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ROLE OF HERBAL MEDICINES IN CANCER

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ABSTRACT

Cancer is a genetic disease. The main causes of cancer are alterations of DNA, mutations, damage etc. Any herbs which may be a plant or a part of the plant that are used to maintain the health are called Herbal supplements or Phytomedicines. Plant extracts are generally prepared by boiling the herb in water. The goals of these herbal medicines include prevention and protection against cancer. The traditional plants like Eleutherococcus senticosis, Astralagaus membranaceous, and medicinal mushrooms are used in cancer treatment. The other herbs used in other parts of the world are Valeriana, Garlic, Curcumin etc. These herbal medicines along with benefits also include some adverse effects. This review summarizes the role of some pharmaceutically important herbal medicines used in treating cancer.

INTRODUCTION: Cancer is a disease that arises from abnormal changes in the genetic make-up of cells that cause them to multiply uncontrollably. The abnormal cells then spread locally or to other regions of the body via the lymphatic or blood circulation [1]. The Cancer may affect people at all ages, even fetuses, but the risk for most varieties increases with age [2]. Cancer causes about 13% of all deaths [3].

Causes of Cancer:

- Cancer is a genetic disease. Alterations to the DNA inside cells can endow cells with morbid "superpowers," such as the ability to grow anywhere and to continue dividing indefinitely.
- Mutations in a relatively small set of cancer-related genes, as the decisive events in the transformation of healthy cells to malignant tumors.
- Breakdown in DNA duplication or repair leading to many thousands of random mutations in cells.
- Damage to a few "master" genes mangles the chromosomes, which then become dangerous.
- Abnormal numbers of chromosomes in a cell may be the first milestone on the road to cancer [4].

Diabolical Superpowers of Cancer:

The six diabolic superpowers of cancer are as follows:

1. Growth even in the absence of normal "go" signals
2. Growth despite "stop" commands issued by neighboring cell
3. Evasion of built-in autodestruct mechanisms
4. Ability to stimulate blood vessel construction
5. Effective immortality
6. Power to invade other tissues and spread to other organs.

HERBAL MEDICINES: Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population [5]. Recognition and development of the medicinal and economic benefits of these plants are on the increase in both developing and industrialized nations [6]. Among the human diseases treated with medicinal plants is cancer, which is probably the most important genetic disease. Every year, millions of people are diagnosed with cancer, leading to death in a majority of the cases. Deaths arising from cancer constitute 2-3% of the annual deaths recorded worldwide [7].

An herb (also called a botanical) is a plant or plant part used for its scent, flavor, and/or therapeutic properties. Products made from botanicals that are used to maintain or improve health have been called herbal supplements, botanicals, or Phytomedicines [8]. The pharmacological treatment of disease began long ago with the use of herbs [9]. Tyler defines herbal medicines as "crude drugs of vegetable origin utilized for the treatment of disease states, often of a chronic nature, or to attain or maintain a condition of improved health" [10] or the Herbal medicines can be defined as "Finished labeled medicinal products that contain ingredients from aerial or underground parts of plant parts or other plant material or combination in the crude state or as plant preparations [11]. It has been estimated that these medicines derived from plants constitute about 25 percent in modern pharmacopoeia [12]. Traditional herbal medicines are naturally occurring; plant-derived substances with minimal or no industrial processing that have been used to treat illness within local or regional healing practices [13].

Common reasons for use of herbal drugs include health promotion; disease prevention; poor outcomes and limited treatment options for a serious illness; exhaustion of conventional therapies; dissatisfaction with, or lack of efficacy of, conventional therapies; significant side effects or risks associated with conventional medicine; belief that herbal and natural products are better or safer; preference for personal involvement in the decision-making process; and Cultural or spiritual preference [14].

Cultivation of wild medicinal plants: The efficacy of medicinal herbs is affected by different environmental factors. Temperature, rainfall, day length and soil characteristics are some of the factors which affect the potency of the medicinal plants. A plant may grow well indifferent situations, but fail to produce the same constituents (e. g., *Cinchonas* growing at altitudes and in plains). The cultivation of some medicinal plants in demand under appropriate environmental conditions will provide

- Better development of plants owing to improved conditions of the soil, pruning, and control of insect pests, and,
- Better facilities for treatment after collection. For example, drying at a correct temperature in the case of colchicum, belladonna and valerian [15]

The age of the plant also decides its medicinal potency. Therefore, the authentic part of medicinal plants of a particular age should be harvested in a particular season before processing for drug manufacture, to avoid any alteration in its medicinal potency [15]. Duration of the drying conditions of the harvested medicinal herb also varies from a few hours to many weeks [16, 17]. Low seed set, poor seed viability, high dormancy and low percentage of seed germination are some of the problems in propagation of some medicinal plants.

Botanical data: Use of herbal medicines in developed countries has expanded sharply in the latter Half of the twentieth century. Monographs on selected herbs are available from a number of sources, including the European Scientific Cooperative on Phytotherapy, German Commission E [18] and the World Health Organization. Other resources that provide detailed information about herbal products in current use include the Natural Medicines Comprehensive Database [19] and NAPRALERT (Natural Products ALERT, 2001) [20]. Information about other available databases has been published by Bhat (1995) [21].

Preparation of Herbal medicines: Herbal medicines are available in several forms and often require preparation before their use. Decoctions are made by boiling the herb in water, then straining out the plant material. More concentrated forms of herbal medicines are available in the form of hydroalcoholic tinctures and fluid extracts [22]. Methods of preparation may differ because of the nature of the plant's active chemical constituents. Volatile oils, resins, alkaloids, glycosides, and fixed oils may be present in varying degrees and possess disparate characteristics in terms of their solubility and heat tolerance [23]. Studies on the effects of certain Ayurvedic herbal preparations for possible cytotoxic activity revealed that these herbal preparations did not kill the cancer cells but transformed them into normal healthy cells [24].

Goals of Herbal Medicine in Cancer Therapy Include:

- Reduction of toxicity from chemotherapeutic and radiation therapies while enhancing tumor killing capacity.

- Reduction of side effects such as fatigue, hair loss, mouth sores, nausea, vomiting, appetite loss, and organ wasting and failure.
- Enhancement of immunity.
- Prevention from cancer spreading via growth, metastasis and local invasion.
- Protection against developing cancer causing effects of radiation and chemotherapy.
- Protection against development of further cancer in cancer prone individuals.
- Improvement of complete or partial remission by exerting direct effects on the tumor by changing the underlying conditions that allows the cancer to exist.
- Augmentation of duration and quality of life.

Some examples of Herbal medicines include foxglove leaf (digitalis), belladonna tops (atropine), poppy herb (morphine), white willow tree bark (salicin), and cinchona bark (quinine). Modern drugs developed from plant products include warfarin from the coumarin anticoagulants found in sweet clover silage, ergotamine from the ergot alkaloids of a fungus that infects rye grass, and the antineoplastic vincristine from the vinca alkaloid fractions of the rosy periwinkle [25]. Many herbal remedies have shown to have anticancer effects.

- Several mushroom derived compounds are approved for use as cancer treatment in Japan.
- A Chinese formula containing herbs was used in the treatment of prostate cancer[26].
- Another Chinese herb was found to have inhibitory properties against breast cancer cells [27].
- Garlic (diallyl- disulfide) inhibited the growth and induced apoptosis in human colon cancer cell lines [28].
- Polyphenolic compound (Resveratrol) found in plant species and food products (grapes, peanuts and herbs) had similar effect [29].
- Major component in green tea, enhanced the growth inhibitory effects of 5-flourouracil (chemotherapeutic agent) [30].
- Research carried out at AIIMS has shown that antioxidants and ginger (*Zingiber officinale*) [31] had useful antiemetic effect in animals (cats and dogs) undergoing cisplatin chemotherapy.
- *Ocimum Sanctum* [32] had anti proliferative and chemo preventive effects; thus it has the potential as an anti-cancer agent.
- Maha Amrit Kalash enhanced immune status of cancer patients undergoing treatment.
- High doses of multiple antioxidant vitamins along with chemotherapy (Carboplatin and Paclitaxel) enhanced apoptosis of non-small cell cancer cells H520 [33].
- Clinical studies demonstrate that combination of chemotherapy and antioxidant vitamins yielded better response rate and longer survival.

Herbal medicines in traditional healing of cancer: Cancer is a major cause of death and the number of new cases, as well as the number of individuals living with cancer, is expanding continuously. Due to the enormous propensity of plants that synthesize mixtures of structurally diverse bioactive compounds, the plant kingdom is potentially a very diverse source of chemical constituents with tumor cytotoxic activity. Despite the successful utilization of few phytochemicals, such as vincristine and taxol, into mainstream cancer chemotherapy, commercial plant-derived anticancer formulations represent only one-fourth of the total repertoire of the available treatment options [34].

Among the cancer patients surveyed, up to three quarters have used these therapies to help them manage their disease [35]. The use of herbal supplements by cancer patients in the preoperative period is prevalent and consistent with the substantial increase in the use of alternative medical therapies by cancer patients [36]. Anywhere from 25% to 85% of cancer patients are seeking alternative and complementary nutritional therapies for prevention or during cancer treatment.

The use of these therapies is highest among patients with breast cancer (80% to 85%) [37], pediatric cancer (46%) [38], prostate cancer (27% to 43%) [39], and head and neck cancer (25%) [40]. Herbs that contain balancing, regulative and tonic properties are known as adaptogens. Adaptogens, or 'harmony-restoring agents', are particularly important for supporting the health of individuals with HIV, AIDS, cancer, autoimmune disorders and chronic illness. The term adaptogen is based on the daily use of herbs for prevention of disease and enhancement of health [41].

Some adaptogen herbs include Siberian Ginseng- the Latin name in parenthesis (*Eleutherococcus senticosis*), the ancient Chinese herb, Huang Qi (*Astragalus membranaceus*) and Medicinal Mushrooms such as Reishi (*Gandoderma lucidum*) and Maitake (*Grifola frondosa*).

1. *Eleutherococcus senticosis:*

- *Eleutherococcus* can inhibit cancer activity through several mechanisms: by both inhibiting angiogenesis (the formation and differentiation of blood vessels):
    - By reducing histamine availability and may block cancer cell proliferation.
    - By inhibiting cyclin dependent kinases (intracellular signals which play a role in cancer cell division) [42].
- *Eleutherococcus* has been shown to both elevate numbers and activate helper / inducer lymphocytes and NK cells [43].

2. *Astragalus membranaceus*:

- *Astragalus* is a member of the Leguminosae (pea) family; some active constituents include triterpenoid saponins, flavonoids and immune stimulating polysaccharides.
- It is a potent immunostimulant and antitumor agent that has been shown to increase survival time in patients with adenocarcinoma, non-small cell lung cancer, and breast cancer (use with Ligustrum fruit) [44].
- Commonly used in Traditional Chinese Medicine, *Astragalus* can support and maintain the bodies' immune function, increasing interferon levels, T cell count, and natural killer cell activity and reducing symptoms of nausea [42].
- *Astragalus* increases NK and T cell activity [45] in both normal and immune compromised hosts [46].
- The polysaccharide fraction of *Astragalus* potentiates the lymphokine-activated killer (LAK) cellinducing activity of IL-2 in cancer and AIDS patients [47].
- Animal studies confirm the adaptogenic properties, enhancing endurance and promoting weight gain. Grouped in a category of herbs known as antiviral, anti bacterial and immune stimulants, *Astragalus* can help inhibit HIV replication in infected cells and prevent secondary infections.

- *Astragalus* has been shown to increase resistance to the immunosuppressive effects of chemotherapy drugs, while stimulating macrophages to produce interleukin- 6 and tumor necrosis factor (TNF) [48].

3. Medicinal Mushrooms:

- Medicinal mushrooms such as Reishi (*Gandoderma lucidum*) and Maitake (*Grifola frondosa*) play an important role in maintaining healthy immunity in individuals with HIV [42].
- All medicinal mushrooms contain a compound called beta glucans, a complex polysaccharide, containing adaptogenic and immunostimulant properties found to:
  - Support components of cellular immunity: Stimulate interferon production, increase natural killer cell activity and has been found (in animal studies) to stimulate macrophage activity
  - Contain chemical substances that inhibit viral, bacteria, and fungal infections specifically benefiting oral and genital herpes, warts, shingles, viral hepatitis and Candida.
- When the immune system is impaired bacteria, fungi and viruses have free reign in the body; cancer cells and other opportunistic infections have occasion to develop. Medicinal mushrooms can offer increased protection from infection.
- *Ganoderma lucidum* is an important part of most fu zheng formulas, used in china to enhance chemotherapy and reduce side effects of cancer treatment [44].
- A hemicellulose/ B 1-3 glucan /mycelial extract from hybrid mushrooms was administered orally, 3 grams per day can effectively cure prostatic cancer, ovarian cancer, multiple myeloma, and breast cancer with full remission, whereas breast cancer patients had partial remission. The Natural killer cells (NKC) function increased 2.5 fold by 2 weeks and maintained. Notable side effects were absent [49].

Herbs from other parts of the world:

1. *Valeriana officinalis:*

- It is used in improving sleep of patients with cancer receiving adjuvant therapy [50].
- Traditionally used to reduce nervousness in adults and children, notably in case of sleeping disorders.
- The root of the valerian herb *(Valeriana officinalis)* is often used for treatment of insomnia and fatigue both common symptoms reported by cancer patients [51].
- This herb has certain anti-tumor effects similar to those of mustard gas. It may be that someday it will play a role in the treatment of cancer. The FDA includes valerian in its list of herbs considered safe.
- The literature generally reports that valerian is a safe product and that there are no side effects or drug interactions.

2. *Matricaria chamomilla:*

- Traditionally used in the symptomatic treatment of digestive upsets such as epigastric distension, slow digestion, eructation and flatulence.
- Traditionally used locally (mouth and throat washes, lozenges) as an analgesic in conditions of the oral cavity and/or larynx.
- Traditionally used for the temporary relief of sore throat and/or transient hoarseness.
- Different preparations of chamomile (CO) (*Matricaria chamomilla*) are used to treat various diseases, including inflammation and cancer [52].

- Exposure of chamomile extracts caused minimal growth inhibitory responses in normal cells, whereas a significant decrease in cell viability was observed in various human cancer cell lines. Chamomile exposure resulted in differential apoptosis in cancer cells but not in normal cells at similar doses [53].

3. *Taxus baccata:*

- The Pacific yew tree (*Taxus brevifolia* Nutt.) was the first plant species to demonstrate anti-cancer properties. These properties were isolated in very low concentrations from extracts found in the bark of the Pacific yew, contains a compound called paclitaxel; like all taxanes, paclitaxel was determined to be toxic to cancerous cells.
- The yew (*Taxus baccata*) particularly the Pacific Yew, *Taxus brefolia* is employed for its taxol content, which is being used very successfully as a chemotherapy treatment for breast and ovarian cancer.
- A novel anticancer diterpene amide, "taxol" from the Pacific yew (*Taxus brevifolia*) extract was isolated and it also had significant activity in the treatment of patients with malignant melanoma, lung cancer, and other solid tumors [54, 55].
- Taxol is considered as the prototype of a new class of cancer chemotherapeutic agents [56].
- Taxol inhibits the replication of human tumor cells. Specifically, Taxol induces tubulin polymerization and inhibits disassembly of microtubules, an activity necessary to complete cell division and showed activity on a human breast cancer xenograft.
- Taxotere was made available in the UK in 1996 and has proven effective in combating lung and prostate cancer, and remarkably successful in the treatment of advanced cases of breast cancer.

4. *Cassia senna:*

- Short-term treatment of occasional constipation. This medicinal product is a stimulant laxative; it stimulates bowel evacuation. It is intended for the short-term treatment of occasional constipation.
- The most widely used species of *Cassia* in herbal medicine is known as senna *(Cassia senna* or *C. acutifolia*). The *Cassia* plants are well known for a group of chemicals with strong laxative actions called anthraquinones [57]. They act as a cellular protector and a preventative to cell damage (immune, liver, kidney, cancer preventative) [58].

5. *Hypericum perforatum:*

- St John's wort (*Hypericum perforatum*) contains active compounds such as naphthodihydro -dianthrones (particularly hypericin and pseudohypericin) and flavonoids (including quercitrin, rutin, and hyperin) [59].
- Cancer patients often take St John's wort to reduce anxiety or depression. Situational depression is common among patients with cancer and may lead to increased use of the herb [59].
- Through a series of experiments, researchers investigated the effect of St. John's wort on leukemia and glioma, a type of brain cancer. The experiments showed that St. John's wort can inhibit the growth of leukemia and glioma cells. Moreover, exposing St. John's wort to light appears to increase the anti-cancer properties of the herb.

- Traditionally used topically as a soothing and antipruriginous application for dermatological ailments and as a protective treatment for cracks, grazes, chapped skin and insect bites.
- *Hypericum perforatum* extract has been tested, as a photosensitizer, for the treatment of bladder cancer both in vitro and in vivo [60].
- The antiproliferative effect of serotonin-reuptake inhibitors (SSRI) and serotonin antagonists has been demonstrated in prostate tumors.

6. *Plantago major* L:

- *Plantago major* (PM), also known as plantain, is a weed found in temperate zones worldwide. PM leaves have been associated with various biological properties ranging from antiinflammatory, antimicrobial and antitumour to wound healing. The regulation of immune parameters induced by plant extracts may be clinically relevant in numerous diseases including chronic viral infections, tuberculosis, AIDS and cancer.
- This is popularly used to treat tumors, infections and as a blood purifier, because of this it is used for the treatment of cancer [61].
- The frequency of tumor formation was decreased in the mice treated with Intracellular fluid of waybread (*Plantago major*) as a prophylactic for mammary cancer in mice.
- The oral administration of *Plantago major* extract caused an aversion to tobacco (cigarette smoking is a major risk factor in coronary artery disease and is the cause of approximately 30% of all cancer deaths. Tobacco chewing has been shown to cause cancers of the mouth and throat) in human subjects who were heavy smokers. Hence the herb *Plantago majo*r has been known as a tobacco deterrent (both smoking tobacco and chewing tobacco) for many years.
- A range of biological activities has been found from plant extracts including wound healing activity, anti-inflammatory, analgesic, antioxidant, weak antibiotic, immuno modulating and antiulcerogenic activity. Some of these effects may attribute to the use of this plant in folk medicine.

7. Curcumin:

- Curcumin is a polyphenol compound from the Indian herb, *Curcuma longa L*, and the dietary spice turmeric which is used for wound healing, skin and gut diseases.
- Evidence from research on the anti-cancer potential of Turmeric has shown particular effectiveness on cancer of the prostate, breast, skin and colon.
- This herb is also known for its beneficial effect on liver health.
- Curcumin is reported to have a wide range of beneficial properties, including anti-inflammatory, anti- oxidant, chemo-preventive and chemo- therapeutic activity [62].
- Curcumin has been shown to potentiate the antitumor effect of gemcitabine in pre-clinical models of pancreatic cancer. Curcumin is relatively non-toxic and exhibits limited bioavailability.
- It has been shown to inhibit cancer in all stages of development (initiation, promotion, and progression) and provide symptom relief when used topically on external cancers.
- Curcumin is currently used in human clinical trials for a variety of malignancies, including multiple myeloma, pancreatic cancer,

myelodysplastic syndromes, and colon cancer [63].

- Curcumin, the active ingredient of the spice turmeric, has been shown to significantly inhibit the incidence and multiplicity of invasive and noninvasive colon adenocarcinomas as well as decrease colon tumor volume.

8. Ashwaganda:

- *Withania somnifera* (Ashwagandha) is also called 'Indian ginseng' and is one of the most important Ayurvedic tonic herbs, assisting with growth, health and vigor.
- Regular use can help to nourish the blood and increase hemoglobin levels.
- A wide range of clinical studies studies have provided strong support for the therapeutic benefits of this herb, which appears to have demonstrated anti-tumor, anti-inflammatory, antioxidant, anti-stress and rejuvenating properties.
- Increases phagocytosis and intracellular killing.

9. Garlic:

- The major putative active constituents of garlic contain sulfur. Intact cloves contain allicin, which is stable. When a clove is cut, the enzyme allicinase (a C-S lyase) reacts with allicin to form various strong-odored compounds associated with garlic, including the thiosulfinate allicin. In addition, garlic contains fructosans and saponins as potentially active substances.
- Garlic has been recommended for multiple purposes including tumors since ancient times.
- Garlic contains many active ingredients including allicin, a thiosulfinanate, which inhibit lactic dehydrogenase a main enzyme in cancer cellular metabolism.
- Garlic inhibits cancer growth in human breast cell lines.
- *Allium sativum* or garlic is known to have a broad range of biologic activities, including immune stimulation and reported antitumor activity [64].
- Garlic has been reported to have antithrombotic properties [65]. It contains inhibitors of adenosine deaminase and cyclic AMP phosphodiesterase, which could account for antithrombotic and vasodilatory actions.
- Concentrations achievable in humans via aged garlic supplementation can decrease cancer cell growth rate upto 70%.

10. Green Tea:

- Researchers at Purdue University have found that green tea contains an antioxidant, epigallocachetin gallate, which selectively shuts down an enzyme needed in cancer cell for cell division, quinol-oxidase. Growth and division of normal cells are not affected.
- When the epigallocachetin gallate treated cancer cells reach critical size for division and cannot divide, they succumb to programmed cell death.
- Black tea contains only a small fraction of this antioxidant compared to green tea.

11. Ginger:

- Ginger is the rhizome part of the plant whose botanical name is *Zingiber officinale*. The active constituents in ginger are thought to be chemicals known as gingerols [1- (3′- methoxy- 4′- hydroxyphenyl)- 5- hydroxyalkan- 3- ones] and shogaols, their

dehydration products, which are responsible for the sharp taste of ginger [66].

- Ginger has been shown to act as a potent inhibitor of thromboxane synthetase, raising levels of prostacyclin without a concomitant rise in prostaglandin E2 or prostaglandin F2 alpha having implications in bleeding times.
- Interestingly, patients at cancer center have been using ginger to manage the nausea they experience from chemotherapy.
- Ginger has been known for its antiemetic properties and has been demonstrated to be as effective in the prevention of postoperative nausea and vomiting after outpatient gynecologic surgery.

12. *Hamamelis virginiana*:

- Witch hazel (*Hamamelis virginiana*) has a long history of use in both traditional herbal medicine and allopathic medical practice for treatment of hemorrhoids, burns, cancer, tuberculosis, colds, and fever.
- Hamamelitannin of *Hamamelis virginiana* inhibits the TNF-mediated endothelial cell death without altering the TNF-induced upregulation of endothelial adhesiveness [67].
- Witch hazel bark (*Hamamelis virginiana*) OPCs, a class of flavonoids prevent nitrosamine formation and their ability to mutate DNA.

13. *Ginkgo biloba*:

- The extract is obtained from the leaves of the *Ginkgo biloba* tree, also known as the maidenhair or kew tree, the oldest known living tree species. The active ingredients in *Ginkgo biloba* are believed to be two compounds — flavonoids (ginkgo-flavone glycosides) and terpene lactones (ginkgolides and bilobalide), found in the extracts of the whole leaf.
- The flavones act as antioxidants, and the terpene lactones (ginkgolides) inhibit blood clotting.
- Ginkgo contains compounds that act as anticoagulants, inhibiting platelet aggregation.
- *Ginkgo biloba* extracts has been reported to cause bleeding into the brain and eyes.
- The therapeutic mechanism of *Ginkgo biloba* exocarp polysaccharide GBEP on human gastric cancer may relate to its effects on the expression of c-myc, bcl-2 and c-fos genes, which can inhibit proliferation and induce apoptosis and differentiation of tumor cells [68].

14. Ginseng:

- The chief constituents responsible for the activity of ginseng are the ginsenosides or panaxocides. Chemical analysis indicates that there are at least four active compounds — saponin glycoside, panaxin, panacene, and panaxic acid.
- Ginsenosides have been shown to inhibit platelet aggregation in vitro. Animal studies have demonstrated that ginsenosides prolong coagulation times of thrombin and activated partial thromboplastin.
- Ginseng was found to protect against cancers of the mouth, esophagus, stomach, colorectum, liver, lung, pancreas and ovaries.
- Recent human studies using Asian Ginseng showed it reduced symptoms of COPD5, improved survival times in patients with gastric cancer, and reduced incidence of metastases [69].
- Ginseng is often taken to slow or decrease the effects of aging, and for such age-

related conditions as hot flashes, diabetes, cancer and Alzheimer's disease.

15. Jiaogulan herb (*Gynostemma pentaphylla*):

- This member of the Curcubitaceae family has a long history of use in Southern China & Taiwan as a folk remedy for fatigue, weakness, asthma, hepatitis, migraines, and cancer.
- Due to its low cost and safety, it has become much more widely used as a "Ginseng" substitute and adaptogen throughout Southeast Asia. Interestingly, some of the active constituents, gypenosides, are chemically identical to ginsenosides.
- Clinically, Jiaogulan is useful for hypertension, congestive heart failure, liver disease, elevated blood lipids, and to strengthen the immune system and inhibit cancer.
- There are other clinical research studies, which indicate jiaogulan's ability to reduce tumor size.

16. Echinacea:

- Among the herbal supplements that potentially interact with corticosteroids, echinacea (purple coneflower) is used commonly by cancer patients, mainly due to "immune boosting" claims.
- Echinacea stimulates non-specific defense mechanisms including alternate complement pathway [70]. It is anti-tumerogenic in animal models.
- All varieties of Echinacea contain four main constituents:glycoproteins, polysaccharides, pigment anthocyanins, and caffeic acid.
- Echinacea extracts have been prescribed to supplement cancer chemotherapy. In a recent study, it was reported that Echinacea purpurea extracts protected noncancerous cells from apoptosis. Cervical and breast cancer cells were treated with the Echinacea [71].

17. *Morinda citrifolia:*

- Roots of *Morinda citrifolia* (Noni or Yor in Thai) are the source of important compounds, anthraquinones, which have been proven to have anti-viral, anti-bacterial, anti-cancer activities.
- The most medicinally valuable anthraquinones in the roots of this plant is damnacanthal, which has been used for treatment of chronic diseases such as cancer and heart disease.
- The compound, damnacanthal, found in the *Morinda citrifolia* (Noni), was found to be an inhibitor of Ras function i.e. on the K-ras-NRK cell (a pre cursor to certain types of cancer).
- The prevention of mammary breast cancer can be brought out by providing a safe, nutraceutical formulation comprising Morinda citrifolia, methylsulfonylmethane (MSM) [72].

18. *Sutherlandia frutescens*:

- This is also traditionally known as 'Cancer Bush' or 'Kankerbossie' is a medicinal herb exclusively found in Southern Africa and has been used by indigenous people for thousands of years to treat cancer, digestive ailments and also as a powerful tonic.
- The extract, which is mainly produced from the leaves, is reported to have anti-proliferative effects on cancer cells [73].
- Sutherlandia contains a number of highly active compounds, including pinitol, L-canavanine and the amino acid, GABA. L-

canavanine has clearly-documented anti-cancer and anti-viral activity.

- This compound L-canavanine is a non-protein amino acid with an anti-cancer capacity that has been demonstrated in abating pancreatic cancer.

19. *Viscum album* (Mistletoe):

- This herb is well known for its ability to maintain healthy blood pressure and improve the functioning of the immune system.
- Mistletoe was effective for cancer survival, tumor response, quality of life, psychological distress, or any other favorable outcomes [74]. However, two of the better designed studies did suggest some benefit for breast cancer patients undergoing chemotherapy.
- Another reported activity that may be relevant to optimum functioning of the immune system in individuals with cancer is stabilization of the DNA in white blood cells, including white blood cells that have been exposed to DNA-damaging chemotherapy drugs.
- Results of both human and animal studies recently suggest that this ancient herb also has an important part to play in the supportive treatment of cancer.

19. *Rhodiola rosea:*

- This is a member of a 50-species genus of plants with northern hemisphere distribution. *Rhodiola rosea* is an authentic adaptogen, non-specifically increasing the resistance of the body without disturbing its normal biological functions.
- Additionally, this amazing root is a strong antioxidant with several anti-cancer effects. It reduces the toxicity of anti-cancer drugs and enhances their anti-carcinogenic effects. It improves urinary tissue and immunity in patients with bladder cancer.
- In other experiments with various types of cancer, including adenocarcinomas, the use of extracts of *Rhodiola rosea* resulted in significant increased survival rate.
- It helps to inhibit tumor growth on its own, and is also anti-mutagenic, substantially reducing the development of chromosomal aberrations [75].

Adverse Effects of Herbal Supplements most commonly used by Cancer Patients: They are certainly associated with both risks and benefits. Even though herbal medicines are not devoid of risk, they could still be safer than synthetic drugs. For example: Kava, an effective herbal Anxiolytics [76] has recently been banned in several countries, including the United Kingdom, because of the suspicion that, in rare cases, it causes hepatotoxicity. These herbal supplements have been demonstrated to have adverse effects, possess antiplatelet activity, adversely interact with corticosteroids and the central nervous system depressant drugs, Have gastrointestinal manifestations, produce hepatotoxicity and nephrotoxicity, and produce additive effects when used concomitantly with opioid analgesics. In one analysis, some botanicals tested had unsafe levels of mercury and other toxic metals, and prescription drug compounds were discovered in more than a third of products tested.

- Turmeric exhibits antiplatelet activity. May enhance effects of anticoagulant medications such as warfarin and (*Curcuma longa*) potentiate bleeding.
- Valerian enhances the effects of sedatives, and hypnotic drugs (*Valeriana officinalis)* [51].
- Garlic appears to contain components that might exert their effects at various stages

involved in the process of platelet aggregation. In addition, serious hematologic side effects have been reported when garlic has been taken in conjunction with blood thinning prescription drugs such as warfarin [77]. A Garlic changes pharmacokinetic variable of paracetamol, decreases blood concentrations of warfarin, and produces hypoglycemia when taken with chlorpropamide.

- More serious side effects may include hypertension from use of ginseng or licorice, anaphylaxis from chamomile teas, and reactivation of systemic lupus erythematosus.
- Nausea, diarrhea, and skin reactions are common side effects of a wide variety of herbal medicines, and are usually considered relatively benign.
- Herbal supplements such as feverfew, *Ginkgo biloba*, echinacea, and St John's wort have been associated with oral manifestations such as aphthous ulcers, lip and tongue irritation and swelling, gingival bleeding tongue numbness, and xerostomia [78].

CONCLUSION: Though significant progress has been made towards the characterization of isolated compounds and their structure-related activities, the complex composition of plant extracts, along with the lack of reproducibility of activity and the synergy between different, even unidentified, components of an extract, prohibits the full utilization of plants. Current data suggest that all herbal medicines should be ceased 2 weeks before surgery. The American Society of Anesthesiologists suggests that all herbal medications should be discontinued 2 to 3 weeks before an elective surgical procedure. Healthy young adults often possess the physiologic capacity to properly metabolize herbal medicines with only limited reactions. This increasing use of herbal products has some very important implications for the older population and for those heading towards their senior years. Seniors have a higher incidence of illness and chronic conditions and because of this take a higher per capita number of different prescription medications. Because of this they need to be especially careful when adding herbal medications to their health regime.

There are several herbs, which should be completely avoided during pregnancy and there are some herbs that can lead to androgynous babies when taken in high doses in pregnancy. In addition, herbal products may be contaminated with hazardous substances: dangerous plant chemicals, toxic metals, disease-causing micro-organisms, fumigants and Pesticides. This is not to say that all these remedies are unsafe, impure or ineffective. Surveys have shown that cancer patients are among the most likely to seek complementary and alternative medical (CAM) remedies, including herbal medicines, with the hope that they would reduce the side effects of conventional treatments, extend life, or at least enhance quality of life. While awaiting outcomes of National Institutes of Health-funded studies of CAM practices in cancer patients, it would be prudent for patients and their oncologists to appreciate that, no matter how beneficial some approaches may appear to be, they are not all safe. Together, patients and oncologists should consider the options and develop a plan regarding which CAM practices to pursue and which to put aside altogether.

It is believed that the pharmacists are active participants in the care of patients who are taking herbal products. Currently, most pharmacists are not educated adequately about herbal products and other types of alternative

medicine. Furthermore, good information about many of these products is not available. These combined factors present a challenge for pharmacists as they seek to provide optimal care and counseling to patients who use herbs or supplements.

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