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A STUDY OF QUERCETIN

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Objective

â€¢ To research the constituent quercetin which forms part of the group of secondary plant metabolites known as flavonoid.
â€¢ Give herbal examples containing quercetin.
â€¢ Give the actions and indications for its use in relation to the constituent group.
â€¢ To document flavonoidâ€™s pharmacokinetic action in the body
â€¢ Discuss the pharmacodynamics of quercetin according to its actions.
â€¢ Provide and critique research articles that substantiate its claims to have beneficial effects on the body.

Introduction

Secondary metabolites are chemicals produced by plants for which no role in growth, photosynthesis, reproduction, or other \"primary\" functions have been found. The apparent lack of primary function in the plant, combined with the observation that many secondary metabolites have specific negative impacts on other organisms such as herbivores and pathogens, leads to the hypothesis that they have evolved because of their protective value. Many secondary metabolites are toxic or repellent to herbivores and microbes and help defend plants producing them. It used to be believed that secondary metabolites were irrelevant for the human diet, however it is now being scientifically proven that secondary metabolites carry out a number of protective functions in the human body. One of the groups of secondary metabolites are known as flavonoid.

The Constituent

Flavonoid

Flavanoids are the most widely found of phenols in the plant world. They occur in plants as flavanoid glycosides and they are found to some degree in every plant. They are found in the leaf cuticle and epidermal cells where they protect against damaging ultra-violet rays and have a role in regulating growth.

Flavanoids are water soluble polyphenolic molecules containing 15 carbon atoms and they belong to the polyphenol family.

Flavanoids are mainly present in plants as glycosides. Aglycones occur less frequently. To date, over 6000 flavonoids have been identified in plants (Mills and Bone2000). The large number is a result of the many possible combinations of flavonoid aglycones and different

sugars.

The flavonoids consist of 6 major subgroups: chalcone, flavone, flavonol, flavanone, anthocyanins and isoflavonoids. Together with carotenes, flavanoids are also responsible for the colouring of fruits, vegetables and herbs. The word â€œflavanoidâ€ is derived from the Latin word flavus meaning yellow and many flavanoids are yellow in colour. However, many others are white, and anthrocyanidins are red, blue or purple (e.g berries).The extracts from these plants are bitter and sweet.
Flavanoids are found in many different families in the plant kingdom:
â€¢ Polygonaceae
â€¢ Rutaceae
â€¢ Fabaceae
â€¢ Umbellieferae
â€¢ Asteraceae
Flavanoids were the first source of â€œvitamin Pâ€ to be found and were found in Ruta graveolens. Flavanoids interact with cell membrane structure and have an effect on improving capillary fragility and therefore reduce capillary permeability. In this way they guard against bruising and inflammation. In decreasing capillary fragility and increasing capillary resistance they are useful for hypertensive states and can also strengthen connective tissue by inhibiting hyaluronidase, an enzyme that breaks down connective tissue.
Other actions flavanoids in general include:
â€¢ Anti-oxidant activity
â€¢ Immune stimulating
â€¢ Weak oestrogenic effect
â€¢ Inhibition of various enzymes â€" lipoxygenase, reverse transcriptase,ATPase, cyclic AMP phosphodiesterase
â€¢ Diuretic
â€¢ Antispasmodic
â€¢ Connective tissue support
Quercetin will be used as an example of a flavanoid.
Quercetin
Quercetin belongs to the flavanoid family and is the most abundant of the flavanoids. It consists of three benzene rings and five hydroxal groups:

Researchers have begun to identify and quantify flavonoids from various foods. A study that compared the flavonoid content of the flesh and peel of apples found the highest concentration of flavonoids in the peel and another study found that green and black tea both contained approximately 200 mg/cup for a typical brew (Bentz 2009).

Food preparation and storage can affect quercetin concentrations in food. Foods that have been fried and boiled show lower quercetin content. Boiling causes the greatest decrease in quercetin due to thermal degradation and the leaching action of boiling water (Bentz 2009). However, this varies between foods, such as onions because they contain quercetin conjugates that can retain their stability up to temperatures of 100oC.
The quercetin content in foods is also dependent on storage effects. Onions can lose 25-33% of their quercetin content in the first twelve days of storage, but suffer minimal losses thereafter (Beecher 2003). In contrast, the quercetin level in strawberries has been shown to increase approximately 32% when stored at -20oC for nine months. The process by which the foods are grown is also pertinent. For example, flavonol content is higher in plants exposed to higher levels of ultraviolet-B rays due to their action as possible defense mechanisms against the UV light. Plants grown in the United Kingdom were found to have a lower flavonol content than those grown in South Africa because of the use of greenhouses, which block the ultraviolet-B rays (Bentz 2009).

Examples of foods containing Quercetin

- â€¢ Apple , with skin
- â€¢ Broccoli
- â€¢ Onions
- â€¢ Spinach
- â€¢ Black / Green tea
- â€¢ Red wine
- â€¢ Berries

Examples of herbs containing Quercetin

- â€¢ Elderberry
- â€¢ Hawthorn
- â€¢ Linden
- â€¢ Shepherdâ€™s Purse
- â€¢ Asthma weed
- â€¢ Black Catechu
- â€¢ Lungwort Herb
- â€¢ Sweet violet
- â€¢ Tansy

For the purpose of this study I will discuss further the herbs Elderberry and Hawthorn in relation to their therapeutic uses due to the constituent quercetin being present.

Elderberry

Common name: Elderberry
Latin name: Sambucus nigra
Family name: Caprifoliaceae
Synonyms: Elder, Black Elderberry, North American Elderberry, Common Elder, Pipe Tree, Bore Tree, Ellhorn , (German) Hollunder, (French) Sureau.
Elderberries have been a folk remedy for centuries in North America, Europe, Western Asia, and North Africa, hence the medicinal benefits of elderberries are being investigated and rediscovered.
A wealth of folk-lore, romance and superstition centre round this English tree. The Elder tree was supposed to ward off evil influences and give protection from witches; if an Elder tree was cut down a spirit known as the Elder Mother would be released and take her revenge, the tree could only be cut down safely while chanting a rhyme to the Elder Mother!
The parts used are the bark, flowers, berries and leaves and the constituents that are found in the plant include tannins, amino acids, carotenoids, flavonoids- (quercetin), sugar, rutin, viburnic acid, vitaman A and B and a large amount of vitamin C.
Actions

- â€¢ Diuretic
- â€¢ Expectorant
- â€¢ Diaphoretic
- â€¢ Anti-catarrahal
- â€¢ Immune stimulating

â€¢ Anti-oxidant
â€¢ Laxative

Hawthorn

Common name: Hawthorn
Latin name: Crataegus oxyacantha
Family name: Rosaceae
Synonyms: English hawthorn, Haw May blossom, May bush, May tree, Quick-set, Shan-cha, Thorn-apple tree, Whitethorn
The leaf, flower and berry of several species of hawthorn are used medicinally. References to Hawthorn are extensive throughout history, and although the berries were traditionally use for therapy, current research is focusing on the leaves and flowers. The key constituents in Hawthorn include oligomeric procyanidins(OPC), flavanoids (quercetin), amines, catechols,carboxylic and triterpene acids. The flowers contain the highest level of flavanoids and the leaves the highest level of OPCs.
Actions
â€¢ Cardio-protective
â€¢ Cardiac tonic
â€¢ Hypotensive
â€¢ Antioxidant
â€¢ Connective tissue support
â€¢ Mild astringent
â€¢ Antiarrhytmic

Pharmacokinetics

Flavonoids are thought to be poorly absorbed because the naturally occurring glycosidesâ€™ sugar moieties elevate the moleculesâ€™ hydrophilicity, and no enzyme is known to split the glycosidic bond (Murota and Terao 2003, Hollman et al. 1997).

It is generally thought that the flavonoid glycosides enter the colon and are hydrolysed to the aglycone by enterobacteria. The aglycone is then absorbed in the large intestine easily because of its lipophilicity, and then metabolised in the liver by O-methylation, glucuronidation, and/or sulfation. Quercetin glucosides are able to pass through the epithelial cell layer, but they have a lower efficiency than the quercetin aglycone. Therefore, the hydrolysis of the glucoside to the aglycone accelerates the absorption of quercetin (Murota and Terao 2003).
Pharmacodynamics according to its three main actions

Anti-oxidant effects
Quercetin is considered to be a strong antioxidant due to its ability to scavenge free radicals and bind transition metal ions. These properties of quercetin allow it to inhibit lipid peroxidation. Lipid peroxidation is the process by which unsaturated fatty acids are converted to free radicals via the removal of hydrogen. Lipid peroxidation can create deleterious effects throughout the body, such as cardiovascular and neurodegenerative diseases; however, it can be terminated by antioxidants, like quercetin, which interfere by reacting with the radicals formed (Hollman and Katan 1997,Beatty et al 2000, Sakanashi et al. 2008).

The oxidation of low-density lipoproteins (LDL) can result in the formation of atherosclerotic plaques, leading to cardiovascular disease (Hollman and Katan 1997).

However, several studies have illustrated quercetinâ€™s ability to inhibit LDL oxidation. One particular study found a 21% reduction in cardiovascular disease mortality when the intake of quercetin was greater than 4mg/d (Graf et al 2005).

The vulnerability of brain lipid membranes to lipid peroxidation is thought to lead to neurodegenerative disease, such as Alzheimerâ€™s and Parkinsonâ€™s disease (Balazs and Leon 1994). Balazs and Leon (1994) found that oxidative stress occurring in the brain membrane lipids is associated with the extracellular accumulation of amyloid beta-peptide, which precedes neural losses in Alzheimerâ€™s patients. Yet, formation of amyloid plaques can be prevented by taking antioxidants (Ansari et al. 2008.) In this situation, quercetin does not only stop the propagation of lipid peroxidation, but also increases glutathione (GSH) levels (Ansari et al. 2008). GSH is part of the neuronâ€™s defense against oxidative damage. When the superoxide radical is formed, the radical can be converted to the hydrogen peroxide radical by superoxide dismutase; however, GSH can convert hydrogen peroxide to oxygen and water, preventing the formation of free radicals.

Quercetin can also protect against the more obvious environmental causes of free radicals, such as smoking. Cigarette tar is a source of free radicals, which has been found to damage erythrocyte membranes. Begum and Terao (2002) found that the quercetin aglycone and its conjugate metabolites (quercetin-3-O-Î²-glucuronide and quercetin-3-O-Î² -glucoside) could protect erythrocytes from the membranous damage that is caused by smoking. The control used in the study was flavone, which has the basic structure of quercetin but no hydroxyl groups, and it had no effect on the erythrocytes. This indicated that the hydroxyl groups are important to the antioxidant properties of quercetin.

Anti-inflammatory effects

Quercetin can also reduce inflammation by inhibiting mast cells involved with inflammation. In one study, men with chronic prostatitis were given 500mg of quercetin twice a day for one month. As a result, 67% of the men had a 25% improvement in symptoms. In 1999, Shoskes et al. gave men with the disease quercetin and Prosta-Q (bromelain and papain), which increases absorption of quercetin, finding that 82% had at least a 25% improvement.

Cardioprotective effects

Quercetin in Hawthorn is thought to be the reason of this herbsâ€™ cardioprotective properties. Quercetin inhibits the proliferation and migration of aortic smooth muscle cells, inhibits platelet aggregation, and improves the health of the endothelium (Br J Nutr 2006). The cardio-protective properties can be sub-divided into, anti-arrythmic and hypotensive. Quercetin acts as a hypotensive agent by dilating blood vessels by blocking the ACE enzyme, which constricts blood vessels. This in turn improves blood flow through arteries and may lower blood pressure. Several studies have proven its hypotensive effects (J Duarte et al 2001).

Its anti-arrythymic effects are due to quercetin blocking certain enzymes that can deteriorate heart muscle, thus correcting irregular heartbeat (S-K Moon et al, 2003).

Conclusion

Quercetin has many health promoting effects, including improvement of cardiovascular health, reducing risk for cancer as well as anti-inflammatory and anti-allergic effects. All

these activities are caused by the strong antioxidant action of quercetin.
As many other flavonoids, quercetin prevents the oxidation of LDLâ€™sl.
The anti-inflammatory action of quercetin is caused by the inhibition of enzymes, such as lipoxygenase, and the inhibition of inflammatory mediators. Quercetin also inhibits the release of histamine, which causes congestion, by basophils and mast cells.
Studies have shown that quercetin reduces the cancer risk of prostate, ovary, breast, gastric and colon cells.
As quercetin is found in most fruit and vegetables increasing our intake of them, is an important factor in preventing chronic disease states.

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