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A Comprehensive Review on Biological Activity of Flavonoids

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ABSTRACT

Plants and herbs consumed by humans are rich sources of phytonutrients compounds synthesized in plants itself. Such bioactive ingredients are responsible for the plant's antioxidant and medicinal values. Flavonoid might recover cancer and cardiovascular diseases. Flavonoids are considered as disease preventing and health promoting dietary supplements. Flavonoids are an important group of naturally occurring polyphenolic compounds, and its flavone nucleus characterizes it. The main purpose of this present review is to deliberate the current trends of research and development on flavonoids, functions, prediction of flavonoids and applications of flavonoids, as potential drugs in inhibiting several chronic diseases and future research guidelines. Flavonoids have the capacity to control the accumulation of reactive oxygen species (ROS) via scavenger ROS when they are designed. Thus, these antioxidant compounds have a significant role in plant stress tolerance and a high significance in human health, mainly due to their anti-inflammatory and antimicrobial properties.

Keywords: ROS, Phytonutrients, Anti-Inflammatory, Antimicrobial Properties.

I. INTRODUCTION

The pigments which is responsible for the color of most fruits, flowers, as well as seeds are flavonoids. Flavonoids are phenolic compounds extensively disseminated in the human diet. The intake of flavonoids has been related through a decreased risk of different diseases like cancer, immune dysfunction and coronary heart disease. Flavonoids has six subgroups that can be considered as major. Chalcones, flavones, flavonols, flavandiols, anthocyanins, and proantho-cyanidins or condensed tannins Flavonoids are a crucial collection of naturally occurring polyphenolic compounds, it is one of the most collective types of compounds accessible in vegetables, fruits, and plant-derived beverages. Moreover, they subsidize to the nutritional merits of vegetables as well as fruits (**Table 1**). Flavonoids are considered as health stimulating and disease avoiding nutritional supplements. It is now measured as an essential component in a variety of pharmaceutical, cosmetic, nutraceutical, medicinal, and further uses. Molecular weight of the flavonoids is low. Many functions and biological utilities are implemented by Flavonoids like comprising protecting from the ultraviolet (UV) radiation and phytopathogens, signaling during nodulation, male

fertility, auxin transport, cell growth regulations, appealing pollinator insects, and protection against biotic and abiotic stresses. Flavonoids are also accountable for the display of fall color in many plants (**Table 2**), which might defend leaf cells by harming from photooxidative, improving the effectiveness of nutrient repossession through senescence In humans, these compounds are connected with a great collection of health benefits rising from their bioactive properties, such as anti-inflammatory, anticancer, anti-aging, cardio-protective, neuroprotective, immunomodulatory, antidiabetic, antibacterial, antiparasitic, and anti-viral properties However, the industrial use of these antioxidants implies extraction processes with high purity and quality. Therefore, several measures for the extraction of flavonoids have been discovered, and in recent years further environmentally approachable extraction methods and strategies that accomplish great yields have been established [1]. Flavonoids are extensively dispersed subordinate metabolites with different metabolic functions in plants. Converse connection can be observed among chronic diseases and dietary flavonoids, which exhibited the significance of reviewing flavonoids. At present have come to the conclusion that the flavonoid might recover cardiovascular diseases and cancer as well.

TABLE 1 : FLAVONOIDS SUBCLASSES AND THEIR OCCURRENCE IN FOODS

Sr. No.	Subclass of Flavonoid	Examples of Compounds	Food source	References
1	Flavonol	Kaempferol, quercetin, Myricetin and tamarixetin	olive oil, red wine, kale, broccoli apples, Onion, cherries, berries, and grapefruit and tea	1
2	Flavones	Chrysin, apigenin Rutin, luteolin, and Glucosidestangeretin	Fruit skins, red wine, buckwheat, red pepper, tomato skin, Parsley, Thyme	2-5
3	Flavonones	Naringin,naringenin, taxifolin, and hesperidin	Citrus fruits, grapefruits, lemons, and oranges	6-7
4	Flavanol	Catechin, epicatechin, epigallocatechin, glausan-3-epicatechin, proanthocyanidins	Apple, tea	1
5	Anthocyanidins	Apigenidin, cyaniding, delphinidin, pelargonidin, malvidin	Cherries, easberry, strawberry, and Grapes	1,5
6	Isoflavones	Genistein, daidzein	Soya beans, Legumes	8, 9

TABLE 2 : FEW COMMON MEDICINAL PLANTS RICH IN FLAVONOIDS

Plant	Flavonoids	References
Aloe Vera	Lucteolin	10
Bacopa Moneirra	Luteolin	10
Acalypha Indica	Kaempferol	10
Azadirachta indica	Quercetin	11
Betula pendula	Quercetin	12
Butea monospermea	Genistein	13

Oroxylum indicum	Chrysin	16
Cannabis sativa	Quercetin	11
Mimosa pudica	Isoquercetin	16
Clitoria ternatea	Kaempferol-3-neohesperidoside	15
Brysonima crassa	Catechin (+)-	14
Pongamia pinnata	Pongaflavonol	17

Plant Sources of Flavonoids:

Flavonoids can be found in numerous beverages and foods, like beer, wine, and tea, but vegetables, fruits, flowers, and seeds are the sources with the maximum quantities of natural flavonoids [19]. Flavonols that comprise, for example, quercetin, kaempferol, isorhamnetin, fisetin, and myricetin are abundant in green fruits, leaves, and grains [20,21]. Flavones are among the most important flavonoids and are represented by lute-olin, isosinensetin, apigenin, sinensetin, nobiletin, galangin, tangeretin, and chrysin [20]. These compounds can be mainly found in leaves, flowers, and fruits as glu-cosides of luteolin, apigenin, and diosmetin [21]. Flavanones, also known as dihydroflavones, are an important class of flavonoids usually found in citrus fruits. Anthocyanins are the flavonoids responsible for the red, blue, purple, and orange color of several leaves, flowers, and fruits.

This class of compounds is usually present as glycosides of anthocyanidins, such as cyanidin, pelargonidin, delphinidin, peonidin, petunidin, and malvidin [18,22]. Natural flavonoids can be taken out and used in the food industry instead of synthetic compounds to increase food quality. In recent years, the limitation imposed on the use of some synthetic antioxidants, such as the case of butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and propyl gallate, improved the interest in natural flavonoids commonly due to their capacity to check oxidative degradation of lipids, increase the quality and nutritional value of food, and diminish toxicity [23]

Biological Activities of Flavonoids:

1. Antioxidant Activity:

Flavonoids have many biochemical properties, but the best described property of nearly every group of flavonoids is their capacity to act as antioxidants. It is depending upon the arrangement of functional groups in the nuclear structure. The benefit of antioxidant activity assay was to simulate cellular biological processes which include uptake, distribution, and metabolism. Antioxidant Activity assay was focused to quantify the capacity of the analyte to prevent the formation of DCF by AAPH-induced peroxyl free radical in HepG2 cells. Other techniques commonly used for measuring chemical antioxidant activity, this assay has been developed a more biologically representative protocol. Antioxidants can act at the cell membrane to break peroxyl radical chain reactions at the cell surface or can be up taken by the cell and react with ROS intracellularly [24]. The efficiencies of membrane binding and cell uptake are two major factors influencing the antioxidant activity of the tested chemical. It is significant that although the antioxidant Activity assay signifies a reliable and cost-effective approach to estimate the potential biological activity of dietary flavonoids on cellular level and conveys significant reference value to the functional food development.

Flavonoids are one of the best phytochemicals that act as antioxidants and thus inhibit the factors of disease-causing. Antioxidant activity depends on the arrangement of functional groups in the flavone nucleus. Flavonoids are also protecting the cell

membranes which are damaged due to lipid peroxidation. Thus, the flavonoids contribute as antioxidants, in the prevention of many diseases caused due to oxidative stress. The antioxidant mechanisms of flavonoids can be by the direct scavenging of ROS, spontaneity of ROS development through the chelation of trace elements (e.g., quercetin has iron-chelating and iron-stabilizing properties).

II. Anti-Inflammatory Activity

Inflammation is a composite biological response of body tissues to harmful stimuli, such as tissue injury, damaged cells, pathogen infection and chemical irritation. It is a defensive response including blood vessels, immune cells, and molecular mediators. Inflammation happens in response to several causes, such as a chemical exposure, tissue physical injury or trauma, and microbial infection. Usually, the inflammation is rapid process and self-limiting, but in some cases, prolonged inflammation periods contribute to the progress of several chronic or degenerative disorders like cardiovascular, cancer, diabetes and neurodegenerative diseases, and obesity [25]. Flavonoids also prevent phosphodiesterases present in cell activation.

III. Antiviral Activity

Since the 1940s and numerous information specify that naturally occurring flavonoids show a significant anti-viral activity. They are useful in the inhibition of several enzymes related with the lifecycle of viruses. Flavon-3-ol was found to be more effective than flavones and flavonones in selective inhibition of HIV-1 & HIV-2 and similar immune deficiency virus triggering infections. The different study shows the quercetin, hesperetin, and naringin also possess anti-dengue activity virus causing infections. The study shows that quercetin, hesperetin, and naringin also have anti-dengue activity.

IV. Anticancer Activity

Because of the anti-inflammatory properties, flavonoids also have a significant influence on cancer expansion. Flavonoids have been reported for their probable applications in the anti-cancer therapies. They have been testified to interfere in the beginning, raise, and development of cancer by modulating different enzymes and receptors in signal transduction pathways related to cellular proliferation, differentiation, apoptosis, Inflammation, Flavonoids significantly impact the cascade of immunological proceedings related with the growth and development of cancer. These compounds utilize their activity by inactivating carcinogen, inducing apoptosis, triggering cell cycle arrest, and inhibiting angiogenesis [27].

V. Antibacterial Action

Flavonoids may exert numerous mechanisms of accomplishment against bacteria. They can obstruct with lipid bilayers by inducing bacterial membrane disruption and inhibit some progressions such as, synthesis of cell envelope, biofilm formation, synthesis of nucleic acid, electron transport chain, and synthesis of ATP. The diverse study indicates that the flavonoid-rich plant extracts from diverse plants possess antibacterial activity.

The approach of antimicrobial action may be associated to their capability to cell envelope, enzymes, and microbial adhesins transport proteins.

VI. Antifungal Action

There are numerous antifungal mechanisms employed by flavonoids, such as plasma membrane disruption, cell division, induction of several mitochondrial dysfunctions, and inhibition of cell wall formation, and RNA and protein synthesis [30]. Some isoflavones, such as glabridin, can inhibit the production of the main

components of fungi cell walls, β-glucans, and chitin [31]. Apigenin interferes with the cell cycle, while naringenin, myricetin, quercetin, luteolin, kaempferol and genistein inhibit DNA, RNA, and protein synthesis [32].

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