursors:

the hydroxycinnamic acids

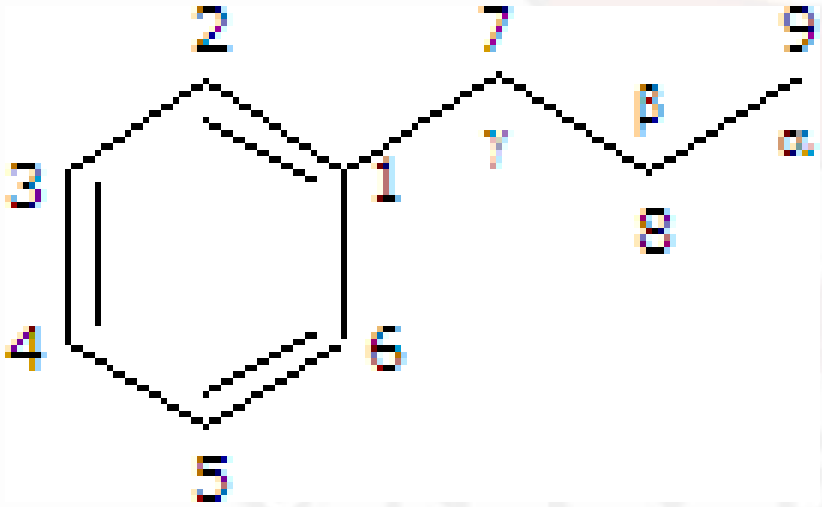


Fig. 1 – Phenylpropane unit

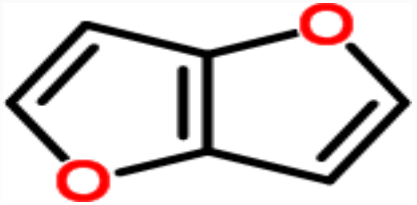
Lignans can be found in more than 60 families of vascular plants and have been isolated from different plant parts, exudates and resins.

Biological activity of Lignans -are Antiviral ,Anticancer ,Cancer prevention, Anti-inflammatory, antimicrobial ,antioxidant , immunosuppressive, Hepatoprotective, Osteoporosis prevention.

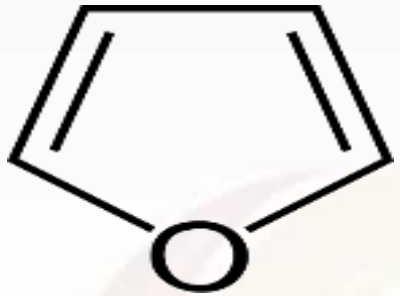
Based on their **carbon skeleton, cyclization pattern**, and the way in which **oxygen is incorporated** in the molecule skeleton, they can be divided **into 8 subgroups**:

Main subclasses of Lignans- 1.Furofuran, 2.Furan, 3.Dibenzylbutane, 4.Dibenzylbutyrolactol, 5.Dibenzylbutyrolactones, 6.Aryltetralin, 7.Arylnaphtalene, 8.Dibenzocyclooctadienes.

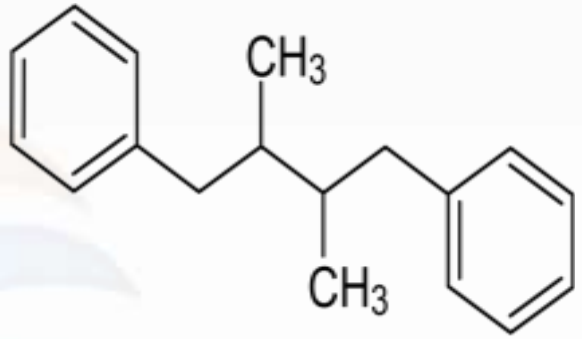
among these subgroups, the furan, dibenzylbutane and dibenzocyclooctadiene lignans can be further classified in “lignans with C9 (9´)-oxygen” and “lignans without C9 (9´)-oxygen”



Furofuran



Furan



Dibenzylbutane

✓They are **not present** in the **free form** in nature, but linked to other molecules, mainly as **glycosylated derivatives**.

✓Among the most <u>common lignans</u>, **secoisolariciresinol** (the most abundant one), **lariciresinol, pinoresinol, matairesinol** and **7- hydroxymatairesinol** are found.

✓**Podophyllotoxin** , a naturally occurring **aryltetralin lignin**, is one of the most important compound due to its **high toxicity** and current use as a local **antiviral agent** . podophyllotoxin, obtained from plants of the genus ***Podophyllum*** (**Berberidaceae** family); it is a mitotic toxin whose **derivatives** have been used as **chemotherapeutic agents**;

➢ **<u>Food rich in lignans</u>**

The richest dietary source is **flaxseed (linseed)**, that contains mainly secoisolariciresinol, but also lariciresinol, pinoresinol and matairesinol in good quantity . They are also found in sesame seeds, **whole grains**.

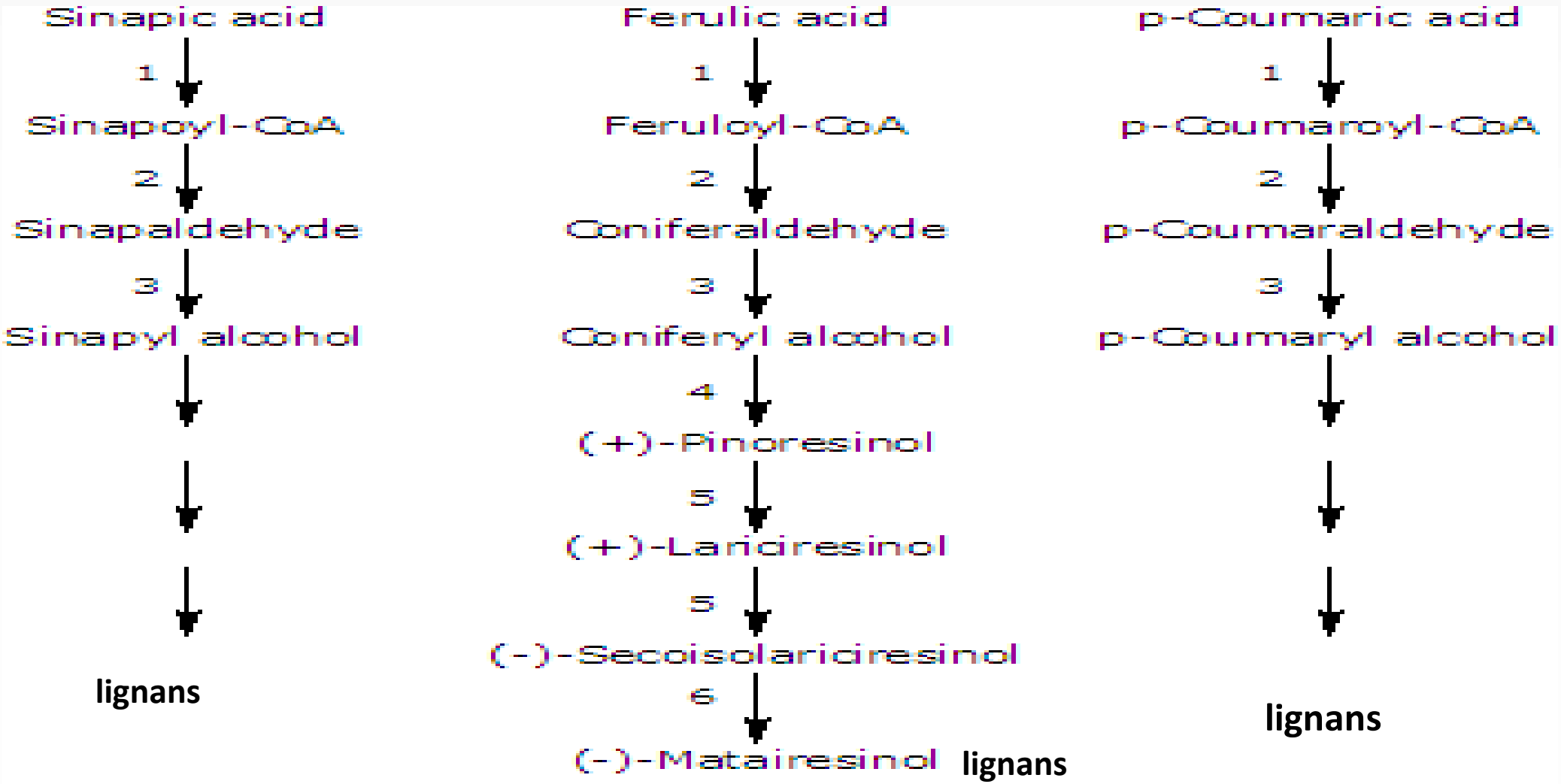
Biosynthesis of lignans

The pathway starts from 3 of the 4 most common dietary **hydroxycinnamic acids**: p-coumaric acid, sinapic acid, and ferulic acid (caffeic acid is not a precursor of this subgroup of poyphenols). Therefore, they arise from the **shikimic acid pathway**, via **phenylalanine**. **The first three reactions reduce** the carboxylic group of the hydroxycinnamates to **alcohol** group, with formation of the corresponding alcohols, called **monolignols**, that is**, p-coumaric alcohol, sinapyl alcohol** and **coniferyl alcohol**. These molecules also enter the pathway of lignin biosynthesis.

- **The first step**, which leads to the **activation of the hydroxycinnamic acids**, is catalysed by hydroxycinnamate:CoA ligases, commonly called p-coumarate:CoA ligases , with formation of the corresponding hydroxycinnamate-CoAs, namely, feruloil-CoA, p- coumaroyl-CoA and sinapil-CoA.
- **In the second step**, a NADPH-dependent cinnamoyl-CoA: oxidoreductase, also called cinnamoyl-CoA reductase catalyzes the **formation of the corresponding aldehydes**, and the release of coenzyme A.
- **In the last step**, a NADPH-dependent cinnamyl alcohol dehydrogenase, also called monolignol dehydrogenase , catalyzes the **reduction of the aldehyde group** to an **alcohol group**, with the formation of the aforementioned **monolignols.**

✓The next step, the **dimerization of monolignols**, involves the intervention of stereoselective mechanisms, or, more precisely, enantioselective mechanisms. **plant lignans** exists as (+)- or (-)- enantiomers,

✓**Hydroxycinnamic acids** (hydroxycinnamates) are a class of aromatic **acids** or phenylpropanoids having a C_6–C_3 skeleton. These compounds are hydroxy derivatives of cinnamic **acid**.



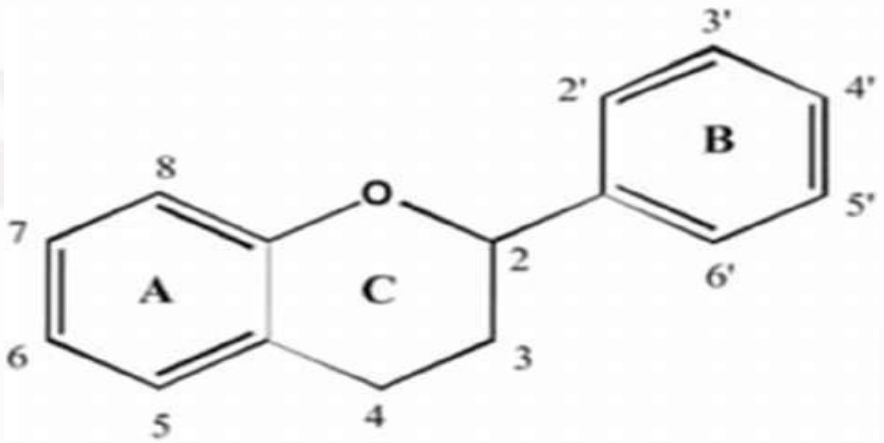
1. Hydroxycinnamate-CoA-ligase
2. NADPH-dependent cinnamoyl-CoA reductase
3. NADPH-dependent cinnamyl alcohol dehydrogenase
4. Pinoresinol syntase (Laccase + "dirigent protein")
5. NADPH-dependent pinoresinol/lariciresinol reductase
6. NAD(P)-dipendent secoisolariciresinol dehydrogenase

Biosynthesis of lignans

Flavonoids

- **Flavonoids** are the most abundant **polyphenols** in human diet, over 4000 have been identified. **Latin** word *flavus* **meaning yellow**, their color in nature. many of which are responsible for the attractive colors of flowers, fruits and leaves. In plants, these compounds afford **protection against ultraviolet radiation**, **pathogens**, and **herbivores .**
- In **fruits and vegetables**, they are usually found in the form of **glycoside**s and sometimes as **acylglycosides** . characterized by the **flavan nucleus**
- Chemically, flavonoids have the general structure of a 15-carbon skeleton, which consists of two phenyl rings (A and B) and heterocyclic ring (C).

flavan nucleus



Classification of flavonoids-

✓They can be subdivided into different subgroups depending on the carbon of the C ring on which B ring is attached, and the degree of unsaturation and oxidation of the C ring.

✓Flavonoids in which B ring is linked in position 3 of the ring C are called **isoflavones;**

✓those in which B ring is linked in position 4, **neoflavonoids**,

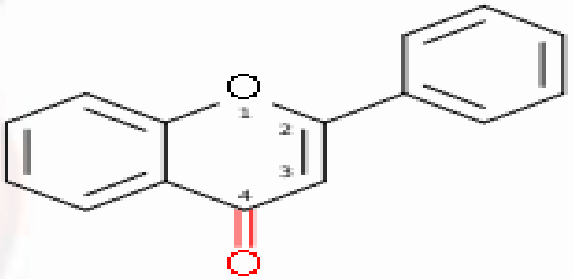
✓while those in which the B ring is linked in position 2 can be further subdivided into several subgroups on the basis of the structural features of the C ring. These subgroup are: **flavones, flavonols or catechins, flavanones, flavanonols, and anthocyanins**.

✓Finally, flavonoids with open C ring are called **chalcones.**

A) Anthoxanthins

1.flavone- Flavones are mainly found in cereals and herbs

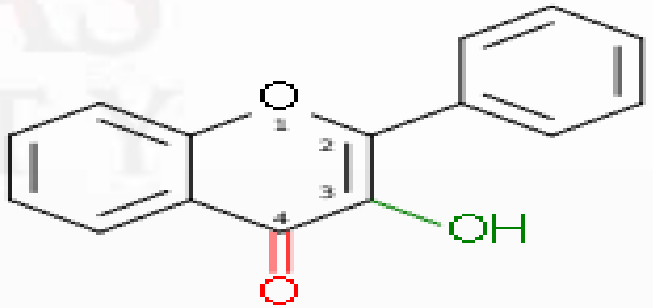
eg luteolin,apigenin,tangeritin



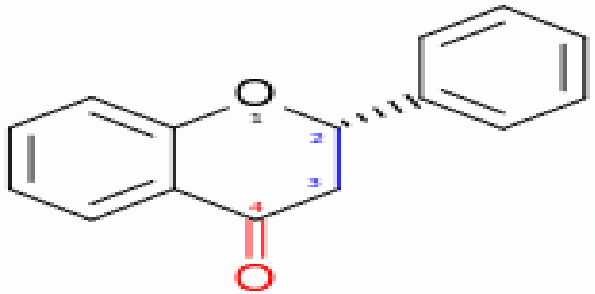
2.Flavonol or 3-hydroxyflavone-

Foods rich in flavonols-The major sources in human diet are:fruit;vegetables;beverages such as red wine and tea.

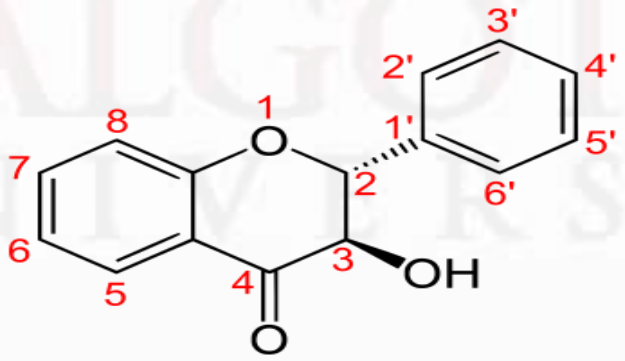
eg. Quercetin,kaempferol,myricetin,fisetin,galangin,isorhamnetin,pachypodol,rhamnazin,pyranoflavonols,furanoflavonols



B) Flavanones: type of flavonoids, are various aromatic, colorless ketones derived from flavone that often occur in plants as glycosides. Flavanone-eg. Hesperetin,naringenin,eriodictyol,homoeriodictyol



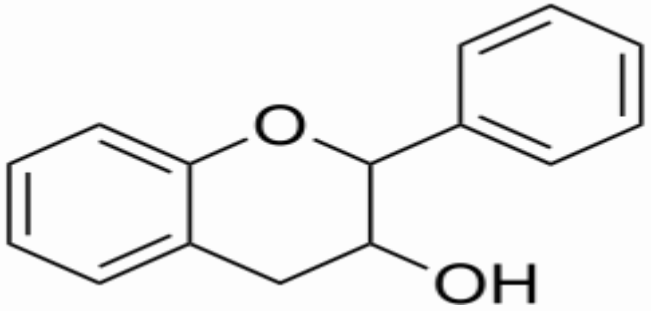
C)Flavanonols:class of flavonoids that use the **3-hydroxy-2,3-dihydro-2-phenylchromen-4-one** (IUPAC name) backbone.
Flavanonol or 3-hydroxyflavanone or 2,3-dihydroflavonol eg.taxifolin or dehydroquercetin,dihydrokaempferol



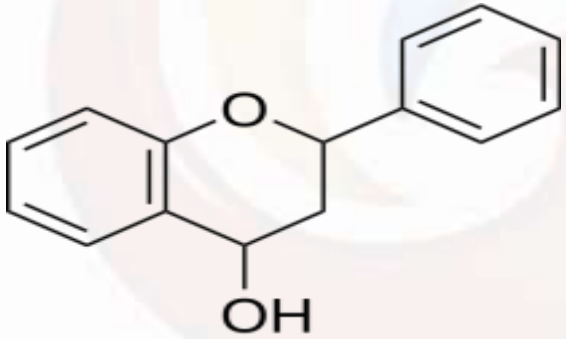
D) Flavans - The **flavans are benzopyran derivatives** that use the 2-phenyl-3,4-dihydro-2H-chromene skeleton include

1.flavan-3-ols (flavanols),- examples are catechin, gallocatechin, catechin 3-gallate, gallocatechin 3-gallate,epicatechins.

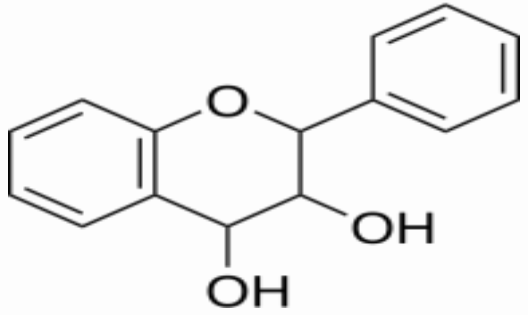
2.flavan-4-ols 3.flavan-3,4-diols.



flavan-3-ols



flavan-4-ols



flavan-3,4-diols

D) **Anthocyanidins - anthocyanidins** are the **aglycones** of anthocyanins;

Anthocyanins are a very large group of **red- blue plant pigments**. Anthocyanins occur in all higher plants, mostly in flowers and fruits but also in leaves, stems, and roots. They are very good **antioxidants**

Health benefits of flavonoids-Their regular consumption is associated with reduced risk of a number of chronic diseases, including **cancer, cardiovascular disease (CVD) and neurodegenerative disorders.** thy are good **antioxidant and anti-inflammatory** ,

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