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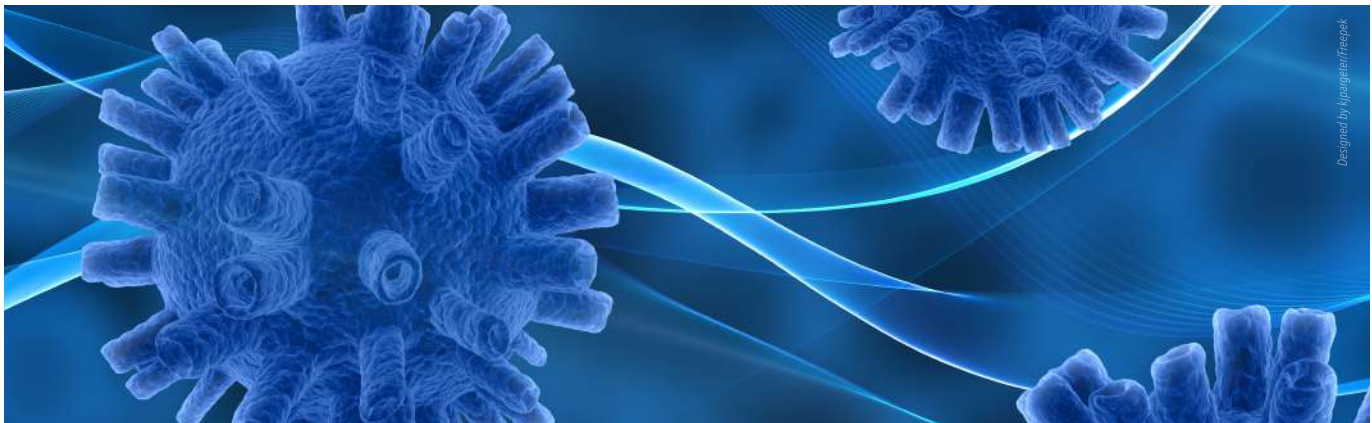
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Botanical Medicine in Cancer Prevention and Treatment

(Article adapted from College of Integrative Medicine Module 25 CIHP2504 Integrative Oncology)

Dr. Wayne Sodano DC, DABCI, DACBN, CFMP, BCTN



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“Plants have been used as medicines since the dawn of animal life. The initial use of plants as medicines by humans is thought to have been a result of ‘instinctive’ dowsing. Animals in the wild still provide evidence that this phenomenon occurs. Animals, with a few notable exceptions, eat plants that heal them and avoid plants that do them harm.”ⁱ “The use of botanicals in oncology is based on the synergistic hypothesis – that combinations of well-selected active constituents from one or more botanical species will together have a synergistic anticancer effect. Some of the ancient Traditional Chinese Medicine combination therapies have been shown to improve efficacy of chemotherapy in pancreatic and colon cancer patients.”ⁱⁱ Unfortunately, but not surprisingly, the use of whole plants or combination plant constituents has not been pursued by mainstream oncology research (mainly in the U.S.)ⁱⁱⁱ. “Even those who have pursued whole-plant botanical oncology have been stymied by the absence of adequate taxonomic, chemical, and bioassay validation of the natural products used in research.”^{iv}

“Botanicals are used in naturopathic oncology in several ways: to prevent cancer and metastasis in high-risk patients, to manage side effects of conventional cancer therapy, as adjuvants to improve efficacy and safety of chemotherapy agents, and as immunomodulators to prevent cancer relapse after treatment.”^v Plant medicines are used by integrative clinicians in several ways^{vi}:

1. In primary prevention of cancer at high risk for malignancy (anti-inflammatory via multiple pathways, pro-apoptosis actions and inhibition of proliferation pathways, antioxidants, and immunomodulators).
2. As phytopharmaceuticals with direct tumoricidal and apoptotic effects.
3. As adjuvants to improve the cytotoxic activity of cancer drugs.
4. As immunomodulators to enhance endogenous immunological tumoricidal activity.
5. To treat radiation-related reactions and fatigue.
6. To mitigate the homological, neurologic, and gastrointestinal toxicities of U.S. FDA - approved chemotherapy pharmaceuticals
7. To improve survival and quality of life in survivorship.

It is my opinion that prescribing a healing substance(s) for chronic conditions in isolation (i.e. scientific reductionism) without using a holistic, integrative medicine approach to care, generally produces little to no positive healing effects. For example, substituting a natural anti-cholesterol or anti-inflammatory for a pharmaceutical drug may have fewer side effects, but it does not address any of the etiological factors and/or triggers known to cause the conditions. In addition, few clinical trials have demonstrated conclusive cancer prevention benefit^{vii}. The majority of the clinical trials use a single substance (e.g. vitamin C, vitamin E, selenium, vitamin D, beta-carotene, curcumin, soy, green tea, fish oils, probiotics, and medicinal mushrooms) when conducting research on the chemoprotective qualities of natural products without giving consideration to subject in integrative/holistic medicine manner.

I would like to someday read about clinical trials that studied the effectiveness of restoring a major system of the body (e.g. gastrointestinal, immune and detoxification system) and/or reducing the toxic load via detoxification protocol or using an anti-inflammatory diet with concomitant use of a natural product such as immune enhancing medicinal mushrooms as it relates to cancer prevention and treatment. For example, the immune system and tumors cells are often concurrent in a dynamic equilibrium and both have a complex interaction and are interlinked^{viii}. An immune system dysfunction can alter the functioning of the natural killer (NK) cells. These cells can lyse tumor cells and viruses infected cells, and play an important role in immune surveillance of cancer and are accomplished to prevent cancer growth. "The ligand on the surface of target cells

(infected or tumor cells) triggers NK cell cytotoxicity and activates the receptors on the NK cells. These ligand are absent on normal cells. NK cells modulate activity of other leukocytes such as dendritic cells and T cells through cytokines."^{ix} There are several natural agents that can increase the cytotoxic activities of the NK cells and increase the level of tumor necrosis factor alpha while decreasing the DNA damage in patients with late stage cancer^x. The research study below highlights the potential use of a nutraceutical approach for the treatment of cancer by boosting the immune system. Although there was no mention of concomitant treatment of any of the body systems or other dietary changes, I believe the study can serve as an inspiration for future studies, even though conventional medicine appears not to be in favor the natural approach to cancer treatment at this time. (As of this writing, I could not find any significant cancer research studies that assess and treat the body systems in combination with prescribing nutraceuticals.)

Studies confirmed that clinical results can be improved by a combination of nutraceuticals. Twenty patients of stage IV (bladder, breast, prostate, lung, neuroblastoma, mesothelioma, lymphoma, ovarian, gastric and osteosarcoma) cancer were treated with natural products such as transfer factor plus (contains bovine colostrum, mushroom extracts and other ingredients), immune modulator mix, ascorbic acid, IMU plus, Agaricus blazei teas, nitrogenated soy extract and Andrographis paniculata. After nutrient application, the function of NK cells, TNF- α and receptor levels were measured by phytohemagglutinin (PHA) and ELISA. Complete blood count and chemistry panels were daily counted. After 6 months, 16 of

the 20 patients were alive, which showed maximum efficiency of NK cell function and TNF- α level in all four cell population. It was observed that hemoglobin, hematocrit and glutathione levels were prominent in investigated patients. It concluded that an aggressive combination of immuno-active nutraceuticals was effective in late stage cancer; while the clinical outcome evaluation are ongoing. (Nouroz F, Bibi F, Noreen S, Masood N, Natural killer cells enhance the immune surveillance of cancer. The Egyptian Journal of Medical Human Genetics. August 2015.)

“Study on various plant constituents revealed that most of the phytochemicals are widely used as immune modulators against cancer and tumors. The important anti-cancerous natural plant products are apigenin (e.g. parsley), crocetin (e.g. saffron), curcumin (e.g. turmeric), cyanidins (e.g. grapes, cranberries, raspberries, etc.), epigallocatechin gallate (e.g. green tea,) fisetic (e.g. strawberries and apples), diindolylmethane (e.g. Brassica vegetables), genistein (e.g. soybean), gingerol (e.g. ginger), kaempferol (e.g. grapefruit, tea and broccoli), lycopene (e.g. tomatoes), resveratrol (e.g. grapes), sulforaphane (e.g. cruciferous vegetables), rosmarinic acid (e.g. rosemary), vitamin D (e.g. mushrooms), and vitamin E for various plant oils.”^{xii} It show be obvious that incorporating this foods in the diet and avoid “junk food” can produce profound positive health benefits.

Natural Compounds and Sources of Promising Cancer Prevention and Cancer Treating Agents ^{xiii}

COMPOUND	NATURAL SOURCE	MODE OF ACTION	TYPE OF CANCERS	SYNERGISTIC
Flavonoid Honokiol	Magnolia officinalis, Magnolia graniflora, Magnolia app.	Antioxidant, antiproliferation (Cell - cycle arrest, apoptosis), anti-inflammation, anti-angiogenesis, anti-autophagy, immunomodulation, anticancer, gastrointestinal disorders, cough, anxiety, and allergies.	Glioblastoma, melanoma, gastric, leukemia, skin, colon, breast, ovarian, pancreatic, hepatocellular, colorectal, lung, prostate, human renal mesangial, head, and neck squamous carcinoma.	Flavonoid Honokiol
Flavonoid Magnolol	Magnolia officinalis, Magnolia obovata.	Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, anti-angiogenesis, anti-anxiety, antidepressant, hepatoprotective effects immunomodulation, anticancer.	Glioblastoma, bladder, breast, colon, gastric, skin, ovaian, lung, prostate, melanoma, liver cancer, cervical epitheloid carcinoma, leukemia, fibrosarcoma, neuroblastoma, thyroid carcinoma	TNF- α , curcumin
Flavonoid Jaceosidin	Artemisia princeps, Artemisia iwayomogi, Artemisia argyi, Artemisia copa, Artemisia vestita, Saussurwa medusa, Eupatorium arnottianum, Eupatorium lindeyanum, Cantaurea	Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation.	Human endometrial, human ovary cancer, glioblastoma, breast, epithelial, prostate, cervical, mammary epithelial.	TNF- α ,

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	<p>phyllocephala, Centaurea nicaeensis, Nipponanthemum nipponicum, Arnica chamissonis, Arnica Montana, Vervain officinalis, Lantana monyevidensis, Eriodicyon californicum</p>			
<p>Flavonoid Casticin</p>	<p>Vitex rotundifolia, V. agnus castus, V. trifolia, V. negundo, Daphne genkwa, Achillea millefolium, Ficus microcarpa, Fructus viticis, Crataegus pinnatifida, Pavetta crassipes, Nelsonia canescens, cutrus unshu, Centipedia minima, Clausena excavate, Croton betulaster, Artimeisia abrotanum, Carmellia sinensis</p>	<p>Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, immunomodulation, premenstrual syndrome, anti-anxiety, antimalarial, antimicrobial, antifungal properties.</p>	<p>Cervical, pancreatic, colon, breast, lung, gastric, ovarian, liver, colorectal, leukemia, prostate.</p>	<p>TRAIL, TNF - α, cisplatin, curcumin</p>
COMPOUND	NATURAL SOURCE	MODE OF ACTION	TYPE OF CANCERS	SYNERGISTIC
<p>Sesquiterpenes Costunolide</p>	<p>Inula helenium, Saussurea lappa, Magnolia grandiflora</p>	<p>Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, anticancer, antiviral, antifungal.</p>	<p>Liver, ovarian, breast, bladder, melanoma, leukemia, prostate, human monocyte gastric, colorectal.</p>	<p>TNF - α, taxol, cisplatin.</p>
<p>Sesquiterpenes Parthenolide</p>	<p>Tanacetum parthenium, Tanacetum vulgare, Centaurea ainetensis, Tanacetum larvatum, Helianthus annus, Anvillea radiate, Magnolia kolus, Magnolia virginiana, Magnolia ovate, Magnolia grandiflora, Liriodendron tulipifera, Magnolia chapaca, Michellia floribunda, Tsoongiodendron odorum, Artemisa ludoviciana, Celea zacatechichi, Polymnia maculate, Achillea falcata</p>	<p>Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, anti-angiogenesis, autophagy, immunomodulation, and cytotoxic effects</p>	<p>Breast, skin, melanoma, malignant glioma, epidermal tumorigenesis, liver, gastric, lung, bladder, prostate, bile duct carcinoma, pancreatic, myeloma, leukemia, colorectal, Burkitt lymphoma, epithelial ovarian, osteosarcoma</p>	<p>TRAIL, gemcitabine, taxol, TNF - α, cisplatin, curcumin, okadaic acid, geldanamycin, buthionine sulfoximine.</p>

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COMPOUND	NATURAL SOURCE	MODE OF ACTION	TYPE OF CANCERS	SYNERGISTIC
Sesquiterpenes Alantolactone	Inula helenium, Inula japonica, Aucklandia lappa, Radix inulae, Inula racemosa	Anti-inflammatory, antimicrobial, anticancer, cytotoxicity, antifungal, oxidoreductase, and antiproliferative	Prostate, glioblastoma, leukemia, liver, lung	
Sesquiterpenes Isoalantolactone	Inula helenium, Inula japonica, aucklandia lappa, Radix inulae, Inula racemosa	Anti-inflammatory, antimicrobial, anticancer, cytotoxicity, antifungal, oxidoreductase, and antiproliferative	Prostate, gastric, pancreatic, leukemia	
COMPOUND	NATURAL SOURCE	MODE OF ACTION	TYPE OF CANCERS	SYNERGISTIC
Diterpenoid Oridonin	Isodon rubescens	Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti - inflammation, autophagy, immunomodulation	Breast, astrocytoma, leukemia, lung, hepatoma, prostate, colorectal, pancreatic, ovarian, human multiple myeloma, human histiocytic lymphoma, hepatocellular, cervical, neuroblastoma, laryngeal, gastric, murine fibrosarcoma, melanoma, apidermoid carcinoma, osteosarcoma	TRAIL, gemcitabine, taxol, TNF - α , cisplatin, curcumin, arsenic trioxide (AS ₂ O ₃), Wogoninleuk emia, liver, lung
Diterpenoid - Pseudolaric acid B	Pseudolarix kaempferi	Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, anti-angiogenesis, anticancer immunomodulation	Micovessell endothelial, prostate, glioblastoma, umbilical vein endothelial, murine fibrosarcoma, bladder, colon, lung, breast, melanoma, ovarian, leukemia, gastric, liver	Taxol, TNF - α .
Polyphenolic Wedelolactone	Eclipta alba, Wedelia calandulaceae, Wedelia chinesis, Eclipta protrata	Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, hepatoprotective effects	Breast, prostate, neuroblastoma, pancreatic, mammary carcinosarcoma, myeloma, leukemia, adenoma, glioma	IFN - γ
Alkaloid Evodimine	Evodia rutaecarpa	Antioxidant, antiproliferation (cell-cycle arrest, apoptosis), anti-inflammation, antimicrobial, anticancer, antimetastatic, anticarcinogenesis	Hepatocellular, leukemia, gastric, pancreatic, colon, human thyroid cancer, melanoma, colorectal, breast, cervix carcinoma, prostate	Gemcitabin, taxol, TNF- α , cisplatin

“The use of botanical and fungal medicines by integrative oncologists in the West is largely evidence based.”^{xiii} The most commonly used botanical medicines for a specific cancer include^{xvi}:

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CANCER TYPE	COMMONLY USED BOTANICALS AND MYCOMEDICINES
Breast cancer	<ul style="list-style-type: none"> Turkey tail mushroom, maitake mushroom, artemisinin, resveratrol, garlic, Quercetin, bromelain, curcumin, green tea, flax seeds, soy, 3,3'-diindolylmethane (DIM) and sulforaphane extracted from cruciferous vegetables
Prostate cancer	<ul style="list-style-type: none"> Garlic, green tea, soy, pomegranate, silymarin, curcumin, lycopene
Lung cancer	<ul style="list-style-type: none"> Turkey tail mushroom, astragalus, green tea, curcumin, silymarin, bromelain, ginseng, garlic, ginkgo, mistletoe
Colorectal and gastric cancer	<ul style="list-style-type: none"> Turkey tail mushroom, maitake mushroom, curcumin, garlic, astragalus, green tea, mushrooms, flax seeds, resveratrol, mistletoe (<i>Viscum alba</i>)
Head and neck cancer	<ul style="list-style-type: none"> Turkey tail mushroom, curcumin, green tea
Glioblastoma multiforme	<ul style="list-style-type: none"> Resveratrol from grape seeds, boswellia, curcumin, aloe vera, lycopene
Melanoma	<ul style="list-style-type: none"> Green tea, curcumin, flavonoids, mistletoe (<i>Viscum alba</i>)
Ovarian cancer	<ul style="list-style-type: none"> Turkey tail mushroom, ginkgo biloba, soy, green tea, curcumin
Hepatocellular carcinoma	<ul style="list-style-type: none"> Turkey tail mushroom, green tea, ginseng, mushroom derivatives beta glucans, milk thistle
Lymphoma	<ul style="list-style-type: none"> Turkey tail mushroom, Lomatium isolatum, curcumin, green tea, flavonoids, astragalus
Leukemia	<ul style="list-style-type: none"> Turkey tail mushroom, green tea, astragalus, soy
Multiple myeloma	<ul style="list-style-type: none"> Plant enzymes, curcumin, green tea, astragalus, soy

- ⁱ Murray MT. *Botanical Medicine - A Modern Perspective*. In: Pizzorno JE, Murray MT. *Textbook of Natural Medicine*. 4th Ed. St. Louis: Elsevier; 2013. P. 257.
- ⁱⁱ Standish LJ, Alschuler IN, Ready AB, Torkelson C, Sivam G, Wenner C. *Botanical Medicine in Integrative Oncology*. In: Abrams D, Weil A. *Integrative Oncology*. Oxford; Oxford University Press; 2009. p.104.
- ⁱⁱⁱ Standish LJ, Alschuler IN, Weaver M, Nezami M. *Botanical and Mycological Medicine in Integrative Oncology*. In: Abrams D, Weil A. *Integrative Oncology*. Oxford; Oxford University Press; 2014.
- ^{iv} *Ibid.*
- ^v *Ibid.*
- ^{vi} *Ibid.*
- ^{vii} Greenlee H. *Natural Products for Cancer Prevention*. *Semin Oncol Nurs*. Feb 2012; 28(1): 29-44.
- ^{viii} Nouroz F, Bibi F, Noreen S, Masood N. *Natural killer cells enhance the immune surveillance of cancer*. *The Egyptian Journal of Medical Human Genetics*. August 2015.
- ^{ix} *Ibid.*
- ^x *Ibid.*
- ^{xi} *Ibid.*
- ^{xii} Millimouno FM, Dong J, Yang L, Li J, Li X. *Targeting Apoptosis Pathways in Cancer and Perspectives with Natural compounds from Mother nature*. *Cancer Prev Res*; 2014; 7(11); 1081-1107.
- ^{xiii} Standish LJ, Alschuler IN, Weaver M, Nezami M. *Botanical and Mycological Medicine in Integrative Oncology*. In: Abrams D, Weil A. *Integrative Oncology*. Oxford; Oxford University Press; 2014.
- ^{xiv} *Ibid.*