Integrative Oncology: Plant Products

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Before reading about plant-based complementary treatments, please see the following:

- **Introduction on Integrative Oncology**
- **Note on Complementary Approaches**
- **Introduction to Scientific Research**

Many different plant products have been studied for their ability to prevent and/or treat cancer. The list below is not meant to be complete, but it does include some of the plant products studied for these activities.

Because the active chemicals in plants that seem to help prevent cancer are often the same ones that help fight cancer once it has developed, we have combined those two activities in the following descriptions.

The following plant-based treatments have shown activity in animal models (*in vivo*) or with human cells in the lab (*in vitro*) as a cancer treatment. Read the individual entries for prevention information.

- Anthocyanin (Berries)
- Bromelain (Pineapples)
- Curcumin (Turmeric)
- EGCG (Green Tea)
- Lycopene (Tomatoes)
- Phytoestrogens (Soy)
- Pycnogenol (Pine Trees)
- Resveratrol (Grapes)
- Selenium (Nuts)

The following plant-based treatments DO NOT have substantial scientific support in any model as a cancer treatment.

- Cannabis and Hemp Oil (Cannabis)
- Essiac®, Flor-Essence® (mixture)
- Gerson Therapy (Mixture)
- Graviola/Soursop

Anthocyanin

Classified as:
Phytochemical, Polyphenol, Flavonoid, Anthocyanidin

Structure of Anthocyanin

Intro and Background
The term anthocyanin refers to a group of compounds found in vegetables, citrus fruits, red wine, and especially in edible berries. Anthocyanins are responsible for the red, blue, and purple colors of many plants. 1 They may help prevent cardiovascular disorders, age complications, obesity, inflammatory responses, cancer, and other degenerative diseases.2, 1 These compounds also exhibit antioxidant behavior* which can help protect DNA and its structure.2 Anthocyanins leave the body quickly after they are eaten, and it is not currently known where and how quickly they are absorbed. 1 These types of compounds may fight cancer by inducing apoptosis and inhibiting proliferation of cancer cells. 3

Scientific Research
Studies have shown that anthocyanins can slow the growth of tumor cells *in vitro*.4, 5, 6, 7 Because it is unclear how anthocyanins will act in animal experiments, 8 no clinical trials seem to have been performed to investigate the ability of anthocyanins to treat cancer in humans. Most of the recent research seems to be focused on the ability of anthocyanins to prevent cancer rather than treat it. Anthocyanins do not seem to have side effects in studies done on cells *in vitro.* 9

Currently, a trial investigating the ability of anthocyanin to modulate the side effects of radiation in breast cancer patients is recruiting participants.10 For information about ongoing clinical trials involving anthocyanins, please visit our section on Finding Clinical Trials.

US Food and Drug Administration Approval
There is not enough evidence to support the effectiveness of anthocyanins in the fight against cancer, and they have not been approved by the FDA for cancer treatment. 11

*It is important to keep in mind that many cancer treatments, including chemotherapy and radiation, work by generating free radicals in order to destroy cancer cells. If a cancer patient takes antioxidants while undergoing radiation or chemotherapy treatment, it is possible that these compounds may protect tumor cells from the desired free radicals. Doctors may recommend that patients undergoing these treatments avoid antioxidants so that the treatment is as effective as possible. 12

Bromelain

pineapple.jpg

Pineapple on plant and sliced (Wikimedia Commons)

Classification
As a phytochemical, the term "bromelain" collectively denotes enzymes, or catalytic polymers of amino acids, found in the Bromeliaceae plant family, whose most recognized member is the pineapple.13Technically, pineapple stem bromelain is not the same enzyme as pineapple fruit bromelain, 13 though in practice both are referred to as bromelain.

Intro and Background
Pineapple has long been used therapeutically in South America and Southeast Asia14 and was called in 1558 "the fruit of which the natives of America make the greatest medicinal use."15 Although bromelain was isolated as the active enzyme in pineapple in 1891,15 it was not commercially produced because pineapple was relatively expensive. However, in 1957 Heinecke discovered that the discarded stem contains more bromelain than the fruit,13 paving the way for bromelain's production as a medicinal compound. Today, nutrition stores throughout America sell it as a supplement that supports digestion,16 though it has multiple biological uses.

Scientific Research
Bromelain has been studied for decades. Not only does it potently fight inflammation,14 a major contributor to cancer,* but it also exhibits anti-cancer activity both in cell culture (*in vitro*) and in mouse models (*in vivo*), blocking growth and causing death of cancer cells.17 So, the way in which bromelain stops cancer is known.18 The enzymes in bromelain are proteloytic; they can break down proteins on the surfaces of cells, influencing cell signaling and behavior. Nonetheless, not all of bromelain's biological activity can be attributed to proteolysis.13

Large amounts of bromelain must reach a tumor site for significant results.18 Even though human beings tolerate bromelain at relatively high doses without side effects,16it is very difficult to get the required levels of the chemical in the body. As a result, studies are currently underway to investigate nanoparticle delivery of bromelain.18

Clinical Trials
A clinical trial exploring the efficacy of bromelain as an anti-cancer treatment has been initiated.19 Another study investigated the use of bromelain, in conjunction with other compounds, to reduce the side effects associated with chemotherapy, but its results are not available.20

US Food and Drug Administration Approval
There is not enough evidence that bromelain treats cancer, and bromelain has not been approved by the FDA for cancer treatment.21

*For more information, see our Inflammation section.

Curcumin

Classified as:
Phytochemical, Polyphenol

Also called:
Diferuloylmethane

Structure of Curcumin

Intro and Background

Curcumin comes from the turmeric plant (*Curcuma longa*). It is

responsible for the yellow color of curry, a traditional spice used in Southeast Asian cuisine and medicine. 22

This agent has been used for centuries by different cultures in Asia. For example, Indian medicinal practices have used curcumin to treat anorexia, cough, rheumatism, and other diseases. 23 Hindu medicine men still use curcumin to treat sprains and swelling. 23 Traditional Chinese medicine uses this same compound to treat diseases that are accompanied by abdominal pain. 23 Western medicine has recently recognized that curcumin may have anti-inflammatory, antioxidant*, anti-bacterial, anti-venom, and anti-HIV activity, as well as the ability to combat Alzheimer's disease. 23, 24

In terms of cancer fighting ability, curcumin may induce apoptosis while reducing angiogenesis, metastasis, proliferation, transformation,25 and epithelial-to-mesenchymal transition.26

Watch the full interview with Dr. Dennis Liotta an Emory researcher working with curcumin to develop cancer prevention and treatment drugs.

Scientific Research

Pre-Clinical/Laboratory Studies

Curcumin has been found to slow tumor cell development 27 and angiogenic processes 28*in vitro* and in rodent experiments. Also, curcumin seems to induce apoptosis in cancer cells without hurting healthy ones. 29 Both *in vitro* (cancer cell lines) and *in vivo* (animals) studies show that it has anti-tumor effects in melanoma,26 breast cancer,30 colon cancer,31, 32 pancreatic cancer,26, 33 and head and neck cancer,32 among others.

Curcumin may also increase the efficacy of standard cancer treatments. For example, as a blocker of the pro-inflammatory protein NF-kB, curcumin has the potential to prevent cells from becoming resistant to chemotherapy.34 As for radiation, pre-clinical evidence, or research done in the laboratory but not in humans, suggests that curcumin can prime cancerous cells to death by radiation and protect normal cells against death by radiation.35

In June of 2017 a study was published which examined different combinations of nutrients on mouse prostate cancer cells, both in culture and in animals. Curcumin showed positive results in these studies. 36, 37

In August 2018, one of curcumin's main hurdles to use in humans was overcome. Curcumin does not dissolve well in water or fat and is therefore hard to get into the body in amounts that are helpful. Research at the University of Illinois were able to combine a platinum-based chemotherapy drug with curcumin in a way that greatly increased the activity of the combined drug against cancer cell lines. The technique needs additional work and testing in animals before it can move to human patients, but is a great step forward.38

Clinical Trials/Studies with Humans

With laboratory studies establishing it as a promising agent in the fight against cancer, curcumin has drawn the attention of many researchers. Over 50 clinical trials are currently investigating its ability to treat and prevent cancer, either alone or in combination with other treatments. Most of these trials are ongoing, and their results have not been posted.39

Curcumin has been demonstrated to be safe taken in pill form in conjunction with chemotherapy.40 As for the side effects of cancer therapy, taking curcumin orally was found to significantly decrease the "burning" (technically, radiation dermatitis and moist desquamation) of the skin associated with radiation treatment,41, 42 though a larger study found no statistically significant improvement.43

Curcumin has run into several problems in clinical trials because it has poor bioavailability (i.e. it has difficulty working and staying inside the human body).26, 44 Researchers are working on stabilizing the molecule via nanotechnology and chemical approaches.26, 30, 44 More bioavailable curcumin analogues have also been made.40

For information about ongoing clinical trials involving curcumin, please visit our section on Finding Clinical Trials.

Find clinical trials at the Winship Cancer Institute of Emory University

US Food and Drug Administration Approval

There is not enough evidence that curcumin effectively kills cancerous cells, and it has not been approved by the FDA for cancer treatment. 11 In fact, a number of curcumin products are on the FDA's list of Fake Cancer "Cures."

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EGCG

Classified as:
Phytochemical, Polyphenol

Also called:
epigallocatechin-3-gallate

Structure of EGCG

Intro and Background
Tea is one of the most widely consumed beverages on the planet, second only to water. 45 Green tea comes from the plant *Canellia sinesis*, an evergreen shrub of the *Theaceae* family. Green, black, and oolong teas all come from this same plant but differ in the way they are prepared. 46 Because it is not allowed to ferment, green tea retains many of the beneficial properties of the tea plant. In general, many plants produce chemicals called polyphenols that protect them from environmental damage. The polyphenol EGCG (epigallocatchin-3-gallate) is present in large amounts in green tea. 45 EGCG has antioxidant properties and has shown to have some preventative effects against skin, lung, esophagus, stomach, liver, small intestine, pancreas, colon, bladder and breast cancers. 47, 48 Worldwide, tea is believed to have a number of beneficial effects varying from improving blood flow, eliminating toxins, increasing resistance to diseases, increasing cardiovascular health, lowering cholesterol and preventing/combating cancer. Green tea has been found to have antioxidant* and health promoting benefits due mostly to its higher content of epigallocatevhin-3-gallate (EGCG). 45

Scientific Research
Studies involving large populations of people suggest that drinking green tea may be associated with a lower risk of some cancer types. 49

These findings have been a basis for research into the cancer-fighting abilities of green tea. EGCG has been found to prevent cancer cells from getting nutrients (angiogenesis), 50 cause cancer cells to die (apoptosis),51 stop cancer cells from traveling,51prevent tumors from growing,51 and inhibit cellular proliferation.52, 51Moreover, EGCG exerts these effects on cancerous cells, not normal cells,51 making it very safe.

There have been numerous clinical trials to determine the ability of EGCG to prevent cancer with mixed results. One study found that it decreased oxidation and NF-kB, an important protein for inflammation, in cancerous prostatic tissue, but it did not significantly affect apoptosis or proliferation.53 In breast cancer patients, EGCG did not significantly decrease VEGF and HGF, markers of angiogenesis and proliferation,54 but in prostate cancer patients, it did, according to another study.55 Many other studies are ongoing; for example, one is investigating how well green tea extract can treat bladder cancer patients.56

Drinking tea (and coffee) has been shown to cause epigenetic changes in women (but not men). Interestingly, many of the changes were found in genes that function in cancer and hormone (estrogen) metabolism. The reason for the sex-specific effects are not known, but could be due to activities of sex hormones.57

Learn more about angiogenesis, apoptosis, metastasis and proliferation.

US Food and Drug Administration Approval
There is not enough evidence that EGCG is effective in the fight against cancer, and it has not been approved by the FDA for cancer treatment. 58

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Please be sure to see our notice on complementary therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Lycopene

Classification
Phytochemical, Carotenoid

Structure of Lycopene

Intro and Background
Lycopene is the compound that gives tomatoes (*Solanum lycopersicum*) their red color. 59 Watermelon, grapefruit, guava, and papaya also contain lycopene but in lower amounts than tomatoes. Consumption of this antioxidant* has long been associated with a decreased risk of prostate cancer.60 Most research about lycopene and cancer involves prostate cancer prevention. Studies have also suggested that lycopene is more effective when it is ingested from a tomato, as opposed to a supplement. 61

Scientific Research
Results of *in vitro* tests are encouraging. For example, treatment with Racimo, a kind of tomato high in lycopene, stopped colorectal cancer cells from growing, 62 and when prostate cancer cells were treated with lycopene, apoptosis was induced in a significant number of cells.63 Lycopene was also shown to inhibit the growth of prostate cancer cells *in vivo*.64 This may occur through increased expression of an enzyme called BCO2, a tumor suppressor that decreases NF-kB activity.65 However, lycopene was only observed to increase BCO2 expression in cells that relied on male hormones for growth (termed "androgen-sensitive").65, 66

Lycopene also has supportive results from *in vivo* tests. For example, in a study involving rats, tomato powder inhibited the creation of cancer cells, prolonged the animals' survival, and reduced animal death rates. 67

Lycopene is the focus of many phase II clinical trials investigating its ability to both prevent and treat prostate cancer. Though some completed trials have published results, the results are either not strong or not generalizable. 68, 69, 61

One trial comparing how well tomato juice and tangerine juice can stop prostate cancer from progressing is recruiting participants.70 For information about ongoing clinical trials involving lycopene, please visit our section on Finding Clinical Trials.

In summary, though pre-clinical evidence is favorable, there is not enough evidence to decide whether lycopene can treat cancer effectively in humans.

Learn more about apoptosis and cancer.

For Further Reading
The National Cancer Institute has published a Physician Data Query (PDQ) summary of prostate cancer, which includes a section on lycopene.

US Food and Drug Administration Approval
There is not enough evidence that lycopene is effective in the fight against cancer, and it has not been approved by the FDA for cancer treatment. 11 In fact, one lycopene product is on the FDA's list of Fake Cancer "Cures."

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Phytoestrogens

Classified as
Phytochemical, Phytoestrogens, Isoflavone

Types of Phytoestrogens
Isoflavones (e.g. genistein, daidzein, glycitein, formononetin) 71

Structure of Genistein

Structure of Daidzein

Lignans (e.g. secoisolariciresinol, matairesinol, pinoresinol, lariciresinol) 71

Structure of Lignan

Coumestan (e.g coumestrol) 72

Structure of Coumestan

Isoflavonoids

Structure of Isoflavonoids

Flavonoids (flavanols, flavanones, flavones, flavonols) 72

Structure of Flavonol

Structure of Flavone

Intro and Background
The term phytoestrogen classifies a large group of compounds derived from plants and naturally found in many foods. Major groups of phytoestrogens are isoflavones, lignans and coumestans. Isoflavones are most commonly found in soy, legumes, meat, cereals, nuts, fruits, and vegetables. Lignans are found in most plants with flaxseed registering the highest concentrations.71 Coumestans can be found in pinto beans, alfalfa sprouts, and vegetables.73

Phytoestrogens have been found to exhibit antioxidant* properties.74 Because antioxidant activity is associated with the health and survival of cells, this discovery has led some to believe that they may able to prevent and combat cancer in humans.75 Another reason phytoestrogens are believed to be anticancer agents is the lower occurrence of prostate and breast cancer in Asian nations. In these countries, much more phytoestrogens from soy and vegetables are consumed than in Western countries. This intake, presumably, contributes to their low rate of these cancer types.76

These compounds are also assumed to inhibit cancer growth because they have structural similarity to steroid hormones like estrogen and testosterone. Estrogen is a known instigator of hormone responsive cancer types, like breast, uterine, endometrial cancers. The resemblance of phytoestrogens to estrogen allows them to bind to molecular receptors intended for this hormone, preventing the hormones from binding and resulting in fewer cancer-causing signals in cells.77 Researchers believe that this class of compounds may also be involved in regulating cell death (apoptosis) as well.74 Phytoestrogens are also being studied for their potential to protect against cardiovascular disease, osteoporosis, and menopausal symptoms.71

Scientific Research
While older population studies from the early and mid-nineties suggest that a diet higher in phytoestrogens may reduce hormone-related cancers, recent studies have yielded conflicting results about the effectiveness of phytoestrogens against cancer.78

Phytoestrogens can hinder metastasis,79 a key to cancer progression. According to one study, high doses of a phytoestrogen from soy (genistein) can slow down the growth of mouse cancer cells *in vitro*.80 In another study, a

combination of soy phytoestrogens (genistein and daizein, pictured above, plus glyceitein) was shown to stop prostate cancer cells from growing in another *in vitro* assay.81 Another research group concluded that coumestrol, pictured above, caused cancer cell death by interacting with copper, of which cancer cells contain high levels, and damaging cellular DNA.82 Flaxseed oil, containing phytoestrogens, has also been shown to prevent estrogen related tumor cell growth *in vitro* and in mice.83 In addition, a preliminary study found that a combination of phytoestrogens and fibers taken orally could be as effective as COX-2 inhibitors, which block an enzyme important for colorectal cancer. The study concluded that the phytoestrogen/fiber dietary supplement may prevent progression of colorectal cancer in patients with familial adenomatous polyposis.84

Research supports a role for phytoestrogens in complementary therapy; genistein has been reported to prevent the bone damage that often accompanies chemotherapy.85 One clinical trial, currently recruiting participants, will investigate whether genistein can improve the effectiveness of chemotherapy in colorectal cancer patients.86

On the other hand, phytoestrogens are also suspected to cause cancer and improper fetal development.76 Some studies have shown that phytoestrogens increase breast cancer cell growth *in vitro.*78, 87Some European countries have even recommended maximum levels of soy intake per day.76

Currently, researchers are conducting several clinical trials designed to investigate the potential role of phytoestrogens in chemoprevention.78 One phase II trial showed that genistein could decrease activation of EGFR, an important receptor involved in growth of cancer cells, in patients with bladder cancer. The study found no significant differences in other markers.88 Other trials are investigating whether phytoestrogens, via dietary supplementation, can decrease prostate cancer progression.89, 90 For information about ongoing clinical trials involving phytoestrogens, please visit our section on Finding Clinical Trials.

Learn more about angiogenesis, apoptosis, metastasis and proliferation.

For Further Reading
The National Cancer Institute has published a Physician Data Query (PDQ) summary on soy and prostate cancer, written specifically for patients.

US Food and Drug Administration Approval
There is not enough evidence that phytoestrogens are effective in the fight against cancer, and they have not been approved by the FDA for cancer treatment.11

*It is important to keep in mind that many cancer treatments, including chemotherapy and radiation, work by generating free radicals in order to destroy cancer cells. If a cancer patient takes antioxidants while undergoing radiation or chemotherapy treatment, it is possible that these compounds may protect tumor cells from the desired free radicals. Doctors may recommend that patients undergoing these treatments avoid antioxidants so that the treatment is as effective as possible.12

Please be sure to see our notice on complementary therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Pycnogenol

Structure of Pycnogenol

Classification
Phytochemical, Polyphenol, Flavonoid, Proanthocyanidin

Intro and Background
Pycnogenol is a product derived from the bark of the French Pine Tree (*Pinus pinaster*). 91 Extract from the bark of this tree contains compounds known as flavonoids, procyanidins, and proanthocyanidins that are also found in grapes and cocoa. 92, 93 This extract is widely used in Europe as a dietary supplement to protect nerve cells, increase sperm activity, increase tissue function, decrease blood pressure, and alleviate asthma symptoms. 91 Pycnogenol and other proanthcyanidins are being investigated for their possible antioxidant, anti-inflammatory, and anti-platelet functionality. 92, 94, 93

Scientific Research
This natural extract has been recognized for its ability to reduce oxidative damage and prevent some processes that can often lead to cancer. 95 It was shown to induce apoptosis and slow down the reproduction of oral,96, 97 leukemia, 98 breast, 99, and ovarian 100 cancer cells *in vitro*.101 A mixture derived from a related tree, the Taiwan short pine (*Pinus morrisonicola*), has also been shown to kill leukemia cells *in vitro*. 102

French Pine trees

Pycnogenol has also been shown to slow the development of skin cancer *in vivo*. 93 What's more, even pycnogenol that has been metabolized, or processed by the human body, can cause fibrosarcoma cells to die *ex vivo*.103 Much of the research pertaining to pycnogenol and proanthocyanidins involves their ability to prevent cancer. Yet, one

group reported that pycnogenol can treat moderate, but not severe, oral mucositis, a painful side effect of chemotherapy that may get in the way of proper nutrition.104

One clinical study, sponsored by the University of Wisconsin and the National Center for Complementary and Integrative Health, investigated whether pycnogenol could benefit breast cancer survivors who suffered from lymphedema, or buildup of fluid in the lymph nodes, a common side-effect of breast cancer treatment. 105 For information about ongoing clinical trials involving pycnogenol, please visit our section on Finding Clinical Trials.

US Food and Drug Administration Approval
There is not enough evidence that pycnogenol is effective in the fight against cancer, and it has not been approved by the FDA for cancer treatment. 11

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Resveratrol

Classification
Phytochemical, Polyphenol, Phytoestrogen, Anthocyanin

Structure of Resveratrol

Intro and Background
Resveratrol is a compound commonly found in the skin and seeds of red grapes. It can also be obtained from berries, nuts, wine, and supplements. 106, 107 In plants, this compound helps defend against fungal infections. 108

Cancer treatment with resveratrol began in 1925 when Johanna Brandt, a South African dietician, claimed that she was able to cure herself of stomach cancer by eating a grape diet. 109 She opened the Harmony and Healing Centre in New York City in 1928 but was quickly charged with practicing medicine without a license. 110, 111 The American Cancer Society has examined Brandt's grape cure four times and found no therapeutic value for its use. 110 Another source of interest regarding resveratrol is the "French paradox": French people typically eat diets high in fat but experience fewer incidences of heart disease. 112

Scientists are researching this compound because of its antioxidant activity 113 and because it may interfere with angiogenesis and metastasis 114 while inducing apoptosis 106 of cancer cells. It is also being studied for potential abilities to prevent cancer, protect endothelial cells, 115 and prevent heart disease. 106 Resveratrol has not shown adverse side effects in animal trials when supplements have been used. 114

Scientific Research
Resveratrol has shown that it can induce apoptosis 116 in cancerous cells and reduce cancer cell growth 106 in *in vitro* studies. Experiments involving mice have also indicated that resveratrol can induce apoptosis in cancer cells. 117 Others have shown that resveratrol can inhibit processes like epithelial-mesenchymal transition, oxidative stress, and inflammation, all of which contribute to cancer progression.118, 79 Resveratrol also has been shown to regulate the progression of cancer stem cells, hindering them from developing into tumors. *In vitro* experiments, however, show that resveratrol is capable of enhancing the anti-tumor growth effects of the chemotherapy drug rapamycin. These experiments also showed a lowered incidence of cancer resistance to rapamycin, which is likely a consequence of reservatrol suppressing AKT signalling 119.

A study using two breast cancer cell lines demonstrated that the effects of resveratrol were dependent on the amount used. Lower doses stimulated breast cancer cell growth *in vitro* and higher doses blocked growth. 107 There is still much to be learned about how resveratrol affects cancer cells and cancer patients.

Some work has been done in people, but because of small patient numbers, differences in study designs, and short

treatment times, researchers have not reached a conclusion about the ability of resveratrol (or similar molecules) to treat cancer. 120 Despite encouraging results in cells, resveratrol, like curcumin, is poorly absorbed by the body, and high concentrations are necessary for significant results.118 Consequently, though laboratory studies indicate that resveratrol can prevent cancer progression, the results of clinical trials have not been as promising. 118, 121

Clinical studies at UC Irvine, The National Cancer Institute, the University of Oslo, the University of Wisconsin, and the University of Michigan are investigating how effectively resveratrol can treat cancer. 122 In the UC Irvine trial, resveratrol was able to negatively affect a pathway key to colon cancer development. 123 This trial, along with the NCI trial, suggests a role for resveratrol in preventing cancer rather than treating it. 124 For information about ongoing clinical trials involving resveratrol, please visit our section on Finding Clinical Trials.

Researchers have also studied the effects of different combinations of nutrients on mouse prostate cancer, both in culture and in a mouse model of prostate cancer. The nutrients with the most effect on prostate cancer cells included: ursolic acid, found in apple peels and rosemary; curcumin; and resveratrol, which is found in red grapes and berries. A lead researcher, Dr. Tiziani, stated, “These nutrients have potential anti-cancer properties and are readily available. We only need to increase concentration beyond levels found in a healthy diet for an effect on prostate cancer cells.” 36, 37

Learn more about angiogenesis, apoptosis and metastasis.

US Food and Drug Administration Approval
There is not enough evidence that resveratrol is effective in the fight against cancer, and it has not been approved by the FDA for cancer treatment. 11

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Please be sure to see our Notice on Complementary Therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Selenium

Often ingested as:
Selenomethionine

Structure of Selenomethionine

Intro and Background

Selenium is a component of the amino acid selenomethionine, commonly found in soil, forages, and grains. 125This naturally occurring amino acid is essential for proper nutrition and is often obtained from meats, seafood, and plants. 126 The amount of selenium in plants, animals, and humans depends on the selenium concentration of the soil where they were raised. Investigators started to look at selenium as an anticancer agent when a report suggested that the average selenium intake was lower among nations that showed an increased risk for cancer. 127

In many studies, selenium is also paired with Vitamin E to investigate their combined cancer fighting abilities. For the most part, research is focused on the ability of selenium to prevent cancer rather than fight it. The exact mechanism by which it works is unknown, but it may fight cancer-causing events in several different ways: it enhances processes that normally fight cancerous cells 128 and prevents harmful molecules from binding to and changing DNA.129

The US Food and Drug administration recommends a daily intake of about 70 µg (with a maximum of 400 µg/day) for adults as part of a normal, healthy diet.130

Scientific Research
Selenium may be an effective agent to prevent cancer, but more research is needed before a conclusion can be made.131, 132 Some studies suggest that a baseline, or minimum, level of selenium intake provides protection from cancer development.133 Studies also show that men are at a reduced risk for prostate cancer when selenium is part of their diet. 130 Treatment of prostate cancer cells with selenium *in vitro* can inhibit tumor growth and induce apoptosis. 125, 134 Selenium-enriched sugars have been found to exert anti-cancer effects, 135 as did a selenium-containing chemical compound called Se,Se'-1,4-phenylenebis(1,2-ethanediyl) bisisoselenourea, with implications for the treatment of liver cancer.136 An ionic compound of selenium, sodium selenite, has also been shown to help treat lymphedema, or swelling of the lymph nodes often caused by radiation therapy and

surgery.137 What's more, methylselenol has been reported to slow down the growth of colon tumors in mice.138

There are some indications that selenium may increase the risk for type II diabetes. 133

Phase II clinical trials are investigating selenium's ability to prevent and/or treat cancer. Though some trials are complete, results have not been published. For more information about clinical trials involving selenium, visit the US database. For information about ongoing clinical trials involving homeopathy, please visit our section on Finding Clinical Trials.

For Further Reading
The National Cancer Institute has published a Physician Data Query (PDQ) summary on selenium and prostate cancer, written specifically for patients.

US Food and Drug Administration Approval
There is not enough evidence that selenium is effective in the treatment of cancer, and it has not been approved by the FDA for cancer treatment. 11

Please be sure to see our Notice on Complementary Therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Cannabis and Hemp Oil

Classified as: Phytochemical, Aromatic Terpenoid

Structure of Cannabis

Introduction and Background
Cannabis belongs to the Cannabaceae family of plants. These include *Cannabis sativa* (pictured above; Wikimedia),*Cannabis indica*, and *Cannabis ruderalis*.139 Cannabinoids are chemicals found in Cannabis plants. Cannabinoids bind to receptor proteins on target cells and produce a variety of effects. Cannabinoids can also be produced by animals and are classified based on their origin. Phytocannabinoids are made in plants, other cannabinoids, called endocannabinoids, are found naturally in humans and animals, and synthetic cannabinoids are man-made. Many cannabinoids that are naturally found in plants can now be produced synthetically. The two main cannabinoids found in *Cannabis* are tetrahydrocannabinol (THC), or more specifically, Î”^{9}-tetrahydrocannabinol (Î”^{9}-THC), shown in the image above (Wikimedia), and cannabidiol (CBD).140, 141 THC is the main psychoactive ingredient. It binds to CB1 and CB2 receptors in the central nervous system and is found in marijuana (from *Cannabis sativa*). THC is thought to be responsible for the euphoria and relaxation felt by marijuana users.140, 141 CBD, on the other hand, has low affinity for the CB1 and CB2 receptors and while the way it works is less understood, studies suggest that CBD produces antipsychotic and anxiolytic effects in humans and lessens THCâ€™s effects in the body 142. Currently, these cannabinoids and others are being studied for their potential use in the treatment of several different cancers. See more details below.143, 144, 145, 146, 147

Hemp Oil
Hemp oil is a common (non-scientific) term for extracts made from many different *Cannabis* species. Hemp oil is obtained when hemp seeds are pressed. Hemp oil is legal in the United States. Modern hemp oil manufacturing methods ensure that almost no THC is found in the hemp oil. The seeds used for the oil come from *Cannabis sativa* strains bred to contain only tiny amounts of THC.148

Scientific Research
Studies have shown that cannabinoids have a wide variety of effects on cells growing in culture and in animals. The following list is not meant to be complete but gives an overview of the types of effects that have been seen. Some of the results are conflicting, with one study showing benefit and another showing either a lack of benefit or, worse, causing cancer to grow or spread more aggressively.

Work in cells grown in dishes in the laboratory (also called cell culture or *in vitro*)

1. Manmade (synthetic) chemicals that activate the same receptors as cannabinoids were shown to inhibit the invasive behavior of lung cancer cells and breast cancer cells.144, 145
2. In a system using the major psychoactive cannabinoid found in *C. sativa* (Î”^{9}-THC), research with different breast cancer cells showed that this chemical was NOT able to kill the cells. The use of this natural product actually enhanced the growth of the cancer cells in animals.146

Work in animals (also called *in vivo*)

1. Synthetic chemicals that bind to cannabinoid receptors were shown to reduce tumr growth and spread of lung cancer grown in mice. The chemicals seemed to cause the cancer cells to die by blocking the activity of a 'survival' protein, AKT.144
2. Also in mice, the same chemcials were shown to reduce the growth and spread of breast cancer.145
3. A study with the natural chemical, Î”^{9}-THC , showed **INCREASED** tumor growth after exposure. The reseach indicated that the increased tumor growth was due to suppression of the immune system by Î”^{9}-THC.146

Work in humans

1. One trial involved the injection of Î”^{9}-THC into the brains of 9 patients with glioblastome multiforme, a type of brain cancer. The results of the trial indicated that, at least for some patients, the drug reduced the division of the cancer cells *in vitro* and *in vivo*, but the patients did not recover from their disease.149
2. In another trial, participants were given spray injections of Î”^{9}-THC and cannabidiol for five weeks. The doses were 1-4, 6-10, or 11-16 sprays a day, and a fourth group was given a placebo. The low dose (1-4 sprays) group showed a statistically significant decrease in pain compared to the placebo group.150

There are indications that the conflicting results seen in some systems are due to different effects caused by different doses of the cannabinoids.This is covered in depth in a 2009 review called "Cannabinoids in the treatment of cancer."143 Several recent reviews of cannabinoids and endocannabinoids in cancer are also available.151, 152

Research published in 2013 shows that the anti-cancer activities of Î”^{9}-THC are, in large part, caused by its effects on a protein called pseudokinase tribbles homologue-3 (TRIB3). TRIB3 is part of a stress response system and when it is present in higher levels, it is able to block the activities of proteins that keep cells alive (including AKT and mTOR). Î”^{9}-THC was shown to increase levels of TRIB3 and cause cancer cell death. It was not able to kill cells missing TRIB3, showing the importance of this protein in the effects of Î”^{9}-THC.153 Because the molecular mechanisms of cannabinoid receptors are still being worked out, further studies on Î”^{9}-THC and other cannabinoids on a variety of cancers are needed.

No studies have shown that Î”^{9}-THC or other cannabinoids found in marijuana or hemp oil cure any form of cancer.

Cannabinoids are also being studied for other reasons. They can help reduce the effects of cancer and side effects of cancer treatments, like pain, nausea, and loss of appetite (anorexia).151, 154, 155, 152, 156They can also increase the effectiveness of radiation in a type of cancer called glioma.157

For Further Reading
The National Cancer Institute has published a Physician Data Query (PDQ) summary about *Cannabis* and cannabinoids. Access the version written for patients here.

Look for more research studies on cannabinoids and cancer. (opens new window - just type in those words in the search bar)

View clinical trials involving cannabinoids and cancer.

US Food and Drug Administration Approval
There is not enough evidence to support cannabiniods as effective in the fight against cancer, and they have not been approved by the FDA for cancer treatment.58However, some synthetic cannabinoids, called nabilone and dronabinol, are approved to treat the nausea and vomiting associated with chemotherapy.158

Please be sure to see our notice on complementary therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Essiac®, Flor-Essence®

Intro and Background
Essiac® is a blend of four herbs: burdock root (*Arctium lappa*), Indian rhubarb (*Rheum palmatum*), sheep sorrel (*Rumex acetosella*) and the inner bark of slippery elm (*Ulmus fulva or U. rubra*). 159 Flor-Essence® contains the previous four herbs as well as red clover (*Trifolum pretense*), blessed thistle (*Carduus benedictus*), kelp (*Laminaria digitata*), and watercress (*Nasturt officinale*). 160 The medicine men of the Ojibwa Native American tribe are believed to be the creators of the four herb mixture found in Essiac**.** 161 The treatment became popular in the early 1920s when a Canadian nurse, Rene Caisse, started treating patients with the herbal blend. 162 She claimed that Essiac® (her last named spelled backwards) improved the quality of life of her patients, prolonged survival, and could even cure cancer. 163 The use of these products by cancer patients is largely fueled by anecdotal evidence (a few rare cases) that they can treat or prevent cancer. 160 Allegedly, it is also is a remedy for allergies, hypertension, and osteoporosis. 164

Scientific Research

Essiac® has shown to block free radicals and exhibited the ability to protect DNA from damage that can lead to cancer. 165 Also, researchers have found that Essiac® prevents prostate cancer cells from growing *in vitro*. 161Another study showed that Essiac® and Flor-Essence® had weak effects on the growth of leukemia and breast cancer cells *in vitro* and only at concentrations higher than would be attained in the body. 162 This study also found that the herbal blend increased cancer cell differentiation. Alternatively, another study found that both Essiac® and Flor-Essence® not only fail to halt tumor enlargement, but can stimulate the growth of breast cancer cells *in vitro.* 160 A clinical trial involving Essiac found that it had no effect on quality of life for women with breast cancer. 166

There are currently no active clinical trials investigating Essiac® or Flor-Essence® and their ability to fight cancer. 167 For information about ongoing clinical trials involving Essiac® or Flor-Essence®, please visit our section on Finding Clinical Trials.

For Further Reading
The National Cancer Institute has published a Physician Data Query (PDQ) summary on Essiac® and Flor-Essence®. Access the patient version here.

US Food and Drug Administration Approval
There is not enough evidence that Essiac® and Flor-Essence® are effective in the fight against cancer,168 and they have not been approved by the FDA for cancer treatment.169 In fact, Essiac is on the FDA's list of Fake Cancer "Cures." Essiac® and Flor-Essence® are available commercially because they're sold as dietary supplements, and dietary supplements do not require FDA approval unless the seller claims that they can cure or prevent disease.170

Please be sure to see our notice on complementary therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Gerson Therapy

The Gerson Therapy targets chronic diseases like cancer using "an organic, vegetarian diet, raw juices, coffee enemas and natural supplements," according to the company's website. Two clinics are licensed to practice it, one in Hungary and one in Mexico.171

However, the FDA has not approved the Gerson therapy, and no preclinical (animal or laboratory) studies examining it are available in the scientific literature. A number of clinical studies (involving humans) are available, most of them as case studies published by Dr. Gerson, but they do not provide conclusive evidence about the regimen.172

For more information, see the National Cancer Institute's Physician Data Query (PDQ) Cancer Information Summary regarding the Gerson therapy.

Please be sure to see our notice on complementary therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

Graviola/Soursop

Image obtained from Wikimedia.

Classification
Phytochemical

Introduction and Background
Graviola (also known as soursop guyabano, and guanÃ¡bana) usually refers to the fruit of the tropical tree *Annona muricata.* Sometimes it is referred to as Brazilian paw paw or custard apple - although these are not the same. Extracts from the bark, leaves, roots, and fruits of *Annona muricata* are traditionally used to treat a variety of ailments including bacterial infections, herpesvirus infections, and cancer. However, few scientific studies have tested the medicinal properties of the extracts.173, 174

Graviola leaves contain derivatives of long-chain fatty acids known as annonaceous acetogenins175, 176, 174, which are believed to exert at least part of their biological effects by inhibiting the production of the cellular energy carrier adenosine triphosphate (ATP).177, 178 Because cancer cells require more ATP than normal cells, annonaceous acetongenins are believed to induce the death of cancer cells by starving them of their energy source. The chemicals in graviola have also been shown to inhibit the production (replication) of DNA.179, 180

Scientific Research

In laboratory studies, graviola extract has been shown to cause impaired function and death of pancreatic cancer cell lines (FG/COL0357 and CD18/HPAF). In immunocompromised mice, oral treatment with graviola extract was shown to reduce the growth and spread of injected pancreatic cancer cells.178Another study reported that it could prevent pancreatic cancer from advancing to a more dangerous stage by decreasing the ability of cancer cells to multiply.181 According to a more recent *in vitro* study, it can also kill squamous cell carcinoma cells.182

Graviola fruit extract has also been shown to downregulate the epidermal growth factor receptor (EGFR) oncogene and inhibit breast cancer cell growth in *in vitro* and *in vivo* studies using EGFR-overexpressing human breast cancer cells (MDA-MB-468). The extract, however, did not have an effect on nontumorigenic human breast epithelial cells.183 In an *in vivo* study, 6-7 week old mice were treated with chemicals that can cause (initiate) and accelerate the growth of (promote) skin cancer. Some of the mice also had extracts from *Annona muricata* put on their skin to see if the extract could slow or prevent the growth of skin cancer. The graviola extract was found to suppress tumor initiation and prevent tumor promotion at the highest dosages. No toxic side effects were seen in the mice (in this short study).184

As for studies in humans, one Phase 0 clinical trial has been completed, in which colorectal cancer patients were given extracts containing graviola, but results are not available.185

Side Effects
Although several studies suggest that graviola extracts may have anti-cancer properties, the major bioactive component of the extract, *Annonaceous acetogenins*, may also cause nervous system and/or mental problems. Consumption of the fruit has been linked to nervous system problems, including a form of atypical Parkinson's disease.186, 187, 188, 189, 190 In a study in which rats were intravenously given *Annonaceous acetogenins* for 28 days, a decrease in brain ATP levels and abnormalities similar to those found in atypical Parkinson patients were observed.191

Several studies suggest that chemicals in graviola (soursop) might be toxic. It should be consumed with caution.

US Food and Drug Administration Approval
There is not enough evidence to support the claim that graviola (soursop) is effective in the fight against cancer, and it has not been approved by the FDA for cancer treatment. 11

Please be sure to see our notice on complementary therapies. To better understand and evaluate the research described above, read our Introduction to Scientific Research.

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