

ANTICANCER POTENTIAL OF DIFFERENT PLANT SPECIES

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ABSTRACT

Although cancer is presently the second most common cause of death among the elderly, it will eventually overtake all other causes. The history of medicine and plants extends back to a time when the sole cure for all illnesses was herbal.^[3] Today, phytotherapy is once again receiving more attention globally. The use of natural remedies made from plants to treat illnesses illustrates how closely connected man is to his environment.^[5] A traditional or folk medical practice known as "herbal medicine" makes use of plant seeds, berries, roots, leaves, bark, flowers, and extracts for therapeutic purposes. Every day, more studies are being done and more herbal medicine is being used to cure illnesses. Traditional medicine has long held that some herbs may be used to cure illnesses including typhoid, cholera, measles, and others.^[6] Additionally, it works as an antioxidant and a free radical scavenger, and it fights weakness and sickness (including cancer).^[7]

INTRODUCTION

A significant proportion of the global population, particularly in developing countries, continues to rely on traditional materia medica, including medicinal plants and other natural resources, to meet their everyday healthcare needs. According to the World Health Organization (WHO), approximately 80% of the world's population depends on plant-derived medicines for their healthcare requirements. Furthermore, one-quarter of all medical prescriptions consist of formulations derived from plant-based substances or synthetic analogs derived from plants.^[8] This is substantiated by the fact that medicinal plants frequently combine different chemical compounds that can improve health either alone, in combination, or in a synergistic way.^[9] They have thus been the subject of an in-depth investigation to ascertain their pharmacological potential.

People have used medicinal plants as a source of medication to treat illness since the dawn of time. Plants have long been used as a source for newly produced modern drugs and pharmacological compounds since they have substantially benefited human health. They perform a dual role in the development of new drugs and/or phytomedicines that could be used to cure diseases.^[10]

For the pharmaceutical, cosmetic, and food industries as well as more recently in agriculture for pest management, active chemicals from medicinal plants provide a plentiful source.^[11] Chemically speaking, bioactive herbs may contain minerals, probiotics, prebiotics, fatty acid and structural, amino acid, isoprenoid derivatives, carbohydrate derivatives, phenolic chemicals, and carbohydrate derivatives.(Ca, Zn, Cu, K, Se).^[12]

Cancer is a group of potentially lethal diseases that are characterized by the unregulated growth and division of aberrant cells. (While the cause of the majority of cancers is unclear, it is known that 5–10% of cases are inherited. Poor diets, some illnesses, inactivity, obesity, smoking, and pollution are additional reasons.

Cancer cells rewire their metabolism to maintain bioenergetics, redox status, cell signaling, and biosynthesis in what is frequently a malnourished, poorly vascularized microenvironment.^[14] To supply precursors for biosynthetic pathways, tumor cells enhance the digestion and absorption of specific nutrients. As a result, medicinal plants and the products derived from them may also possess anti-mutagenic and anti-cancer characteristics. By aiding in anti-mutagenicity and cancer treatment, natural compounds (secondary metabolites) from plants have been demonstrated to have a very important role in the improvement of many diseases^[15] (Fig).

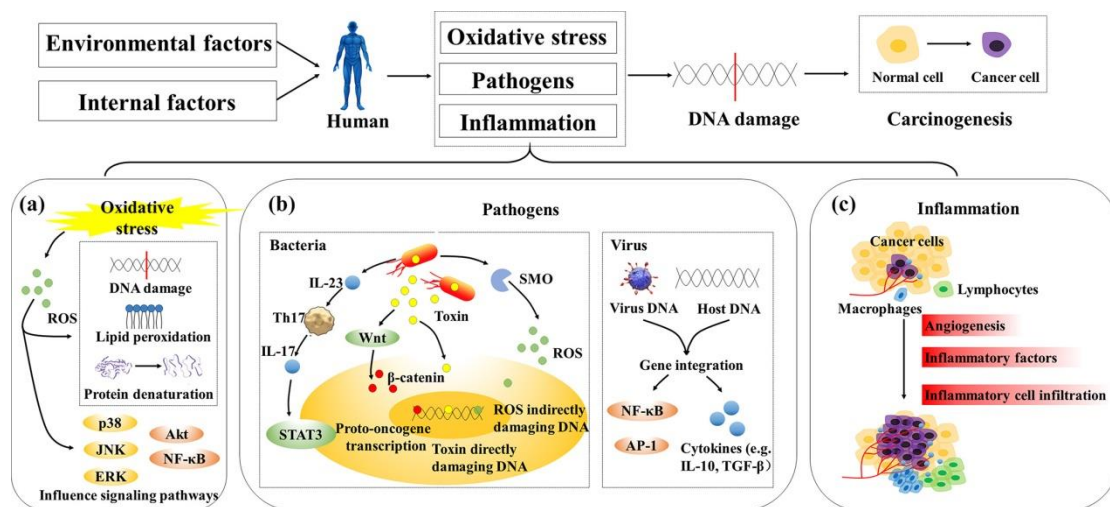


Figure 1: Shown variables have an impact on how normal cells become cancer cells.

The aforementioned figure explained the factors that influence the onset and incidence of cancer. Both internal and environmental factors affect how much oxidative stress, inflammation, and pathogen exposure there is in humans, all of which can lead to DNA damage and eventually carcinogenesis. Stress from oxidation is (a). There is an excess of reactive oxygen species (ROS). Protein denaturation, lipid peroxidation, and DNA oxidation are all processes that ROS may directly influence. The excessive activation of several signaling pathways, including p38, c-Jun N-terminal kinase (JNK), extracellular regulated protein kinases (ERK), protein kinase B (Akt), and nuclear factor B (NF-B), by ROS, might result in cancer. contaminants (b). By creating toxins, spermine oxidase (SMO), and gene integration, bacteria and viruses can harm an organism's DNA both directly and indirectly.

Wingless-type MMTV integration site family (Wnt)/-catenin signaling is another one of these pathways. In addition, pathogens have a role in regulating the frequency of inflammatory cells such as T helper cell 17 (Th17), cytokine production, and other signaling molecules like interleukin 23 (IL-23), IL-17, IL-10, and transforming growth factor (TGF-). Inflammation is also involved in the promotion of tumor cell survival, proliferation, invasion, and angiogenesis

once cancer cells have formed. Macrophages and lymphocytes participate in this inflammatory process. Significant efforts have been made in recent decades to improve the available therapy options as a result of the disease's societal and financial repercussions. Although many powerful chemotherapy drugs have been discovered and effectively used in clinical settings, their potential side effects have been kept to a minimum. However, most of these drugs are not selective for cancer cells, which limits their effectiveness. Additionally, various physiological barriers can hinder the drugs from reaching their intended targets, and chemotherapy resistance is responsible for treatment failure in over 90% of patients with metastatic cancer. widespread use of herbal plants and plant-based medications as all-natural alternatives to produce new pharmaceutical compounds for the treatment of illnesses.^[18] Greater people are consuming plant extracts and their constituent parts, and scientists are discovering greater advantages to human health. Several herbs have been investigated in clinical studies to understand their tumoricidal actions against various malignancies, and they are now being examined phytochemically.^[19]

Iraq is home to the interesting flora of the ancient Mesopotamian culture, including hundreds of species of medicinal plants. The Iraqi Center for Cancer and Medical Genetic Research (ICCMGR) has conducted numerous studies on the properties of native plants that are beneficial against cancer. These studies have demonstrated the cytotoxic or anticancer activities of some plants and herbs.^[20]

Several plant species have anticancer properties, some of which are mentioned below:

- *Ficus religiosa*: Pharmacological study on the plant's constituents supports the variety of traditional uses for the *Ficus religiosa*. Its bark, fruits, leaves, adventitious roots, latex, and seeds are among the parts used medicinally, occasionally in combination with other plants.^[21]

Numerous scientists^[22] advocated for a full investigation of its potential against parasitic infections, cancer, cardiovascular disease, and neuro-inflammatory illnesses. Many studies have focused on the pharmacological properties of this substance to confirm its traditional use in healing wounds, as well as its effectiveness against bacterial infections, diabetes, inflammation, and anxiety.^[23] *Ficus* spp. has been used in ethnopharmacology for its anti-inflammatory and anti-cancer properties, both in ancient and modern times. The combination of medieval and ancient beliefs along with modern knowledge of the role of inflammation in cancer development highlights the strong connection between inflammatory, infectious, and cancerous disorders. The F. methanol extract from the leaves of the *religiosa* plant was found to be cytotoxic against various human cancer cell lines, such as MDA-MB-4435s (breast), HT-29 (colon), and AGS (gastric), using the MTT test.^[25] The fractions of *religiosa* were also tested on cancerous MCF7 cell lines and were recommended by Choudhari and colleagues.^[27] It may be worthwhile to look into *religiosa*'s potential as an anticancer agent with specific regard to cervical cancer. The effect that the acetone extract of *F.* When a religious leaf was utilized in multiple apoptotic signals in human breast cancer cells, the results demonstrated a drastically induced permanent reduction of breast cancer cell proliferation with little harm to normal breast epithelial cells. Intriguingly, acetone extract accelerated cell mortality in continuous live cell imaging mode in a mitochondrial-dependent manner, exposing its potential photosensitizing effect. The creation of reactive oxygen species (ROS) within cells by the acetone extract was crucial in causing cell death and photosensitization. The extract also prevented the growth of cancer cells in a manner that was dependent on the amount and duration of exposure. Overall, the acetone extract effectively slowed down the proliferation of cancer cells in a dose- and time-dependent manner. The suppression of cancer cells was linked to the translocation of the Bax protein and mitochondria-mediated apoptosis,

which activated the caspase 9-dependent caspase cascade. Additionally, the acetone extract showed a significant ability to sensitize cancer cells to treatment. This was due to a quick decrease in mitochondrial transmembrane potential and partial activation of caspase, resulting in the formation of intracellular ROS.^[28]

- Cardamom is the most extensively used spice in the world and is growing in popularity because of its good health benefits, according to *Elettaria cardamomum*. It's a dietary phytoproduct. The traditional use of little cardamom [*Elettaria cardamom* (L.) Maton (Family: Zingiberaceae)] has included the treatment of heart, stomach, kidney, and asthma problems as well as infections of the teeth and gums, cataracts, nausea, and diarrhea. Numerous research has demonstrated the biological benefits of cardamom and its polyphenols, which include antioxidant, anticancer, anti-inflammatory, and metabolic regulation capabilities. The 1,8-cineole and its esters, the Limonene terpinyl Acetates, make up the majority of the cardamom's bioactive components. They are acknowledged as multifunctional chemicals that could help treat or prevent a number of cancers, cardiovascular diseases, chronic inflammatory issues, digestive disorders, as well as contagious bacterial and fungal infections. Several nations cultivate it, including Tanzania, India, Guatemala, Sri Lanka, Nepal, Indonesia, Costa Rica, and Tanzania.^[29] The false cardamom, huge cardamom, or black cardamom, which belongs to the related genus *Amomum*, is native to Nepal, Sikkim, Bengal, and southeast Asian countries. The scientific name for African cardamom is *Aframomum danielli*, and it is primarily grown in Tanzania, Cameroon, Madagascar, and Guinea.^[30] Small cardamom capsules have been used by ancient Greek and Roman physicians as well as Indian Ayurvedic practitioners since the fourth century BC to treat a range of medical conditions, including bronchitis, asthma, constipation, colds, coughs, tooth and gum infections, urinary and kidney disorders, congestion of the lungs, pulmonary tuberculosis, irritation of eyelids and cataracts, nausea, diarrhea, and cardiac disorders.^[31] Ayurvedic medicine has historically used cardamom to cure food poisoning, while traditional Chinese medicine has used it to treat dysentery, bladder infections, and constipation in children who have dysentery. Currently, cardamom oils are used in several plant-based hand lotions and soaps, and numerous studies have demonstrated that eating enough veggies reduces the incidence of colon cancer.^[32]

- Plantago, a family of about 265 species in the Lamiales (order) suborder. The tiny plants often have long, leafless stalks with a terminal spike of tiny flowers, dense clusters of basal leaves, and no leaves.^[33] *Plantago heterophylla*, *Plantago incisa*, *Plantago krajinai*, *Plantago bigelovii*, *Plantago canescens*, *Plantago debilis* (Shade plantain, feeble plantain), *Plantago erosa*, *Plantago fernandezia*, *Plantago gentianoides*, and *Plantago lanceolata* (Ribwort plantain) The seeds of this plant have laxative properties because they contain polysaccharides. The hydrophilic property of polysaccharides. The seeds promote peristalsis, hold on to water, bulk up the stool, and ease bowel movements. The mucilage can also be used to treat loose stools successfully. The seeds can be utilized to treat parasitic worms as well.^[35] Due to its abilities as an antifungal, antioxidant, analgesic, and even a small antibiotic, *Plantago lanceolata* appears to be a very adaptable addition to the medical supply cupboard.^[36] The leaves of *Plantago lanceolata* are ophthalmic, astringent, demulcent, mildly expectorant, and have a bitter flavor. If your children are wounded and you can't find any Plantain, *Plantago lanceolata*, an antihistamine, works far better than Dock, which is effectively a placebo, for healing insect bites or stings or stings from nettles.^[37]

The leaves may also be used to create a tea that works well as a cough suppressant. The synthesis of butyric acid during the colonic fermentation of dietary fiber, which triggers apoptosis and is involved with the regulation of various

malignancy traits, has been suggested as a contributing factor to *Plantago ovata*'s anti-cancer effects. After consuming *Plantago ovata*, it has been shown that the production of butyric acid increases.^[38]

the rotund *Cyperus* The Cyperaceae family, according to Linn^[39], encompasses various plants. Among them, an Indian plant stands out as the worst one. This plant grows in small clusters that can reach up to 100 cm in height. Nut grass, as it is commonly known, is highly adaptable to different soil types, elevations, temperatures, moisture levels, and soil pH, which explains its wide distribution across different regions.^[40] It is capable of thriving in diverse environments and has been found to have medicinal and pharmacological benefits.^[41] According to Ayurveda, these medicinal plants are a rich source of ingredients for synthesizing and producing medicines. The rhizomes of *C. rotundus* are attributed with numerous properties such as astringent, diaphoretic, diuretic, analgesic, antispasmodic, aromatic, carminative, antitussive, emmenagogue, lithophytic, sedative, stimulant, stomachic, vermifuge, tonic, and antibacterial. The ingredients in these plants contain multiple enzymes for carbohydrates and minerals that act as catalysts for various metabolic reactions, which can aid in indigestion. Therefore, they may be a helpful treatment for indigestion. These plants are commonly used to treat various health conditions such as amenorrhea, dysmenorrhea, inadequate lactation, memory loss, insect bites, food poisoning, indigestion, nausea, dyspepsia, coli, flatulence, diarrhea, dysentery, intestinal parasites, fever, malaria, cough, bronchitis, renal and vesical calculi, urinary tenesmus, skin diseases, and wounds. A natural plant called rotundus, also known as Nutgrass and part of the Cyperaceae family, has gained popularity in pharmaceutical applications due to its anti-inflammatory, antipyretic, anti-rheumatic, anti-ulcer, and antineuronal characteristics. The phytochemical elements that makeup *C. Sesquiterpenes*, flavonoids, phenylpropanoids, phenolic acids, alkaloids, and saponins having an anticancer action are found in the rotundus rhizome. In recent findings, iridoid glycosides isolated from *C. The lipoygenase* activity in the rotundus rhizome was important in suppressing hepatic malignancy. The rhizome's methanolic extract also exhibited antioxidant and hepatoprotective properties, as well as a suppression of lipid peroxidation. It is known as ama-pancake, or the corrected elimination of endotoxins, in ancient literature.^[44] Studies on the tubers of *C. rotundus* have shown that they have antigenotoxic, antimutagenic, and anti-aging effects.^[45] Research on the oil and samples taken from the aerial regions of *C. rotundus* has also revealed an anticarcinogenic antioxidant activity. When tested on various cell lines including MCF-7, HeLa, Hep G2, PC-3, and HT-29, the MRCr demonstrated cytotoxic activity which induced apoptosis in all the cells. However, the difference in IC50 value between each cell line was relatively small, with MCF-7 having the lowest value and HT-29 having the highest. The MRCr's ability to scavenge free radicals has contributed to the elimination of harmful substances.^[46] Unlike oolong teas and black teas, which have through the same withering and oxidation procedures, green tea is made from *Camellia sinensis* leaves and buds.^[47] There are numerous sorts of green tea, and they change greatly depending on the *C* variety. Since its invention in China, green tea has spread to other East Asian countries. "Catechins" and "theanine," the two main components of green tea, are gaining a lot of attention for their health advantages both in Japan and internationally. Based on its antioxidant and anti-inflammatory qualities, it has been proposed that it may suppress cancer genesis and proliferation by reducing "cell damage." Anyone using the chemotherapeutic drug bortezomib (Velcade) or any other boronic acid-based proteasome inhibitors shouldn't drink green tea.^[48] Drinking green tea did not significantly lower plasma levels of C-reactive protein, a measure of inflammation, according to a study of 11 randomized controlled studies from 2015.^[49] Inflammation is one condition for which green tea may be used medically.

THE ANTICANCER ACTIVITY OF TEA INGREDIENTS: It is common knowledge that tea offers health advantages and might shield against cancer. Nevertheless, diverse results have been observed between trials, which may be accounted for by changes in the type and doses of the tea that is the subject of the study. Additionally, tea's useful elements play a major role in its anti-cancer effect. The anti-cancer properties of tea polyphenols, such as epigallocatechin-3-gallate (EGCG)^[50], tea polysaccharides, L-theanine, tea pigments, and caffeine, have been demonstrated in a number of in vivo and in vitro investigations. In contrast, very little research has looked at the efficacy of the minor components, such as tea saponin, tea protein, vitamins, lipids, trace minerals, -aminobutyric acid, and enzymes, to prevent cancer.^[51] The present focus of tea's anti-cancer mechanisms is the management of redox equilibrium in the tissues and organs of the entire body. This focus has already been extensively outlined, detailing the role tea's anti-oxidative and pro-oxidative activities play during cancer prevention.^[52] The ability of tea to treat or prevent cancer may be influenced by a number of pathways, including those that are anti-inflammatory, anti-pathogen, and those that promote specific cell survival.^[53]

- Pomegranate consumption has been associated with a reduced risk of cancer mortality and incidence, as evidenced by a negative correlation with these outcomes.^[54] The interest in specific fruits enriched with polyphenolic compounds has surged due to their potential in chemoprevention and/or chemotherapy. Pomegranate (*Punica granatum* L.) has been extensively studied for its anticancer properties owing to its abundance of polyphenols, including ellagitannins, ellagic acid, and various flavonoids such as quercetin, kaempferol, and luteolin glycosides. Among the three parts of the pomegranate — the seed, peel, and juice — the peel exhibits the highest concentration of polyphenols (A. Forai and C. Calhau, "The Bioactivity of Pomegranate: Impact on Health and Disease".^[56] Ellagitannins are present in this particular component, with punicalagin being a prominent polyphenol belonging to the ellagitannin family, along with punicalin and gallagic acid as lesser tannins. Punicalagin, a bioactive compound with a molecular weight exceeding 1000, is exclusive to pomegranates and contributes to over 50% of the antioxidant activity found in pomegranate juice.^[57] Recent research suggests that pomegranate polyphenols have anti-tumor properties that can impede the growth and spread of cancer by targeting various genes and proteins. This means that pomegranate could be used in cancer prevention or treatment. To determine the effectiveness of pomegranate in different preclinical models, researchers conducted extensive mechanistic investigations. Cell-cycle arrest and apoptosis induction have been described as the two main methods. Angiogenesis and metastasis, two other critical pathways involved in the development of cancer, have also been identified by some writers to be significantly inhibited. DNA damage, a factor in the early stages of cancer formation, has been shown to be inhibited by pomegranates and their constituents. Only a small portion of their antigenotoxic action is reliant on their antioxidant activity. When given to mice, pomegranate extract (400, 600, and 800 mg/kg b.w.) dramatically decreased the DNA damage caused by cyclophosphamide while simultaneously increasing the activity of antioxidant enzymes such as glutathione S-transferase, superoxide dismutase, and catalase.^[58] Pomegranate's ability to prevent benzo[a]pyrene-induced DNA adducts may be due to direct conjugation with benzo[a]pyrene metabolites, a drop in cytochrome P450 activity, an increase in phase II enzymes, or a combination of the three. Punicalagin has been shown to inhibit cytochrome P450 1A1, which is essential for benzo[a]pyrene's bioactivation.^[59] The evidence disproves the assertion that it can degrade benzo[a]pyrene metabolites.^[60] Inflammatory signaling pathways are a focus for cancer prevention due to their potential to activate cellular signaling, cause DNA damage, and change epigenetic patterns. intestinal inflammation that persists specifically increases the likelihood of developing intestinal cancer.^[61] Using a human colon cancer cell line, the effects of pomegranate juice, whole pomegranate tannin extract, and punicalagin on inflammatory cell signaling proteins were investigated. Free fatty acids

are thought to be converted into prostanoids by the enzymes cyclooxygenase (COX) 1 and cyclooxygenase (COX) 2. For example, while COX-1 is responsible for the generation of prostanoids that regulate the normal tissue homeostasis, COX-2 produces prostanoids that induce inflammation. Consequently, the overexpression of COX-2 facilitates the progression of cancer. The pathways involving protein kinase B (AKT), nuclear factor kappa B (NF-B), and phosphatidylinositol 3-kinase (PI3K) exert positive influences on COX-2 expression. The administration of Punicalagin (25–200 mg/L), pomegranate juice (6–50 mg/L), and whole pomegranate tannin extract all led to significant reductions in COX-2 protein expression. This observation was corroborated by the ability of pomegranate juice to suppress NF-B activation and inhibit AKT activity. Notably, pomegranate juice exhibited greater efficacy compared to punicalagin and total pomegranate tannin, as evidenced by a 79% reduction in COX-2 protein expression for pomegranate, 55% total pomegranate tannin, and 48% for punicalagin.^[62] This that other bioactive polyphenols present in pomegranate, such as anthyanins andonols, may contribute to its anti-inflammatory properties.

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