Materia Medica for Managing Cancer Cyto-toxic Herbs

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"In America we are becoming a nation of nervous, hysterical people. You must realize that if the nerve power falls below the normal standards there is danger of the invasion of cancer.

What our people need to be taught is how to live. Good pure water, good pure air helps you make good healthy blood. Unadulterated food, mostly vegetables, which are easily digested, keep the nervous system strong and vigorous".

Eli Jones 1909

THERAPEUTIC INTENTIONS

Improve quality of life and increase longevity

- Build vitality and healing capacity
- Delay or inhibit progression of cancer
- Enhance potencies and efficacy of conventional treatment
- Relieve side effects of conventional treatments
- Address underlying imbalances including stress, blood stagnation, redox cycling and mitochondrial efficiency.

THERAPEUTIC STRATEGIES

- Restore vitality tonics, adaptogens, bitters, nutritives
- Optimize internal chemistry diet (sugars, proteins, fats, fruits and vegetables)
- Detoxify alteratives, cholagogues, diaphoretics, aperients
- Support immune system deep immune tonics
- Induce apoptosis in cancer cells flavonoids, cytotoxics anti-neoplastics

THERAPEUTIC STRATEGIES

Increase mitochondrial energy transfer

•Normalize gene expression and gene repair

•Disrupt cancer cell metabolism and normalize growth factors, signal transduction and signal transcription

•Promote hepatic and other metabolic detox pathways

•Support bone marrow and immune activity, reduce local inflammation

Normalize angiogenesis

•Strengthen blood vessel walls, inhibit collagenases and proteases, inhibit hyper coagulation

Factors to Consider in Integrative Oncology

- Specifics of the patient (constitutional weaknesses, psychological and physical environment)
- Specifics of the cancer (growth factors, hormones; gene mutations, angiogenic rate, etc.)
- Symptoms present (nausea, pain, indigestion, etc.)
- Other treatments (interactions between NHP's and conventional medicine: chemotherapy, radiotherapy or other medication)
- Other co-existing health conditions

Major cell behaviors to target

- 1) Cellular mitochondrial energy transfer
- 2) Neuro-endocrine dysregulation
- 3) Anabolic / catabolic balance
- 4) Redox balance
- 5) Immune surveillance
- 6) Inflammatory response
- 7) Connective tissue
- 8) Cytotoxics
- 9) Anti-angiogenesis
- 10) Coagulopathy

Phytochemicals in herbal extracts

• Curcumin, genistein, resveratrol, catechins = block EGFR

• Curcumin, catechins, silymarin, sanguinarine, emodin, resveratrol, capsaicin = inhibit the NF-κB pathway

• Curcumin, capsaicin, resveratrol, green tea catechins, 6-gingerol = inhibit AP-1 pathway

• EGCG = block the MAPK signaling pathway

(Phytother Res. 2006 Apr;20(4):239-49)

Categories of herbs used in cancer treatment

- primary adaptogens
- · companion or adjunctive adaptogens
- immune system modulators and mediators of inflammation
- alteratives and hepatics
- specific cytotoxics
- connective tissue tonics
- symptomatics (including pain, cachexia, anemia etc)

Classes of terpenoid compounds with anti-cancer activity

- Sterols beta sitosterol, stigmasterol, ampesterol
- Phytoecdysterones luzeasterone, ecdysone
- Monoterpenes limonene
- Diterpenes forskolin, parthenolide, taxanes
- Sesquiterpenes artemisinin
- Terpenpid quinones ubiquinone (CoQ10)
- Triterpenes ginsenosides, eleutherosides, astragalosides, withanolides, ursolic acid
- Tetraterpenes carotenoids, luetin, lycopene

Plant compounds that inhibit telomerase:

- Silibinin, from Milk thistle (Silybum marianum)
- Baicalein, from Baical skullcap (Scutellaria
- baicalensis)
- beta-Lapachone, from Pau d'arco, Taheebo
- Podophyllotoxin from May apple (Podophyllum
- peltatum)
- Gossypol from Cotton seed

Anti-tumorigenics

Potent cytotoxics	Adjunctives
Asimina triloba	Calendula officinalis
Artemisia annua	Camellia sinensis
Camptotheca acuminata	Corydalis ambigua
Chelidonium majus	Curcuma longa
Larrea divaricata	Ganoderma lucidum
Phytolacca decandra	Thuja occidentalis
Podophyllum peltatum	
Taxus sp.	
Vinca rosea	
Viscum album	

Artemisia annua L. annual wormwood, sweet wormwood, sweet annie

A highly aromatic annual herb of Asiatic and eastern European origin; widely dispersed throughout the temperate region; naturalized in the United States

Bitter, acrid and cooling. Used in TCM to clear damp heat.

Essential oils of *A. annua* are comprised of many constituents with the major compounds including (in relative % of total essential oil) alpha-pinene (0.032%), camphene (0.047%), ß-pinene (0.882%), myrcene (3.8%), 1,8-cineole (5.5%), artemisia ketone (66.7%), linalool (3.4%), camphor (0.6%), borneol (0.2%), and ß-caryophyllene (1.2%).

Analysis of artemisinin is difficult because the compound is unstable, concentrations in the plant low, the intact molecule stains poorly, and other compounds in the crude plant extracts interfere in its detection. *Artemisinin* is a sesquiterpene lactone with 2 oxygen atoms linked by an endo-peroxide bridge.

This readily reacts with iron to form free radicals \rightarrow oxidative stress to cell.

Preferentially taken up with iron therefore test for iron, ferritin, total iron binding capacity and soluble transferrin receptors

Artemisinin and its derivatives, artemether and artesunate, have been studied for their efficacy as antimalarial agents.

In vitro trials conducted in China (WHO 1981), showed all three compounds to be effective against the erythrocytic stages of two chloroquine-resistant Hainan strains of *Plasmodium falciparum*, the malarial parasite, at lower minimum effective concentrations than chloroquine, the most commonly used drug.

Artemisinin and its derivatives have effectively treated malaria and cerebral malaria in human subjects with no apparent adverse reactions nor side effects (Klayman 1985). In vitro studies indicate that artemisinin may be an effective treatment for other protozoal infections such as leishmaniasis, Chagas' disease, and African sleeping sickness.

Leaves have 89% of the total artemisinin in the plant with the uppermost foliar portion of the plant (top 1/3 of growth at maturity) containing almost double that of the lower leaves.

Artemisinin is absorbed faster from the tea preparations than from capsules. The maximum plasma concentrations were observed after 30 minutes following intake. Artesunate is rapidly absorbed and reaches maximum plasma level within 45-90 minutes. It is metabolized in the liver by hydrolysis to dihydroartemisinin Upregulation of CYP 2B6, CYP 2C19 and CYP 3A4

 $\rightarrow\,$ increased hepatic clearance so plasma levels drop off after 5 – 7 days.

Women clear up to twice as fast as men.

Therefore need to pulse dose to allow enzymes to normalize periodically

Adverse Reactions

Oral (high doses): Artemisia may cause abdominal pain, bradycardia, diarrhea, nausea, vomiting, decreased appetite, flu-like symptoms, fever, liver enzyme elevations and decreased reticulocyte count. Topical: Artemisia may cause dermatitis

Herb-Drug Interactions

Antacids: Artemisia interferes with antacids, sucralfate, proton pump inhibitors, and histamine-receptor antagonists because it increases the production of stomach acid.

Anti-seizure medications: Artemisia can induce seizures resulting in decreased efficacy of anti-seizure medications

Artemisinin and derivatives:

ART in blood absorbed across cell membrane with iron. ROS formed in cell cytoplasm

 \rightarrow

- Inhibits ras proteins
- Inhibits multi drug resistance pathways
- Decreases mitochondrial membrane potential in cancer cells leading to 30 – 50% decrease in available cellular energy.
- · Inhibits VEGFr expression, anti-angiogenesis

Artesunate is a synergist with Tarceva in glioblastoma

Dihydroartemisin is a synergist with radiotherapy in glioblastoma

<u>Dosing plan</u> Pulse dose alternate weeks in increasing doses

Week onetaken with grapefruit juiceART 150 mg (1 cap) twice dailyButyric acid up to 10 gVitamin C to bowel toleranceH2O2 if desiredIron if levels are lowGLA 1000 mg, DHA 500 mg, EPA 750 mg

<u>Week two</u> Cytotoxics blend

<u>Week three</u> ART 150 mg (1 cap) three times daily

<u>Week four</u> Cytotoxics blend

<u>Week five</u> ART 300 mg (2 caps) three times daily

<u>Week six</u> Cytotoxics blend

<u>Week seven</u> ART 450 mg (3 caps) three times daily Butyrate is a naturally occurring, short-chain fatty acid that is a potent inducer of cellular differentiation. The effects on differentiation are mediated through its inhibition on histone deacetylase.

Inhibition of this enzyme leads to an increase in histone acetylation, changes in chromosome structure, and increased DNA transcription.

Experimental concentrations of 1.0 millimolar plasma levels produced a ten fold increase in artemisinin effect.

To attain such plasma levels you need to take at least 10 grams (10,000 mg) a day. In brain tumors, doses up to 20 g /day have been used.

Butyrate is totally non toxic (its a food ingredient found typically in butter) and is a selective nutrient for colonocytes.

At these high doses the main side effect is body odor.

Chelidonium majus Greater celandine

Traditional indications

Full, pale tongue and mucous membranes, sallow complexion Hepatic congestion, jaundice, throbbing pain in right Hypochondrium Bilious headaches

Modern research Inhibits mitotic cyclins A and B, and cyclin dependent kinases CDK1 and CDK2 Upregulates CDK inhibitor p27 Inhibits BcI-2 Induces apoptosis Habitat

A wild hedgerow plant of Europe, preferring sunny and slightly rocky, sheltered spots.

Botany

Herbaceous perennial. Glaucous finely divided foliage. Bright yellow-orange flower with four petals in a cross shape.

Parts used **Aerial parts, picked shortly before flowering.**

Actions Stimulant, acrid, alterative, diuretic, diaphoretic, purgative, and vulnerary.

Latex is bright orange and slightly caustic.

Crude extracts of *Chelidonium majus*, and purified compounds derived from crude extracts, exhibit antiviral, anti-inflammatory, anti-tumor and anti-microbial properties both in vitro and in vivo.

Chelidonium is used against various liver disorders including cancer in humans.

The juice, when applied to the skin, produces inflammation, and even vesication, and has long been known as a caustic for the removal of warts, indolent ulcers, fungal growths, etc.

It has tissue specificity for the parts supplied with nerve force from the branches of the solar plexus, and with blood from the hepatic artery, and to some extent by the splenic artery. Indicated for

Migraine, bilious headaches, supraorbital neuralgia, bilious dyspepsia, with headache, and other gastric and intestinal disturbances, due to faulty action of the liver

Hemorrhoids, hepatic and splenic congestion, and gastro-intestinal disorders, due to capillary engorgement of the viscera

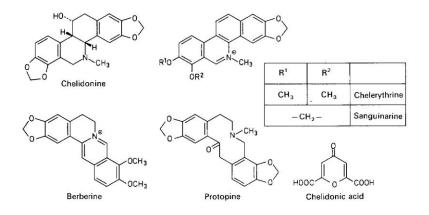
Specific Indications and Uses

"Full, pale, sallow tongue and mucous membranes; skin pale and sallow, sometimes greenish;" hepatic congestion; jaundice, due to swollen bile ducts; sluggish hepatic action; cough, with hepatic pain; fullness, with tensive or throbbing pain in the right hypochondrium, and pain extending to right shoulder; melancholia, headaches, and gastric disorders, dependent upon faulty action of the liver.

Felter, Harvey Wickes, Lloyd, John Uri, 1898, King's American Dispensatory

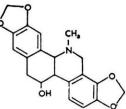
Alkaloids

Chelidonine, chelerythrine, sanguinarine and sometimes protopine.



Alkaloids

Chelidonine is a major component in the roots but not in the tops.



Alkaloids are maximized when the plants grow in open sunshine in soils with a neutral pH Treatment for patients with bile, liver, and digestive troubles.

Stimulates bile flow in guinea-pigs.

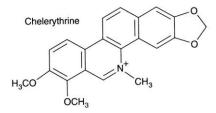
Chelidonium extracts and their alkaloidal fractions relieve histamine-induced spasms of guinea-pig ileum in vitro.

Chelerythrine and protopine stimulate the isolated small intestine and uterus of rabbits and guineapigs, and chelidonine also stimulates the uterus.

In frogs, mice, and rats an extract reduced pain sensation for 4-48 hours and relieved gastralgia from ulcers.

It also toned the small intestine and stimulated the uterus of the rat while relaxing its colon.

Chelerythrine and sanguinarine are anti-inflammatory with low toxicity and have been recommended for use in the treatment of oral inflammatory processes.



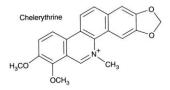
They also inhibit liver alanine aminotransferase activity and along with a number of minor *Chelidonium* alkaloids inhibit acetyl-cholinesterase activity

Chelidonium root possesses potent in vitro antimicrobial activity specifically against *Staph. aureus, Klebsiella pneumoniae, Mycobacterium smegmatis,* and *Candida albicans.* The activity of chelerythrine and sanguinarine is much greater against gram-positive than gram-negative bacteria.

Sanguinarine has slightly greater fungistatic activity than chelidonine and protopine against *Epidermophyton floccosum* in vitro.

Chelerythrine and sanguinarine produced an antifungal effect in vitro against *Trichophyton mentagrophytes* and *T. rubrum, Microsporum canis, Epidermophyton floccosum*, and *Aspergillus fumigatus*.

The activity of chelerythrine was comparable to that of the commercial preparations nitrofungin and myco-decidin.



The antiviral activity of *Chelidonium* root includes activity against the measles virus, inhibition of Herpes virus *in vitro* and viral encephalomyocarditis.

Neutralizes influenza virus *in vitro*, and prolongs the survival of mice infected with influenza A virus.

The more potent thiophosphamide derivatives of chelidonine have been shown to reverse the T-helper cell deficiency and diminish the T-suppressor cell overgrowth in patients with AIDS

Celandine has traditionally been used to treat cancer and recently has been tested for cytotoxic effects. It was comparable to many commonly used chemotherapeutic drugs

Celandine has traditionally been used to treat cancer and recently has been tested for cytotoxic effects. It was comparable to many commonly used chemotherapeutic drugs A study in 2002 suggested that the homeopathic drug Chelidonium exhibited anti-tumor and anti-genotoxic activities and also favorably modulated activities of some marker enzymes and that microdoses of Chelidonium may be effectively used in combating liver cancer.

A Thiophosphate derivative of alkaloids from *Chelidonium majus* (Ukrain) was found to significantly enhance the quality of life and prolong life of patients with pancreatic cancer. Ukrain exerted selective cytotoxic and cytostatic effects on tumor cells, simultaneously acting as an immune response modifier and showing good tolerance and lack of side effects even after long-term application.

Uglyanitsa KN, Nefyodov LI, Doroshenko YM, Nowicky JW, Volchek IV, Brzosko WJ, Hodysh YJ.

Ukrain: a novel antitumor drug. Drugs Exp Clin Res 2000;26(5-6):341-56

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Gansauge F, Ramadani M, Pressmar J, Gansauge S, Muehling B, Stecker K, Cammerer G, Leder G, Beger HG., NSC-631570 (Ukrain) in the palliative treatment of pancreatic cancer. Results of a phase II trial. Langenbecks Arch Surg 2002 Mar;386(8):570-574

Taxus brevifolia

Contains 27 different diterpene taxanes \rightarrow potent anti-cancer activity

Decreases availability of tubulin to form spindles during mitosis \rightarrow prolonging of Gap 1 phase and inhibition of cell replication

Taxol is one of the 27 diterpenes Taxotere is a synthetic analogue

Taxus sp. also contains

four flavonoids, including quercetin

three plant sterols, which include beta-sitosterol, daucosterol, and ponasterone A.

Anti-oxidant, anti-inflammatory and immune modulating effects

Taxus brevifolia (Pacific Yew or Western Yew) is a conifer native to the Pacific Northwest rangeing from southernmost Alaska south to central California, mostly in the Pacific Coast Ranges.

It is a small to medium-sized evergreen tree, growing 10-15 m tall and with a trunk up to 50 cm diameter, rarely more.

Taxus baccata is a conifer native to western, central and southern Europe, northwest Africa, northern Iran and southwest Asia.

It is a small- to medium-sized evergreen tree, growing 10–20 metres (33–66 ft) (exceptionally up to 28 m/92 ft) tall, with a trunk up to 2 metres (6 ft 7 in) (exceptionally 4 m/13 ft) diameter.

Yew is slow growing, but very long-lived, with the maximum recorded trunk diameter of 4 metres probably only being reached in about 2,000 years.

The age of yews is impossible to determine accurately and is subject to much dispute. There is rarely any wood as old as the entire tree, while the boughs themselves often hollow with age, making ring counts impossible.

Taxus baccata is the longest living plant in Europe.

Fossil yew over 1 million years old is identical with yew today.

The yew's reputation for long life is due to the unique way in which the tree grows. Its branches grow down into the ground to form new trunks, which then rise up around the old central growth as separate but linked trunks. After a time, they cannot be distinguished from the original tree. So the yew has always been a symbol of death and rebirth, the new that springs out of the old.

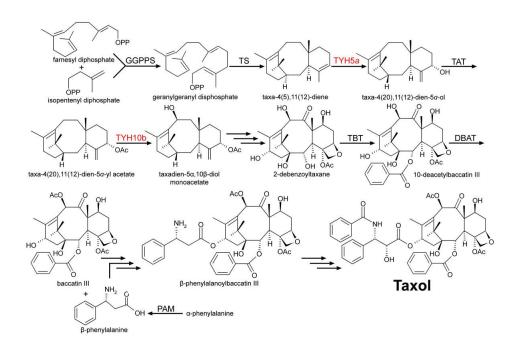
The life of a Yew, the length of an Age

"The lives of three wattles, the life of a hound; The lives of three hounds, the life of a steed; The lives of three steeds, the life of a man; The lives of three eagles, the life of a yew; The life of a yew, the length of an age; Seven ages from Creation to Doom.

Most parts of the tree are toxic, except the bright red aril surrounding the seed, enabling ingestion and dispersal by birds.

The major toxin is the diterpenoid taxane. The foliage remains toxic even when wilted or dried. Horses have the lowest tolerance, with a lethal dose of 200–400 mg/kg body weight, but cattle, pigs, and other livestock are only slightly less vulnerable.

Symptoms include staggering gait, muscle tremors, convulsions, collapse, difficulty breathing, and eventually heart failure. However, death occurs so rapidly that many times the symptoms are missed.



Paclitaxel (taxol), first isolated from Taxus brevifolia as antitumor agent in the late 1960's.

Semi-synthetic taxane called docetaxel (taxotere) derived from 10-deacetylbaccatin III was introduced in the 1990's.

Paclitaxel and docetaxel are two of the most effective chemotherapeutic drugs used today. They are used to treat many types of cancers including ovarian, breast, and non-small cell lung cancer. Taxanes act by inhibiting microtubule dynamics, inducing cell cycle arrest in M phase and consequent activation of the apoptotic program.

Rather than inhibiting microtubulin formation at the M phase (the mitotic phase of the cell during which time the cell is dividing) the way other plant alkaloids do, Taxol inhibits cell division by inhibiting availability of tubulin required for assembly. This keeps it in the Gap I phase longer than it should and not allowing the cell to get to the Mitotic phase for division.

Clinical treatment with synthetic taxane agents often causes undesirable side effects and multidrug resistance (MDR) caused by overexpression of P-glycoprotein (Pgp).

Some non-taxol-type taxanes, in the yew demonstated an ability to enhances the cytotoxcitiy of other cytotoxic compounds inhibiting multi-drug resistance. These taxanes increased cellular accumulation of vincristine (VCR) in multidrug-resistant cells as potently as verapamil.

Various taxanes, other than taxol, from the yew tree may be candidates for pharmaceuticals for reversing multi-drug resistance (MDR) and also may be good modifiers of MDR in cancer chemotherapy. **Clinical applications**

Yew extract is an excellent general alterative with a high affinity for suppressing cancerous growth. It is also is advantage to use with taxane-derrived drugs such as Taxol and Abraxane; for it potentiates and reduces MDR.

Energetically speaking, Yew is an invaluable ally for those who have cancer and facing death, as it can assist in breaking through dogma, doubts, fear and conditioning by elevating our spirit – the "Shen." The Yew helps to make the connection between our brief mortal lives and eternity.

Asimina triloba

Contains over 50 acetogenins, concentrated mostly in the seed. These are derivatives of long chain (C-32 or C-34) fatty acids. They represent a large class of naturally occurring polyketides exhibiting potent anticancer activities.

Powerful inhibition of mitochondrial NADH:ubiquinone oxidoreductase and therefore inhibition of mitochondrial ATP production

Up-regulates p21

Inhibition of multi drug resistance

Polyketides are secondary metabolites from bacteria, fungi, plants, and animals. They are biosynthesized by the polymerization of acetyl and propionyl subunits in a similar process to fatty acid synthesis.

They are the building blocks for a broad range of natural products. Polyketides are structurally a very diverse family of natural products with diverse biological activities and pharmacological properties.

Polyketide antibiotics, antifungals, cytostatics, anticholesterolemics, antiparasitics, animal growth promoters and natural insecticides are in commercial use

Pawpaw is a large shrub or small tree growing to a height of 11 meters (rarely to 14 m) with a trunk diameter of 20-30 cm. The leaves are deciduous,

It is native to eastern North America, from southernmost Ontario and New York west to eastern Nebraska, and south to northern Florida and eastern Texas. The fruit is rich in fatty acids, especially octanoate. They also contain *cis*- δ 9- and *cis*- δ 11-hexadecenoate, *cis*- δ 9-, *cis*- δ 11- and *cis*- δ 13-octadecenoate.

The seeds contain the polyketide acetogenins asimitrin and 4-hydroxytrilobin.

These chemicals have selective cytotoxicity against prostate adenocarcinoma and colon adenocarcinoma cell lines.

The leaves also contain toxic annonaceous acetogenins, making them unpalatable to most insects. The one notable exception is the zebra swallowtail butterfly (*Eurytides marcellus*), whose larvae feed on the leaves. This confers protection from predation throughout the butterfly's life, as trace amounts of acetogenins remain present, making them unpalatable to birds and other predators.

The bark contains other acetogenins, including asimin, asiminacin and asiminecin.

Acetogenins are especially effective against multi-drug resistant (MDR) tumors in which the resistance is due to ATP-dependent efflux pumps.

Successful *in vivo* studies, against murine leukemia, myeloma, and human ovarian carcinoma in athymic mice, attest to the antitumor effectiveness of several of the acetogenins and demonstrate potencies in animals as high as 300 times that of taxol with concurrent weight gain rather than the drastic weight loss caused by taxol.

Clinical applications

Antitumor, pesticidal, antimalarial, anthelmintic, piscicidal, antiviral, and antimicrobial

Shampoo for treating infestations of head lice, fleas, and ticks pesticidal sprays, which protects host plants against a diversity of pests

Ointment for treatment of oral herpes (HSV-1) and other viral skin infections.

The extract (in capsule form) enhances a mixture of natural anthelmintics

Viscum album

A species of mistletoe native to Europe and western and southern Asia.

It is a hemi-parasitic shrub, which grows on the stems of other trees. It has stems 30–100 centimetres (12– 39 in) long.

Used in magic and mysticism for millenia

That which grows on black or water elm is considered the most efficacious in hermetic traditions

Balder, the god of Peace, was slain with an arrow made of Mistletoe. He was restored to life at the request of the other gods and goddesses, and Mistletoe was afterwards given into the keeping of the goddess of Love, and it was ordained that everyone who passed under it should receive a kiss, to show that the branch had become an emblem of love, and not of hate

Viscum album

Traditional indications Anti-spasmodic nervine for seizures, hysteria and hypertension

The leaves and young twigs are antispasmodic, cardiac realaxant, cytostatic, diuretic, hypotensive, narcotic, nervine, tonic and vasodilator.

They are harvested just before the berries form and are dried for later use.

Mistletoe is traditionally used to lower blood pressure and heart rate, ease anxiety and promote sleep.

In low doses it can also relieve panic attacks and headaches, and also improves the ability to concentrate

Modern research

Contains cytotoxic lectins including viscumin that binds to galactose residues of cell surface glycoproteins and may be internalised by endocytosis. Viscumin strongly inhibits protein synthesis and the lectins inhibit agglutination of tumor cells

Contains cytotoxic polypeptides

Contains polysaccharides that stimulate non-specific immunity

VA lectins thus have an immunomodulating activity to enhance the host defense system against tumors, and its prophylactic and therapeutic effect on tumor metastasis is associated with the activation of NK cells and macrophages.

Viscum album

Upregulates apoptosis Inhibits tumor growth and metastases Upregulates NK cells and macrophages Increases survival Viscum lectins, peptides and polysaccharides:

↑ phagocytic and cytotoxic actions of macrophages

↑ neutrophil production and maturation

 \uparrow thymic weight and thymocyte activity, \uparrow Th1 cytokines

↑ natural killer cell activity

Induction of IL1, IL6, TNF, interferon Induction of DNA repair

Lectins further inhibit tumor growth and metastasis by increasing apoptosis and inhibiting angiogenesis.

Iscador is a homeopathic complex made from the fermented fruits, and given by subcutaneous injection for cancer. It reduces the leukocytopenia produced by radiation and chemotherapy **Clinical applications**

Hypertension with dizziness and headaches Nervous tachycardia Seizure disorders – epilepsy, tourettes, palsies, torticollis Anxiety and hysteria

Pharmacy:

Dried herb decocted	2 – 6 g three times daily
Tincture 1 : 5 45% EtOH	1 – 3 mL three times daily, starting low and working up

Over dose leads to vomiting, catharsis, bloody stool and bowel spasms, prostration, coma and death.

<u>Camptotheca acuminata – happy tree / cancer tree</u> (Nyssaceae).

A a deciduous tree in the Tupelo family that grows quickly to about 75 feet high and can make a canopy about 40 feet wide indigenous to southern China

Seeds and leaves are used Contains quinoline alkaloids notably *camptothecin* (CPT) which inhibits topoisomerase 1 required for cell replication.

Hydroxycamptothecin and methoxycamptothecin have also been identified and appear active

Camptothecin is an anticancer and antiviral alkaloid

Camptothecin accumulates to approximately 0.4% of the dry weight of young leaves. This level is 1.5-fold higher than that of the seeds and 2.5-fold higher than that of the bark, the two currently used sources of the drug.

As the leave mature, the concentration and absolute amount of camptothecin decreases rapidly.

Camptothecin and its analog compounds can inhibit the nuclear DNA topoisomerase I enzyme and has the effect of interrupting the replication and transcription of cancer cells.

Camptothecin is not water-soluble and can be highly toxic, making it difficult to administer as a medicine.

Camptosar by Pharmacia, Hycamtin by GlaxoSmithKline, and CPT11 by Aventis.

Worldwide sales of these drugs have collectively reached about \$1 billion annually. The raw material for these drugs is still only available from the C. acuminata trees.

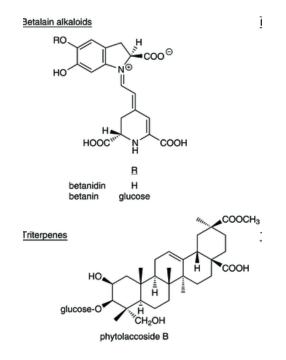
The harvesting of C. acuminata for the pharmaceutical industry has decimated the population of the endemic trees in China. The tree may now be considered as "Endangered" by the government of China and export is severely restricted. It is estimated that less than 4,000 of the trees remain in the wild in China

Phytolacca decandra and sp.

Part used is the root

Constituents include:

triterpene saponins called phytolaccosides an alkaloid called phytolaccine a resin containing phytolaccic acid



Phytolacca decandra and sp.

Traditional applications

As an alterative, anti-phlogistic and drainage herb used for the lymphatic system, to stimulate lymph glands and lymphocytes

Actions

Leucocytic Lymph node and lymphocyte activator Alterative / lymphatic decongestant Anti-inflammatory Thyroid stimulant

5/18/2017

Changes can be induced in lymphocytes by certain plant mitogens, one of the most important being phytohaemaglutinin (PHA). It is termed a polyclonal T-cell activator because it reacts with the T-cell surface nonspecifically (i.e. not as an antigen) and produces the same series of cellular events as does antigen, locking onto its specific surface receptor.

Unlike the situation with antigen stimulation where only a small fraction of the cells are sensitive, PHA transforms a major portion of the T-cells. Additionally, some B-cells are affected although their response appears to be T-cell dependent. The picture is emerging that helper T-cells are preferentially stimulated by PHA. Poke weed derived PHA activates both T- and B-lymphocytes.

Tissue specific to skin, lymph glands, mucus membranes, serous membranes and fibrous tissues

Slows the heart Slows respiration and makes it shallow

Higher doses \rightarrow slow onset but persistent emetic and drastic cathartic, ksin prickling and tingling / crawling, diplopia, vertigo, stupor

In toxic doses it paralyzes the medulla

Clinical applications

- Auto-immune inflammations (RA, SLE, PR)
- Lymphadenopathy and lowered immune states
- · Cysts, boils, acne, dry eczema, psoriasis
- Inflamamtion or ulceration of mucus membranes
- · Laryngitis, tonsillitis, mastitis, otitis, sinusitis
- Hypothyrodism, goitre

Specific indications

White / leaden tongue with a slick or glossy sheen but little coating Pallor of the mucus membranes

Dosage

Tincture 1 : 10 fresh @ 65% EtOH 5 – 15 mL / week

<u>Larrea divaricata / tridentata</u>

Contains the phenolic lignan compound Nordihydroguairetic acid (NDGA), first isolated in 1942 by scientists at the University of Minnesota.

NDGA and the derivative tetramethyl-Onordihydroguaiaretic acid inhibits the IGF-1 receptor and the Her2/neu receptor. Causes S phase arrest and inhibits apoptosis. Inhibits glycolysis and electron transfer chain

Increases cancer cell sensitivity to herceptin.

Additional 18 known flavones and flavanol glycosides contribute to an anti-oxidant effect

Larrea tridentata

creosote bush or chaparral

family Zygophyllaceae.

It is a prominent species in the Mojave, Sonoran, and Chihuahuan Deserts of western North America, including portions of California, Arizona, Nevada, Utah, New Mexico and western Texas in the United States, and northern Chihuahua in Mexico.

It is closely related to the South American *Larrea divaricata*, and was formerly treated as the same species.

It is an evergreen shrub growing to 1-3 m tall, rarely 4 m. The stems of the plant bear resinous, dark green leaves.

Actions

Anti-oxidant Anti-inflammatory Anti-allergenic Hypolipidemic Anti-fungal Anti-bacterial Anti-viral Hepatic stimulant Anti-cancer

NDGA

Inhibits COX $\rightarrow \qquad \downarrow$ PGE2 series, \downarrow thromboxanes

Inhibits LOX $\rightarrow \qquad \downarrow$ leukotrines

Decreases histamine and slow-release substance of anaphylaxis in lungs, decreases bronchial spasm

Flavonoids

Inhibit aerobic glycolysis by bacteria and cancer cells through inhibition of mitochondrial NADH oxidases, succinoxidase and folate dehydrogenase Flavonoids inhibit lipid peroxidation and protect the liver from rancid fats

Volatile oil is antibacterial, anti-viral and anti-fungal

Polysaccharides are immuno-modulating

Phytosterols are anti-inflammatory and alterative

Clinical applications

Hypercholesterolemia (lowers LDL and triglycerides, prevents peroxidation) Blood poisoning Chronic and sub-clinical infections Toxin accumulation Candida or chronic mold exposures Gonorrhoea and syphilus

Cancers, especially of the skin and the breast

Dosage

Tincture 1 : 5 @75 – 90 % EtOH 2.5 mL daily

Take it for 2 months on and one month off in rotation

Podophyllum peltatum

Cathartic / purgative

Anti-viral

Alterative

Anti - neoplastic / anti-tumorigenic

Cytotoxic

Cholagogue

Digestive stimulant

May apple acts as a certain, but slow and gentle cathartic. It exerts a powerful influence upon the whole glandular system.

It acts as a gentle stimulant tonic, improves the appetite, and is particularly valuable in *atonic dyspepsia, gastric* and *intestinal catarrh*, and all *atonic forms of indigestion*, when the patient complains of dizziness, loss of appetite and heavy headache.

By its slow and thorough action, yet permanent in its effects in restoring and maintaining the normal hepatic and intestinal secretions, podophyllum is one of the very best agents to overcome *habitual constipation*, and more especially if it be due to portal engorgement

May apple contains a group of resinous lignan components, found in the alcohol extract, one of which podophyllotoxin, possess antitumor activity in both animal and human studies.

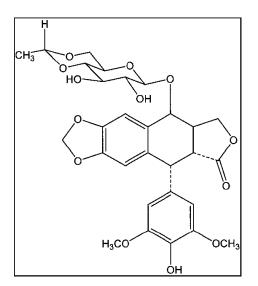
One of the podophyllotoxins, podophyllin, is used externally to treat venereal warts (condyloma acuminata) and herpes.

The podophyllotoxin derivatives etoposide and teniposide are active in the treatment of a variety of cancers.

Etoposide arrests cell growth by inhibiting DNA topoisomerase II which causes double strand breaks in DNA

It does not inhibit tubulin polymerization, however, its parent compound, podophyllotoxin, which has no inhibitory activity against DNA topoisomerase II, is a potent inhibitor of microtubule assembly.

Etoposide acts primarily in the G2 and S phases of the cell cycle



Etoposide

Dosage

Tincture 1 : 10 @65% EtOH

up to 10 drops daily

Vinca rosea / Catharanthus roseus

Madagasgar periwinkle

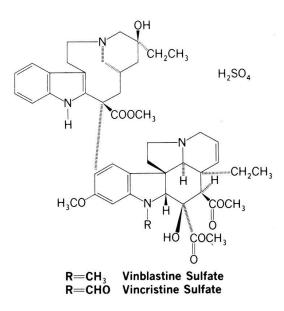
family (Apocynaceae) which includes a number of medicinal plants, among them rauwolfia and Canadian hemp, *Apocynum cannabinum*.

The plant has a long tradition in medicine, particularly in the treatment of diabetes.

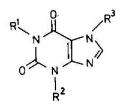
Vincristine and vinblastine, two of 500 alkaloids named from Catharanthus roseus.

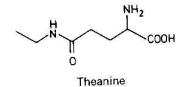
The anticancer activity (mostly for leukemia and lymphoma) of these alkaloids were discovered serendipitously in 1954 when scientists were looking for antidiabetic activities behind the West Indian belief that the periwinkle was good for diabetes.

Many Vinca alkaloids are anti-mitotic and antimicrotubule agents; they are now established as cytotoxic and chiefly block mitosis through metaphase arrest.



Camellia sinensis (Green tea)





Green tea (*Camellia sinensis*), is a member of the Theaceae family that grows in central and southern Asia.

Black and oolong tea require partial fermentation of the leaves but green tea is produced by steaming fresh leaves, which inactivates oxidizing enzymes in the leaves and preserves the polyphenol content. The polyphenols (flavonols or catechins) in tea comprise 30-40 percent of the extractable solids of dried green tea leaves.

In an aqueous infusion of dried unfermented leaves of Camellia sinensis numerous biological activities have been reported including antimutagenic, antibacterial, hypocholesterolemic, antioxidant, antitumor and cancer preventive activities

The polyphenolic fraction contains four main catechins: epicatechin (EC), epicatechin-3-gallate (ECG), epigallocatechin (EGC), and epigallocatechin-3-gallate (EGCG), with the latter being the highest in concentration.

EGCG has shown antioxidant, anti-viral, and anti-cancer effects, both in vitro and in vivo studies. EGCG inhibits histadine decarboxylase, spares vitamin C oxidation, is anti-viral and anti-bacterial, and enhances pancreatic function. Epigallocatechin gallate (EGCG), also known as Epigallocatechin 3-gallate, is the ester of epigallocatechin and gallic acid and a type of catechin

EGCG is the most abundant catechin in tea and an antioxidant.

The non-polyphenolic fraction was found to contain pheophytins a and b in relative abundance, and chlorophylls a and b, beta-carotene and lutein in lower concentrations.

Although all these pigments exhibited significant antioxidant activities, the ranks of suppressive activity against hydroperoxide generation were chlorophyll a > lutein > pheophytin a > chlorophyll b > beta-carotene > pheophytin b.

These results suggest that the non-polyphenolic fraction of residual green tea has a potent suppressive activity against hydroperoxide generation from oxidized linoleic acid

Researchers found that Japanese adults drinking five or more cups of green tea daily were 16 per cent were less likely to die from a range of illnesses, and particularly heart disease, than those only drinking one cup per day.

Anti-carcinogenic:

- · Inhibits NF-Kappa Beta; up-regulates cancer-suppressor genes
- · Suppresses tumor initiation and growth; Inhibits genetic mutations
- Triggers Fas-mediated apoptosis in U937 cells
- Activates caspase-3CPP32-like proteases
- Inhibits VEGF and Protein Kinase C
- Inhibits topoisomerase I
- · Decreases the activity of ornithine decarboxylase
- Inactivates matrix metalloproteinase (MMP)
- Reduces the formation of of N-nitrosodimethylamine (NDMA)
- Reduces viability in Ehrlich ascites tumor cells
- Inhibits multi-drug resistance (MDR)
- · Blocks tumor formation (bladder, prostate, colon, breast, ovarian)
- Protects skin from UV radiation.

Anti-oxidant Promotes hepatic detoxification pathways Anti-inflammatory Protects against the progression of atrophic gastritis Prevents cardiac toxicity in chemotherapy Modulates androgenic activity Protective effect on lipid peroxidation Enhances fat metabolism Reduces serum lipids and lipoproteins Thermogenic effect Decreases muscle necrosis Inhibits aromatase activity Neuroprotective

Anti-viral: HPV; HIV; HSV-2; EBV; Adenovirus

Anti-bacterial: Staph Enterotoxin B (SEB); Staph superantigens (SsAgs) in atopic dermatitis;

Enhances beta lactans in MR Staph, H. Pylori; E. coli in bladder; E. coli, Strep salivarius and Strep mutans in dental caries

Note on dosage:

It is more efficacious to take powdered green tea extract (95% polyhenols/40% EGCG) rather than drinking tea as a cancer adjuvant therapy.

An appropriate dose for cancer inhibition including VEGF blockade would be 3-4 grams of standardized green tea extract (95% polyphenols/60% catechins)

Caffeine has been shown to potentiate tea polyphenols, such as EGCG, so it is preferable not to decaffeinate the tea.

A recent study using mouse models at USC showed that, in contrast to the myriad benefits commonly associated with green tea and GTE, EGCG binds with the anti-cancer drug Velcade, significantly reducing its bioavailability and thereby rendering it therapeutically useless.

Dr. Schönthal, who headed the study, suggests that consumption of green tea and GTE products be strongly contraindicated for patients undergoing treatment for multiple myeloma and mantle cell lymphoma. Turmeric (*Curcuma longa*) is a member of the ginger family and is thought to be indigenous to the Indian subcontinent. It is grown and harvested commercially in India, China, Costa Rica, and many regions of tropical south Asia.

3-5% curcuminoids - a group of lipid soluble natural phenolic compounds:

Curcumin I (diferulomethane) Curcumin II (demethoxycurcumin) Curcimin III (bisdemethoxycurcumin) Curcumin IV (cyclocurcumin)

2-7% essential oil, comprised mainly bisabolane, guaiaane, and germacrane sesquiterpenes: turmerone, arturmerone, zingiberene, curlone, etc;

The high content of bisbolane derivatives distinguishes turmeric from other Curcuma species.

Curcuminoids

Anti-inflammatory, antioxidant, antineoplastic, antiviral, and immune-modulation activity in animals, and in some human studies as well.

Curcuminoids inhibit leukotriene biosynthesis via the lipoxygenase pathway and decrease prostaglandin formation. Curcumin has caused apoptosis in various cancer cell lines and animal tumor cells and inhibits angiogenesis.

Curcumin has antiseptic and antiparasitic activity. It preferentially inhibits platelet aggregation induced by platelet-activating factor and arachidonic acid



α-Turmerone

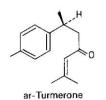


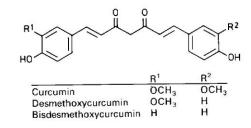




Curlone

Zingiberene





Anti-Inflammatory: Inhibits NF-kappaB, COX-2, LOX-5 & 12, IL-6, TNF- α , and suppresses PG2

Anti-Angiogenesis & Anti-Metastatic: Inhibits VEGF, bFGF, EGF, PDGF, and MMP-2

Anti-Oxidant/ Free Radical Scavenger: Protects Against Lipid Peroxidation, increases glutathione peroxidase, glutathione S-transferase and NADPH: quinone reductase

Pro-oxidant: Selective cancer cell pro-oxidant: increases the production of reactive oxygen species (ROS) selective to cancer

Anti-Mutagenic

Anti-Thrombotic: inhibits platelet aggregation and platelet-derived growth factor (PDGF)-stimulated proliferation

Anti-Tumor: activates T-cells, tumor-fighting cytokines, inhibits NF-kappa B

Normalizes cellular behavior and gene expression: downregulates the anti-apoptotic gene Bcl-2, IkappaBalpha, cyclin D1, and interleukin-6, activates caspases-3,7,8 and 9, igniting cancer cell apoptosis

Chemotherapy Enhancement and chemo-related protection (heart, liver, kidney and brain), overcomes chemo-resistance (MDR) and induces chemo-sensitivity

Radiation protective

Neuro-protective: reduces beta-amyloid, inhibits Alzheimer's Disease and other forms of dementia

Adrenal Health: enhances adrenal steroidogenesis – adaptogenic – stress protection

Anabolic – stimulates muscle regeneration

Cardiovascular Health: lipid lowering - Elevates HDL Cholesterol while Lowering VLDL + LDL Cholesterol, improves blood motility, anti-atherosclerotic, inhibits platelet aggregation, plaque formation and lipid oxidation

Gastrointestinal Health: Anti-ulcerogenic, choleretic, dyspeptic conditions, including loss of appetite, postprandial feelings of fullness, and liver and gallbladder complaints

Anti-viral: Inhibits HIV Replication

Liver Protective: modulates Phase I & II enzyme systems, prevents alcohol and chemically-induced liver disease

Antioxidative Detoxification of heavy metals (iron, mercury, copper etc.)

Anti-arthritic

Ocular Health: prevents age-related cataracts – via antioxidative; inhibits corneal vascularization (Macular Degeneration), treats chronic anterior uveitis

Skin Health: treatment for skin/mucosal conditions: protective against skin cancer, age-related and oxidative damage; treat scabies and other skin disorders

Thuja occidentalis (Eastern Arborvitae, Northern Whitecedar)

An evergreen coniferous tree, in the cypress family Cupressaceae

Grows to a height of 10-20 m tall with a 0.4 m trunk diameter, exceptionally to 30 m tall and 1.6 m diameter

The name arborvitae or "tree of life" dates from the 16th century when the French explorer Jacques Cartier learned from the Indians how to use the tree's foliage to treat scurvy

The rot- and insect-resistant wood is used principally for products in contact with water and soil such as rustic fencing, posts and saunas. Other important products include cabin logs, lumber, poles, and shingles.

Ancient peoples burned thuja's aromatic wood along with sacrifices.

"Thuja" comes from the Latin form of the Greek word thero (to sacrifice).

Other species of thuja were used in Egypt for embalming the dead.

Antiviral and anti-fungal activity. Used to treat warts and polyps, being prescribed both internally and externally for these conditions.

Stimulating expectorant and decongestant remedy, and may be used to treat acute bronchitis and other respiratory infections.

Diuretic and used to treat acute cystitis and bed-wetting in children.

Extracts may be painted on painful joints or muscles as a counter-irritant, improving local blood supply and easing pain and stiffness.

Young leaves and growing tips are harvested in the spring

Contains:

Oleo-resin up to 4%

dicyclic ketones: (-)thujone, isothujone, α and β thujone monoterpene hydrocarbon: pinene ketone: carvone

7 diterpenoids Polysaccharides Glycoprotein A bitter principle called pinipicrin Tannins Actions

Astringent / cicatrant Stimulating expectorant Diuretic Anti-neoplastic Anti-fungal Anti-viral Moth and insect repellant

Diterpenoids induce IL1, IL2, IL3, IL6, gamma interferon, TNK β

Polysaccharides are immuno-modulating

Thujones are neuro-toxic and cumulative

Dosing

Tincture 1:5 90% EtOH up to 3 mL three times daily One month on, one month off

Traditional applications

Topically for warts, fungal and viral skin afflictions, herpes, bed sores, scabies, lice

Steam inhalation for viral or fungal chest infections

Snuff or lavage for nasal polyps

Douche for leucorrhoea, cervical dysplasia, HPV

BPH, prostatitis, eneuresis, incontinence

Turkey corn

Habitat

Arizona, New Mexico, and northwards, anywhere from 2,000 to 10,500 feet. Often found along old cuts, roads, mine tailings, ski lodges, and new burn areas.

Botany

Low bluish green fleshy biennial or short lived perennial. The weak hairless stems, diffusely branched and spreading from the base, are often prostrate with the tips turning upward. The leaves are dissected into many small segments.

Part used Tuber and Root

Narrow bright yellow, pink, blue or white flowers, 3/8 to 3/4 inch long, have a short conspicuous spur at the base, and 2 sepals.

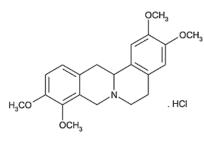
In short spike-like inflorescences at the end of the stems.

Bluish green seed pods are usually curved, and often hang downward. They are cylindrical, 1/2 to 1 inch long, and produce many black and shining seeds. Smooth seeds have rounded margins, and are about 1/12 inch in diameter. Constituents

Alkaloids - corydaline, protopine, tetrahydropalmatine, dl-Tetrahydropalmatine (dl-THP), tetrahydrocoptisine, corybulbine, tetrahydrocolumbamine

Protoberberine type alkaloid (leonticine)

Tetrahydropalmatine analgesic, sedative and tranquilizing effects.



Tetrahydropalmatine

Indications

Pain relief

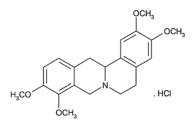
Rarely taken on its own, but used in combinations to alleviate pain from almost any cause.

Study in mice showed that *Corydalis yanhusuo* strengthened the analgesic function produced by electro-acupuncture.

According to Chinese Medicine it is taken where there is Qi and blood stagnation. Frying the root in vinegar may help increase the pain relieving properties **Cardiovascular effect**

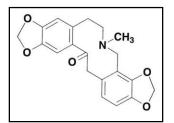
Invigorates blood in TCM. At least two clinical trials have been done on rabbits and rats showing that the tetrahydroberberine isolated alkaloid extract prevented platelet aggregation both in-vitro and in-vivo.

dI-THP has been shown to both decrease the stickiness of platelets and protect against stroke, as well as lower blood pressure and heart rate in animal studies. Additionally, it seems to exert an anti-arrhythmic action on the heart.



Tetrahydropalmatine

Protopine, another of the alkaloids present in Corydalis anti-arrhythmic anti-hypertensive negative inotropic effects



Anti-viral

Clinical trial done Japan found that eighteen isoquinoline alkaloids including protoberberines, benzophenanthridines and an aporphine isolated from *Corydalis* species showed inhibitory effects on Epstein-Barr virus.

It has been suggested that these alkaloids could be useful as anti-tumor agents.

In TCM *Corydalis* invigorates the blood, moves qi and alleviate all types of pain, including menstrual, abdominal, hernial and pain associated with cancer, especially abdominal pain.

Corydalis relieves pain by reducing B-endorphin-like substances in cerebrospinal fluid and serum, decreasing monoamines, and increasing ACT levels.

Improves sleep

Human clinical trials with dI-THP have shown the ability to fall asleep was improved in people suffering from insomnia after taking 100–200 mg of dI-THP at bedtime. No drug hangover symptoms such as morning grogginess, dizziness or vertigo were reported by people taking the alkaloid extract. Relieves pain, spasm and inflammation

75 mg of THP daily was effective in reducing nerve pain in 78% of the patients tested [54]

Indicated for

Painful menstruation (dysmenorrhea), abdominal pain after childbirth, and headache

Anti-inflammatory

- *Corydalis* extract inhibited an increase in vascular permeability in mice induced by acetic acid, and reduced induction of acute paw edema in rats
- *Corydalis* suppressed the development of adjuvantinduced edema in arthritic rats.
- *Corydalis* also inhibited histamine release from peritoneal mast cells.
- Effective in both the acute and chronic phases of inflammation.

Corydalis has shown cytotoxicity to many cancer-cell lines, in particular, liver tumors. It's mechanism includes suppression of the oncogene N-ras mRNA

THP is a very effective anti-epileptic and anticonvulsant agent

Dosage

For an analgesic or sedative effect, the crude, dried rhizome is usually recommended at 5–10 grams per day.

Alternatively, 10–20 ml per day of a 1:2 extract.

Corydalis 400:1 80% THP 50-100 mg. 2-3x per day, 50-200 mg. before bed.