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Review Article

Biological Activities Of Ginseng And Its Application To Human Health

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ABSTRACT

Ginseng, the root of Panax species is a well-known conventional and perennial herb belonging to Araliaceae of various countries China, Korea, and Japan that is also known as the king of all herbs and famous for many years worldwide. It is a short underground rhizome that is associated with the fleshy root. Pharmacognostic details of cultivation and collection with different morphological characters are discussed. Phytocontent present is saponins glycosides, carbohydrates, polyacetylenes, phytosterols, nitrogenous substances, amino acids, peptides, vitamins, volatile oil, minerals, and enzymes details are discussed. The main focusing of the bioactive constituent of ginseng is ginsenosides are triterpenoid saponin glycosides having multifunctional pharmacological activities including anticancer, anti-inflammatory, antimicrobial, antioxidant and many more will be discussed. Ginseng has been used as a traditional herb in Asian countries for thousands of years. It contains a large number of active ingredients including steroidal saponins, protopanaxadiols, and protopanaxatriols, collectively known as ginsenosides.

INTRODUCTION

The origin of ginseng dates back to prehistory. In China, Shennong (Divine Peasant) also known as Emperor Yan, the Yellow Emperor, or one of the "Three Emperors" (the Emper- or who is said to have started herbal medicine about 5,500 yr ago) is reported to have tasted hundreds of plants to discover many medicinal herbs. The original work was lost long ago, however, studies performed by Shennong were handed down verbally over many generations and were com- piled into a commentary book "Shennong Bencao Jing (Shen-

nong's Herbal)" by Tao Hongjing during the Liang Dynasty, 502-557 A.D..

THE KING OF ALL HERBS

Ginseng, called the king of all herbs, has been used as a traditional medicine for the treatment of diseases for thousands of years in East Asian countries. In the last three decades, it has become one of the most popular herbs worldwide. It is used in agricultural products, dietary and health supplements, and medicines in different countries. The signature bioactive ingredients of ginseng are ginsenosides, which are triterpene saponins.

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However, the therapeutic effects of ginseng are not solely dependent on ginsenosides. Recently, the active ingredient gintonin was identified. Nevertheless, most pharmacological and medical studies of ginseng have focused primarily on ginsenosides. They show various anti-inflammatory, antioxidant, antibacterial, antiviral, and anti-fungal activities. Moreover, they have been demonstrated to have therapeutic potential in hypertension, stress, and different neurological disorders such as Alzheimer's disease (AD), Parkinson disease (PD), and Huntington disease. Numerous molecular targets for ginseng have been identified in recent years. Plants are an important natural resource for the development of drugs. Different pathological conditions can be treated by plant-derived medicines. A number of modern drugs originate from traditional medications. Ginseng has been used in clinical settings all over the world and may provide the basis for the development of novel therapeutic agents. The objective of this article is to review the state of ginseng research and to evaluate the use of its bioactive compounds as therapeutic agents. The medicinal and pharmacological potential of ginseng and ginsenosides in different diseases is discussed based on documentation of their therapeutic applications in various *in vitro* and *in vivo* models. Ginseng (a medicinal herb) and its derived natural products are amongst the most popular natural remedies and are used to treat various diseases and conditions such as diabetes, anti-oxidative, inflammation, cancers, fungal, bacterial, viral, stress, and neurodegenerative diseases (ND), as well as brain ischemia, hypertension, obesity, cardiovascular diseases and stroke, sarcopenia, muscle-wasting conditions, muscle aging, and cancer cachexia including headaches, diarrhea, blood pressure changes, skin irritations, and vaginal bleeding. Overall, ginseng has been reported to be a useful management option for many diseases as it suggests by its name

- panax is derived from Greek pan akheia, meaning "cures all disease". Ginseng has been well known as an immune modulator. Roots (mostly), stems, leaves of ginseng, and their extracts have been used for maintaining immune homeostasis and enhancing resistance to illness or microbial attacks through effects on immune system.

WHAT IS GINSENG ?

Many commercially available products are labeled 'ginseng' or 'ginseng-derived'. However, many of these are not derived from ginseng. Authentic ginseng products or plants have distinguishable compounds. Saponins and saponogenins or ginsenosides are signature compounds of the genus *Panax*, known popularly as ginseng after the scientific name of Asian or Chinese ginseng, *Panax ginseng*. To the best of our knowledge, there are 8-13 species within the genus *Panax*, and three of these species are widely used as major sources of medicinal constituents: *P. ginseng*, commonly known as Asian or Chinese ginseng; *P. quinquefolius* or American ginseng; and *P. notoginseng*, commonly named sanchi.

MEDICINAL IMPORTANCE OF GINSENG

Ginseng is highly valued for its therapeutic applications since it contains a variety of potent compounds that are advantageous to human health. The pharmacological action of it has been investigated globally. Numerous consumer goods have been created as a result of ginseng's discovery as being very useful for human health.

TRADITIONAL USES OF GINSENG

For more than a thousand years, ginseng was used as traditional herbal medicine as a healer of every type of disease. It was considered the best medicine for main fatigue and spiritlessness. In traditional Chinese medicine, it was used for the treatment of heart and blood vessel disorder and also to make people feel calmer. In the ayurvedic system of medicine, traditionally ginseng was utilized as a cardioprotective, anticancer, and also as antioxidant.



PHARMACOLOGICAL POTENTIAL OF GINSENG

Ginseng is considered a miracle source of multifaceted pharmacological activities such as anti-inflammatory, anticancer, antifungal, antibacterial, antiviral, immune-booster, antidiabetic, and antioxidant activities. The bioactive of ginseng has the power of interaction with membrane-bound ion channels, cell membranes, and extracellular and intracellular receptors which as consequences causes alteration at the transcriptional level. The extracts of Ginseng had shown protective effects on hepatocytes and liver injury. Previously demonstrated that both neurotrophic effects in learning and memory enhancement and also cause neuroprotective action for prevention of neuron degeneration.

WHY DO CHINESE CALL GINSENG A MAN ROOT ?



Fig 1 Panax Ginseng C.A Meyer Shaped Like A Person

The herb is believed to restore and enhance well-being by boosting energy levels, lowering blood sugar and cholesterol levels, reducing stress and assisting relaxation. This year, it has been used in many traditional Chinese medicines that have been effective in preventing COVID-19 and also relieving symptoms of the disease. A common name for ginseng is "man-root." This is because the root is shaped like a person. It has benefits for the whole body. The medicinal part is made of the dried main and lateral root and root hairs. The word ginseng derives from the Chinese character

"Renshen" meaning "man root", which refers to the ginseng root's characteristic forked shape. The botanical name Panax is derived from the Greek word meaning "all-heal" as in the term panacea. Ginseng is taken promote health and healing, as an adaptogen (to treat stress and enhance recovery from illness), aphrodisiac (to aid in sexual desire and performance) and a stimulant (wakefulness and mental acuity). Ginseng is also claimed to lower blood glucose levels and to be beneficial in diabetes. Ginseng is found in energy drinks as well as in many cosmetic preparations. The herb is believed to restore and enhance well-being by boosting energy levels, lowering blood sugar and cholesterol levels, reducing stress and assisting relaxation.

TAXONOMIC CLASSIFICATION

Kingdom: Plantae
Clade: Tracheophytes
Clade: Angiosperms
Clade: Eudicots
Clade: Asterids
Order: Apiales
Family: Araliaceae
Genus: Panax
Species: P. ginseng
Binomial name: Panax Ginseng C.A. Mey.

SYNONYMS

Aralia ginseng Baill., Panax verus Oken.

COMMON NAME

American ginseng, Asiatic ginseng, Chinese ginseng, five-fingers, Japanese ginseng, jintsam, Korean ginseng, ninjin, Oriental ginseng, schinsent, seng and sang, tartar root, Western ginseng.

GEOGRAPHICAL SOURCE

Ginseng is found in Northern Hemisphere, North America, Eastern Asia (mostly Korea, northern China (Manchuria), Eastern Siberia, Typically in cooler climates. In India the genus is known from Sikkim, West Bengal (Darjeeling district) Arunachal Pradesh (Tawang district) arid

Meghalaya (Khasia Misty). It grows wild in the temperate forest and is represented by three species namely *P. assamicus* Banerji, *P. fruticosus* L. and *P. pseudoginseng* Wall. with its two varieties. Only *P. pseudoginseng* (the Himalayan Ginseng) is known to have ginseng properties like other commercial ginseng species. Although about a century ago this species were frequent in the Eastern Himalaya but now their population is disappearing alarmingly mainly due to demographic pressure, deforestation and commercial exploitation. Therefore, some necessary information about this species for helping administrative and scientific measure regarding conservation would be of immense importance for rescuing its security before extinction.

MORPHOLOGY

FLOWER

The flowers are born in a solitary inflorescence that is a terminal umbel with 30 to 50 flowers. The peduncles of the flowers are 15 to 30 cm long. The flower ovary is 2-carpellate, with each carpel having two distinct styles. Flowers begin to bloom when the ginseng is 3 years old.

FRUITS/BERRIES

Mature fruits are 4-5 x 6-7 millimeters in size, red in color, and round with flattened ends. The white seeds are kidney-shaped. The (2n) diploid chromosome count is 48. The berries, which are initially green, turn red as they become ripe. The berries are picked and dried to be used as seeds.

LEAVES

Plants produce 3 to 6 leaves that are palmately compound, with each leaf having 3 to 5 leaflets. The margins of the leaflets are densely serrated. Ginseng leaves have a long petiole, and the leaf blades divide into five sections, with several smaller leaves attached to a single leafstalk. The tip is sharp, and the edges have a saw-toothed shape.

ROOTS

Plants have a spindle- or cylinder-shaped taproot, usually with 1 or 2 main branches. This is the part of ginseng that is widely used for consumption and medicinal purposes.

MAIN ROOT

This is the central part of the ginseng. It is processed into various forms for consumption and medicinal purposes.

ROOTLETS

A single ginseng typically have two to five rootlets. The number of rootlets varies depending on the soil quality, cultivation method, age, etc. Fine roots alone are called Misam in Korean. They are used to make ginseng tea, etc.

CULTIVATION

A. Propagation:

Ginseng is best propagated by seed. The seeds are recalcitrant and immature at the time of harvest. Thus, they are kept moist and require special handling and stratification treatments till they germinate after about 18 months.

B. Site selection:

The plant can be grown in rain shade temperate areas of the inner Himalayas where the summer monsoons are scanty, but with ensured supply of water to maintain moisture. Areas with deciduous broad leaved trees such as, Acer, Walnut, Oak, Poplar are considered good for forest grown ginseng. Herbaceous plants like *Trillium* spp., *Podophyllum* sp., *Fragaria* spp. etc. in temperate forests are indicators where ginseng can be grown under natural conditions. The inner temperate forest areas of Chamba, Kullu and Kinnaur districts of Himachal Pradesh have the potential for producing forest grown ginseng.

C. Soil:

Ginseng grows best in slightly acid soils with a pH of 5-6.5. Ginseng is a shallow rooted plant and the water requirement is less compared to other conventional crops.

It is desirable to select a site with slight gradient for avoiding water logging situation.



The ideal soil is loam with high organic matter content or humus.

D. Bed preparation:

The field is ploughed 3-4 times. The seeds or plants are planted in raised beds 10-12.5 cm high, prepared across the contour of land in terraces.

The beds should be 120 cm wide and the length can be adjusted according to the contour of soil or the shading infrastructure at the site.

The use of farm yard manure (FYM) is not recommended, as it is laden with undesirable weed seeds and insects.

E. Seed sowing and nursery development:

Depending on the site and soil conditions the seeds are sown 12 mm to 25 mm deep. The seeds are covered with enough soil or mulch so that these do not dry. It is essential to cover the seed beds with 2.5-5.0 cm of mulch. The sowing should be done at a uniform depth and spacing to avoid uneven stands. High density sowing, is usually done for nursery development or natural stratification of green seeds in field. Furrows are prepared 15 cm apart along the length of the bed. Seeding is done 2.5 cm apart in each row. However, in low density sowing which is usually adapted in woodland natural shade conditions, the seeds are sown 15-30 cm apart. Consequently, the seeding rate is about 35-100 kg/ ha depending upon the seeding density adopted. The actual seeding rate and other cropping parameters are location specific.

F. Transplantation:

The rootlets produced in first year of growth in the nursery, known as planting stock are transplanted in main field. Plantation is done with proper spacing to obtain disease free plants till the harvest after 5 years of growth. The rootlets are dug out and transplanted immediately to the already prepared beds. The usual spacing for rootlets is 10-15 cm plant to plant, in 15-20 cm apart rows. It is essential to plant the rootlets well before the onset of apical growth to avoid unnecessary damage to the plants.

COLLECTION

The ginseng plants flower in its third year of growth. The berries ripen in September, when they turn into bright red colour. Since ginseng is propagated by seed, the ensured indigenous seed production should be the first priority for any effort to domesticate the crop in Himachal Pradesh. Under ideal growth conditions, a yield of about 400-500 kg/ ha fresh seeds is achieved in traditional ginseng growing countries. The berries in the outer circle mature first by bright red colour. The collected berries are mashed to rupture the skins and placed in a water bucket. The bucket is covered and placed in shade for 4-5 days, stirring daily until the pulp has disintegrated. The seeds can now be washed through an appropriate sieve or mesh using a pressure hose. The washed seeds are then put again into bucket containing clean water and allowed to settle for about 1 minute to remove the floaters and remaining pulp, if any. The seeds are then surface dried in shade for a few hours to avoid their sticking together. Seed stratification and storage.

PHARMACOLOGICAL USES OF GINSENG

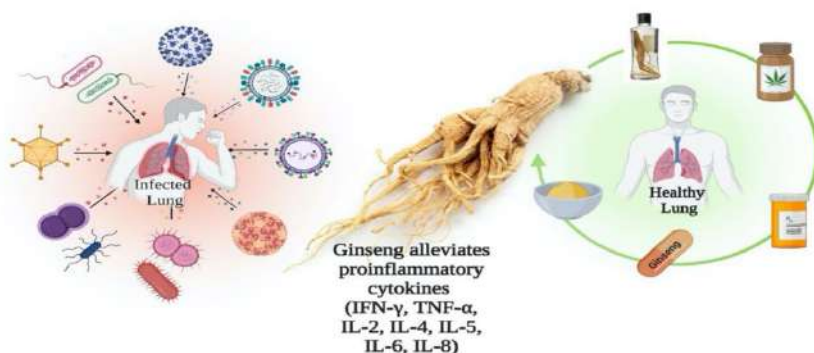


Fig 2 Pharmacological Effects Of Ginseng

Antioxidant Activity

Free radicals, reactive oxygen species (ROS), and reactive nitrogen species originate from both exogenous and endogenous sources. Major exogenous sources are pollution, alcohol, tobacco consumption, smoking, heavy metals, transition metals, industrial solvents, pesticides, and certain drugs such as halothane, paracetamol, and radiation. Endogenous sources include mitochondria, peroxisomes, the endoplasmic reticulum, and phagocytic cells.

Anti-inflammatory Activity

Inflammation is a normal response to infection that involves both the innate and adaptive immune systems. Heat, pain, redness, swelling, and loss of function are the cardinal features of inflammation. A number of *in vitro*, *in vivo*, and clinical studies suggest that ginseng has some degree of anti-inflammatory activity. Dong- Hyun Kim et al found that ginsenosides Re and Rpl can suppress the NF- κ B signaling pathway. In another study, Yu et al revealed that ginsenoside Rc can inhibit the expression of macrophage-derived cytokines. Moreover, it can suppress the activation of tumor necrosis factor receptor-associated factor family member-associated NF- κ B activator (TANK)-binding kinase-1/1 κ B kinase -E interferon regulatory factor-3 and p38/ATF-2 signaling in activated RAW264.7 macrophages, human synovial cells, and HEK293 cells.

Anti-microbial Activity

Antibiotic resistance is on the rise, and there is great need to develop new classes of antimicrobial agents. In this context, novel antimicrobial agents, especially from an herbal source, would be well received. A number of studies have reported that ginseng extract or its components individually or combined possess antiviral and/or antimicrobial properties. Korean Red Ginseng (KRG) extract blocked 22 respiratory syncytial virus-induced inflammatory cytokines and increased the levels of IFN- ν , CD8+ T cells, and CD11c + dendritic cells and hence decreased lung disease in mice. In another study, ginsenosides Rg1, Re, Rf, Rh1, Rg2(s), Rg2(r), Rb1, Rc, Rb2, Rd, Rg3(s), and Rg3 stimulated the antiviral cytokines IN- γ and IFN- α in response to H5N1 influenza virus challenge. In addition, this herb has activity against H1N1, H3N2, and H9N2 influenza viruses.

Anti-Cardiovascular Disease Activity

Cardiovascular disease comprises a range of conditions involving the heart or blood vessels and is one of the leading causes of death around the globe. Active components of ginseng can stimulate nitric oxide production, inhibit ROS production, increase blood circulation, and help in adjusting lipid profiles. In the cardiovascular system, calcium ions (Ca²⁺) play a critical role in the regulation of contraction and intracellular signaling, which are vital for heart function. Different studies have revealed that ginsenosides can inhibit Ca²⁺ entry, and thus improve cardiac functions. One *in vivo* study showed that

ginsenoside Rb1 (GRb1) can inhibit cardiac hypertrophy in a rat model. Studies showed that *P. ginseng* can help maintain proper blood circulation and can boost vascular endothelial cell-derived nitric oxide secretion, which decreases blood pressure. Other studies have reported that the components of ginseng also function as anticoagulation agents in the circulatory system. In vitro and in vivo studies have demonstrated that ginsenosides Rg1, Rg3, and water extract of KRG suppressed platelet aggregation by downregulating thrombin-enhanced fibrinogen binding and P-selectin expression via downstream signaling elements, for example, cAMP and ERK2, in addition to the release of 1,2-diacylglycerol. The n-butanol extract (NE3) and saponins from *P. notoginseng*, as well as radix notoginseng have been shown to regulate total cholesterol, triglyceride (TG), and low-density lipoprotein-cholesterol (LDL-C) levels based on in vivo experiments

Antidiabetic Effect

Diabetes mellitus (DM) is a metabolic condition that impairs the ability of the body to process blood

glucose due to defects in insulin secretion, insulin action, or both. There are two major categories of DM: type 1 diabetes mellitus, commonly known as insulin-dependent DM, and type 2 diabetes mellitus, commonly known as non insulin-dependent DM. Ginseng is used as a traditional medicine for treating DM in China, Korea, and Japan. Yun et al investigated the antidiabetic effects of wild ginseng ethanol extract on high-fat diet-induced Institute of Cancer Research (ICR) mice for 8 weeks. Wild ginseng ethanol extract significantly reduced fasting blood glucose in a dose-dependent manner. Different in vitro and in vivo studies have shown that compound K, an active metabolite of ginsenosides, can stimulate insulin secretion by primary cultured islets (Fig. 2.15). Compound K enhanced insulin secretion in a concentration-dependent manner through K-channel dependent pathways. Vuksan et al examined the clinical efficacy of KRG in 19 participants with well-controlled type 2 diabetes, and after 12 weeks of supplementation, found that it improved glucose and insulin regulation.

Table 1 Chemical Constituent Of Ginseng

Groups	Contents	Ingredients
Saponin	Saponin (3–6%)	- PPD ginsenosides
		- PPT ginsenosides
		- Oleanane ginsenosides
Non-saponin	N-containing substances (12–15%)	- Proteins, amino acids
		- Peptides, nucleic acids
		- Alkaloids
Non-saponin	Fat-soluble components (1–2%)	- Fat, fatty acids
		- Essential oils
		- Phytosterol
		- Organic acids
		- Phenolics
		- Polyacetylenes
Others	Carbohydrates (50–60%)	- Terpenes
		- Polysaccharides
		- Oligosaccharides
Others	Ash (4–6%)	- Sugar, fiber, pectin
		- Minerals
Others	Vitamin (0.05%)	- Water-soluble vitamins

CONCLUSION

There is great interest in pharmacological agents from natural sources that have predictable health benefits against inflammation, oxidative stress, microbial infection, cancer, diabetes, sexuality problem, central nervous system disorders, and cardiovascular disorders with no toxicity property. However, the job of discovering new ginseng constituents is still underway. Ginseng is distributed in 35 countries around the globe, and the ginseng market is estimated to be worth \$2,084 million. The pharmaceutical industry is a rapidly growing industry; in 2014, global pharmaceutical revenues had surpassed one trillion dollar benchmark. Traditional herbs are a great source of therapeutic agents, for example, artemisinin from *Artemisia annua*. Several studies have revealed that ginsenosides and their derivatives have great pharmaceutical potential to prevent and treat different diseases. We strongly believe that traditional herbs will open up new horizons for the pharmaceutical industry in the future. Biochemical approaches, such as immunoassays and genetic marker analyses, are being used with increasing frequency in ginseng analysis and are likely to contribute more significantly in the future. Relevant technical advances may help in understanding the *Panax* species, thereby contributing to the creation of beneficial bioengineered species. The major applications of ginseng analysis are in species authentication, quality control, pharmacokinetic profiling, and biomarker identification in biological systems.

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