-Review Article-

Development and optimization of fenugreek extract loaded nanoemugel for the treatment Anti-inflammatory Activity

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**Introduction of Quercetin-**

Quercetin is a polyphenolic Flavonoid with potential chemo preventive activity.

Quercetin also produces anti-inflammatory and anti-allergy effect. Quercetin

is a Flavonoid found in many food and herbs and is regular component of a normal

diet. Extract of Quercetin have been used to treat or prevent diverse conditions including cardiovascular Quercetin as a disease. Nutritional supplement is well tolerated.

Quercetin has been separated from a crude plant extract by high-performance liquid chromatography.Human cannot make quercetin in their body but many fruits, vegetables, and drinks contain it.Flavonoids occur either as free molecules or as glyco- sides. They have widespread occurrence in plant kingdom. They occur in families like compositae, leguminoceae, po- lygonaceae, rutaceae etc. contain a large number of flavono- ids. Flavonoids have been reported in some green algae also. Chemically, flavonoids show a fifteen-carbon skeleton. Most of the Flavonoid have a carbonyl function situated at one end of the bridge. Quercetin is the most abundant of the Flavonoid. Plants containing various flavonoids have a long history of use in traditional medicines in many cultures, but the flavonoids themselves were not discovered until the 1930’s. Quercetin first gained attention several decades ago when it was found to cause DNA mutations in bacteria, a possible sign that it might actually contribute to causing cancer

**Foods and drinks that contain Quercetin include-**

|  |  |  |  |
| --- | --- | --- | --- |
| Sr.no | Name  | Biological source | Part |
| 1 | Grapes | Vitis venifera | Fruit |
| 2 | Berries(blue) | Rubus | Fruit |
| 3 | Cherries | Prunus avium  | Fruit |
| 4 | Apple | Malus sieversil | Fruit |
| 5 | Citrus  | Citrus lemon  | Flower |
| 6 | Onion | Allium cepa  | Skin |
| 7 | Buckwheat | Fagopurum tatarium | Seed |
| 8 | Broccoli | Brassica oleracea | Flower, bud |
| 9 | fenugreek seed | Trigonella foenum graecum | Seed |
| 10 | Tomatoes | Solanum lycopersicum | Fruit |
| 11 | Black tea | Camellia sinensis | Leaves |
| 12 | Coffee | Coffea arabica | Fruit, flowers |
| 13 | Wine | Vitis venifera | Fruit |
| 14 | Audhumber | Ficus racemosa | Seed |
| 15 | Amla | Phyllanthus embllica | Fruit |

Quercetin is also present in herbal remedies such as Ginko-biloba and John’s wort people can also take quercetin as a supplement

**The pharmacological and biological functions of quercetin**

Quercetin is a kind of ﬂavonoid compound that human can get from food and plants. Compared with quercetin, the conjugated form of quercetin glycoside is better absorbed. Quercetin is mainly absorbed into intestinal cells in the form of glycosides, hydrolyzed into aglycone and enters the intestinal lumen, and its mechanism may be related to glucose transport. The transformation process occurs mainly in the intestines, and some can be done in the liver and blood.

**Therapeutic activity of quercetin in cancer**

Quercetin has shown signiﬁcant beneﬁcial eﬀects on many diseases. Due to reasonable doses of quercetin have no obvious toxic side eﬀects on normal cells, more and more researchers are paying attention to the therapeutic eﬀect of quercetin on tumors. Numerous studies have shown that quercetin can exert anti-tumour functions in a variety of mechanisms and has been conﬁrmed in in vitro and in vivo models of various tumors, with encouraging results Quercetin signiﬁcant pre- vents cell cycle, promotes apoptosis, and inhibits angiogenesis and metastasis in vitro (Fig. 1). In in vivo studies, the conclusions indicate that the selected dose of quercetin is eﬀective in inhibiting the growth of xenograft tumor models.

**Cell cycle arrest**

**Decreased Cyclin D, Cyclin E, E2F**

**Increased Cyclin B**

 **Apoptosis**

**LC3I- LC3II VOA Formed**

VOA formed

 **Quercetin**

**Decreased Bcl-XL, Bcl-2, Mcl-1**

**Increased Bax, Bad**

**Autophagy**

**Decreased N-Cadherin, Vimenthin, Snail**

**Increased E-cadherin**

**Decreased VEGF**

**Metastatis**

 **EMT**

**Angiogenesis**

 **Fig 1 overview of the Anticancer effect of Quercetin**

**In vitro studies**

Eﬀect of quercetin on cell cycle of cancer cells The cell cycle is the basic process of cell division and is mainly divided into four phases: G1 phase (pre-DNA synthesis), S phase (DNA synthesis phase), G2 phase (late DNA synthesis phase), and M phase (mitotic phase), which is mainly regulated by Cyclin, Cyclin dependent kinesis (CDKs) and Cyclin dependent kinase inhibitor (CKI). The cell cycle is mainly regulated by the pRb network regulatory pathway. Cycling forms a complex with its corresponding CDK, which phosphorylates Rb, and then releases E2F and cAb1.Subsequently, E2F enters the nucleus to promoteG1 phase into S phase for cell autonomy division. In the cell cycle progression, one kind of CKI, INK4 (including p15, p16, p18, p19) competes with cyclinD1 for binding to CDK4/CDK6, inhibiting phosphorylation of Rb and inhibiting cell cycle progression. Another important pathway is mainly regulated by p53, which induces the expression of p21, GADD45, and Bax to regulate cell cycle division However, in studies of tumour pathogenesis, abnormal cell cycle activity and uncontrolled replication of tumour cells were found due to the abnormal expression of cycling.

**Ethno pharmacological actions of Quercetin-**

1. **Fighting free radicals.**

**2) Reducing inflammation.**

**3) Reducing the risk of cancer.**

**4) Preventing neurological disease.**

**5) Relieving allergy symptoms.**

**6) Preventing infections.**

**7) Reducing the risk heart disease.**

**8) showering high blood pressure.**

**Dose -** people can get quercetin through their diet by eating a range of fruit and vegetables each day.Fenugreek have the highest level of quercetin compared to other tested produce containing approximately 300mg per kilogram.

**Side effect of quercetin-**

1. headach (oral use)
2. Numbling and tingling (oral use)
3. Shortness of breath (intravenous use)
4. Nausea and vomiting (intravenous use)
5. Kidney damage

**Structure of Quercetin-**



**Classification- Flavonoid**

 Properties-crystalline nature

Solubility- solubility in water-practically in soluble in water soluble in aqueous alkaline Solution

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Sr.no | Plant | Family | Part | Method of extraction | Solvent extraction | Reference |
| 1 | Enonymus alatus | Celastruceae | Flower | Maceration Refluxing | Ethanol-methanol | 1 |
| 2 | Cuscata campestris | Cuscutaceae | Seed | Extractionincubation | ACN (acetonitrile)0.1 Formic acid | 2 |
| 3 | Buckwheat | Fagopyrum tataricum | Grains | Extraction steaming | Methanol | 3 |
| 4 | Ginko-leaves | Ginkgoaceae | Leaves | Solid phase extraction | 0.1% sodium hydrochlorideEthylene glycol | 4 |
| 5 | Black tea and green tea | Theaceae | Leaves | Hydrolysis | Ethanol HCL | 5 |
| 6 | Nicotiana attenuata | Solancaceae | Flower | Extraction | ACN dimethyl ether | 6 |
| 7 | Magnifera indica | Anacardiaceae | Fruit | Supercritical fluid extractionSubcritical fluid extraction | Ethanol | 7 |
| 8 | Umbelliferaceae | Apiaceae | Fruit | Extraction | HCL | 9 |
| 9 | Grapes | Vitaceae | Fruit | Fermentation maceration | Sulphur dioxide | 10 |
| 10 | Citrus | Rutaceae | Flower | Extraction | Methanol acetonitrile | 11 |
| 11 | Broccoli | Brassicaceae | Flower | Extraction | Ascorbic acid | 12 |
| 12 | Fenugreek seed | Fabaceae | Seed | Soxhlet apparatus extraction | HCL ethanol acetone methanol | 13 |
| 13 | Kiwi fruit | Actinidiaceae | Fruit  | Extraction /TLC | Sodium hydrochloride | 17 |

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| Antimicrobial (ethylantus alatus) | Agar disk diffusion method was used | It inhibits gram-positive and gram- negative bacteria through inactivating extracellular proteins. Apart from antimicrobial activity, it also displays other beneficial effects: |  14 |
| Anti-inflammatory(cuscata campestris) | MTT cell viability Cytotoxicity performed | The effect of Flavonol (rutin and quercetin) and flavanone (hesperidin)  |  15 |
| Buckwheat(antioxidant) | Radical scavenging activity on DPPH | evaluated the stability constant, coordination aspects of quercetin in presence of Cd(II) ion and its antioxidant behaviour. |  16 |
| Anti-inflammatory(ginko leaves) | DPPH scavenging ability | The results derived from the extraction test and further validated directlytrapping active compounds of certain structuralfeatures by MIP technology was operable |  17 |
| Anti-inflammatory(citrus) | GSK-3b protein model by using the DOCK function | Among the citrus compounds tested acid), the ﬂavonoids had the overall highest inhibitory activity |  18 |
| Anti-inflammatory(broccoli) | LCMSD software | The broccoliphenolic fractionwas analysed by HPLC/UV- DAD and the characteristic sinapoyl/feruloyl gentiobio- sides were detected |  19 |
| Anti-inflammatory(coffee) | DPPH radical scavenging activity | It is known that ﬂavonoids inhibit oxidative stress in- vitro by acting either as free radical scavengers or as metal chelating agents |   20 |
| Anti-arrthmatic (nicotina attenuate) | LDH measurement | Sequential and serial extractions (see Experimental) of leaf surface, trichomes and laminar components demonstrated the localization of particular compounds |  21 |
| Anti-oxidant(magnifera indica) | DPPH method | Peroxyl radical-driven peroxidation of methyl linoleatewas carried out in a solution of n-hexane and 2-propanol  |  22 |
| Anti-oxidant(rasbeery fruit) | HPLC-MS and diode array ananlysis of raspberries | For the synthesis of complex first Job’s method [23] (continual variation method) was applied to validate the stoichiometric comp  |  23 |
| anti-oxidant (kiwi fruit) | In vitro by DPPH and FRAP assays, as well as by evaluation of potential to inhibit LP. Signiﬁcant diﬀerences were observed for the tested compounds, as well as between the assays employed | The eﬀects of diﬀerent concentrations of quercetin on mycelial growth are shown in Table 2. Quercetin at a concentration of 0.25 mg/ mL signiﬁcantly inhibited the growth of P. expansum by 30%. |  24 |
| Anti-inflammatory (fenugreek) |  | plant quercetin has been extracted successfully from the leaves of Trigonella foenum-graecum. It is found that solvent plays the ma |  25 |
| Anti-hypertensive(onion) | The IR spectra were recorded using KBr disk method on a Shimadzu FT-IR, Model 8300. | Total ﬂavonol and quercetin conjugate contents in baked and saut!eed onions increased, as these compounds were concentrated in the tissues, as water and other volatiles were lost during cooking. |  26 |

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