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A REVIEW ON IMPORTANCE AND PHARMACOLOGICAL APPLICATIONS OF FLAVONOIDS

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ABSTRACT

Flavonoids, a class of plant secondary metabolites having a polyphenolic structure, are found in fruits, vegetables, grains, bark, roots, stems, flowers, tea, and wine. They have miscellaneous favorable biochemical and antioxidant effects associated with various diseases such as cancer, Alzheimer's disease (AD), atherosclerosis. Flavonoids are classified into six groups, including flavones, flavonol, flavanone, isoflavone, flavan-3-ol, and anthocyanin, this classification depending on which carbon of the C ring attached to the B ring and the degree of unsaturation and oxidation potential of C ring. The B ring is linked at the position 3 of C ring re called isoflavones. In which the B ring is linked at the position 4 are called neoflavonoids. In this present study give the details about nomenclature, structure, and its biological activities of flavonoids.

KEYWORDS: Flavones, flavonol, flavanone, isoflavone, Applications of flavonoid.

INTRODUCTION

Flavonoids, a class of plant secondary metabolites having a polyphenolic structure, are found in fruits, vegetables, grains, bark, roots, stems, flowers, tea, and wine. They have miscellaneous favourable biochemical and antioxidant effects associated with various diseases such as cancer, Alzheimer's disease (AD), atherosclerosis, etc.Flavonoids are an indispensable component in a variety of nutraceutical, pharmaceutical, medicinal, and cosmetic applications. This is due to their antioxidative, anti inflammatory, anti-mutagenic and anti-carcinogenic properties coupled with their capacity to modulate key cellular enzyme functions. They are also have potent inhibition action several enzymes, such as xanthine oxidase (XO), cyclo-oxygenase (COX), lipoxygenase and phosphoinositide 3-kinase. In nature, flavonoid compounds are extracted from plants and they are found in various parts of the plant (Panche.A et al., 2016).

Their activities are structure dependent. Functional hydroxyl group in flavonoids mediate the antioxidant effects by scavenging free radicals. This review deals with the chemistry, classification and pharmacological applications of flavonoids (shashank kumar and k.pandey,2013).

Chemical Structure

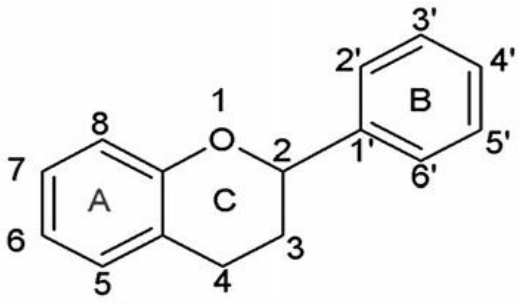


Fig 1: Basic flavonoid moiety.

Their basic structure is a skeleton of diphenylpropane, namely two benzene rings (A and B ring) linked by three carbon chain that forms a closed pyron ring (heterocyclic ring contain oxygen the C ring) with benzene ring A (shashank kumar and k.pandey, 2013).

Classifications

Flavonoids are classified into six group, including flavones, flavonol, flavanone, is of flavone, flavan-3-ol, and anthocyanin. This classification depending on carbon atom of the C ring attached to the B ring and the degree of unsaturation and oxidation potential of C ring. The B ring is linked at the position 3 of C ring re called isoflavones. In which the B ring is linked at the position 4 are called neoflavonoids , while those in which the B

ring is linked at the position 2 can be sub sub divided in to subgroup (Panche et al.,2016).

Flavones are one of the important subgroup of flavonoids. It will be characterized by a planar structure because of a double bond in the central benzene ring. Flavone found in onions, apples, broccoli, and berries (Robert J nijveldt et al., 2001).

The next class is flavonol it's structurally similar to flavones but differ in various pharmacological properties, physiological properties is due to different positions of the phenolic groups. Good sources of flavonols in diet are onion, kale, broccoli, tomato, grapes, tea, berries, and red wine (Eleonora Corradini et al., 2010).

Flavanones occur as two glycosides which are attached at position 7. The chiral center at position 2 and absence of double bond between positions 2 and 3 describes that it's a flavanones. The main sources of flavanones are lemon, lime, sweet orange, and grapes (Yogesh Murti and Pradeep Mishra., 2014).

Isoflavonoid can be divided in to 14 classes and it again classified into 23 subclasses depending on their skeletal modification. In isoflavonoids B ring is linked to position 39. The good source of isoflavonoids was soys beans, red clover, psoralea, fava beans, kudzu (Eleonora Corradini et al., 2010).

Flavanols are the 3-hydroxyl derivative of flananones, it also called as dihydroflavanols or catechins. In flavanol the hydroxyl group is bound to position 3 of the C ring. Flavanol found in bananas, apples, blue berries, peaches and pears.

Anthocyanin is a natural colorant molecule which comes under flavonoids. It has very higher antioxidant activity, and it rich in black berries, red raspberries, black raspberries and strawberries (padma S. vankar and Jyoti srivastava., 2010).

Pharmacological Applications

Anti-Inflammatory property

Inflammation is a immune response of the organism to detect and destroy harmful agents. During inflammation, the Pro-inflammatory mediators (nitric oxide (NO), reactive oxygen species (ROS), cytokines and prostaglandins (PG_S), inducible nitric oxide synthase (iNOS), and cyclooxygenases (COXs) synthesis was activated. Flavonoids will produce inhibition action on these pro-inflammatory mediators synthesis by suppress the action of enzymes essential for the synthesis of pro-inflammatory mediators(Erick P.Gutierrez-Grijalva et al.,2017).

Hepatoprotective property

Many flavonoids such as catechin, apigenin, quercetin, naringenin, rutin, and venoruton are reported for their hepatoprotective activities. Chronic diseases like diabetes may lead to development of hepatic clinical manifestation (J.B.Harborne and C.A.Williams.,2000). The glutamate-cysteine ligase catalytic subunit (Gclc) expression, glutathione, and ROS level are reported to be decreased in liver of diabetic mice. Flavonoids have drawn increasing attention due to their preventive action against various diseases. They will increase the Gclc expression by increasing cAMP levels to activate the (PKA) which regulate the cAMP response element binding protein phosphorylation to promote CREB-DNA binding and increase the Gclc transcription (shashank kumar and k.pandey.,2013).

Vascular activity

Flavonoids act in a number of different ways on the various blood components such as platelets, monocyte, low density lipoprotein (LDL) and smooth muscles. Platelets are very important component in antherosclerosis and pro-inflammatory mediators like thromboxane A_2, PAF and serotonin are synthesized from them (Nijveldt et al.,2001). Flavonoids may be inhibit platelet adhesion, aggregation and secretion. Quercetin and kaempferol derivatives are reported to their inhibition activity on platelet aggregation caused by various inducer (J.B.Harborne and C.A.Williams.,2000).

Antimicrobial properties

Flavonoids are effective antimicrobial agents against a wide range of microorganism. This is due to their complex action with the extracellular and soluble proteins and also with the bacterial cell wall. Flavonoids present in the plants are known to be toxic to microorganism (Mohammad asif and Elham khodadai.,2013). Rutin shows antiviral activity and flavones, flavanones were show mild anti-tuberculosis activity (D K sharma.,2006).

Neurodegenerative diseases

Flavonoids may perform a major role in enzyme and receptor system of the brain, and also exerting significant effects on the central nervous system, such as prevention of neurodegeneration associated with AD and Parkinson's diseases. Flavonoids hve ability to inhibiting enzymes, as their exist strong reports about inhibitory enzymes like aldose reductase, XO, phosphodiesterase, Ca^{2+} ATPase, lipoxygenase and COX in preventive neurodegenerative diseases (Panche.A et al.,2015).

Anticancer property

Cancer is described as "a group of disease characterized by unregulated cell growth and the invasion and spread of cells from the site of origin, or primary site (Pecorino.L.,2012). Several factors are involved in the onset of action of cancer such as age, alcohol, cancer-causing substances, diet, hormone, obesity, radiation, tobacco, etc.; and they may play a direct or indirect role in the development and progressions of different type of cancers. Cancer includes five known stages: initiation, promotion, progression, invasion and metastasis. Dietary factors play an important role in the prevention of

cancers. Fruits and vegetables having high flavonoids content have been reported as cancer chemopreventive agent (A. Mishra et al.,2013). Flavono quercetin is inversely associated with the incidence of cancer of the prostate, lung, stomach, and breast. Various mechanisms have been proposed for the anticancer activity of flavonoids on the initiation stages of the cancer including influences on development and hormonal activities (G.G.Duthie et al.,2000). Major molecular mechanism of action of flavonoids are given below:

1) Dowmregulation of mutant P^{53} protein,
2) Cell cycle arrest,
3) Tyrosine kinase inhibition,
4) Inhibition of heat shock proteins,
5) Estrogen receptor binding capacity,
6) Inhibition of expression of Ras proteins.

Quercetin is known to produce cell cycle arrest in proliferating lymphoid cells. In addition to it's anticancer activity, it will exerted growth-inhibitory effects on various malignant tumor cell lines in vitro.

Antiosteroporotic effect

According to the reference, bone mineral density was compared between older women who consumed tea and those who did not. Women in the study consumed tea had higher bone mineral density measurement than did those did not consumed tea. The presence of flavonoids in tea might be responsible for the prevention of osteoporosis (J.B.Harborne and C.A.Williams.,2000).

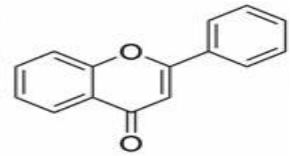
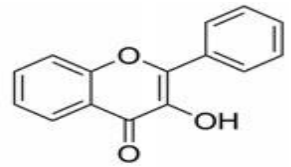
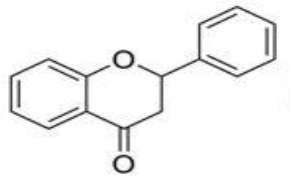
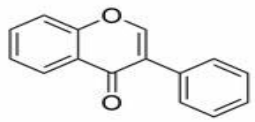
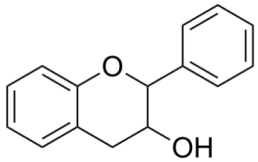
Flavonoid classes	Subclasses	Natural sources
Flavones 	Asigenin Tangeretin Baicalein Rpoifolin	Fruits Medicinal plants and other
Flavonol 	Quercetin Myricetin Rutin Morin Kaempferol	Fruits Vegetables Medicinal plants and other
Flavanones 	Hespertin Naringin Naringenin Eriodictyol Hesperidin	Fruits Medicinal plants and other
Isoflavonoids 	Genistin Genistein Daidzein Glycitein Daidzin	Legumes Medicinal plants
Flavanols 	Catechin Fisetinidol Afzelechin Robinetindol	Fruits Medicinal plants
Anthocyanin 	Cyanidin Malvidin Delphinidin Peonidin	Fruits Vegetables Nuts and dried fruits Medicinal plants and other

Fig 2: Classifications of Flavonoid.

CONCLUSION

This study was provided the detailed information about structure, classification, and pharmacological application of the flavonoids. According to the structure the flavonoid can be classified as follows flavones, flavonol, flavanone, isoflavone, flavan-3-ol, and anthocyanin. Flavonoid have potent anti oxidant property and also have anti inflammatory property, hepato protective property and vascular activity, anti microbial activity, anticancer activity, antisteropotic effect and active against neurodegenerative diseases.

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