

## PANAX GINSENG - A UNIVERSAL PANACEA IN THE HERBAL MEDICINE WITH DIVERSE PHARMACOLOGICAL SPECTRUM –A REVIEW

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### ABSTRACT

The use of medicinal plant either as a single drug or in combination is increasing in the health care of human being. Medicinal plants can be important source of previously unknown chemical substances with potential therapeutic effect. The herbal remedies referred to as “ginseng” are derived from the roots of several plants. One of the most commonly used and researched of the ginseng is Panax ginseng, also called Asian or Korean ginseng. The main active components of Panax ginseng are ginsenosides, which have been shown to have a variety of beneficial effects, including anti-inflammatory, antioxidant, and anticancer effects. Panax ginseng also improve psychologic function, immune function, and conditions associated with diabetes. This review gives a bird's eye view mainly on the pharmacognostic characteristics, traditional uses, phytochemistry and pharmacological actions of the plant.

**Keywords:** *Panax ginseng*, Pharmacological action, Ginsenosides, Anti oxidant, Anti diabetic activity.

### INTRODUCTION

Medicinal plants are part and parcel of human society to combat diseases, from the dawn of civilization <sup>1</sup> Medicinal plants can be important source of previously unknown chemical substances with potential therapeutic effects.

The medicinal use of plants is an ancient tradition, far older than the contemporary sciences of medicine, pharmacology and chemistry. The world health organization has estimated that over 75% of the world's population still relies on plant derived medicines, usually obtained from traditional healers, for its basic health care needs <sup>2</sup> Herbal medicines are in great demand in the developed as well as developing countries for primary healthcare because of their wide biological and medicinal activities, higher safety margins and lesser costs <sup>3</sup> *Panax ginseng* belongs to the Araliaceae family Panax is derived from the Latin word panacea, which refers to its historical usage for many conditions.

*Panax ginseng*, used medicinally for thousands of years in China, Korea, and Japan,<sup>4</sup> is well known as an adaptogen and a restorative tonic that is widely used in traditional Chinese medicine (TCM) and Western herbal preparations.<sup>5,6</sup> Eclectic uses for *Panax ginseng* include infertility, liver disease, amnesia, colds, menopause, and erectile dysfunction.<sup>5-7</sup>

There are many species of Panax, which leads to some confusion in the literature. However, the two species that have been the most extensively researched and used are *Panax ginseng* and *Panax quinquefolius*. Panax ginseng is one of the most commonly used and highly researched species of ginseng. This species, which is native to China, Korea, and Russia, has been an important herbal remedy in traditional Chinese medicine for thousands of years, where it has been used primarily as a treatment for weakness and fatigue.<sup>8</sup> The main active agents in Panax ginseng are ginsenosides, which are triterpene saponins. Ginseng has been used for a variety of purposes for about 5000 years.

It has been used to increase physical endurance and lessen fatigue, to improve the ability to cope with stress, and to improve concentration. It is also used for anemia, diabetes, gastritis, neurasthenia, erectile dysfunction, impotence and male fertility, fever, hangover, and asthma. Panax ginseng is also used for bleeding disorders, loss of appetite, vomiting, colitis, dysentery, cancer, insomnia, neuralgia, rheumatism, dizziness, headache, convulsions, disorders of pregnancy and childbirth, hot flashes due to menopause, and to slow the aging process. It may also improve your overall being.

### Plant Profile

#### Plant taxonomy <sup>9</sup>

Kingdom:	Plantae
Division:	Angiosperms
Sub division:	Eudicots
Class:	Asterids
Order:	Apiales
Family:	Araliaceae
Subfamily:	Aralioideae
Genus:	Panax
Species	Ginseng

#### Common names <sup>10</sup>

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

### Plant Descriptions

#### Botanical description

*Panax ginseng* belongs to the Araliaceae family and is found throughout East Asia and Russia.<sup>11,12</sup> It grows natively in remote forests of Manchuria and North Korea, but has become over-harvested in other parts of Asia.<sup>4</sup> It is cultivated in Korea, China, and Japan for export and use as a medicinal herb. *Panax ginseng* is a shade-loving, deciduous perennial with five-fingered leaves, tiny white flowers, red berries, and a yellowish-brown root.<sup>5-7</sup>

The root is utilized medicinally, although active compounds are present in all other parts of the plant. The root of *Panax ginseng* is a thick structure that resembles a human-like form, which is responsible for its name in Chinese, jen shen, or “man-root.”<sup>5</sup> Panax is derived from the Latin word panacea, which refers to its historical usage for many conditions. There are two distinct forms of *Panax ginseng*, red and white ginseng.

The difference is the method of processing that results in different pigment compositions; white ginseng is produced by harvesting the root and drying it in the sun,<sup>6</sup> while red ginseng is steamed after harvest and dried. The content of ginsenoside compounds differs slightly between the red and white forms. Growing time also impacts ginsenoside content, with roots from plants older than five years being more potent than roots from one- to two-year-old plants.<sup>6,7</sup> Ginseng is a perennial herb long known for the reputed medicinal and aphrodisiac properties of its aromatic root. The genus name *Panax* reflects the reputed value of various species of ginseng as a cure all--or panacea. The unbranched stem is 20 - 40 cm (8 - 15 in.)

high and is topped by a single whorl of 1 to 5 palmately compound leaves. Usually, three compound leaves are produced, each with five serrate (pointed and toothed) leaflets. The tiny flowers are produced in a single, ball-like cluster in the fork where the leaf stalks meet the stem.

The five-petaled flowers are white or greenish-yellow and are scented like lily-of-the-valley. They appear from late June to mid July. The fruits, bright red drupes one cm (0.4 in.) in diameter, are easily seen in the fall. (Ginseng plants less than three years old usually bear no fruit, and it takes 18-22 months between the time when the ripe fruit drops to the ground and the time the seed will germinate.)

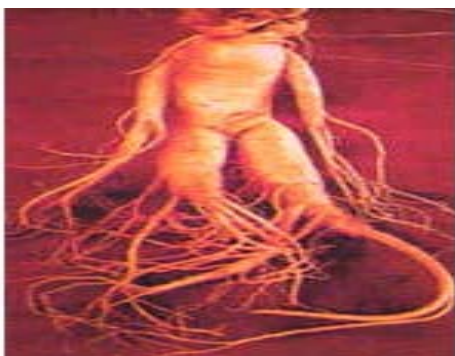


Fig. 2.1: Root of panax ginseng



Fig. 2.2: Leaves, flowers and root of panax ginseng



Fig. 2.3: Fruit of panax ginseng

#### Habitat<sup>11,12</sup>

Ginseng favors cool, well-drained soils of rich, moist deciduous woods. It may also be found on rocky talus slopes. Among the specific habitats in Massachusetts are a variety of rocky habitats, including the tops of ledges, rocky talus slopes and jumbles, and rocky rich mesic woods; along a creek at the base of a fern-covered slope; and various rich mesic forest habitats, including ones at the

base of a dolomitic limestone ledge and one in a ravine. None of the current sites is in full sun

#### Phenology

Flowers in late June to mid July.

**Propagation:** By harvesting the root

#### Parts Used

The root of the plant is used medicinally.

#### Phyto chemical constituents<sup>6-14</sup>

*Panax ginseng* contains triterpene glycosides, or saponins, commonly referred to as ginsenosides. Many active compounds can be found in all parts of the plant, including amino acids, alkaloids, phenols, proteins, polypeptides, and vitamins B1 and B2.<sup>6</sup> Up to 40 distinct ginsenosides have been identified by thin layer chromatography (TLC) and methanol extraction experiments.<sup>6,13</sup> The nomenclature of ginsenosides is by the designation Rx, where x represents the retention factor (Rf) value from the sequence of spots on TLC from bottom to top. The two major sub-types of ginsenosides, protopanaxadiol and protopanaxatriol, are classified according to the arrangement and number of sugar residues glucose, rhamnose, xylose, and arabinose – on the ginsenoside. Rb1, Rb2, Rc, and Rd are examples of protopanaxadiol ginsenosides. Re, Rf, Rg1, and Rg2 are examples of protopanaxatriols.<sup>5-7,13</sup> These ginsenosides have varying concentrations in red and white *Panax ginseng* extracts due to different processing methods that affect deacetylating enzymes within the raw plant material.<sup>14</sup>

#### Active Components

The triterpenoid saponins referred to collectively as ginsenosides or panaxosides.

#### Pharmacokinetics<sup>15</sup>

Recent research supports the hypothesis that ginsenosides are activated by intestinal bacteria through deglycosylation and esterification.<sup>15</sup> Protopanaxadiol and protopanaxatriol glycosides are absorbed into the blood or lymph and transported to target tissues for esterification with stearic, oleic, or palmitic fatty acids.

The transformation into ginsenoside metabolites, M1 (20S-protopanaxadiol 20-O-B-D-glucopyranoside) and M4 (20S-protopanaxatriol) affect excretion and utilization of the metabolites.

#### Mechanism of action

*Panax ginseng* is often referred to as an adaptogen, which suggests it has varied actions and effects on the body that support non-specific resistance to biochemical and physical stressors, improve vitality and longevity, and enhance mental capacity.<sup>3,10,11</sup> Reviews suggest *Panax ginseng* has immuno-modulating activity by affecting the hypothalamic-pituitary-adrenal (HPA) axis.<sup>6,16</sup> *In vitro* experiments reveal enhanced natural killer (NK) cell activity and increased immune cell phagocytosis after ginsenoside exposure.<sup>6</sup>

According to a 1999 World Health Organization review, ginsenosaponins “are thought to decrease serum prolactin, thereby increasing libido” in male impotence.<sup>10</sup>

#### Pharmacology

The main active agents in *Panax ginseng* are ginsenosides, which are triterpene saponins. The majority of published research on the medicinal activity of *Panax ginseng* has focused on ginsenosides.<sup>17</sup> These are the compounds to which some ginseng products are now standardized. Research reviews postulate that extracts of *Panax ginseng* affect the hypothalamus-pituitary-adrenal axis and the immune system, which could account for many of the documented effects. Animal models and *in vitro* studies mentioned in these reviews<sup>8,18</sup> indicate that *Panax ginseng* enhances phagocytosis, natural killer cell activity, and the production of interferon; improves physical and mental performance in mice and rats; causes vasodilation; increases resistance to exogenous stress factors; and affects hypoglycemic activity

## Pharmacological Activity

### Anti sterility activity<sup>19</sup>

A study was designed using an untreated control group found indications that *Panax ginseng* might improve sperm count and motility, thereby enhancing male fertility.

### Anti proliferative activity<sup>20,21</sup>

*Panax ginseng* is also said to help prevent cancer and fight chemical dependency, but the scientific evidence for these uses is minimal at best. Numerous in vitro and animal studies have examined the interaction of *Panax ginseng* with carcinogenesis, apoptosis, angiogenesis, and metastasis.<sup>13,22-25</sup>

### Adaptogenic activity

Numerous studies have evaluated the effects of oral *Panax ginseng* on animals under conditions of extreme stress. The results suggest that ginseng increases physical endurance and causes physiological changes that may help the body adapt to adverse conditions.<sup>26,27, 28- 31</sup> In addition, studies in mice found that consuming *Panax ginseng* before exposure to a virus significantly increased the survival rate and the number of antibodies produced.<sup>32,33</sup> However, most of these studies fall far beneath modern scientific standards

### Treatment for cold and flu

A double-blind, placebo-controlled study of 323 people found meaningful evidence that an extract of American ginseng taken at 400 mg daily may help prevent the common cold.<sup>33</sup> Participants who used the extract over 4 months experienced a reduced number of colds as compared to those taking the placebo. Comparative benefits were also seen regarding the percentage of participants who developed two or more colds, and the severity and duration of cold symptoms that did develop. Similar benefits were also seen in a study of 43 people.<sup>34</sup> In addition, two double-blind, placebo-controlled studies indicate that *Panax quinquefolius* may be able to prevent flu-like illness in seniors.<sup>35</sup>

A double-blind, placebo-controlled study suggests that *Panax ginseng* can also help prevent flu-like illnesses.<sup>36</sup> This trial enrolled 227 participants at three medical offices in Milan, Italy. Half were given ginseng at a dosage of 100 mg daily, the other half placebo. Four weeks into the study, all participants received influenza vaccine. The results showed a significant decline in the frequency of colds and flus in the treated group compared to the placebo group (15 versus 42 cases). Also, antibody measurements in response to the vaccination rose higher in the treated group than in the placebo group.

A double-blind, placebo-controlled study found that *Panax ginseng* can improve some aspects of mental function.<sup>37</sup> Over a period of 2 months, 112 healthy, middle-aged adults were given either ginseng or placebo. The results showed that ginseng improved abstract thinking ability. However, there was no significant change in reaction time, memory, concentration, or overall subjective experience between the two groups. Another double-blind, placebo-controlled study of 50 men found that 8-week treatment with a *Panax ginseng* extract improved ability in completion of a detail-oriented editing task.<sup>38</sup> Also, a double-blind trial of 16 healthy males found favorable changes in ability to perform mental arithmetic in those given *Panax ginseng* for 12 weeks.<sup>39</sup>

### Memory power enhancing activity

Several studies have found indications that *Panax ginseng* might enhance mental function. More comprehensive benefits were seen in a double-blind, placebo-controlled trial involving 60 elderly people. Researchers found that 50 or 100 days of treatment with *Panax ginseng* produced improvements in numerous measures of mental function, including memory, attention, concentration, and ability to cope.<sup>40</sup> Benefits were still evident at the 50-day follow-up. However, virtually no improvement

was seen in the placebo group, a result that is highly unusual and raises doubts about the accuracy of the study.

### Sports performance

The evidence for *Panax ginseng* as a sports supplement is mixed at best. An 8-week, double-blind, placebo-controlled trial evaluated the effects of *Panax ginseng* with and without exercise in 41 individuals.<sup>41</sup> The participants were given either ginseng or placebo, and then underwent exercise training or remained untrained throughout the study. The results showed that ginseng improved aerobic capacity in individuals who did not exercise, but offered no benefit in those who did exercise. In a 9-week, double-blind, placebo-controlled trial of 30 highly trained athletes, treatment with *Panax ginseng* alone or in combination with vitamin E produced significant improvements in aerobic capacity.<sup>42</sup> Another double-blind, placebo-controlled trial of 37 individuals also found some benefit.<sup>43</sup>

### Sense of well being effects

A double-blind study compared the effects of a nutritional supplement with and without *Panax ginseng* extract on the feeling of well-being in 625 people whose average age was just under 40 years old.<sup>44</sup> Quality of life was measured by a set of 11 questions. People taking the ginseng-containing supplement reported significant improvement compared to those taking the non-ginseng supplement (the control group). Similar findings were reported in a double-blind, placebo-controlled study of 36 people newly diagnosed with diabetes.<sup>45</sup> After 8 weeks, participants who had been taking 200 mg of ginseng daily reported improvements in mood, well-being, vigor, and psychophysical performance that were significant compared to the reports of control participants,

### Anti diabetic activity

Eclectic medicine texts reference *Panax ginseng* for its beneficial use in blood sugar regulation.<sup>2,10</sup> In a double-blind RCT, Sotaniemi et al examined the efficacy of *Panax ginseng* in newly diagnosed type 2 diabetics.<sup>45</sup> Parameters measured included physical performance, mood, serum lipids, fasting blood glucose, hemoglobinA1c (HbA1c), amino terminal propeptide (PIIINP) concentration, and body weight. PIIINP serum levels are associated with coronary artery disease and were used as a safety parameter in this study. The study participants (n=36) were given 100 mg ginseng extract, 200 mg ginseng extract, or placebo daily for eight weeks. Compared to the placebo group, the 200-mg ginseng group experienced elevated mood, improved physical performance, and reduced fasting blood glucose. The authors concluded ginseng warrants further study as an adjuvant to diabetes.

A double-blind, 12-week RCT examined the effect of red *Panax ginseng* on HbA1c levels in 19 subjects with well-controlled type 2 diabetes.<sup>46</sup> Study participants received 2 g ginseng or placebo three times daily before meals. Plasma glucose and insulin, insulin sensitivity, and oral glucose tolerance were secondary measures of efficacy, while blood pressure checks and liver and kidney function tests assessed safety. Although no change was seen in HbA1c levels with ginseng, the participants remained well controlled throughout the study without pharmaceutical intervention – with average levels of HbA1c of 6.5 percent. A significant 8- to 11-percent decrease in glucose on the oral glucose tolerance test and 33-percent decrease in plasma insulin (p<0.05) was seen in the ginseng group compared to placebo. No change was reported in safety parameters throughout the study, which led the authors to conclude

red *Panax ginseng* is safe to use in the treatment of type 2 diabetes management

### Anti inflammatory activity

A recent paper proposed an anti-inflammatory role of *Panax ginseng* in the sequence of progression to promotion in a model of carcinogenesis.<sup>47</sup> *Panax ginseng* affects multiple points within the inflammatory cascade, including inhibition of cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and nuclear factor kappaB.<sup>48,49</sup> In a review, Lee et al concluded *Panax ginseng* has a

radioprotective effect associated with antioxidant and immunomodulation properties<sup>14</sup>

#### Drug-Botanical Interactions

According to a review by Blumenthal et al, there are no known interactions between Panax ginseng and pharmaceuticals, as reported by the German Commission E.<sup>50,51</sup> Caution is advised with concomitant use with phenelzine, coumadin, oral hypoglycemics, insulin, and caffeine, based on preclinical studies and proposed mechanisms of action. A recent review by Seely et al suggests cautious use of Panax ginseng in pregnancy and lactation, although no specific teratogenic or hormone disrupting activity was noted<sup>11</sup>

#### Side Effects and Toxicity

Panax ginseng is associated with low toxicity; few adverse events have been reported with proper usage.<sup>6,50</sup> Adverse events have been associated with high doses and long-term usage, producing what has been cited in the literature as ginseng abuse syndrome,<sup>8,16</sup> although case studies associated with ginseng abuse syndrome have been discounted by several authors. Side effects such as hypertension, nausea, diarrhea, headache, mastalgia, insomnia, and skin rash have been noted.<sup>5,8,16</sup>

#### Warnings and Contraindications

The German Commission E and the World Health Organization report no known contraindications for Panax ginseng.<sup>6,51</sup> It is advised during pregnancy and lactation due to a lack of controlled human clinical studies.<sup>3,8</sup> Teratogenicity has been documented in an in vitro rat embryo model, but the implication for human health is questionable due to dosages used that exceed possible human consumption.<sup>52</sup> In Asian countries the use of Panax ginseng in TCM formulas is common throughout pregnancy and lactation.<sup>5</sup>

#### Safety issues

Ginseng appears to be nontoxic, both in the short- and long-term, according to the results of studies in mice, rats, chickens, and dwarf pigs.<sup>53-56</sup>

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#### CONCLUSION

Medicinal plants have provided copious leads to combat diseases, from the dawn of civilization. The extensive survey of literature revealed that *Panax ginseng* is highly regarded as a universal panacea in the herbal medicine with diverse pharmacological activity spectrum. This versatile medicinal plant is the unique source of various types of chemical compounds, which are responsible for the various activities of the plant.

Hence extensive investigation is needed to exploit their therapeutic utility to combat diseases. A drug development programme should be undertaken for the development of modern drugs with the compounds isolated from *Panax ginseng*. As the global scenario is now changing towards the use of non-toxic plant products having traditional medicinal use, development of modern drugs from *Panax ginseng* should be emphasized for the control of various diseases. *Panax ginseng* imbining a tremendous potential deserves a special attention of the scientific fraternity to emerge as a milestone for medical science of this millennium due to its various medicinal uses. Further evaluation needs to be carried out on *Panax ginseng* in order to explore the concealed areas and their practical clinical applications, which can be used for the welfare of the mankind.

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