Review Article
ISSN: 0974-6943

Anita S et al. / Journal of Pharmacy Research 2010, 3(12),2834-2835

Available online through
www.jpronline.info

Bio-flavonoid Quercetin in oncology : A review

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Received on: 20-09-2010; Revised on: 16-10-2010; Accepted on:15-11-2010

ABSTRACT

Among chemopreventers, one of the most studied group of antioxidant compounds are flavonoids.Quercetin (2-(3,4-dihydroxyphenyl)- 3,5,7-trihydroxy-4*H*chromen-4-one) is a flavonoid, an aglycone form of a number of other flavonoid glycosides found in citrus fruits. Quercetin has exhibited a wide range of beneficial biological activities including antioxidant, radical scavenging, anti-inflammatory, anti-atherosclerotic, anti-tumoral and anti-viral effects. A number of its actions make it a potential anti-cancer agent, including cell cycle regulation, interaction with type II estrogen binding sites, and tyrosine kinase inhibition. This article reviews the cancer-preventive effects of natural compound quercetin.

Keywords: Quercetin, natural compound, aglycon, chemoprventer,antioxident

INTRODUCTION

The field of cancer chemoprevention, defined as the long-term intervention with natural or synthetic molecules to prevent, inhibit or reverse carcinogenesis, is gaining increasing importance, especially at a time when the use of complementary and alternative medicine (CAM) and natural health products is consistently increasing [1].

Consumption of fruits, particularly citrus fruit, as well as vegetables, likely correlates with decreased esophageal cancer risk [2,3]. Green leafy vegetables, rather than fruit, might also have a protective effect against lung cancer [4,5]. High intake of cruciferous vegetables may be associated with reduced risk of aggressive prostate cancer [6].

Flavonoids occur as aglycones, glycosides and methylated derivatives. 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 [7]. The Flavonoids can be divided into various classes on the basis of their molecular structures Figure.1 [8].

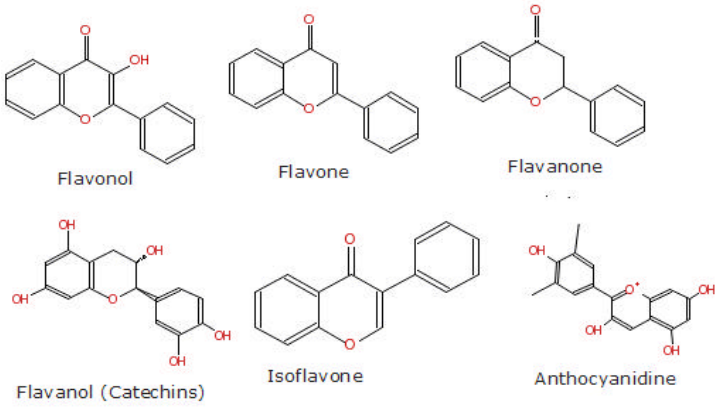

Figure 1: Structures of the major classes of flavonoids

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Quercetin is a member o f a group o f naturally occurring compounds, the flavonoids, which have a common flavone nucleus composed of two benzene rings linked through a heterocyclicpyrone ring. Frequently quercetin occurs as glycosides (sugar derivatives); e.g., rutin in which the hydrogen of the R-4 hydroxyl group is replaced by a disaccharide Figure.2. Quercetin is termed the aglycone, or sugarless form of rutin[9].

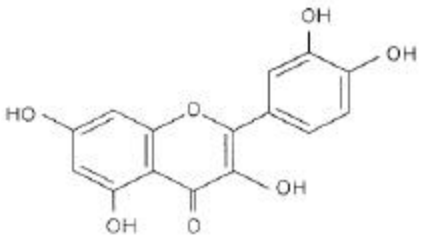

Figure.2 Quercetin (Chemical Formula: $C_{15}H_{10}O_7$ Molecular Weight: 302.23)

Synonyms: C.I. Natural Yellow, 10; C.I. 75670; Cyanidelonon 15:2;,Flavin Meletin; Quercetine; Quercetol; Quertin; Quertin, Sophoretin; Xanthaurine; 3,3 ,4 ,5,7-Pentahydroxyfiavone; 3,5,7,3 ,4 -Pentahydroxyflavone; 2-(3,4-DihydroxyphenyI)-3,5,7-trihydmxy 4H-l-benzopn-4-one [10].

Physical, chemical properties and occurrence of quercetin
Quercetin is a yellow, crystalline solid with a bitter taste, which is insoluble in water, slightly soluble in alcohol, and soluble in glacial acetic acid and aqueous alkaline solutions[10]. Animals are unable to synthesize the flavone nucleus; thus, flavonoids are found exclusively in the plant kingdom. Quercetin is found in various food products and plants, including fruits, seeds, vegetables, tea, coffee, bracken fern, and natural dyes[11].

Metabolism and distribution
Quercetin glycosides are relatively poorly absorbed by the small intestine[12]. Quercetin obtained from plant source is in the form of Quercetin –glucose conjugates (Quercetin glucosides), which are absorbed in the apical membrane of the enterocytes. Once absorbed, Quercetin glucosides are hydrolyzed to generate Quercetin aglycone which is further metabolized to the methylated, sulfonylated and glucuronidated forms by the enterocytic transferases. Quercetin metabolites are then transported first to the intestinal lumen[13], and then to the liver, where other conjugation reactions take place to form Quercetin -3-glucuronide and Quercetin -3'-sulfate, which are the major Quercetin -derived circulating compounds in human plasma[14, 15]. According to recent studies on Quercetin bioavailability[16], when Quercetin is absorbed in the form of Quercetin glucosides, the peak plasma concentration ranges from 3.5 to 5.0 µmol l^{-1}. In the unconjugated form, Quercetin