



Evidence from Clinical Research for the Use of Phytochemicals in Cancer Treatment

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Abstract

In both industrialized and developing nations, cancer continues to be one of the leading causes of death. Many patients now have dismal prognoses despite receiving comprehensive therapy. The search for novel anticancer drugs with improved effectiveness and fewer side effects has so continued. Numerous medicinal herbs have been found to have an anticancer effect, according to traditional advice and experimental investigations. Several phytochemicals have also been demonstrated to have antiproliferative, pro-apoptotic, anti-metastatic, and anti-angiogenic properties in in vitro and animal investigations. There is, however, no evidence of their therapeutic efficacy and very few have been evaluated on cancer patients. Additionally, there are certain phytochemicals that have only been shown to improve quality of life or symptoms associated with cancer; there are no conclusive data to support any anticancer benefits. The favorable benefits of phytochemicals overall on different forms of cancer have been substantiated by clinical studies, which was the review's main focus. The clinical evidence for curcumin, green tea, resveratrol, and *Viscum album*'s anticancer benefits was adequate, according to the literature evaluation. Additionally, a summary and discussion of these phytochemicals' key results was provided.

Keywords: Cancer; Phytochemical; Plant; Tumor

Introduction

Both emerging and developed nations are dealing with an increasing number of cancer cases. In 2012, 8.2 million people died from cancer, according to a World Health Organization data dated February 2014. Additionally, it has been predicted that over the next 20 years, there would be an increase in yearly cancer cases from 14 million in 2012 to 22 million. Chemotherapy, radiation, and surgery are the primary cancer therapies now available. Antimetabolites (like methotrexate), DNA-interactive agents (like cisplatin, doxorubicin), antitubulin agents (like taxanes), hormones, and molecular targeting agents are some of the most used chemotherapy medications. However, there are a number of undesirable side effects associated with their therapeutic usage, including hair loss, bone marrow suppression, drug resistance, gastrointestinal lesions, neurologic dysfunction, and heart toxicity. Furthermore, many patients have dismal prognoses even with the current rigorous therapies [1]. The hunt for novel anticancer drugs that are more effective and have fewer adverse effects has thus

continued. For the creation of novel treatments for many ailments, natural substances are excellent sources. Numerous medicinal plants and herbal compounds have been shown in studies to have anticancer properties. Additionally, it has been demonstrated that a variety of phytochemicals that have been extracted from medicinal plants can reduce cell proliferation, trigger apoptosis, slow metastasis, and block angiogenesis. Some of these plant-derived substances are being utilized often in the treatment of cancer patients. For instance, the therapy of such individuals has made use of taxol analogues, vinca alkaloids (vincristine, vinblastine), and podophyllotoxin analogues.

Using the search phrases cancer, clinical, plants, herbs, and patients, a literature search was undertaken on Google Scholar, Medline, and Science Direct to find the clinical trials that were included in this review. The publication only contains clinical trials that looked at how phytochemicals affected cancer patients. There have been no conclusive findings about the anticancer effects of various phytochemicals (such as Aloe vera and *Withania somnifera*), but only good effects on symptoms associated to cancer (such as fatigue, pain, vomiting, and anorexia) or on quality of life have been noted. These clinical trial reports weren't included. Additionally, for several phytochemicals, the number of studies demonstrating their ability to treat cancer patients with tumors was not greater than the number of studies indicating no such ability. These phytochemicals (such as *Punica granatum*) were not included because more research is needed to determine how effective they are [2].

Discussion

Anticancer phytochemicals

Allium sativum: Numerous therapeutic properties of *Allium sativum*, or garlic, have been noted, including antidiabetic, hypolipidemic, antibacterial, antihypertensive, and anticancer activities. Consuming garlic may have a preventive impact against gastrointestinal malignancies, according to epidemiologic research. Garlic consumption has recently been shown to slow the growth of colorectal adenomas in people. Additionally, a randomized double-blind placebo-controlled experiment revealed that giving garlic to patients with advanced digestive system cancer enhances the number and activity of natural killer cells. Garlic may reduce the risk of cancer-related mortality because an increase in natural killer cells is linked to a good tumor outcome [3].

Camptothecin: *Camptotheca acirminata* and *Mappia foetida* are two plant species from which camptothecin, a natural alkaloid, may be isolated. Targeting topoisomerase I, an enzyme involved in the relaxing of DNA supercoils, it is a strong anticancer phytochemical. Camptothecin derivatives have been created and are now undergoing clinical studies. In a phase I clinical research, 52 and 29 patients with refractory malignancies, respectively, received 20-(S)-camptothecin and 20-(S)-9-nitrocamptothecin. In a number of individuals with breast cancer (disappearance of liver mass), prostate cancer (fall in the rapidly rising PSA level), and melanoma (regression of skin tumor nodules), both substances demonstrated anticancer activity. Several patients with cholangiocarcinoma (decrease in extensive liver metastases), breast carcinoma (disappearance of cutaneous metastases), and ovarian carcinoma also showed partial responses.

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Another research showed that some patients with advanced lung malignancies experienced good outcomes (stabilization and partial remissions) after receiving aerosolized liposomal 9-nitrocamptothecin. A novel camptothecin derivative, CPT-11, was also said to have the ability to fight metastatic colorectal cancer by inducing an antitumor impact [4].

Curcumin: The rhizome of the turmeric plant (*Curcuma longa* Linn) yields curcumin, a yellow polyphenol (diferuloylmethane). Its therapeutic benefits against a number of ailments, including diabetes, cardiovascular disease, arthritis, gastrointestinal ulcers, nephropathy, and hepatic disorders, have been the subject of extensive experimental and clinical studies during the past 10 years. Curcumin's anti-inflammatory, antioxidant, and cytoprotective qualities are what give it its positive effects. Additionally, it has been claimed that curcumin has anticancer properties due to a variety of activities it has on mutagenesis, cell cycle control, apoptosis, oncogene expression, and metastasis. Curcumin has the ability to influence cancer in all of its stages, including start, promotion, and progression [5]. 25 patients with pancreatic cancer participated in an oral curcumin treatment in a nonrandomized open-label research. Two of them achieved clinical responses, with one having stable illness for more than 18 months and the other seeing tumor regression. When curcumin was ingested, lymphocyte Glutathione S-Transferase (GST) activity was also significantly reduced. It has been established that the GSTs, a family of phase II detoxifying enzymes, play a role in the emergence of chemotherapeutic drug resistance. Curcumin's anticancer impact is achieved by its inhibitory effect on transcription factors and downstream gene products, modulatory effect on growth factor receptors and cell adhesion molecules involved in angiogenesis, tumor development, and metastasis, and antiproliferative effect in a variety of malignancies [6].

Green tea: Green tea is a widely consumed beverage, particularly in Asia, Europe, and North America. A number of biological features, including anti-inflammatory, anti-arthritic, antibacterial, antioxidative, neuroprotective, antidiabetic, antiangiogenesis, and anticancer activities, have been described for this beverage. Proteins, amino acids, carbs, minerals, lipids, vitamins, and volatile components are all present in green tea. Recent research has shown that the majority of the biological effects of green tea are caused by catechins, a kind of polyphenol [7].

Panax ginseng: In Asia, ginseng roots have been used medicinally for thousands of years. The three most often utilized ginsengs in the world are *Panax quinquefolius* (American ginseng), *Panax japonicus* (Japanese ginseng), and *Panax ginseng* (Korean or Chinese ginseng). Clinical research have shown that *P. ginseng* both lowers cancer incidence and has positive benefits on cancer patients. According to case-control studies, drinking ginseng tea, juice, or fresh slices lowers the incidence of most cancers, including those of the pharynx, larynx, esophagus, stomach, colon, pancreatic, liver, lung, and ovary. It was shown that ginseng use before to cancer diagnosis was related with a higher overall survival rate in a group of 1455 breast cancer patients. Additionally, a randomized placebo-controlled experiment revealed that *P. ginseng* helped certain patients with gynecologic or hepatobiliary cancers in terms of their physical and mental health [8,9].

Other anticancer phytochemicals: Along with the ones already listed, the following phytochemicals have also been discovered to be helpful for cancer patients: *Aloe arborescens*, combretastatins, *Ganoderma lucidum*, *Nigella sativa*, *Panax quinquefolius*, and

Scutellaria barbata. Only one or two clinical trials from independent authors could be located to substantiate the anticancer effects of each one, though. Therefore, more clinical studies are required to validate their therapeutic efficacy in the treatment of cancer [10].

Conclusion

Finding novel treatments is urgently needed since cancer is a frequent cause of death and is becoming more prevalent worldwide. The study of medicinal plants has always been crucial for the development of novel treatments for human ailments. Therefore, the discovery of new anticancer drugs may be a suitable fit for this source. Only a few of the hundreds of plants that have been researched for their ability to prevent cancer have successfully passed in vitro tests and animal studies and are currently undergoing clinical trials. *Allium sativum*, camptothecin, curcumin, green tea, *Panax ginseng*, resveratrol, *Rhus verniciflua*, and *Viscum album* all provided sufficient clinical data to support their anticancer benefits, according to our literature search. As a result, it appears that they can be used in conjunction with modern chemotherapy medications to treat a variety of cancers. Although a number of other phytochemicals might be included in this list, it is preferable to wait until further clinical research confirms their anticancer efficacy before adding them. A general drawback of cancer phytotherapy is that the majority of relevant research has methodological errors, such as small sample numbers, short trial durations, and the absence of a control or placebo group. Therefore, it is too early to make conclusions about the anticancer effects of numerous phytochemicals. Furthermore, there is still much to learn about the pharmacokinetics, pharmacological interactions, optimal doses, long-term safety, and negative consequences of phytochemicals that have been suggested as cancer treatments.

On the other hand, thankfully, in vitro investigations have identified the molecular processes behind the anticancer effects of various medicinal plants. These defense mechanisms may consist of a mix of antioxidation, carcinogen inactivation, antiproliferation, cell cycle arrest, induction of apoptosis, and suppression of angiogenesis. Multiple phytochemicals in herbal medicines are thought to have stronger effects than just one phytochemical alone. According to this theory, combinations of the anticancer phytochemicals may have a greater impact and produce more effective cancer treatment agents. Future clinical trials on this subject are especially necessary given the promising early results.

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