

# Pharmacology of Ginseng

Jin Sup Oh

*Professor Emeritus, College of Medicine, Seoul National University*

*Seoul 110, Korea*

## I. Introduction

*Panax ginseng* (from a Greek word meaning cure-all) was first named taxonomically by C. A. Meyer in 1843.

Due to its curative and restorative properties, the ginseng has been recognized as a miraculous medicament in oriental medicine.

Even 2000 years old literatures described about *Panax ginseng*.

Several of them are 神農本草經, 名醫別錄, 傷寒論.

Combining modern pharmacological knowledge with the result of long experiences in the ginseng medication, chinese scientists proposed the seven effects of the ginseng as the followings,

- 1) 補氣救脫 : The effects of tonic, and stimulating the recovery of tiredness.
- 2) 益血復脈 : The enhancement of blood cells production and strengthen the puls, effects on anemia, hypotension and cardiac system.
- 3) 養心安神 : Sedative actions and effects on sympathetic nerve system.
- 4) 生津止渴 : Stimulating secretions and appeasing effect on thirst.
- 5) 補肺定喘 : Strengthen lung and effect on asthma.
- 6) 健脾止瀉 : Strengthen stomach and enhancing appetite, and antidiarrheal activity.
- 7) 托毒合瘡 : Antidotal action against intoxication, anti-inflammatory activity and cosmetic effect on skin.

In the orient the studies on ginseng research with modern scientific aspects began about 60 years ago. Furthermore, in the west, the ginseng research has only 20

years old history.

The tonic effect is one of the most important effects of ginseng. It has appeared so many times in oriental medical literatures.

Brekhman and his group proposed a hypothesis to explain the impact of tonic effect of ginseng, and finally many scientists involved in ginseng research now begin to believe in his hypothesis.

The tonic effect of ginseng appears most often times in old oriental medical literatures as mentioned before.

Brekhman and his group have intensively studied the nature of this effect and they reached a conclusion, in which the certain active component of ginseng gives rise a nonspecific resistance as the living organisms are under undesirable environments like disease and stress.

And they named the substances giving nonspecific resistance as the adaptogen.

Furthermore they have made efforts to find out the substances exhibiting adaptogenic activity among many oriental folk medicines, and they concluded such substances mainly consisted of glycosides chemically.

Many oriental folk medicines and medical plants have mild actions and they are usually administered long time till their actions appear. The ginseng as a herb-drug is not an exception. Therefore many laboratory workers and scientists involved in ginseng research often meet the difficulty with handling the ginseng as a experimental material.

Because it is not easy to keep the experimental animals and other conditions consistent for long time for experiments.

Thus, such difficulty may be one of the reasons why the experimental data about the ginseng pharmacology have appeared to be unreproducible often and to be inconsistent.

One of biologically active components of ginseng is saponin as the form of glycosides, about 12~13 analogs consisting of panaxadiol forms were isolated and most of their structures were determined.

As Hong(1972) reviewed 467 oriental medical prescriptions, he found 132 prescriptions among them contained ginseng. It means 28% of the total.

In addition, about 1200 publications about ginseng were reported through the world, and 490 publications were found to be concerned with pharmacological action of ginseng or ginseng components.

Among them one hundred ninety publications were reported by Korean scientists.

**Table I.** Number of ginseng-containing oriental medical prescriptions.

Classification* Total	Number of Prescriptions (a)	Number of Prescriptions Containing Ginseng (b)	% (b/a × 100)
Upper Group	123	70	56.9
Middle Group	181	54	29.8
Lower Group	163	8	4.9
Total	467	132	28.3

\* Upper group of prescriptions is tonic remedy, middle group is mild remedy, and lower group is attacking remedy of toxic property.

**Table II.** Publications related with ginseng research

Field	Total Number of Publications (a)	Number of Publications by Korean Scientists (b)	Ratio (b/a × 100) %
Pharmacology	488	190	38.9
Chemistry	219	38	17.4
Total (including others)	1199	279	23.3

## II. Pharmacology of Ginseng

### 1) Effects on Body Weight, Basic Metabolism and Sexual Behavior

It has been well known that the ginseng enhances the synthesis of proteins and nucleic acids, that it maintains the metabolic balances, and that it stimulates sexual activity.

However the exact mode of action has not been elucidated yet.

Since 1929, Min(1929) reported that feeding ginseng to experimental mice produced the gain of body weight and that it stimulated the growth rate. Oh(1964), Park (1962), and Kim(1970, 1935, and 1960), also reported similar growth-stimulating effects on chicken, rabbit and albino mice.

Oura(1967) reported that prostsol, one of protopanaxatriol, which stimulated synthesis of serum proteins especially, albumin, and enhanced protein and nucleic acid synthesis in liver and stomach cells.

Similar observation was made with purified Korean ginseng saponin by Han(1973).

Notsu(1941) observed that when mice fed with food containing ginseng, their copulation time was extended during mating, and that not only the weight of uterus but the production of follicle increased.

Yamata(1955), Yonekawa(1927), and Hashimoto(1932) observed that ginseng exhibited aphrodisiac action to experimental animals, in addition, Brekhman(1967) reported that ginseng showed some gonadotropic action to young animal, and that it helped them to reach the puberty age earlier.

With summarizing the publications mentioned, the ginseng appears to exhibit slight effects under normal conditions, but it gives stimulatory effects to animal under stressed and undesirable environments.

Although the ginseng showed enhancement of sexual activity, it does not seem to have direct stimulatory effect to sex hormone secretion.

### 2) Longevity and Recovery of Tiredness

In order to observe the longevity of experimental animals during fairly short time, animals received no food or toxic food, or they were exercised severely, and consequently they resulted in death.

Through such experiments, it was observed that the administration of ginseng extended longevity significantly or reduced the death rate.

Brekhman's experiments (1971) about recovering tiredness and enhancing human labor working ability are interesting us. When mice received ginseng, their swimming capacity, that is, the duration of swimming markedly increased in comparison with control group.

In case of human working efficiency test, the human who received the ginseng not only performed the elevated reading efficiency about 12% compared with the control group, but also error such as misreading was reduced about 54%. Similar result was observed as the radio-telegrapher who received ginseng also reduced their mistakes. Furthermore, after long administration of ginseng, the marked enhancement of mental and physical endurance appeared and continued for one to one and half month.

### 3) Effects on Stomach

Sorekhtin(1958) observed that when chronic gastritis patients received ginseng, their appetite was recovered and enhanced and that uncomfortable symptom was diminished.

Yoon(1960) reported that when alcoholic extract of ginseng was injected intravenously into cat, movement of stomach was temporarily reduced, and shortly after, that its movement appeared to be stimulated.

Therefore it was suggested that such action might be a direct effect of ginseng on gastrointestinal tracts.

In addition, when Ahn(1962) administered ginseng to human for several months and X-ray picture was taken to follow the movement of contents in gastrointestinal tract, the picture showed the rate of movement of administered food appeared to be faster. This result suggested that ginseng directly stimulated the GI tract movement.

All these observations suggest that ginseng gives effects to rather directly periphe-

ral smooth muscle than to reflectory system and central nerve system. Otherwise it gives no effect to stomach juice secretion.

#### 4) Carbohydrate and Methanol Metabolism

Ginseng was well known to inhibit the hyperglycemia and maintain normal conditions of bodies.

Saito(1921, 1922), Abe(1922), Kim(1932), Petkov(1959) and Yamada *et al.*(1955) reported that ginseng inhibited the hypoglycemia of diabetic patients, adrenaline hyperglycemia and appetite hyperglycemia.

Imamura(1923), Kim(1932) and Kang(1962) reported that both extracts and saponin of ginseng components suppressed the glycolysis in liver and muscle, while these substances increased directly the rate of glucose oxidation in liver.

With summarizing the papers mentioned, we can conclude that the ginseng has dual functions, always maintaining the blood sugar level normal.

In other words the ginseng not only reduced the blood sugar level of hyperglycemia by controlling carbohydrate metabolism, but also it increased the low blood sugar level of hypoglycemia caused by insulin to normal.

Another interesting observation is that ginseng can exhibit some effect on ethanol metabolism as it reduces the ethanol content in blood.

In addition, even it was reported that ginseng stimulated pathologically damaged liver.

Such evidence may support that hangover can be diminished as ginseng is taken before or after drinking alcoholic beverages.

#### 5) Lipid Metabolism and Arteriosclerosis

It is well known that the diseases of cardiac system like hypertension and arteriosclerosis have some connexion with cholesterol content in blood.

Many publications concerning the effects of ginseng on lipid metabolism, especially cholesterol metabolism, have been reported.

Iimai(1941) observed that administering dried ginseng powder to experimental animals had prevented the development of arteriosclerosis.

Lim(1963) also reported that when house rabbits were fed with the food containing ginseng, the contents of blood serum cholesterol and phospholipid appeared to be lower than those of control animals.

Similar observations were reported by Kim(1962), Nahm(1961), Lee(1964), Choi(1968), Kwon(1969) and Park(1969).

Therefore all these observations suggest that the ginseng has certain effects on lipid, especially cholesterol, metabolism and furthermore that it may prevent arteriosclerosis

or and may have direct therapeutic effects.

#### 6) Effects on Hypertension

In 1936, Kim observed that when the alcoholic extract of ginseng or saponin was administered to rabbits, the blood pressure temporarily dropped.

Therefore he suggested that such effects might be due to paralysis of central nerve system.

With respect to this observation I would like to refer to Burkat(1947) observation: the small amount of ginseng increased the blood pressure but large amount of ginseng decreased the blood pressure.

Lee(1960) observed that when alcohol extract of the ginseng was administered to dogs, its blood pressure was dropped suddenly and then immediately it was recovered to normal, and simultaneously the histamine was secreted, and therefore, he suggested that the ginseng might have histamine releasing factor.

When Lim(1963) fed rabbits with non-saponin fraction of the ginseng extracts, the content of blood serum serotonin increased, and thus he suggested that sudden decrease of blood pressure caused by ginseng might be due to the increase of serotonin content in blood.

Although many ginseng researchers agree that the ginseng has some such blood pressure lowering effects, its exact mode of actions is not understood yet. Furthermore, Oh *et al.*(1968) reported that ginseng appeared to be effective to the animal model of hypertension derived from massive administering cholesterol and thyroxin, and Lee(1971) observed that ginseng appeared to lower the blood pressure caused by kidney removal. But such effect was not understood fully either.

#### 7) Effects on Blood and Blood Forming Activity

When house rabbits were fed with food containing ginseng, the numbers of red blood cells, white blood cells and platelets were not changed(Kim, 1931). However, Oh(1961) made an interesting observation that female mice were fed with dried ginseng powder for one month, the incorporation rate of radioisotope  $Fe^{59}$  into red blood cells increased in comparison with that of control group.

Similar observations have been made by Kim *et al.*(1969, and 1955). They found that the numbers of red blood cells of white mice which received the ginseng increased significantly and Park(1970) also reported that the blood forming factor was markedly increased in house rabbit fed with ginseng.

With summarizing all these results, ginseng may give some effects to production of red and white blood cells and platelets and it seems to give significant

increase of incorporation rate of iron into red blood cells and activation of blood forming factors as well.

#### 8) Effects on Central Nerve Systems

Among many biological actions of ginseng, the effects on CNS have been interest of many ginseng researcher. And a number of reports in this area of study have been published. Fujidani(1905) observed first that the panaquilon isolated from ginseng relaxed the voluntary muscle of frog and and that suppressed the central nerve system. Following this, Sakai(1914) found that small amount of the ginseng might stimulates the CNS but fairly large amount brought about sedation of the CNS.

In addition they also found the function of cerebral cortex was brought about in sedation from the beginning.

Similar observations were made by Yonekawa(1926), Min(1930) and Kim (1931) as well. When alcoholic extracts of ginseng was administered to white mice, the sleeping time caused by hexobarbital was extended(Kim, 1969).

Moon(1964) and Lee(1965) observed that convulsion caused by metrazol or pic-rotoxin or strychnine was suppressed by administering ginseng.

Furthermore, Oh(1769) reported that while small amount of ginseng shortened the sleeping time of white mice derived from nembutal uptake, large amount extended it longer, and convulsive seizure caused by metrazol or cocaine was not suppressed with small amount of ginseng, but large administration of ginseng extended the time of appearance of convulsion and death.

Therefore, it may be concluded that ginseng has dual effects on CNS, that is, small amount exhibits stimulatory action, whereas large amount shows sadative. Recently, psychological methodology in the area of ginseng researeh has been introduced to study the effects of ginseng on CNS.

Petkov(1959) found that Korean ginseng had stimulatory effects on multiple functions of cerebral cortex, and that it maintained the balance of such activation state.

Unlike amphetamine, a synthetic drug, the effects of Korean ginseng showed long duration of action, but no side-effects, and therefore, he concluded Korean ginseng had certain effects on maintaining balance and releaving psychological stress.

Brekhman's suggestions(1969) are of more interest, since ginseng showed slight or no effects on normal sleeping, so thatit could be administered for long time without side-effects.

Furthermore Takagi *et al.*(1972, 1973) suggested that panaxadiol isolated from

ginseng saponin possessed sedative effects, while panaxatriol had stimulatory effects on CNS.

This observation indicated also that ginseng contained both stimulatory and sedative components at certain proportion.

Similar observations were made by Hong(1970, 1974) and Shin(1973) with total ginseng saponin fraction.

All the results mentioned suggest the ginseng has significant effects on CNS; however, it is uncertain whether the action of ginseng itself is stimulatory and/or sedative(suppressive).

Generally, it seems to be stimulatory under stressed condition like disease, whereas it showed slightly sedative or no action to normal condition.

#### **9) Protection against Stress**

The living organisms including human body react to every stress no matter what its sources would be physical or emotional in order to protect themselves from harmful conditions.

One of important biological actions of ginseng is the protection effects against stress.

Min(1929) reported first that he fed white mice ginseng, and then no foods were given till all mice were dead, the death rates of mice received ginseng were significantly reduced compared with those of the control group.

Since then Park(1962), Kim(1963) and Kim(1966) found similar results in the experiments in which the mice which received ginseng showed marked increase of resistance to physical stress like excessive coldness and X-ray irradiation.

In addition, Kim(1966) and Oh(1969) also observed such a increased protection effects on chemical stresses, too.

Egg-laying efficiency of chicken which received food containing ginseng was rather increased under excessive cold and heat, while there was no difference under normal conditions(Oh, 1964).

Kim(1965), Hu(1967) and Lee(1968) reported that the reduction of the adrenal ascorbic acid content was prevented when they received ginseng under the stress.

In addition the Oura(1967) found that when experimental animals under stress were fed with ginseng, their DNA, RNA and protein syntheses increased.

Such protection effects of ginseng on stress was called adaptogenic action by Brekhman(1969), in and addition the effects of ginseng on every stress appeared to be non-specific.



### 10) Toxicities and Side Effects of Ginseng

Hong(1974) measured LD<sub>50</sub> of ginseng saponin in mice and it was 272 ± 52 mg/kg, while Takagi(1972) reported that LD<sub>50</sub> of the saponin was estimated as 600~900mg/kg in mice.

Although less than 10 g/day of crude form of ginseng are being usually taken for human, we can observe significant biological activity with less than 10 mg/kg of purified saponin isolated from ginseng.

Thus it can be said that ginseng is one of very safe medicinal drugs.

### III. Summary

1) Ginseng exhibits slight effects on body-building tonic action and basic metabolism under normal condition, whereas it shows markedly stimulatory effects on them under undesirable environment and conditions like disease and stresses.

Feeding ginseng does not seem to stimulate the secretion of sex hormone, however it appears to give indirect effects on sexual activity when the living organism and animals exposed to some abnormal conditions.

2) Ginseng enhances physical endurance and mental concentration ability, and such effects increases work efficiency and prompts the recovery of tiredness.

3) Generally ginseng stimulate the movement of G-I tracts and smooth muscles. However, such effects vary depending on individuals.

4) Ginseng gives effect on hyperglycemia and lowers the content of blood sugar. Its mode of action is not fully understood.

5) Ginseng lowers blood cholesterol content slightly in normal healthy animal but its effect appears to be remarkable in experimental model of hypercholesterolemia. Therefore it appears to prevent and cure arteriosclerosis.

6) Ginseng lowers temporarily blood pressure, and such effects may be related with CNS suppression and release of histamine and serotonin. Its exact mechanism of action is still unknown.

7) Ginseng does not enhance the production of blood cells. But it produces increased incorporation rate of radioisotope <sup>59</sup>Fe into red blood cells and it seems to activate the blood forming factor.

8) Many contradictory and, to some extent, confusing reports have been published in the studies of ginseng effects on central nerve system. However, generally ginseng acts as stimulant to CNS, especially, its small amount shows stimulatory.

9) Ginseng gives not only protecting effect against harmful stress, but also it

increases the ability of mental concentration and working efficiency.

Although its exact mode of action is uncertain, the protection effects may be produced either in peripheral organ and adrenal or cerebral cortex and CNS.

10) Ginseng enhances the synthesis of DNA, RNA and protein and causes to release histamine and serotonin. And the toxicity and side effects of ginseng appear to be negligible.

As closing this review, it was impossible for me to cover all tracks of ginseng research and I hope this review was not biased too much to my personal opinions.

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