Chinese Scullcap (Baicalein)

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General Features

Scutellaria baicalensis or Chinese scullcap is a member of the mint family and grows in China and Russia.[1,2] The plant root is a rich source of over 35 flavonoids, giving it a yellow color, and hence its traditional name of golden root or Huang qin, the Chinese term for yellow gold (known as Ogon in Japanese).[3,4] One of the major flavonoids contained in the root of the plant is baicalin, a flavone glycoside (12-17% of all scullcap root flavonoids), which yields the aglycone flavone baicalein, once hydrolyzed by gut bacteria.[3] Baicalein is readily absorbed into the bloodstream where it has been shown to exert a broad spectrum of important biological activities.[5] Baicalein has been incorporated into a number of herbal combinations in Traditional Chinese Medicine that treat a wide array of health conditions, including the widely used Asian herbal remedy, "Sho-saiko-to".[6,7] Currently, baicalein is being studied for its anti-cancer, anti-inflammatory, anti-viral, anti-bacterial and anti-allergy effects.[8,9,10,11] As explained below, its ability to halt the replication of various human cancer cell lines, via the inhibition of the 12 lipoxygenase enzyme system, is attracting a great deal of attention from the scientific community as a premiere agent in cancer research.

Active Constituents

Primarily Flavonoids – The flavonoid Baicalein within Chinese scullcap is considered to be its most important active constituent.[3,5]

Clinical Application and Mechanism of Action

a. Anti-Cancer Effects

Many experimental studies indicate that baicalein (5,6,7-trihydroxyflavone) prevents and inhibits cancer growth via a number of direct and indirect physiological actions:

Inhibits 12-lipoxygenase enzyme and induces apoptosis of cancer cells - Baicalein has been shown to inhibit the 12-lipoxygenase enzyme, which converts arachidonic acid into a specific leukotriene (eicosanoid) that is required for cancer cells to proliferate. Studies demonstrate that by inhibiting the 12-lipoxygenase enzyme baicalein has been shown to inhibit cancer cell proliferation and induce apoptosis (programmed cell death) of human gastric cancer cell lines.[12] Further, activation of arachidonic acid by the 12-lipoxygenase enzyme has been shown to be critical for metastasis of human prostate cancer cells. Experimental evidence demonstrates that after intraprostatic injection of mice with human prostate cancer cells, the prostate cells pre-treated with baicalein failed to metastasize to the lung and failed to express activity of the 12-lipoxygenase enzyme. This evidence suggests that, in the presence of baicalein, various cancer cells can be prevented from multiplying and metastasizing to other tissues and that a primary mechanism through which this occurs is via the inhibition of the 12-lipoxygenase enzyme.[13] The inhibition of cancer cell proliferation also lends itself to increased apoptosis and a better opportunity for immune cells to destroy tumor cells.[12,13] Other studies testing baicalein as an anti-tumor agent have shown that it selectively induces apoptosis in human hepatoma cell lines (liver cancer cells) with minimal influence on

non-cancer cells.[14,15,28,29] Its ability to induce apoptosis is under intensive investigation as many studies provide evidence that baicalein exhibits an extraordinary ability to selectively encourage apoptosis of many different human cancer cells. This is likely one of the primary ways in which it has been a useful addition to herbal combinations that have been used in cancer treatment.[16,17,18]

Anti-proliferative - Baicalein has also demonstrated anti-proliferative effects on human bladder cancer cell lines and a murine bladder cancer cell line, in vitro. In an in vivo experiment, mice were injected with bladder cancer cells with concurrent oral administration of a high baicalein-yielding supplement in one group, or with no baicalein supplementation in the control group. All the control mice showed a progressive increase in tumor volume over the ensuing days of the study, whereas the mice treated with baicalein (scutellaria) showed a significant inhibition of tumor growth.[19] In other experiments, baicalein has demonstrated anti-proliferative effects on human pancreatic cancer cell lines and T lymphoid leukemia cells. The mechanism of action was shown to be through the reduction of protein tyrosine kinase activity and protein kinase C activity. Both of these enzyme activities are required for normal cellular proliferation to occur. Thus, in addition to inhibiting the 12 lipoxygenase enzyme pathway and inducing apoptosis of cancer cells, baicalein is also known to reduce cancer cell proliferation by directly or indirectly inhibiting specific enzymes (protein tyrosine kinase and protein kinase C) required for cellular division and proliferation.[28]

Antioxidant - Baicalein is also a strong antioxidant, and has been shown to protect DNA from undergoing cancerous mutations in challenge studies using potent carcinogens such as benzo{a}pyrene, and toxins such as aflatoxin (AF) B.[1,20,21]

Stimulates DNA repair enzymes - In vitro evidence indicates baicalein stimulates recombination and repair of damaged DNA, supporting its traditional inclusion in cancer formulas, and suggesting possible use after sunburn and radiation damage.[22]

Inhibits the 5alpha-reductase enzyme - Baicalein has been shown to inhibit the 5alpha-reductase enzyme, which converts testosterone to dihydrotestosterone (DHT). DHT is strongly associated with the development of prostate enlargement (benign prostatic hyperplasia) and prostate cancer. As such, baicalein is reported to be potentially useful for the prevention and/or treatment of androgen-dependent (testosterone-driven) disorders, including prostate enlargement and prostate cancer.[23]

Human Studies Involving Prostate Cancer Patients

Studies on humans have primarily involved patients with advanced prostate cancer, who were shown to be unresponsive to traditional medical drugs and other interventions. In a study performed by researchers from the University of California at San Francisco and Memorial Sloan-Kettering Cancer Center in New York, the oral administration of a herbal combination containing baicalein to patients with metastatic prostate cancer (previously unresponsive to standard treatments) demonstrated reversal and/or stabilization of their condition with significantly improved survival, quality of life scores and other positive outcomes in almost all patients receiving the supplement. After a median treatment period of 57 weeks, 100% of patients with androgen-dependent cancer had a decline of 80% or more in their prostate-specific antigen (PSA) levels, and these levels were undetectable in 81% of the patients. In 31 of 32 patients, the testosterone level declined to that seen in castrated men. Of nine men with elevated prostatic acid

phosphatase levels (a marker for cancer progression), all had declines of more than 50%. Of two patients with positive bone scans, one had a complete disappearance of cancerous bone lesions, and the other showed improvement. One patient had a complete disappearance of a bladder mass, demonstrated by CT scan.

Of 35 patients with androgen-independent prostate cancer 54% showed a drop in their PSA levels by 50% or more, and of 25 patients with metastasis to bone, 2 showed marked improvement, 7 remained stable, 11 progressed, and 5 had no further bone scan follow up due to an increasing trend in their PSA levels.[24] Other studies involving men with known prostate cancer, taking this herbal combination, have demonstrated similar results. In one study PSA levels dropped from 100ng/mL to 24 and from 386ng/mL to 114 within 16 months of supplementation in a two case report of hormone-refractory prostate cancer.[25] Studies following larger groups of men with prostate cancer for up to four years have also shown this herbal formula to significantly reduce PSA levels and improve survival and quality of life scores.[26,27]

Researchers attribute much of the anti-tumor effects of this herbal combination to the presence of baicalein. According to researchers, baicalein has demonstrated impressive anti-cancer effects against androgen-dependent and androgen-independent human prostate cancer cells lines, and many of its anti-cancer mechanisms have been uncovered in recent years, in vitro and in vivo experiments.[16,17,18,24,25,26,27,28] It appears to be of particular benefit in prostate cancer treatment and in combination with other phytonutrients (plant-based nutrients) and micronutrients (vitamins and minerals) may help to prevent the development of clinically important prostate cancer, reducing prostate cancer incidence.[26] Animal studies indicate that baicalein may be effective in the treatment of other cancers as well, with experimental evidence supporting its potential use in stomach, pancreatic, bladder, liver[12, 14, 15,19, 28] and breast cancer. [29, 30, 31]

Hepatoma and Leukemia Patients

Based on its traditional use, and the documentation of its anti-tumor effects against various human cancer cell lines, Baicalein has been used recently by doctors in Asia as a complementary supplemental agent in the treatment of hepatomas and leukemia in human subjects.[29]

b. Anti-viral/Anti-HIV

Baicalein has been shown in experimental studies to inhibit the activity of HIV-1 integrase enzyme, which is an essential enzyme in the life cycle of the HIV-virus. This enzyme is responsible for catalyzing the insertion of the viral genome into the host cell chromosome. It is an attractive target for the design of a HIV antiviral drug because the integrase enzyme has no human counterpart.[32] In a review of all herbal medicines frequently used as an alternative medical therapy by HIV positive patients and AIDS patients, JA Wu et al, emphasized that experimental data suggest that the flavonoid, Baicalein inhibits infectivity and replication of HIV, and shows great promise as an important component to be included in herbal remedies used for HIV treatment.[33]

c. Asthma and Allergies

Baicalein inhibits type I and II hypersensitivity reactions, confirming its traditional use in asthma34,35 and allergic dermatitis.[3]

d. Anti-inflammatory

Baicalein has shown impressive anti-inflammatory effects that appear to be mediated via repression of leukotriene B4 (inhibition of the 5-lipoxygenase enzyme), inhibition of

interleukin-1B, and prostaglandin E2. Studies reveal it may be of benefit in the treatment of gingivitis (gum inflammation).[29, 36, 37]

e. Alzheimer's and Dementia

In a rat model Baicalein has been shown to prevent the build up of amyloid beta peptide (Abeta), which is known to generate free radical damage to brain cells and participate to a significant degree in the development and progression of Alzheimer's disease. Additionally, chronic inflammation occurs in Alzheimer's pathogenesis and Baicalein was shown to inhibit the 12- lipoxygenase enzyme responsible for brain inflammation, to a large degree. When tested against other known 12-lipoxygenase inhibitor agents, only Baicalein was able to attenuate both nerve cell death (apoptosis) and over-expression of Abeta production. As such, Baicalein may help to prevent or forestall the development of Alzheimer's disease by reducing the build up of the toxic brain protein, Abeta and inflammatory mediators, and preventing brain cell death, which has been shown to be triggered by the accumulation of Abeta in affected brain cells. [38] In studies using human neuroblastoma cells, the antioxidant properties of Baicalein were shown to inhibit free radical damage to these nerve cells induced by treatment with hydrogen peroxide (a powerful free radical generating agent). The researchers argue that oxidative (free radical) stress plays an important role in the development of neurodegenerative diseases (e.g. Alzheimer's disease, Multiple Sclerosis, Parkinson's disease) and that antioxidants such as Baicalein and Quercetin (also a flavonoid) may be useful bioactive agents in the prevention and/or management of these conditions, pending further studies. Both of these flavonoids have shown impressive protective effects under experimental conditions.[39]

f. Inhibition of Xanthine Oxidase (Gout Treatment)

Baicalein is one of few bioactive agents that has been shown to inhibit the enzyme xanthine oxidase, which is responsible for the conversion of hypoxanthine to xanthine, and xanthine to uric acid, in the pathway for degradation of purines in the body. High levels of uric acid is a hallmark feature of gout and thus, Baicalein supplementation may be an effective complementary intervention in the long-term management of this condition.[40] The drug Allopurinol is a Xanthine Oxidase inhibitor and is a primary medication prescribed for the treatment of gout.

Dosage

1. Therapeutic Purposes: The usual doses for therapeutic purposes ranges from 150 to 200 mg per day of Baicalein.[6]
2. General wellness: Consider 50-100mg per day.

Toxicity and Adverse Side Effects

Baicalein supplementation at therapeutic doses appears to be safe with no reports of significant side effects or toxicity. Baicalein or Chinese scullcap are not known to be contraindicated for any health conditions.[41,42]

Drug-Nutrient Interaction

There are no known drug-nutrient interactions for Baicalein or Chinese skullcap.[42]

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