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Medicinal plants used in the prophylactic treatment of cancer

Debolina Dattaray
West Bengal University of Animal and Fishery Sciences, Belgachia, Kolkata

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Introduction

The word cancer was derived from the Greek word "Karkinos" given by the father of medicine, Hippocrates, who used this term to describe "tumors". Cancer is the second leading cause of death and a major public health burden in both developed and developing countries of the world. The main causative agent of cancer may be a genetic predisposition, inappropriate diets, and sedentary lifestyle, and occupational and environmental reasons as well.

To combat this emerging disease threat, various alternative treatment approaches are trying to be explored besides, chemotherapy, hormonal therapy, and radiation. Nowadays, phytomedicines are a recent trend, where people from all states are focusing on these natural remedies for their primary health care benefits and also to avoid severe possible ailments. Moreover, plants have been serving not only as food but also as medicines for both human and animals from the time immemorial. The multiple chemical constituents present in the plant either have an additive or synergistic effect in preventing multidrug-resistant strains and improving the cell signaling network. The record of Egyptian medicine is the "Ebers Papyrus" (1500 BCE) which documents over 700 drugs, mostly of plant origin, that is used for the treatment of cancer.

The interest in the consumption of green tea for different detoxification remedies and other healthcare benefits has noticeably increased worldwide. Moreover, the antioxidant compound present in green tea is, EGCG (epigallocatechin-3-gallate), which has significantly reduced breast cancer growth in animal studies. The high levels of catechins, in green tea, have also significantly increased apoptosis in colon cancer cells and reduced the expression of the vascular endothelial growth factor (VEGF) and its promoter activity in various studies.

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The juice, peel, and oil of *Punica granatum* (pomegranate) have also some beneficial anticancer property, which interferes with tumor cell proliferation, cell cycle invasion, and angiogenesis. The numerous phytochemicals present in *Punica granatum*, such as punicalagin, ellagitannins, ellagic acid, and other flavonoids, like quercetin, kaempferol, and luteolin glycosides indicate the anticancer property through reduction of phosphorylation of the p65 subunit. It also inhibits the activity of the TNF receptor-induced by Akt, which is required for the activity of NFκB and thus causes subsequent inhibition of nuclear factor-κB (NFκB).

Grapes also contain an abundant amount of flavonoids and procyanidins, which play a role in reducing the proliferation of cancer cells by increasing dihydroceramide and p53 and p21 (cell cycle gatekeeper) protein levels. It can also trigger an antioxidant response by activating the transcriptional factor nuclear factor erythroid 2-related factor 2 (Nrf2). Grape seeds are therefore helpful in preventing the growth of colon cancer cells by altering the cell cycle, which would lead to causing the caspase-dependent apoptosis.

Garlic, being a remarkable plant, has multiple beneficial effects such as antimicrobial, hypolipidemic, antiarthritic, hypoglycemic, and antitumor activity. The roots of garlic have allicin and organosulfur, allyl cysteine, and S-allylmercapto-L-cysteine compound which are known to exhibit anticancer properties. They have inhibited cancer cell growth and induced apoptosis through the inhibition of the phosphoinositide 3-kinase/Akt pathway in different studies. Simultaneously, they can also increase the expression of phosphatase and tensin homolog (PTEN) and reduce the expression of Akt and p-Akt. Moreover, the chemopreventive action of garlic in carcinogenesis is mediated by the induction of phase II detoxification enzymes including glutathione transferases, quinone reductase, epoxide hydrolase, and glucuronosyl-transferase that have a detoxifying role in the metabolism of electrophilic carcinogens. Thus consumption of garlic on daily basis can reduce the chance of cancer development in individuals.

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Garlic Cloves

Myrrh is derived from the dried resin of *Commiphora myrrh* resin. The active compounds, obtained from *C. myrrh* gum are 2-methoxyfuranodiene and 2-acetoxyfuranodiene, which are members of the Furano-sesquiterpenoid family. It not only kills cancer cells in general but also kills those cancer cells that are resistant to other anti-cancer drugs. Cancer cell generally produce an inactivating protein called Bcl-2, a natural factor mainly overproduced in breast and prostate cancer, which is significantly down regulated by myrrh. One of the major advantages of this plant is that it harms only the cancer cells without affecting healthy ones.

***Commiphora myrrh* resin**

One of the other most effective drugs against breast and ovarian cancer which has also been approved clinically for cancer patients is obtained from the Pacific Yew tree, *Taxus brevifolia*. Paclitaxel derived from *Taxus brevifolia* exerts its anticancer activity by inhibiting mitosis, by binding to the β subunit of microtubules, therefore chromosomes cannot undergo spindle formation and thus apoptosis occurs. Paclitaxel induces the release of tumor necrosis factor-α (TNF- α) causes a decrease in the expression of TNF receptors.

Vinca alkaloids are isolated from the periwinkle plant *Catharanthus roseus*, also known as *Vinca rosea*. Vincristine, vinblastine, and vindesine are the first vinca alkaloids with anti-tumor activity. Vinca alkaloids bind to the tubulin protein, therefore tubulin is unable to undergo polymerization to form microtubules, the cell does not separate its chromosome during the metaphase stage, and this cause interference in the cell division and thus undergo apoptosis Classical vinca alkaloids, mainly vincristine are largely used in the treatment of hematological and lymphatic neoplasms as vincristine molecule inhibit leucocyte production and maturation and are useful in various other solid tumors (such as vinblastine in breast, testicular cancer, choriocarcinoma; vindesine in non-small cell lung cancer, breast cancer, etc.)

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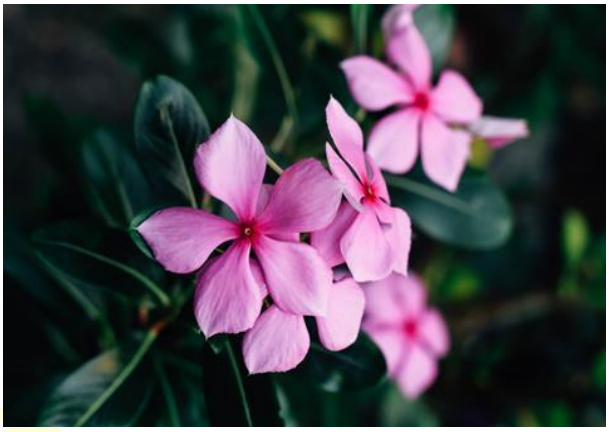
Flower and leaves part of *Catharantus roseus* plant

Saffron (*Crocus sativus*) is an ancient spice, where dried stigmas are used for flavoring and coloring food. Due to the heavy manual work involved in collecting the stigmas, it is considered to be one of the most expensive spices. Crocetin, which is an important chemical constituent of saffron, has shown significant potential as an antitumor agent in various animal models and cell culture systems. Crocetin affects the growth of cancer cells by inhibiting nucleic acid synthesis, strengthening the antioxidant defense system, inducing apoptosis, and hindering growth factor signaling pathways.



Curcumin is the yellow pigment that is found in the rhizomes of *Curcuma longa*, which is a commonly used medicinal plant. The anticancer potential of curcumin is mainly manifested by its ability to inhibit or inactivate various intracellular transcription factors, thus regulating the expression of various proteins that participate in tumor growth and development. Curcumin can inhibit the activation of NF-κβ which aids in reducing the expression of pro-inflammatory cytokines, COX-2, nitric oxide synthase, and many other factors thus diminishing cell proliferation, growth, and tumor angiogenesis.

The aswagandha plant is already known for its multiple medicinal values and is extensively used in Ayurvedic medicine and also its availability as a dietary supplement has a high demand. The root, stem, and leaves of *the Withania Somnifera* plant have been effective against various Human cancer cell lines used in various *in vitro* studies. The active component of Withania is Withaferin A, which shows the anticancer activity by inducing p53-dependent apoptosis by downregulating the

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expression of HPV E6/ E7 oncogenes and restoring the p53 pathway, thus resulting in apoptosis of cervical cancer cells.

Ashwagandha plant (*Withania Somnifera)*

Podophyllotoxins are another compound having long therapeutic history. They are obtained from the root of the Indian podophyllum plant (*Podophyllum peltatum*). Topoisomerase II is a nuclear enzyme that alters DNA tertiary structure by creating transient double-stranded breakage of the DNA backbone, allowing subsequent passage of a second intact DNA duplex through the break. Etoposide and teniposide are the two most important podophyllotoxins, which form a ternary complex with topoisomerase II and DNA and prevent resealing of the DNA break. Due to the presence of epipodophyllotoxins, the topoisomerase II-DNA intermediate cannot be reversed, thus the DNA double-strand break will lead to cell death. Teniposide has already been approved for central nervous system tumors, malignant lymphoma, and bladder cancer.

The rhizome of *Zingiber Officinalis* is ginger, one of the most widely used spices in Indian families. It is being tremendously used across the globe for traditional treatment purposes against various ailments such as indigestion, diarrhea, nausea. The anticancer properties of ginger are attributed to the presence of certain biologically active compounds, such as [6]-gingerol and [6]-paradol, as well as some other constituents like shogaols, zingerone, etc. Various studies have revealed that [6]-gingerol has inhibited angiogenesis of human endothelial cells and caused cell cycle arrest in the G1 phase through the down-regulation of cyclin D1. Apoptosis induced by gingerol is accompanied by a down-regulation of anti-apoptotic protein Bcl-2 and causes an enhancement of proapoptotic protein Bax expression. Zingerone was also found to inhibit liver microsomal lipid peroxidation and act as an effective free radical scavenger. [6]-gingerol and [6]-paradol are also known to suppress TNFα production.

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Rhizome of *Zingiber Officinalis*

Plant and their chemical compounds mediate their anticancer effects via various mechanisms such as induction of antioxidant defense mechanisms such as superoxide dismutase, reduction of DNA oxidation, induction of apoptosis by inducing a cell cycle arrest in S phase, G1 and G2 phase, reduction of PI3K, P-Akt protein activity, reduction of anti-apoptotic Bcl-2, Bcl-xL proteins, and decrease of proliferating cell nuclear antigen (PCNA). Certain plant compounds can also increase the expression of both cell cycle inhibitors, such as p53, p21, and p27, and Bax, caspase 3, caspase 7, caspase 8, and caspase 9 proteins levels.