Herbal medicine and cancer prevention: myth or not?

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Abstract
Introduction
Cancer is a major health problem worldwide. Many studies have been conducted to investigate the prevention and treatment of cancer. Till date, no absolute preventative and curable agent has been found. Complementary and alternative medicine modalities are commonly used for cancer prevention and care. A very well-known type of these modalities is herbal medicine. Many of the drugs in cancer care originated from natural products. As a healthy diet, rich in vegetables and fruits, is one of the protective factors for cancer; plants and derivatives are the focus of many studies. Green tea, lycopene and selenium are some of them. In this review, the association between cancer prevention and herbal medicine is discussed.

Conclusion
Although a healthy diet that is rich in fruits and vegetables is crucial for cancer prevention, herbal remedies and specific dietary supplements have not been shown to prevent cancer, till date. Further studies should be conducted on this issue regarding standardisation, possible side effects, drug interactions and personal characteristics.

Discussion
Back to the Future: Herbal Medicine
The WHO definition of traditional medicine (including herbal drugs) is ‘comprising therapeutic practices that have been in existence, often for hundreds of years, before the development and spread of modern medicine and are still in use today’ and another definition is ‘the synthesis of therapeutic experience of generations of practising physicians of indigenous systems of medicine’. We can define two terms related to this issue: one is traditional preparation (which consists of medicinal plants, minerals, organic matter, etc.) and the other is herbal drug (traditional medicines which are composition of medicinal plant preparations used for therapy). Herbal medicine is one of the biologically based practices of complementary/alternative therapies. Especially in recent years, plants are getting more attention as drugs worldwide. It has been in use for about 80% of the world for thousands of years. They are used for several health-related issues including chronic diseases and cancer care. They are especially used for disorders, which have no conventional medicinal cure.

Many people expect cure for many diseases from herbal medicine; however, we have to accept that there are pros and cons for herbal medicine as well. People prefer herbal medicine as conventional drugs can be very toxic, while herbs are presumed innocent. Besides, other efforts to prevent cancer are more expensive as compared with the use of plants. Although there are many studies on herbal medicines, some queries still remain. Ingredients of some remedies have not been well established. The remedies can vary depending on the change in location, culture and religion. Standardisation, another problem of herbal remedies, remains unsolved as their compositions can vary even in the same brand due to...
several factors\textsuperscript{13}. This results in different pharmacological effects. WHO, also, pointed out major challenges in regulation of herbal medicine as regulatory status, monitoring and controlling of safety, quality, efficacy issues and lack of knowledge about these drugs\textsuperscript{14}.

Cancer Prevention: Is it Utopia?

Cancer is a major health problem and a leading cause of death worldwide. One-third of the world’s population suffers from cancer and it is responsible for one-fifth of all deaths\textsuperscript{3}. In 2007, 11.3 million people developed cancer and 7.9 million died because of cancer\textsuperscript{9}.

As about 40% of all cancer deaths appear preventable\textsuperscript{15}, cancer prevention is regarded very important and should be the basis of cancer control programmes. Among patients with chronic diseases including cancer, consumption of herbal preparations and drugs is very common. Some of the epidemiological data support the beliefs of their benefits. For instance, cancer rates are higher in Western countries than in Asian countries where traditional medicine is much more common\textsuperscript{17}.

There are three stages in the development of cancer: initiation, promotion and progression\textsuperscript{16}. Prevention activities can target each step of this process. Chemoprevention, either natural or synthetic, can be applied in these three steps. Causes of cancer include viruses, exposure to radiation, ultraviolet rays, alkylating agents, tobacco, ethanol, inheritance and high-fat, low-fibre diet\textsuperscript{5}. Although carcinogenesis is not completely understood, it can be stated that cancer is the result of a process, in which cellular pathways are affected by multiple risk factors and agents within a certain time\textsuperscript{2}. DNA damages occur within this process and result in conversion of normal cells into cancer cells. Oncogenes and tumour suppressor genes play controlling role in carcinogenesis. Oncogenes, their products and enzymes that play a role in the division of cancer cells are the focus of cancer therapy\textsuperscript{4}.

Primary prevention of cancer is less expensive and easier, as it is mainly based on control and modification of the risk factors. Risk factors are often regarded as modifiable and fixed (such as sex and inheritance)\textsuperscript{17}. As fixed ones cannot be changed, focus of cancer prevention programs is the modifiable risk factors that can be simply divided into two groups—lifestyle and environmental. Environmental risk factor generally means the exposure of carcinogetic substances. Avoiding and controlling this kind of risk factors sometimes appear impossible. Although cancer prevention actions have included reducing carcinogenic exposure, clinical interventions for chemoprevention and health promotion, lifestyle changes (healthy diet, weight control, etc.) have the precedence in a cancer prevention programme\textsuperscript{17}.

Healthy diet is accepted as one of the most important lifestyle changes to reduce the risk of cancer\textsuperscript{4}, so natural dietary agents such as fruits, vegetables and spices have drawn the interest of scientific and general population to their probable cancer prevention features. Fruits and vegetables can provide not only fibre and vitamins, but also substances such as polyphenols and alkaloids. Many trials have been held to show if micronutrients in fruits and vegetables reduce cancer incidence\textsuperscript{4}. Some epidemiological studies have indicated an inverse relationship between consumption of vegetables and fruits, and risk for many types of cancer\textsuperscript{5,15,17}. The important point is most of the trials on herbal drugs are in vitro studies\textsuperscript{9,13,18–23}.

Help From an Old Friend

The term ‘dietary supplement’ is used commonly for a natural product that contains vitamins, minerals, herbs or other botanicals, to supplement the diet\textsuperscript{8,11}. Many types of dietary components have been evaluated, either in whole-food forms or as nutritional supplements, to prove beneficial in cancer prevention, treatment and care. According to the literature, specific dietary supplements are not recommended for cancer prevention, though certain populations may benefit from their use\textsuperscript{11}.

‘Food, Nutrition and the Prevention of Cancer: a global perspective’ report suggests that higher consumption of several plant foods protects against cancers\textsuperscript{4}. This report defines ‘plant-based’ as ‘diets that give more emphasis to those plant foods that are high in nutrients, high in dietary fibre (and so in non-starch polysaccharides), and low in energy density’. It also supposes non-starchy vegetables and fruits, including broccoli, carrots, turnips and so on, as protective against some cancers and weight control. Although there are pros and cons in the literature, evidence-based guidelines do not recommend specific dietary supplements for cancer prevention\textsuperscript{11}. They also recommend dietary supplements including botanicals and vitamins and minerals to be evaluated for their harm/benefit ratio including side effects and drug interactions\textsuperscript{11,25,26}.

Some Examples of ‘Anticancer’ Herbals and Derivatives

Many of the plants and their derivatives have been under evaluation for their effects in cancer prevention. Among them, there are biologically active components such as curcumin, lycopene, capsaicin, gingerol, catechins, isothiocyanates, isoflavones, vitamin E and C and selenium. Flavonoids, tannins, isoprenoids and phytosterns are commonly investigated. All of these agents are thought to have anti-inflammatory effect that may influence the carcinogenesis. Because 69% of anticancer drugs originated from natural products, searching for new anticancer drugs from herbal medicine is quite understandable\textsuperscript{3}.
**Critical review**

Tannins are natural constituents of green tea that are thought to prevent cancer by inducing cell death in cancer cells, at certain doses. Iso-prenoids are shown to suppress the proliferation of promyelocytic leukaemia cells. Phytosterols are considered as protective agents against cardiovascular diseases and cancer development. They tend to improve lipid profiles (red clover, soy and flax), arterial compliance (red clover and soy) and bone density (red clover and soy).

Cortés-Jofré et al. analysed drugs for lung cancer prevention and found no evidence for recommending supplements of vitamins A, C, E, and selenium for the prevention of lung cancer and lung cancer mortality in healthy people. On the contrary, they found association between use of beta-carotene and increase in lung cancer incidence among smokers or persons exposed to asbestos.

Daily intake of 1 g dietary calcium is found to have moderate protective effect on colorectal adenomatous polyposis but no preventive effect on colorectal cancer.

Again in a review, 20 randomised clinical trials were assessed and no protective effects of antioxidant supplements (beta-carotene, vitamin A, vitamin C, vitamin E, and selenium vs. placebo) against gastrointestinal tract cancers were found. Besides, these supplements appear to increase mortality. Although selenium alone is reported to have protective effects, it needs to be confirmed by further studies.

There is no evidence for a relationship between low selenium exposure and an increased risk of cancer. Still, it is not suggested to be used in men, women or children for protection.

Green tea (Camellia sinensis), which can also provide catechins, is another product, which is under scrutiny. Although drinking green tea appears to be safe at regular, habitual use and may have some beneficial effects on cancer patients, there is no convincing proof for their cancer preventive effects. Besides, patients on bortezomib therapy should avoid using it.

In vitro studies, cumin and saffron components are shown to have some beneficial effects in tumour cells, but there is no evidence on availability for cancer prevention.

Lycopene is another popular supplement and its effects on prostate cancer and oral cancers were studied; however no advantage has been reported till date.

Flavonoids are very common. Based on the literature, they are accepted to have antibacterial, anti-viral, anti-inflammatory, anticancer and anti-allergic features; however, their effects on colorectal neoplasm prevention remain conflicting and unproven. Some beneficial effects on leukaemia, as an adjuvant agent, have been reported.

Another famous plant, Panax ginseng, is known as immune system modulator, anti-stressor, and anti-hyperglycemic, but is not proven as a cancer preventative agent currently.

*Aegle marmelos* (stone apple) is presumed to have antioxidant activity. *Allium cepa* (onion) and *Allium sativum* (garlic) are thought to inhibit cancer cells in addition to their other benefits. *Aloe vera* is assumed to have anticancer activity by stimulating the immune system. *Gingko biloba* is a kind of tree that is said to have antioxidant feature. *Brassica oleracea* (broccoli) and other cruciferous vegetables have been investigated for their potential chemopreventive features.

Antioxidant and anticancer activities of phytochemicals are thought to come from their synergistic effects. This explanation can be true as they cannot prevent cancers alone, and whole vegetables and fruits are needed to decrease cancer incidences.

There are many studies in the literature suggesting that all these vegetables and derivatives mentioned earlier are cancer protective. However, systematic reviews report that further trials, especially in vivo, well-established, randomised controlled ones, are needed for the investigation of their actual effects.

**Conclusion**

Although a healthy diet that is rich in fruits and vegetables is crucial for cancer prevention, herbal remedies and specific dietary supplements have not been shown to prevent cancer; till date. Further studies should be held on this issue regarding standardisation, possible side effects, drug interactions and personal characteristics. Natural products appear to continue to be the favourite and the focus of cancer prevention studies hereafter. At present, lifestyle changes, such as healthy diet, exercise and weight control and so on, should be targeted in prevention programmes. Cancer is hoped to be completely eliminated in the future. Every effort to prevent cancer will be worthwhile and valuable.

**Abbreviations list**

WHO, World Health Organization.

**References**


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