

# Quercetin Supplementation May Reduce Risk of Colon Cancer

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Quercetin is a flavonoid that serves as the backbone for many other flavonoids in nature, including the citrus flavonoids rutin, quercitin and hesperidin. These derivatives differ from quercetin in that they have sugar molecules attached to their quercetin backbone. Experimental studies reveal that many medicinal plants owe much of their biological activity to their high quercetin content. Abundant evidence indicates that quercetin supplementation provides anti-inflammatory effects, may inhibit the formation and/or progression of cataracts, and has anti-tumor properties. In a recent human trial conducted by M. Cruz-Correa and D.A. Shoskes, quercetin supplementation (in conjunction with curcumin, another natural supplement) reduced colon cancer incidence in high-risk subjects. The study is discussed further in this review article.

## Anti-Inflammatory Effects

Quercetin inhibits the manufacture and release of histamine and other allergic/inflammatory mediators, which gives quercetin supplementation application in a variety of inflammatory and allergic reactions (arthritis, joint inflammation, asthma, hay fever, lupus, etc.). It also demonstrates impressive anti-inflammatory and antioxidant properties, and like some other flavonoids (e.g. genistein, diadzein), appears to possess phytoestrogen effects. In one human trial, quercetin supplementation demonstrated improvement in prostatitis, with 67 percent of patients experiencing significant improvement in the quercetin group compared to 20 percent of patients in the placebo group. This benefit may be due to its phytoestrogen activity and/or its anti-inflammatory properties.

## Inhibits Formation of Diabetic Cataracts

Quercetin inhibits the aldose reductase enzyme, which converts glucose into sorbitol. Sorbitol buildup in the lens of the eye (secondary to diabetes and hyperglycemia) is involved in the development of cataracts. Elevated sorbitol also may contribute to the development of diabetic neuropathy and retinopathy. Thus, quercetin may be beneficial in diabetes management for a number of reasons. Animal studies reveal that quercetin effectively delays the onset of cataracts in diabetic animals.

## Anti-Tumor Effects

Many flavonoids inhibit tumor formation, but quercetin has demonstrated a very consistent effect in this regard. Under experimental conditions, quercetin demonstrates a significant antiproliferative effect in regards to squamous cell carcinoma, leukemia, and cancers of the breast, ovaries, colon, rectum and brain. It is thought that quercetin down-regulates enzymes that control the rate of cellular division (i.e., protein kinase, DNA-topoisomerase, ornithine decarboxylase), in addition to its mild phytoestrogen effects. Under experimental conditions, these phytoestrogen effects have been shown to inhibit the proliferation of human breast cancer cells in test tube experiments.

## Does Quercetin Supplementation Decrease Colon Cancer Risk?

Experimental evidence has shown the mechanism of action through which quercetin can protect against the development of colon cancer in a number of experimental and animal studies: slows colon cancer cell replication, induces programmed cell death of cancer cells (apoptosis), encourages normal differentiation of colon cells and colon cancer cells, and acts as an antioxidant and anti-inflammatory agent. The addition of quercetin to cultured human colon cancer cells (Caco-2 cells: human adenocarcinoma colon cancer cells) inhibited the ability of the colon cancer cells to replicate. After exposure to quercetin, cell replication rates decreased to 51.3 percent compared to cancer cells not exposed to quercetin.

Some animal studies have shown that oral administration of quercetin reduces the development of colon cancer in animals exposed to cancer-causing agents known to induce colon cancer development. (Animals given the quercetin showed significantly lower rates of cancers than those not given quercetin.) As well, experimental studies indicate that quercetin can cause undifferentiated cancer cell lines to differentiate, and that it can protect against hydrogen peroxide-induced DNA strand breaks in human adenocarcinoma cells (Caco-2 cells).

A study in *The European Journal of Nutrition* (M.J. van Erik, et al.; 2005) demonstrated that quercetin inhibited proliferation of human colonic Aden carcinoma cells (Caco-2 cells) via a number of biological actions. These include down-regulation expression of cell cycle genes (e.g., CDC6, CDK4 and cyclin D1), down-regulation of cell proliferation, and induced cell cycle arrest.

The strong experimental and animal research cited above led researchers to test whether quercetin could prevent colon cancer in human subjects, who are known to be at high risk for colon cancer development. Individuals with a hereditary condition known as familial adenomatous polyposis are known to have a high risk of developing colon cancer, as they produce numerous polyps in the large bowel, which are prone to undergoing conversion to malignancy. In a study involving five patients with familial adenomatous polyposis (FAP: an autosomal-dominant disorder characterized by the development of hundreds of colorectal adenomas and eventual colorectal cancer) and prior colectomy (four with retained rectum and one with an ileal anal pouch), supplementation with curcumin and quercetin reduced the number and size of ileal and rectal adenomas.

The five patients received oral supplementation with 480 mg of curcumin and 20 mg quercetin, three times a day. At treatment end, the number and size of the polyps had decreased in all five patients, with a 60.4 percent mean decrease in the number of polyps and a 50.9 percent mean decrease in the size of polyps. Additionally, minimal adverse side effects and no laboratory abnormalities were observed in the patients during the treatment period. Thus, the findings of this study indicate that supplementation with curcumin and quercetin may reduce the number and size of ileal and rectal adenomas in patients with FAP, and may help to prevent colon cancer development in general.

Curcumin was tested with quercetin in this study because it also shares many of the same anti-colon cancer properties as quercetin, according to experimental and animal studies. Curcumin is a constituent of the spice turmeric and can be found in many supplements used to reduce joint inflammatory conditions?

In regards to the preventive dosages of quercetin, large bowel concentrations of quercetin can reach 100 micromoles in the intestinal lumen after ingestion of a quercetin supplement (250-500 mg). Studies show that the addition of only 50 micromoles to human adenocarcinoma cells (Caco-2 cells)

can inhibit their proliferation by more than 50 percent.

## Dosage

*Anti-inflammatory/anti-allergy:* As a single agent: 200-400 mg, three times per day. Combinations of bromelain and quercetin have been shown to potentiate or enhance each other's anti-inflammatory activity. The amount of bromelain should be equal to the amount of quercetin. Bromelain also enhances the absorption of quercetin.

*Diabetes (neuropathy or cataract protection):* Consider 200-400 mg, three times per day.

*Colon support:* The recent study by M. Cruz-Correa and D.A. Shoskes suggests supplementation with 60 mg of quercetin and 1,440 mg of curcumin per day may reduce the risk of colon cancer.

## Colon Cancer

Colon cancer is the second leading cause of cancer death in North America, after lung cancer. Studies reported in the *Journal of the National Cancer Institute* indicate that 70 percent to 90 percent of all colon cancer cases are produced by faulty dietary and lifestyle factors. In addition to quercetin and curcumin supplementation, a number of other lifestyle practices are associated with decreased risk of colon cancer, some of which include:

- low animal fat diet;
- calcium intake above 1,200 mg per day;
- blood levels of vitamin D above 85 nmol/L;
- regular exercise;
- alcohol consumption below two drinks per day (average);
- reduced intake of foods containing nitrate salts, heterocyclic amines, and polycyclic aromatic hydrocarbons (from smoked, BBQ, charred and pan-fried meats) smoked, BBQ, charred and pan-fried meats);
- high intake of cruciferous vegetables and dietary fiber;
- selenium supplementation at 100-200 mcg per day (which can be from a multiple vitamin and mineral);
- folic acid intake of 400 mcg per day from a supplement (can be from a multiple vitamin and mineral supplement);
- at least 1 gram per day of omega-3 fats;
- higher-than-average intakes of vitamin C and supplementation with vitamin E (at least 100 IU per day);
- not smoking.

## Adverse Side Effects and Toxicity of Quercetin

Animal studies demonstrate that quercetin is extremely nontoxic and noncarcinogenic. In rare cases, allergic reactions to quercetin can occur in humans.

## Quercetin Drug-Nutrient Interactions of Importance

Estradiol (found in oral contraceptives and hormone replacement therapy) may interact with quercetin. Quercetin may slow down the detoxification of estradiol by liver enzymes. There are no human reports of quercetin potentiating the effects of estradiol through this mechanism at this time.

Felodipine is a calcium channel blocker used in the treatment of congestive heart failure, hypertension and Raynaud's syndrome. Test-tube studies indicate quercetin inhibits the enzyme in the liver that is responsible for the breakdown of felodipine. This may result in higher, more potentially dangerous levels of felodipine in the bloodstream, although no human reports of adverse effects have been reported to date.

## Resources

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