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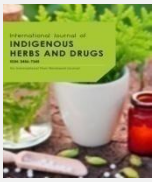

PANAX GINSENG: THE MEDICINAL HERB

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Abstract

Panax ginseng, particularly valued in China and Korea, has long been considered a "paternal herb" in traditional medicine. First recorded in the Shennong Herbal Classic around 200 AD, it is attributed to Shennong, one of the "Three Emperors" of ancient China, who is believed to have pioneered herbal medicine over 5,000 years ago. Recognized as a modern tonic and traditional complementary medicine, Panax ginseng contains ginseng saponins (GS), which are the main bioactive compounds. These saponins exhibit hypoglycemic effects, support wound healing, and have demonstrated superior anticancer properties compared to Panax quinquefolium. Ginseng is considered safe with minimal reported side effects, prompting the development of various analytical techniques, especially high-performance liquid chromatography, to study its complex composition. Ginseng's pharmacological potential has led to its use in clinical research, particularly in exploring its chemopreventive, anti-inflammatory, and immunosuppressive effects. These properties suggest applications in treating inflammatory conditions and boosting overall immune health.Despite its historical use and promising properties, clinical evidence, especially regarding ginseng's efficacy in treating erectile dysfunction, remains inconclusive due to small sample sizes and subjective results in human trials. Still, growing interest in herbal alternatives is driving further research. With well-designed, large-scale clinical trials and stricter safety standards, ginseng holds strong potential as a validated alternative therapy in modern healthcare.For centuries, humans have relied on plants like ginseng not just for medicine but also for food, cosmetics, and overall wellness, reinforcing its continued relevance in both traditional and modern practices.

Keywords: Panax ginseng, Ginseng saponins (GS), Traditional complementary medicine, Anticancer effects, High-performance liquid chromatography (HPLC), Chemo preventive effects.

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Introduction

panax ginseng is widely used as a physical, chemical and biological resistance enhancer. Regulating blood lipid and decreasing blood sugar levels. Cancer prevention, liver, kidney and heart protection and immunostimulatory effects. [1-3]. Seng extract could be used as a natural feed additive in poultry feed due to the phenolic compound contained in it because of its strong antioxidant,anti-radical, antimicrobial, mineral and High vitamin content. The present research was conducted to determine the effect of supplementing graded level of a commercial PGLE on egg production performance, egg quality and some blood serum biochemical parameters in laying hens at 20 week of age [4].

Panax ginseng is one of the most widely used herbs in the world. it has been frequently used in East Asia since ancient times based a traditional Asian medicine theory and clinical experience-[5]. In recent years many clinical trials have been conducted to reveal the efficacy of panax ginseng has effect on pathological conditions, such as ischemic heart disease, common cold, obstructive pulmonary disease, and erectile dysfunction [6-9]. It is commonly believed that most pharmacological effect of panax ginseng are attributed to ginsenosides including the stimulatory and inhibitory effect on the nervous system, antineoplastic effect, immunomodulatory effect, and nitric oxide release [6-10].

Ginseng is believed to improve energy, physical and emotional health, and wellbeing. Central nervous system and to have antioxidant and anti-inflammatory properties, as well as cortisol - modulating effect [11-14]. It has been used to treat a variety of disorders including anaemia, insomnia, dystonia , memory impairment, confusion, decreased libido, chronic fatigue, angina, diabetes mellitus and herpes simplex type-II infection [15-16].

SAFETY AND EFFICACY OF P. GINSENG DURING PREGNANCY AND LACTATION

Panax should be eaten with caution during pregnancy, particularly during the first trimester, and throughout nursing. Ginseng is not regarded as a plant unique to women's health difficulties However; the wide popularity will unavoidably include its use by women of reproductive age and those who may be pregnant. Ginseng saponins, particularly ginsenosides Rg1,Rg2,Rd,Rf, and Re, have been demonstrated to trigger a significant recovery of cerebellar growth [17]. The researchers were unable to confirm whether the claims made by Chinese herbalists on the efficacy of panax ginseng in pregnancy were true or not.(18). The authors reported no harmful effects linked with the usage of panax ginseng during breastfeeding [3]. Panax ginseng has been linked to hypertension, diarrhoea, insomnia, mastalgia, eruptions, and vaginal bleeding [19]. This plant is not especially utilised during pregnancy or lactation.

1. **Limited Breastfeeding Data**
   There has been little research into the usage of Panax ginseng when breastfeeding. While lactating moms have traditionally utilised the plant, there is inadequate information to determine whether it goes into breast milk or what effects it may have on the infant.
2. **Potential risks: Infant Safety**
   Because of a lack of clear research, there is uncertainty about Panax ginseng's influence on newborn health, particularly its potential hormonal effects or impact on development. Effect on Milk Supply: Ginseng has been shown to have different effects on lactation. Some argue that it may boost milk production, while others believe it may have the reverse effect.

Panax ginseng clinical trials: current status and future perspectives

Diseases classification of R-GCTS

Among these trials we retrieved from ICTRp, the primary purpose of ginseng trials is the treatment of different diseases, including metabolic diseases, cardiovascular disorders, cognitive diseases, fatigue, cancer, sexual function, and pulmonary diseases (fight.2B). Removed 9 records which are difficult to classify by disease, we found that most of the R-GCTs researched in 37 trials for metabolic diseases (22.8), such as type 2 diabetes and impaired glucose tolerance . The cardiovascular disease, fatigue, sexual function, quality of life and cognitive diseases have similar count from 15 to 20 [20-21].

Current status of published ginseng clinical trials

Since lots of the registrars did not update the results of clinical trials in real-time, when they completed their researches. Therefore, we collected published clinical trials of ginseng to obtain current status and tract the conclusion of the efficacy of ginseng in different subjects. After removing the duplicates from 966 records are excluded from 345 p-GCTs: articles not be related to ginseng [102], animal or in vitro studies [68], systematic review articles [27], or no control group [4] are excluded as primary reason to retrieve144 records [22].

Panax ginseng: a network pharmacological approach

Respiratory Effects

P. ginseng is known to have a variety of effects on the respiratory system, particularly on asthma, and It also has antiallergic qualities. For instance, ovalbumin Sensitizes a murine model of chronic asthma. All of the chronic histopathologic alterations of the airways (the thicknesses of the basement membrane, epithelium, and subepithelial smooth muscle, as well as the quantity of goblet cells and mast cells) were considerably improved in the P. ginseng group as compared to the placebo group. Accordingly, P. ginseng was found to inhibit the generation of inflammatory cytokines, ovalbumin-specific IgE, and airway hyper responsiveness. Kim and Yang looked into the underlying mechanism and showed that P. ginseng decreased airway inflammation in a model of allergic asthma in mice. In addition to restoring the mRNA and protein levels of the cytokines [interleukin (IL)-1b, IL-4, IL-5, and tumor necrosis], the P. ginseng-treated group also restored the expression of inflammatory cells, including EMBP, Muc5ac, CD40, and CD40L [23-25]

Cardiovascular effects

Numerous effects on the cardiovascular system are also produced by P. ginseng. Research has indicated that P. ginseng may be effective in treating hypertension [56–60]. P. ginseng is recognized to help raise low blood pressure and lower high blood pressure by regulating blood pressure to normal. According to reports, encouraging the release of nitric oxide from vascular endothelial cells has the impact of controlling excessive blood pressure [62e64]. According to recent research, P. ginseng and angiogenesis are closely related [65, 66]. According to reports, P. ginseng and its ginsenosides influence several stages of angiogenesis, including preventing the growth of endothelial cells, the development of capillary tubes, and chemo invasion brought on by vascular endothelial growth factor (VEGF) . Choi et al. claim that Korean red ginseng extracts effectively reduce a number of angiogenic factors, including matrix metalloproteinases, VEGF, IL-6, IL-8, and hypoxia inducible factor-1a, suggesting the underlying mechanism of anti-angiogenesis.

Parkinson's Disease

According to a number of recent research, P. ginseng exhibits a variety of central nervous system functions, including encouraging results for Parkinson's disease. The neuroprotective properties of the P. ginseng extract were shown by Van et al. In animals used as models for chronic Parkinson's disease, it prevented the development of locomotor impairments by substantially decreasing

dopaminergic cell death. Hu et al. showed that P. ginseng water extract effectively shields mice from cytotoxic chemicals that cause parkinsonism, including 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine and its active metabolite 1-methyl-4-phenylpyridinium. It controlled the overproduction of reactive oxygen species, boosted the release of cytochrome c, reduced cell death, and raised the Bax/Bcl-2 ratio. 5.5. Pain P. ginseng has been shown to havepain-relieving properties.

Pain

P. ginseng has been reported to have pain-relieving properties According to Nah et al. ginsenosides may control, in a dose-dependent way, the behaviour of mice experiencing discomfort from capsaicin. In models of inflammatory pain in mice, Lee et al. showed that the fraction of P. ginseng has analgesic and anti-inflammatory properties. Using acetic acid-induced writhing and hot-plate experiments, Wang et al.demonstrated that glycoproteins isolated from P. ginseng had a dose-dependent analgesic effect in mice. A recent study also demonstrated P. ginseng's impact in animal models of neuropathic pain.

Panax ginseng components and the pathogenesis of Alzheimer's disease.

Neuronal ginsenosides and calcium ion levels, Numerous studies have examined the mechanism of neuronal injury brought on by an increase in intracellular calcium ion (Ca^{2+}) levels, which are triggered by glutamate. An increase in Ca^{2+} levels contributes to the excitotoxic process by excessively stimulating proteolytic enzymes, increasing lipid peroxidation, and increasing the production of ROS and nitrogen. Aβ increases the flow of calcium and starts neurodegeneration by phosphorylating already-existing calcium channels in addition to creating new ion channels in the cell membrane. Through MAPK, Aβ increases the phosphorylation of membrane-bound proteins and lowers that of cytosolic proteins, which raises the intracellular Ca^{2+} level [94]. In the PC12 cell model, ginsenoside Rg2 can significantly decrease the intracellular levels of Ca^{2+} and ROS brought on by Aβ [25–35]. Ginsenoside Rg2 has been shown in another investigation to lower lipid peroxidation as well as the Ca^{2+} level [26-29].

Ginsenosides and other factors

Neurotrophic hormones like BDNF and insulin-like growth factor-1 (IGF-1) can be inhibited by elevated Aβ levels. BDNF has been identified as a synapticplasticity regulator implicated in cognition and memory processes. It contributes to a number of the events that make up AD's pathogenic cascade [30]. Decreases in IGF-1 levels in the brain are thought to have a significant role in the development of Aβ deposition and cognitive impairment [31]. According to a study on a mouse model of AD, ginsenoside Rg5 can raise the expression of BDNF and IGF-1. In addition to raising BDNF expression in a transgenic mouse model of AD, ginsenoside Rg1 has also been shown to activate TrkB, the BDNF receptor, which in turn activates the BDNF/TrkB pathway . Only after the activation of four transcription factors, including CREB, does BDNF start to be effectively transcribed. Most of the time, changes in BDNF expression are largely caused by CREB failure. The primary mechanism by which CREB is activated is by PKA phosphorylation at Ser133, whose activity is inhibited in the AD model caused by Aβ [32].

Ginsenosides and individuals with Alzheimer's Disease

The most widely used set of criteria for diagnosing AD was developed by the Alzheimer's Disease Association and the American National Institute of Neurological and Communication Disorders and Stroke. Thus, the neuropsychological tests listed below are frequently used to evaluate cognitive impairment: The Mini-Mental Status Examination (MMSE) is one of the tests; the AD assessment scale (ADAS), which comprises the cognitive (ADAS-cog) and non-cognitive (ADAS-non-cog) subscales; the "Frontal Assessment Battery" (FAB) test is another; and the clinical dementia rating (CDR) is the last measurement .

AChE inhibitors have been shown in numerous long-term (more than two-year) studies to be effective, although they were unable to stop or reverse cognitive deterioration. The American National Institute of Neurological and Communication Disorders and Stroke and the Alzheimer's Disease Association created the most popular set of diagnostic standards for AD. Therefore, the following neuropsychological tests are commonly used to assess cognitive impairment: One of the tests is the Mini-Mental Status Examination (MMSE); another is the "Frontal Assessment Battery" (FAB); the final measurement is the clinical dementia rating (CDR); and the AD assessment scale (ADAS), which includes the cognitive (ADAS-cog) and non-cognitive (ADAS-non-cog) subscales [33-34].

Numerous long-term (greater than two-year) investigations have demonstrated the effectiveness of AChE inhibitors, despite their inability to prevent or reverse cognitive decline [35, 36]. In comparison to the initial estimate, the 2-year MMSE drop usually varied between 2.5 and 4.0 points. In patients on conventional medication, the typical picture of cognitive decline is an early improvement lasting three or six months, followed by a fall to baseline over around a year. After that, the illness worsens once more. In contrast, there was no discernible decline in the ADAS-cog and K-MMSE scores at the registration periods throughout the course of two years [37]. Ginseng and anticholinesterase have different primary mechanisms of action, which explains this clinical presentation. It has been examined how ginseng affects cognitive function and the underlying mechanisms of influence [38].

Effects on Physical Performance

No clinical benefit has been found in the majority of clinical research looking into Panax ginseng's potential to improve physical performance [14]. One study15 found no change in oxygen absorption, energy metabolic reactions, or physical work performance in 19 healthy adult women using 200 mg of G115 daily. Similarly, no change in physiologic or psychological responses to submaximal or maximal activity was observed in a trial of 31 healthy males who took 200 or 400 mg of G115 daily for eight weeks.16 [B-level evidence,

lower-quality RCT] Another study17 involved giving 28 healthy young adults a different product that was standardized to contain 7% ginsenosides at a daily dose of 200 mg for 21 days.

Effects on Immune System

Daily injection of 100 mg of G115 for 12 weeks improved the effectiveness of the polyvalent influenza vaccination, according to a study18 involving 227 healthy volunteers. The ginseng-treated individuals exhibited higher antibody titers, higher levels of natural killer cell activity, and a decreased incidence of colds and influenza. In a different study19, 60 healthy individuals who received 100 mg of G115 twice a day for eight weeks demonstrated improved phagocytosis, chemotaxis, total lymphocyte count, and T helper cell counts.

In a study of 75 patients treated with antibiotics or antibiotics with ginseng for acute exacerbations of chronic bronchitis, the ginseng group demonstrated quicker bacterial clearance [2].

According to certain articles, ginseng abuse syndrome can occur in those who use it for an extended length of time or who consume more than three grams of ginseng daily. Nonetheless, there is some evidence of ginseng-related patient risk based on case reports and research articles. For example, a 56-year-old lady experienced a manic episode after consuming ginseng, and the symptoms were managed with benzodiazepines and low neuroleptics [17]. Another example of an allergic reaction to ginseng syrup was documented, resulting in low blood pressure, erythematous papules, pulmonary allergies, and angioedema in the body [17]. Electrocardiograms showed a prolonged QT interval in cardiovascular patients, which might cause syncope, convulsions, cardiac arrest, or even death.

After consuming ginseng for the first week, a correlation between cardiovascular disease and renal disease was found, and an 83-year-old woman with chronic renal insufficiency was reported to have developed atrial fibrillation with bradycardia. After taking ginseng orally for cosmetic purposes, a 39-yearold woman developed menometrorrhagia, and a 12-year-old kid with breast soreness experienced gynecomastia after consuming ginseng for a month [17]. This is because ginsenosides, the active component, have the ability to behave like an estragon. Ginseng has been shown to have a variety of impacts on drug metabolism and can induce numerous drug interactions that might result in hepatotoxicity. People taking medications like warfarin should be especially cautious since ginseng can intensify the anticoagulant effects of warfarin [17].

Human immunodeficiency virus type 1 (HIV-1)

80–90% of HIV/AIDS patients have benefited from the development of highly active antiretroviral medication therapy (HAART); however, long-term HAART has numerous side effects and eventually leads to virological treatment failure, with a high frequency of resistance mutations in patients infected with HIV-1 [32,33]. According to recent studies, long-term ingestion of Korean Red Ginseng (KRG) increased HIV-1 patient survival before starting HAART by delaying the onset of resistance mutations in HIV-1 patients [37] and decreasing the fall in CD4þ T cell count [34, 36].

Coronavirus

Due to the low fidelity of RNA replication, coronaviruses-which cause Middle Eastern respiratory syndrome (MERS), severe acute respiratory syndrome (SARS), and coronavirus disease 2019. (COVID-19)-tend to mutate and recombine readily, increasing the virus's diversity and evolution in the wild [94, 95]. During the 2002–2003 pandemic, Panax ginseng was demonstrated to be efficacious against both COVID-19 and SARS. In SARS-CoV-2 intensive care unit patients, PEGylated nanoparticle albumin-bound (PNAB) has been shown to inhibit NF-kB, SREBP2-, and H4-mediated NET cytokine storms. This nanotherapeutics may also reduce vascular inflammation and blood clot formation [97]. This research confirms that PNABsteroidal ginsenoside nanotherapeutics show promise as possible treatments for Patients with severe COVID-19.

Phytochemical analysis of Panax species

A prior study discovered a number of bioactive components in P. ginseng, including ginsenosides, polysaccharides, alkaloids, glucosides, and phenolic acids [3]. They comprise C-17 side chain type, ocotillol, oleanolic acid, protopanaxadiol, and protopanaxatriol [4,5]. The glucose moiety of protopanaxadiol is joined to C-20 and C-3, while the glycosylation sites of protopanaxatriol are located at C-20, C-3, and C-6. In processed conditions, the breakage of the glucose bond at C-20 is hydrolyzed before the bonds at C-3 and C-6 [6]. 20(S)-ginsenosides are always eluted more readily than 20(R)ginsenosides, and the quantity of isomer pairs is identified [6]. Additionally, ginsenosides with a D20(21) elute before those with a D20(22) derivative. The side chain of ocotillol-type and oleanane-type is located at C-20. From P. notoginseng leaves, Yao et al. have isolated 945 ginsenosides and 662 potentially unique ginsenosides [7]. The chemical components of herbal medicines are greatly influenced by different species, parts, processing methods, geographical locations, and growing seasons.

Long-term safety study Test conditions and experimental specimens

Koatech Inc. (Pyeongtaek-si, Korea) provided 120 male and female SpragueDawley (SD) rats that were 4 weeks old and specified pathogen-free (SPF). The rats were housed in polycarbonate plastic cages (one per cage) with aspen porous good laboratory practice (GLP) bedding (Samtako, Osan-si, Korea) for seven days prior to administration. They were kept in a room with a 12-hour light/dark cycle, a controlled temperature (22°C±3°C), and humidity levels of 50%, 50% ± 20%. Standard rodent food (Purina, USA) and unlimited access to filtered water were given to the rodents. The rats were randomly assigned to 12 groups at five weeks of age (10 males and 10 females per group), which included a KRG-treated group (300 mg/kg/day) and male and female vehicle controls (distilled water).

Side Effects and Toxicity

Low toxicity is linked to Panax ginseng; when used properly, minimal side effects have been documented. Although some authors have disregarded case cases linked to ginseng abuse syndrome, adverse outcomes have been linked to large dosages and prolonged use, resulting in what has been cited in the literature as ginseng abuse syndrome [22, 28].[20] There have been reports of side effects such skin rash, headache, mastalgia, nausea, diarrhea, and hypertension.[19]

Dosage

The root of ginseng can be consumed as a powder, liquid extract, decoction, infusion, or chewed. The type of preparation and steeping period can affect the amount of ginsenosides. The range of the ginsenoside content is between 64– 77 percent. The German Commission E.29 recommends that crude formulations of 1-2 g dried root powder be taken daily for up to three months. To make a decoction, simmer 3–9 grams of dried root in 720–960 milliliters (24–32 ounces) of water for 45 minutes. One to six milliliters of a crude root fluid extract (1:2 concentration) can be administered every day. 31To make an infusion, cover 12 g of root with 150-250 mL (5-8 oz) of boiling water, soak for 10 minutes, filter, and then consume. Divided dosages of 200 mg of Panax ginseng extract, standardized to 4 percent ginsenosides, provide 8 mg of ginsenosides per day. According to some accounts, in certain situations, far greater dosages of 80–240 mg of ginsenosides per day may be necessary [20].

Conclusion

In conclusion, Panax ginseng is a highly versatile medicinal plant with well-established therapeutic potential across multiple body systems. Its diverse pharmacological actions make it valuable in managing metabolic, cardiovascular, neurological, infectious, and immune-related disorders. However, caution must be exercised in special populations such as pregnant and lactating women, individuals with hormone-sensitive conditions, or those taking anticoagulants. More robust, long-term human clinical trials are needed to confirm its safety and efficacy across various health domains, optimize dosing strategies, and understand potential herb-drug interactions. Given the current evidence, Panax ginseng remains a promising natural agent in integrative health approaches, particularly when used within recommended dosages and under professional supervision.

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Conflict of Interest

No Conflict of Interest

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Inform Consent and Ethical Statement

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Author Contribution

All authors are contributed equally.

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