

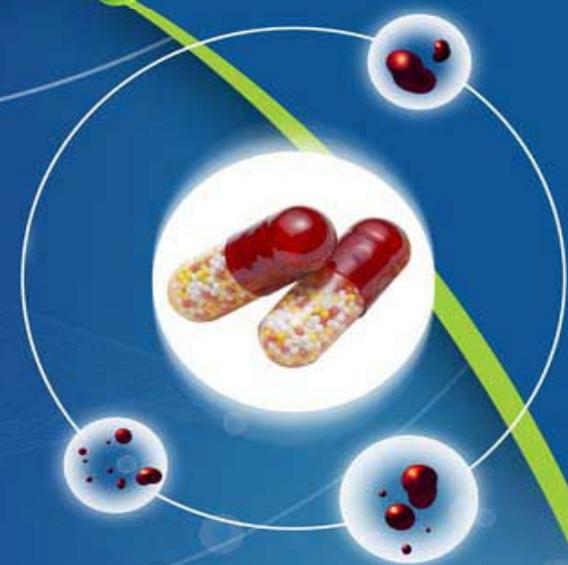


ISSN : 2320 4850

BI
MONTHLY

Asian Journal of Pharmaceutical Research And Development

(An International Peer Reviewed
Journal of Pharmaceutical
Research and Development)



A
J
P
R
D

Volume - 01

Issue - 02

MAR-APR 2013

website: www.ajprd.com
editor@ajprd.com



Review Article

A REVIEW ON FLAVONOIDS**Hitesh Kumar*, Ravi Singh Chauhan, M.P.Kabra, S.S. Bhandari.**

Department of Pharmaceutics, Kota College of Pharmacy, Kota (Raj.) India

Received: 07 February 2013,

Revised and Accepted: 05 March 2013

ABSTRACT

Flavonoids are low molecular weight polyphenolic compound present in all vascular plants. They are primary recognised as the pigments responsible for autumnal burst hues and yellow, orange and red shades in flowers and fruits. Flavonoids have been show to possess a variety of biological activity at non-toxic concentration in living organism compelling data from various in vivo and invitro experimental. Several epidemiological studies have demonstrated the beneficial effect of dietary Flavonoids. They are ubiquitous in photosynthesis cells and are commonly found in fruits, nuts, seeds, tea, wine and honey. The mechanism of their cardio productive effect have been thought to stem from their free radical Scavenging antioxidant, antithrombotic, antiapoptotic and antihypertensive effect.

Keywords: Flavonoids, Antifungal, Antibacterial, Antihypertensive, Cardio productive.

INTRODUCTION

Flavonoids are a group of water-soluble substances that occur mainly as natural pigments in plants and flowers. It occurs as natural dyes and in citrus fruit and found in the white portion of the peel. It is a compounds found in fruits, vegetables, and certain beverages that have diverse beneficial biochemical and antioxidant effects. [1]Flavanoids are antioxidants in fruits, vegetables, tea, and wine - plant nutrients that belong to the polyphenol family.

and reds which cannot be attributed to carotenoids (found in carrots). Carotenoids are fat-soluble, while flavanoids are predominantly water-soluble. Flavanoids are found in more concentrated forms in red wine, green tea, and soy products, as well as many common fruits and veggies. Flavonoids are most commonly known for their antioxidant activity. However, it is now known that the health benefits they provide against cancer and heart disease are the result of other mechanisms. The antioxidant activity of flavonoids depends on their molecular structure, and structural characteristics of certain flavonoids found in hops and beer confer surprisingly potent antioxidant activity exceeding that of red wine, tea, or soy. [2]

Flavonoids also called Vitamin P are not strictly speaking a vitamin. The term flavonoids refer to many different ingredients eg.hesperin, hesperidin, eriodictyol, quercetin, rutin etc. This

Correspondence Author*Hitesh Kumar**Department of Pharmacology,
Kota College of Pharmacy, Rajasthan, IndiaEmail: hiteshsiyana@gmail.com

+91-8430827154, +91-8302686102

Flavanoids are responsible for brilliant blues, purples, and greens, as well as yellows, oranges,

nutrient cannot be manufactured by the body and must be supplied in the diet. [3]

Flavonoids refer to phytochemical compounds in plants that are absorbed by the body but then rapidly excreted as if they were a foreign substance, but without causing damage. Flavonoids do not function like conventional hydrogen-donating antioxidants, but have an interesting hodgepodge of effects inside the cells. Flavonoids are like dust mops for toxins that get thrown out along with the dust that they collect. Flavonoids are present in our food and their role in the prevention of heart disease is well documented. They are anticarcinogenic, that is, they destroy and inhibit the growth of cancer cells. This cytotoxic quality the actual ability of potent flavonoids to kill cancer cells – is one of the most effective weapons in our antibacterial arsenal today.

Flavonoids may help provide protection against cancer, aging, atherosclerosis, ischemic injury, inflammation and neurodegenerative diseases (Parkinson's and Alzheimer's) diseases by contributing, along with antioxidant vitamins and enzymes, to the total antioxidant defence system of the human body. Epidemiological studies have shown that flavonoid intake is inversely related to mortality from coronary heart disease and to the incidence of heart attacks. [4, 5]

CLASSIFICATION & BIOSYNTHESIS

Classification

Flavonoid (or bioflavonoid) refers to a class of plant secondary metabolites.

According to the IUPAC nomenclature, they can be classified into:

- Flavonoids, derived from 2-phenylchromen-4-one (2-phenyl-1,4-benzopyrone) structure
- Isoflavonoids, derived from 3-phenylchromen-4-one (3-phenyl-1,4-benzopyrone) structure
- Neoflavonoids, derived from 4-phenylcoumarine (4-phenyl-1, 2-benzopyrone) structure.

Flavonoids 2-phenylchromen-4-one (2-phenyl-1, 4-benzopyrone):

Flavonoids belong to a group of natural substances with variable phenolic structures and are found in fruit, vegetables, grains, bark, roots, stems, flowers, tea, and wine. These natural products were known for their beneficial effects on health long before flavonoids were isolated as the effective compounds. More than 4000 varieties of flavonoids have been identified, many of which are responsible for the attractive colors of flowers, fruit, and leaves.

The association between flavonoid intake and the long-term effects on mortality was studied subsequently and it was suggested that flavonoid intake is inversely correlated with mortality due to coronary heart disease. [6] Over 5000 naturally occurring flavonoids have been characterized from various plants. They have been classified according to their chemical structure, and are usually subdivided into the following subgroups.

Flavonols -3-hydroxy-2-phenylchromen-4-one:

These compounds are very widespread in higher plants where they occur usually as O-glycosides in the leaves and outer parts of the plant, while only trace amounts are found in parts of the plant below the soil surface. There are far fewer detailed quantitative studies on fruit flavonols than on anthocyanins particularly in relation to genetic and environmental variability. Nevertheless, over 200 flavonol glycosides have been identified in plants, although only four of these, quercetin, kaempferol, myricetin and isorhamnetin, are common in fruits.

Glycosylation occurs preferentially at the 3-hydroxyl group and the predominant types in fruits are 3-O-monoglycosides in the following order: 3-glucosides > 3-galactosides > 3-rhamnosides > 3-glucuronides. The only diglycosides observed with any frequency in fruit are the 3-rutinosides of quercetin and kaempferol. Complete characterization of a flavonol monoglycoside requires a knowledge of whether the sugar–glycone bond is an a or b

linkage and whether the sugar is in furanose or pyranose form. In general, it has been found that sugars with a d-configuration, namely glucose, galactose, xylose and glucuronic acid, are usually linked to the aglycone by β bonds whilst α linkages occur to l-arabinose and l-rhamnose.

This is illustrated by the characteristic flavonoid glycosides of apple, which include quercetin α -l-rabinofuranoside, β -d-galactopyranoside, β -d-glucopyranoside, α -l-rhamnopyranoside and β -d-xylopyranoside. The occurrence of flavones and flavonols has been thoroughly reviewed. The flavonol content of Rosaceae fruits, e.g., strawberry, raspberry and blackberry is dominated by quercetin and kaempferol and their glycosides.

Flavones -2-phenylchromen-4-one:

These compounds are not common in fruits and are never predominant. Citrus is again a special case containing a number of polymethoxylated flavones as minor flavonoids. Some of these, e.g., nobiletin and sinensetin (sweet orange peel) and tangeretin (tangerine oil).

Flavanone -2, 3-dihydro-2-phenylchromen-4-one:

In most of the plant kingdom, flavanones occur in small amounts compared with other flavonoids, yet they are the predominant flavonoid in citrus. In terms of its flavonoid composition, citrus is exceptional, some citrus flavanones being found nowhere else. Four aglycones are common, namely naringenin, eriodictyol, isosakuranetin and hesperetin. Further, citrus flavanones usually occur as glycosides whereas in other plants flavanones are seldom found in glycosidic form. Glycosylation occurs at position 7 either by rutinose or neohesperidose, disaccharides formed by a glucose and rhamnose molecule differing only in the type of linkage.

This has formed the basis for classification of citrus. Thus, most commercial citrus cultivars contain only the non-bitter rutosides whereas

sour orange and pummelo have only bitter flavanone neohesperidosides. Further distinction is possible on the basis of the predominant flavanone; in the case of sweet oranges, mandarins, lemons and citrons this is hesperidin, whereas naringin is the major flavanone in grapefruit and pummelo. It is now accepted that naringin is absent from sweet orange varieties. Nevertheless, the evidence is contradictory and a recent publication reported concentration data for naringin in a number of sweet orange varieties. The latter data were obtained by HPLC using coulometric array detection. [4, 5]

Flavanonol-3-hydroxy-2, 3-dihydro-2-phenylchromen-4-one:

Flavonoids are either not widely distributed in fruits or are present as minor components of the total flavonoid content. This section is intended to provide an indication of flavonoid diversity rather than a comprehensive treatise on flavonoid distribution. Nevertheless, the flavanols, particularly dihydrokaempferol and chalcones, should be noted. [7]

Bioflavonoids -3-phenylchromen-4-one (3-phenyl-1, 4-benzopyrone):

Bioflavonoids are also referred to as vitamin P, a name that nutrition scientists object to because it has not been proved that they are essential to human nutrition and health. Many researchers are studying bioflavonoids and many reports have been given about their possible functions. Some researchers believe that bioflavonoids help maintain capillaries. Capillaries are microscopic blood vessels that allow the oxygen, hormones, nutrients, and antibodies to pass from the body's bloodstream to individual cells.

Bioflavonoids also in recent studies have been shown to help the blood clot, this alone can be helpful in treating phlebitis and other clotting disorders. Many bioflavonoids prevent the cellular damage caused by free radicals; these are unstable molecules that are formed when the body burns oxygen. Some bioflavonoids are

used as food preservatives to prevent fats from oxidation. Some reports show bioflavonoids are useful in enhancing the antioxidant action of certain nutrients. Bioflavonoids and vitamin C are found in many of the same foods and the body metabolizes both of these in the same manner.

Since they work so close together numerous reports have stated that vitamin C and many bioflavonoids need each other to produce the effects that they have on the immune system. All these uses of bioflavonoids are the main reason that they are accredited with the use they have at preventing many heart diseases. Many laboratory studies show how bioflavonoids stop or slow the growth of malignant cells, they also help protect against cancer-causing substances invading the heart and blood cells. Bioflavonoids also act as natural antibiotics for the human body. Some bioflavonoids destroy certain bacteria that are found in foods; this prevents food spoilage and protects humans from food-borne infections. [8]

The major classes of Bioflavonoids

- Proanthocyanidins - (or PCO for short), which included both pycnogenol, derived from the bark of the French maritime pine tree, and grape seed extract, derived from grapes
- Green tea extract - derived from the tea plant *Camellia sinensis*, prepared by preventing oxidation that could inactivate the bioflavonoids. While green tea extract also contains PCO, it also contains other bioflavonoids such as catechin, epicatechin, and gallate compounds
- Quercetin - a bioflavonoid with potent anti-inflammatory action and protective action in diabetes
- Citrus bioflavonoids - high in compounds called isoflavones, such as hesperidin and rutin, that are formed by the addition of sugars to quercetin
- Soy bioflavonoids - Because each of these classes of bioflavonoids has its own unique

set of compounds, each category also has its own unique benefits. This is a complex topic and is appropriately dealt with by considering each major category separately. In future articles we will describe these classes of bioflavonoids and discuss their health benefits.

Sources of Bioflavonoids

Many foods are excellent sources of bioflavonoid compounds and should be included in the diet. In fact, the recommendation of eating a diet rich in fruits and vegetables is partly because of the health-promoting effects of these compounds. Excellent sources of bioflavonoids are citrus fruits, a wide range of berries, tomatoes, legumes, onions, parsley, green tea (not black tea), and grape-derived products such as grape juice and red wine (but not white wine). While it is quite possible to obtain an excellent intake of bioflavonoids with a well balance diet rich in appropriate fruits, vegetables, green tea, and grape products, the typical American diet is lacking in consistent intake of these very important dietary components. Of course, the same individuals who have poor dietary habits are also not likely to take supplements to further enhance their intake of bioflavonoid. [12]

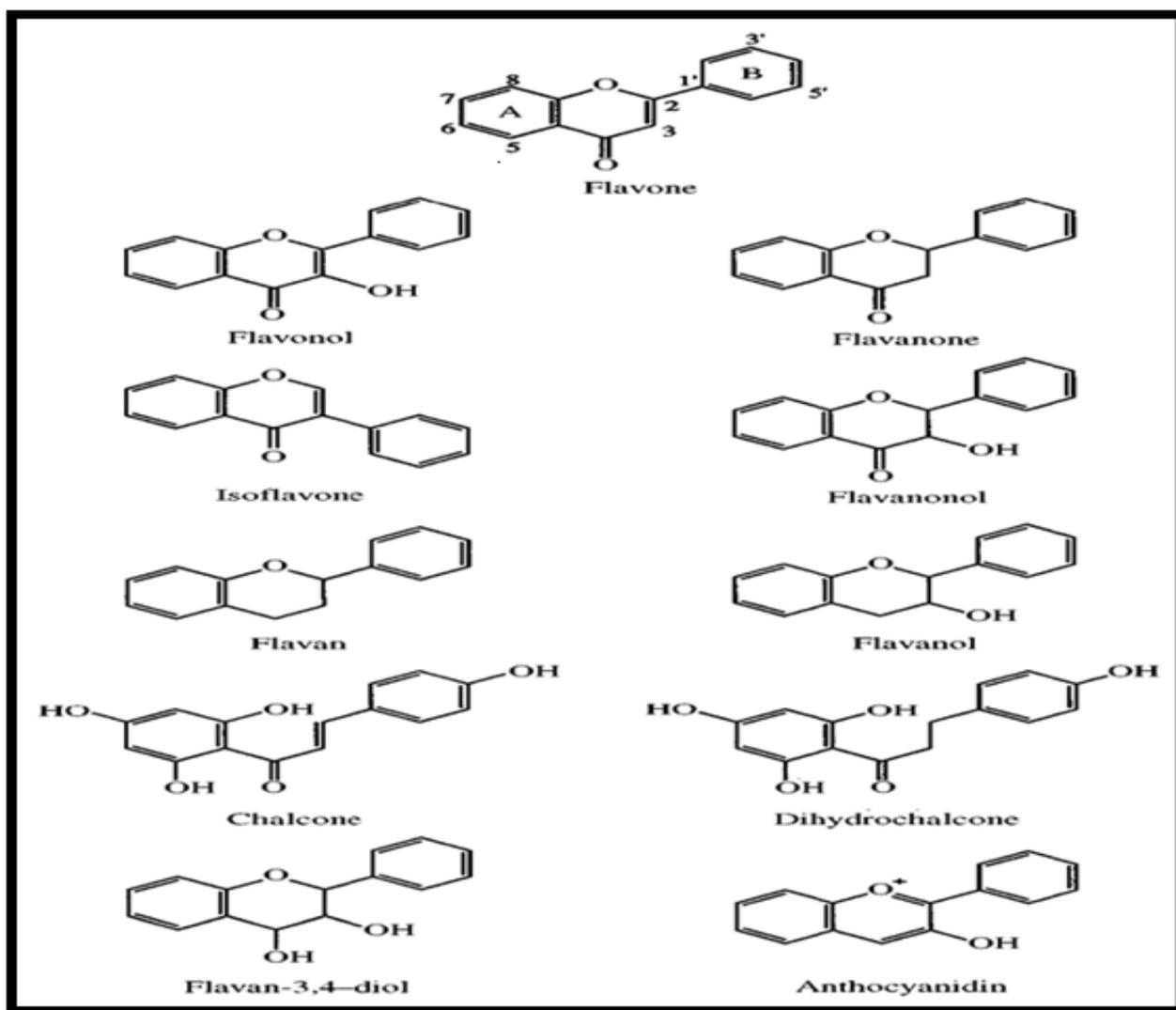
Structure of Flavonoids:

Flavonoids occur as aglycones, glycosides and methylated derivatives. The flavonoid aglycone consists of a benzene ring condensed with a six membered ring in the 2-position carries a phenyl ring as a substituent. Six-member ring condensed with the benzene ring is either a pyrone (flavonols and flavonones) or its dihydroderivative (flavanols and flavanones). The position of the benzenoid substituent divides the flavonoid class into flavonoids (2-position) and isoflavonoids (3-position). Flavonols differ from flavonones by hydroxyl group the 3-position and a C2-C3 double bonds.[9]

Common Structure of Flavonoids:

Flavonols differ from flavonones by hydroxyl group the 3-position and a C₂-C₃ double bonds. Flavonoids are often hydroxylated in position 3,5,7,2',3',4',5'. Methylethers and acetylestere of

the alcohol group are known to occur in nature. When glycosides are formed, the glycosidic linkage is normally located in positions 3 or 7 and the arbohydrate can be L-rhamnose, D-glucose, glucor-hamnose, galactose or arabinose. [10]

Fig: Nomenclature of the classes of flavonoids

Nomenclature of the subclasses of flavonoids based on the position of their substituents:

Flavonols

Kaempferol	OH	OH	OH	H	H	OH	H
Morin	OH	OH	OH	OH	H	OH	H
Rutin	O-R1	OH	OH	H	OH	OH	H
Myricetin	OH	OH	OH	H	OH	OH	OH
Quercetin	OH	OH	OH	H	OH	OH	H

Flavonones

Hesperitin	H	OH	OH	H	OH	O-Me	H
Naringin	H	OH	O-R	H	H	OH	H
Naringenin	H	OH	OH	H	H	OH	H
Eriodictyol	H	OH	OH	H	OH	OH	H
Hesperidin	H	OH	O-Me	H	OH	O-Me	H

Flavones

Rpofolin	H	OH	O-R	H	H	OH	H
Apigenin	H	OH	OH	H	H	OH	H
Tangeretin	H	O-Me	O-Me	H	H	O-Me	H

Flavone

Baicalein	H	OH	OH	H	H	H	H
Luteolin	H	OH	OH	H	OH	OH	H
Techtochrysin	H	OH	O-Me	H	H	H	H
Diosmetin	H	OH	OH	H	OH	O-Me	H
Diosmin	H	OH	O-R1	H	OH	O-Me	H

Flavanolols

Silibinin	OH	OH	OH	H	H	O-L-O	H
Silymarin	OH	OH	OH	H	OH	OH	H
Taxifolin	OH	OH	OH	H	OH	OH	H
Pinobanksin	OH	OH	OH	H	H	H	H

-O-Me = Methoxy -O-Glu = Glucosyl -O-R' = Alkoxy -O-L-O = Sene

BIOSYNTHESIS

Flavonoids are synthesized by the phenylpropanoid metabolic pathway in which the amino acid phenylalanine is used to produce 4-coumaroyl-CoA. This can be combined with malonyl-CoA to yield the true backbone of flavonoids, a group of compounds called chalcones, which contain two phenyl rings. Conjugate ring-closure of chalcones results in the familiar form of flavonoids, the three-ringed structure of a flavone. The metabolic pathway continues through a series of enzymatic modifications to yield flavanones → dihydroflavonols → anthocyanins. Along this pathway, many products can be formed, including the flavonols, flavan-3-ols, proanthocyanidins (tannins) and a host of other polyphenolics. An understanding of the essential features of flavonoid biosynthesis is important to understanding their diversity and to the design of sound analytical procedures.

Flavonoid biosynthesis involves the interaction of at least five different pathways, namely the glycolytic pathway, the pentose phosphate pathway, the shikimate pathway that synthesizes phenylalanine, the general phenylpropanoid metabolism that produces activated cinnamic acid derivatives (4-coumaroyl-CoA) and also the plant structural component lignin and finally the diverse specific flavonoid pathways. The last three should be viewed as segments of a single unit, that of aromatic metabolism. Enzymes responsible for the formation of different flavonoid classes and for structural modifications, such as hydroxylation, methylation, glycosylation and acylation, have been identified. Moreover, amino acid and nucleic acid sequences are now available for several of these enzymes.

ACTION OF FLAVONOIDS

Pharmacological action

CNS activity

Synthetic flavonoids like 6-bromoflavone and 6-bromo-3'-nitro-flavones were shown to displace

flumazenil binding to membranes from rat cerebellum but not from spinal cord, indicating selectivity for the BZ Omega receptor subtype, but latter was very potent than 6 bromoflavone. Results from two conflict tests in rats showed that these synthetic flavonoids possess anxiolytic like properties similar or superior to that of diazepam.

Cardiotonic activity

Flavonoids have been reported to have action on the heart. The unsubstituted parent flavone exerts coronary dilatory activity and was commercially available under the name 'Chromocor' and its combination with routine and isoquercetin was also available with brand name 'flavoce', useful in the treatment of atherosclerosis. 3-methyl quercetin has positive chronotropic effect on guinea pig right atrium and antiarrhythmic effect on left atrium. In recent report the cardiotoxicity of doxorubicin on the mouse left atrium has been inhibited by flavonoids, 7-mono-hydroxy ethyl rutoside and 3',4'- trihydroxyethylrutoside. The glycosides of luteolin, apigenin and genistein produced antihypertensive activity even more than the reference drug papaverine. Three flavonoids showed vasorelaxant effect in order of potency, luteolin > eriodictyol > naringenin on rat thoracic aorta.

Lipid lowering activity

Oxidative modification of low-density lipoproteins (LDL) by free radicals is an early event in the pathogenesis of atherosclerosis. The rapid uptake of oxidatively modified LDL via a scavenger receptor leads to the formation of foam cells. Oxidized LDL also has a number of other atherogenic properties. A number of mechanisms are likely to contribute to inhibition of LDL oxidation by flavonoids. Flavonoids may directly scavenge some radical species by acting as chainbreaking antioxidants. In addition, they may recycle other chain-breaking antioxidants such as tocopherol by donating a

hydrogen atom to the tocopheryl radical. Transition metals such as iron and copper are important pro-oxidants, and some flavonoids can chelate divalent metal ions, hence preventing free radical formation. [14]

GITactivity

Antiulcer activity

Some recent reports have indicated that many flavonoids possess antiulcerogenic activity. Oral treatment with the ether fraction of the flavonoid extract demonstrated a good level of gastric protection. Mucous content was increased and accompanied by proportionate increase in proteins and hexosamines. Hydroxy ethyl rutosides, gossypin, naringin, naringenin and (+)-Cyanidanol-3 were shown to exhibit anti-ulcer activity. Quercetin, rutin and kaempferol administered intraperitoneally (25- 100 mg/kg) inhibited dose-dependent gastric damage produced by acidified ethanol in rats.

Flavone was inactive while naringin was active at a higher dose (200 mg/kg). Quercetin, kaempferol, morin, myricetin and rutin when tested were found to inhibit the mucosal content of platelet activating factor (P AF) in a dose dependent manner suggesting that the protective role of these substances may be mediated by endogenous PAF. Quercetin, kaempferol, rutin produced an inhibitory effect on intestinal functions, and that their actions are mediated through 2-adrenergic and calcium systems. This result may show the beneficial effects in diarrhea and other intestinal secretions.

Hepatoprotective activity

Many flavonoids have also been found to possess hepato-protective activity. In a study carried out to investigate silymarin, apigenin, quercetin and naringenin as putative therapeutic agents against microcrystin LR- induced hepatotoxicity, silymarin was found to be the most effective one. Rutin and venorutin showed regenerative and hepato-protective effects in experimental cirrhosis. The results of several clinical investigations showed the efficacy and

safety of flavonoids in the treatment of hepato-biliary dysfunction and digestive complaints, such as sensation of fullness, loss of appetite, nausea and abdominal pain. Silymarin normalizes cell phospholipids synthesis without showing any demonstrable effect on undamaged cells where by counteracting fatty liver. Moreover, earlier findings on a hepato-protective effect and the prevention of NSAIDs-induced gastropathy may be confirmed.

Anti-inflammatory activity

A number of flavonoids are reported to possess anti-inflammatory activity. Hesperidin, a citrus flavonoid possesses significant antiinflammatory and analgesic effects. Recently, apigenin, luteolin and quercetin have been reported to exhibit anti-inflammatory activity. Quercetin, gallic acid ethyl ester and some as yet unidentified flavonoids might account for the antinociceptive action reported for the hydroalcoholic extract of *Phyllanthuscaroliniensis*. Treatment with silymarin demonstrated reversal of the carrageenin induced biochemical changes. Detailed biochemical studies to establish mechanism of action of flavonoids have been carried out.

Antineoplastic activity

A number of flavonoids have exhibited antineoplastic activity. quercetin exerted a dose dependent inhibition of cell growth and colony formation. The flavonoids kaempferol, catechin, toxifolin and fisetin also suppressed cell growth. On screening antileukaemic efficacy of 28 naturally occurring and synthetic flavonoids on human promyelocyticleukaemic HL-60 cells, genistein, an isoflavone was found to have strong effect. Genistein is also reported to inhibit in a dose dependent manner the growth of HGC-27 cells derived from human gastric cancer. Of the 14 flavonoids tested against murine and human cancer cell lines, 2',6'-diacetoxy -4,4' -

dimethoxydihydrochalcone was the most potent and showed selectivity for the cell line. Trifolirhizintetraacetate showed greater selectivity for the human cell lines.

Antimicrobial activity

Flavonoids and esters of phenolic acids were investigated for their antibacterial, antifungal and antiviral activities. All samples were active against the fungal and gram-positive bacterial test strains and most showed antiviral activity.

Antibacterial Activity: Antibacterial activity has been displayed by a number of flavonoids. Twenty-five out of one hundred and eighty two flavonoid studies were found to be active against many bacteria. Most of the flavonones having no sugar moiety showed antimicrobial activities where as none of the flavonols and flavonolignans tested showed inhibitory activity on the microorganisms.

Antifungal Activity: Number of flavonoids isolated from peel of tangerine orange, when tested for fungistatic activity towards *Deuterophomatracheiphila* showed promising activity. Chlorflavonin was the first chlorine containing flavonoid type antifungal antibiotic produced by strains of *Aspergillus candidus*.

Antiviral Activity: Flavonoids also displayed antiviral, including anti-HIV activity. It has been found that flavonols are more active than flavones against herpes simplex virus type 1 and the order of importance was galangin>kaempferol>quercetin. Recently, a natural plant flavonoid polymer of molecular weight 2100 Daltons was found to have antiviral activity against two strains of type-1 herpes type simplex, virus, including a thymidine-kinase deficient strain and type -2 herpes simplex virus.

Effects on blood vessels

Quercetin and rutin have been used as effective constituents of several pharmaceuticals used for treatment of capillary fragility and phlebosclerosis. The activities of certain flavonoids in inhibiting capillary permeability and Arthus phenomenon were found to be in the following order,

hesperitin>rutin>quercetin>naringenin>kaempferol>isoquercitol. It has been suggested that flavonoids, which contain free hydroxyl groups at 3, 3' and 4' positions exert beneficial physiological effects on capillaries.

Patuletin reduced the capillary permeability and was also reported to have antispasmodic and hypotensive effects.

Effect on heat shock proteins

Heat shock proteins (HSP) have been recognized against physiological stress such as heat shock, heavy metals and glucose starvation. Recent progress has revealed the role of HSPs in various diseases. HSP27 has been shown to be involved in the acquired resistance of tumour cells, hyperthermic and chemotherapeutic treatment. Aberrant expression of HSP could cause various autoimmune diseases.

Antioxidant activity:

Free radical production in animal cells can either be accidental or deliberate. With the increasing acceptance of free radicals as common place and important biochemical intermediates, they have been implicated in a large number of human diseases. Quercetin, kaempferol, morin, myricetin and rutin by acting as antioxidants exhibited several beneficial effects, such as antiinflammatory, antiallergic, antiviral as well as an anticancer activity.

They have also been suggested to play a protective role in liver diseases, cataracts, and cardiovascular diseases. Stabilization of meat lipids with flavonoids has been studied and morin, myricetin, kaempferol and quercetin at a level of 200 ppm were found to be most effective. Induction period of lipid oxidation in canola oil was delayed with the flavonoid myricetin by upto fifteen days. Morin, myricetin, kaempferol and quercetin have also been suggested as stabilizers for fish oil as an alternative to synthetic antioxidants [11, 13].

INTERACTION & TOXICITY

Interactions

Certain medicines interact with flavonoids: Some interactions may increase the need for flavonoids. Other interactions may be negative.

Interaction with acyclovir

The flavonoids quercetin, quercitrin, and apigenin enhanced the antiviral activity of acyclovir in test tube studies. Controlled research is needed to determine whether taking quercetin or other flavonoid supplements would increase the effectiveness of acyclovir in humans. [15]

Toxicity

A team of University of California Berkeley (UC Berkeley) scientists led by C.F. Skibola and M.T. Smith has found that high concentrations of flavonoids in supplements sold at health stores actually may promote cancer formation. In a study of the impact of flavonoid intake on the cell, scientists found that excessively high levels of flavonoids in the body can damage the chromosomes and DNA in cells, leaving them more susceptible to cancer.

When consumed in excessive quantities of flavonoids act as mutagens and contribute to free radical formation. They can damage DNA, break chromosomes, and act as endocrine disrupters, inhibiting enzymes such as DNA topoisomerase, which could lead to DNA breaks that potentially lead to cancer.

RECENT TRENDS

From the major medical universities and research centers of Italy, Japan, India, Turkey, Russia, China, England, the USA and the Netherlands, have come marvelous reports of bioflavonoid investigation. Following are the abstracts of just a few of the research reports of the flavonoids:-

EnteroVirus

Synthetic flavans with modified chloro-, cyano- and amidino- groups were found to possess powerful antiviral activity, higher than most original compounds studied, and they were found to be effective in the early stages of viral replication.

Coronary Flow

Researchers at the Kohu University, Germany, using the main flavonoids from crataegus species found, it can favorably influence heart rate, left ventricular pressure, velocity of heart muscle contraction and relaxation, and it improves coronary artery blood flow.

Flavonoids as Oxygen Radical Scavengers

Faculty at the Vrije University, Amsterdam, have confirmed research identifying flavonoids as a group of natural occurring compounds that are excellent and potent scavengers of oxygen radicals. This is the primary reason bioflavonoids are therapeutically effective. It is this action that bolsters the immunity and counters aging, heart disease and cancer.

Inhibition of Leukemia Cells Synthesis

The School of Medicine at Loyola University, in Chicago, investigating quercetin, a flavonoid, found it inhibits the DNA synthesis of human leukemia cells. Flavonoids possess analgesic and anti-inflammatory qualities. R. Ficarra et al, researching extracts of Cordia has proven these flavonoids to have significant analgesic, anti-inflammatory, and antiarthritic activity.

Preventing Spinal Cord Injury Damage

The experimental research center at the University of Erciyes, using Ginkgo biloba flavonoids, has shown they significantly decrease malondialdehyde. This is the substance that causes ischemic spinal cord damage following spinal cord injuries.

More Potent Than Vitamin E

Two plant-derived flavonoids, quercetin and cyanidin, were found to have four times the antioxidant potential of vitamin E analogues.

Tumor Prevention

The department of Internal Medicine, at Kanazawa, Japan, has documented the antitumor properties of nine herbal components investigated and has found all to have potent antitumor activity.

Alcohol Abuse

Kering and Vallee, at the Harvard Medicine School have shown the flavonoid Radix pueraric, found in an herb long used in Chinese medicine, to prevent and treat alcohol abuse.

CONCLUSION

REFERENCES

1. Kirtikar K., Basu B., *Indian medical plant*, 1st ed. Delhi: International book Publication, 1995; 499-502
2. <http://www.wikipedia.org/wiki/flavonoids>
3. <http://www.anyvitamins.com/vitamin-p-flavonoids>
4. <http://www.altavista.org/flavonoids/toxicity>
5. <http://www.pharma.com/flavonoids/history>
6. Clinnutr A. J. *American society for clinical nutrient. USA.* 2001. 74; 418-25.
7. Robards K., Antolovich M. *Analytical Critical Review Chemistry of Fruit Bioflavonoids.* NSW Australia. CharlsSturt University Riverina. 1997.122;1-20
8. <http://www.ejirich.net/bioflavonoids/journal>
9. Kokate C.K., Purohit A.P., Gokhale S.B. *Pharmacognosy.* 37ed. Nirali Prakashan. 2007; 231-32.
10. <http://answer.com/topic/flavonoids/structure>
11. Narayana R.K., Reddy S.M., Chaluvadi M.R., Krishana D.R. *Drug Metabolism & Clinical Pharmacokinetic.* University College of Pharmaceutical Science. 2000; 230-238.
12. <http://www.ajcn.org/sources/flavonoids>
13. Narayana R.K. *Indian Journal of Pharmacolgy.* 2001.33; 2-16
14. Nijveldt R.J., Nood E.V., Boelens P.G., Norren K.V., Paul A.M. *Flavonoids A Review of Probable Mechanism of Action & Potential Application.* Netherland. Vrije University Medical Center. 2001; 418
15. <http://www.altavista.org/flavonoids/topic/interaction>.

Flavonoids are antioxidants in fruits, vegetables, tea, and wine - plant nutrients that belong to the polyphenol family. Flavonoids are responsible for brilliant blues, purples, and greens, as well as yellows, oranges, and reds which cannot be attributed to carotenoids (found in carrots).

Flavonoids are most commonly known for their antioxidant activity. However, it is now known that the health benefits they provide against cancer and heart disease are the result of other mechanisms. The antioxidant activity of flavonoids depends on their molecular structure, and structural characteristics of certain flavonoids found in hops and beer confer surprisingly potent antioxidant activity exceeding that of red wine, tea, or soy.

Flavonoids also called Vitamin P are not strictly speaking a vitamin, but for easy classification, we are listing it as a vitamin. The term flavonoids refer to many different ingredients and includes hesperin, hesperidin, eriodictyol, quercetin, rutin etc. This nutrient cannot be manufactured by the body and must be supplied in the diet.