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ARTICLE

PHOTOPROTECTIVE ACTIVITY OF FLAVONOIDS: A REVIEW

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Abstract:

In the recent years, there has been a high rise in the magnitude of ultraviolet light reaching the earth surface due to the fact that stratospheric ozone is being depleted at a fast rate, which in turn has led to increased cases of skin cancer and other skin disorders. UVC radiation is extremely detrimental to the skin even in a small amount but fortunately it is absorbed by the molecular oxygen and the ozone layer. UVB radiation makes 4-5% of the UV light and is 1000 times more capable of causing sunburn than UVA. UVA can cause instant tanning effect and chronic exposure to UVA can cause detrimental effects to the underlying structures of the skin and cause premature photo-aging. Flavonoids are natural secondary plant phenolics which are sub-divided into 6 sub-classes. They possess anti-oxidant and chelating properties. The biochemical activities of flavonoids and their metabolites depend on their chemical structure and the relative orientation of various moieties on the molecule. Natural flavonoids are one of the many candidates as a defence barrier against the UV damage due to their UV absorbing properties, chelating properties, anti-oxidant properties and their ability to modulate several signalling pathways. However these substances must denote their safety in inclusion to its efficacy as a photoprotective agent.

Keywords: photoprotective, flavonoids

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Introduction:

Sunlight comprises of electromagnetic radiation of various wavelengths which include wavelengths from UV to visible range. In the recent years, there has been a rise in the magnitude of ultraviolet light reaching the earth surface due to the fact that stratospheric ozone is being depleted at a fast rate, which in turn has led to increased cases of skin cancer and other skin disorders. Solar UV radiation is grouped in 3 classes based on their wavelengths:

1. UV-A (320-400 nm)
2. UV-B (290-320 nm)
3. UV-C (200-290 nm)

UV-C radiation is filtered by the ozone layer whereas UV-A radiation penetrates deeper into the layers of the skin and is barely able to stimulate the DNA molecule directly and exerts its mutagenic and carcinogenic action through oxidative stress. If UVB is directly absorbed it leads to direct disruption of DNA, which produces photoproducts like cyclobutane pyrimidine dimers (CPD) and pyrimidine-pyrimidone dimers, which if remained un-repaired may commence photo-carcinogenesis. Thus protection against the radiations is vital for thwarting the damage. Dermatological preparations like sunscreens are available for providing a defense barrier to the skin. These preparations contain organic or inorganic filters which act as a medium for filtering the radiations. [1,8]

Consequences of UV radiation on the skin:

UVC is extremely deleterious to the skin even in a little amount but fortunately it is taken up by the molecular oxygen and the ozone layer.

UVB radiation makes 4-5% of the UV light and is 1000 times more capable of causing sunburn than UVA. It induces the formation of pyrimidine photoproducts, induction of ornithine decarboxylase activity, photoaging, and photo-carcinogenesis, and is responsible for causing skin cancer due to its ability to penetrate into deeper layers of the skin.

In comparison to UVB, UVA can cause prompt tanning effect, and chronic exposure to UVA can cause detrimental effects to the underlying structures of the skin and cause premature photoaging, causing sagging of the skin rather than wrinkling. It can also damage the DNA structures and weaken the immune system and is also responsible for malignant melanoma. [2,7,9]

Flavonoids:

Flavonoids are natural secondary plant phenolics which are divided into 6 sub-classes namely:

- Flavanols
- Flavonols
- Flavones
- Iso-flavones
- Flavanolols
- Anthocyanidins

These flavonoids possess anti-oxidant and chelating properties. They are also responsible for giving appealing look to flowers, fruits, leaves, etc. Apart from fruits, vegetables flavonoids are present in variety of other substances like tea, beer, wine (particularly red wine), grains, nuts and seeds. (Table 1) [4,6]

Table-1 Sources of flavonoids

Flavonoid sub- class	**Major food sources**
Flavonols	Tea, onion, apple, kale, red wine, berry, cherry, broccoli, carrots, tomato, lettuce, nuts, walnut, ginger
Flavones	Thymes, parsley, citrus peels
Flavanones	Citrus peels
Isoflavones	Red clover, peanuts, chickpeas, alfalfa sprouts, soy, other legumes
Catechins	Apple, grape wine, lentils, tea
Anthocyanidins	Cherry, grape, bilberry, cranberry, peach, plum, hawthorn, loganberry, cocoa

Chemistry of flavonoids:

The biochemical activities of flavonoids and their metabolites depend on their chemical structure and the relative orientation of various moieties on the molecule.

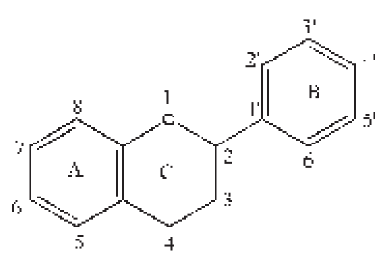

Figure-1 Basic skeleton of flavonoids

The three phenolic rings are designated as the A, B, and C (or pyrane) rings, the flavonoid aglycone consists of a benzene ring (A) condensed with a six membered ring (C) which in the 2-position carries a phenyl ring (B) as a substituent. Six-membered ring condensed with the benzene ring can be either a pyrone or its dihydro derivative.

The position of the benzenoid substituent divides the flavonoid class into either flavonoids at 2nd position or iso-flavonoids at 3rd position. Flavonols differ from flavonones by the presence of hydroxyl group at 3rd position and C2-C3 double bonds. Flavonoids are often hydroxylated at position 3, 5, 7, 2′, 3′, 4′, 5′. Methyl ethers and acetyl esters of the alcohol group are known to occur in nature. [3]

Classification:

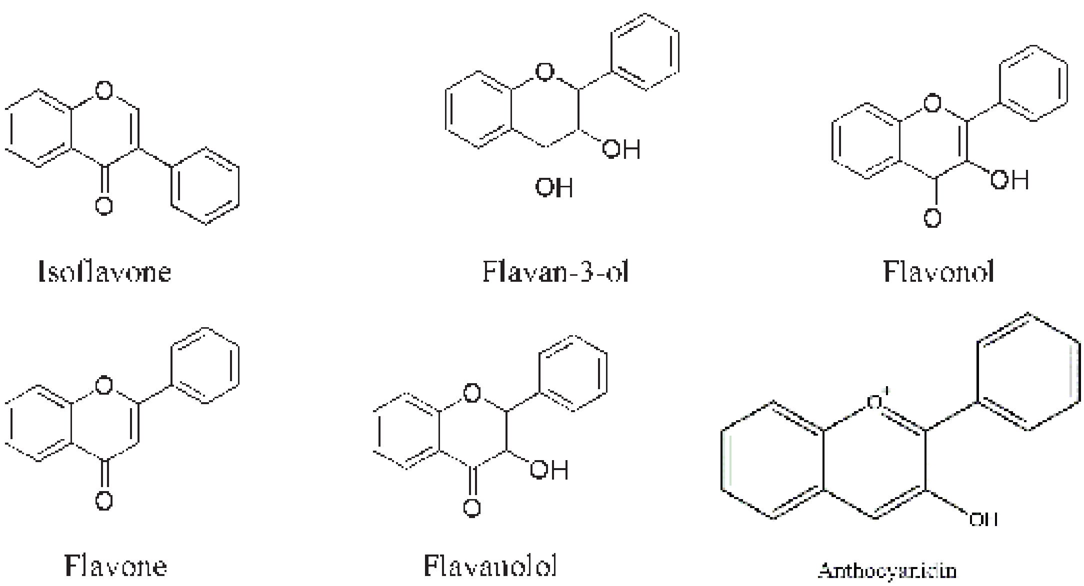

Figure-2 Basic chemical structures of classes of flavonoids

1. Flavones: The prime flavones available in nature are Apigenin and Chrysin. Apigenin is widely distributed in parsley, rosemary, apple, cherries, beans, broccoli etc. When apigenin applied topically it results in significant inhibition of UV induced activity of ornithine decarboxylase which in turn results in reduction in tumor incidence activity and an increased survival rate from tumors. [5]

2. Flavonols: The prime flavonols available in nature are Kaempferol, Myricetin, Isorhamnetin and

Quercetin. Quercetin is widely distributed in apples, grapes, kale, lettuce, red wine, propolis from bee hives etc. The ultraviolet energy absorbed by this flavonol is either dissipated as heat or light. When applied topically it has shown to be successful in avoiding UVC instigated liposomal peroxidation. Topical formulations when applied to animals shows significant inhibition of skin damage due to UVB. [5]

3. Flavanolols: Well-known flavanonol available in nature are Silymarins. They are obtained from seeds of the *Silybum marianum*. Silymarins prevents UV instigated carcinogenesis via prevention of UVB radiation produced oxidative stress, also suppresses the immune system. In normal human epidermal keratinocytes (NHEK), treatment done with silymarins proved to be effective in reduction or rectifying the volume of damage done due to UVB radiation. [5, 9]

4. Isoflavones: Iso-flavones are found most commonly in legumes, including black beans, chick peas, green beans, soybeans. Major isoflavones found in nature are Genistein, Equol, Diadzein. Genistein a soybean isoflavone which is a formidable anti-oxidant and is specific inhibitor of protein tyrosine kinase and phytoestrogen. Genistein also protects UVB-induced senescence-like characteristics in human dermal fibroblasts. [4,5]

5. Flavanols: Flavanols are often commonly called catechins. The biggest source of catechins in the human diet was found to be from various types of teas like oolong tea, black tea and green tea. Epigallocatethin gallate (EGCG) is the most abundant catechin found in green tea. In animal study, topical treatment and oral feeding to the animals were done using green tea polyphenolics or prior to the exposure to the UV radiation and the treatment was found to protect against UVB induced carcinogenesis and immunosuppression. [4]

6. Anthocyanidins: Anthocyanidins are the principal agents responsible for giving colors to many flowers, vegetables, fruits and cereal grains. They absorb visible as well as UV radiation and are operative antioxidants and scavengers of ROS. Cyanidin-3-glucoside is the most common anthocyanin found in nature. Pre-treating the cells with this glucoside clearly inhibited the adverse effects of UVB. The complex provided operative barrier against detrimental consequences of photo-oxidation to skin when applied topically immediately after skin exposure to UV radiations. [5,10]

Conclusion:

Many synthetic sunscreens are available in the market have constraints due to their probability to cause photo-reaction and their harmful reaction on skin. Natural compounds may work in various ways such as by stimulating the immune response and inducing gene suppression. Natural flavonoids are one of the many candidates for the protection of skin against the UV damage due to their UV absorbing properties, chelating properties, anti-oxidant properties and their ability to modulate several signalling pathways. However these new agents must be evaluated for their safety in addition to their efficacy to develop them as novel photoprotective agents.

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