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Diabetic Nephropathy – Using Herbals in Diabetic Nephropathy Prevention and Treatment – The Role of Ginger (*Zingiber officinale*) and Onion (*Allium cepa*) in Diabetics' Nephropathy

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1. Introduction

Diabetic nephropathy is a kidney disease or damage that results as a complication of diabetes. See also: Type 1 diabetes, Type 2 diabetes, Risk factors for diabetes, Chronic kidney disease causes, incidence, and risk factors. The exact cause of diabetic nephropathy is unknown, but it is believed that uncontrolled high blood sugar leads to the development of kidney damage, especially when high blood pressure is also present. In some cases, your genes or family history may also play a role. Not all persons with diabetes develop this condition.Each kidney is made of hundreds of thousands of filtering units called nephrons. Each nephron has a cluster of tiny blood vessels called a glomerulus. Together these structures help remove waste from the body. Too much blood sugar can damage these structures, causing them to thicken and become scarred. Slowly, over time, more and more blood vessels are destroyed. The kidney structures begin to leak and protein (albumin) begins to pass into the urine.Persons with diabetes who have the following risk factors are more likely to develop this condition:

- African American, Hispanic, or American Indian origin
- Family history of kidney disease or high blood pressure
- Poor control of blood pressure
- Poor control of blood sugars
- Type 1 diabetes before age 20
- Smoking

Diabetic nephropathy generally goes along with other diabetes complications including high blood pressure, retinopathy, and blood vessel changes. Early stage diabetic nephropathy has no symptoms. Over time, the kidney's ability to function starts to decline. Symptoms develop late in the disease and may include: Fatigue, Foamy appearance or

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excessive frothing of the urine, Frequent hiccups, General ill feeling, Generalized itching, Headache, Nausea and Vomiting, Poor appetite, Swelling of the legs, Swelling usually around the eyes in the mornings; general body swelling may occur with late-stage disease.

1.1 Signs and tests

The main sign of diabetic nephropathy is persistent protein in the urine. (protein may appear in the urine for 5 to 10 years before other symptoms develop.) If your doctor thinks you might have this condition, a microalbuminuria test will be done. A positive test often means you have at least some damage to the kidney from diabetes. Damage at this stage may be reversible. The test results can be high for other reasons, so it needs to be repeated for confirmation.High blood pressure often goes along with diabetic nephropathy. You may have high blood pressure that develops rapidly or is difficult to control.

1.2 Expectations (prognosis)

Nephropathy is a major cause of sickness and death in persons with diabetes. It is the leading cause of long-term kidney failure and end-stage kidney disease in the United States, and often leads to the need for dialysis or kidney transplantation.The condition slowly continues to get worse once large amounts of protein begin to appear in the urine or levels of creatinine in the blood begin to rise.Complications due to chronic kidney failure are more likely to occur earlier, and get worse more rapidly, when it is caused by diabetes than other causes. Even after dialysis or transplantation, persons with diabetes tend to do worse than those without diabetes.Complications,Possible complications include: Anemia, Chronic kidney failure (rapidly gets worse), Dialysis complications, End-stage kidney disease, Hyperkalemia, Severe hypertension, Hypoglycemia, Infections, Kidney transplant complications, Peritonitis (if peritoneal dialysis used).

1.3 Prevention

All persons with diabetes should have a yearly checkup with their doctor to have their blood and urine tested for signs of possible kidney problems.Persons with kidney disease should avoid contrast dyes that contain iodine, if possible. These dyes are removed through the kidneys and can worsen kidney function. Certain imaging tests use these types of dyes. If they must be used, fluids should be given through a vein for several hours before the test. This allows for rapid removal of the dyes from the body.Commonly used nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen, naproxen, and prescription COX-2 inhibitors such as celecoxib (Celebrex), may injure the weakened kidney. You should always talk to your health care provider before using any drugs.

2. Herbalism

Herbalism is a traditional medicinal or folk medicine practice based on the use of plants and plant extracts. Herbalism is also known as botanical medicine, medical herbalism, herbal medicine, herbology, herblore and phytotherapy. The scope of herbal medicine is sometimes extended to include fungal and bee products, as well as minerals, shells and certain animal parts. Traditional use of medicines is recognized as a

way to learn about potential future medicines. In 2001, researchers identified 122 compounds used in mainstream medicine which were derived from "ethnomedical" plant sources; 80% of these compounds were used in the same or related manner as the traditional ethnomedical use.

Plants have evolved the ability to synthesize chemical compounds that help them defend against attack from a wide variety of predators such as insects, fungi and herbivorous mammals. By chance, some of these compounds, whilst being toxic to plant predators, turn out to have beneficial effects when used to treat human diseases. Such secondary metabolites are highly varied in structure, many are aromatic substances, most of which are phenols or their oxygen-substituted derivatives. At least 12,000 have been isolated so far; a number estimated to be less than 10% of the total. Chemical compounds in plants mediate their effects on the human body by binding to receptor molecules present in the body; such processes are identical to those already well understood for conventional drugs and as such herbal medicines do not differ greatly from conventional drugs in terms of how they work. This enables herbal medicines to be in principle just as effective as conventional medicines but also gives them the same potential to cause harmful side effects. Many of the herbs and spices used by humans to season food yield useful medicinal compounds.

Similarly to prescription drugs, a number of herbs are thought to be likely to cause adverse effects. Furthermore, "adulteration, inappropriate formulation, or lack of understanding of plant and drug interactions have led to adverse reactions that are sometimes life threatening or lethal.

2.1 Biological background

All plants produce chemical compounds as part of their normal metabolic activities. These are divided into primary metabolites, such as sugars and fats, found in all plants, and secondary metabolites, compounds not essential for basic function found in a smaller range of plants, some useful ones found only in a particular genus or species. Pigments harvest light, protect the organism from radiation and display colors to attract pollinators. Many common weeds, such as nettle, dandelion and chickweed, have medicinal properties.

The functions of secondary metabolites are varied. For example, some secondary metabolites are toxins used to deter predation, and others are pheromonesused to attract insects for pollination. Phytoalexins protect against bacterial and fungal attacks. Allelochemicals inhibit rival plants that are competing for soil and light.

Plants upregulate and downregulate their biochemical paths in response to the local mix of herbivores, pollinators and microorganisms. The chemical profile of a single plant may vary over time as it reacts to changing conditions. It is the secondary metabolites and pigments that can have therapeutic actions in humans and which can be refined to produce drugs.

Plants synthesize a bewildering variety of phytochemicals but most are derivatives of a few biochemical motifs.

- Alkaloids contain a ring with nitrogen. Many alkaloids have dramatic effects on the central nervous system. Caffeine is an alkaloid that provides a mild lift but the alkaloids in datura cause severe intoxication and even death.

- polyphenol, also known as phenolics, contain phenol rings. The anthocyanins that give grapes their purple color, the isoflavones, the phytoestrogens from soy and the tannins that give tea its astringency are phenolics.
- Terpenoids are built up from terpene building blocks. Each terpene consists of two paired isoprenes. The names monoterpenes, sesquiterpenes,diterpenes and triterpenes are based on the number of isoprene units. The fragrance of rose and lavender is due to monoterpenes. The carotenoids as terpenoids produce the reds, yellows and oranges of pumpkin, corn and tomatoes.
- Glycosides consist of a glucose moiety attached to an aglycone. The aglycone is a molecule that is bioactive in its free form but inert until the glycoside bond is broken by water or enzymes. This mechanism allows the plant to defer the availability of the molecule to an appropriate time, similar to a safety lock on a gun. An example is the cyanoglycosides in cherry pits that release toxins only when bitten by a herbivore.

The word drug itself comes from the Dutch word "droog" (via the French word Drogue), which means 'dried plant'. Some examples are inulin from the roots of dahlias, quinine from the cinchona, morphine and codeine from the poppy and digoxin from the foxglove.

The active ingredient in willow bark, once prescribed by Hippocrates, is salicin, which is converted in the body into salicylic acid. The discovery of salicylic acid would eventually lead to the development of the acetylated form acetylsalicylic acid, also known as "aspirin", when it was isolated from a plant known as meadowsweet. The word *aspirin* comes from an abbreviation of meadowsweet's Latin genus *Spiraea*, with an additional "A" at the beginning to acknowledge acetylation, and "in" was added at the end for easier pronunciation. "Aspirin" was originally a brand name, and is still a protected trademark in some countries. This medication was patented by Bayer company.

2.2 Popularity

A survey released in May 2004 by the National Center for Complementary and Alternative Medicine focused on who used complementary and alternative medicines (CAM), what was used, and why it was used. The survey was limited to adults, aged 18 years and over during 2002, living in the United States.

According to this survey, herbal therapy, or use of natural products other than vitamins and minerals, was the most commonly used CAM therapy (18.9%) when all use of prayer was excluded.

Herbal remedies are very common in Europe. In Germany, herbal medications are dispensed by apothecaries (e.g., Apotheke). Prescription drugs are sold alongside essential oils, herbal extracts, or herbal teas. Herbal remedies are seen by some as a treatment to be preferred to pure medical compounds which have been industrially produced.

In the United Kingdom, the training of medical herbalists is done by state funded Universities. For example, Bachelor of Science degrees in herbal medicine are offered at Universities such as University of East London, Middlesex University, University of Central Lancashire, University of Westminster, University of Lincoln and Napier University in Edinburgh at the present. Avid public interest in herbalism in the UK has been recently confirmed by the popularity of the topic in mainstream media, such as the prime-time hit

TV series BBC's Grow Your Own Drugs,which demonstrated how to grow and prepare herbal remedies at home.

In the United States, a Bachelor of Science degree in herbal sciences is offered at Bastyr University, and a Master of Science in herbal medicine is offered at Tai Sophia Institute. There are also many smaller organizations and teachers offering certifications.

A 2004 Cochrane Collaboration review found that herbal therapies are supported by strong evidence but are not widely used in all clinical settings.

2.3 Types of herbal medicine systems

Use of medicinal plants can be as informal as, for example, culinary use or consumption of an herbal tea or supplement, although the sale of some herbs considered dangerous is often restricted to the public. Sometimes such herbs are provided to professional herbalists by specialist companies. Many herbalists, both professional and amateur, often grow or "wildcraft" their own herbs.

Some researchers trained in both western and traditional Chinese medicine have attempted to deconstruct ancient medical texts in the light of modern science. One idea is that the yin-yang balance, at least with regard to herbs, corresponds to the pro-oxidant and anti-oxidant balance. This interpretation is supported by several investigations of the ORAC ratings of various yin and yang herbs.

In America, early settlers relied on plants imported from Europe, and also from local Indian knowledge. One particularly successful practitioner, Samuel Thomson developed a hugely popular system of medicine. This approach was subsequently broadened to include concepts introduced from modern physiology, a discipline called Physiomedicalism. Another group, the Eclectics, were a later offshoot from the orthodox medical profession, who were looking to avoid the current medical treatments of mercury and bleeding, and introduced herbal medicine into their practices. Both groups were eventually overcome by the actions of the American Medical Association, which was formed for this purpose. Cherokee medicine tends to divide herbs into foods, medicines and toxins and to use seven plants in the treatment of disease, which is defined with both spiritual and physiological aspects, according to Cherokee herbalist David Winston.

In India, Ayurvedic medicine has quite complex formulas with 30 or more ingredients, including a sizable number of ingredients that have undergone "alchemical processing", chosen to balance "Vata", "Pitta" or "Kapha."

In Tamil Nadu, Tamils have their own medicinal system now popularly called the Siddha medicinal system. The Siddha system is entirely in the Tamil language. It contains roughly 300,000 verses covering diverse aspects of medicine such as anatomy, sex ("kokokam" is the sexual treatise of par excellence), herbal, mineral and metallic compositions to cure many diseases that are relevant even to-day. Ayurveda is in Sanskrit, but Sanskrit was not generally used as a mother tongue and hence its medines are mostly taken from Siddha and other local traditions.

In addition there are more modern theories of herbal combination like William LeSassier's triune formula which combined Pythagorean imagery with Chinese medicine ideas and

resulted in 9 herb formulas which supplemented, drained or neutrally nourished the main organ systems affected and three associated systems. His system has been taught to thousands of influential American herbalists through his own apprenticeship programs during his lifetime, the William LeSassier Archive and the David Winston Center for Herbal Studies. Different chemicals in herbs are more abundant than in a single drug. Some chemicals in herbs may work as growth hormones or antibiotics, nutrients, and toxin neutralizers.

Many traditional African remedies have performed well in initial laboratory tests to ensure they are not toxic and in tests on animals. Gawo, a herb used in traditional treatments, has been tested in rats by researchers from Nigeria's University of Jos and the National Institute for Pharmaceutical Research and Development. According to research in the African Journal of Biotechnology, Gawo passed tests for toxicity and reduced induced fevers, diarrhoea and inflammation.

2.4 Routes of administration

The exact composition of a herbal product is influenced by the method of extraction. A tisane will be rich in polar components because water is a polar solvent. Oil on the other hand is a non-polar solvent and it will absorb non-polar compounds. Alcohol lies somewhere in between. There are many forms in which herbs can be administered, these include:

- Tinctures - Alcoholic extracts of herbs such as Echinacea extract. Usually obtained by combining 100% pure ethanol (or a mixture of 100% ethanol with water) with the herb. A completed tincture has a ethanol percentage of at least 25% (sometimes up to 90%). The term tincture is sometimes applied to preparations using other solvents than ethanol.
- Herbal wine and elixirs - These are alcoholic extract of herbs; usually with an ethanol percentage of 12-38% Herbal wine is a maceration of herbs in wine, while an elixir is a maceration of herbs in spirits (e.g., vodka, grappa, etc.)
- Tisanes - Hot water extracts of herb, such as chamomile.
- Decoctions - Long-term boiled extract of usually roots or bark.
- Macerates - Cold infusion of plants with high mucilage-content as sage, thyme, etc. Plants are chopped and added to cold water. They are then left to stand for 7 to 12 hours (depending on herb used). For most macerates 10 hours is used.
- Vinegars - Prepared at the same way as tinctures, except using a solution of acetic acid as the solvent.
- Whole herb consumption - This can occur in either dried form (herbal powder), or fresh juice, (fresh leaves and other plant parts).
- Syrups - Extracts of herbs made with syrup or honey. Sixty five parts of sugar are mixed with 35 parts of water and herb. The whole is then boiled and macerated for three weeks.
- Extracts - Include liquid extracts, dry extracts and nebulisates. Liquid extracts are liquids with a lower ethanol percentage than tinctures. They can (and are usually) made by vacuum distilling tinctures. Dry extracts are extracts of plant material which are evaporated into a dry mass. They can then be further refined to a capsule or tablet. A nebulisate is a dry extract created by freeze-drying.
- Inhalation as in aromatherapy can be used as a mood changing treatment to fight a sinus infection or cough , or to cleanse the skin on a deeper level (steam rather than direct inhalation here)

Topicals:

- Essential oils - Application of essential oil extracts, usually diluted in a carrier oil (many essential oils can burn the skin or are simply too high dose used straight – diluting in olive oil or another food grade oil such as almond oil can allow these to be used safely as a topical).
- Salves, oils, balms, creams and lotions - Most topical applications are oil extractions of herbs. Taking a food grade oil and soaking herbs in it for anywhere from weeks to months allows certain phytochemicals to be extracted into the oil. This oil can then be made into salves, creams, lotions, or simply used as an oil for topical application. Any massage oils, antibacterial salves and wound healing compounds are made this way.
- Poultices and compresses - One can also make a poultice or compress using whole herb (or the appropriate part of the plant) usually crushed or dried and re-hydrated with a small amount of water and then applied directly in a bandage, cloth or just as is.

2.5 Examples of plants used as medicine

Few herbal remedies have conclusively demonstrated any positive effect on humans, possibly due to inadequate testing. Many of the studies cited refer to animal model investigations or in-vitro assays and therefore cannot provide more than weak supportive evidence.

- Aloe vera has traditionally been used for the healing of burns and wounds. A systematic review (from 1999) states that the efficacy of aloe vera in promoting wound healing is unclear, while a later review (from 2007) concludes that the cumulative evidence supports the use of aloe vera for the healing of first to second degree burns.
- Artichoke (*Cynara cardunculus*) may reduce production cholesterol levels according to *in vitro* studies and a small clinical study.
- Blackberry (*Rubus fruticosus*) leaf has drawn the attention of the cosmetology community because it interferes with the metalloproteinases that contribute to skin wrinkling.
- Black raspberry *(Rubus occidentalis)* may have a role in preventing oral cancer.
- Boophone (*Boophone disticha*) This highly toxic plant has been used in South African traditional medicine for treatment of mental illness. Research demonstrate *in vitro* and *in vivo* effect against depression.
- Butterbur *(Petasites hybridus)*
- Calendula *(Calendula officinalis)* has been used traditionally for abdominal cramps and constipation. In animal research an aqueous-ethanol extract of *Calendula officinalis* flowers was shown to have both spasmolytic and spasmogenic effects, thus providing a scientific rationale for this traditional use. There is "limited evidence" that calendula cream or ointment is effective in treating radiation dermatitis.
- Cannabis, see also medical cannabis.
- Cranberry *(Vaccinium oxycoccos)* may be effective in treating urinary tract infections in women with recurrent symptoms.
- Echinacea (*Echinacea angustifolia, Echinacea pallida, Echinacea purpurea*) extracts may limit the length and severity of rhinovirus colds; however, the appropriate dosage levels, which might be higher than is available over-the-counter, require further research.
- Elderberry (*Sambucus nigra*) may speed the recovery from type A and B influenza. However it is possibly risky in the case of avian influenza because the immunostimulatory effects may aggravate the cytokine cascade.

- Feverfew (*Chrysanthemum parthenium*) is sometimes used to treat migraine headaches. Although many reviews of Feverfew studies show no or unclear efficacy, a more recent RTC showed favorable results Feverfew is not recommended for pregnant women as it may be dangerous to the fetus.
- Gawo (*Faidherbia albida*), a traditional herbal medicine in West Africa, has shown promise in animal tests
- Garlic (*Allium sativum*) may lower total cholesterol levels
- German Chamomile (*Matricaria chamomilla*) has demonstrated antispasmodic, anxiolytic, antiinflammatory and some antimutagenic and cholesterol-lowering effects in animal research. *In vitro* chamomile has demonstrated moderate antimicrobial and antioxidant properties and significant antiplatelet activity, as well as preliminary results against cancer. Essential oil of chamomile was shown to be a promising antiviral agent against herpes simplex virus type 2 (HSV-2) *in vitro*.
- Ginger (*Zingiber officinale*), administered in 250 mg capsules for four days, effectively decreased nausea and vomiting of pregnancy in a human clinical trial.
- Grapefruit (Naringenin) components may prevent obesity.
- Green tea (*Camelia sinensis*) components may inhibit growth of breast cancer cells and may heal scars faster.
- Purified extracts of the seeds of *Hibiscus sabdariffa* may have some antihypertensive, antifungal and antibacterial effect. Toxicity tested low except for an isolated case of damage to the testes of a rat after prolonged and excessive consumption.
- Honey may reduce cholesterol. May be useful in wound healing.
- Lemon grass (*Cymbopogon citratus*), administered daily as an aqueous extract of the fresh leaf, has lowered total cholesterol and fasting plasma glucose levels in rats, as well as increasing HDL cholesterol levels. Lemon grass administration had no effect on triglyceride levels.
- Magnolia
- Marshmallow Root (althaea officinalis L.), a mucilage used for various inflammitory diseases including bronchitis and peptic ulcers.
- Meadowsweet (*Filipendula ulmaria, Spiraea ulmaria*) can be used for a variety of anti-inflammatory and antimicrobial purposes due to presence of salicylic acid. Effective for fevers and inflammations, pain relief, ulcers and bacteriostatic. Listed as therapeutical in 1652 by Nicholas Culpeper. In 1838, salicylic acid was isolated from the plant. The word Aspirin is derived from spirin, based on Meadowsweet's synonym name Spiraea ulmaria.
- Milk thistle (*Silybum marianum*) extracts have been recognized for many centuries as "liver tonics.". Research suggests that milk thistle extracts both prevent and repair damage to the liver from toxic chemicals and medications.
- Morinda citrifolia (noni) is used in the Pacific and Caribbean islands for the treatment of inflammation and pain. Human studies indicate potential cancer preventive effects.
- Nigella sativa (Black cumin) has demonstrated analgesic properties in mice. The mechanism for this effect, however, is unclear. In vitro studies support antibacterial, antifungal, anticancer, anti-inflammatory and immune modulating effects. However few randomized double blind studies have been published.
- Ocimum gratissimum and tea tree oil can be used to treat acne.
- Oregano (*Origanum vulgare*) may be effective against multi-drug resistant bacteria.
- Pawpaw can be used as insecticide (killing lice, worms).

- Peppermint oil may have benefits for individuals with irritable bowel syndrome.
- Phytolacca or Pokeweed can be applied topically or taken internally. Topical treatments have been used for acne and other ailments. It is used as a treatment for tonsilitis, swollen glands and weight loss.
- Pomegranate contains the highest percentage of ellagitannins of any commonly consumed juice. Punicalagin, an ellagitannin unique to pomegranate, is the highest molecular weight polyphenol known. Ellagitannins are metabolized into urolithins by gut flora, and have been shown to inhibit cancer cell growth in mice.
- Rauvolfia Serpentina, high risk of toxicity if improperly used. used extensively in India for sleeplessness, anxiety, and high blood pressure.
- Rooibos (*Aspalathus linearis*) contains a number of phenolic compounds, including flavanols, flavones, flavanones, flavonols, and dihydrochalcones. Rooibos has traditionally been used for skin ailments, allergies, asthma and colic in infants. In an animal study with diabetic mice, aspalathin, a rooibos constituent improved glucose homeostasis by stimulating insulin secretion in pancreatic beta cells and glucose uptake in muscle tissue.
- Rose hips – Small scale studies indicate that hips from *Rosa canina* may provide benefits in the treatment of osteoarthritis. Rose hips show anti COX activity.
- Salvia lavandulaefolia may improve memory
- Saw Palmetto can be used for BPH. Supported in some studies, failed to confirm in others.
- Shiitake mushrooms (*Lentinus edodes*) are edible mushrooms that have been reported to have health benefits, including cancer-preventing properties. In laboratory research a shiitake extract has inhibited the growth of tumor cells through induction of apoptosis. Both a water extract and fresh juice of shiitake have demonstrated antimicrobial activity against pathogenic bacteria and fungi in vitro.
- Soy and other plants that contain phytoestrogens (plant molecules with estrogen activity) (black cohosh probably has serotonin activity) have some benefits for treatment of symptoms resulting frommenopause.
- St. John's wort, has yielded positive results, proving more effective than a placebo for the treatment of mild to moderate depression in some clinical trials. A subsequent, large, controlled trial, however, found St. John's wort to be no better than a placebo in treating depression. However, more recent trials have shown positive results or positive trends that failed significance. A 2004 meta-analysis concluded that the positive results can be explained by publication bias but later analyses have been more favorable. The Cochrane Database cautions that the data on St. John's wort for depression are conflicting and ambiguous.
- Stinging nettle In some clinical studies effective for benign prostatic hyperplasia and the pain associated with osteoarthritis. In-vitro tests show antiinflammatory action. In a rodent model, stinging nettle reduced LDL cholesterol and total cholesterol. In another rodent study it reduced platelet aggregation.
- Umckaloabo (*Pelargonium sidoides*): an extract of this plant showed efficacy in the treatment of acute bronchitis in a controlled trial and is approved for this use in Germany.
- Valerian root can be used to treat insomnia. Clinical studies show mixed results and researchers note that many trials are of poor quality.
- Vanilla

- Willow bark (*Salix alba*) can be used for a variety of anti-inflammatory and antimicrobial purposes due to presence of salicylic acid and tannins. Has been in use for aprox. 6000yrs and was described in the 1st century AD by Dioscorides.

3. Herbals and diabetes

Using herbal remedies and plant derivatives to help in the treatment of diabetes should certainly not be discounted. Although numerous 'miracle herbal cure' companies exist, and champion the ability of herbal compounds to supplement insulin as a treatment, these should not be taken at face value without thorough research and consultation with experts.That is not to say that some of the following herbs do not have properties that some diabetics will find beneficial.The herbs and plant derivatives listed below have been employed traditionally by native people in the treatment of diabetes, in the areas in which they grow. Many suffer from an inadequate knowledge base.Allium sativum is more commonly known as garlic, and is thought to offer antioxidant properties and micro-circulatory effects. Although few studies have directly linked allium with insulin and blood glucose levels, results have been positive.Allium may cause a reduction in blood glucose, increase secretion and slow the degradation of insulin. Limited data is available however, and further trials are needed. Further herbs that have been studied and may have positive effects for diabetic patients include berberine, Cinnamomym tamala, curry, Eugenia jambolana, gingko, Phyllanthus amarus, Pterocarpus marsupium, Solanum torvum, Vinca rosea, Trigonella foenum graecum, Silybum marianum, Opuntia streptacantha (nopal), Ocimum sanctum, Ginseng, Gymnema sylvestre, Coccinia indica, Bauhinia forficate, Myrcia uniflora and Aloe vera.

3.1 Ginger (Zingiber officinale)

3.1.1 Scientific classification

Kingdom: Plantae
Clade: Angiosperms, Monocots, Commelinids
Order: Zingiberales
Family: Zingiberaceae
Genus: Zingiber
Species: Z.officinale
Binominal name: Zingiber officinale

3.1.2 Medical properties and research

The Zingiber officinale plant, common ginger, has medicinal properties. Traditionally used as a digestive aid, ginger also helps fight diabetes, cancer and anxiety. The roots of this plant, sold at grocery stores, can affect the reproductive system as well. A 2010 article in "Food and Chemical Toxicology" looked at the impact of ginger on hormone levels in an animal model of diabetes. Rats were given extracted ginger or no treatment for 65 days. The results indicated that ginger enhanced testosterone levels relative to controls. It also reduced diabetic lesions. No adverse events appeared, but long-term treatment may have a different effect.

Ginger have been claimed to decrease the pain from arthritis, though studies have been inconsistent. It may also have blood thinning and cholesterol lowering properties that may make it useful for treating heart disease.

Preliminary research also indicates that nine compounds found in ginger may bind to human serotonin receptors, possibly helping to affect anxiety.

Advanced glycation end-products are possibly associated in the development of several pathophysiologies, including diabetic cataract for which ginger was effective in preliminary studies, apparently by acting through antiglycating mechanisms.

Ginger compounds are active against a form of diarrhea which is the leading cause of infant death in developing countries. Zingerone is likely to be the active constituent against enterotoxigenic *Escherichia coli* heat-labile enterotoxin-induced diarrhea.

Ginger has been found effective in multiple studies for treating nausea caused by seasickness, morning sickness and chemotherapy, though ginger was not found superior over a placebo for pre-emptively treating post-operative nausea. Ginger is a safe remedy for nausea relief during pregnancy. The television program *Mythbusters* performed an experiment using one of their staff who suffered from severe motion sickness. The staff member was placed in a moving device which, without treatment, produced severe nausea. Multiple treatments were administered. None, with the exception of the ginger and the two most common drugs, were successful. The staff member preferred the ginger due to lack of side effects. Several studies over the last 20 years were inconclusive with some studies in favor of the herb and some not.

3.1.3 Folk medicine

The traditional medical form of ginger historically was called *Jamaica ginger*; it was classified as a stimulant and carminative and used frequently fordyspepsia, gastroparesis, slow motility symptoms, constipation, and colic. It was also frequently employed to disguise the taste of medicines.

Tea brewed from ginger is a common folk remedy for colds. Ginger ale and ginger beer are also drunk as *stomach settlers* in countries where the beverages are made.

- In Burma, ginger and a local sweetener made from palm tree juice (*htan nyat*) are boiled together and taken to prevent the flu.
- In China, ginger is included in several traditional preparations. A drink made with sliced ginger cooked in water with brown sugar or a cola is used as a folk medicine for the common cold."Ginger eggs" (scrambled eggs with finely diced ginger root) is a

common home remedy for coughing. The Chinese also make a kind of dried ginger candy that is fermented in plum juice and sugared, which is also commonly consumed to suppress coughing. Ginger has also been historically used to treat inflammation, which several scientific studies support, though one arthritis trial showed ginger to be no better than a placebo or ibuprofen for treatment of osteoarthritis.

- In Congo, ginger is crushed and mixed with mango tree sap to make tangawisi juice, which is considered a panacea.
- In India, ginger is applied as a paste to the temples to relieve headache, and consumed when suffering from the common cold. Ginger with lemon and black salt is also used for nausea.
- In Indonesia, ginger (*jahe* in Indonesian) is used as a herbal preparation to reduce fatigue, reducing "winds" in the blood, prevent and cure rheumatism and control poor dietary habits.
- In Nepal, ginger is called *aduwa*, अदुवा and is widely grown and used throughout the country as a spice for vegetables, used medically to treat cold and also sometimes used to flavor tea.
- In the Philippines, ginger is known as *luya* and is used as a throat lozenge in traditional medicine to relieve sore throat. It is also brewed into a tea known as *salabat*.
- In the United States, ginger is used to prevent motion and morning sickness. It is recognized as safe by the Food and Drug Administration and is sold as an unregulated dietary supplement. Ginger water was also used to avoid heat cramps in the United States.
- In Peru, ginger is sliced in hot water as an infusion for stomach aches as *infusión de Kión*.

3.2 Onion (Alluim Cepa)

3.2.1 Scientific classification

Kingdom: Plantae
Clade: Angiosperms, Monocots
Order: Asparagales
Family: Amaryllidaceae
Subfamily: Allioideae
Genus: Allium
Species: A.cepa
Binominal name: Allium cepa

The onion (*Allium cepa*), also known as the bulb onion, common onion and garden onion, is the most widely cultivated species of the genus *Allium.* The genus *Allium* also contains a number of other species variously referred to as onions and cultivated for food, such as the Japanese bunching onion (*A. fistulosum*), Egyptian onion (A. *proliferum*), and Canada onion (*A. canadense*). The name "wild onion" is applied to a number of *Allium*species.

The vast majority of cultivars of *A. cepa* belong to the 'common onion group' (*A. cepa* var. *cepa*) and are usually referred to simply as 'onions'. The 'Aggregatum group' of cultivars (*A. cepa* var. *aggregatum*) includes both shallots and potato onions.

Allium cepa is known only in cultivation, but related wild species occur in Central Asia. The most closely related species include *Allium vavilovii* (Popov & Vved.) and *Allium asarense*

(R.M. Fritsch & Matin) from Iran. However, Zohary and Hopf warn that "there are doubts whether the *A. vavilovii* collections tested represent genuine wild material or only feral derivatives of the crop.

3.3 Possible medicinal properties and health effects of onion

Wide-ranging claims have been made for the effectiveness of onions against conditions ranging from the common cold to heart disease, diabetes,osteoporosis, and other diseases. They contain chemical compounds believed to have anti-inflammatory, anticholesterol, anticancer, and antioxidantproperties, such as quercetin. Preliminary studies have shown increased consumption of onions reduces the risk of head and neck cancers.

Raw Onions	
Nutritional value per 100 g (3.5 oz)	
Energy	166 kJ (40 kcal)
Carbohydrates	9.34 g
Sugars	4.24 g
Dietary fiber	1.7 g
Fat	0.1 g
saturated	0.042 g
monounsaturated	0.013 g
polyunsaturated	0.017 g
Protein	1.1 g
Water	89.11 g
Vitamin A equiv.	0 µg (0%)
Thiamine (Vit. B_1)	0.046 mg (4%)
Riboflavin (Vit. B_2)	0.027 mg (2%)
Niacin (Vit. B_3)	0.116 mg (1%)
Vitamin B_6	0.12 mg (9%)
Folate (Vit. B_9)	19 µg (5%)
Vitamin B_{12}	0 µg (0%)
Vitamin C	7.4 mg (9%)
Vitamin E	0.02 mg (0%)
Vitamin K	0.4 µg (0%)
Calcium	23 mg (2%)
Iron	0.21 mg (2%)
Magnesium	0.129 mg (0%)
Phosphorus	29 mg (4%)
Potassium	146 mg (3%)
Sodium	4 mg (0%)
Zinc	0.17 mg (2%)
Percentages are relative to US recommendationsfor adults. Source: USDA Nutrient database	

Table 1. Possible medicinal properties of onions

Among all varieties, Asian white onions have the most eye irritating chemical reaction. Regular use of white onion, if eaten raw, is good for male sexual power due to its antioxidant and anti-inflammatory properties.

In India some sects do not eat onions as they believe them to be an aphrodisiac; various schools of Buddhism also advise against eating onions and other vegetables of the Allium family.

In many parts of the undeveloped world, onions are used to heal blisters and boils. A traditional Maltese remedy for sea urchin wounds is to tie half a baked onion to the afflicted area overnight. A similar traditional cure is known in Bulgaria. Half-baked onion with sugar is placed over the finger and fingernail in case of inflammation.

An application of raw onion is also said to be helpful in reducing swelling from bee stings. In the United States, products that contain onion extract are used in the treatment of topical scars; some studies have found their action to be ineffective, while others found that they may act as an anti-inflammatory or bacteriostatic and can improve collagen organization in rabbits

Onions may be beneficial for women, who are at increased risk for osteoporosis as they go through menopause, by destroying osteoclasts so they do not break down bone.

An American chemist has stated the pleiomeric chemicals in onions have the potential to alleviate or prevent sore throat. Onion in combination withjaggery has been widely used as a traditional household remedy for sore throat in India.

Shallots have the most phenols, six times the amount found in Vidalia onion, the variety with the lowest phenolic content. Shallots also have the mostantioxidant activity, followed by Western Yellow, pungent yellow (New York Bold), Northern Red, Mexico, Empire Sweet, Western White, Peruvian Sweet, Texas 1015, Imperial Valley Sweet, and Vidalia. Western Yellow onions have the most flavonoids, eleven times the amount found in Western White, the variety with the lowest flavonoid content.

The Allium cepa plant also affects the reproductive system. Bulbs from this plant, onions, are used as a vegetable and as a condiment. Yet, onions may treat erectile dysfunction as well. The underlying cause of these benefits remains unclear, but it could involve sex steroids. In a 2009 study conducted by Arash Khaki and colleagues that was published in the journal of "Folia Morphologica," researchers evaluated the impact of onion on sperm production in subjects. They discovered that animals consuming fresh onion juice for three weeks experienced significant improvements in testosterone production compared to the control groups. Scientists suggest that onion boosts testosterone levels by increasing the output of luteinizing hormone, which signals to the testes to stimulate testosterone production. Our previous study since 2005 up to 2011 showed onion and Ginger can regulate nephropathy disorders by their anti-oxidant capacity.

For all varieties of onions, the more phenols and flavonoids they contain, the more reputed antioxidant and anticancer activity they provide. When tested against liver and colon cancer cells in laboratory studies, 'Western Yellow', pungent yellow (New York Bold) and shallots were most effective in inhibiting their growth. The milder-tasting cultivars (i.e., 'Western White,' 'Peruvian Sweet,' 'Empire Sweet,' 'Mexico,' 'Texas 1015,' 'Imperial Valley Sweet' and 'Vidalia') showed little cancer-fighting ability.

Shallots and ten other onion (*Allium cepa* L.) varieties commonly available in the United States were evaluated: Western Yellow, Northern Red, pungent yellow (New York Bold), Western White, Peruvian Sweet, Empire Sweet, Mexico, Texas 1015, Imperial Valley Sweet, and Vidalia. In general, the most pungent onions delivered many times the effects of their milder cousins.

The 3-mercapto-2-methylpentan-1-ol in onion was found to inhibit peroxynitrite-induced mechanisms *in vitro*.

While members of the onion family appear to have medicinal properties for humans, they can be deadly for dogs and cats.

4. Syzygium jambolanum

4.1 Scientific classification:

Kingdom: Plantae
Order: Myrtales
Family: Myrtaceae
Genus: Syzygium
Species: S.cumini
Binominal name: Syzygium cumini
Synonyms: Eugenia cumini(L.) Druce
Eugenia jambolana Lam.
Syzygium jambolanum DC.

Syzygium jambolanum (Lam.) DC (henceforth to be denoted as SJ) tree belongs to Myrtaceae family and consists of about 90 genera and 2800 species, commonly called Jamun, Jambol fruit in India and Rose apple in English. Jambol is also known as jambu/jambula/jamboola, Javaplum, jamun, jaam/kalojaam, jamblang, jambolan, black plum , Damson plum , Duhat plum , Jambolan plum or Portuguese plum. Malabar plum may also refer to other species of Syzygium. In Tamil, this fruit is called Naaval Pazham or Navva Pazham.

It is a large, evergreen tree found primarily in India, Pakistan, Southern Asia and Brazil. The leaves and bark are used for controlling blood pressure and gingivitis. It has a high source in vitamin A and vitamin C. The powdered seeds of Syzygium Jambolanum are a well known Indian folk medicine for treatment of diabetes mellitus. They also have anti-bacterial and anti-inflammatory activities.

Syzygium jambolanum seeds are used by the village people to treat illnesses caused by bacterial, fungal and viral pathogens. The seed extract of Syzygium jambolanum is used to treat cold, cough, fever and skin problems such as rashes and the mouth, throat, intestines and genitourinary tract ulcers (infected by Candida albicans).

The chemical composition of the seed extract has only been recently reported by a lone study to contain glycoside (jamboline), tannin, ellagic acid and gallic acid as principal ingredients. The seeds are sweet, astringent to the bowels and good for diabetes. It also stops urinary discharges.

In recent years, in view of toxic side-effects of most of the modern medicines, there is a growing popularity of scientifically validated natural products as alternative medicines. Though ethanolic extract of SJ (EESJ) has long been used as a good anti-diabetic drug in various traditional and folk medicines (Samadder et al, 2011).

Achrekar et al in 1991 have described that the seeds or fruit of this tree, in which various methods were used to prepare the medicine and administer it to normal and diabetic animals, the following effects were observed: reduction of glycaemia and glycosuria, anti-oxidant activity and partial restoration of altered liver and skeletal muscle glycogen content and liver glucokinase, hexokinase, glucose-6-phosphate and phosphofructokinase levels. In India, it has been used, in a mix with honey or milk, to treat diabetes and digestive diseases and the fresh fruits has been taken orally to treat stomachache.

4.2 Nutrients and phytochemicals

Java Plum, raw	
Nutritional value per 100 g (3.5 oz)	
Energy	251 kJ (60 kcal)
Carbohydrates	15.56 g
Fat	0.23 g
Protein	0.72 g
Water	83.13 g
Vitamin A	3 IU
Thiamine (Vit. B_1)	0.006 mg (1%)
Riboflavin (Vit. B_2)	0.012 mg (1%)
Niacin (Vit. B_3)	0.260 mg (2%)
Pantothenic acid (B_5)	0.160 mg (3%)
Vitamin B_6	0.038 mg (3%)
Vitamin C	14.3 mg (17%)
Calcium	19 mg (2%)
Iron	0.19 mg (1%)
Magnesium	15 mg (4%)
Phosphorus	17 mg (2%)
Potassium	79 mg (2%)
Sodium	14 mg (1%)
Percentages are relative to US recommendationsfor adults. Source: USDA Nutrient database	

Table 2. Some nutrients of Java Plum

The leaf composition is shown in the tables below.

Java Plum Leaf	
Compound	**Percent**
Crude Protein	9.1
Fat	4.3
Crude Fiber	17.0
Ash	6.0
Calcium	1.3
Phosphorus	0.19

Table 3. The leaf composition of Java Plum

5. Antioxidants

An antioxidant is a molecule capable of inhibiting the oxidation of other molecules. Oxidation is a chemical reaction that transfers electrons or hydrogen from a substance to an oxidizing agent. Oxidation reactions can produce free radicals. In turn, these radicals can start chain reactions. When the chain reaction occurs in a cell, it can cause damage or death to the cell. When the chain reaction occurs in a purified monomer, it produces a polymer resin, such as a plastic, a synthetic fiber, or an oil paint film. Antioxidants terminate these chain reactions by removing free radical intermediates, and inhibit other oxidation reactions. They do this by being oxidized themselves, so antioxidants are often reducing agents such as thiols, ascorbic acid, or polyphenols.

Antioxidants are important additives in gasoline. These antioxidants prevent the formation of gums that interfere with the operation of internal combustion engines. Although oxidation reactions are crucial for life, they can also be damaging; hence, plants and animals maintain complex systems of multiple types of antioxidants, such as glutathione, vitamin C, and vitamin E as well as enzymes such as catalase, superoxide dismutase and various peroxidases. Low levels of antioxidants, or inhibition of the antioxidant enzymes, cause oxidative stress and may damage or kill cells.

As oxidative stress appears to be an important part of many human diseases, the use of antioxidants in pharmacology is intensively studied, particularly as treatments for stroke and neurodegenerative diseases. However, it is unknown whether oxidative stress is the cause or the consequence of disease.

Antioxidants are widely used as ingredients in dietary supplements and have been investigated for the prevention of diseases such as cancer, coronary heart disease and even altitude sickness. Although initial studies suggested that antioxidant supplements might promote health, later large clinical trials did not detect any benefit and suggested instead that excess supplementation is harmful. (Concerning the previous studies cited the first only shows that antioxidant supplements were not effective in helping against "mountain sickness", and in the second study showed that the supplements beta carotene, vitamin A ,

and vitamin E, "singly or combined, significantly increased mortality." Though it says that "Most trials investigated the effects of supplements administered at higher doses than those commonly found in a balanced diet" whereas it says "Vitamin C and selenium had no significant effect on mortality.") In addition to these uses of natural antioxidants in medicine, these compounds have many industrial uses, such as preservatives in food and cosmetics and preventing the degradation of rubber and gasoline.

6. Measurement and levels of antioxidants in food

Measurement of antioxidants is not a straightforward process, as this is a diverse group of compounds with different reactivities to different reactive oxygen species. In food science, the oxygen radical absorbance capacity (ORAC) has become the current industry standard for assessing antioxidant strength of whole foods, juices and food additives. Other measurement tests include the Folin-Ciocalteu reagent, and the Trolox equivalent antioxidant capacity assay.

Antioxidants are found in varying amounts in foods such as vegetables, fruits, grain cereals, eggs, meat, legumes and nuts. Some antioxidants such as lycopene and ascorbic acid can be destroyed by long-term storage or prolonged cooking. Other antioxidant compounds are more stable, such as the polyphenolic antioxidants in foods such as whole-wheat cereals and tea. The effects of cooking and food processing are complex, as these processes can also increase the bioavailability of antioxidants, such as some carotenoids in vegetables. In general, processed foods contain fewer antioxidants than fresh and uncooked foods, since the preparation processes may expose the food to oxygen.

Antioxidant compounds	**Foods containing high levels of these antioxidants**
Vitamin C (ascorbic acid)	Fresh Fruits and vegetables
Vitamin E (tocopherols, tocotrienols)	Vegetable oils
Polyphenolic antioxidants (resveratrol, flavonoids)	Tea, coffee, soy, fruit, olive oil, chocolate, cinnamon, oregano and red wine
Carotenoids (lycopene, carotenes, lutein)	Fruit, vegetables and eggs.

Table 4. Antioxidant compounds of some food

Other antioxidants are not vitamins and are instead made in the body. For example, ubiquinol (coenzyme Q) is poorly absorbed from the gut and is made in humans through the mevalonate pathway. Another example is glutathione, which is made from amino acids. As any glutathione in the gut is broken down to free cysteine, glycine and glutamic acid before being absorbed, even large oral doses have little effect on the concentration of glutathione in the body. Although large amounts of sulfur-containing amino acids such as acetylcysteine can increase glutathione, no evidence exists that eating high levels of these glutathione precursors is beneficial for healthy adults. Supplying more of these precursors may be useful as part of the treatment of some diseases, such as acute respiratory distress syndrome, protein-energy malnutrition, or preventing the liver damage produced by paracetamol overdose.

Other compounds in the diet can alter the levels of antioxidants by acting as pro-oxidants. Here, consuming the compound causes oxidative stress, which the body responds to by inducing higher levels of antioxidant defenses such as antioxidant enzymes. Some of these compounds, such as isothiocyanates and curcumin, may be chemopreventive agents that either block the transformation of abnormal cells into cancerous cells, or even kill existing cancer cells.

7. Health effects of antioxidants

7.1 Disease treatment

The brain is uniquely vulnerable to oxidative injury, due to its high metabolic rate and elevated levels of polyunsaturated lipids, the target of lipid peroxidation. Consequently, antioxidants are commonly used as medications to treat various forms of brain injury. Here, superoxide dismutase mimetics, sodium thiopental and propofol are used to treat reperfusion injury and traumatic brain injury, while the experimental drug NXY-059 and ebselen are being applied in the treatment of stroke. These compounds appear to prevent oxidative stress in neurons and preventapoptosis and neurological damage. Antioxidants are also being investigated as possible treatments for neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis, and as a way to prevent noise-induced hearing loss. Targeted antioxidants may lead to better medicinal effects. Mitochondria-targeted ubiquinone, for example, may prevent damage to the liver caused by excessive alcohol.

7.2 Disease prevention

People who eat fruits and vegetables have a lower risk of heart disease and some neurological diseases, and there is evidence that some types of vegetables, and fruits in general, protect against some cancers. Since fruits and vegetables happen to be good sources of antioxidants, this suggested that antioxidants might prevent some types of diseases. This idea has been tested in clinical trials and does not seem to be true, as antioxidant supplements have no clear effect on the risk of chronic diseases such as cancer and heart disease. This suggests that these health benefits come from other substances in fruits and vegetables (possibly flavonoids), or come from a complex mix of substances.

It is thought that oxidation of low density lipoprotein in the blood contributes to heart disease, and initial observational studies found that people taking Vitamin E supplements had a lower risk of developing heart disease. Consequently, at least seven large clinical trials were conducted to test the effects of antioxidant supplement with Vitamin E, in doses ranging from 50 to 600 mg per day. None of these trials found a statistically significant effect of Vitamin E on overall number of deaths or on deaths due to heart disease. Further studies have also been negative. It is not clear if the doses used in these trials or in most dietary supplements are capable of producing any significant decrease in oxidative stress. Overall, despite the clear role of oxidative stress in cardiovascular disease, controlled studies using antioxidant vitamins have observed no reduction in either the risk of developing heart disease, or the rate of progression of existing disease.

While several trials have investigated supplements with high doses of antioxidants, the "Supplémentation en Vitamines et Mineraux Antioxydants" (SU.VI.MAX) study tested the

effect of supplementation with doses comparable to those in a healthy diet. Over 12,500 French men and women took either low-dose antioxidants (120 mg of ascorbic acid, 30 mg of vitamin E, 6 mg of beta carotene, 100 µg of selenium, and 20 mg of zinc) or placebo pills for an average of 7.5 years. The study concluded that low-dose antioxidant supplementation lowered total cancer incidence and all-cause mortality in men but not in women. Supplementation may be effective in men only because of their lower baseline status of certain antioxidants, especially of beta carotene.

Many nutraceutical and health food companies sell formulations of antioxidants as dietary supplements and these are widely used in industrialized countries. These supplements may include specific antioxidant chemicals, like the polyphenol, resveratrol (from grape seeds or knotweed roots), combinations of antioxidants, like the "ACES" products that contain beta carotene (provitaminA), vitamin C, vitamin E and Selenium, or herbs that contain antioxidants - such as green tea and jiaogulan. Although some levels of antioxidant vitamins and minerals in the diet are required for good health, there is considerable doubt as to whether these antioxidant supplements are beneficial or harmful, and if they are actually beneficial, which antioxidant(s) are needed and in what amounts. Indeed, some authors argue that the hypothesis that antioxidants could prevent chronic diseases has now been disproved and that the idea was misguided from the beginning. Rather, dietary polyphenols may have non-antioxidant roles in minute concentrations that affect cell-to-cell signaling, receptor sensitivity, inflammatory enzyme activity or gene regulation.

For overall life expectancy, it has even been suggested that moderate levels of oxidative stress may increase lifespan in the worm Caenorhabditis elegans, by inducing a protective response to increased levels of reactive oxygen species. The suggestion that increased life expectancy comes from increased oxidative stress conflicts with results seen in the yeast Saccharomyces cerevisiae, and the situation in mammals is even less clear. Nevertheless, antioxidant supplements do not appear to increase life expectancy in humans.

7.3 Adverse effects

Relatively strong reducing acids can have antinutrient effects by binding to dietary minerals such as iron and zinc in the gastrointestinal tract and preventing them from being absorbed. Notable examples are oxalic acid, tannins and phytic acid, which are high in plant-based diets. Calcium and iron deficiencies are not uncommon in diets in developing countries where less meat is eaten and there is high consumption of phytic acid from beans and unleavened whole grain bread.

Foods	**Reducing acid present**
Cocoa bean and chocolate, spinach, turnip and rhubarb.	Oxalic acid
Whole grains, maize, legumes.	Phytic acid
Tea, beans, cabbage.	Tannins

Table 5. Some acid reducing foods

Nonpolar antioxidants such as eugenol—a major component of oil of cloves—have toxicity limits that can be exceeded with the misuse of undiluted essential oils. Toxicity associated with high doses of water-soluble antioxidants such as ascorbic acid are less of a concern, as these compounds can be excreted rapidly in urine. More seriously, very high doses of some antioxidants may have harmful long-term effects. The beta-Carotene and Retinol Efficacy Trial (CARET) study of lung cancer patients found that smokers given supplements containing beta-carotene and vitamin A had increased rates of lung cancer. Subsequent studies confirmed these adverse effects.

These harmful effects may also be seen in non-smokers, as a recent meta-analysis including data from approximately 230,000 patients showed that β-carotene, vitamin A or vitamin E supplementation is associated with increased mortality but saw no significant effect from vitamin C. No health risk was seen when all the randomized controlled studies were examined together, but an increase in mortality was detected only when the high-quality and low-bias risk trials were examined separately. However, as the majority of these low-bias trials dealt with either elderly people, or people already suffering disease, these results may not apply to the general population. This meta-analysis was later repeated and extended by the same authors, with the new analysis published by the Cochrane Collaboration; confirming the previous results. These two publications are consistent with some previous meta-analyzes that also suggested that Vitamin E supplementation increased mortality, and that antioxidant supplements increased the risk of colon cancer. However, the results of this meta-analysis are inconsistent with other studies such as the SU.VI.MAX trial, which suggested that antioxidants have no effect on cause-all mortality. Overall, the large number of clinical trials carried out on antioxidant supplements suggest that either these products have no effect on health, or that they cause a small increase in mortality in elderly or vulnerable populations.

While antioxidant supplementation is widely used in attempts to prevent the development of cancer, it has been proposed that antioxidants may, paradoxically, interfere with cancer treatments. This was thought to occur since the environment of cancer cells causes high levels of oxidative stress, making these cells more susceptible to the further oxidative stress induced by treatments. As a result, by reducing the redox stress in cancer cells, antioxidant supplements could decrease the effectiveness of radiotherapy and chemotherapy. On the other hand, other reviews have suggested that antioxidants could reduce side effects or increase survival times.

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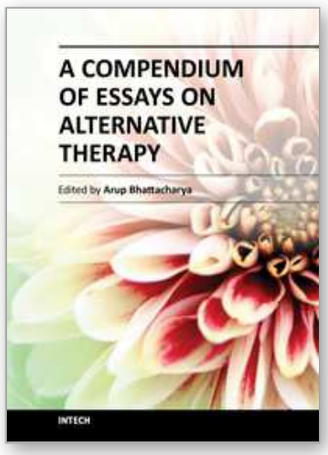

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A Compendium of Essays on Alternative Therapy is aimed at both conventional and alternate therapy practitioners, besides serving as an educational tool for students and lay persons on the progress made in the field. While this resource is not all-inclusive, it does reflect the current theories from different international experts in the field. This will hopefully stimulate more research initiatives, funding, and critical insight in the already increasing demand for alternate therapies that has been evidenced worldwide.

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