

# Chemistry of flavonoids and their therapeutic effects: A Review

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**ABSTRACT:** One important class of natural compounds is flavonoids. Flavonoids belong specifically to a group of secondary metabolites from plants with polyphenolic structures. Fruits, vegetables, tea, wine, grains, bark, and stems are all primary sources of flavonoids. The general molecular structure of flavonoids is defined by a 15-carbon skeleton composed of two benzene rings (A and B) connected by a heterocyclic ring (C), often a pyran ring. The structure can be altered by the C ring's oxidation state and substitution patterns, as well as those of the A and B rings. Methylated, glycoside, and aglycone derivatives are all forms of flavonoids. The basic flavonoid molecule is aglycone. In addition to these flavonoid groups, there are also other subgroups such as bioflavonoids, flavonolignans, prenylflavonoids, chalcones, glycosidic ester flavonoids, and proanthocyanidins. Flavonoids' medicinal, pharmacological, and therapeutic properties, such as anti-ageing, anti-bacterial, anti-tumour, anti-viral, anti-inflammatory, cardiovascular, anti-cancer, neuroprotective, anti-microbial, and anti-diabetic activity have been investigated. The major classifications and replacements of flavonoids, such as hydrogenation, hydroxylation, methylation, malonylation, sulphation, and glycosylation, result in a wide range of structural variations. Based on the location of the benzenoid substituent, the flavonoid class is divided into flavonoids (2-position) and isoflavonoids (3-position). Anthocyanidins, flavones, flavonols, flavan-3-ols, flavanones, and isoflavonoids are the different types of flavonoids.

**Keywords:** Flavonoids, medicinal, pharmacological, therapeutic.

## INTRODUCTION

Flavonoids, which have a basic 15-carbon flavone skeleton with two benzene rings (A and B) joined by a three-carbon pyran ring (C), which are chromene in structure, have been referred to by the more general term "C<sub>6</sub>-C<sub>3</sub>-C<sub>6</sub>' compounds" since 1952. Flavonoids are composed of two types of compounds: a phenyl-substituted propylbenzene derivative (rotenoids) compounds with a C<sub>16</sub> skeleton, and compounds structurally based on derivatives of a phenyl-substituted propylbenzene with a C<sub>15</sub> skeleton. Flavonoids are therefore categorised as heterocyclic rings with oxygen contained in them (Liga *et al.*, 2023).

A significant family of natural products, flavonoids are specifically categorised as dietary flavonoids because they

are a type of secondary metabolite from plants that have a polyphenolic structure and are frequently found in fruits, vegetables, tea, cocoa, wine, and some beverages. Chalcones, flavones, flavanols, anthocyanins, and isoflavones are some of the subgroups of flavonoids. The main sources of these subgroups are distinct. For instance, two important food sources of flavonols and flavones are tea and onions (Panche *et al.*, 2016). Until recently, it was thought that the oldest plants that produced flavonoids were mosses and liverworts. Flavonoids comprise more than 9,000 molecules and are one of the main classes of specialised metabolites (Bowman *et al.*, 2017).

Flavonoids serve a variety of biological purposes in

plants, animals, and microbes. Flavonoids, which are known to be synthesised in specific areas in plants, are responsible for the colour and aroma of flowers, the ability of fruits to attract pollinators and subsequently aid in fruit dispersal, seed germination, seedling growth and development. Flavonoids protect plants against a range of biotic and abiotic stresses by acting as unique UV filters, signal molecules, allelopathic substances, phytoalexins, detoxifying agents, and antimicrobial defensive compounds. Plants are protected from cold and drought by flavonoids, and they may also play a crucial role in their capacity to adapt to cold and heat (Mutha *et al.*, 2021).

In animals, flavonoids possess antioxidant, anti-inflammatory, and antimicrobial properties, which can promote health and enhance the quality of animal products. Flavonoids exhibit various biological activities against bacteria, including antibacterial effects through mechanisms like membrane disruption, inhibition of nucleic acid synthesis, and energy metabolism, as well as biofilm formation and pathogenicity reduction (Syed *et al.*, 2024; Kang *et al.*, 2018).

## BASIC STRUCTURE AND CLASSIFICATION OF FLAVONOIDS

### Basic structure of flavonoids

The basic structure of flavonoids is shown in Figure 1.

### C<sub>6</sub>-C<sub>3</sub>-C<sub>6</sub> Skeleton

Flavonoids are structurally made up of 15 carbon atoms arranged in two benzene rings, called the A and B rings, which are connected by an oxygen-containing pyrene ring (C). Most flavonoids have a fundamental structure made up of a carbon skeleton that is derived from the flavan system (C<sub>6</sub>-C<sub>3</sub>-C<sub>6</sub>) (Rauter *et al.*, 2018).

### Polyphenols

They are a subgroup of polyphenols, meaning they contain multiple phenolic (aromatic hydroxyl) groups (Rauter *et al.*, 2018)

### Variations

The structure can vary depending on the oxidation state and substitution patterns of the C ring, as well as the A and B rings (Rauter *et al.*, 2018).

### Classification of flavonoids

The chemical structure, degree of oxidation, and chain-

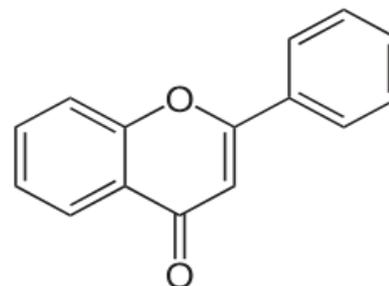


Figure 1. Structure of flavonoids.

linked unsaturation of flavonoids allow for their classification into six major groups: flavanols, flavan-3-ols, flavones, flavanones, isoflavonoids, and anthocyanins. Flavones (e.g., rutin, chrysin, apigenin, and luteolin), flavonols (e.g., quercetin, kaempferol, myricetin, and fisetin), flavan-3-ols (e.g., proanthocyanidins, catechin, epicatechin, and epigallocatechin), flavanones (e.g., flavanone, hesperetin, naringin, and naringenin), isoflavonoids (e.g., genistein and daidzein), anthocyanidins (e.g., apigenidin, malvidin, cyaniding, and delphinidin) (Karak, 2019; Panche *et al.*, 2016). Besides these flavonoid classes, there are more subgroups such as proanthocyanidins, glycosidic ester flavonoids, prenyl-flavonoids, chalcones, bioflavonoids, and flavonolignans (Majewska and Czczot, 2009; Shen *et al.*, 2022).

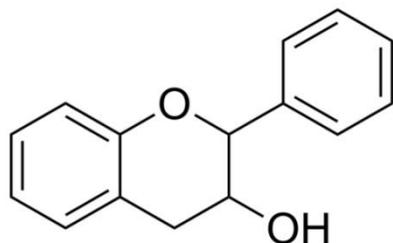
### Flavanols (Flavan-3-Ols)

Flavanols, commonly referred to as flavan-3-ols, have a simple 2-phenyl-3,4-dihydro-2-H-chromen-3-ol structure (Figure 2). Dihydroflavonols, sometimes referred to as flavanols, flavan-3-ols, or catechins, are a complex class of flavonoids. (Kang *et al.*, 2018).

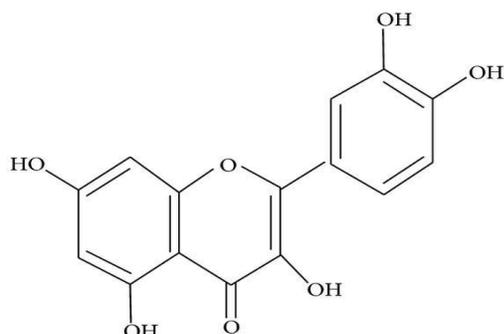
Pecans and hazelnuts are common foods high in flavanols, whereas almonds, cashews, roasted peanuts, and pistachios have moderate levels. Significant quantities of flavanols can also be found in a variety of fruits, beans, teas, red wines, dark chocolate, mint, sage, dill, and rosemary. Flavanols are responsible for certain food quality parameters such as sweetness, sourness, bitterness, astringency, colour formation, and scent. The inflammatory activities of flavanols are due to its modulation of cell redox status and ability to inhibit activation of the NF-κB (Mena *et al.*, 2014)

### Flavonols

Flavonols are flavonoids with a ketone group at position 4 of the C ring and a double bond between C-2 and C-3 (Figure 3). They are the proanthocyanins' building blocks. Flavonols are the most prevalent type of flavonoid found in fruits, leaves and vegetables. Apples, kale, onions, leeks,



**Figure 2.** Structure of flavanol (Flavan-3-Ols).



**Figure 3.** Structure of flavonol.

grapes, berries, broccoli, red lettuce, tomatoes, tea and red wine are the predominant foods that contain flavonols (De Pascual *et al.*, 2010). Flavonols possess a basic structure of 3-hydroxy-2-phenyl chromen-4-one. The major flavonols studied are quercetin, kaempferol, fisetin, myricetin, rhamnetin, isorhamnetin, azaleatin, and their respective glycosyl derivatives (Barreca *et al.*, 2021).

Because of flavonols' scavenging reactive oxygen species (ROS) and pro-oxidant activity due to auto-oxidation, they have anti-inflammatory, anti-allergy, and anti-cancer properties. In addition to flavonols' ability to scavenge reactive oxygen species (ROS), flavonols exhibit a variety of therapeutic functions, such as antispasmodic, antiviral, and antibacterial properties, indicating a complicated mode of action (Barreca *et al.*, 2021; Brodowska, 2017).

Numerous health advantages, such as antioxidant potential and a lower risk of vascular disease, have been linked to flavonol intake. Flavonol may be the most prevalent and sizable class of flavonoids found in fruits and vegetables as a result of their various glycosylation patterns. For example, many plant meals contain quercetin. (Panche *et al.*, 2016; Iwashina, 2013).

## Flavones

Flavones are a group of flavonoids that play several major therapeutic roles and are mainly distributed in higher

plants (Figure 4). The majority of fruit and vegetable flavones include a hydroxyl group at position 5 of the A ring. However, the taxonomic classification of the specific vegetable or fruit may affect the hydroxylation in other locations, primarily in positions 7 of the A ring or 3' and 4' of the B ring (Panche *et al.*, 2016). The main pigments in flowers that are white or cream in colour are flavones. Flavones are differentiated from other flavonoid groups by a double bond between C2 and C3 in their basic flavonoid structure. Apigenin and luteolin are the widely studied flavones (Ganjare *et al.*, 2011). Flavones have been shown in studies to have strong anti-inflammatory, anti-cancer, antibacterial, anti-allergy, and antispasmodic properties (Brodowska, 2017; Kang *et al.*, 2018).

## Flavanones

One of the biggest subgroups of flavonoids is flavanones (Figure 5). This subgroup's fundamental structure is 2,3-dihydro-2-phenyl chromen-4-one. Flavanones are found in the form of glycosides and are widely dispersed in fruits, flowers, and leaves, particularly in the citrus family. Aglycones such as hesperetin, sinensetin, nobiletin, tangeretin, eriodictyol, and isosakuranetin, together with their corresponding glycosides, are the most researched flavanones (Kang *et al.*, 2018; Khan and Dangles, 2014). Flavanones like naringenin (5,7,4'-trihydroxy flavanone) are mostly found in sour oranges and grapefruit, while hesperetin (4'-methoxy-5,7,3'-trihydroxy flavanone) is prominently found in orange, lime, lemon, and tangelo. Flavanones are mostly recognised for their cardioprotective, antiviral, anticancer, and anti-inflammatory effects. The amount and spatial distribution of phenolic OH groups determine the antioxidant properties of flavanones. Flavanones have a stronger antioxidant impact under a hydrophilic environment (Brodowska *et al.*, 2017).

## Isoflavone

Through a process known as aryl migration, the 3-phenyl chromen skeleton of isoflavone is chemically generated from the 2-phenyl chromene skeleton. Legumes, especially soybeans and soy products, are the main source of isoflavones (Figure 6). Among the many medicinal benefits of isoflavones are their lipid-lowering, antioxidant, and anticancer properties. It is well known that isoflavones improve bone health (Poppy *et al.*, 2024).

Some isoflavones have also been reported to be present in microbes. Additionally, during plant-microbe interactions, they are discovered to be crucial precursors for the synthesis of phytoalexins. Because of their oestrogenic activity in specific animal models, isoflavones like genistein and daidzein are frequently considered phyto-oestrogens. Szkudelska and Nogowski (2017) reviewed the effect of genistein, which induces hormonal

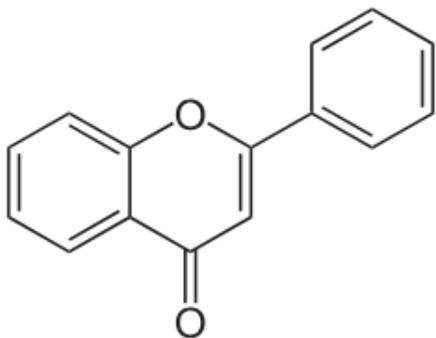


Figure 4. Structure of flavone.

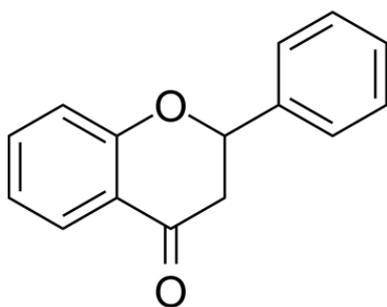


Figure 5. Structure of flavonone.

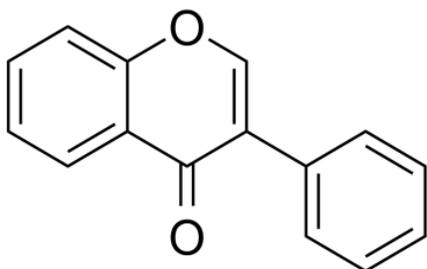


Figure 6. Structure of Isoflavone.

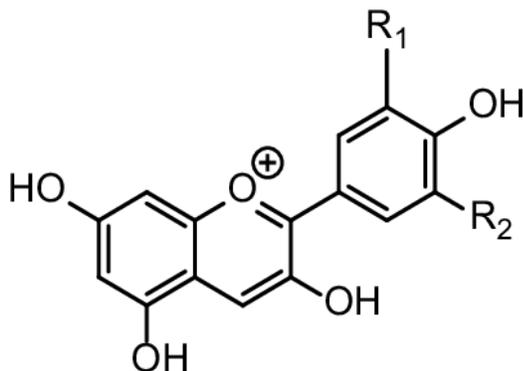


Figure 7. Structure of anthocyanins.

and metabolic changes which can influence various disease pathways.

### Anthocyanins

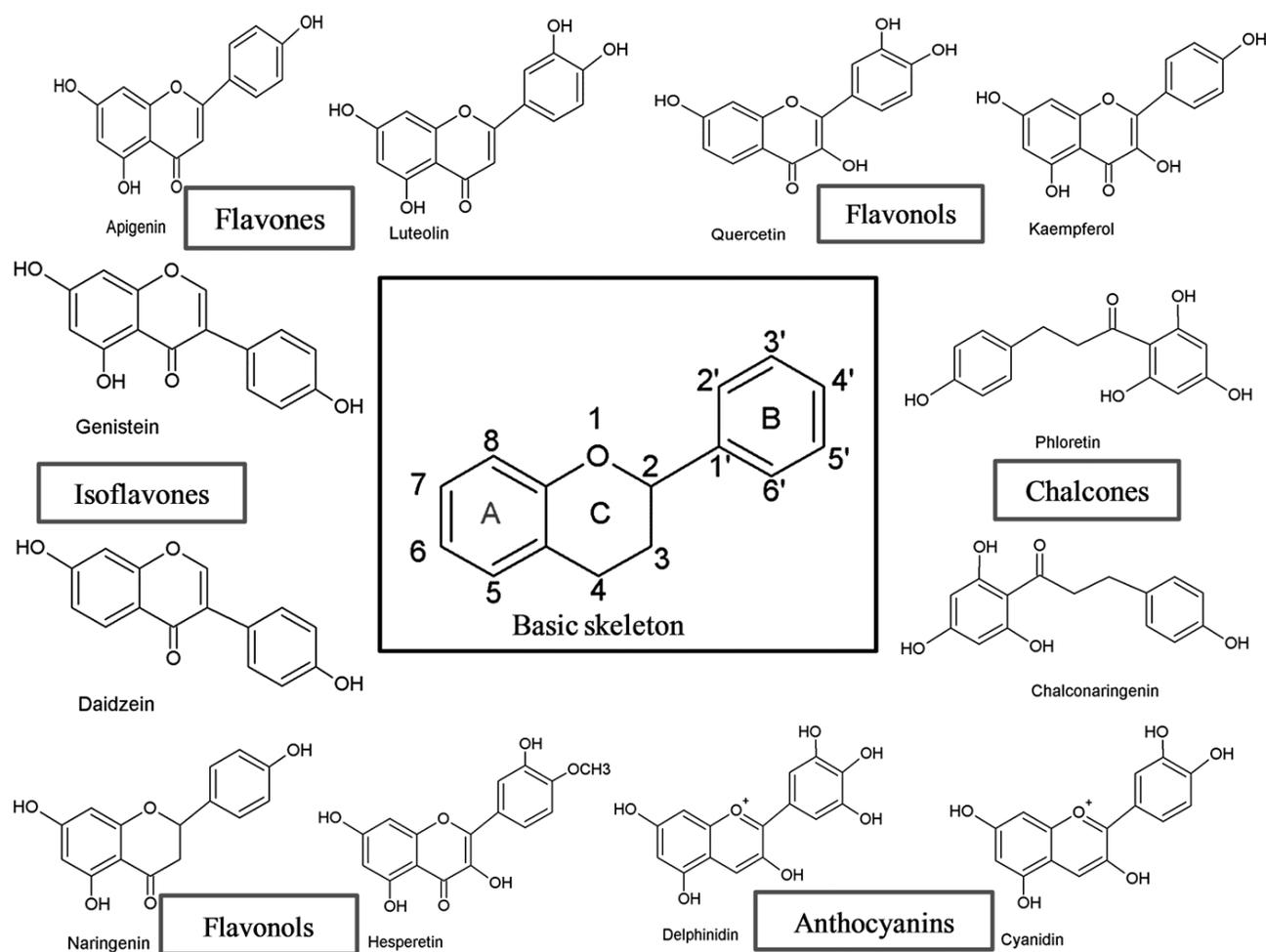
A subgroup of the flavonoid family with a C<sub>3</sub>-C<sub>6</sub>-C<sub>3</sub> carbon structure is called anthocyanins (Figure 7). Glycosylated substances called anthocyanins are polymethoxy and polyhydroxy derivatives of flavylium salts. Anthocyanins are predominantly present in tea, vegetables, fruits, honey, nuts, cocoa, olive oil, and cereals. Furthermore, berries like elderberries, blueberries, strawberries, blackcurrants, and red wine contain anthocyanins in different proportions, while Pelargonidin, cyanidin, delphinidin, petunidin, malvidin, and peonidin are the most common anthocyanins found in fruits and vegetables. The critical function of anthocyanins in cardiovascular health, visual acuity, cholesterol breakdown, and cytotoxicity has been validated by scientific research. Also, anthocyanins have been studied for their potential to improve cognitive function (Wallace, 2011; Poppy *et al.*, 2024). Figure 8 shows the full classes of flavonoids, examples and their chemical structures.

Plants, flowers, and fruits get their colour from anthocyanin pigments. They occur predominantly in the outer cell layers of various fruits such as cranberries, black currants, red grapes, merlot grapes, raspberries, strawberries, blueberries, bilberries and blackberries. These compounds' stability and health advantages allow for a wide range of applications in the food industry. The pH and methylation or acylation at the hydroxyl groups on the A and B rings determine the anthocyanin's colour (Iwashina, 2013).

### DIETARY SOURCE OF FLAVONOIDS

Flavonoids are widely distributed; physiologically active phytochemicals found in plants that have long been utilised in a variety of herbal remedies. They are a crucial part of our everyday nutrition and are mostly found in plants' edible portions (Luthra *et al.*, 2021). Fruits and vegetables are significant sources of dietary flavonoids, along with several other potentially bioactive ingredients like potassium, fibre, folate, antioxidants and vitamins. Additionally, tea that is high in flavonoids and Cocoa (*Camellia sinensis*) represent relatively concentrated sources, and their impact on vascular function is becoming apparent. Due to their widespread occurrence, flavonoids are regularly ingested by humans (Kaur and Roy, 2021).

The individual intake of flavonoids varies substantially depending on the type of diet consumed. *Raphanus sativus* (radish) root and *Lactuca sativa* (salad) were shown to contain flavonoids (Sarah and Gerald, 2011; Rodriguez *et al.*, 2019). Flavonoids can be found in a variety of foods and drinks, such as wine, beer, and tea. The largest concentrations of natural flavonoids are found in fruits, vegetables, flowers, and seeds. However, a



**Figure 8.** Classes of flavonoids, examples and their chemical structures.

number of variables, including plant cultivar or genotype, growing conditions, soil properties, harvest, and storage, affect the quantity of these chemical compounds present (Rodriguez *et al.*, 2019).

Flavonols that comprise, for example, quercetin, kaempferol, fisetin, isorhamnetin, and myricetin are abundant in green leaves, fruits, and grains, including lettuce, cranberries, apples, peaches, and red pepper are rich in quercetin and kaempferol. Spinach leaves have a high quantity of rutin, spinacetin glycosides, and patuletin glycosides, while broccoli, kale, endive, potatoes, onions, grapes, and tomatoes contain more kaempferol 3-O-glycosides. Myricetin also, can also be gotten from nuts, berries, tea, and red wine (Panche *et al.*, 2016; Terahara, 2015).

The flavones, which include luteolin, apigenin, sinensetin, isosinensetin, nobiletin, tangeretin, galangin, and chrysin, are among the most significant flavonoids. These compounds are mainly found in leaves, flowers, and fruits as glucosides of apigenin, luteolin, and diosmetin (Kozłowska and Szostak, 2017). For example, celery is rich in apigenin 7-O-glycoside; glycosides of luteolin and

apigenin are abundant in several citrus fruits, green and red peppers, lettuce, broccoli, olive oil, cacao, oregano, thyme, rosemary, peppermint, and parsley (Terahara, 2015). Flavones like Chrysin, apigenin, rutin, luteolin, and luteolin glucosides are found in Fruit skins, red wine, buckwheat, red pepper, and tomato skin.

Flavanols, or flavan-3-ols, contain catechin, epicatechin, epicatechin gallate, galocatechin, epigallocatechin, and epigallocatechin gallate (Bae *et al.*, 2020). Flavanols are found in high quantities in *Camellia sinensis*, the tea plant, as (-)-epigallocatechin gallate, (-)-epicatechin gallate, (-)-epigallocatechin, (-)-epigallocatechin, and (-)-epicatechin, tea consumption being one of the most important sources of these flavonoids. In addition, fruits like apples, red grapes, peaches, mangoes, pears, plums, nectarines, and raspberries are very rich in (+)-catechin, (-)-epicatechin, and (-)-epigallocatechin. Cocoa and red wine are good sources of catechins (Panche *et al.*, 2016). Flavonols such as Naringin, naringenin, taxifolin, and hesperidin are found in Tea.

Dihydroflavones, another name for flavanones, are a significant class of flavonoids that are frequently present in

citrus fruits. For example, flavanone glycosides, like naringin, naringenin, and naringenin 7-O-neohesperidide, can be found in grapefruits, hesperidin, hesperetin, and hesperetin 7-O-rutinoside in oranges, mandarins, limes, lemons, eriocitrin, eriodictyol, and eriodictyol 7-O-rutinoside in lemons (Terahara, 2015). Flavanones like Naringin, naringenin, taxifolin and hesperidin are found in Citrus fruits, grapefruits, lemons and oranges.

Isoflavones are mostly generated in legumes and are less common in other plants. Isoflavones, particularly present in soybeans, are genistin, glycitin, daidzin, glycosides, and malonylated isoflavones. Soya bean contains, Lupin, fava beans, and kudzu roots also contain genistin. Small quantities of isoflavones like Genistin and daidzin are present in common beans, peanuts, and chickpeas (Panche *et al.*, 2016).

Many flowers, foliage, and fruits have blue, purple, red, and orange colours due to the presence of anthocyanin flavonoids. This group of substances is frequently found as anthocyanidin glycosides, such as cyanidin, pelargonidin, delphinidin, peonidin, petunidin, and malvidin. For example, cranberries, blueberries, raspberries, bilberries, strawberries, blackberries, plums, grapes, cherries, and sweet potatoes have a high quantity of anthocyanins (Khoo *et al.*, 2017). Vegetables such as red cabbage, red turnips, and purple sweet potatoes are rich in acylated anthocyanins. Also, black beans and purple corn contain cyanidin 3-O-glucoside. The blue colour of some flowers is due to delphinidin, while the orange colour is associated with pelargonidin. Anthocyanidins like Apigenidin, cyanidin are found in cherry, raspberry, and strawberry.

## CHEMISTRY OF FLAVONOIDS

The degree of oxidation and the pattern of heterocyclic pyrane substitution vary among the different classes of flavonoids, and the pattern of substitution of the two benzene rings varies among individual compounds within a class. Flavonoids can be found as methylated derivatives, glycosides, and aglycones. Aglycone is the fundamental flavonoid structure. The flavonoid class is separated into flavonoids (2-position) and isoflavonoids (3-position) by the location of the benzenoid substituent. (Zahra *et al.*, 2017). Flavonoids often share a C<sub>6</sub>-C<sub>3</sub>-C<sub>6</sub> flavone skeleton, with oxygen typically enclosing the three-carbon bridge connecting the phenyl groups. Depending on how unsaturated and oxidised the three-carbon segment (C-ring) is, flavonoids are classified according to their chemical structure. The major flavonoid classes include flavonols, flavones, flavanones, catechins (or flavanols), anthocyanidins, isoflavones and chalcones (Rees *et al.*, 2018; Yingxue *et al.*, 2024; Kopustinskiene *et al.*, 2020).

Hydrogenation, hydroxylation, methylation, malonylation, sulphation, and glycosylation are among the substitutions that occur in the structure of flavonoids, which vary greatly among the major classifications of flavonoids. (Hardeep *et*

*al.*, 2023; Vauzour *et al.*, 2008). Many flavonoids occur naturally as flavonoid glycosides and carbohydrate substitutions, including D-glucose, L-rhamnose, glucorhamnose, galactose, lignin, and arabinose (Biswajit *et al.*, 2025). The three most prevalent flavonoid glycosides in the diet are quercitrin, rutin, and robinin. Intestinal flora hydrolyses them to create the physiologically active aglycone. (sugar-free flavonoid) (Mohammad *et al.*, 2023; Syed *et al.*, 2021; Gorniak *et al.*, 2019).

## THERAPEUTIC AND PHARMACOLOGICAL APPLICATIONS OF FLAVONOIDS

The physiological and pharmacological activities of flavonoids have been studied extensively in recent years, such as antioxidant, anti-ageing, anti-bacterial, anti-tumour and anti-viral (Shen *et al.*, 2022; Sun *et al.*, 2021). Flavonoids, naturally occurring compounds in plants, have diverse therapeutic uses, including antioxidants, anti-inflammatory agents, and having anticancer, antiviral, and neuroprotective properties, making them potential treatments for various diseases. These therapeutic uses include;

### Anti-oxidant activity

Flavonoids have the basic 15-carbon flavone skeleton C<sub>6</sub>-C<sub>3</sub>-C<sub>6</sub>, which is connected by a three-carbon pyran ring (C) to two benzene rings (A and B). The antioxidant capacity of flavonoids is influenced by the quantity and location of hydroxy groups on the catechol B-ring as well as the position of the B-ring on the pyran C-ring (D'Amelia *et al.*, 2018).

Free radicals can be scavenged by flavonoids, which lower inflammation and oxidative stress, two factors linked to a number of illnesses. By scavenging dangerous free radicals and reactive oxygen species (ROS), flavonoids function as antioxidants, averting oxidative stress and cell damage. By stabilising free radicals with electrons or hydrogen atoms, flavonoids can successfully stop chain reactions that harm tissues and cells. Well-known flavonoids with potent antioxidant properties include quercetin, kaempferol, and apigenin (Samec *et al.*, 2024). Flavonoids' antioxidative qualities have made them promising in the fight against cancer. As signalling molecules, flavonoids control cell division, initiate apoptosis, and reduce reactive oxygen species generation. These capabilities present viable substitute approaches to cancer prevention and treatment. Numerous fruits and vegetables naturally contain quercetin, a flavonoid that has demonstrated a range of biological benefits in experimental models. One of its noted benefits is the reduction of major asthma symptoms, such as airway inflammation, mucus production, and bronchial hyperactivity (Goulas and Manganaris, 2012).

### Anti-inflammatory activity

Flavonoids can stop the production of inflammatory mediators such as cytokines (including IL-1 $\beta$ , TNF- $\alpha$ , and IL-6) and enzymes linked to inflammation (lipoxygenase and cyclooxygenase-2). Flavonoids can help treat inflammatory conditions, including arthritis and irritable bowel syndrome, as well as chronic pain. Naringenin is one of the flavonoids that can help with neurological diseases, neurotoxicity, and neuroinflammation. The activity of immune cells and immunological systems involved in inflammatory processes can be modulated by flavonoids. Examples of substances with known anti-inflammatory properties include quercetin, genistein, apigenin, kaempferol, and epigallocatechin 3-gallate (Al-Khayri *et al.*, 2022; Brodowska, 2017).

### Cardiovascular health activity

Research indicates that a higher dietary flavonoid consumption is linked to a decreased risk of Atherosclerotic cardiovascular illnesses, including coronary heart disease and stroke. The therapeutic benefits of flavonoids for atherosclerosis, hypertension, and other conditions are becoming more and clearer. There has been much research done on the possible therapeutic benefits of flavonoids for cardiovascular disorders. For instance, studies have assessed the functions of flavonoids in controlling blood pressure through both endothelium-dependent and non-endothelium-dependent pathways, as well as in controlling the systolic and diastolic functions of the heart by affecting calcium homeostasis and the expression of proteins related to smooth muscle.

In order to maintain healthy blood flow and stop atherosclerosis from developing, flavonoids can improve the function of the endothelium, the inner lining of blood vessels. According to research, dietary flavonoids found in foods like cocoa, apples, tea, citrus fruits, and berries have several beneficial impacts on cardiovascular risk factors, such as high blood pressure and endothelial dysfunction. They are thought to have a significant effect on both vascular and cerebrovascular health, and ultimately, they may help avoid neurological and cardiovascular disorders that have a vascular component, such as vascular dementia (Rees *et al.*, 2018).

### Anti-cancer activity

Flavonoids have shown anticancer properties through controlling reactive oxygen species (ROS), halting the cell cycle, inducing apoptosis, and lowering the proliferation and invasiveness of cancer cells. In cancer pharmacology and drug screens, they are regarded as significant anticancer prospects. Important enzymes involved in angiogenesis (the development of new blood vessels that supply tumours) and tumour promotion may also be

disrupted by them. flavonoids can stop cancer cells from surviving by inducing apoptosis, a natural mechanism in which damaged or undesired cells destroy themselves. By stopping the cancer cell cycle at particular stages, flavonoids can stop unchecked cell division. They can reduce a tumour's potential to metastasise by preventing the development of new blood vessels, which are necessary for the tumour to grow and spread, and suppress angiogenesis as a result. Additionally, flavonoids help lessen inflammation, which is a major contributor to the onset and spread of cancer (Hardeep *et al.*, 2023; Hostetler *et al.*, 2017). Examples of flavonoids with anticancer effects are Quercetin, Genistein, Epigallocatechin-3-gallate (EGCG), Luteolin, Myricetin, Apigenin and kaempferol.

### Neuroprotective effects

One potential method for preventing or lessening the impact of neurodegenerative illnesses is the ability of flavonoids to shield neurones from harm caused by neurotoxins. They can also slow the progression of Alzheimer's disease and reverse cognitive deficits. Diets high in flavonoids may help prevent neurodegeneration, according to studies. Certain flavonoids, like as naringenin, have demonstrated promise as a treatment for neurotrophic effects, depression, and amyloidogenesis. Flavonoids may also improve cognitive function, memory, and learning (Biswajit *et al.*, 2025).

In the brain, flavonoids have a number of neuroprotective properties, including the ability to lower neuroinflammation, protect neurones from harm caused by neurotoxins, and improve cognitive function, memory, and learning by encouraging synaptic plasticity and neuronal survival. Two common pathways seem to underlie these effects. First of all, they interfere with important protein and lipid kinase signalling cascades in the brain, which promote synaptic plasticity and neuronal survival while inhibiting apoptosis brought on by neurotoxic species. Second, they have positive effects on the vascular system, which alters the flow of blood throughout the brain and can lead to angiogenesis, neurogenesis, and morphological changes in neurones. By lowering oxidative damage and inflammation, flavonoids may delay the onset and progression of age-related illnesses like Parkinson's and Alzheimer's. (Kumar and Pandey, 2013).

Eating foods rich in flavonoids throughout life may reduce neurodegeneration and prevent or repair age-dependent decreases in cognitive function through this mechanism. Flavonoids may be significant precursor chemicals in the pursuit of creating a new generation of brain-enhancing medications, given the strong interest in creating medications that can improve brain function. (Vauzour *et al.*, 2008).

Flavonoids included in foods and diets can also prevent ageing and enhance cognitive performance. Flavonoids prevent neuronal death from neurotoxic substances,

enhance vascular blood flow, and encourage neurogenesis. Flavonoids rich in neuroprotective properties include Quercetin, Epicatechin, Naringin, Myricetin, Kaempferol and Luteolin.

### Antiviral and antimicrobial activity

Flavonoids have the potential to be antiviral agents because they can prevent viruses from replicating and entering cells. They also have antibacterial and antifungal properties by potentially breaking down cell membranes, inhibiting the development of cell walls, or interfering with essential metabolic processes. Flavonoids have the ability to connect to particular extracellular areas of viruses, prevent them from attaching or entering host cells, and disrupt viral infections. Certain flavonoids have demonstrated antifungal and antibiofilm properties. By disrupting host components necessary for infection or controlling the immune system to lower the viral content, flavonoids can be utilised to treat viral infections (Kozłowska and Szostak, 2019).

Flavonoids have the ability to decrease viral protease activity, prevent viral replication (DNA/RNA synthesis), and obstruct viral entry into cells. (Syed *et al.*, 2021). According to numerous studies, flavonoids have antiviral properties against enteroviruses through a variety of mechanisms, such as preventing viral entry, preventing viral reproduction, and reducing viral protease activity (Jing *et al.*, 2025). Flavonoids have the ability to target the attachment, entrance, replication, and release phases of viral infection. Their antiviral effects can be strengthened by combining various flavonoid mixtures or by combining them with synthetic antiviral medications. Certain flavonoids, such as apigenin, vitexin, quercetin, rutin, and naringenin, have demonstrated antiviral properties against a variety of viruses.

Flavonoids have the ability to inhibit bacterial energy metabolism, cytoplasmic membrane function, and nucleic acid production. Numerous bacteria have been demonstrated to be susceptible to the antibacterial properties of flavonoids such as rutin, quercetin, and morin. Certain flavonoids have the ability to reverse antibiotic resistance, suppress viral factors, and specifically target bacterial cells. Biofilm development, a key component of bacterial persistence and antibiotic resistance, can be inhibited by certain flavonoids. Additionally, some flavonoids have antifungal properties. (Arpita *et al.*, 2022)

Notably, plants produce flavonoids in response to microbial infection, and *in vitro* studies have shown that these chemicals are effective antimicrobials against a variety of pathogenic bacteria. Flavonoids' diverse biological activities, which may not initially appear to be highly specific, are what give them their antimicrobial effect. Nonetheless, there are promising antibacterial flavonoids that can decrease virulence factors and other microbial dangers, such as the formation of biofilms, in

addition to specifically targeting bacterial cells. Additionally, several plant flavonoids show promise in reversing antibiotic resistance and improving the effectiveness of existing antibiotic medications. Creating and using medications based on flavonoids may be a potential strategy for treating illnesses that are resistant to antibiotics (Gorniak *et al.*, 2019).

### Antidiabetic activity

Considering the potential for flavonoids to shield the body from pro-oxidative substances like free radicals, and the proposed link between diabetes and inflammation. Eating foods high in flavonoids or flavonoids themselves could lower the chance of developing diabetes. This movement has given rise to new ideas, including nutritional treatment, phytonutrients, nutraceuticals, and phytotherapy. In order to prevent certain types of diabetes, these functional foods and phytomedicines help to manage blood glucose levels, insulin secretion, glucose uptake, and immunological function. Many strategies have been developed recently to use flavonoids *in vitro* and *in vivo* models, adding a few new techniques to enhance their antidiabetic action (Vinayagam, 2015)

By shielding pancreatic  $\beta$ -cells, triggering insulin signalling, and blocking enzymes involved in carbohydrate metabolism, flavonoids can reduce blood glucose levels. Flavonoids have been acknowledged as potential diabetes mellitus treatment agents due to their antidiabetic and anti-inflammatory qualities (Proenca *et al.*, 2021).

### CONCLUSION

Flavonoids are secondary metabolites which are readily available in different parts and classes of plants. Flavonoids can be found as methylated derivatives, glycosides, and aglycones. The major flavonoid classes include flavonols, flavones, flavanones, catechins, anthocyanidins, isoflavones and chalcones. Flavonoids' therapeutic and pharmacological properties, such as anti-ageing, anti-bacterial, anti-tumour, anti-viral, anti-inflammatory, cardiovascular, anti-cancer, neuroprotective, anti-microbial, and anti-diabetic activities, are investigated for the treatment of diseases and future trends on further medicinal uses.

### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

### REFERENCES

- Al-Khayri, J. M., Sahana, G. R., Nagella, P., Joseph, B. V., Alessa, F. M., & Al-Mssallem, M. Q. (2022). Flavonoids as Potential Anti-Inflammatory Molecules: A Review. *Molecules* (Basel, Switzerland), 27(9), 2901.

- Arpita, R., Ariba, K., Irfan, A., Saad, A., Bodour, S. R., Ahmad, O. B., Mohammad, Y. A., Saiful, I., & Md Rabiul, I. (2022). Flavonoids a bioactive compounds from medicinal plants and its therapeutic applications. *BioMed Research International* 2022(1), 5445291
- Bae, J., Kim, N., Shin, Y., Kim, S.Y., & Kim, Y.J. (2020). Activity of catechins and their applications. *Biomedical Dermatology*, 4, 8.
- Barreca, D., Trombetta, D., Smeriglio, A., Mandalari, G., Romeo, O., Felice, M. R., Gattuso, G. & Nabavi, S. M. (2021) Food flavonols: Nutraceuticals with complex health benefits and functionalities, *Trends Food Science*, 117, 194-204
- Biswajit, K. U., Baishakhi, S., Mehrukh, Z., Sherouk, H. S., Trupti, P. D., Uppuluri, V. N., Venkata, A., Thukani, S. S., Shruthi P. K., P. Dharani, P., Md. Rageeb, Md. Usman, Konatham T. K., Rokeya, S., Mohammed, A. A., Safia O. R., Muath S., Talha, B. E. (2025). Cellular stress response and neuroprotection of flavonoids in neurodegenerative diseases: Clinical insights into targeted therapy and molecular signaling pathways, *Brain Research*, 1847, 8993.
- Bowman, J. L., Kohchi, T., Yamato, K. T., Jenkins, J., Shu, S., Ishizaki, K., Yamaoka, S., Nishihama, R., Nakamura, Y., Berger, F., Adam, C., Aki, S. S., Althoff, F., Araki, T., Arteaga-Vazquez, M. A., Balasubramanian, S., Barry, K., Bauer, D., Boehm, C. R., Briginshaw, L., & Schmutz, J. (2017). Insights into Land Plant Evolution Garnered from the Marchantiopolymorpha Genome. *Cell*, 171(2), 287–304.
- Brodowska, K. M. (2017). Natural flavonoids: classification, potential role, and application of flavonoid analogues. *European Journal of Biological Research*, 7(2), 108-123.
- D'Amelia, V., Aversano, R., Chiaiese, P., & Carputo, D. (2018). The antioxidant properties of plant flavonoids: Their exploitation by molecular plant breeding. *Phytochemistry Reviews*, 17, 611–625.
- De Pascual, T., S., Moreno, D. A., García-Viguera, C. (2010). Flavanols and anthocyanins in cardiovascular health: a review of current evidence. *International Journal of Molecular Sciences*, 11(4) 1679-1703.
- Ganjare, A.B., Nirmal, S.A., & Patil, A.N (2011). Use of apigenin from *Cordia dichotoma* in the treatment of colitis, *Fitoterapia*, 82(7) 1052-1056.
- Górnjak, I., Bartoszewski, R., & Króliczewski, J. (2019). Comprehensive review of antimicrobial activities of plant flavonoids. *Phytochemistry Reviews*, 18(1), 241-272.
- Goulas, V., & Manganaris, G. A. (2012). Exploring the phytochemical content and the antioxidant potential of Citrus fruits grown in Cyprus. *Food Chemistry*, 131(1), 39-47.
- Hardeep, S. T., Vivek, K. G., Sakshi, B., Vivek, U., Uttam, S., Aklank, J., Katrin, S., Vikas, Y., Jose, M. L., Kuldeep, D., Tapan, B., & Gautam, S. (2023) Natural flavonoids exhibit potent anticancer activity by targeting microRNAs in cancer: A signature step hinting towards clinical perfection, *Translational Oncology*, 27,1936-5233.
- Hostetler, G.A., Ralston, R. A., & Schwartz, S. J. (2017). Flavones: Food sources, bioavailability, metabolism, and bioactivity, *Advances in Nutrition*, 8(3) 423-435.
- Iwashina, T. (2013). Flavonoid properties of five families newly incorporated into the order Caryophyllales (Review). *Bulletin of the National Museum of Nature and Science*, 39, 25–51
- Jing, C., Yi, Z., Xiao, C., Yadi, L., Li, K., & Yuwei, L. (2025). The antiviral properties of flavonoids, *Clinical Traditional Medicine and Pharmacology*, 6(1), 2097-3829.
- Kang, H. W., Lee, S. G., Otiemo, D., & Ha, K. (2018). Flavonoids, potential bioactive compounds, and non-shivering thermogenesis. *Nutrients*, 10(9) 1168.
- Karak, P. (2019). Biological activities of flavonoids: An overview. *International Journal of Pharmaceutical Sciences and Research*, 10(4)1567-1574.
- Kaur, S., & Roy, A. (2021). A Review on the nutritional aspects of wild edible plants. *Current Traditional Medicine*, 7(4), 552-563.
- Khan, M. K., & Dangles, O. (2014). A comprehensive review on flavanones, the major citrus polyphenols. *Journal of Food Composition and Analysis*, 33(1), 85-104.
- Khoo, H. E., Azlan, A., Tang, S. T., & Lim, S. M. (2017). Anthocyanidins and anthocyanins: Colored pigments as food, pharmaceutical ingredients, and the potential health benefits. *Food & Nutrition Research*, 61, 1361779.
- Kopustinskiene, D. M., Jakstas, V., Savickas, A., & Bernatoniene, J. (2020). Flavonoids as anticancer agents. *Nutrients*, 12(2), 457.
- Kozłowska, A., & Szostak, W. D. (2019). Flavonoids – Food sources, health benefits, and mechanisms involved. In: Mérillon, J. M., Ramawat, K. G. (eds.). *Bioactive molecules in food. reference series in phytochemistry*. Springer, Cham.
- Liga, S., Paul, C., & Peter, F. (2023). Flavonoids: Overview of Biosynthesis, Biological Activity, and Current Extraction Techniques. *Plants*, 12(14), 2732.
- Luthra, R., Roy, A., Pandit, S., & Prasad, R. (2021). Biotechnological methods for the production of ginsenosides, *South African Journal of Botany*, 141, 25-36.
- Majewska, M., & Czacot, H. (2009). Flavonoids in prevention and therapy of diseases, *Farm Policy Journal*, 65, 369-377.
- Mena, P., Domínguez-Perles, R., Gironés-Vilaplana, A., Baenas, N., García-Viguera, C., & Villaño, D. (2014). Flavan-3-ols, anthocyanins, and inflammation, *IUBMB Life*, 66(11) 745-758.
- Mohammad, T., Navid, M., Arash, S., Reza, K., Forough, T., Mohsen, M., Alireza, K., Sara, A., Mobina, B., Abbas, S. K., & Javid, S. N. (2023). Chapter 6 - Neuroprotective effects of flavonoids. In: Khan, H., Aschner, M., & Mirzaei, H. (eds.). *Phytonutrients and neurological disorders* (pp. 133-200) Academic Press.
- Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). Flavonoids: an overview. *Journal of Nutritional Science*, 5, 1-15.
- Poppy, A. Z., Yogi, S., Evamarie, H., Muhammad, F. L., Ade, S. R., Moon, N. P., Bonglee, K., & Rony, A. S. (2024). Unlocking the potential of flavonoids: Natural solutions in the fight against colon cancer, *Biomedicine & Pharmacotherapy*, 176, 116827.
- Proença, C., Ribeiro, D., Freitas, M., Carvalho, F., & Fernandes, E. (2021). A comprehensive review on the antidiabetic activity of flavonoids targeting PTP1B and DPP-4: a structure-activity relationship analysis. *Critical Reviews in Food Science and Nutrition*, 62(15), 4095-4151.
- Rauter, A., Ennis, M., Hellwich, K., Herold, B., Horton, D., Moss, G., & Schomburg, I. (2018). Nomenclature of flavonoids (IUPAC Recommendations 2017). *Pure and Applied Chemistry*, 90(9), 1429-1486.
- Rees, A., Dodd, G. F., & Spencer, J. P. (2018). The Effects of Flavonoids on Cardiovascular Health: A Review of Human Intervention Trials and Implications for Cerebrovascular Function. *Nutrients*, 10(12), 1852.
- Rodríguez, G. C., Sánchez, Q. C., & Gaforio, J. J. (2019). Dietary flavonoids as cancer chemopreventive agents: An updated review of human studies. *Antioxidants*, 8, 137.
- Roy, A., Khan, A., Ahmad, I., Alghamdi, S., Rajab, B. S., Babalghith, A. O., Alshahrani, M. Y., Islam, S., & Islam, R. (2022). Flavonoid: A bioactive compound from medicinal plants

- and its therapeutic applications. *BioMed Research International*. Volume 2022, Article ID 5445291, 9 pages.
- Kumar, S., & Pandey, A. K. (2013). Chemistry and biological activities of flavonoids: an overview. *The Scientific World Journal*, 58(4), 145-148.
- Mutha, R. E., Tatiya, A. U., & Surana, S. J. (2021). Flavonoids as natural phenolic compounds and their role in therapeutics: an overview. *Future Journal of Pharmaceutical Science*, 7, 25.
- Samec, D., Karalija, E., Sola, I., Bok, V. V., & Salopek-Sondi, B. (2021). The role of polyphenols in abiotic stress response: The influence of molecular structure. *Plants*, 10, 118.
- Sarah, E., & Gerald, R. (2011). Which Sources of flavonoids: Complex diets or dietary supplements? *Advances in Nutrition*, 2(1), 8-14.
- Shen, N., Wang, T., Gan, Q., Liu, S., Wang, L., & Jin, B. (2022). Plant flavonoids: classification, distribution, biosynthesis, and antioxidant activity. *Food Chemistry*, 383:132531.
- Shen, N., Wang, T., Gan, Q., Liu, S., Wang, L., & Jin, B. (2022). Plant flavonoids: classification, distribution, biosynthesis, and antioxidant activity. *Food Chemistry*, 383.
- Sun, C., Liu, Y., Zhan, L., Rayat, G. R., Xiao, J., Jiang, H., Li, X., & Chen, K. (2021). Anti-diabetic effects of natural antioxidants from fruits. *Trends Food Science Technology*, 117, 3-14.
- Syed, L. B., Shah, F., Akhtar, M., Benjamin, Gabriel, P., Abdul, H. E., & Mariusz, J. (2021). Antiviral activities of flavonoids, *Biomedicine & Pharmacotherapy*, 140, 0753-3322.
- Szkudelska, K., & Nogowski, L. (2007). Genistein – a dietary compound inducing hormonal and metabolic changes. *The Journal of Steroid Biochemistry and Molecular Biology*, 105, 37–45.
- Terahara, N. (2015). Flavonoids in foods: A Review. *Natural Product Communications*, 10, 521–528.
- Vauzour, D., Vafeiadou, K., Rodriguez-Mateos, A., Rendeiro, C., & Spencer, J. P. (2008). The neuroprotective potential of flavonoids: a multiplicity of effects. *Genes & Nutrition*, 3(3-4), 115-126.
- Vinayagam, R., & Xu, B. (2015). Antidiabetic properties of dietary flavonoids: a cellular mechanism review. *Nutrition & Metabolism*, 12(1), 60.
- Wallace, T. C. (2011). Anthocyanins in cardiovascular disease. *Advances in Nutrition*, 2(1) 1-7.
- Yingxue, L., Jing, L., Lin, P., Qi, Z., Xi, R., Yuhao, L., & Jiafu, Li. (2024). Flavonoids: Potential therapeutic agents for cardiovascular disease, *Heliyon*, 10,12, 2405-8440.
- Zahra, M., Abrahamse, H., & George, B. P. (2024). Flavonoids: antioxidant powerhouses and their role in nanomedicine. *Antioxidants* (Basel, Switzerland), 13(8), 922.
- Khajuria, R., Singh, S., & Bahl, A. (2019). General introduction and sources of flavonoids. In: Tuli, H. (ed.). *Current aspects of flavonoids: Their role in cancer treatment* (pp. 1-7). Springer, Singapore.