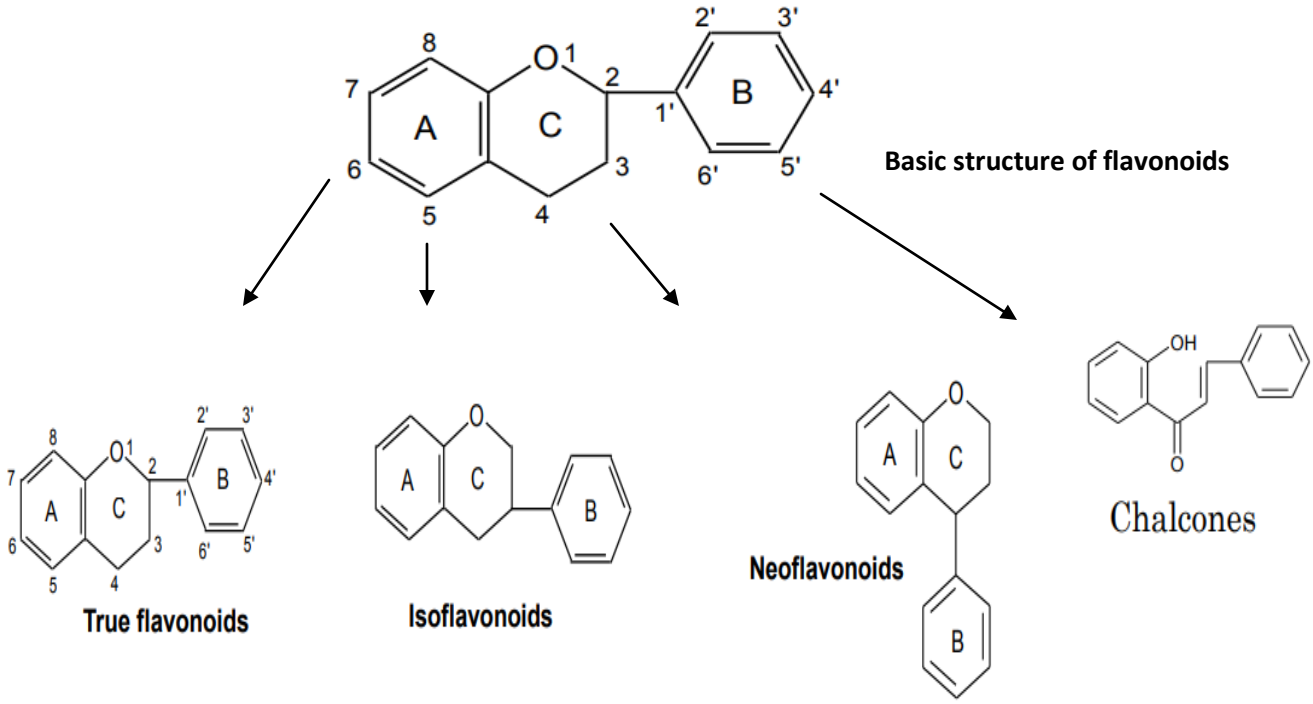
Flavonoid glycosides :

Large group of glycosides which widely distributed in the plants kingdom and in all plants parts (leaves, roots, rhizomes, fruits peels) . having a polyphenolic structure and very important activity such as antioxidant effects associated with various diseases such as cancer and Alzheimer's disease .

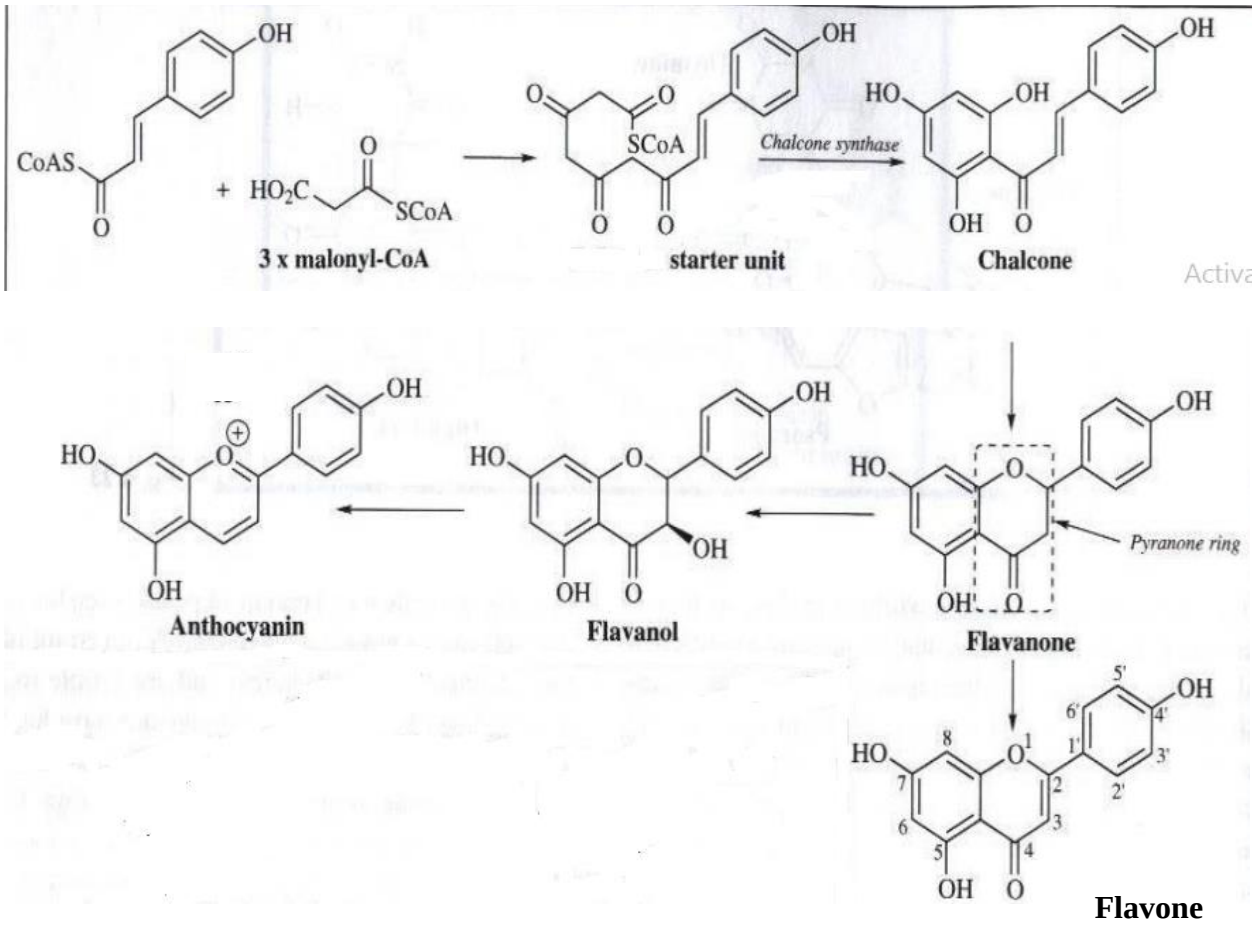
Flavonoids are associated with a broad spectrum of health-promoting effects and are an indispensable component in a variety of nutraceutical, pharmaceutical, medicinal and cosmetic applications. This is because of their antioxidative, anti-inflammatory, anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme functions.

Classification

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 called **true flavonoids** which include : **flavones , flavonols , flavanones , flavanonols , catechins** and **anthocyanins**. Finally, flavonoids with open C ring are called **chalcones**.



Biosynthesis: Flavonoids are products from a cinnamoyl-CoA starter unit, with chain extension using three molecules of malonyl-CoA **.** Flavonoids are mixed biosynthesis, consisting of units derived from both shikimate and acetate pathways.



The starter unit undergoes cyclization by the enzyme chalcone synthase to generate the chalcone group of flavonoids. Cyclization can then occur to give a C ring containing flavanone nucleus, which can either have the C2-C3 bond oxidized (unsaturated) to give the flavones or be hydroxylated at position C3 of the C ring to give the flavanol group of flavonoids. The flavanols may then be further oxidized to yield the anthocyanins .

Quercetin :

Its flavonoid classified under flavonols (true flavonoids) found in various food products and plants, including fruits, seeds, vegetables, tea, coffee, bracken fern, and natural dyes .

Example on quercetin sources :

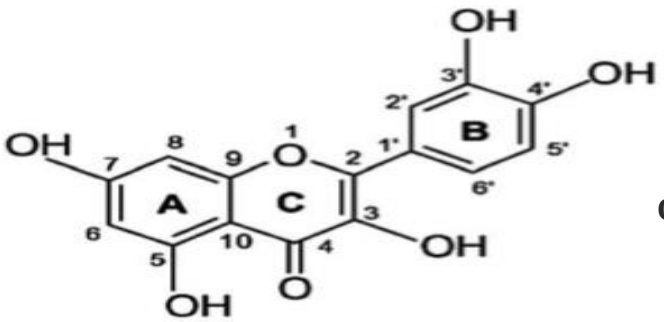
Common name	Scientific name	Family	Quercetin content (mg)
Apple with skin	*Malus domestica*	Amaryllidaceae	4.42
Raw Onions	*Allium cepa*	Rosaceae	13.27

Quercetin glycosides are relatively poorly absorbed by the small intestine. Micro flora of the lower bowel hydrolyze the flavonide-glycoside to quercetin and the sugar, and quercetin is then absorbed into the enterohepatic system.

ANTIOXIDANT PROPERTIES

Quercetin is considered to be a strong antioxidant due to its ability to scavenge free radicals and bind transition metal ions. These properties of quercetin allow it to inhibit lipid peroxidation. Lipid peroxidation is the process by which unsaturated fatty acids are converted to free radicals via the abstraction of hydrogen. Lipid peroxidation can create deleterious effects throughout the body, such as cardiovascular and neurodegenerative diseases; however, it can be terminated by antioxidants, like quercetin, which interfere by reacting with the radicals formed. Quercetin can also reduce inflammation by scavenging free radicals. Free radicals can activate transcription factors that generate pro-inflammatory cytokines, which are often found, elevated in patients that suffer from chronic inflammatory diseases.

Note : Oxidative DNA damage is a known risk factor of cancer. Antioxidants, such as quercetin, are thought to play an important role in protecting cells from oxidative stress induced by reactive oxygen species.



Quercetin

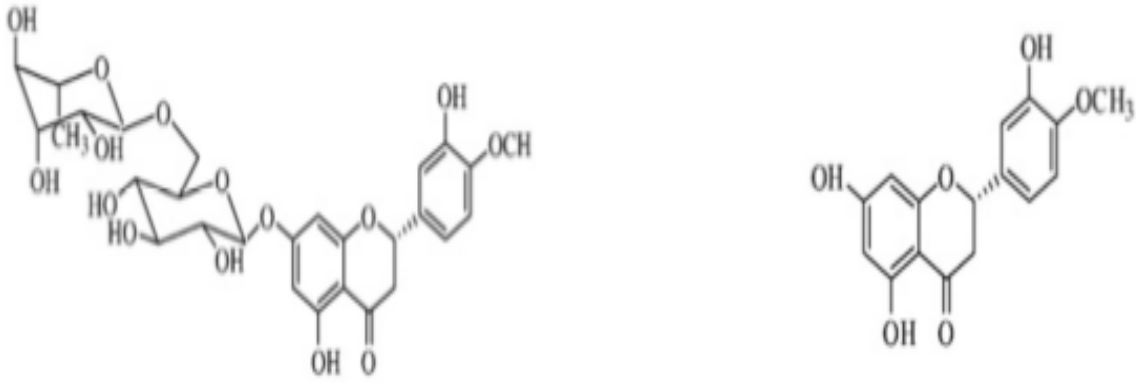
Hesperdine :

Its flavonoid classified under important group Flavanones (true flavonoids) another important class which is generally present in all citrus fruits such as oranges, lemons and grapes .

Example on hesperdine sources :

Common name	Scientific name	Family
Orange (peel)	*Citrus sinensis*	Rutaceae
Lemon (Peel & Seed)	*Citrus limon*	Rutaceae

Hesperidin or also called Vitamin P (is a flavanone glycoside comprised of the flavanone hesperitin and the disaccharide rutinose. The flavonoid hesperidin is primarily found in citrus fruits such as oranges and lemons. Maximum of the hesperidin in these fruits are found in the membranes and peel. A lack of this bioflavonoid in the diet has been linked with abnormal capillary leakiness as well as pain in the extremities causing aches, weakness and night leg cramps. Hesperidin alone, or in combination with other bioflavonoids, is usually used for vascular conditions such as varicose veins and hemorrhoids. Hesperidin has multiple biological properties such as antioxidant and anti-inflammatory, hypertensive, anticarcinogenic and antimicrobial activity . Its most often used for blood vessel conditions such as hemorrhoids, varicose veins, and poor circulation. In numerous widely spread dietary supplements, Hesp is present as Citrus complex of bioflavonoids, usually in a combination with Vitamin C. In those kinds of products, the content of total bioflavonoids is usually declared by the producer, without the concentration of Hesp alone. Hesperidin provides necessary support molecules for vitamin C absorption and is most effective when taken at the same time. Hesperidin with Vitamin C may assist in the cure of colds by reducing the severity and duration of symptoms, relaxation of the symptoms of hay fever, assist in the maintenance of peripheral circulation. Also in combination with a flavone called diosmin, the tablets (trade name Daflon®) for treatment of chronic venous insufficiency and hemorrhoids are broadly available on the European market.



1 2

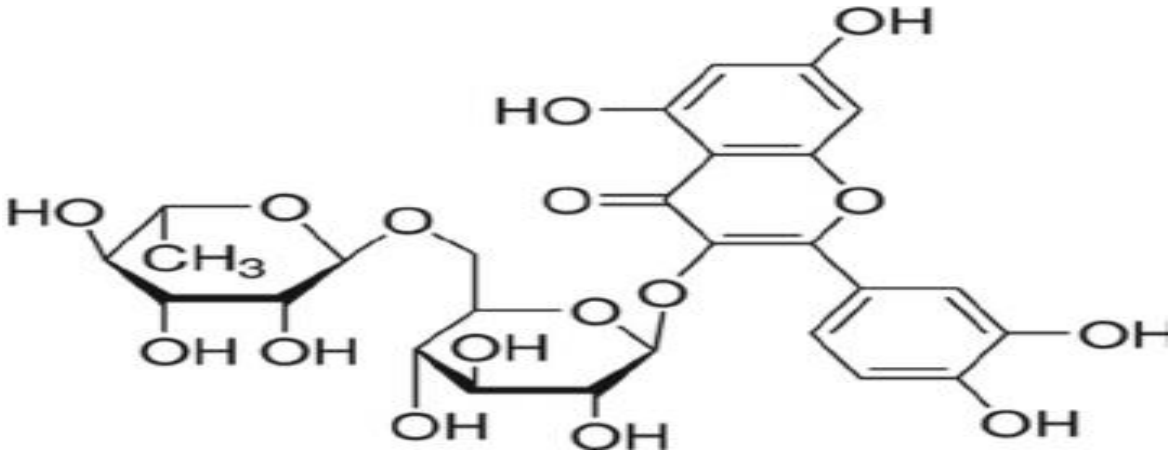
chemical structures of Hesperidin (1) and Hesperitin (2)

Hesperdine and coronavirus:

Coronavirus disease 2019 (COVID-19), being a new and largely unknown disease , Although clinical trials are underway to test several antivirals and other agents, an important question for the population is whether there are any nutrients and food/nutrition patterns that can prevent viral infection or mitigate its severity , one of the most important compound which is used as antiviral agents, hesperidin and vitamin C,these compounds support and improve the body's defenses against oxidative stress and in the prevention of cardiovascular diseases, atherosclerosis and cancer. In addition, they show anti-inflammatory, antiviral and antimicrobial activities. Also recent research indicate to use these compound as potential medicines against Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), for their activities as antiviral, antioxidants, and modulators of inflammation. The discovery that the molecule of hesperidin has a chemical-physical structure suitable for binding to key proteins in the functioning of the SARS-CoV-2 virus (these research fo hesperdine called " In-silico" (using docking software).

3- Rutin :

Rutin is a flavonol, abundantly found in plants, such as tea, and apple. It is a vital nutritional component of food stuff . Rutin, also called as rutoside, quercetin-3-rutinoside, and sophorin is a citrus flavonoid glycoside . The name 'rutin' comes from the plant *Ruta graveolens*, which also contains rutin. Chemically it is a glycoside comprising of flavonolic aglycone quercetin along with disaccharide rutinose. It has demonstrated a number of pharmacological activities, including antioxidant, anti-carcinogenic, neuroprotective.



One of the most important role of rutin and also quercetin studied in 2013, this study illustrate using of this flavonoids inhibit oxaliplatin-induced chronic painful peripheral neuropathy. [third-generation platinum compound, has evolved as one of the most important therapeutic agents in colorectal cancer chemotherapy]. The main limiting factor in oxaliplatin treatment is painful neuropathy that is difficult to treat. The flavonoids rutin and quercetin have been described as cell-protecting agents because of their antioxidant and anti-inflammatory actions. Flavonoids occur as glycosides and contain several phenolics hydroxyl groups, many flavonoids are found to

be strong antioxidants effectively because of their phenolics hydroxyl groups the comprehensive model of action of flavonoids includes: quenching free radical elements, chelating metal, suppressing the enzymes associated with the free radical generation, and stimulation of internal antioxidant enzymes, The best-described antioxidant property of flavonoids derives from its ability to directly scavenge the reactive oxygen species, flavonoids can chelate free radicals immediately by donating a hydrogen atom or by single-electron transfer.