



FLAVONOIDS AND PHENOLIC ACIDS AS ANTIOXIDANTS IN PLANTS AND HUMAN HEALTH

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ABSTRACT

Flavonoids and phenolic acids are the most persistent groups of plant phenolics therefore they play significant role in plants and human health, thus it is important to better understanding of flavonoid awareness with biological behavior that could indicate their potentials as therapeutic agents. Plants and herbs consumed by humans may contain different phenolic acid and flavonoid components therefore the effect of dietary phenolics is currently of great interest due to their antioxidative activities although Phenolic acids and flavonoids function as reducing agents and free radical scavengers. So it will be significant to examine the possible role of flavonoids and phenolic acids in disease prevention, especially the current status of the subject matter and future prospects, in this review.

Keywords: Flavonoids, phenolic acids, antioxidants.

INTRODUCTION

In recent years there is an increase in the areas related to newer developments in prevention of disease especially the role of flavonoids and phenolic acids as antioxidants moreover flavonoids and phenolic acids components play important roles in the control of different human diseases. Flavonoids and phenolics acids are the most important groups of secondary metabolites and bioactive compounds in plants and good sources of natural antioxidants in human diets¹. They are also a kind of natural product and antioxidant substance capable of scavenging free superoxide radicals, reducing the risk of cancer and protecting biological systems against the harmful effects of oxidative processes on macromolecules, such as carbohydrates, proteins, lipids and DNA². Flavonoids and phenolics acids are more correctly referred as antioxidant inside this review. Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as ROS (reactive oxygen species) and free radicals. Free radicals are responsible for causing a wide number of health problems which include cancer, heart diseases and gastric problems etc. Flavonoids and phenolics may assist make available security against these diseases by contributing, along with antioxidant vitamins and enzymes, to the total antioxidant defense system of the human body even though Phenolics and flavonoids possess diverse biological activities, for instance, antiulcer and anti-inflammatory³, antidibatic⁴, antiviral⁵, antioxidant⁶, cytotoxic and antitumor⁷. The aim of this review is to present evidence for the role of flavonoids and phenolics acids as antioxidants in health promotion by preventing oxidative damage responsible of many diseases.

PHENOLIC ACIDS

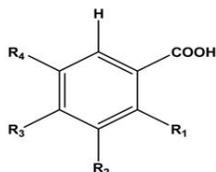
Phenolic acids are aromatic secondary plant metabolites broadly distributed throughout the plant kingdom. Phenolic compounds confer unique taste, flavour, and health-promoting properties found in vegetables and fruits⁸. The term "phenolic acids", in general, designates phenols that possess one carboxylic acid functionality, moreover the reason for including phenolic acids in the family of plant polyphenols lies in the fact that they are bioprecursors of polyphenols and, more importantly, they are metabolites of polyphenols. Naturally occurring phenolic acids contain two distinctive carbon frameworks: the hydroxycinnamic and hydroxybenzoic structures (Table 1). Hydroxycinnamic acid compounds are produced as simple esters with glucose or hydroxy carboxylic acids. Plant phenolic compounds are different in molecular structure, and are characterized by hydroxylated aromatic rings⁹. These compounds have been studied mainly for their properties against oxidative damage leading to various degenerative diseases, such as cardiovascular diseases, inflammation and cancer. Indeed, tumour cells, including leukaemia cells, typically have higher levels of reactive oxygen species (ROS) than normal cells so that they are particularly sensitive to oxidative stress¹⁰. Many papers and reviews describe studies on bioavailability of phenolic acids, emphasizing both the direct intake through food consumption and the indirect bioavailability deriving by gastric, intestinal and hepatic metabolism¹¹. In addition Phenolic acid compounds and functions have been the subject of a great number of agricultural, biological, chemical and medical studies. In recent years, the importance of antioxidant activities of phenolic compounds and their potential usage in processed foods as a natural antioxidant compounds has reached a new level and some evidence suggests that the biological



actions of these compounds are related to their antioxidant activity¹².

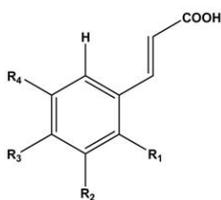
Table 1: Structures of the important naturally occurring phenolic acids

Hydroxybenzoic Acids



Position	R ₁	R ₂	R ₃	R ₄
Benzoic acid	H	H	H	H
Gallic acid	H	OH	OH	OH
Vaillinic acid	H	OCH ₃	OH	H
Salicylic acid	OH	H	H	H

Hydroxycinnamic Acids



Position	R ₁	R ₂	R ₃	R ₄
Cinnamic acid	H	H	H	H
Ferulic acid	H	OCH ₃	OH	H
Sinapic acid	H	OCH ₃	OH	OCH ₃
Caffeic acid	H	OH	OH	H

FLAVONOIDS

Like as phenolic acids, flavonoids are secondary metabolites of plants with polyphenolic structure thus flavonoid groups of poly phenolic compounds have low toxicity in mammals and are widely distributed in plant kingdom¹³. Major dietary sources of Flavonoides in the form of flavonols, flavones, isoflavones, flavonones are, tea, red wine, apple, tomato, cherry, onion, thyme, parsley, soyabeans, and other legumes, grape fruit, orange, lemon, ginkgo, and neem¹⁴. Flavonoids have gained recent attention because of their broad biological and pharmacological activities in these order Flavonoids have been reported to exert multiple biological property including antimicrobial, cytotoxicity, anti-inflammatory as well as antitumor activities but the best-described property of almost every group of flavonoids is their capacity to act as powerful antioxidants which can protect the human body from free radicals and reactive oxygen species¹⁵. The capacity of flavonoids to act as antioxidants depends upon their molecular structure. The position of hydroxyl groups and other features in the chemical structure of flavonoids are important for their antioxidant and free radical scavenging activities. Quercetin, the most abundant dietary flavonol, is a potent antioxidant because it has all the right structural features for free radical scavenging activity¹⁶.

The acknowledged dietary antioxidants are vitamin C, vitamin E, selenium, and carotenoids. However, recent studies have demonstrated that flavonoids found in fruits and vegetables may also act as antioxidants¹⁷. On the other hand flavonoids such as luteolin and catechins, are better antioxidants than the nutrients antioxidants such as vitamin C, vitamin E and β-carotene¹⁸. The function of an antioxidant is to intercept and react with free radicals at a rate faster than the substrate. Since free radicals are able to attack at a variety of target including lipids, fats and proteins, it is believed that they may damage organisms, leading to disease and poisoning¹⁹.

STRUCTURE AND CLASSIFICATION OF FLAVONOIDS

Flavonoids contain C₁₅ atoms in their basic nucleus and C₁₅ atoms composed of two aromatic rings linked through a heterocyclic pyrane ring. All flavonoids share the basic C₆-C₃-C₆ Structural skeleton, consisting of two aromatic C₆ rings (A and B) and a heterocyclic ring (C) that contains one oxygen atom (Figure 1). They can be subdivided into six subclasses (Table 2).²⁰

Figure 1: Basic structure of flavonoid

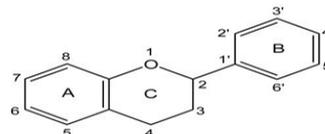
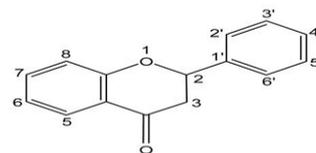


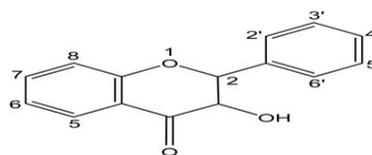
Table 2: Different classes of flavonoids and their substitution patterns.

Flavones



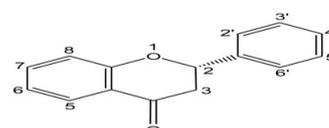
Position	5	7	3'	4'
Apigenin	OH	OH	—	OH
Luteolin	OH	OH	OH	OH
Chrysin	OH	OH	—	—

Flavonols



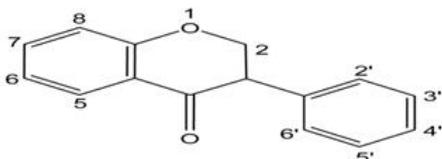
Position	5	7	3'	4'	5'
Quercetin	OH	OH	OH	OH	—
Kaempferol	OH	OH	—	OH	—
Galangin	OH	OH	—	—	—

Flavanone



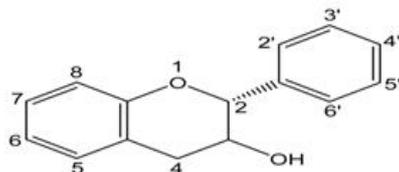
Position	5	7	3'	4'
Naringenin	OH	OH	–	OH
Hesperetin	OH	OH	OH	OCH ₃

Isoflavones



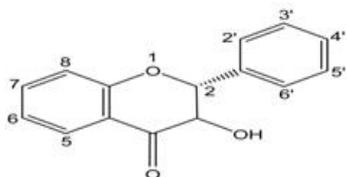
Position	5	7	4'
Ganistein	OH	OH	OH
Daidzein	–	OH	OH

Flavan-3-ol



Position	3	5	7	3'	4'	5'
(+)-Catechin	βOH	OH	OH	OH	OH	–
(-)-Epicatechin	αOH	OH	OH	OH	OH	–
(-)-Epigallocatechin	αOH	OH	OH	OH	OH	OH

Flavanol



Position	5	7	3'	4'
Taxifolin	OH	OH	OH	OH

Role of flavonoids and phenolic acids in plants

The role of flavonoids in flowers is to provide colors attractive to plant pollinators²¹ and in leaves, these compounds are increasingly believed to promote physiological survival of the plant, protecting it from, for example, fungal pathogens and UV-radiation.²² In addition, flavonoids are involved in photosensitization, energy transfer, the actions of plant growth hormones and growth regulators, control of respiration and photosynthesis, morphogenesis and sex determination²³. Although Flavonoids are amongst of the chemicals that give the plant a rich taste and the flavour may act as an attractant or repellent to pollinators or pests²⁴.

Insoluble phenolics are dispersed in the cell walls, while soluble phenolics are compartmentalised within the plant cell vacuoles²⁵. Various phenolic acids have been found during the different stages of maturation²⁶ while growing conditions are known to have an impact on the phenolic acid content²⁷. Many of the phenolic acids like cinnamic and benzoic acid derivatives exist in all plant and plant-derived foods (e. g., fruits, vegetables, and grains)²⁸. Although much knowledge is to be obtained with respect

to the role of phenolic acids in plants, they have been associated with diverse functions, including nutrient uptake, protein synthesis, enzyme activity, photosynthesis, structural components, and allelopathy²⁹.

Flavonoids and phenolic acids as antioxidant properties

Flavonoids and phenolics are well known for their antioxidant activity and we know that Antioxidants are specific compounds that protect human, animal and plant cells against the damaging effects of free radicals in addition an imbalance between antioxidants and free radicals results in oxidative stress, will lead to cellular damage³⁰. Oxidative stress is a harmful condition that occurs when there is an excess of ROS and decrease in antioxidant levels, this may caused tissue damage by physical, chemical that lead to tissue injury in human and causes different diseases³¹. Researchers have shown that the antioxidants of plant origin with free-radical scavenging properties could have enormous importance as therapeutic agents in diseases caused due to oxidative stress³².

Plants are potential sources of invaluable antioxidants. Natural or phytochemical antioxidants are secondary metabolites in plants such as phenolic acids and flavonoids which are amongst the antioxidants produced by plants for their sustenance³³. Recently, phenolics and flavonoids have been considered as great antioxidants and proved to be more effective than Vitamin C, E and carotenoids³⁴. The flavones and catechins seem to be the most powerful flavonoids for protecting the body against reactive oxygen species (ROS)³⁵. Quercetin, kaempferol, morin, myricetin and rutin, by acting as antioxidants, exhibited beneficial effects such as anti-inflammatory, antiallergic, antiviral, as well as anticancer activity. They have also been suggested to play a protective role in liver diseases and cardiovascular diseases³⁶. The reduction activity of phenolic and flavonoid compounds depends on the number of free hydroxyl groups in the molecular structure, which would be strengthened by steric hindrance.

Several researches have been demonstrate that the significant role of flavonoids and phenolics as antioxidant activities in these order Braca *et al.*, isolated several flavonoids from the leaves of *Licania licaniaeflora* and reported quercetin derivatives to possess strongest antioxidant activity and flavonone 8-hydroxy-naringen and kaempferol 3-O-α-rhamnoside possesses lowest antioxidant activity³⁷. Shariffer *et al.*, reported antioxidant activity of methanolic extract of *Teucrium polium* and rutin and apigenin were found to be potent inhibitors of lipid peroxidation and oxidation of beta-carotene³⁸. Salucci *et al.*, reported that dietary flavonoids like epicatechin, galate, gallic acid, quercetin-3-glucoside possess strong antioxidant activity³⁹. Ghasemzadeh *et al.*, reported that high level of total phenolic and flavonoid in *Halia Bara* variety possess potent antioxidant activities⁴⁰. All these pharmacological benefits of flavonoids are generally thought to be due to their

antioxidant and free radical scavenging properties. Apart from antioxidant positive effects on improving health, antioxidants are also added in food to prevent or delay the oxidation of food, initiated by free radicals formed during their exposure to environmental factors such as air, light and temperature⁴¹.

Flavonoids and phenolic acids as antioxidants protection against human disease

Requirement for antioxidants in Indian conditions differ from that of industrialized western countries due to the nutritional differences. There are also a number of dietary supplements rich in antioxidants tested for their efficacy. There are many laboratories from India working on the antioxidant effect of plant compounds, mainly derived from natural sources that are capable of protecting against cell damage and different diseases. Such studies show that compounds with potent antioxidant activity include carotenoids, curcumin from turmeric, flavonoids, phenolic acids, etc⁴². Ayurvedic Indian systems are living great traditions and have important roles in bioprospecting of new medicines from medicinal plants, which are also rich sources of antioxidants.

Apart from their physiological roles in the plants, flavonoids and phenolics are considered as important components in the human diet therefore Flavonoids have been used extensively since centuries for the treatment of various diseases. Cardiovascular diseases are today the principal cause of death in both developing and developed countries. Cardiovascular diseases include atherosclerosis, coronary heart disease, arterial hypertension, and heart failure. The major reason behind CVS diseases is oxidative stress and hence with the help of antioxidant decreases the oxidative stress. It is generally accepted that most of, if not all, the beneficial health effects of flavonoids are attributed to their antioxidant and chelating capacities⁴³. Phenolics have an array of health-promoting benefits they are of current interest due to their important biological and pharmacological properties, especially the antioxidant activity⁴⁴. Phenolic antioxidants have been shown to play important roles in delaying the development of chronic diseases such as cardiovascular diseases, cancer, inflammatory bowel syndrome and Alzheimer's disease⁴⁵. Furthermore, epidemiologic studies suggest a protective role of dietary flavonoids and phenolics against coronary heart disease⁴⁶. The health-promoting effects of flavonoids and phenolics may relate to interactions with key enzymes, signaling cascades involving cytokines and transcription factors, or antioxidant systems⁴⁷.

CONCLUSION

Antioxidant activity is the foundation of many actions which lead to its beneficial effects in majority of the diseases. Usually HPLC, HPTLC and UV spectrophotometric methods can be used effectively for the qualitative and quantitative estimation of Flavonoids and phenolic acids for their therapeutical action. Researchers are Underway to study the effect of several

flavonoids and phenolics in diseases such as pneumonia, cancer, amoebic dysentery. Therefore the rapid and systematic measurement of phenolic acids and flavonoids is a serious challenge for analytical chemists, phytochemists, and biochemists because of their inherent structural diversity and dietary impact.

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