# LFT – Lifetime


Photo Courtesy of APLGO, LLC 2024

Mary Esther Gilbert, MSc HN, BSc NSP ©2024

## Product Ingredients

Black Pepper (Fruit) (*Piper nigrum*)
Japanese Knotweed (Root) (*Reynoutria japonica*)
Milk Thistle (Seeds) (*Silybum marianum*)
Pomegranate (Fruit) (*Punica granatum*)
Red Grape (Fruit) (*Vitis vinifera*)
Rosemary (Leaf) (*Vitis vinifera*)
Siberian Larch (Bark) (*Larix sibirica*)
Spirulina (*Arthros[ora platensis*)
Turmeric (Root) (*Curcuma longa*)
Molasses
Sugar
Citric Acid
Natural Mango Flavor
Curcumin Natural Coloring

## Black Pepper *(Piper nigrum)*

H. Zell - Wikimedia Commons 2009

K Hari Krishnan
Wikimedia Commons 2012

- Pepper has been increasingly studied for its potential for improving a diverse amount of metabolic malfunctions.
- *Piper nigrum* contains a bioactive pungent alkaloid isomer, piperine, found to improve blood lipids by lowering cholesterol levels, including low-density lipoprotein cholesterol (LDL), and triglycerides in overweight and obese individuals—while increasing blood levels of high-density lipoprotein (HDL).
- In research studies on those with metabolic syndrome, it was shown that intake of piperine had antioxidant and anti-inflammatory properties through increased serum levels of the body's antioxidant production of superoxide dismutase (SOD), while reducing cell-damaging free radical reactions of malonaldehyde and C-reactive proteins.

- Further clinical evidence shows pepper improves chronic conditions such as osteoarthritis, oropharyngeal dysphagia (difficulty swallowing), neuromuscular fatigue, digestive disruptions, and in hemodialysis.
- In preclinical trials, piperine and another bioactive compound, capsaicin, together displayed antimicrobial, gastro-protective, and antidepressant properties.
- Other bioactive compounds in pepper include cis–trans isomer (isopiperine), cis–cis isomer (chavicine), and trans–cis isomer (isochevicine) as well as other alkaloids piperanine, piperettine, piperolein, piperylin, and pipericine.
- The biochemical compounds in pepper are utilized in detoxification processes within the liver , and improving brain efficacy, especially when combined with the compound in turmeric, curcumin.
- Piperine has been found to improve the digestive system functions while reducing oxidative stress and inflammatory responses, including reducing arthritis, hepatic steatosis (excess fat storage in the liver), type 2 diabetes, and obesity.
- Piperine has been shown to improve cell functions by modulating or inhibiting inflammatory signaling pathways of the nervous system's response to stress (such as those of protein-kinase-activated NLR family pyrin domain containing-3 inflammasome, nuclear factor-κB, Jun *N*-terminal kinase/p38 mitogen-activated protein kinase).
- Piperine in pepper is known to ameliorate the toxic effects of oxidative stress through the activation of inflammation-blocking bioactions of nuclear factor erythroid 2-related factor 2, peroxisome proliferator-activated receptor-gamma, cyclooxygenase-2, and nitric oxide synthases-2.
- In an 8-week study, subjects were administered piperine with turmeric's curcuminoids, which improved oxidative and inflammatory conditions by increasing the production of the body's antioxidant superoxide dismutase (SOD), which reduced inflammatory malonaldehyde (MDA)and C-reactive protein in those with metabolic syndrome (health conditions associated with obesity).
- Predominant symptoms that perpetuate metabolic syndrome are due to damaging free radicals of lipid peroxidation and the presence of malonaldehyde; studies found that a three-month application of piperine, resveratrol (from grapes) and alpha tocopherol (vitamin E) effectively reduced levels of ferritin and C-reactive protein.
- Pepper's active compound capsaicin was administered to individuals, and in 2 hours, was shown to reduce plasma glucose levels and maintain normal insulin levels in those who underwent glucose tolerance tests.
- Pepper's nutrient-dense phytochemistry includes active essential oils, oleoresins, and various alkaloids proved to have protective effects against the toxic impact of oxidative stress and inflammation in the body (Dludla et. al., 2023).
- Pepper's constituents contain essential oils found to contain antimicrobial, anti-mutagenic, cell-protective attributes that also effectively scavenge free radicals, improve breathing and the swallowing reflex.
- Pepper's oleoresins, phenolics, and alkaloids piperine and chavicine aid in efficient digestion and absorption of dietary nutrients, aid immune cells in destroying invading, illness-causing microorganisms, and are anti-cancer agents.
- Pepper's constituents have been found to inhibit the proliferation, invasion, migration, and metastasis of cancer cells through damaging their DNA and inducing apoptosis (self-imposed cancer cell death).

- Research has found that pepper's and other spices' anticancer actions against breast and prostate cancer are linked to hormone regulatory processes of hormone receptor sites such as estrogen and androgen receptors.
- The piperine alkaloid in pepper is known to kill malignant growth cells.
- Black pepper has anti-atherosclerotic actions by improving the digestion and regulation of lipids or fats , and the inhibition of the free radical ROS or reactive oxygen species production.
- Due to the high content of alkaloids, *Piper nigrum* has shown to have strong antiviral properties; pepper's bioactive piperdardine and piperanine are found to be highly effective antiviral compounds.
- Piperine studies show it prevents memory impairment, and prevents epilepsy by elevating the cortical and hippocampal serotonin, norepinephrine, and GABA levels,
- Piperine has been found to enhance intellectual development by inhibiting AChE and secretase proteins, and is thought to pass through the blood brain barrier; has been found to help increase perception while lowering oxidative effects on the brain's hippocampus.
- Piperine has been shown to help improve learning and memory insufficiencies caused by aluminum chloride, a health-hazardous substance that leads to nerve degeneration associated with Alzheimer's and Parkinson's disease.
- Black pepper is an effective antibacterial against *Staphylococcus aureus* and other microbials, and fungicidal against Fusarium oxysporum.
- Black pepper as a supplement is marketed as a bioavailability nutrient enhancer; its piperine and piperopiperidine compounds are thermonutrients known to invigorate thermogenic activity or induce the production of heat in small intestinal epithelial cells and therefore improve nutrient absorption.
- Researchers found that after ingestion of piperine, intestines viewed via electron scanning microscopy revealed an increase in size of intestinal microvilli, thereby improving the intestinal mucosa epithelia's layer's permeability or capacity for nutrient and fluids absorption (Singh, 2021).

## Japanese Knotweed (Root) (*Reynoutria japonica*)

W. Carter – Wikipedia 2019

Bibliothèque de l'Université Laval
Creative Commons Wikipedia 2023


Ohio State University Weed Lab
Creative Commons 2018

- Contains a high concentration of the phytonutrients resveratrol and glycosides.
- Japanese Knotweed root has been used for respiratory tract infections (RTIs).
- *Reynoutria japonica* is traditionally known as clearing heat in the body, improving blood and Qi circulation, clearing phlegm, and relieving cough.

- Peer-reviewed studies showed *R. japonica's* symptom improvement rate and fever reduction time in all age groups, and showed to have antiallergic, antimutagenic, antioxidant, antibacterial, and antiviral effects (Wang, et. al., 2022).
- *Reynoutria japonica* is native to China, Japan, Taiwan, North and South Korea, and North America.
- The rhizomes (underground shoots) are found to contain a great variety of phytochemicals:
    - Anthraquinones: emodin, citreorosein, fallacinol, physcion.
    - Flavonoids: rutin, apigenin, quercetin, quercitrin, isoquercetrin, hyperoside, reynoutrin, and kaempferol.
    - Stilbenes: resveratrol, emodin, and polydatin.
    - Coumarins, lignans, essential oils.
    - Polyphenols.
    - The most studied compounds are resveratrol, piceid, polydatin, emodin, and physcion for their antioxidant, antimicrobial, anti-inflammatory, neuroprotective, antidiabetic, and anticancer actions (Cucu, 2021).
- In dental gingiva, *R. japonica* was found to be an effective bacteriostatic and was bactericidal against the bacteria *S. mutans, S. salivarius, S. sanguinis,* and *S. pyogenes*, when tested against human fibroblasts (cells that form the connective tissue of the upper and lower jaw that surrounds the teeth), due to the high content of stilbene aglycons and anthraquinone aglycons in the plant's extract.
- *R. japonica* extract protected human fibroblasts against the cytotoxicity (cell damage) of those pathogens (especially *S. mutans*) that lead to dental caries; it therefore is a likely candidate as a natural antimicrobial for controlling dental caries (Nawrot-Hadzik, et. al., 2019).
- Studies indicate the presence of alkaloids, sterol terpenes, tannins, and flavonoid phytochemicals in *R. japonica* effectively destroy the plaque and dental caries-causing bacteria *S. mutans* and *S. sobrinus*.
- Synonymous with *R. japonica* is the name *Polygonum cuspidatum*; both names refer to the Japanese knotweed, which is used for menoxenia (abnormal menstruation), skin burn, gallstones, hepatitis, osteomyelitis (infection affecting the bone marrow), and other inflammatory conditions.
- Research findings include this plant contains a large number of flavonoid glucosides, phenyl alcohols, sterols, essential oils, and amino acids (Song, et. al., 2006).
- Further studies on the Japanese knotweed show its plant compounds to have cancer antiproliferative properties, as well as its established anti-inflammatory, antiatherosclerotic, antibacterial, antiviral actions.
- *R. japonica* antioxidant activity includes preventing the cellular damage by free radicals and highly oxidating singlet oxygen, aiding in metal chelation for detoxification, inflammatory enzyme inhibition, reducing agents (electron donors), and hydrogen donors for achieving an acid/base balance.
- The concentrated amounts of epicatechin compounds in the rhizomes of this botanical are considered to be very potent and stable antioxidants (Jug, 2021).

## Milk Thistle (Seed) (*Silybum marianum*)

Zaca Blog 2024

Tony Hisgett - Birmingham UK Wikimedia 2011

Fir0002 Wikimedia 2005

- Primary activities are antioxidant and hepatoprotective (protects the liver).
- Contain phytonutrient antioxidants: apigenin, betaine, flavonolignans, silybonol.
- In India, silymarin is used to treat various forms of liver diseases, including degenerative necrosis (liver cell death), alcoholic cirrhosis (scarring in the liver), and viral hepatitis (liver inflammation due to a virus).
- Improves liver enzyme levels and serum bilirubin.
- Restores liver back to normal functioning by stimulating liver tissue regeneration through increased production of proteins in the liver.
- Has been shown to have anti-inflammatory, immunomodulatory, antiviral, and antitumor properties (Bhattacharya, 2011).
- Milk thistle contains the active phytochemical compound, silybin, also known as silybinin; it is derived from its seeds and is a well-known antioxidant and the most commonly used hepatoprotectant (liver protectant) in U.S. gastrointestinal clinics.
- Milk thistle is known for its use in treatment of dyspepsia or a group of symptoms that cause upper abdominal pain, and of cirrhosis or the late stage of scarring of the liver, and damage to the liver caused by toxins.
- Intravenous silybinin, a phytochemical component of *Silybum*, has been effectively used against the amatoxin released by amanita or deathcap mushrooms on patients who have ingested the poisonous mushrooms.
- Effective for detoxing the liver and helping with hangovers.
- In preclinical studies (research on animals before human trials are performed), milk thistle compounds have demonstrated anticancer activities, such as colon cancer cells self-destruction (apoptosis), causing breast cancer cell senescence (blocking a cancer cell's ability to divide and grow), and blocking angiogenesis or the development of new blood vessels in prostate cancer cells.
- Milk thistle compounds applied to the skin of mice after exposure to harmful ultraviolet radiation prevented skin cancers from spreading; the actions of those compounds blocked the cancer cells' developmental pathways (Siegel, Stebbing, 2013).
- Common uses are for pain due to gallstones, bronchitis, detoxifying the organs such as in jaundice, toxic kidney damage, nerve disorders, clogged arteries, dialysis, eczema, and gallbladder disease (Mayo,1998-2017).
- Milk thistle contains silymarin that protects cell membranes and helps build new cells.
- Contains flavonoids and flavonoid derivatives, the flavonolignans, which are involved in the detoxification process as well as the conversion in the body to bioflavonoids or vitamin P, which enhances capillary permeability and strength.

- Studies show silymarin's ability to stabilize cell membranes, preventing toxic chemicals from entering the cell, and to stimulate actions in the body's detoxification pathways.
- Helps improve vitamin C levels in the body's cells, aids in the scavenging of free radicals or foreign toxic substances that damage cells, protects against destruction of collagen needed in the repairing of the body's tissues.
- Has direct anticancer actions against breast, ectocervical (the part of the cervix that protrudes into the vagina), and prostate tumors.
- Prevents the release and synthesis of immune compounds in the body that result in allergies and inflammation (PDQ, National, 2002)
- Phenolic compounds in milk thistle are known to improve how the neutrophils or white blood cells of the immune system work to protect against structural, functional and aesthetic changes to skin in the aging process.
- Various intrinsic (genetic) and extrinsic (environmental) factors generate changes to skin cell structure, one of which is solar radiation, which wavelengths reaching the Earth stimulate a complex skin reaction that can generate reactive oxygen species (ROS), a cell-damaging free radical.
- ROS, produced by the body under stress, modify proteins and lipids, form carbonylated proteins, lipid peroxides, and the active enzymes collagenase, elastase, and hyaluronidase, which impact the skin's extracellular matrix composed of collagen, elastin, and hyaluronic acid.
- Neutrophils are activated through utilizing calcium and zinc to produce metalloproteinases, collagenase, and elastase, enzymes that break down collagen and elastic fibers in the skin cell matrix and results in skin dehydration and formation of wrinkles.
- Phenolic compounds in milk thistle have been found to diminish the structural and functional changes caused by the above extrinsic factors that degrade skin cell structures.
- *Silybum marianum* also contains flavonolignan SB, flavonolignans isosilybin, silydianin, silychristin, 2,3-dehydrosilybin, and the flavonoid taxifolin, which contain immunomodulating, antioxidant, and anti-inflammatory properties that help modulate nerve signaling pathways.
- Studied extensively for its potential in slowing down the degenerative disease process and providing protection against UVB light from the sun for over thirty years, *Silybum marianum* and its flavonolignan have also been studied for its reactions against UVA light.
- Chronic and acute UVA solar radiation reaches into the deep dermal skin layers; therefore, the blood vessels and the skin's elastin, collagen, and hyaluronic acid are prone to degenerative tissue damage; the body responds by producing ROS (reactive oxygen species) leading to oxidative stress and degradation of skin hydration and elasticity, and the formation of wrinkles and pigment spots.
- Research has focused on finding plants containing inhibitors of this photo-aging process.
- Milk thistle seeds are found to contain the potent polyphenols (flavonolignans), which are antioxidant, anti-inflammatory, bioactive compounds that are effective free radical scavengers found to prevent UVA damage to human dermal fibroblasts (connective tissue cells that synthesize collagen and other extracellular proteins) (Cao, 2023) (Vostalova, 2019).

## Pomegranate (Fruit) (*Punica granatum*)

Aamiredwardes 2018
Wikimedia Commons

Fir0002Flagstaffotos 2005
Wikimedia Commons

- Seed consists of oil high in vitamin E and polyunsaturated fatty acids.
- Chinese used pomegranate seeds to enhance male power.
- Biochemicals contained in pomegranate seeds have been found to help lower blood pressure and relieve headaches.
- Helps improve hemoglobin levels, reducing the risk of anemia.
- Used for centuries for improving various inflammatory conditions, and preventing diabetes, diarrhea, intestinal parasites such as dysentery, malaria and other infections, and reducing dental plaque (Ismail, 2012).
- Tonic, stimulant, analgesic (pain killer) effects.
- Has astringent properties (causes the contraction of body tissues, typically for protecting the skin and to reduce bleeding from minor abrasions).
- In addition to being an anthelmintic (antiparasitic), studies show pomegranate is a hemostatic (arrests bleeding), antipyretic (reduces fever) and aids in wound healing.
- Concentrated phytochemicals (also known as phytonutrients) found in the peels include phenolics and flavonoids, which have been shown to inhibit Listeria monocytogenes, Staphylococcus aureus (Staph), Escherichea coli, and Yersinia enterocolitica, as well as Salmonella enteritidis (Al-Zoreky, 2009).
- Is also a valuable source of the essential mineral potassium, vitamin C and contains polyphenols, which are excellent antioxidants.
- A fatty acid found in the seeds called punicic acid, has anti-atherogenic properties (helps prevent heart disease from clogged heart vessels), and reduces cholesterol, as shown through improved lipid profiles on human test subjects in a double blind, placebo-controlled clinical trial (Mirmiran, et. al., 2010).
- Studies also show pomegranate can also help prevent cancer and aging.
- Plays an important role in regulating low-density lipoprotein (LDL) by reducing lipid peroxidation that damages polyunsaturated fatty acids such as linoleic acid and arachidonic acid and results in reactive, toxic byproducts such as the aldehydes malondialdehyde and 4-hydroxynonenal. This damage affects the body's DNA and many critical, normal functions of specific proteins, leading to alterations in cell functioning, which in turn leads to various diseases such as atherosclerosis or damage to and hardening of the arteries (Nam, 2011).
- Has neuroprotective effects, protects against memory dysfunction.

- Pomegranate's phytochemicals ellagitannin and ellagic acid are converted to urolithins in the body, found to improve microbiota (beneficial aerobic bacteria) conditions in the colon, known as *Gordonibacter urolithinfaciens*, and other bacteria (Wonderful, 2013).
- The pomegranate contains different polyphenols, including hydrolizable (able to break molecular bonds when reacting with water) ellagitannins such as punicalagin, punicalin, and pedunculagin, which are known for their actions in improving the skin microbiome, thereby helping to reduce wrinkles.
- Phytonutrients in pomegranate have been found to counter the damage of reactive oxygen species (ROS), the free radical that is produced in cells under stress, leading to photodamage, photoaging, and skin cancers as a result of chronic and intense exposure to solar UVA and UVB radiation.
- Different components of pomegranate fruit have been well-researched for their antioxidant, anti-inflammatory, anti-microbial, anti-neuroinflammatory, anti-glycation (preventing or countering a worsening cascade of toxic biochemical reactions), and immunomodulatory properties.
- Pomegranate's antioxidant capacity is reportedly the highest compared to milk thistle, green tea, grape seed, goji (Chinese wolfberry) and acai berry extracts, and is thus able to reduce oxidative stress (an imbalance of free radicals and antioxidants leading to cell damage), DNA damage, and cytotoxicity or cell poisoning.
- Antioxidants in pomegranate have been shown to have improved effects on the liver, the gut microbiome (the established beneficial microorganisms that exist in the colon), and obesity (Chakkalakal, et. al., 2022) (Hao Guo, et. al., 2021).
- The pomegranate tree dates back to the bronze age about 3500-2000 B.C., discovered in South and Central Asia, the Middle East and Caucasus region, the Mediterranean, North and tropical Africa and currently cultivated in North and South America.
- Historically, the pomegranate was known as a symbol of life, prosperity, and fertility; the Bible's Old Testament referred to it as for good luck, abundance, and fertility.
- Research shows pomegranate's prebiotic properties due to the array of its phytochemicals that include ellagitannins, gallotannins, anthocyanins, anthocyanidins, flavonoids, flavonones, flavonols, organic acids, fatty acids and lipids, phenolic acids, alkaloids and lignans.
- The fruit of *Punica granatum* are known for maintaining biochemical homeostasis attributed to its lignans, organic acids gallic and ellagic acid, fatty acids, alkaloids, triterpenoids, phytosterols, hydrolysable tannins and flavonoids.
- The rind or pericarp contains hydrolysable tannins, flavonoids, ellagitannins, and punicalagins, and the seeds contain polyphenols, isoflavones, and ascorbic, citric, and malic acids.
- Pomegranate seeds contain a high concentration of lipids punicic, oleic, stearic, and palmitic acid, as well as the polyunsaturated fatty acids linolenic and linoleic acid (Lavoro, et. al., 2021).
- The polyphenols anthocyanins and hydrolysable tannins in pomegranate fruit have been purportedly effective for expelling parasites; the seeds and peels for diarrhea, flowers for controlling diabetes, tree bark and roots for arresting bleeding and healing of ulcers, leaves for reducing inflammation and digestive system problems.
- Phenolic metabolites known as urolithins have been found to improve gut microbiota.
- The phytochemicals ellagic acid, caffeic acid, luteolin and punicic acid were found to work synergistically to suppress prostate cancer cells, and polyphenols worked on eliminating colon cancer cells.

- Anthocyanins in pomegranate were found to be cardioprotective by halting free radicals such as inhibiting the free radical actions of xanthine oxidase, superoxide dismutase (ROS) and reactive nitrogen species (RNS).
- Anthocyanins bind to metal ions involved in the degenerative actions in the oxidation of low-density lipoproteins (LDLs), and also help regulate the articulation of endogenous (produced in the body) antioxidant enzymes.
- The anti-inflammatory properties of anthocyanins were found to have anti-obesity effects through attenuating the inflammatory responses in adipose tissue triggered by a high-fat diet.
- Anthocyanins have also been shown to impede the formation of tumors, prevent malignant cells from forming and inhibiting cancer cell proliferation and inducing cancer cell apoptosis (destruction of cancer cells).
- Pomegranate juice's cardioprotective effect is the result of its anti-atherosclerotic and cholesterol activities against oxidized lipids, and its antidiabetic activities are largely due to the antioxidant actions of reducing oxidative stress and lipid peroxidation.
- The urolithins in pomegranate fruit are anti-cancer, anti-inflammatory and anti-aging.
- Urolithins have been shown to reduce the risks of breast and endometrial cancers, impair the proliferation of prostate cancer cells, and induce apoptosis in lymphoma.
- Urolithins were found to impair the behavior of neutrophils and monocytes during inflammatory responses in the development of cardiovascular diseases.
- Urolithins through enzyme actions were predicted to be able to penetrate the blood-brain barrier in their anti-Alzheimer actions.
- Urolithins have been found to improve mitochondrial energy-producing function and maintain muscle quality (Wu, 2017).

## Different Classes of Phytochemicals Identified in Pomegranate

### Ellagitannins, Gallotannins and Derivatives

Brevifolin, Brevifolin carboxylic acid, Brevifolin carboxylic acid 10-monopotassium sulphate, Castalagin, Casuariin, Casuarinin, Corilagin, Isocorilagin, Hippomanin A, Gemin D, Diellagic acid rhamnosyl(1→4) glucopyranoside, 1,2-Di-*O*-galloyl-4,6-*O*-(*S*)-hexahydroxydiphenoyl β-d-glucopyranoside, Ellagic acid, 3,3'-Di-*O*-methylellagic acid, 3,3',4'-Tri-*O*-methylellagic acid, 3-*O*-Methylellagic acid, 4,4'-Di-*O*-methylellagic acid, 3'-*O*-Methyl-3,4-methylenedioxy-ellagic acid, Eschweilenol C (Ellagic acid 4-*O*-α-l-rhamnopyranoside), Ethyl brevifolincarboxylate, Eucalbanin B, Eucarpanin $T_1$, Pomegraniin A, Pomegraniin B, Gallagic acid, Gallic acid 3-*O*-β-d-(6'-*O*-galloyl)-glucopyranoside, 6-*O*-Galloyl-2,3-(*S*)-hexahydroxydiphenoyl-d-glucose, 5-Galloylpunicacortein D, 2-*O*-Galloylpunicalin (2-*O*-Galloyl-4,6-(*S*,*S*)-gallagyl-d-glucose), Granatin A, Granatin B, 2,3-(*S*)-Hexahydroxydiphenoyl-d-glucose, Lagerstannin B, Lagerstannin C, 3-*O*-Methylellagic acid 4-*O*-α-l-rhamnopyranoside, 3,4'-*O*-Dimethylellagic acid 4-*O*-α-l-rhamnopyranoside, Oenothein B, Pedunculagin I, Pedunculagin II, 1,2,3,4,6-Penta-*O*-galloyl-β-d-glucose, 3,4,8,9,10-Pentahydroxydibenzo [*b,d*] pyran-6-one (Urolithin M-5), Phyllanthusiin E, Pomegranatate, Punicacortein A, Punicacortein B, Punicacortein C, Punicacortein D, Punicafolin, Punicalagin A, Punicalagin B, Punicalin, Punicatannin A, Punicatannin B, Punigluconin, Strictinin [1-*O*-Galloyl-4,6-(*S*)-hexahydroxydiphenoyl-d-glucose], Tellimagrandin I, Tercatain [1,4-Di-*O*-galloyl-3,6-(*R*)-hexahydroxydiphenoyl-β-glucopyranose], Terminalin (Gallagyl dilactone), 1,2,4,6-Tetra-*O*-galloyl-β-d-glucose, 1,2,3-Tri-*O*-galloyl-β-glucopyranose, 1,2,4-Tri-*O*-galloyl-β-glucopyranose, 1,2,6-Tri-*O*-galloyl-

β-glucopyranose, 1,3,4-Tri-*O*-galloyl-β-glucopyranose, 1,4,6-Tri-*O*-galloyl-β-glucopyranose, 3,4,6-Tri-*O*-galloyl-β-glucopyranose, Valoneic acid dilactone.

**Flavonoids**

Hovetrichoside C, Phloretin, Phlorizin, Eriodictyol-7-*O*-α-l-arabinofuranosyl (1-6)-β-d-glucoside, Granatumflavanyl xyloside, Naringin (Naringenin-7-*O*-rhamnoglucoside), Naringenin-4'methyl ether 7-*O*-α-l-arabinofuranosyl(1-6)-β-d-glucoside, Pinocembrin, Punicaflavanol, Apigenin, Apigenin 4'-*O*-β-glucopyranoside, Luteolin, Luteolin 3'-*O*-β-glucopyranoside, Luteolin 4'-*O*-β-glucopyranoside, Cynaroside (Luteolin 7-*O*-glycoside), Luteolin 3'-*O*-β-xylopyranoside, Tricetin, Daidzein, Genistein, Amurensin (Noricaritin 7-β-d-glucopyranoside), Kaempferol, Astragalin (Kaempferol 3-*O*-glucoside), Kaempferol-3-*O*-rhamnoglucoside, Myricetin, Phellatin, Quercetin, Hirsutrin (Quercetin-3-*O*-glucoside), Quercimeritrin (Quercetin-7-*O*-glucoside), Quercetin 3-*O*-rhamnoside, Rutin (Quercetin-3-*O*-rutinoside), Quercetin-3,4'-dimethyl ether 7-*O*-α-l-arabinofuranosyl(1-6)-β-d-glucoside, Cyanidin, Chrysanthemin (Cyanidin-3-*O*-glucoside), Cyanin (Cyanidin-3,5-di-*O*-glucoside), Antirrhinin (Cyanidin-3-*O*-rutinoside), Catechin-cyanidin-3-hexoside, Delphinidin, Myrtillin (Delphinidin-3-*O*-glucoside), Delphinidin-3,5-di-*O*-glucoside, Pelargonidin, Callistephin (Pelargonidin-3-*O*-glucoside), Pelargonin (Pelargonidin-3,5-di-*O*-glucoside), Catechin, Epicatechin, Epicatechin gallate, Epigallocatechin-3-*O*-gallate, Gallocatechin-(4→8)-catechin, Gallocatechin-(4→8)-gallocatechin, Catechin-(4→8)-gallocatechin, Procyanidin A2, Procyanidin B1, Procyanidin B2, Procyanidin B3.

**Lignans**

Conidendrin, Isohydroxymatairesinol, Isolariciresinol, Matairesinol, Medioresinol, Phylligenin, Pinoresinol, Secoisolariciresinol, Syringaresinol, Pomegralignan, Punicatannin C.

**Triterpenoids and Phytosterols**

Asiatic acid, Betulinic acid (Betulic acid), Friedooleanan-3-one (Friedelin), Maslinic acid, Oleanolic acid, Punicanolic acid, Ursolic acid, Campesterol, Cholesterol, Daucosterol, β-Sitosterol, β-Sitosterol laurate, β-Sitosterol myristate, Stigmasterol.

**Alkaloids and Indolamines**

*N*-(2',5'-Dihydroxyphenyl)pyridinium chloride, Hygrine, Norhygrine, Pelletierine, *N*-Methylpelletierine, Norpseudopelletierine, Pseudopelletierine, 2-(2'-Hydroxypropyl)-$\Delta^1$piperideine, 2-(2'-Propenyl)-$\Delta^1$piperideine, Punigratane (2,5-Diheptyl-*N*-methylpyrrolidine), Sedridine, Melatonin, Serotonin, Tryptamine.

**Fatty Acids and Lipids**

Caproic acid (Hexanoic acid), Caprylic acid (Octanoic acid), Capric acid (Decanoic acid), Lauric acid (Dodecanoic acid), Myristic acid (Tetradecanoic acid), Myristoleic acid (9-*cis*-Tetradecanoic acid), Palmitic acid (Hexadecanoic acid), Palmitoleic acid (Hexadec-9-enoic acid), Punicic acid (9*Z*, 11*E*, 13*Z*-octadecatrienoic acid), Linoleic acid (*cis*, *cis*-9,12-Octadecadienoic acid), α-Linolenic acid (All-*cis*-9,12,15-octadecatrienoic acid), γ-Linolenic acid (All-*cis*-6,9,12-octadecatrienoic acid), Oleic acid (9*Z*-octadecenoic acid), Stearic acid (Octadecanoic acid), α-Eleostearic acid (9*Z*, 11*E*, 13*E*-octadecatrienoic acid), β-Eleostearic acid (9*E*, 11*E*, 13*E*-octadecatrienoic acid), Catalpic acid (9*E*, 11*E*, 13*Z*-octadecatrienoic acid), Arachidic acid (Eicosanoic acid), Gadoleic acid (9*Z*-icosenoic acid), Behenic acid (Docosanoic acid), Nervonic acid (*cis*-15-Tetracosenoic acid), 1-*O*-9*E*,11*Z*,13*E*-

| |
|---|
| Octadecatrienoyl glycerol, 1-*O*-Isopentyl-3-*O*-octadec-2-enoyl glycerol, Tri-*O*-punicylglycerol, Di-*O*-punicyl-*O*-octadeca-8*Z*, 11*Z*, 13*E*-trienylglycerol, *N*-palmitoyl cerebroside. |
| **Organic Acids and Phenolic Acids**<br><br>Ascorbic acid, Citric acid, Fumaric acid, l-Malic acid, Oxalic acid, Quinic acid, Succinic acid, Tartaric acid, Caffeic acid, Chlorogenic acid, Cinnamic acid, *o*-Coumaric acid, *p*-Coumaric acid, *cis*-*p*-Coumaric acid, Coutaric acid, 7,8-Dihydroxy-3-carboxymethylcoumarin-5-carboxylic acid, Ferulic acid, Gallic acid, Methyl gallate, Neochlorogenic acid (5-*O*-Caffeoylquinic acid), Protocatechuic acid, Vanillic acid, Coniferyl 9-*O*-[*β*-d-apiofuranosyl(1→6)]-*O*-*β*-d-glucopyranoside, Sinapyl 9-*O*-[*β*-d-apiofuranosyl(1→6)]-*O*-*β*-d-glucopyranoside. |
| **Other Compounds**<br><br>Catechol, Coumestrol, Icariside D1, Phenylethylrutinoside, Syringaldehyde. |

(Wu, 2017)

## Red Grape (Fruit) (*Vitis vinifera*)

Silverije 2012 Wikimedia Commons

- Red grapes contain many phytochemical compounds that have been shown to have therapeutic and chemopreventive actions against many health conditions.
- Grapes contain a phytoalexin compound, resveratrol, which is a trihydroxy derivative of the compound stilbene (3,5,4'-trihydroxystilbene).
- Resveratrol occurs naturally in berries, peanuts, red wine, and many other plants since its production is a form of defense against harmful stimuli in the plant's environment, such as fungal infections and scavenging insects.
- Researchers have shown resveratrol's protective effects against ultraviolet radiation mediated oxidative stress on human cells, including cutaneous damages that result in skin aging and skin cancer.
- Ultraviolet (UV) sun radiation is a main factor in the pathogenesis leading to skin disorders since it directly causes DNA damage, setting off a cascade of oxidative stress and inflammatory reactions, including nerve signaling leading to mutations in the genetic code.
- Besides much accomplished research regarding resveratrol's protective effects against cardiovascular disease, an added focus in the areas of cancer chemoprevention, inflammation, and oxidative stress has revealed resveratrol's effects in balancing the body's natural production of reactive oxygen species (ROS) when under stress or injury, with the body's counter-balancing

production of its natural antioxidants superoxide dismutase (SOD), catalase, and glutathione peroxidase.

- Under prolonged stress conditions, the balance is disrupted, and the ROS overwhelms the cells, leading to impaired cellular processes, such as from:
    - Cigarette smoke
    - Extreme change in temperatures
    - UV radiation exposure (UVA, UVB, and UVC)
    - UVA – the longest wavelength linked to skin aging and skin cancer.
    - UVB – a mid-range wavelength linked to skin cancer, with a role in other skin damage and aging.
    - UVC – the shortest wavelength that can play a role in mutagenesis (when the genetic information is changed due to a mutation), causing DNA damage.
- Resveratrol has been found to have chemopreventive (preventing formation of cancer cells) activity against the three major stages of carcinogenesis: initiation, promotion, ad progression.
- In a clinical trial testing resveratrol against melanoma, it was shown that it decreased levels of IGF-1 and IGFBP-3, messenger hormones that affect growth and other cell actions, including cancer cells.
- Resveratrol was shown to affect enzymes involved in activation of cancer cells, while providing detoxification pathways, demonstrating its other chemopreventive properties:
    - As an antioxidant and antimutagen.
    - Preventing the initiation of phase II in cancer cell formation by inducing metabolization of enzymes.
    - Mediating anti-inflammatory actions.
    - Inhibiting inflammatory enzymes cyclooxygenase and hydroperoxidase.
    - Induce anti-progression actions in cancer cell development, growth, and proliferation.
- Resveratrol's other chemopreventive properties:
    - Protects collagen from UV radiation degradation.
    - Regulates normal cell apoptosis (cell turnover in aged cells), and effects cancer cell apoptosis self-destruction.
    - Prevents abnormal cell proliferation leading to DNA mutations.
    - Inhibited growth of various *in vitro* (generations of laboratory cell cultures) cancer cell lines, and protected cells from oxidative DNA damage.
    - Generations of human keratinocyte cell lines *in vitro* have thus far been immortalized since the application of resveratrol to the skin tissues have continued to thrive, showing much promise for skin diseases and skin cancers.
    - Protected cells from UVA and UVB exposure damage and oxidative stress, showing improved cell viability after exposure (Ndiaye, 2011).
- Grape polyphenols have been studied for the interconnected mechanisms of oxidative stress and inflammation in aging when the major free radical molecules reactive oxygen species (ROS) and reactive oxygen and nitrogen species (RONS) are present.
- Other frequently researched free radicals include superoxide ($O_2^-$), hydrogen peroxide($H_2O_2$), hydroxyl radical ($\cdot OH$), peroxynitrite ($ONO_2^-$), and nitric oxide (NO), are necessary for:
    - Immune cell actions as defense against invading illness-causing microorganisms, eliminating cellular debris, and arresting and preventing cancer cell formation.
    - Acting as signaling molecules.
    - Regulating regular cell repair, growth and routine apoptosis.
    - RONS are involved in the electron transport chain in mitochondrial energy production.

- By contrast, the necessary metabolic actions of some free radicals as shown above have the roles of oxidation, adversely affecting signaling messengers, DNA, healthy cell structures and their critical membranes.
- The body must be provided with full range nutrient density to counteract this occurrence of oxidative stress and allow for the production of its own antioxidants SOD, glutathioneperoxidase, catalases, glutathione/TrxR, and peroxiredoxins.
- Only with the proper intake of antioxidant foods such as grapes that aid the production of endogenous antioxidants can the body develop the efficient defenses to outweigh the effects of oxidative stress and accelerated aging.
- It was found that the risk for dementia induced by stroke in correlation with oxidative stress was associated with the shortening of telomere lengths in both fibroblasts (cell material that secretes collagen proteins in building tissue structural frameworks) and peripheral blood mononuclear cells (PBMCs) or immune cells that protect the body against harmful pathogens, which include T cells, B cells, NK cells, monocytes, and dendritic cells.
- Telomere shortening is the result of a cascade of oxidative events that damage cells and impair their ability to replicate, repair and regenerate themselves, leading to cell senescence, cell death, and premature aging of an individual.
- Grapes also contain rutin, a potent antioxidant shown to protect against aging-related metabolic malfunctions.
- The flavonoids quercetin and dihydro-quercetin, proanthocyanins and anthocyanins in grapes are known antioxidants and anti-inflammatory agents.
- Researchers found that resveratrol delayed age-dependent degeneration of locomotor and cognition, and reduced neurofibrillary tangled bundles of twisted protein filaments within neurons called tau that form brain lesions and are associated with Alzheimer's disease.
- Grape polyphenols have been shown to modulate inflammatory cytokine signaling and attenuate the motility and functions of leukocytes, white blood cells that circulate in the blood and initiate inflammatory and cellular actions in response to injury or invading pathogenic organisms (bacteria, viruses, fungi, parasites) (Petersen, 2016).
- Because of resveratrol's antioxidant and anti-inflammatory actions, it has been shown to have anti-platelet properties that prevent abnormal clots from forming and growing, and inhibit apoptotic or programmed cell death in conditions such as myocardial ischemic reperfusion injury (blood flow restored to the heart yet causes further damage), atherosclerosis, ventricular arrhythmias, and cerebral ischemia (insufficient blood flow to the brain).
- More evidence reveals that resveratrol mimics the effects of calorie restriction in efforts to promote longevity; resveratrol and safe calorie restriction both improve insulin sensitivity and in turn reduce insulin and blood glucose levels, as such blocking of insulin receptors in adipose tissue was found to extend the life spans of animal test subjects by approximately 18% (Lekli, 2010).

## Rosemary (Leaf) (*Rosmarinus officinalis L.)*

Photos By: Samueles, Bluesnap, JoannaSz, A Different Perspective - Pixabay

- *Rosemarinus officinalis L.* is native to the Mediterranean regions and is cultivated throughout the world.
- Contains active phytochemical compounds with anti-inflammatory, antioxidant, antimicrobial, antiviral, antiproliferative, and antitumor properties.
- Phytochemicals include derivatives of eugenol and luteolin, and caffeic acid, camphor, carnosol, carnosol acid, chlorogenic acid, alpha-pinene, eucalyptol, monomeric acid, oleanolic acid, rosmarinic acid, rosmadial, rosmanol, rosmaquinones A and B, secohinokio, and ursolic acid.
- *R. officinalis L.* has demonstrated actions for attenuating asthma, and prevent atherosclerosis, cataracts, renal colic, hepatotoxicity, peptic ulcer, inflammatory conditions, ischemic heart disease.
- Shown to be anti-hypercholesterolemia, provides protection against oxidative stress and physical and mental fatigue.
- Contains rosmarinic acid, shown to reduce myocardial blood pressure, demonstrated antiulcer actions, and as an antioxidant, was shown to reduce lipid peroxidation in the heart and brain.
- Rosemary's phytochemicals carnosic acid and carnosol showed antiangiogenic (prevents tumors from growing blood vessels) and neuroprotective properties.
- Is hepatoprotective, neuroprotective, protects against radiation with anti-mutagenic properties, helps attenuate blood glucose, skin allergies, and has demonstrated to help with depressive behavior.
- Found to function as an antioxidant enzyme, able to remove superoxide radicals from cardiac tissue and improve gene encoding and transcription in forming antioxidant enzymes.
- Demonstrated protection against liver injuries.
- Has been compared to harmful effects on the liver by antibiotics and shown to reverse those damaging effects.
- Has been shown to reduce total cholesterol, phospholipids, triacylglycerols and atherogenesis (fatty plaques in the arteries).

- *R. officinalis L.* is rich in catechins, coumarins, and cinnamic acid, quercitin, luteolin, kaempferol, rosmarinic, hydrocafeic and caffeic acids, phytochemicals with high antioxidant activity that protect liver and heart functions.
- Shown to stimulate excretion of fecal matter, along with cholesterol and bile acids, thereby helping to reduce cholesterol levels in the body.
- Was shown to protect against cerebral edema and rupturing of the blood-brain barrier, and prevent molecules that create oxidative stress and harm the brain.
- Promotes the reduction of free radicals that can damage cerebral, cardiac, renal, and serum, such as lipid peroxidation, hydroxyl radical, and hydrogen peroxide.
- Is found to be a natural cyclooxygenase (COX) inhibitor without the side effects of COX inhibiting medications used for pain, which are known to lead to cardiovascular and renal (kidney) disorders, and gastric (stomach) problems.
- Studies show how *R. officinalis L.* can inhibit pain.
- Found to be effective against the forming of typical biofilms by the fungi *Candida albicans*, and the bacteria *Staphylococcus aureus*, *Enterococcus faecalis*, *Streptococcus mutans*, and *Pseudomonas aeruginosa* that cause a variety of infections in teeth and oral mucosal tissues.
- Protects against the life-threatening effects of lead (Pb), which adversely affects the liver and kidneys, causes blood disorders and a severely compromised immune system, and causes cardiac, nervous, metabolic and reproductive harm.
- Rosemary has been found to improve levels of anemia and white blood cells, and eliminate peroxyl radicals and inhibit the forming of hydroxyl radicals.
- Has been shown to have an antianxiety or anxiolytic effect with no side effects, compared to antianxiety medications.
- High in phytochemical compounds known as flavonoids, including apigenin, and enhance the functioning of the central nervous system.
- *R. officinalis L.* helps create the proper biochemical balance of oxygenation and pH acidity/alkalinity in the body that prevents cancer, and prevents circulation of nutrients to tumors, and therefore disrupts their development, inhibits tumor cell growth, and induces apoptosis (cancer cell self-destruction).
- Has exhibited positive effects on blood lipids and improved circulation, protecting blood flow through the circulatory system, which reduces risk of heart attack, angina or stroke (De Oliveira, 2019).
- A study showed that *R. officinalis* essential oil was active in healing wounds in diabetic test animals, indicating evidence for use of this herb for wounds (Abu-Al-Basal, 2010).
- The essential oils in the rosemary leaf have been shown to have telomere-protective effects through the mediation of the TERF-1 telomere-suppressive protein, which is critical when cells become cancerous and begin to proliferate and which telomeres in those gene expressions begin to replicate with the aid of the elongated telomeres.
    - In aging, as the body's cells perpetually divide over a lifespan, theoretically the protective telomeres or end-caps at the end of each chromosome gradually shorten.
    - By contrast and in maintaining necessary balance and accurate gene transcriptions during cell replication, TERF-1 as part of the telomere protein complex, is critical for maintaining telomere length in healthy cells while inhibiting the enzyme telomerase that limits the elongation of the telomere chromosome ends.
    - In each cell DNA replication process, a small amount of gene sequences at the ends of the chromosomal DNA are lost each time a cell divides, and when this duplication process reaches its replicative potential limit (aka the "Hayflick limit"), the cell senesces or retires.

    - A cell's senescence can be prevented through actions of the telomerase protein/RNA complex that allows chromosome telomere ends to be replicated without losing the correct genetic sequences, including stem cells responsible for replacing skin and blood cells that necessarily must express telomerase and are therefore not imposed on by the replicative limit.
    - Telomerase enzyme activation is an indication of cancer as tumor cells reveal their limitless replicative potential.
    - TERF-1 can act to inhibit telomere lengthening by blocking the binding sites for telomerase; however as more binding sites for TERF-1 are formed due to the action of telomerase, a threshold is reached where telomerase can no longer effect its actions.
    - As telomeres shorten eventually, that threshold can not be met; therefore, telomerase can resume its binding and extending of the telomere chromosome ends to maintain telomere length equilibrium.
    - Other pathways of telomere erosion are prolonged oxidative stress through inflammation or the presence of reactive oxygen species (ROS) generated by the body's production of stress chemicals, which directly damage DNA, including the telomeric regions, causing telomere shortening.
- Rosemary leaf oils have been shown in live cell cultures to counter the telomere-shortening effects from exposure to the free radical hydrogen peroxide, which reduced the telomere specific signal, yet the oils increased and restored the size of telomeres by 60-80% compared to the untreated control cells.
- Administering subtoxic doses of *Rosmarinus officinalis* has been confirmed in many research findings to increase the length of telomeres while protecting cells against losing telomeric DNA due to oxidative stress.
    - The antioxidants in rosemary leaf are able to absorb or neutralize ROS directly even as the oils do not induce telomerase production.
    - The telomere-regulating protein TERF-1 is downregulated in the presence of rosemary leaf oils which allows telomere length to be maintained without increasing telomerase expression.
    - Research suggests that *Rosmarinus officinalis* oils can maintain telomere length, while preventing cellular senescence "without cancer risk" (Plant, 2016).

## Siberian Larch (Bark) (*Larix sibirica*)

Ugraland - 2004 - Creative Commons

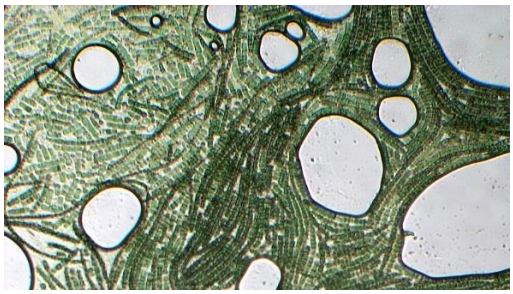
Jerzy Opiola - 2022 - CC BY-SA 4.0

- Siberian larch is a deciduous tree native to Russia, Mongolia, and China.

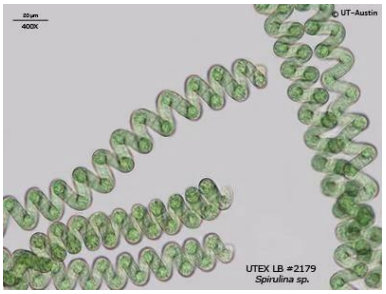
- The major constituents of *L. sibirica* are the flavonoids dihydroquercetin, dihydrokaempferol, quercetin, kaempferol, secoisolariciresinol, (+)-catechin, naringenin, resveratrol, and eriodictyol (Myungsuk, et. al, 2016).
- Flavonoids contain protective anti-oxidative, anti-inflammatory, anti-carcinogenic and anti-mutagenic properties, which modulate critical enzyme functions in the human cell.
- Flavonoids:
    - Are associated with preventing coronary heart disease.
    - Quercetin and kaempferol are known to demonstrate anti-cholinesterase activity.
    - Are found to inhibit the acetylcholinesterase (AChE) enzyme, helping to increase acetylcholine levels, a neurotransmitter known to help relieve symptoms of Alzheimer's disease.
    - Have been instrumental in understanding the biochemical pathways of attenuating inflammatory enzymes such as cycooxygenase-2 (COX-2).
- Studies also indicate that flavonoids such as naringenin and eriodictyol are effective inhibitors of the methicillin-resistant bacteria, *Staphylococcus aureus*. Certain enzymes such as β-Ketoacyl acyl carrier protein synthase III (KAS III), which initiates the process of essential fatty acid production in bacteria and is important to their reproduction, are being targeted to solve the serious problem of antibiotics no longer being effective against the overgrowth of illness or disease-causing bacterial populations in the human body.
- The flavonoid group of flavones and catechins appear to be highly effective for protecting cells from damage by free radical scavengers such as reactive oxygen species (ROS) and lipid peroxidation as a result of exposure to environmental toxins, and being normally produced during the body's normal oxygen metabolism (Gilbert, 2024) (Panche, 2016).
- The bark of *Labix sabirica* contains a unique composition of chemical compounds shown to possess medicinal (health restorative) properties:
    - Carotene, lignin, glycosides, organic acids, anthocyanins, flavonoids, gum and resins.
- In lesser amounts found in young larch needles are additional biologically active complexes: ascorbic acid (vitamin C) and essential oils pinene, borneol, bornyl acetate.
- Resins in *L. sabirica* include rosin, phytoncides, and dihydroquercetin.
- In plant raw materials analysis tested for levels of toxic trace elements (lead, cadmium, arsenic, mercury), Siberian larch was found to meet the requirements and standards for quality and safety by the General Pharmacopoeia Articles of the State Pharmacopoeia of the Republic of Belarus, Kazakhstan (Sayakova, et. al., 2022).
- Studies report the Siberian larch tree to have antioxidant, anti-viral, antibacterial, and neuroprotective properties.
- When studied for the effects of its various flavonoids, *L. sabirica* was found that its anti-allergenic actions:
    - Reduced the release and actions of inflammatory proteins by the immune system such as β-hexosaminidase, histamine, and inflammatory mediators (prostaglandin D2, leukotriene C4, interleukin-4, and tumor necrosis factor-α).
    - Suppressed and reduced the actions of inflammatory signaling proteins such as protein kinase, phospholipase and various other protein kinases.
- Contains phytoncides, carotene, lignin, glycosides, organic acids, anthocyanins, flavonoids, gum, fats, phytosterols, mannitol, glucose, arabinogalactan (water-soluble polysaccharide), dihydroquercetin, and rosin (solid resin).
- Resin contains essential oils pinene, borneol, bornyl acetate, α-pinene, dipentene, sylvestrene, and α-sylvic acid.

- Bark is particularly rich in tannins, coniferin glycoside, gum, catechins, flavonols, anthocyanins, organic acids (Myungsuk, et. al., 2016).
- Contains the arabinogalactan polysaccharide shown to be useful for correcting upper respiratory infections and dyslipidemia (abnormally high levels of fats in the blood).
- USDA-approved nutritional supplements in the form of concentrated powders and extracts have contraindications due to their immune-stimulating effects on those with autoimmune disorders and taking immunosuppressant drugs.
- Other cautions refer to the dietary fiber in supplement powders that, like other fiber, may cause bloating, flatulence, or other mild gastrointestinal upsets (Larch, 2024).
- L. sibirica contains phenolic compounds in the knot zones of its wood, which have been found to potentially ameliorate acute and chronic trauma of the nervous system.
- Severe damage to nerve cells or neurons leading to Alzheimer's, Parkinson's, acute spinal cord injury or stroke is due to oxidative stress and neuronal excitotoxicity or abnormally high levels of neurotransmitters that result in excessive stimulation of nerve cell receptors.
- Damage to nerve cells occur with the presence of inflammatory stress reactions, producing the biochemicals:
    - *Amyloid beta* – an abnormally formed protein, a primary component of plaques found in the brains of those with Alzheimer's conditions.
    - *Neurofibrillary tangles (NFT)* – causing normal amyloid protein groups near abnormal amyloid plaque deposits to mutate to form larger plaques or fibrils.
    - *Myelin debris* – debris accumulated from myelin sheath damage, the demyelination or breakdown of the nerve cell's protecting myelin sheath that is broken down and removed by the immune system's process of phagocytosis.
    - Causing a *loss of neurotrophic support* – molecules that enhance the growth and survival of neurons.
    - *Causing a loss of glial support* – glial cells are non-neuronal cells that do not participate directly in synaptic transmissions but nonetheless protect neurons in the nervous system.
    - Causing *ischemia* – insufficient blood flow that can affect the brain, heart, muscle, intestines and other organs, which can result in life-threatening conditions such as heart attacks and strokes.
- Studies of the flavonoid (+)-dihydroquercetin and two lignans (-)-secoisolariciresinol and (+)-isolariciresinol also known as cyclolariciresinol were found to:
    - Exhibit neuroprotective effects by scavenging cell-damaging free radicals and stimulating other nerve functions such as migration and neurite outgrowth, or the bringing together of developing neurons for proper interactions and forming new neuronal connections or transmission pathways.
    - Stimulate the formation, proper elongation, proper regeneration, and functional viability of Schwann cells, a type of glial cell in the peripheral nervous system that forms the myelin sheath protective coating around cell axons, which are responsible for signal transmissions.
    - After injury and at the lesion site, prevent glial cell scarring from forming obstructions that otherwise inhibit axonal regrowth and prevent functional recovery (Loers, et. al., 2014).
    - The effects of the flavonoid dihydroquercetin from larch wood on test animals demonstrated a lowered inflammatory response and no signs of tissue destruction in pancreatitis (Galochkina, 2016).

## Spirulina (*Arthrospira platensis*)



MaCameron 2023 – Wikimedia




UTEX, Austin - 2024

- Spirulina is a microscopic filamentous cyanobacterium that is a sustainable, ecofriendly microalga beneficial for bioremediation (decontaminating environments), nitrification (filling in of nitrogen compounds), and carbon dioxide ($CO_2$) fixation, and therefore a good candidate for detoxification of heavy metals and removal of other toxicants.
- The highly nutritious and ecofriendly *A. platensis* is hypolipidemic, hypoglycemic, and antihypertensive properties.
- Contains the phytochemical groups of phenolics, phycocyanins, and polysaccharides, all of which are antioxidants, anti-inflammatories, and immunostimulatory, promoting natural killer immune cell actions.
- Studies show spirulina's positive effects on inflammatory cytokines and lymphocyte proliferation, as related to aging and obesity associated with chronic inflammation, impaired immunity, and intestinal dysbiosis (an imbalance or lack of diversity in the populations of the various beneficial microorganisms in the gut's microbiome).
- *In vitro* studies show spirulina as a probiotic can improve the growth of beneficial intestinal microbiota.
- Is protein-rich, hypolipidemic (reduces the levels of lipids and lipoprotein complexes in the blood), hypoglycemic (lowers blood sugar levels), and antihypertensive (preventing high blood pressure).
- Animal studies show that spirulina and its phytochemical phycocyanin increases lipoprotein lipase enzyme actions that degrade circulating triglycerides or fats in the bloodstream.
- Promotes pancreatic secretion of insulin, and is therefore thought to be helpful in preventing metabolic syndrome, which is associated with low grade inflammation, oxidative stress, and intestinal dysbiosis or disruption of the microbiome in the gut.
- *Arthrospira platensis* was shown to decrease cholesterol, triglycerides, and malondialdehyde (an aldehyde produced during the oxidation of unsaturated fats) with an increase in serum total antioxidant capability.
- There are indications of spirulina's positive effects on systolic and diastolic blood pressure of hypertensive test animals.
- Studies show spirulina's phenolic and phycobiliprotein C-phycocyanin phytochemicals are functional bioactives with antioxidant and anti-inflammatory activities.
- Spirulina also contains antioxidant, anti-inflammatory phytochemicals: flavonoids and allophycocyanins; and immunostimulating polysaccharides.
- *Arthrospira platensis* produces extracellular metabolites that inhibit the growth of illness-causing bacteria, including the gram-negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa*, the gram-positive bacteria *Staphylococcus aureus*, *Bacillus subtilis*, and *Bacillus pumulis*, and *Streptococcus faecalis*, *Staphylococcus epidermidis*, and the yeast *Candida albicans*.

- Spirulina is thought to prevent or help regulate changes in metabolites that are generated in the gut, which are essential for maintaining gut homeostasis and promoting probiotic species growth.
- Cell cultures indicate that spirulina can promote the growth of lactic acid bacteria used in carbohydrate and dairy fermentation: *Lactococcus lactis*, *Streptococcus thermophilus*, *Lactobacillus casei*, *Lactobacillus acidophilus*, and *Lactobacillus bulgaricus*, as well as promote probiotics, including the genera *Lactobacillus* and *Bifidobacterium* used to produce yogurt.
- All evidence suggests that spirulina may be important for promoting beneficial bacteria to prevent microbiota-related conditions such as gastrointestinal, immunological, inflammatory bowel, and metabolic diseases, as well as helping to prevent metabolic syndrome (Finamore, 2017).

## Turmeric (Root) (*Curcuma longa*)

Photos By: Stevepb, Karenski1, Cgdsro - Pixabay

- Effective in the fight against various forms of gastritis and liver problems.
- Useful in weight loss; effectively breaks down fats and significantly simplifies the process of digestion.
- Reduces the adverse consequences of obesity such as diabetes by inhibiting the inflammatory effect of macrophages, which produce cytokines that cause inflammation in the heart and pancreas and prevent glucose absorption or uptake into the muscles and liver, resulting in hazardously high levels of blood sugar in the bloodstream.
- Increases the effectiveness of skin cancer treatment when directly applied to the damaged area.
- Used for the treatment of acne, inflammation caused by osteoarthritis, and diseases of the cardiovascular system.
- Helps the immune system deal with psychological stress.
- Supports the health of bones and joints; reduces joint pain and swelling through decreased production of cyclo-oxygenase 2 enzymes; it is a COX-2 inhibitor.
- Keeps cholesterol levels in the normal range and has a lipid-lowering effect (reduces fats in the circulatory system).
- Evidence shows that the curcumin in turmeric exhibits several cardio-protective properties: anti-inflammatory actions prevent cardiac injury; its antioxidant properties help improve circulatory pathways in the heart while destroying free radicals such as cytokines; suppresses atherosclerotic lesions in heart tissues; decreases thrombosis or abnormal clotting; may prevent strokes and lessen inflammation and blood vessel spasms after a stroke.
- Contains at least ten antioxidants that scavenge free radical molecules (foreign molecules such as synthetic chemicals from processed foods, agrichemicals, industrial chemicals); its antioxidants protect against free radical damage to cell membranes and DNA while stimulating the immune system to neutralize free radicals by producing its own antioxidant enzymes.

- Contains an important group of compounds called curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin, and bisdemethoxycurcumin.
- Contains beneficial essential oils: termerone, curlone, curumene, cineole, and *p-cymene,* as well as various natural sugars, proteins and resins.
- Improves brain function through helping the brain produce more Brain-Derived-Neurotrophic Factor (BDFNF), found to be effective in delaying or even reversing many brain and age-related diseases and depression, and in preventing the shrinking of the brain's hippocampus, the area of the brain that functions for learning and memory.
- Curcumin in turmeric has been shown to cross the blood-brain barrier and improve the neurodegenerative process of Alzheimer's disease by blocking B-amyloid, the substance that causes plaques that narrow circulatory passages in the brain.
- Strong anti-allergic, antibacterial, anti-carcinogenic (anti-cancer), anti-inflammatory antifungal, anti-mutagenic, anti-septic and anti-spasmodic and anti-viral.
- Found to hinder the development of chronic inflammation, tumors, and leukemia.
- Found to prevent the development of Type 2 diabetes in pre-diabetics by lessening insulin resistance.
- The curcumin and other antioxidants in turmeric have been found to destroy cancer cell cultures taken from the bloodstream, ovaries and the skin; studies show curcumin reduces growth of new blood vessels in tumors and prevents metastasis (spreading of cancerous cells).
- Overwhelming scientific evidence shows that turmeric can prevent cancer altogether by blocking certain enzymes needed for cancer growth; researchers have attested that there was not any type of cancer cell upon which turmeric did not work, including colon, mammary, prostate, liver cancer, esophageal, and oral cancers.
- Researchers have also found that turmeric's curcumin treatments prevent cervical cancer cell proliferation by altering their HPV-associated (Human Papillovirus) pathways.
- Turmeric has been proven to be effective in the treatments of many serious ailments, including multiple sclerosis, anemia, atherosclerosis, back pain, fibromyalgia, bloating and intestinal gas, bronchitis, conjunctivitis, bursitis, Crohn's disease, dyspepsia (heart burn), diarrhea, stomach pain, hepatitis, gallbladder infections and gallstones, genital herpes, hemorrhoids, irritable bowel syndrome, gingivitis (gum disease), kidney inflammation and infections, peptic ulcer (stomach ulcers caused by Helicobacter pylori bacteria), skin inflammatory conditions including eczema, liver disease, leprosy, food poisoning, fever, poor circulation, menstrual disorders, lung infections, edema (intercellular water retention), parasites, poor circulation, urinary tract infections (UTI), worms, ringworm.
- Used for healing wounds.
- Balances the reproductive system, lactation, purifies reproductive organs and breast milk, purifies the semen.
- Is an astringent (tightening, toning), carminative (relieves flatulence), cholagogue (promotes the flow of bile from the gall bladder to the duodenum, the first and shortest segment of the small intestine), diuretic (promotes increased production of urine), stimulant (increases alertness, attention and energy), and vulnerary (heals wounds).
- Aids digestion.
- Mosquito repellant (Vyas, 2015).
- Anti-tumor effects of curcumin have focused on how it binds to cell surface membranes and enters the cytoplasm to perform apoptotic and down-regulating actions that result in higher cytotoxicity in glioblastoma and medulloblastoma cancer cells expressing the telomerase enzyme and affecting telomere lengths.

- Telomeres, the specific DNA proteins residing at both ends of each chromosome, protect the genome from damage and from fusing with other DNA molecules inside the cell, therefore preventing the loss of genetic information.
- The enzyme telomerase is key to maintain proper lengths of the telomeres, which under oxidative stress conditions, undergo a shortening or loss of genomic information during the cell replication process, leading to senescence and eventual apoptosis or aged cell destruction.
- Curcumin was found to inhibit the telomerase activity that leads to telomere shortening; this inhibitory effect indicates its use in adjuvant cancer therapy in suppressing secondary tumor formation (Khaw, 2013).
- The polyphenolic curcumin compound is studied for its anti-aging, lifespan extension properties such as antioxidative, anti-inflammatory, anticancer, chemopreventive, anti-neurogenerative, and how it enhances the body's antioxidant superoxide dismutase (SOD) activity and reduces free radical malondialdehyde and lipofuscin levels.
- Curcumin's anti-aging, anti-cancer, anti-microbial, anti-inflammatory and antioxidant actions have led to research on how it modulates major signaling pathways that determine longevity.
- Oxidative stress, a cause of cellular aging or senescence, leads to a defect in cellular renewal and functionality and reduces cell regeneration capacity; yet, turmeric's phenolic compounds and flavonoids are found to prevent oxidation by modulating proper signal transduction communication between nerve cells, maintaining critical mitochondrial permeability, and modulating gene expression for longevity for telomere maintenance.
- In 1961 Leonard Hayflick, PhD. discovered that somatic cells' ability to divide and repair themselves occurs between 40-60 times in vitro before reaching senescence—this growth arrest that restricts a cell's lifespan and proliferative capacity is referred to as the "Hayflick limit".
- Research has since improved understanding of the regulatory pathways of replicative senescence that leads to progressive shortening of telomeres, the DNA protein structures that cap the ends of chromosomes, particularly when under prolonged, oxidative stress conditions.
- Since aging and age-related "disease" are thought to be caused by oxidative damage to DNA, lipids, and proteins, the curcumin phytonutrient has been proven to counter that damage through improving cellular antioxidant defenses by preventing lipid peroxidation degradation and promoting the body's natural antioxidants glutathione-s-transferase (GST), glutathione (GHS), superoxide dismutase (SOD), and glutathione peroxidase (GPx).
- Curcumin's anti-aging activity includes its anti-tumor effects of uncapping chromosome telomere ends of cancer cells, ensuring their senescence and apoptosis by down-regulating hTERT mRNA.
- Human telomerase reverse transcriptase (hTERT) is the replicating rate-limiting component of the telomerase enzyme, and its increased activity indicates the upregulating of most cancers; thus, inhibiting their telomerase activity prevents lengthening of their telomeres, which is a marker used to predict the survival of cancer, and therefore prevents their proliferation.
- Research into the human genome has discovered that telomeric DNA shortening and uncapping is especially due to oxidative damage by the body's scavenging stress chemical, ROS; however, cellular nourishment and exercise have been shown to have a positive effect on the rate of cell division, decrease telomere shortening and inhibit telomere attrition, and therefore prevent or delay the onset of age-related disorders and increase one's lifespan (Aliabbas, 2021) (Pawlikowski, 2013) (Wang, 2018).

Reference:

Abu-Al-Basal MA. Healing potential of Rosmarinus officinalis L. on full-thickness excision cutaneous wounds in alloxan-induced-diabetic BALB/c mice. J Ethnopharmacol. 2010 Sep 15;131(2):443-50. doi: 10.1016/j.jep.2010.07.007. Epub 2010 Jul 13. PMID: 20633625.

Aliabbas Zia, Tahereh Farkhondeh, Ali Mohammad Pourbagher-Shahri, Saeed Samarghandian. The role of curcumin in aging and senescence: Molecular mechanisms. *Biomedicine & Pharmacotherapy*. Volume 134. 2021. https://doi.org/10.1016/j.biopha.2020.111119. https://www.sciencedirect.com/science/article/pii/S0753332220313123.

Al-Zoreky, N.S., (2009). Antimicrobial activity of pomegranate (Punica granatum L.) fruit peels. *Int. J. Food Microbiology,* 134(3):244-8. doi:10.1016/j.ijfoodmicro.2009.07.002. Epub 2009 Jul 12

Bhattacharya, S. (2011). Chapter 90, Pages 759-766, Milk Thistle (Silybum marianum L. Gaert.) Seeds in Health. In *Nuts and Seeds in Health and Disease Prevention*. doi:10.1016/B978-0-12-375688-6.10090-8

Cao Y, Lin FH, Zhu Z, Sakamoto T. *Tissue Engineering*. 3rd ed. 2023. https://www.sciencedirect.com/topics/engineering/dermal-fibroblast

Chakkalakal M, Nadora D, Gahoonia N, Dumont A, Burney W, Pan A, Chambers CJ, Sivamani RK. Prospective Randomized Double-Blind Placebo-Controlled Study of Oral Pomegranate Extract on Skin Wrinkles, Biophysical Features, and the Gut-Skin Axis. *J Clin Med*. 2022 Nov 14;11(22):6724. doi: 10.3390/jcm11226724. https://pmc.ncbi.nlm.nih.gov/articles/PMC9699032/.

Cucu A-A, Baci G-M, Dezsi Ş, Nap M-E, Beteg FI, Bonta V, Bobiş O, Caprio E, Dezmirean DS. New Approaches on Japanese Knotweed (*Fallopia japonica*) Bioactive Compounds and Their Potential of Pharmacological and Beekeeping Activities: Challenges and Future Directions. *Plants*. 2021; 10(12):2621. https://doi.org/10.3390/plants10122621. https://www.mdpi.com/2223-7747/10/12/2621.

Dludla PV, Cirilli I, Marcheggiani F, Silvestri S, Orlando P, Muvhulawa N, Moetlediwa MT, Nkambule BB, Mazibuko-Mbeje SE, Hlengwa N, Hanser S, Ndwandwe D, Marnewick JL, Basson AK, Tiano L. Bioactive Properties, Bioavailability Profiles, and Clinical Evidence of the Potential Benefits of Black Pepper (*Piper nigrum*) and Red Pepper (*Capsicum annum*) against Diverse Metabolic Complications. *Molecules*. 2023 Sep 11;28(18):6569. doi: 10.3390/molecules28186569. https://pmc.ncbi.nlm.nih.gov/articles/PMC10534530/#molecules-28-06569-t002.

Finamore A, Palmery M, Bensehaila S, Peluso I. Antioxidant, Immunomodulating, and Microbial-Modulating Activities of the Sustainable and Ecofriendly *Spirulina*. Oxid Med Cell Longev. 2017;2017:3247528. doi: 10.1155/2017/3247528. Epub 2017 Jan 15. https://pmc.ncbi.nlm.nih.gov/articles/PMC5274660/#:~:text=Abstract,%2Dinflammatory%2C%20and%20immunostimulating%20effects.

Galochkina AV, Anikin VB, Babkin VA, Ostrouhova LA, Zarubaev VV. Virus-inhibiting activity of dihydroquercetin, a flavonoid from Larix sibirica, against coxsackievirus B4 in a model of viral pancreatitis. Arch Virol. 2016 Apr;161(4):929-38. doi: 10.1007/s00705-016-2749-3. Epub 2016 Jan 18. https://pubmed.ncbi.nlm.nih.gov/26780775/.

Gilbert, M. E. (2024). The APL Product Reference Nutritional Health Guide, 2nd Edition, Ageo Product Line, Acumullit SA Technology. AZ: Mary Esther Gilbert, Holistic Choices Publishing.

Hao Guo, Chang Liu, Qi Tang, Deyu Li, Yinsheng Wan, Jiu-Hong Li, Xing-Hua Gao, Navindra P. Seeram, Hang Ma, Hong-Duo Chen. Pomegranate (Punica granatum) extract and its polyphenols reduce the formation of methylglyoxal-DNA adducts and protect human keratinocytes against methylglyoxal-induced oxidative stress. *Journal of Functional Foods*. Volume 83. 2021. https://doi.org/10.1016/j.jff.2021.104564. https://www.sciencedirect.com/science/article/pii/S1756464621002139

Ismail, T., & Sestill P., Akhtar, S., (2012). Pomegranate peel and fruit extracts: a review of potential anti-infllammatory and anti-infective effects. *Journal of Ethnopharmacology,* 143(2):397-405. doi: 10.1016/j.jep.2012.07.004. Epub 2012 Jul 20.

Jug U, Naumoska K, Vovk I. (−)-Epicatechin—An Important Contributor to the Antioxidant Activity of Japanese Knotweed Rhizome Bark Extract as Determined by Antioxidant Activity-Guided Fractionation. *Antioxidants*. 2021; 10(1):133. https://doi.org/10.3390/antiox10010133

Khaw AK, Hande MP, Kalthur G, Hande MP. Curcumin inhibits telomerase and induces telomere shortening and apoptosis in brain tumour cells. J Cell Biochem. 2013 Jun;114(6):1257-70. doi: 10.1002/jcb.24466. https://pubmed.ncbi.nlm.nih.gov/23192708/

*Larch*. Drugs.com. (2024). https://www.drugs.com/npp/larch.html

Lavoro, A., Falzone, L., Gattuso, G., Salemi, R., Cultrera, G., Leone, G. M., Scandurra, G., Candido, S., Libra, M. Pomegranate: A promising avenue against the most common chronic diseases and their associated risk factors (Review). *International Journal of Functional Nutrition*. Volume 2, Issue 2. March-April 2021. https://doi.org/10.3892/ijfn.2021.16. https://www.spandidos-publications.com/10.3892/ijfn.2021.16.

Lekli I, Ray D, Das DK. Longevity nutrients resveratrol, wines and grapes. Genes Nutr. 2010 Mar;5(1):55-60. doi: 10.1007/s12263-009-0145-2. Epub 2009 Sep 4. https://pmc.ncbi.nlm.nih.gov/articles/PMC2820197/.

Loers G, Yashunsky DV, Nifantiev NE, Schachner M. Neural cell activation by phenolic compounds from the Siberian larch (Larix sibirica). *J Nat Prod.* 2014 Jul 25;77(7):1554-61. doi: 10.1021/np4009738. Epub 2014 Jun 25. PMID: 24963869. Neural cell activation by phenolic compounds from the Siberian larch (Larix sibirica) - PubMed. https://www.researchgate.net/publication/263394211_Neural_Cell_Activation_by_Phenolic_Compounds_from_the_Siberian_Larch_Larix_sibirica

Mayo Clinic. (1998-2017). Milk thistle (Silybum marianum). Retrieved from http://www.mayoclinic.org/drugs-supplements/milk-thistle/evidence/hrb-20059806

Mirmiran, P., & Fazeli, M. R., Asghari, G., Shafiee, A., Azizi, F. (2010). Effect of pomegranate seed oil on hyperlipidaemic subjects: a double-blind placebo controlled clinical trial. *Br J Nutr,* 104(3): 402-6. doi: 10.1017/S0007114510000504. Epub 2010 Mar 25

Myungsuk Kim, Sun Young Kim, Ahmad Randy, Sue Ji Lim, Banzragch Dorjsembe, Chu Won Nho, Inhibitory effect of the Larix sibirica and its various flavonoids on the IgE-stimulated mast cell activation and anaphylaxis. *Journal of Functional Foods*. Volume 27. 2016, Pages 631-644. https://doi.org/10.1016/j.jff.2016.10.009. https://www.sciencedirect.com/science/article/pii/S175646461630322X. https://www.researchgate.net/publication/364151695_Actual_prospects_of_using_some_types_of_larch_growing_in_Kazakhstan_in_medicine

Nawrot-Hadzik I, Hadzik J, Fleischer M, Choromańska A, Sterczała B, Kubasiewicz-Ross P, Saczko J, Gałczyńska-Rusin M, Gedrange T, Matkowski A. Chemical Composition of East Asian Invasive Knotweeds, their Cytotoxicity and Antimicrobial Efficacy Against Cariogenic Pathogens: An In-Vitro Study. *Med Sci Monit*. 2019 May 4;25:3279-3287. doi: 10.12659/MSM.913855. https://pmc.ncbi.nlm.nih.gov/articles/PMC6512351/

Ndiaye M, Philippe C, Mukhtar H, Ahmad N. The grape antioxidant resveratrol for skin disorders: promise, prospects, and challenges. *Archives in Biochem and Biophys*. 2011 Apr 15;508(2):164-70. doi: 10.1016/j.abb.2010.12.030. Epub 2011 Jan 4. https://pmc.ncbi.nlm.nih.gov/articles/PMC3060966/.

Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. *J Nutr Sci*. 2016 Dec 29;5:e47. doi: 10.1017/jns.2016.41. PMID: 28620474; PMCID: PMC5465813. https://pmc.ncbi.nlm.nih.gov/articles/PMC5465813/

Pawlikowski JS, Adams PD, Nelson DM. Senescence at a glance. J Cell Sci. 2013 Sep 15;126(Pt 18):4061-7. doi: 10.1242/jcs.109728. Epub 2013 Aug 22. https://pmc.ncbi.nlm.nih.gov/articles/PMC3772382/

PDQ Integrative, Alternative, and Complementary Therapies Editorial Board. Milk Thistle (PDQ®): Health Professional Version. 2018 Aug 17. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002-.Available from: https://www.ncbi.nlm.nih.gov/books/NBK65780/

Petersen, K. S., Smith, C. Ageing-Associated Oxidative Stress and Inflammation Are Alleviated by Products from Grapes. Oxidative Medicine and Cellular Longevity.
*Medicinal Plants in Therapy: Antioxidant Activities*. Volume 2016, Article ID 6236309, 12 pages. February 2016. https://onlinelibrary.wiley.com/doi/epdf/10.1155/2016/6236309

Plant J (2016) Effects of Essential Oils on Telomere Length in Human Cells. Med Aromat Plants 5: 230. doi:10.4172/2167-0412.1000230. https://www.longdom.org/open-access-pdfs/effects-of-essential-oils-on-telomere-length-in-human-cells-2167-0412-1000230.pdf
Siegel, A. B., & Stebbing, J. (2013). Milk thistle: Early seeds of potential. *The Lancet. Oncology,14*(10), 929-930. doi:10.1016/S1470-2045(13)70414-5

Sayakova G, Boshkayeva A, Ibadullayeva G, Khamitova A, Begimova G. Actual prospects of using some types of larch growing in Kazakhstan in medicine. *J Med Life*. 2022 Aug;15(8):1038-1046. doi: 10.25122/jml-2021-0373. PMID: 36188655; PMCID: PMC9514822. https://pmc.ncbi.nlm.nih.gov/articles/PMC9514822/

Singh, S., & Jogdand, S. (2021). Black Pepper: Its Health Benefits. *Journal of Pharmaceutical Research International*, *33*(60B), 2043–2049. https://doi.org/10.9734/jpri/2021/v33i60B34843. https://journaljpri.com/index.php/JPRI/article/view/6901

Song, J.H., Kim, S.K., Chang, K. W., Han, S.K., Yi, H. K., Jeon, J.G. In vitro inhibitory effects of Polygonum cuspidatum on bacterial viability and virulence factors of *Streptococcus mutans* and *Streptococcus sobrinus*. *Archives of Oral Biology*. Volume 51, Issue 12. 2006. Pages 1131-1140. https://doi.org/10.1016/j.archoralbio.2006.06.011. https://www.sciencedirect.com/science/article/pii/S0003996906001609.

Vostálová J, Tinková E, Biedermann D, Kosina P, Ulrichová J, Rajnochová Svobodová A. Skin Protective Activity of Silymarin and its Flavonolignans. *Molecules*. 2019 Mar 14;24(6):1022. doi: 10.3390/molecules24061022. https://pmc.ncbi.nlm.nih.gov/articles/PMC6470681/.

Vyas, K. (2015). The Cure is in the Roots: Turmeric. *Journal of Nutritional Disorders & Therapy,* 5(3): 1-6. doi: 10.4172/2161-0509.1000163. https://www.walshmedicalmedia.com/open-access/the-cure-is-in-the-roots-turmeric-2161-0509-1000163.pdf.

Wang K, Wang RL, Liu JJ, Zhou J, Li X, Hu WW, Jiang WJ, Hao NB. The prognostic significance of hTERT overexpression in cancers: A systematic review and meta-analysis. Medicine (Baltimore). 2018 Aug;97(35):e11794. doi: 10.1097/MD.0000000000011794. https://pmc.ncbi.nlm.nih.gov/articles/PMC6392887/#:~:text=hTERT%20is%20the%20rate%2Dlimiting,telomerase%20activity%20in%20most%20cancers.&text=It%20was%20hypothesized%20that%20the,predict%20the%20survival%20of%20cancer.

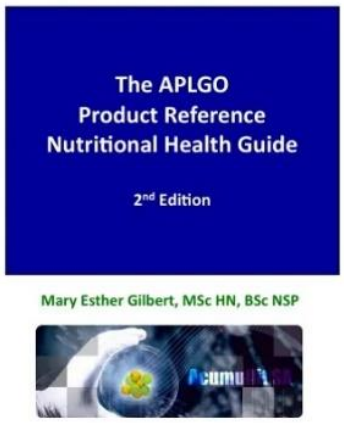
Wang ZJ, Trill J, Tan LL, Chang WJ, Zhang Y, Willcox M, Xia RY, Jiang Y, Moore M, Liu JP, Hu XY. *Reynoutria japonica* Houtt for Acute Respiratory Tract Infections in Adults and Children: A Systematic Review. *Front Pharmacol*. 2022 Feb 24;13:787032. doi: 10.3389/fphar.2022.787032. https://pmc.ncbi.nlm.nih.gov/articles/PMC8911541/.

Wonderful Variety Pomegranate Research. (2013). All Studies on the Wonderful Variety Pomegranate. Antioxidants and Bioavailability. Retrieved from: www.wonderful pomegranateresearch.com/studies/html

Wu S, Tian L. Diverse Phytochemicals and Bioactivities in the Ancient Fruit and Modern Functional Food Pomegranate (*Punica granatum*). *Molecules*. 2017; 22(10):1606. https://doi.org/10.3390/molecules22101606.

## The New APLGO BOOK 2nd Edition is Now Available for APLGO Associates

Please allow at least 3 weeks for order processing, printing, and delivery.




**Order the Printed Version**

**Use this Private Link:**
https://www.holisticchoices.com/product-page/the-aplgo-product-reference-nutritional-health-guide

**eBook PDF Format**

**To order, use this private link:**
https://www.holisticchoices.com/product-page/the-aplgo-product-reference-nutritional-health-guide-2nd-edition

**Contact**

**https://www.holisticchoices.com/contact**