Anti-Cancerous Guide

Rainforest Plants & Formulas with anti-cancerous properties

AMAZON VITALITY

Description: The 8 rainforest plants in this formula have been documented with cytoprotective, antimutagenic, and/or immunomodulatory actions. This product has been formulated to be taken chronically at low dosages for general health, well being and cellular protection.
Traditional Uses: For cancer protection, brain cell protection, skin cell protection, and anti-aging.
Ingredients: A herbal blend of calaguala (Polypodium leucotomos), samambaia (Polypodium decumanum), chanca piedra (Phyllanthus niruri), cat's claw (Uncaria tomentosa), fedegoso (Cassia occidentalis), picão preto (Bidens pilosa), gervâo (Stachytarpheta jamaicensis), and tayuya (Cayaponia tayuya).
Suggested Use: Take 1-2 capsules twice daily with food (depending on body weight).
Contraindications: Not to be used during pregnancy or while breast-feeding.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: Possible weight loss is a reported side effect of this formula.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

- Calaguala and samambaia extracts are manufactured and sold in Europe as herbal drugs for the treatment of psoriasis, and more recently, for dementia and Alzheimer's Disease. A 1997 U.S. patent and several *in vivo* clinical studies report that these plants protect against brain cell degeneration, promotes repair of damaged brain cells in Alzheimer's and dementia patients, and provides a protective effect to brain cells in general. The same cytoprotective effects to brain cells seems to extend to skin cells as well. Another U.S. patent was filed in 1997 which indicated these rainforest ferns are effective in preventing sunburn and skin damage (taken internally, as well as applied topically prior to exposure). Its protective effect was reported to be due, in part, to an antioxidant effect, as well as by protecting and increasing the amount of elastin in skin cells. An *in vivo* study conducted at Harvard medical school in 1999, reported that a samambaia extract applied topically helped to avoid skin damage and sun-associated skin aging, as well as reduced the number of UV-induced skin tumors in mice. The Harvard researchers published a human study in 2004 reporting that samambaia evidenced substantial benefits of skin protection to prevent sunburn and prevent skin aging when it was taken internally. Based on *in vitro* tests, other researchers suggested that samambaia may help prevent sun damage and skin aging at low dosages while higher dosages may actually reverse the loss of normal elastic fibers associated with intrinsic aging of the skin. A pharmaceutical company in Spain has also published a study indicating that samambaia is suitable to use as a preventative treatment for sunburn and skin damage.
- Chanca piedra has demonstrated hepatoprotective and antihepatotoxic in animal and human studies. The plant has also been reported with antimutagenic and radiation-protective properties.
- Cat's claw has been documented to possess antimutagenic, cytoprotective, antioxidant, and immunostimulant actions. Research also reports its ability to reduce amyloid plaque.
- Fedegoso has demonstrated antimutagenic, anticancerous, hepatotonic, hepatoprotective, antihepatotoxic, cytoprotective, immunostimulant, and cellular repair actions in various studies in animals, humans and *in vitro* tests.
- Picão preto has demonstrated in various studies over the years antihepatotoxic, antioxidant, antitumorous, cardiotonic, COX-inhibitor, gastroprotective, hepatoprotective, hepatotonic, and immunomodulator actions.
- Gervâo is documented by research with antioxidant, gastroprotective, gastrototonic, hepatoprotective, and antiulcerous actions. In addition, it has been documented with analgesic, anti-anaphylactic, antidysenteric, antihistamine, anti-inflammatory, bronchodilator, and neurasthenic properties and actions.
- Tayuya contains 24 novel cucurbitacins plant chemicals called cayaponosides. These phytochemicals have been documented to have antioxidant, anti-inflammatory and analgesic properties and, more recently, to have anticancerous and antimutagenic potential.

ANAMU

Description: Many biologically active compounds have been discovered in anamu, including flavonoids, triterpenes, steroids, and sulfur compounds. Anamu contains a specific sulfur compound named dibenzyl trisulfide. In a University plant-screening program anamu was one of 34 plants identified with active properties against cancer. The researchers reported that dibenzyl trisulfide was one of two of the active compounds in anamu with anticancerous actions. Anamu also contains the phytochemicals astilbin, benzaldehyde, and coumarin, all three of which have been documented with antitumorous and/or anti-cancerous properties as well.
Traditional Uses: For cancer and leukemia and to stimulate immune function and immune cell production.
Suggested Use: Take 2 capsules 2-3 times daily.
Contraindications: Methanol extracts of anamu were reported to cause uterine contractions in animals studies, therefore, it is contraindicated in pregnancy.
Drug Interactions: None published. Due to anamu's natural coumarin content, however, it is conceivable that it may potentiate the effects of coumadin (Warfarin®).
Other Practitioner Observations and Possible Precautions:

- Anamu contains a low concentration of coumarin, which has a blood thinning effect. People with blood disorders such as hemophilia should be monitored closely for this possible effect.
- This plant has been shown to have hypoglycemic effects in mice. People with hypoglycemia should be monitored more closely for this possible effect.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

Research published on anamu (and its plant chemicals) reveals that it has antileukemic, antitumorous, and anticancerous activities against several types of cancer cells. In an *in vitro* study by Italian researchers in 1990, water extracts and ethanol extracts of anamu retarded the growth of leukemia cells and several other strains of cancerous tumor cells. Three years later, they reported anamu was directly cytotoxic to leukemia and lymphoma cancer cells but only inhibited the growth of breast cancer cells. A study published in 2002 documented an *in vitro* toxic effect against a liver cancer cell line; another *in vitro* study in 2001 reported that anamu retarded the growth of brain cancer cells (neuroblastoma).

Anamu has been found in both *in vivo* and *in vitro* studies to be an immunostimulant. In a 1993 study with mice, a water extract stimulated immune cell production (lymphocytes and Interleukin II). In the same year, another study with mice demonstrated that anamu increased natural killer cell activity by 100% and stimulated the production of even more types of immune cells (Interferon, Interleukin II, and Interleukin IV). Additional research from 1997 to 2001 further substantiated anamu's immunostimulant actions in humans and animals. In one study they reported: “Based on these findings we suggest that *P. alliacea* [anamu] up-regulates anti-bacterial immune response by enhancing both Th1 function and the activity of NK cells.”

Other research suggests anamu's traditional use as a remedy for arthritis and rheumatism has been validated by documenting analgesic, antinociceptive, and anti-inflammatory properties. One research group in Sweden reported that anamu possesses COX-1 inhibitory actions. Another research group in Brazil documented significant anti-inflammatory effects in rats using various models, and researchers in 2002 noted a significant analgesic effect in rats. The analgesic and anti-inflammatory effects were even verified when an ethanol extract was applied topically in rats, again validating traditional use.

Many *in vitro* laboratory studies document that anamu shows broad-spectrum antimicrobial properties against numerous strains of bacteria, mycobacteria, mycoplasma, viruses, fungi, and yeast.

BELLACO CASPI

Description: Bellaco caspi is a tropical rainforest tree growing 8-16 meters in height with a tall, narrow, pyramidal crown. This tree is known by two botanical names: *Himatanthus sucuuba* and *Plumeria rubra*. The bark and the latex of the bellaco caspi tree has a long history of use among the Indians in the Amazon for ovarian, cervical, and uterine disorders.
Traditional Uses: For tumors and cancer (uterine, cervical, & ovarian), for endometriosis, uterine fibroid tumors, menstrual irregularities and pain, and for ovarian cysts and ovarian inflammation.
Suggested Use: Take 60 drops (2 ml) three times daily.
Contraindications: None reported.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: In estrogen-positive cancers this product is best in combination with graviola or Graviola Max and cat's claw.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

A review of some of the chemicals found in bellaco caspi might explain some of the many traditional uses of this tropical rainforest tree. An antitumor iridoid compound and two depside chemicals have been isolated from bellaco caspi bark. In addition, two iridoid chemicals called *plumericin* and *isoplumericin* have been found in the tree bark and the latex. These two chemicals have been reported with cytotoxic, anticancerous, antifungal and antibacterial actions in laboratory research.

In 2001, researchers in the United States reported that the bark of bellaco caspi was significantly cytotoxic *in vitro* to 5 different human cancer cell lines (breast, colon, prostate, lung, & lymphoma). They related this anticancerous action to the iridoids and triterpenoids chemicals discovered in the tree bark. It also passed a brine shrimp assay (which predicts antitumor activity) in 2003 and was shown to be active *in vitro* against malignant ascites at less than 20 mcg per ml.

Toxicity studies in laboratory animals indicate that the use of bellaco caspi at traditional dosages is non-toxic. Even when a bark extract was given to pregnant rats, there were no toxic, abortive, or birth defects reported.

Antitumorous & Cytotoxic Actions:

Guignard, E., et al. "Screening of plants found in Amazonas state for lethality towards brine shrimp." *Acta Amazonica.* 2003; 33(1): 93-104.
Bolzani, V., et al. "Search for antifungal and anticancer compounds from native plant species of Cerrado and Atlantic Forest." *An. Acad. Bras. Cienc.* 1999; 71(2): 181-7.
Persinos-Perdue, G., et al. "South American plants. III. Isolation of fulvoplumierin from *Himatanthus sucuuba* (Apocynaceae). *J. Pharm. Sci.* 1978; 67: 1322.
Kardono, L., et al. "Cytotoxic constituents of the bark of *Plumeria rubra* collected in Indonesia." *J. Nat. Prod.* 1990 Nov-Dec; 53(6):1447-55.
Wood, C. A., et al. "A bioactive spirolactone iridoid and triterpenoids from *Himatanthus sucuuba*." *Chem. Pharm. Bull.* 2001; 49(11): 1477-1478.
De Silva, J. R., et al. "Triterpenic esters from *Himatanthus sucuuba* (Spruce) Woodson." *Quimica Nova* 1998; 21(6): 702-704.
Abdel-Kader, M., et al. "Bioactive iridoids and a new lignan from *Allamanda cathartica* and *Himatanthus fallax* from the Suriname rainforest." *J. Nat. Prod.* 1997; 60(12): 1294-7.
Hamburger, M., et al. "Traditional medicinal plants of Thailand. XVII. Biologically active constituents of *Plumeria rubra*." *J. Ethnopharmacol.* 1991 Jul; 33(3): 289-92.

CAT'S CLAW

Description: Cat's Claw has been shown to boost immune function and to have a direct anti-cancerous effect in published research .
Traditional Uses: As an immune stimulant and an adjunctive therapy for cancer (to reduce side effects of chemotherapy and protect cells) and for estrogen-positive breast cancer.
Suggested Use: Take 2 capsules 2-3 times daily.
Contraindications:

- Cat's claw has been clinically documented with immunostimulant effects and is contraindicated before or following any organ or bone marrow transplant or skin graft.
- Cat's claw has been documented with antifertility properties and is contraindicated in persons seeking to get pregnant.
- Cat's claw has been documented with chemicals which can reduce platelet aggregation and thin the blood. It is contraindicated in persons with bleeding disorders such as hemophilia.

Drug Interactions: Based upon *in vivo* rat studies, cat's claw may protect against gastrointestinal damage associated with NSAIDs such as ibuprofen. May potentiate coumadin and blood-thinning drugs.
Other Practitioner Observations and Possible Precautions:

- Cat's claw requires sufficient stomach acid to help break down the tannins and alkaloids during digestion and to aid in absorption. Avoid taking capsules at the same time as antacids.
- Large dosages of cat's claw (3-4 gram dosages) have been reported to cause some abdominal pain or gastrointestinal problems including diarrhea (due to the tannin content of the vine bark). The diarrhea or loose stools tend to be mild and go away with continued use. Discontinue use or reduce dosage if diarrhea persists longer than 3-4 days.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

In addition to its well documented and patented immunostimulant activity, *in vitro* anticancerous properties have been documented for several constituents in cat's claw. Five of the oxindole alkaloids have been documented with *in vitro* antileukemic properties, and various root and bark extracts have demonstrated antitumorous and anticancerous properties. Italian researchers reported in a 2001 *in vitro* study that cat's claw directly inhibited the growth of a human breast cancer cell line by 90%, while another research group reported that it inhibited the binding of estrogens in human breast cancer cells *in vitro*. Swedish researchers documented it inhibited the growth of lymphoma and leukemia cells *in vitro* in 1998.

Early reports on observatory trials with cancer patients taking cat's claw in conjunction with such traditional cancer therapies as chemotherapy and radiation reported fewer side effects to the traditional therapies (such as hair loss, weight loss, nausea, secondary infections, and skin problems). Subsequent researchers have shown how these effects might be possible: they have reported that cat's claw can aid in DNA cellular repair and prevent cells from mutating; it also can help prevent the loss of white blood cells and immune cell damage caused by many chemotherapy drugs, thereby reducing or preventing leukopenia.

Antitumorous & Cytotoxic Actions:

Santos Araújo Mdo, C., et al. "Uncaria tomentosa-Adjuvant Treatment for Breast Cancer: Clinical Trial." Evid Based Complement Alternat Med. 2012;2012:676984.
Farias, I., et al. "Uncaria tomentosa for Reducing Side Effects Caused by Chemotherapy in CRC Patients: Clinical Trial." Evid Based Complement Alternat Med. 2012;2012:892182.
Anter, J., et al.. "Antigenotoxicity, cytotoxicity, and apoptosis induction by apigenin, bisabolol, and protocatechuic acid." J Med Food. 2011 Mar;14(3):276-83.
Gurrola-Díaz, C., et al. "Inhibitory mechanisms of two Uncaria tomentosa extracts affecting the Wnt-signaling pathway." Phytomedicine. 2011 Jun 15;18(8-9):683-90.
Pilarski, R., et al. "Anticancer activity of the Uncaria tomentosa (Willd.) DC. preparations with different oxindole alkaloid composition." Phytomedicine. 2010 Dec 1;17(14):1133-9.
Dreifuss, A., et al. "Antitumoral and antioxidant effects of a hydroalcoholic extract of cat's claw (Uncaria tomentosa) (Willd. Ex Roem. & Schult) in an in vivo carcinosarcoma model." J Ethnopharmacol. 2010 Jul 6;130(1):127-33
García Giménez, D., et al. "Cytotoxic effect of the pentacyclic oxindole alkaloid mitraphylline isolated from Uncaria tomentosa bark on human ewing's sarcoma and breast cancer cell lines." Planta Med. 2010 Feb; 76(2):133-6.

GRAVIOLA

Description: Some of the active ingredients documented, researched, and verified in graviola are a group of Annonaceous acetogenins which are only found in the *Annonaceae* family to which graviola belongs. These phytochemicals are being researched and patented around the world for their active antitumorous and anticancerous actions and uses.
Traditional Uses: For cancer (all types).
Suggested Use: Take 3 capsules 3-4 times daily.
Contraindications:
- Not to be used during pregnancy or breast-feeding.
- Graviola has demonstrated hypotensive, vasodilator, and cardiodepressant activities in animal studies. People with low blood pressure should monitor their blood pressure accordingly.

Drug Interactions: None have been reported; however, graviola may potentiate antihypertensive and cardiac depressant drugs.
Other Practitioner Observations and Possible Precautions:
- Graviola has demonstrated significant *in vitro* antimicrobial properties. Supplementing the diet with probiotics and digestive enzymes is advisable if this product is used for longer than 30 days.
- One of three documented mechanisms of action of graviola is by decreasing ATP energy to abnormal cells. Taking supplements that increase ATP energy (like CoQ10) may counteract or disable this one mechanism of action of graviola (however, the other two mechanisms of action will be unaffected).
- Graviola has demonstrated emetic properties in one animal study with pigs. Large single dosages may cause nausea or vomiting. Reduce the usage accordingly or take with a meal if nausea occurs.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

To date, over 80 Annonaceous acetogenins have been recorded in graviola which have shown in laboratory studies to be selectively cytotoxic to cancer cells without toxicity to healthy cells. Many of the acetogenins have demonstrated selective cytotoxicity to tumor cells with as little as 1 part per million. Thus far, specific acetogenins in graviola and/or extracts of graviola have been reported to be selectively toxic *in vitro* to these types of tumor cells: lung carcinoma cell lines; human breast solid tumor lines; prostate adenocarcinoma; pancreatic carcinoma cell lines; colon adenocarcinoma cell lines; liver cancer cell lines; human lymphoma cell lines; skin cancer cell lines, and multi-drug resistant human breast adenocarcinoma. Researchers in Taiwan reported in 2003 that the main graviola acetogenin, annonacin, was highly toxic to ovarian, cervical, breast, bladder and skin cancer cell lines at very low dosages saying; ". . . annonacin is a promising anti-cancer agent and worthy of further animal studies and, we would hope, clinical trials."

Researchers have reported several mechanisms of actions including inhibition of NADH oxidase in the plasma membranes of cancer cells (an enzyme only transiently expressed in normal healthy cells). Acetogenins also inhibit complex I (NADH/ubiquinone oxidoreductase) in mitochondrial electron transport systems, inhibiting oxidative phosphorylation and resulting in lower ATP levels. In addition, increased expression of a plasma membrane pump, P-glycoprotein, is a contributor to multidrug resistance. The pump activity in these multi-drug resistant cells requires large amounts of ATP. The acetogenins were found, through depletion of ATP, to reduce the activity or shut down the P-glycoprotein pump. Finally, acetogenins in graviola have shown to directly induce apoptosis to cancer cells. Cells at the S phase of their cell cycle were shown to be more vulnerable to the main graviola acetogenin, annonacin. Annonacin was able to arrest the cell cycle in the G1 phase, and inhibit the S phase progression. In addition, it was reported that p53 and p21 cell cycle checkpoint proteins, were enhanced by annonacin.

GRAVIOLA MAX

Description: Some of the active ingredients documented, researched, and verified in graviola are a group of Annonaceous acetogenins which are found only in the Annonaceae plant family. These phytochemicals are being researched and patented around the world for their active biological properties and potential uses. Graviola (*Annona muricata)* has 82 different acetogenin chemicals (in 10 distinct types). Mountain Graviola (*Annona montana*) contains the main annonacin chemical that graviola does—and it has 26 more acetogenin chemicals not found in regular graviola (in 6 distinct types). Graviola Max combines both species of graviola (Annona muricata and Annona montana) to provide 12 different types of acetogenins—108 distinct powerful chemicals in all. Compare that to only 28 acetogenin chemicals found in the American paw paw. . . Graviola Max delivers almost four times more acetogenins than paw paw!
Traditional Uses: For cancer (all types).
Suggested Use: Take 3 capsules 3-4 times daily.
Contraindications:
- Not to be used during pregnancy or breast-feeding.
- Graviola has demonstrated hypotensive, vasodilator, and cardiodepressant activities in animal studies. People with low blood pressure should monitor their blood pressure accordingly.

Drug Interactions: None have been reported; however, graviola may potentiate antihypertensive and cardiac depressant drugs.
Other Practitioner Observations and Possible Precautions:
- Graviola has demonstrated *in vitro* antimicrobial properties. Supplementing the diet with probiotics and digestive enzymes is advisable if this product is used for longer than 30 days.
- Graviola has demonstrated emetic properties in one animal study with pigs. Large single dosages may cause nausea or vomiting. Reduce the usage accordingly or take with a meal if nausea occurs.
- One of three documented mechanisms of action of graviola is by decreasing ATP energy to abnormal cells. Taking supplements that increase ATP energy (like CoQ10) may counteract or disable this one mechanism of action of graviola (however, the other two mechanisms of action will be unaffected).

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

Graviola (*Annona muricata*) contains over 80 Annonaceous acetogenins; many of which have confirmed through laboratory research to be selectively cytotoxic to cancer cells without toxicity to healthy cells. Much of the research has focused on one acetogenin named annonacin which has been reported to be highly toxic to most types of cancer cells at very low dosages. Studies and *in vitro* testing report the ED50 values for annoncin to be as low as 0.010 ug//ml in comparison with control drugs like Adriamycin of 0.15 or higher for most cancer cell lines tested.

Mountain Graviola (*Annona montana*) contains as much annonacin as regular graviola does. In addition, this graviola species contains 26 other Annonaceous acetogenins that are not found in regular graviola. These new and novel acetogenins (like most others) have shown selective toxicity to cancer cells in laboratory research reported in 9 studies from 1991 to 2005. Researchers discovering these new acetogenins in mountain graviola reported in 2005: “All of these compounds showed significant selective cytotoxicity toward hepatoma cells (Hep G2) and two compounds also were active against ovarian cancer cells (1A9).”

Annonacin was reported with *in vivo* actions against tumors in research published in 2002. Researchers inoculated mice with lung cancer cells; one third received the chemotherapy drug adriamycin, one third received annonacin (at a dosage of 10 mg/kg) and the last group received nothing (control group). At the end of two weeks, five of the six in the untreated control group were still alive and lung tumor sizes were then measured. The adriamycin group showed a 54.6% reduction of tumor mass over the control group but 50% of the animals died from toxicity. The mice receiving annonacin were all still alive, and the tumors were inhibited by 57.9%—slightly better than adriamycin—and without toxicity.

GUACATONGA

Description: Some of the active ingredients documented, researched, and verified in guacatonga are a group of chemicals called clerodane diterpenes. These phytochemicals are being researched and patented for their active biological properties and potential uses against sarcomas and other tumorous cancers.
Traditional Uses: For cancer (sarcoma, carcinoma, and adenocarcinoma).
Suggested Use: Take 3 capsules 2-3 times daily.
Contraindications: Not to be used during pregnancy or while breast-feeding.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: None reported.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

The research on guacatonga's anticancerous properties began in 1988 by Japanese researchers from the Tokyo College of Pharmacy and Pharmacognosy. They published one preliminary trial in 1988 on their discovery of these novel clerodane diterpenes and their anticancerous and antitumorous activities. They named these chemicals *casearins*. The study indicated that an ethanol extract of the leaf showed strong antitumorous activity in laboratory mice with sarcomas. As soon as they made this discovery, they rushed to patent it, filing a Japanese patent for the casearin chemicals they'd discovered as new antitumorous agents. They published a follow-up study in 1990, again reporting their results from injecting mice with sarcomas with an ethanol extract of guacatonga leaves and confirming their previous findings. They then tested individual casearins against various human cancer cell lines and published two more studies in 1991 and 1992. These studies reported newly isolated casearin chemicals and their antitumorous and anti-cancerous actions against various cancerous tumor cells. Oddly, the Japanese researchers have not published any further studies and, since they had already filed patents, other research groups have not been forthcoming in funding research dollars on these now patented anti-tumorous plant chemicals.

In 2002, however, a well-known research group in North Carolina discovered three new casearins in the leaves and stems of guacatonga that the Japanese had not (and, obviously, hadn't patented). They named the new chemicals casearvestrin A, B and C, and published their first study in February, 2002, stating: "All three compounds displayed promising bioactivity, both in cytotoxicity assays against a panel of tumor cell lines and in antifungal assays . . ." Their research tested the new plant chemicals against human lung, colon and ovarian tumor cells and indicated all three compounds had toxicity to cancer cells in very small amounts. This research was supported by a grant from the National Cancer Institute, the National Institutes of Health (NCI) and performed by a non-profit biotech company, a large pharmaceutical company and a major university. The NCI has also performed research in-house on clerodane diterpenoids found in another *Casearia* plant species documenting the antitumor properties of its novel diterpenoids and another university research group has documented the anticancerous properties of this class of chemicals in a *Casearia* plant from the Madagascar rainforest as well.

Antitumorous & Cytotoxic Actions:

Prieto, A., et al. "Assessment of the chemopreventive effect of casearin B, a clerodane diterpene extracted from Casearia sylvestris (Salicaceae)." Food Chem Toxicol. 2012 Nov 28.
Faiella, L., et al. "A chemical proteomics approach reveals Hsp27 as a target for proapoptotic clerodane diterpenes." Mol Biosyst. 2012 Oct;8(10):2637-44.
Vieira-Júnior, G., et al. "Cytotoxic clerodane diterpenes from Casearia rupestris." J Nat Prod. 2011 Apr 25;74(4):776-81.
Ferreira, P., et al. "Casearin X exhibits cytotoxic effects in leukemia cells triggered by apoptosis." Chem Biol Interact. 2010 Dec 5;188(3):497-504.
dos Santos, A., et al. "Casearin X, its degradation product and other clerodane diterpenes from leaves of Casearia sylvestris: evaluation of cytotoxicity against normal and tumor human cells." Chem Biodivers. 2010 Jan;7(1):205-15.
Vieira, G., et al. "Cytotoxic clerodane diterpenoids from Casearia obliqua." J Nat Prod. 2009 Oct;72(10):1847-50.
de Oliveira, A., et al. "Ethanolic extract of Casearia sylvestris and its clerodane diterpen (caseargrewiin F) protect against DNA damage at low concentrations and cause DNA damage at high concentrations in mice's blood cells." Mutagenesis. 2009 Nov;24(6):501-6.
de Mesquita, M., et al. "Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines." J Ethnopharmacol. 2009 Jun 25;123(3):439-45.

HUACAPU EXTRACT

2 Fluid Ounces / 60 ml

Description: Raintree's concentrated huacapu extract uses new and proprietary extraction methods to concentrate and preserve the active ingredients found in this wonderful plant. Concentration and extraction methods provide the equivalent of 500 mg huacapu bark per milliliter of extract. Huacapu is a huge canopy tree that can be found throughout the Amazon rainforest.
Traditional Uses: For cancer and viral infections.
Suggested Use: Take 60 drops (2 ml) three times daily, Best taken in combination with N-Tense capsules.
Contraindications: Not to be used during pregnancy or while breast-feeding.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: Large dosages are reported to have a laxative or purgative effect.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

Huacapu bark contains triterpenes, xanthones, lipids, tannins, and acids. The main bioactive chemical in the bark is a lipid called minquartynoic acid. This plant chemical has been the subject of research and various scientists have reported that it is cytotoxic to a large diverse line of cancer cells including human lung cancer cell lines, ovarian, colon, and neuroblastoma cancer cell lines. Another research group reported it passed the initial screening test for antitumor activity as well as demonstrated actions against the malaria and leishmania parasites. A research group reported in 2000 that minquartynoic acid demonstrated effective antiviral actions against the HIV virus at as little as 2.2 mcg/ml which might explain why the tree bark has been so popularly used for other viruses like hepatitis and herpes.

The research on huacapu to date is quite preliminary since scientists now seem more focused on its main bioactive chemical instead. Researchers in the United States first reported in 1988 and 1989 that a water extract of huacapu bark passed the initial antitumor screening test, as well as an *in vitro* cell culture test against cancer cells in amounts less than 4 mcg/ml. This was reconfirmed by a European research group who published similar reports in 2003 and 2004. In earlier research in 1996 researchers reported that a methanol extract of huacapu bark demonstrated antibacterial actions against two antibiotic-resistant strains of *Staphylococcus*, as well as *Pseudomonas* and *Bacillus*.

In herbal medicine systems in Ecuador huacapu bark is a respected remedy for herpes, lung cancer, hepatitis, and tuberculosis. It is also used for intestinal worms and parasites, muscular pain, and externally for skin irritations. In Peruvian herbal medicine systems huacapu is employed for many of the same conditions. It is highly regarded for hepatitis, malaria, herpes, and rheumatism. It is also used for leishmaniasis, and used externally on lacerations and wounds.

While little research on the tree bark exists, research has been more forthcoming on huacapu's main active plant chemical which is documented with antimalarial, antiviral, antitumoral, and antibacterial actions. The actions of minquartynoic acid do help to explain and support huacapu's main traditional uses for microbial diseases such as herpes, hepatitis, and tuberculosis, for lung cancer, and malaria. The tree bark is a significant source of this highly active plant chemical. Huacapu is quite popular in Ecuador and Peru, however it is not very well known here in the United States.

Cytotoxic & Anti-tumorous Actions:

Gung, B., et al. "Total synthesis of (-)-minquartynoic acid: an anti-cancer, anti-HIV natural product." Org Lett. 2002 Jul 25;4(15):2517-9.
Marles, R. J., et al. "Isolation of a novel cytotoxic polyacetylene from a traditional anthelmintic medicinal plant, Minquartia guianensis." J. Nat. Prod. 1989; 52(2): 261-266.
Farnsworth, N. R., et al. "Isolation of a novel cytotoxic polyacetylene from a traditional anthelmintic medicinal plant: Minquartia guianensis Aubl. (Olacaceae). Abstr International Congress on Natural Products Research Park City, UT July 17-21 1988: Abstr-22 .
Quignard, E. L. J., et al. "Screening of plants found in Amazonas state for lethality towards brine shrimp." Acta Amazonica. 2003; 33(1): 93-104.
Quignard, E. L. J., et al. "Medium lethal concentrations of amazonian plant extracts in the brine shrimp assay." Pharmaceutical Biology. 2004; 42(3): 253-257.

N-TENSE

Description: A combination of 8 plants which have been independently documented around the world with anticancerous, antitumorous, antimutagenic, cytoprotective, and/or immunostimulant properties.
Traditional Uses: The plants in this formula have been traditionally used for cancer.
Ingredients: A herbal blend of graviola (Annona muricata), mullaca (Physalis angulata), guacatonga (Casearia sylvestris), espinheira santa (Maytenus ilicifolia), bitter melon (Momordica charantia), vassourinha (Scoparia dulcis), mutamba (Guazuma ulmifolia), and cat's claw (Uncaria tomentosa).
Suggested Use: Take 3-4 capsules three times daily.
Contraindications:

- Not to be used during pregnancy or while breast-feeding.
- Several ingredients in this formula have demonstrated hypotensive, vasodilator, and cardiodepressant activities in animal studies. People with low blood pressure should monitor their blood pressure for this possible effect.

Drug Interactions: This product may potentiate antihypertensive and cardiac depressant drugs.
Other Practitioner Observations and Possible Precautions:

- Several ingredients in this formula have demonstrated significant *in vitro* antimicrobial properties. Supplementing the diet with probiotics and digestive enzymes is advisable if this product is used for longer than 30 days.
- Taking CoQ10 and other supplements which increase cellular ATP may reduce the effects of N-Tense.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

- Graviola contains over 80 Annonaceous acetogenins which have shown in laboratory studies to be selectively cytotoxic to cancer cells without toxicity to healthy cells. Over 30 published studies report that these acetogenins have demonstrated selective cytotoxicity to tumor cells with as little as 1 part per million.
- Mullaca, and its novel plant steroids, have shown strong *in vitro* and *in vivo* (mice) cytotoxic activity against numerous types of cancer including leukemia, lung, colon, cervix and melanoma cancer cells. It has also evidenced significant immunostimulant actions.
- Guacatonga contains a group of chemicals called *clerodane diterpenes* which are being researched and patented for their anticarcinomic actions.
- Espinheira santa contains a group of chemicals called maytansinoids which have showed potent antitumorous and anticancerous activities at very low dosages. Other compounds in the plant named cangorins have shown in research to possess cytotoxic and/or inhibitory activity against various leukemia and cancer tumor cells.
- Bitter melon has been shown in studies over the last 10 years to have antitumorous and anticancerous properties. The plant contains the phytochemicals 5-hydroxytryptamine, zeaxanthin, cryptoxanthin, and lanosterol—all of which are documented to be anticancerous, antimutagenic and/or cytoprotective.
- A crude extract of vassourinha was reported to be active against human oral epidermoid carcinoma cells (66% inhibition) *in vitro*. Crude extracts from the plant demonstrated cytotoxicity towards six human stomach cancer cell lines. These antitumor actions were linked to two phytochemicals, scopadulcic acid B and betulinic acid. These two chemicals have been documented with anticarcinomic, antimelanomic, cytotoxic, and antiviral properties in other research studies.
- Mutamba, in one *in vitro* study, exhibited strong activity against human oral epidermoid carcinoma cells by inhibiting growth by 97.3%. Mutamba also contains procyanidin B-2 which has shown in other *in vitro* studies to have antitumor activity. In one study it showed activity towards melanoma cells with an ED50 of 1-4 mcg/ml. Some of the latest research on mutamba has focused on the antioxidants in the plant and their ability to interfere with prostaglandin synthetase.
- Cat's claw has been documented with immunostimulant, antitumor, and antimutagenic actions in laboratory research.

N-TENSE TOPICAL

2 Fluid Ounces / 60 ml

Description: A combination of 10 plants which have been independently documented in research with antimelanomic, anticancerous, and antitumorous properties.
Traditional Uses: The plants in this formula have been traditionally used for skin cancer.
Ingredients: A herbal blend of sangre de grado (Croton lechleri), copaiba (Copaifera officinalis), graviola (Annona muricata), espinheira santa (Maytenus ilicifolia), suma (Pfaffia paniculata), bellaco caspi (Himatanthus sucuuba), huacapu (Minquartia guianensis), pau d'arco (Tabebuia impetiginosa), mullaca (Physalis angulata), vassourinha (Scoparia dulcis), and mutamba (Guazuma ulmifolia) extracted in distilled water and 20% alcohol.
Suggested Use: Shake well and apply liberally on affected area several times daily. Allow to dry completely before covering with clothing.
Contraindications: None documented.
Drug Interactions: None documented.
Other Practitioner Observations and Possible Precautions: This extract will stain clothing and other textiles.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

- Sangre de grado contains an alkaloid called taspine which has been documented in several *in vitro* and *in vivo* laboratory studies to possess antitumorous, antiviral, anti-inflammatory and vulnerary actions.Copaiba contains kolavenol, methlyl copalate, and kaurenoic acid which have been documented with anticarcinomic, antimelanomic, and antitumorous actions in various *in vitro* and *in vivo* studies.
- Graviola contains over 80 Annonaceous acetogenins which have shown in laboratory studies to be selectively cytotoxic to cancer cells without toxicity to healthy cells.
- Espinheira santa contains a group of chemicals called maytansinoids which have showed potent antitumor and antimelanomic activities at very low dosages. Ointments and salves of espinheira santa are widely sold in Brazilian pharmacies for skin cancers.
- Suma contains novel saponins called pfaffosides which have been documented to inhibit melanoma *in vitro* in laboratory studies. In other research, suma demonstrated analgesic and anti-inflammatory activities in various *in vivo* rat and mouse studies.
- Bellaco Caspi was reported to be significantly cytotoxic *in vitro* to human cancer cell lines. Researchers related this anticancerous action to the iridoids and triterpenoids chemicals discovered in the tree bark.
- Huacapu contains minquartynoic acid. This chemical has been reported with cytotoxic actions against a large diverse line of cancer cells..
- Pau d'arco contains two chemicals called lapachol and beta-lapachone which have widely been documented with strong anticancerous and antitumorous actions in many studies over the last 30 years.
- Mullaca and its novel plant steroids have shown strong *in vitro* and *in vivo* (mice) cytotoxic activity against numerous types of cancer cells including: melanoma, leukemia, lung, colon, and cervical cancer.
- A crude extract of vassourinha was reported to be active against human oral epidermoid carcinoma (66% inhibition) *in vitro*. Crude extracts of vassourinha demonstrated cytotoxicity towards six human stomach cancer cell lines. These antitumor actions were linked to two phytochemicals, scopadulcic acid B and betulinic acid. These two chemicals have been documented with antimelanomic, anticarcinomic, cytotoxic, and antiviral properties in other research studies.
- Mutamba, in one *in vitro* study, exhibited strong activity against human oral epidermoid carcinoma cells, inhibiting growth by 97.3%. Mutamba also contains procyanidin B-2 which has shown in other *in vitro* studies to have antitumor activity. In one study it showed activity towards melanoma cancer cells in a range of 1-4 mcg/ml.

NTENSE-2

Description: A combination of 8 plants which have been independently documented around the world with active antileukemic and/or immunostimulant properties.
Traditional Uses: The plants in this formula have been traditionally used for leukemia.
Ingredients: A herbal blend of mullaca (Physalis angulata), anamu (Petiveria alliacea), vassourinha (Scoparia dulcis), simarouba (Simarouba amara), picão preto (Bidens pilosa), suma (Pfaffia paniculata), cat's claw (Uncaria tomentosa), and espinheira santa (Maytenus ilicifolia).
Suggested Use: Take 3-4 capsules three times daily.
Contraindications:
- Not to be used during pregnancy or while breast-feeding.
- Several plants in this formula have demonstrated immunostimulant effects therefore this formula is contraindicated before or following any organ or bone marrow transplant or skin graft.

Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: This product is best used in combination with Amazon Lymph Support.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

- Mullaca has been the subject of recent clinical research which is still ongoing based upon the preliminary studies showing that it is an effective immune stimulant, is cytotoxic to numerous types of cancer and leukemic cells and that it has antiviral properties. Researchers demonstrated that two chemicals in mullaca inhibited the growth of several human leukemia cells: erythroleukemia, acute T lymphoid leukemia, acute promyelocytic leukemia, acute myeloid leukemia, acute monocytic leukemia, and acute B lymphoid leukemia. In several *in vivo* animal tests and *in vitro* lab tests, an extract of the entire plant of mullaca and/or its steroidal fractions demonstrated immune stimulant properties by strongly enhancing blastogenesis, antibody responses and increased T and B lymphocyte production.
- Anamu has demonstrated *in vitro* antileukemic and antitumorous properties in several studies. Anamu has also been documented with *in vivo* and *in vitro* immunostimulant properties. In a 1993 study, a water extract demonstrated the ability to stimulate lymphocyte and interleukin II production in mice. In the same year, another study with mice demonstrated that an anamu extract increased natural killer cell activity by 100% and stimulated interferon, interleukin 2 and interleukin 4 production.
- Vassourinha contains the chemicals scopadulcic acids A and B, scopadiol, scopadulciol, scopadulin, scoparic acids A, B, and C, and betulinic acid. These chemicals have shown in laboratory tests to have antileukemic and antitumor actions.
- Simarouba contains quassinoid chemicals named glaucarubinone, holacanthone, alianthinone, and dehydroglaucarubinone. In laboratory studies from 1977 to 1998 these chemicals are reported with antileukemic and antitumor actions. See page A-15 for more information on simarouba.
- Picão preto first was reported to have antileukemic actions in 1995. Then researchers from Taiwan reported (in 2001) that a simple hot-water extract of picão preto could inhibit the growth of five strains of human and mouse leukemia at less than 200 mcg per ml *in vitro*. They summarized their research by saying that picão preto ". . . may prove to be a useful medicinal plant for treating leukemia."
- Suma was reported to inhibit the proliferation of lymphoma and leukemia in mice and, otherwise, delay mortality in research published in 2000.
- Cat's claw, in addition to its well documented immunostimulant actions, has been shown in laboratory research to possess antileukemic and antimutagenic actions.
- Espinheira santa contains a group of chemicals called maytansinoids which have showed potent antitumor and antileukemic activities at very low dosages. Other triterpene compounds in the plant (named cangorins) have shown in laboratory studies to possess cytotoxic and/or inhibitory activity against various leukemia and cancer tumor cells.

PAU D'ARCO

Description: Scientists around the world have documented the active properties of pau d'arco and its chemicals. This rainforest canopy tree goes by several names including taheebo, lapacho, tahuari and, of course, pau d'arco. The main active chemicals in pau d'arco require heat and alcohol to extract them as they are not very water soluble. Raintree's extract is rich in active and beneficial phytochemicals which occur naturally in this plant because we employ the best methods required based upon this plant's individual phytochemistry—with heat and alcohol. The extraction method utilized provides the equivalent of approximately 500 mg of pau d'arco bark per milliliter of extract—resulting in a highly potent extract.
Traditional Uses: For leukemia and cancer.
Suggested Use: Take 60 drops (2 ml) two or more times daily.
Contraindications: Not to be used during pregnancy or while breast-feeding.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: Large single dosages of pau d'arco may cause gastrointestinal upset and/or nausea.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

In the 1960s, extracts of pau d'arco demonstrated marked antitumorous effects in animals, which drew the interest of the National Cancer Institute (NCI). Researchers decided that the most potent single chemical for this activity was a naphthoquinone chemical named *lapachol* and they concentrated solely on this single chemical in their subsequent cancer research. In a 1968 study, lapachol demonstrated highly significant activity against cancerous tumors in rats.

By 1970, NCI-backed research already was testing lapachol in human cancer patients. The institute reported, however, that their first Phase I study failed to produce a therapeutic effect without side effects—and they discontinued further cancer research shortly thereafter. These side effects were nausea and vomiting and anti-vitamin K activity. Interestingly, other chemicals in the whole plant extract (which, initially, showed positive antitumor effects at very low toxicity) demonstrated positive effects on vitamin K and, conceivably, compensated for lapachol's negative effect. Once again, instead of pursuing research on a complex combination of at least 20 active chemicals in a whole plant extract (several of which had anti-tumor effects and other positive biological activities), research focused on a single, patentable chemical—and it didn't work as well. Despite NCI's abandonment of the research, another group developed a lapachol analog (which was patentable) in 1975. One study reported that this lapachol analog increased the life span of mice inoculated with leukemic cells by over 80%. In a small, uncontrolled, 1980 study of nine human patients with various cancers (liver, kidney, breast, prostate, and cervix), pure lapachol was reported to shrink tumors and reduce pain caused by them—and three of the patients realized complete remissions.

Another chemical in pau d'arco, beta-lapachone, has been studied closely of late and a number of recent patents have been filed on it. It has demonstrated in laboratory studies to have activities similar to lapachol (antimicrobial, antifungal, antiviral, antitumorous, antileukemic, and anti-inflammatory), with few side effects. Research published from 2003 to 2005 provides important new insights into the possible molecular mechanisms of the anti-cancer activity of beta-lapachone specifically against prostate, colon, pancreatic, and lung cancers. In a 2002 U.S. patent, beta-lapachone was cited to have significant anticancerous activity against human cancer cell lines including: promyelocytic leukemia, prostate, malignant glioma, colon, hepatoma, breast, ovarian, pancreatic, multiple myeloma cell lines and drug-resistant cell lines. In yet another U.S. patent, beta-lapachone was cited with the *in vivo* ability to inhibit the growth of prostate tumors.

SANGRE DE GRADO RESIN

Description: A pure natural resin extracted from the sangre de grado tree which is also called dragon's blood. It has been independently documented with anticancerous, antimicrobial, and vulnerary actions.
Traditional Uses: For stomach cancer, skin cancer, and ulcers.
Suggested Use: Take 15 drops (.5 ml) 2 or more times daily. Can also be applied topically on the skin as desired.
Contraindications: Not to be used during pregnancy or while breast-feeding.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions:

- When taking internally, this resin tastes quite bad. Adding it to a small amount of a strong-flavored beverage (like cranberry juice) is recommended.
- This red resin will permanently stain clothing and other textiles.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

Sangre de grado has traditionally been used in South America for stomach ulcers, ulcerative colitis, and stomach and colon cancer. Some of these traditional uses are beginning to be verified by independent research. Peruvian researchers reported in 2002 that sangre de grado was active against the stomach ulcer-causing bacteria, *Heliobacter pylorii*, *in vitro* and *in vivo* (mice). Another research group designed a study in 2000 to evaluate its gastrointestinal effects. These researchers concluded that "Sangre de grado is a potent, cost-effective treatment for gastrointestinal ulcers and distress via antimicrobial, anti-inflammatory, and sensory afferent-dependent actions." In 2002, these same researchers reported that sangre de grado evidenced an *in vitro* effect against stomach cancer and colon cancer cells as well. In 2003, Italian researchers reported that the resin inhibited the growth of a human myelogenous leukemia cell line and also evidenced an antimutagenic effect *in vitro*.

Scientists have attributed many of the biologically active properties of sangre de grado to one of its main bioactive constituents: an alkaloid named taspine. In the early 1990's a Japanese research group published three studies about taspine's antitumorous and anticancerous actions. This chemical has also been reported with anti-inflammatory, wound healing, immunostimulant, and antiviral actions in other published research.

Anticancerous and Cytotoxic Actions:

Montopoli, M., et al. "Croton lechleri sap and isolated alkaloid taspine exhibit inhibition against human melanoma SK23 and colon cancer HT29 cell lines." J Ethnopharmacol. 2012 Dec 18;144(3):747-53.
Zhang, Y., et al. "Antitumor activity of taspine by modulating the EGFR signaling pathway of Erk1/2 and Akt in vitro and in vivo." Planta Med. 2011 Nov;77(16):1774-81.
Alonso-Castro, A., et al. "Antitumor effect of Croton lechleri Mull. Arg. (Euphorbiaceae). J Ethnopharmacol. 2012 Mar 27;140(2):438-42.
Lu, W., et al. "A novel taspine analog, HMQ1611, inhibits growth of non-small cell lung cancer by inhibiting angiogenesis." Oncol Lett. 2012 Nov;4(5):1109-1113.
Zhang, Y., et al. "A novel angiogenesis inhibitor impairs lovo cell survival via targeting against human VEGFR and its signaling pathway of phosphorylation." Cell Death Dis. 2012 Oct 11;3:e406.
He, H., et al. "Tas13D inhibits growth of SMMC-7721 cell via suppression VEGF and EGF expression." Asian Pac J Cancer Prev. 2012;13(5):2009-14.
Zhan, Y., et al. "A novel taspine derivative, HMQ1611, suppresses adhesion, migration and invasion of ZR-75-30 human breast cancer cells." Breast Cancer. 2012 Aug 9.
Zhang, Y., et al. "Facile synthesis and biological evaluation of novel symmetrical biphenyls as antitumor agents." Med Chem. 2012 Mar;8(2):145-50.
Zhang, Y., et al. "Effects of taspine on proliferation and apoptosis by regulating caspase-3 expression and the ratio of Bax/Bcl-2 in A431 cells." Phytother Res. 2011 Mar;25(3):357-64.
Takami, Y., et al. "Proanthocyanidin derived from the leaves of Vaccinium virgatum suppresses platelet-derived growth factor-induced proliferation of the human hepatic stellate cell line LI90." Hepatol Res. 2010 Apr;40(4):337-45.
Fayed, W., et al. "Identification of a novel topoisomerase inhibitor effective in cells overexpressing drug efflux transporters." PLoS One. 2009 Oct 2;4(10):e7238.
Zhang, Y., et al. "[Inhibitory effect of taspine on mouse S180 sarcoma and its mechanism]." Zhongguo Zhong Yao Za Zhi. 2007 May;32(10):953-6.

SIMAROUBA

Description: Raintree's simarouba extract uses proprietary extractions methods which provide the equivalent of 500 mg simarouba bark per milliliter of extract. The main active group of chemicals in simarouba are called quassinoids. Several of the quassinoids found in simarouba, such as ailanthinone, glaucarubinone, and holacanthone, are considered the plant's main therapeutic constituents and are the ones documented to be toxic to cancer and leukemia cells.
Traditional Uses: For cancer and leukemia.
Suggested Use: Take 60 drops (2 ml) 2 or more times daily.
Contraindications: Not to be used during pregnancy or while breast-feeding.
Drug Interactions: None reported.
Other Practitioner Observations and Possible Precautions: Reported side effects at high dosages (approx. 5 times the suggested use) include increased perspiration and urination, nausea, and/or vomiting.

Synopsis of research: (Please see the Tropical Plant Database for all cited research.)

An important area of research on simarouba and its plant chemicals has focused on cancer and leukemia. The quassinoids responsible for the anti-amebic and antimalarial properties of simarouba bark have also shown in clinical research to possess active cancer-killing properties. Early cancer screening performed by the National Cancer Institute in 1976 indicated that an alcohol extract of simarouba root (and a water extract of its seeds) had toxic actions against cancer cells at very low dosages (less than 20 mcg/ml). Following up on that initial screening, scientists discovered that several of the quassinoids in simarouba (glaucarubinone, alianthinone, and dehydroglaucarubinone) had antileukemic actions against lymphocytic leukemia *in vitro* and published several studies in 1977 and 1978. Researchers found that yet another simarouba quassinoid, holacanthone, also possessed antileukemic and antitumorous actions in 1983. Researchers in the UK cited the antitumorous activity of two of the quassinoids, ailanthinone and glaucarubinone, against human epidermoid carcinoma of the pharynx. A later study in 1998 by U.S. researchers demonstrated the antitumorous activity of glaucarubinone against solid tumors (human and mouse cell lines), multi-drug-resistant mammary tumors in mice, and antileukemic activity against leukemia in mice.

Anticancerous & Antileukemic Actions:

Reynertson, K., et al. "Induction of murine embryonic stem cell differentiation by medicinal plant extracts." Exp Cell Res. 2011 Jan 1;317(1):82-93.
de Mesquita, M., et al. "Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines." J Ethnopharmacol. 2009 Jun 25;123(3):439-45.
Rivero-Cruz, J. F., et al. “Cytotoxic constituents of the twigs of Simarouba glauca collected from a plot in Southern Florida.” Phytother. Res. 2005; 19(2): 136-40.
Mata-Greenwood, E., et al. “ Novel esters of glaucarubolone as inducers of terminal differentiation of promyelocytic HL-60 cells and inhibitors of 7,12-dimethylbenz[a]anthracene-induced preneoplastic lesion formation in mouse mammary organ culture.” J. Nat. Prod. 2001; 64(12): 1509-13.
Morre, D. J., et al. “Mode of action of the anticancer quassinoids--inhibition of the plasma membrane NADH oxidase.” Life Sci. 1998; 63(7) :595-604.
Valeriote, F. A., et al. “Anticancer activity of glaucarubinone analogues.” Oncol Res. 1998; 10(4): 201–8.
Ohno, N., et al. “Synthesis of cytotoxic fluorinated quassinoids.” Bioorg. Med. Chem. 1997; 5(8): 1489-95.
Klocke, J. A., et al. "Growth inhibitory, insecticidal and antifeedant effects of some antileukemic and cytotoxic quassinoids on two species of agricultural pests." Experientia. 1985 Mar 15; 41(3): 379-82.
Handa, S. S., et al. “Plant anticancer agents XXV. Constituents of Soulamea soulameoides.” J. Nat. Prod. 1983; 46(3): 359–64.
Polonsky, J. “The isolation and structure of 13,18-dehydroglaucarubinone, a new antineoplastic quassinoid from Simarouba amara.” Experientia. 1978; 34(9): 1122–23.
Ghosh, P. C., et al. “Antitumor plants. IV. Constituents of Simarouba versicolor.” Lloydia. 1977; 40(4): 364–69.
Ogura, M. et al. “Potential anticancer agents VI. Constituents of Ailanthus excelsa (Simaroubaceae)." Lloydia. 1977; 40(6): 579–84.