

## Points to Consider When Using Herbal Supplements in Cancer Patients

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Received: 19 July 2019

Published: 24 October 2019

**Keywords:** *Herbal Supplements; Colon Cancer; Chemotherapy*

Herbal supplements are being increasingly recognized as useful complementary treatments for cancer patients. These types of supplements are widely used by those recently diagnosed with cancer, in current treatment, and long-term survivors. The most common reasons for using herbal supplements are the ability to help oneself, boost the immune system, provide more energy, and help prevent cancer recurrence [1]. During cancer treatment, the use of the herbal supplement can help to decrease and alleviate symptoms caused by chemotherapy, while supporting the body in its recovery period.

Herbal supplements are generally self-prescribed; this could pose a problem because consumers are unable to make truly informed decisions about their use since most information available in the media and on the internet is misleading [2]. It is not uncommon that manufacturers overstate herbal supplements efficacy and minimizes their potential toxic effects. When properly combined with conventional chemotherapy treatment, certain herbs may help people to live longer, decrease chemotherapy side effects, and help to prevent cancer recurrence [3]. However, due to possible interactions with anticancer medication, it is imperative that patients considering using herbals supplement should consult with their treating physician first. Among the most popular herbal supplements used, we can find the following:

### Green Tea

This popular drink is rich in polyphenols, a substance with antioxidant and anti-inflammatory properties. The active component in green tea is epigallocatechin-3-gallate (EGCG). EGCG, at a dose of 200mg twice daily, appears to be safe. The anticancer effects of EGCG are thought to be via inhibition of enzymes

involved in cell replication and DNA synthesis, interference with cell-to-cell adhesion or inhibiting intracellular communication pathways essential for cell division. Concentrations of 30 $\mu$ g/mL of EGCG were shown to inhibit lipoxygenase-dependent arachidonic acid metabolism in human colon mucosa and colon tumors, which may alter the risk for colon cancer [4]. Other studies suggest that EGCG inhibits topoisomerase I (essential for cell survival) in colon carcinoma cells and may hold therapeutic potential. EGCG was also shown to inhibit DNA replication in leukemia cell lines and to modulate vascular endothelial growth factor leading to apoptosis in leukemic cells.

Among the possible interactions of green tea, we find that EGCG and other polyphenols in green tea can inhibit the therapeutic effects of bortezomib (Velcade) and other boronic acid-based proteasome inhibitors. In a murine model, EGCG was able to increase the oral bioavailability of tamoxifen. However, the clinical relevance of this finding remains unknown. EGCG was reported to inhibit transport of irinotecan and its metabolite SN-38 into biliary elimination, resulting in their enhanced half-life, which can increase toxicity. Green tea modulates UGT enzymes *in vitro* and can amplify the adverse effects of drugs metabolized by them. Green tea extract inhibits CYP3A4 and may affect the intracellular concentration of drugs metabolized by this enzyme [5].

## Ginger

This herb can decrease nausea and vomiting from chemotherapy. The rhizome of ginger possesses an array of bioactive compounds, such as gingerols, shogaols, zingiberene, zingerone, and paradol, that may stimulate oral and gastric secretions, regulate gastrointestinal motility, interact with the 5HT3 and NK1 receptors involved in nausea and vomiting reflex, and act as a scavenger for free radicals [6]. Gingerols are the primary active component in fresh ginger and shogaols are the most abundant active component in dried ginger. Most studies agree that a dosage of up to 4 grams a day can be considered safe. The most significant reduction in nausea occurred with 0.5-g and 1.0-g doses of ginger. Also, time of day had a substantial effect on nausea, with a linear decrease in nausea symptoms over 24 hours on day 1 of chemotherapy for patients using ginger.

Most importantly, ginger has not been shown to inhibit the effectiveness of chemotherapeutic drugs

Ginger inhibits NF- $\kappa$ B activation and suppressed NF- $\kappa$ B-regulated gene expression induced by carcinogens. Other studies suggest that ginger decreased lipid peroxidation and increased enzymatic and nonenzymatic antioxidant levels to reduce oxidative stress and inflammation [7]. Additionally, ginger effectively suppresses ultraviolet B-induced skin carcinogenesis. However, it might increase the possibilities of hemorrhages, so it should be avoided before surgery. Moreover, ginger, along with other herbs such as feverfew, garlic, and ginkgo, can alter bleeding time and is recommended not to combine them with warfarin sodium [8]. Ginger has been shown to cause diarrhea, heartburn, and gastric irritation at doses of 6 grams and higher.

## Ginseng

Ginseng is an “adaptogen” that allows the body to respond to physical and emotional stress. Ginseng contains various active components, such as ginsenosides, polysaccharides, flavonoids, volatile oils, amino acid, and vitamins. Among these active components, ginsenosides and ginseng polysaccharides appear to be

for the anticancer effect [9]. The quality of ginseng is directly related to age at harvesting. When ginseng is harvested at 5 to 6 years, it is considered the “best” because ginsenoside content is at its highest. In high doses, ginseng can reduce cancer-related fatigue and is regarded as a great chemotherapy adjuvant, due of its low toxicity and many desirable properties such as antiangiogenesis, antiproliferation, anti-inflammation, antioxidation, apoptosis, and immune modulation effects [10]. In *in-vitro* studies, ginseng anticancer activity was demonstrated in cell cultures of ER+ breast cancer tissue. American ginseng inhibited cell growth and was synergistic with tamoxifen, cyclophosphamide, methotrexate, doxorubicin, and 5-fluorouracil. Cell cultures of human colorectal cancer were impacted by American ginseng, which caused apoptosis, possibly through mitochondrial damage.

Due to additive effects, ginseng should not be used with estrogens or corticosteroids. This property is likely two-fold. First, a fungus was identified on the roots, which in one study did not account for adverse events but may be associated with possible estrogenic activity. The second is related to the extraction method. Alcohol extraction confers estrogenic properties to the ginseng and should be avoided, especially by those for whom estrogen is contraindicated. Consumers should be aware of the type of ginseng they are purchasing, including whether it is ground root or an extract. Ginseng seems to be effective in preventing or treating cancer-related fatigue and may improve quality of life.

## Astragalus

Astragalus might decrease the side effects of chemotherapy, such as nausea and vomiting. The antitumor effect of astragalus may be related through activation of the antitumor immune mechanism of the cancer patient stimulating and increasing the immune system and reducing inflammation [11]. The recommended dose is between 250 and 500mg, three to four times a day, standardized to 0.4% 4-hydroxy-3-methoxy isoflavone 7-sug. When making tea, boil three to six grams of dried root per 12 ounces of water three times a day. Astragalus can decrease the effect of other medicines such as cyclophosphamide, basiliximab, cyclosporine, daclizumab, and prednisone.

## Guarana

Guarana is a natural stimulant present in a plant native to the Amazon basin. It can help with chemotherapy-related fatigue, especially in breast cancer patients. Guarana may help reduce, stabilize weight, and increase appetite due to its chemical composition, which includes a higher content of purinic alkaloid caffeine (1,3,7-trimethylxanthine) [12]. Caffeine, the most widely used neuroactive compound in the human diet, has antiproliferative activity and can induce cell cycle arrest and apoptosis. Guarana is also rich in tannins and the stimulants theophylline and theobromine. Guarana demonstrated antioxidant effects by inhibiting lipid peroxidation. Chronic exposure to Guarana seed extract can produce an anxiolytic effect involving the dopaminergic and serotonergic neurotransmission systems [13].

Considering these effects, Guarana is currently commercialized in herbal and energetic beverages due to its stimulant properties. Studies of breast cancer patients using 50 milligrams (mg) dose twice daily showed anti-fatigue effects. Guarana has some antiplatelet activity and can, therefore, have additive effects; thus, it should be avoided when using anticoagulant or antiplatelet drugs.

Despite the increased use of herbal supplements over the past decade, most compounds did not generate significant interest and acceptance by medical practitioners. The main issue noticed by many medical practitioners is the lack of evidence-based information and guidelines for the routine and regulatory application of herbal medicines as “drugs.” Because all herbal supplements products are complex mixtures that usually include several active ingredients, it is not surprising to find little evidence-based information regarding the biologic effects of these substances. Herbal supplements sold in health food stores and pharmacies must meet quality standards as well as provide information about their composition. This includes the specific content, dose of the product, and how safe it is. The dosage of the active ingredient can also vary widely between products [14]. These differences are due to the lack of regulations and knowledge of adequate doses of such products. Standardization and monitoring for adulteration are needed to limit the present problem of variation in the composition of active constituents. In orders to sell, some manufacturers also make inflated claims about their supplements.

In summary, cancer patients interesting in using herbal supplements should first discuss potential benefits and contraindications with their doctors. Then when buying herbal supplements, patients should purchase single-ingredient products, verify the dosage, look for a certification which indicates that the product has met specifics manufacturing standards, and check the label to see if researchers have tested the product [15]. Lastly, patients should be skeptical of claims on labels, particularly those that say the product will cure cancer. No single remedy or treatment can successfully treat all cancers. And no dietary or natural product can cure cancer.

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