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Ginseng- Multipurpose Herb

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ABSTRACT:
Ginseng is the most popular herb. Ginseng is often referred as the ultimate tonic; the herb boosts general well-being, immune function, libido, and athletic performance. Ginseng is popularly used for its adaptogenic, antineoplastic, immunomodulatory, cardiovascular, CNS, endocrine, and ergogenic effects, but these uses have not been confirmed by clinical trials. A number of ginseng species used in herbal products grow around the world. Some of these plants include American ginseng, Korean ginseng, Sanchi ginseng, Chikusetsu ginseng. Ginseng is also known as Siberian ginseng, devil's shrub, eleuthero, touch-me-not, and wild pepper. Ginseng has been used to improve the body's resistance to stress and to increase vitality. However, the mechanisms underlying ginseng's effects remain to be investigated. Biological effects of ginseng are due to its anti-inflammatory effects, antineurological effect, hypoglycemia effect. Research has shown that drinking a cup of hot ginseng tea has an anti-inflammatory effect.

INTRODUCTION:

Ginseng is one of the most popular and widely available of all herbal supplements. A common name for ginseng is "man-root" because of its resemblance to the human body. The name also implies that it has benefits for the whole body. Ginseng is each of eleven species of slow-growing perennial plants with fleshy roots, in the *Panax* genus, in the family Araliaceae. It grows in the Northern Hemisphere in eastern Asia (mostly northern China, Korea, and eastern Siberia), typically in cooler climates; *Panax vietnamensis*, discovered in Vietnam, is the southernmost ginseng found. This article focuses on the Series Panax ginsengs, which are the adaptogenic herbs, principally *Panax ginseng* and *P. quinquefolius*.

MAJOR SPECIES OF GINSENG:

1. Panax Quinquefolium is American ginseng found in North America, cultivated mainly in Wisconsin. The term 'Panax' is a combination of two Greek words; pan or 'all' and akos or 'cure', which fully translated means 'cure all'.
2. Panax Ginseng; Korean, Asian, or Chinese ginseng cultivated in Korea, Manchuria, and china.
3. Panax Trifolium, also called Dwarf Ginseng and Ground Nut, is much smaller than Panax Quinquefolium American Ginseng, and at one time, was harvested by Indians and settlers for food.
4. Panax Pseudo ginseng, also called Himalayan Ginseng, Panax Notoginseng or Tien Chi Ginseng. It is found in Korea, China and Japan.
5. Panax Japonicum, called Japanese ginseng, is found in Japan.
6. Eleutherococcus Senticosus, or Siberian Ginseng, is not considered 'true' ginseng and does not contain ginsenosides as does the Panax varieties. Its active substance is called eleutheroside.

COMMON CLASSIFICATION:

1. *P. quinquefolius* American ginseng (root)

American ginseng promotes Yin (shadow, cold, negative, female) while East Asian ginseng promotes Yang (sunshine, hot, positive, male). This is because, according to traditional Chinese medicine, things living in cold places or northern side of mountains or southern side of rivers are strong in Yang and vice versa, so that the two are balanced. Chinese/Korean ginseng grows in northeast China and Korea, the coldest area known to many Koreans in traditional times. Thus, ginseng from there is

supposed to be very *Yang*. Originally, American ginseng was imported into China via subtropical Guangzhou, the seaport next to Hong Kong, so Chinese doctors believed that American ginseng must be good for *Yin*, because it came from a hot area.Nonetheless the root is legitimately classified as more *Yin* because it generates fluids. The two main components of ginseng are in different proportions in the Asian and American varieties, and may well be the cause of the excitatory versus tonic natures.[3] The ginseng is sliced and a few slices are simmered in hot water to make a decoction. Most North American ginseng is produced in the Canadian provinces of Ontario and British Columbia and the American state of Wisconsin, according to Agri-food Canada. *P. quinquefolius* is now also grown in northern China. A randomized, double-blind study shows that an extract of American ginseng reduces influenza cases in the elderly when compared to placebo.[1]

2. *Panax ginseng* Asian ginseng (root)

According to Traditional Chinese Medicine Panax Ginseng promotes Yang energy, improves circulation, increases blood supply, revitalizes and aids recovery from weakness after illness, and stimulates the body. Panax Ginseng is available in two forms:

The form called white ginseng is grown for four to six years, and then peeled and dried to reduce the water content to 12% or less. White Ginseng is air dried in the sun and may contain less of the therapeutic constituents. It is thought by some that enzymes contained in the root break down these constituents in the process of drying. Drying in the sun bleaches the root to a yellowish-white color. The form called red ginseng is harvested after six years, is not peeled and is steam-cured, thereby giving them a glossy reddish-brown coloring. Steaming the root is thought to change its biochemical composition and also to prevent the breakdown of the active ingredients. The roots are then dried.

a. Red ginseng

Red ginseng is *P. ginseng* that has been heated, either through steaming or sun-drying. It is frequently marinated in an herbal brew which results in the root becoming extremely brittle. This version of ginseng is traditionally associated with stimulating sexual function and increasing energy. Red ginseng is always produced from cultivated roots, usually from either China or South Korea. In 2002, a preliminary double-blind, crossover study of Korean red ginseng's effects on impotence reported that it can be an effective alternative for treating male erectile dysfunction.[2] A study shows that Red ginseng reduces the relapse of gastric cancer versus control.[3] A study of ginseng's effects on rats shows that while both white ginseng and red ginseng reduce the incidence of cancer, the effects appear to be greater with red ginseng.[3] Falcarinol, a seventeen-carbon diyne fatty alcohol was isolated from carrot and red ginseng, shown to have potent anticancer properties on primary mammary epithelial (breast cancer) cells.[4] Other acetylenic fatty alcohols in ginseng (panaxacol, panaxydol, panaxytriol) have antibiotic properties.[5]

b.Wild ginseng

Wild ginseng is ginseng that has not been planted and cultivated domestically, rather it is that which grows naturally and is harvested from wherever it is found to be growing. Wild ginseng is relatively rare and even increasingly endangered, due in large part to high demand for the product in recent years, which has led to the wild plants being sought out and harvested faster than new ones can grow (it requires years for a ginseng root to reach maturity). Wild ginseng can be either Asian or American

and can be processed to be red ginseng. There are woods grown American ginseng programs in Maine, Tennessee, Virginia, North Carolina and West Virginia. [6,4] and United Plant Savers has been encouraging the woods planting of ginseng both to restore natural habitats and to remove pressure from any remaining wild ginseng, and they offer both advice and sources of rootlets.

MODERN SCIENCE AND GINSENG:

It has been difficult to verify the medicinal benefits of ginseng using science, as there are contradictory results from different studies, possibly due to the wide variety and quality of ginseng used in studies. High-quality studies of the effects of ginseng are rare.[7] Ginseng is promoted as an adaptogen (a product that increases the body's resistance to stress), one which can to a certain extent be supported with reference to its anticarcinogenic and antioxidant properties,[8] although animal experiments to determine whether longevity and health were increased in the presence of stress gave negative results.[11] A comparative, randomized and double-blind study at the National Autonomous University of Mexico indicates it may be "a promising dietary supplement" when assessed for an increase in quality of life .[12] A recent study at the University of Hong Kong has identified Ginseng to have anti-inflammatory effects. The study found that out of the nine ginsenosides they identified, seven could selectively inhibit expression of the inflammatory gene CXCL-10. [13] *P. ginseng* appear to inhibit some characteristics associated with cancer in animal models; nevertheless, this effect is unclear in humans.[14] A randomized, double-blind pilot study noted ginseng appeared to reduce fatigue in cancer patients.[15]

CHEMICAL CONSTITUENTS:

Like *Panax ginseng*, American ginseng contains dammarane-type ginsenosides as the major biologically active constituents. Dammarane type ginsenosides include two classifications: the 20(S)-protopanaxadiol (ppd) and 20(S)-protopanaxatriol (ppt) classifications. American ginseng contains high levels of Rb1, Rd (ppd classification) and Re (ppt classification) ginsenosides—higher than that of P. ginseng in one study[16] Like P. ginseng, P. quinquefolius and P. vietnamensis, notoginseng contains dammarane-type ginsenosides as the major constituents. Dammarane type ginsenosides includes 2 classifications: the 20(S)-protopanaxadiol (ppd) and 20(S)-protopanaxatriol (ppt) classifications. P. notoginseng contains high levels of Rb1, Rd (ppd classification) and Rg1 (ppt classification)ginsenosides. Rb1, Rd and Rg1 content of P. notoginseng is found to be higher than that of P. ginseng and P. quinquefolius in one study.[16]

APPLICATION OF GINSENG:

1) Antiparkinson's effects of ginseng:

Recently, it has been shown that ginseng and its components, ginsenosides, have a wide range of actions in the central nervous system [19]. These effects include increased cell survival, extension of neurite growth and rescuing of neurons from death due to different insults either in vivo or in vitro. Sugaya et al. [20], Himi et al. [17] and Mizumaki et al. [21] reported that ginseng roots appeared to facilitate survival and neurite extension of cultured cortical neurons and Kim et al. [22] showed that ginsenosides Rb1 and Rg3 protected neurons from glutamate-

induced neurotoxicity. Following forebrain ischemia in gerbils, Wen et al. [18] and Lim et al. [23] demonstrated that central infusion of ginsenoside Rb1 rescued the hippocampal CA1 neurons against lethal damage of cellular hypoxia. Using a spinal neuron model, ginsenosides Rb1 and Rg1 proved to be potentially effective therapeutic agents for spinal cord injuries as they protected spinal neurons from excitotoxicity induced by glutamate and kainic acid, and oxidative stress induced by hydrogen peroxide [24].A number of studies have recently described the beneficial effect of ginseng and its main components, ginsenosides, on some neurodegenerative disease models. Special interest has been paid to Parkinson's disease (PD) models either in vivo or in vitro. In an in vivo model, Van Kampen et al. [19] reported that prolonged oral administration of ginseng extract G115 significantly protected against neurotoxic effects of parkinsonism- inducing agents such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and its active metabolite 1- methyl-4-phenylpyridinium (MPP+) in rodents. He found that ginseng-treated animals sustained less damage and TH+ neuronal loss in substantia nigra pars compacta (SNpc) after MPP+ exposure. Likewise reduction of TH immunoreactivity in striatum was effectively diminished as a result of ginseng treatment compared to MPP+ exposed animals. Similarly, striatal dopamine transporter (DAT) was significantly preserved due to ginseng treatment. In *in vitro* studies, it has been shown that ginseng saponins enhanced neurite growth of the dopaminergic SK-N-SH neuroblastoma cells [25]. As mentioned above, we showed recently that ginsenosides Rb1 and Rg1 increased the survival of primary cultured dopaminergic cells and promoted their neuritic growth after exposure to either MPP+ or glutamate [26, 27] .Interestingly, Tanner and Ben-Schlomo [28] speculated that geographic variations in PD prevalence might reflect ginseng consumption as in North America, PD occurs in approximately 200 cases per 100,000 persons compared to only 44 cases per 100,000 in China.

2) CVS effects of ginseng:

Ginseng has been shown to produce a number of actions on the cardiovascular system. Intravenous administration of ginseng to anaesthetized dogs resulted in reduction, followed by an increase in blood pressure, and transient vasodilatation [29]. In rats and rabbits, Lei and Chiou [30] and Kim et al. [31] found that extracts of Panax notoginseng decreased systemic blood pressure and ginsenosides exerted relaxing effects in rings of rat and rabbit aorta, respectively. This relaxing effect of ginseng and its active constituents on the cardiovascular system is partially due to the release of endothelial NO. Researchers have reported that chronic feeding of rabbits with ginsenosides may enhance indirectly vasodilatation by preventing NO degradation by oxygen radicals such as superoxide anions [32]. Ginsenosides have depressant action on cardiomyocyte contraction which may be mediated, in part, through increased NO production [33]. Korean red ginseng can improve the vascular endothelial dysfunction in patients with hypertension possibly through increasing NO [34]. In addition to endothelium- derived NO release, Li et al. [35] reported that ginsenosides-induced vasorelaxation also involves Ca2+ activated K+ channels in vascular smooth muscle cells. It has also been reported that crude saponin fractions of

Korean red ginseng enhanced cerebral blood flow in rats [36] and ginsenosides reduced plasma cholesterol levels and the formation of atheroma in the aorta of rabbits fed on a high cholesterol diet [32]. This ntiatherosclerotic action of ginseng components is apparently due to the correction in the balance between prostacyclin and thromboxane [37], inhibition of 5- hydroxytryptamine (5-HT) release from, and adrenaline and thrombin-induced aggregation of platelets [38], regulation of cGMP and cAMP levels and prolongation of the time interval between conversions of fibrinogen to fibrin [39]. Also, ginsenosides have been shown to be relatively potent platelet activating factor antagonist [41]. In parallel with these findings, Nakajima et al. [40] found red ginseng to promote the proliferation of vascular endothelial cells, to inhibit the production of endothelin which is known to constrict blood vessels resulting in raising blood pressure and to increase the production of interleukin 1 beta, which suppresses the formation of thrombin in blood coagulation. In the same direction, Yuan et al. [42] used cultured human umbilical vein endothelial cells to conclude that American ginseng, *Panax quinquefolium* L. extracts, significantly decreased endothelin concentration in a dose and time dependent manner after thrombin treatment. The role of ginseng in angiogenesis has also been studied. Ginsenoside Rg1 promoted functional neovascularization into a polymer scaffold in vivo and tubulogenesis by endothelial cells in vitro [43]. Therefore, ginsenoside Rg1 might be useful in wound healing as it can induce therapeutic angiogenesis.

3) Anti-inflammatory and Anti-allergic effects of ginseng

More recently, the role of ginseng in modulation of inflammatory and allergic processes has been documented by some researchers. For example, Ginseng root saponins exerted an inhibitory effect on IL-1β and IL-6 gene expression in a chronic inflammation model of aged rats, ginsenosides Rb1 and Rg1 decreased TNF-α production by murine macrophages, pretreatment with ginsenoside Rg3 abrogated cyclooxygenase-2 expression in response to 12-0-tetradecanoylphorbol-13- acetate (TPA) in mice skin and in senosides Rb1 and Rc suppressed histamine and leukotrienes release during the activation of guinea pig lung mast cells in vitro [44-47]. An additional anti-inflammatory action by ginseng has been mentioned by Li and Li [48]. They reported that total saponins of Sanchi (Panax pseudo-ginseng notoginseng) reduced the level of the intracellular Ca2+ concentration in neutrophils and Kim et al. [49] found that ginseng had radioprotective effect against γ-rayinduced DNA double strand breaks in cultured murine spleen lymphocytes. Furthermore, it was found that ginseng promoted apoptosis in renal interstitial fibroblasts and thus could affect renal interstitial fibrosis [50]. Ginseng also has immunostimulant effects as it enhances interferon induction, phagocytosis, natural killer (NK) cell, and B and T cells in various animal species including mice and guinea pigs and also in humans [51-54]. Hu et al. [55] reported that ginseng stimulated the immune system of dairy cows as it activated the innate immunity of cows and contributed to the cow's recovery from mastitis.

4) Anti-carcinogenic effect of ginseng:

Researchers have reported that chronic intake of Panax ginseng C. A. Meyer decreased the incidence of cancers such as lung, gastric, liver and colorectal tumors [56,57]. Ginsenoside Rh2 has been shown to suppress proliferation in a number of human cancer cells including breast, prostate, hepatic and intestinal cancer, but also in animal cell lines [58-61].

Ginsenosides Rb1, Rb2 and Rc inhibited tumor angiogenesis and metastasis [62] while ginsenoside Rh1 inhibited proliferation of the NIH 3T3 mouse fibroblast cell line [63]. Some of the mechanisms and processes underlying the former beneficial effects of ginseng against cancer have been stated by Surh et al. [64] and others. Using both in vivo and in vitro models, Surh et al [64] reported that ginsenoside Rg3 treatment caused marked suppression of TPA-induced cyclooxygenase-2 (COX- 2) expression in mouse skin and in human breast epithelial cells (MCF-10A). Also, he observed the same suppressive effect on NF-κB in mouse skin and extracellular regulated protein kinases (ERK) activation in TPAstimulated MCF-10A cells. Consistent with the results of Surh et al. [64], Keum et al. [65] reported that topical application of ginseng extract prior to each topical dose of the tumor promoter TPA markedly lowered the papilloma formation in mouse skin and caused substantial reduction in epidermal ornithine decarboxylase (ODC) activity and suppressed the expression of its mRNA. All of the above mentioned enzymes and factors are, in part, involved in tumorogenesis. COX-2 was upregulated in transformed cells and in various forms of cancer. Its overexpression inhibited apoptosis and increased the invasiveness of tumor cells [66]. ODC is a rate-limiting enzyme in the biosynthesis of polyamines that play a pivotal role in cell proliferation and tumor promotion [67]. Mitogen-activated protein kinase (MAPK) cascade is responsible, in part, for upregulation of COX-2 as specific inhibitors of the corresponding MAPK abolish the induction of COX-2 and result in production of prostaglandin E2 [64]. NF-κB is a ubiquitous eukaryotic transcription factor implicated in cellular proliferation and malignant transformation. Its activation is an essential early event prior to malignant transformation by inhibiting cell death signal activated by oncogenic Ras [68].

5) Ginseng on Hyperglycemia:

Studies have shown that ginseng and its components attenuate hyperglycemia in two ways, the first through enhancing pancreatic β-cell function and the other through reducing insulin resistance. This leads us to believe that ginseng may have benefits for both type I and type II diabetes. American ginseng root extracts have been shown to affect pancreatic β-cells through altering cell metabolism, increasing insulin production and reducing apoptosis in a dosage dependent manner [73] Ginseng extracts were able to enhance ATP production and in turn increase insulin production, as insulin deficiency is often linked to a lack of ATP produced [74,75]Along with an increase in ATP production, ginseng reduced mitochondrial protein UCP-2, which negatively regulates insulin secretion [71,76-79] Aside from affecting insulin production, ginseng may have the ability to target various glucose receptors, creating an antilipolytic effect, thus attenuating hyperglycemia [70,80] This suggests that there exist other pathways through which ginseng acts through. Overall, ginseng is able to enhance insulin production through regulating cell metabolism. Though UCP-2 regulates insulin secretion, it has also been reported to decrease cell longevity[81]. Apoptosis is one of the common causes of cell death in pancreatic β-cells. Resulting in the destruction of genetic material, apoptosis is regulated by factors such as Bcl-2, which protects against apoptosis and Caspase-3/9, which promotes death through the caspase cascade [69,82,83] American ginseng reduces apoptosis by promoting caspase-3/9 and enhanced cell protective Bcl-2 protein levels, resulting in protecting cells against apoptosis .Preventing apoptosis allows for

further cell function and insulin production in pancreatic β-cells. Aside from affecting cell metabolism and longevity, ginseng has the ability to change neuropeptide through Rh2, a ginsenoside derived from Panax ginseng, in STZ-diabetic rats. Rh2 lowered plasma glucose due to an increase in beta-endorphin secretion that activates opioid mu-receptors thereby resulting in an increased expression of GLUT 4, a glucose transporter in fat and muscle tissue [72]. Protopanaxatriol, a ginsenoside metabolite, also increased GLUT4 and improved insulin resistance.The up-regulation of GLUT-4 signalizes that ginseng has an effect on fat/muscle tissue, possibly decreasing insulin resistance.

SIDE EFFECTS:

a) Major side effects

Infants given Panax ginseng may develop a condition, resembling alcohol intoxication that has lead to at least one reported death of a newborn.Rarely, taking Panax ginseng by mouth has been associated with non-infectious hepatitis. In other rare reports, Panax ginseng may have caused inflammation of blood vessels in the brain – a condition that could result in headaches or strokes.One case has been reported of an individual who developed anaphylaxis-like symptoms shortly after ingesting a small amount of Panax ginseng syrup. Anaphylaxis is a potentially life-threatening allergic reaction that may involve the development of a rash or hives, a sudden fall in blood pressure, swelling of the mouth and throat, or unconsciousness.

b) Less severe side effects

Other side effects associated with taking Panax Ginseng are generally mild and temporary. They usually diminish after a few days and they may include:

- Blood pressure changes
  • Insomnia
- Breast pain
  • Heart rate changes.
- Diarrhea Itching
  •Itching
- Dizziness
  • Loss of appetite
- Headache
  • Nervousness
- Mood changes

In very rare cases, Panax ginseng may have caused a very serious skin reaction called Stevens - Johnson syndrome. A doctor should be contacted right away if a high fever, swollen eyelids, blisters in the mouth, or red marks on the skin develop while Panax ginseng is taken.

DRUGS AFFECT GINSENG:

- Any heart or blood pressure medicines; a medicine to control blood sugar levels such as insulin, glipizide (Glucotrol), glyburide (Glynase, Diabeta, Micronase), chlorpropamide (Diabinese), tolbutamide (Orinase), tolazamide (Tolinase), troglitazone (Rezulin), rosiglitazone (Avandia), repaglinide (Prandin), metformin (Glucophage), and others; warfarin (Coumadin);
- A nonsteroidal anti-inflammatory drug (NSAID) including ibuprofen (Advil, Motrin, Nuprin, others), naproxen (Aleve, Naprosyn, Naprelan, Anaprox, others), ketoprofen (Orudis KT, Orudis), indomethacin (Indocin), etodolac

(Lodine), nabumetone (Relafen), oxaprozin (Daypro), piroxicam (Feldene), sulindac (Clinoril), tolmetin (Tolectin).

CONTRAINDICATIONS:

Hypersensitivity to any of the components of ginseng. Ginseng is contraindicated in patients who take warfarin, loop diuretics, or phenelzine. Patients with high blood pressure should not take ginseng and patients who must control their blood glucose level should use ginseng with caution. One postmarketing report documents an anaphylactic-like reaction (mouth and tongue swelling) with the use of CVT-E002. CVT-E002 should be avoided in autoimmune diseases such as inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, and systemic lupus erythematosus. Patients with allergic rhinitis, asthma, or eczema should avoid using ginseng products.

CONCLUSION:

The active ingredients of ginseng are ginsenosides which are also called ginseng saponins. Recently, there is increasing evidence in the literature on the pharmacological and physiological actions of ginseng. Ginseng had been used primarily as a tonic to invigorate week bodies and help the restoration of homeostasis. However current in vivo and in vitro studies have shown its beneficial effects in a wide range of pathological conditions such as cardiovascular diseases, cancer, immune deficiency and hepatotoxicity. Moreover, recent research has suggested that some of ginseng's active ingredients also exert beneficial actions on aging, CNS disorders and neurodegenerative diseases. In general, antioxidant, anti-inflammatory, anti-apoptotic and immunostimulant activities are mostly underlying the possible ginseng-mediated protective mechanisms. Based on limited animal research and anecdotal reports of nosebleeds and vaginal bleeding in humans, ginseng may increase the risk of bleeding when taken with herbs and supplements that are believed to increase the risk of bleeding. Scientific research is now providing preliminary evidence supporting its medicinal potential in a variety of body systems and disorders.

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