高麗人蔘學會誌
Korean J. Ginseng Sci. Vol. 1, No. 1, pp. 33—49 (1976)

A Study on the Psychopharmacological Actions of *Panax ginseng* in Animals

Sa Ack Hong, Hyun Kap Chang and Myung Suk Kim

Department of Pharmacology, College of Medicine, Seoul National University
Seoul 110, Korea

Abstract

As a continuation of series of works on the pharmacological actions of Panax ginseng, three kinds of behavioral experiments were carried out using rats and mice.

The occurrence of component patterns of general behavioral activity in rat was examined by visual scanning using the time sample method in the ad lib. and the hunger deprivated situation.

In normal ad lib. situation, the eating behavior of rat treated with 100mg/kg of ginseng saponin was significantly more frequent than that of saline control rat at night and throughout the 24 hr period. But grooming was less frequent thna the control at the same period.

In the hunger situation followed by 90~120 hrs of food deprivation, the locomotive activity and rearing were significantly more often and sleeping was less frequent in the two dosage groups of ginseng saponin (10 and 100 mg/kg) than in the saline group through out the observation period.

Training of avoidance conditioning in rats was done in a two-way shuttle box. The number of conditioned response (CR) in which the animal avoided sucessfully an electric shock by running in to the other compartment of the box was regarded as an index of learning performance.

Ginseng saponin in doses of 2.5 mg/kg produced a significantly increased CR in total avoidance trials compared with the control. Although other dosage groups of ginseng saponin (5.0, 50mg and 100 mg/kg) showed no significant statistical difference from the normal control, it tended to increase in CR in the ginseng groups than in the control.

An aggressive behavior in mice was observed in a shock-generating fighting box. The occurrence of reflexive fighting between two animals induced by an electric shock applied to the feet was checked as an index of aggression.

The occurrences of reciprocal fighting episode immediately after the onset of the shock was significantly decreased in the dosage group of 400 mg/kg ginseng saponin, but it did not differ in the 100 mg/kg group of ginseng saponin from the control group. The dose, 400 mg/kg of ginseng saponin, inhibited fighting behavior in more than 80% of the pairs, but 100 mg/kg of ginseng did inhibit it in less than 20% of the pairs.

Although so called a tonic effect of *Panax ginseng* can be a total effect of the actions on the various organs, we have been thinking that this effect may be due to its effect on the central nervous system. With this thought in mind, we have studied on the effects on CNS from various points of view.

The studies on the psychopharmacological actions of ginseng which we have carried out include three fields: a relationship between ginseng and general behaviors, a relationship between ginseng and learning, and a relationship between ginseng and emotional activities.

Our first report on the studies on the relationship between ginseng and general behaviors was published in 1972. We fed on rats the feed containing the alcohol extract of *Panax ginseng* for a comparatively long period of time and then observed their activities for 24 hours. In that study we observed that the ginseng-fed rat group showed no difference in their activities during the daytime compared with the control group.

However, we observed that during the night the sleeping time decreased, that the rats ate more feeds, and that the behaviors increased when they were fed with the ginseng extract. On the basis of this evidence it is assumed that ginseng has the CNS stimulating action which increases the behavioral activity by elevating the level of sensation.

In 1973 Shim and Oh[1] observed a decrease in the sleeping time in the rats fed with ginseng saponins and an increase in the behavioral activity. And therefore these results support our suggestion. In 1974 when we thoroughly studied on the effects of ginseng saponin on the voluntary activities of rats and mice using the light interception apparatus, we found that the activivies of the ginseng-fed group increased, compared with that of the control group in the doses below 50 mg/kg and that, on the contrary, the activities decreased in the large doses over 100 mg/kg. These results show that the activities can vary depending on the saponin doses administered. We also observed the similar tendency in the experiments of general behavioral activities.

In these two studies, however, only single dose of ginseng saponin was given to rats, followed by an observation in a short period of time. And therefore this is contrary to the traditional method of administering ginseng to humans. Since the behaviors in daytime were observed and the experimental animals were nocturnal animals, the results may not reflect adequate responses. For these reasons the behaviors observed may not be so normal as the general behavioral activities of rats and mice.

In the present study, therefore, we observed behavioral activities after the eight-day administration of ginseng saponins in order to diminish these incomplete conditions in the previous reports. We also observed the alteration in the general behavioral activities in the animals given with ginseng for a long period of time in the hunger situation caused by food deprivation, as compared with the normal control group.

Studies on the relationship between ginseng and learning activity were first conducted by the authors[3]. In that study the conditioned response (CR), which is an index of learning of the conditioned avoidance(CAR), of the ginseng-administered rat group was observed as compard with the control group. It was shown that CR of the ginseng-administered group was increased as compared with the control group, and this indicates an increase of CAR achievement and a decrease of disappearance rate, suggesting that ginseng stimulated the conditioned avoidance response.

Chang[2] (one of the authors) observed in his experiments that the ginseng-administered mice group performed better than the control group in the learning performance in water. And he suggested that ginseng might enhance the learning activity by stimulating the central nervous system.

These two experiments cited above appear to have some shortcomings: the sample used in the conditioned avoidance response test was ginseng extract; the doses of the extract were inaccurate because it was mixed with the feeds; The performance after the only one dose in the learning performance of the mice in water was observed. In order to diminish these shortcomings, therefore, our experiment used ginseng saponin instead of the extract and a method of repeated administrations of the saponin instead of a single dose, obtaining relatively accurate values of CR, the index of learning CAR.

In our previous studies of the relationship between ginseng and the emotional activity, we observed primitive physiological responses such as the changes of defecation and urination of mice in CAR process and the spontaneous activity in an open field. On the contrary to this, Nabata[13] *et al.* reported that the reflex fighting activity was significantly decreased in the mice group which was given 4000mg/kg of ginseng saponin and an electric shock. In this study we attempted to observe in detail the effects of ginseng on the emotional activity of mice by checking an aggressive behavior, a more concrete aspect of the emotional activity.

Experimental Materials and Methods

1) Experimental Materials

The methanol extract of *Panax ginseng* was dissolved in water and ether was used three times to remove oily matters. To the water layer was added the same volume of *n*-butanol and was vigrously shaken. Then the butanol layer was separated. This procedure was repeated four times to extract the saponin into butanol. The combined butanol layer was evaporated under reduced pressure. The acquired residue was separated into several saponin fractions by preparative thin layer chromatography. To conduct TLC, 2.1 grams of the total saponin were dissolved in 10m*l* of cold methanol and stored in a refrigerator for a week. After the precipitate was removed by filtration, the filtrate was applied to TLC by streaking 0.4m*l* of the filtrate (40 mg of the total saponin) on TLC plates of 0.5mm thickness of the absorbant. The preparative TLC plates were prepared by placing 40g. of silica gel G (type 60, E. Merck Co.) into an Erlenmeyer flask with 95m*l* of distilled water-methanol(2:1) and shaking vigrously for two minutes. A uniform 500 μ layer of the gel was spread on 20×20cm glass plates, using Camag Apparatus (Camag Co., Switzerland). The plates were allowed to stand for 20-30 minutes at room temperature and activated in an oven at 110-120° for one hour. The solvent system used was the lower layer of a mixture of chloroform-methanol-distilled water (65:35:10). A half of the developed chromatogram was sprayed with 3% cerric sulfate in $3N$-H_2SO_4 as a coloring reagent. The unsprayed half of the chromatogram was visualized under UV light. By comparing the two halves, seven saponin bands were located. These saponin bands were scraped from the plates and one gram of the respective band was extracted with about 10m*l* of methanol. The methanol solution was concentrated under reduced pressure and the crystalline saponin fractions were obtained.

2) Experimental Methods

(1) Effects on Sleeping and General Behaviors

A). Experimental animal and apparatus

Male Sprasue Dowley hybrid rats whose body weight was about 200g were used. Cages with a size of 30×30×30 cm whose front side and bottom were made of iron wire and the other side was of iron plate were used for preservation and observation. Thirty cages of this type were displayed on the six shelves of the observation stage, with five cages on each shelf. Solid feeds and a water tub were supplied to each cage with one rat in it. An animal room which was relatively little affected by the

environment was used as the laboratory. The natural light was used during the daytime, but two red fluorescent lamps(60 w) were used during the night (6 p.m.~6 a.m.) in order to make it easy to observe behaviors of the animals. The temperature of the laboratory had been kept around 20° and animals were adapted to this atmosphere for a week before the initiation of the experiments.

B). Experimental Procedure

After 30 rats were adapted to the environment for a week, the animals were divided into three groups: saline control group, 10 mg/kg ginseng saponin groups, and 100 mg/kg ginseng saponin group. Consequently there were ten rats in each group. Doses of 10 mg/kg and 100 mg/kg ginseng saponin dissolved in 0.5 m*l* of saline per 200-gram body weight of rats were injected subcutaneously to each animal of the groups every morning between 4:00~9:30 a. m. for eight days. From 11.00 a.m. (an hour and a half later) after injecting the last dose on the eighth day, the observation of the behaviors was initiated.

A modification of the methods designed by Bindra[6] and Kim *et al.*[8] was adopted in evaluating general behaviors by time schedule. First, the observer entered silently the laboratory at 10:57 a.m. and sat quietely on the chair about one meter distant from the observation stage for three minutes and then began to observe from 11:00 a.m.

At first the behaviors of the five animals on the highest shelf were observed from the left to the right cage for five minutes and were recorded on the prepared charts. After the behaviors of each animal on the highest shelf were scanned ten times during the five minutes, the observation of the behaviors of the rats on the second shelf was followed. It took 30 minutes to finish all observations on the lowest shelf and this was called one session. After resting for 30 minutes, the second session was initiated. The behaviors of each animal were observed ten times in a session. Therefore the observations were made 240 times for each animal (10 times×24 sessions) in a day.

The general behaviors observed are as follows:

i) Sleeping: lying, crouching down the body, covering the head and closing the eyes.

ii) Lying: lying silently without moving or smelling.

iii) Locomotion: moving the body with four legs.

iv) Rearing: placing the front legs on the wall, or rearing the front legs and looking around or smelling.

v) Eating and drinking: eating feeds or drinking water.

vi) Grooming: licking the hair or scraching successicely, or motioning like washing the face.

vii) Miscellaneous: behaviors not mentioned above, for example, yawning or stretching the body.

The general behavioral activities were observed one time in the normal *ad lib.* condition and also observed one more time in the hunger situation followed by 96~120 hours of feed deprivation.

(2) Effects on the Conditioned Avoidance Response

A) Experimental animal and apparatus

Fifty Sprague Dowley rats whose body weight was about 200 grams were used. These animals were raised in iron-cages of 36×18×20 cm size with one animal in each cage receiving sufficient water and feeds for a week to adapt them to the laboratory environment. The size of the shuttle box used was 81×125×23 cm and the right, left, back and upper sides of the cage, were made of black bakelite, but the front was of transparent acrylic material, which was used for observing behaviors as well as for placing in or takin out the animals as a door. The brass rods of 3 mm diameter were attached 1.2 cm apart to the bottom of the cage from the front to the rear.

This cage was separated into two compartments by a board in the middle, which had an arch door of 5 cm width and 8 cm height, and through the door the animals could move freely.

The unconditioned stimulus(US) used was an electric shock, 700v, 155 mA a.c. which came through the bottom of the cage. The conditioned stimulus(CS) was ten-second light beam of a 60 W electric lamp attached to the ceiling of the cage. Operation of CS and US was manually controlled through the stimulator attached.

B) Experimental procedure

The experimenter took out the animals from the cage ten minutes before the initiation of the experiment and weighed them for body weight. The given amount of drug whose volume was 1 m*l* per 200 grams of the body weight was administered intraperitoneally.

Five minutes after the administration, the animals were adapted to the environment of the shuttle box without giving CS and US. After the completion of the adaptation, the light(CS) was turned on for ten seconds from the ceiling. CS stopped automatically if the animal moved into the other compartment during ten seconds. The electric shock was given as soon as the light beam was turned off.

The resting period between the trials was one minute, and 30 trials were conducted in a day(one session) for six consecutive days(6 sessions). The number of CR which the animals showed during the achievement period of the conditioned avoidance response was used as an index of learning performance.

(3) Effects on Aggressive Emotional Activities

A) Experimental animals and apparatus

For the experiment 180 grown-up male white mice whose body weight was about 20 grams were used. These mice were divided into 90 pairs by selecting two mice of similar body weight into a pair. Each pair of animal was placed into the fighting box which will be described below and was given electric shock for three minutes at 10 seconds intervals.

Sixty pairs (120 mice) which fought at a rate of more than 50 per cent were selected for the experiments. These animals were raised as a group of five mice in each cage of 15×15×15 cm size. A shock-induced fighting box by Tedech *et al.*[11] was slightly modified and used.

A transparent acrylic plate was attached to the front of the small plastic box of 15×15×15 cm size to observe easily the behaviors of the animals. Black opaque acrylic plates were used or the other three sides and the ceiling. Copper rods of 3mm diameter were installed at 1 cm intervals, 8 cm apart from the bottom. These rods were connected alternately to the same electrode so that the electric shock could be felt if the animal stepped on the two adjacent rods. The strong electric shock of 700 v, 0.23 mA a.c. was used to eliminate individual difference due to the innate resistance of the animals and was operated by a remote control.

B) Experimental Procedure

For the experiment 120 animals which fought at a frequency of more than 50% in the preliminary experiment were divided into 60 pairs by selecting two animals of relatively similar body weight as a pair.

Six kinds of drugs to be described below were administered intraperitoneally into mice 30 minutes before the onset of the experiment.

The six groups were: 100 mg/kg ginseng saponin group, 400 mg/kg ginseng saponin group, saline control group, stimulant control group (amphetamine 1 mg/kg) and two sedative control groups (chlorpromazine 2 mg/kg and meprobamate 80 mg /kg), and each group had 20 animals. Thirty minutes after the injection, the animals were simultaneously placed into the fighting cage.

Thereafter, a spontaneous fighting between two animals was checked for two mi-

nutes without giving any shock and then the main experiment was carried out. The first shock was manually operated to give five times of short instant stimuli within two seconds. Whether a reflexive fighting between two animals occurred or not was checked during the treatment with electric shock.

Results

1. Analysis of Sleeping and General Behaviors

Table I shows the mean numbers of the occurrences of 7 component patterns of general behavioral activity including sleeping displayed by the three animal groups, i.e., saline control group, 100 mg/kg ginseng saponin group and 10 mg/kg ginseng saponin group during the day and night and in 24 hours in normal *ad lid.* condition. As shown in Table I, the grooming of the rats treated with 100 mg/kg ginseng saponin was significantly less frequent than that of the saline control rats during the night and throughout the 24 hours period. However, the eating behavior was more frequent than that of the control during the same period. The grooming of the 10 mg/kg ginseng group was less frequent, but the difference was insignificant. The eating and drinking behaviors were significantly more frequent than those of the control group during the daytime. There was no significant difference between the ginseng groups and the control group in the other behaviors. Table II shows the mean numbers of the appearances of general behavioral activities dispalyed by the three groups during the day and night and in 24 hours after 96~120 hours deprivation of feeds. Even in hunger situation the animal was allowed to drink water freely.

Sleeping was significantly less frequent in two ginseng groups (10 mg/kg and 100 mg/kg) than that of the saline control group throughout the observation periods.

Table I. Mean numbers of occurrences of 7 component patterns of general behavioral activity displayed by the three animal groups in the daytime, at night, and in 24 hours, in normal *ad lib.* condition

Groups / Behavior component	Saline			Ginseng 100mg/kg			Ginseng 10mg/kg		
	Day	Night	24hrs.	Day	Night	24hrs.	Day	Night	24hrs.
Sleeping	88.4	56.8	145.2	90.3	62.8	153.1	93.7	58.7	152.4
Lying	11.8	18.4	30.2	12.2	14.7	26.9	5.4	11.8	17.2
Locomotion	1.5	4.4	5.9	1.6	5.3	6.9	1.9	9.8	8.8
Rearing	1.1	3.0	4.1	1.5	1.5	3.0	0.4	4.2	4.6
Grooming	13.6	23.3	36.9	9.3	15.0*	24.3*	8.7	221.9	31.6
Eating & Drinking	2.7	12.2	14.9	3.8	19.4*	23.2*	7.4*	13.6	21.0
Miscellaneous	0.9	1.9	2.8	1.3	1.3	2.6	1.0	1.8	2.8

*The value is significantly different from that of the saline control.

Table II. Mean numbers of occurrences of 7 components patterns of general behavioral activity displayed by the three animal groups in the daytime, at night, and in 24 hours, in 96~120 hrs. deprivation of food.

Behavior component \ Groups	Saline			Ginseng 100mg/kg			Ginseng 10mg/kg		
	Daytime	night	24hrs.	Day	Night	24hrs.	Day	Night	24hrs.
Sleeping	69.2	70.7	139.9	46.4*	42.6*	89.0*	55.3*	51.9*	107.2*
Lying	8.6	11.4	20.0	18.0	15.3	28.3	8.5	9.5	18.0
Locomotion	21.5	22.1	43.6	32.8*	33.6*	66.4*	29.2*	33.6*	62.8*
Rearing	12.9	8.8	21.7	18.2*	17.0*	35.2*	12.2	16.0*	22.2
Grooming	8.0	6.8	14.8	9.1	9.1	18.2	11.0	9.3	20.3
Eating & Drinking	0.2	0.2	0.4	0.1	0.3	0.4	0.6	0.1	0.7
Miscellaneous	0.2	0.1	0.3	0.5	0.0	0.5	1.6	0.1	1.7

*The value is significantly different from that of the saline control.

On the other hand, the diurnal cycle of sleeping disappeared in all three groups under this condition of food deprivation. The locomotive activity, an index of behavioral activity, was significantly more frequent in the two ginseng groups than in the saline group throughout the day, at night and in 24 hours. The rearing, which has a close relationship with the locomotion, increased significantly in the 100 mg/kg ginseng group throughout the observation periods. In the 10 mg/kg ginseng group, the rearing increased significantly only at night, but the increase was insignificant in other periods.

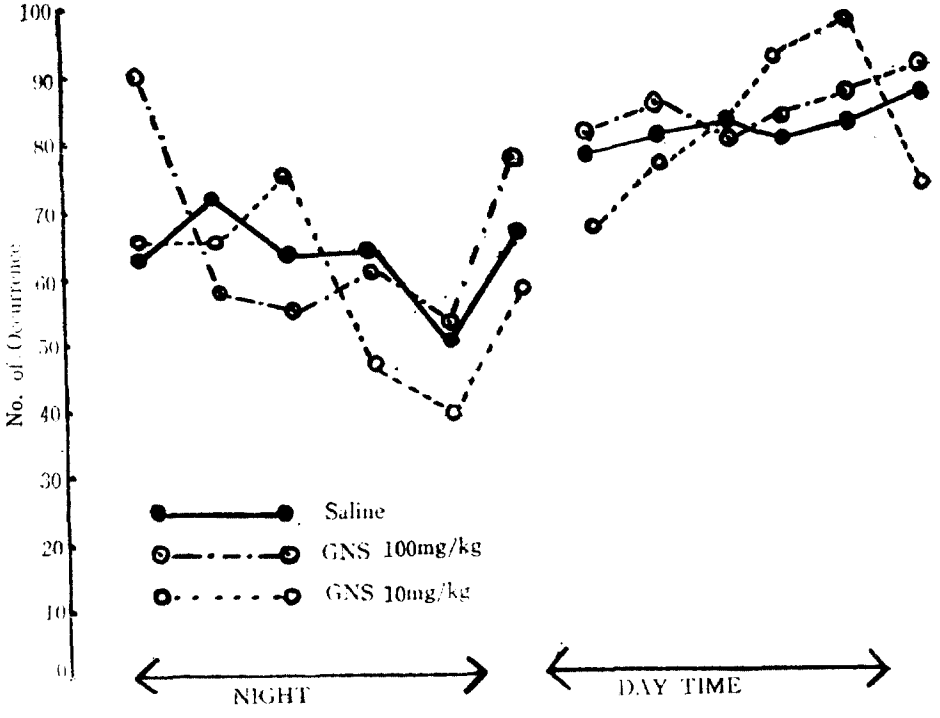

Fig. 1. Occurrence of total inactivity (sleep+lying) in normal *ad lib.* condition.

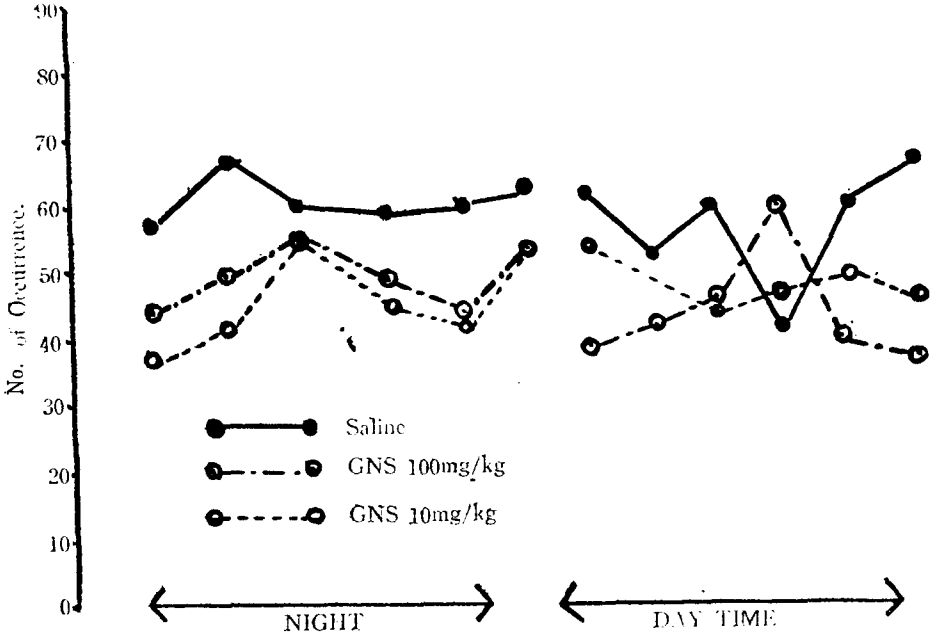

Fig. 2. Occurrence of total inactivity(sleeping+lying) in 96~120 hrs. hunger condition.

Figure 1 shows the occurrence of total inactivity(sleeping plus lying) in three groups in normal *ad lib.* condition. As shown in Figure 1, the total inactivity was less during the night than during the day in all the three groups. Although the diurnal cycle appeared, there was no significant difference between the three groups both during night and day.

Figure 2 shows the occurrence of total inactivity (sleeping plus lying) in the three groups in 96~120 hours deprivation of feeds. As shown in Figure 2, the total inactivity was markedly much more in the saline control group than in the two ginseng groups both during night and day.

2. Conditioned Avoidance Response

Table 3 shows the total mean numbers and its standard error of conditioned response (CR) during six days of training of avoidance conditioning in the ginseng groups and the control group. As shown in Table 3, all the ginseng groups produced more CR than the control. However, only the 2.5 mg/kg ginseng group produced a significantly more CR than the control and the other dosage groups of ginseng showed no significant difference from the normal control group. The mean numbers of CR during six days are shown in Figure 3, which indicates a tendency of increased CR in all the ginseng groups from the second day of the experiment. An ascending line at a relatively same rate was shown in the 215 mg/kg and 5.0 mg/kg ginseng groups,

Table III. Total mean number of conitioned response(CR) displayed by various dosages of ginseng saponin.

Group	No. of case	Total mean No. of CR	SD
Saline control	12	35.1	29.9
Ginseng 2.5mg/kg	12	59.8*	39.1
Ginseng 5.0mg/kg	12	56.3	30.4
Ginseng 50mg/kg	12	44.9	36.5
Ginseng 100mg/kg	12	55.1	38.3

*The value is significantly different from that of the saline control.

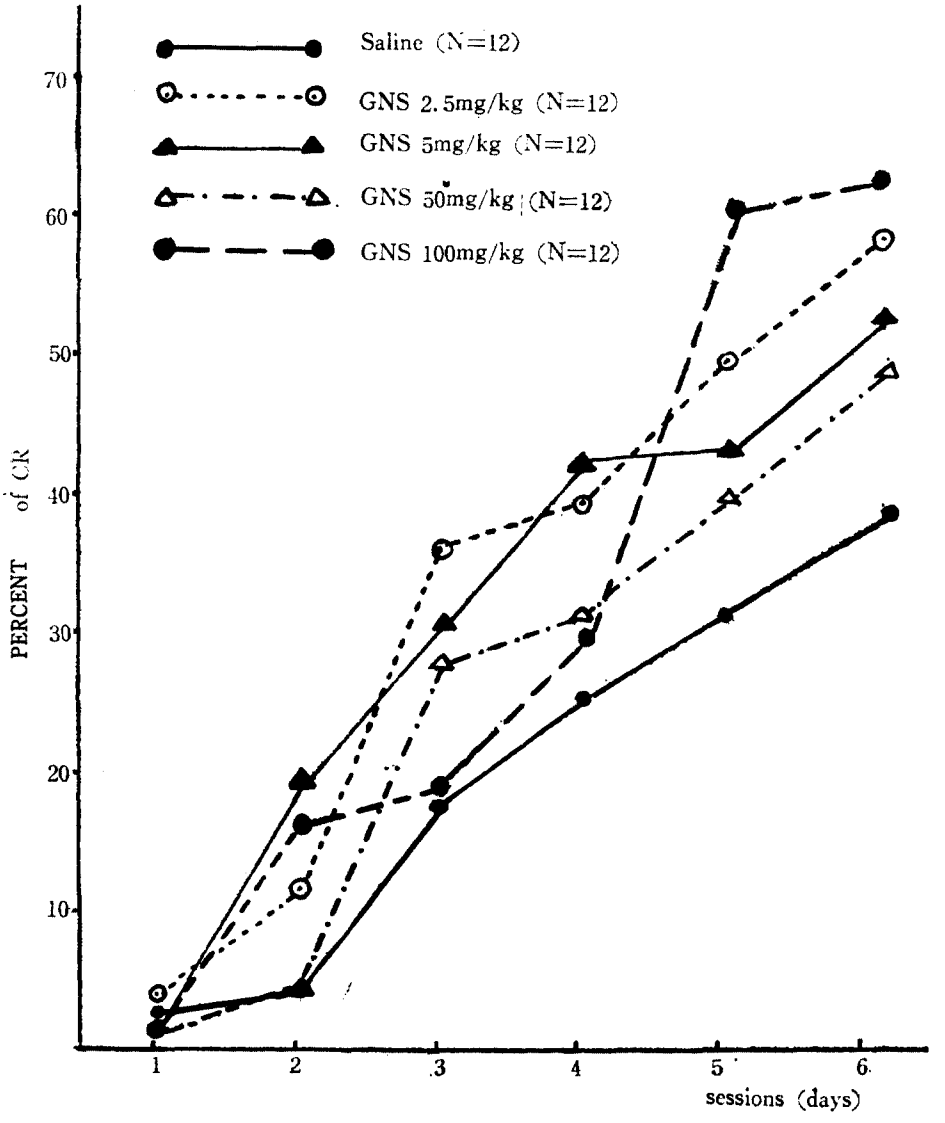

Fig. 4. Conditioned avoidance response(CAR).

respectively. Especially, the 100 mg/kg ginseng group showed a sharp increase in CR on the fifth and sixth days, and this increase is significant(p.c. 0.5) as compared with the control.

3. Aggressive Emotional Behavior

Table IV shows the total mean numbers and standand errors of shock-elicited reflexive fightings in the ten trials after administering several drugs. As shown in Table IV, the occurrence of reciprocal fighting episode of the 400 mg/kg ginseng group was significantly decreased to 2.8, i.e., about a half of that of the saline group(6.0), but it showed no difference in the 100mg/kg ginseng group. On the other hand, the occurrence was significantly increased in the amphetamine group and significantly decreased both in the chlorpromazine and meprobamate groups as compared with the saline control group.

Table V shows the number of those pairs that fought less than half of the 10 fighting episodes after the shock was given to the six groups. There was a tendency of decrease in the aggressive activity by the administration of the drugs, although only those animals that had fought at more than 50% were selected prior to the experiment. This tendency appears to be due to the adaptation of the animals to the environment. The dose of 400mg/kg ginseng saponin inhibited the fighting behavior to 80%, whereas the saline inhibited only 20% of the behavior. The dose of 100mg/kg inhibited only 20% of the behavior, chlorpromazine 50%, and meprobamate 60%.

Table IV. Total mean numbers of shock elicited reflexive fighting in various kinds of drugs

Groups	Mean No. of occurrences of fighting episode	SD	Significance
Saline control	6.0	1.7	
Ginseng 400mg/kg	2.8	1.2	$P<.01$
Ginseng 100mg/kg	6.2	2.4	None
d-Amphetamine 1.0mg/kg	7.3	11.3	$P<.05$
Chlorpromazine 2.0mg/kg	4.2	1.7	$P<.05$
Meprobamate 80mg/kg	4.4	1.9	$P<.05$

Table V. The number of pairs that fought less than half of the fighting episode after receiving shock.

Groups	No. of pairs	No. of pairs inhibited
Saline control	10	2
Ginseng 400mg/kg	10	8
Ginseng 100mg/kg	10	2
d-Amphetamine 1.0mg/kg	10	1
Chlorpromazine 2.0mg/kg	10	5
Meprobamate 80mg/kg	10	6

Discussion

1) Analysis of Sleeping and General Behavior

In the first experiment of this study it was observed that eating activity increased in the ginseng-administered groups in normal *ad lib.* situation an and that grooming decreased. It was also observed that in the hunger situation followed by 96~120 hours of food deprivation, sleeping decreased, whereas locomotive activity increased in the ginseng groups. The increase of eating activity in normal *ad lib.* situation in this study agrees with the results of the previous study by Hong *et al.*[4], but the decrease of rearing does not agree with the previous result. The previous study by Hong *et al.*[4] showed that sleeping at night decreased and that eating activity increased in the ginseng extract group. There is no difference in methodology between this study and the previous one by Hong[4] *et al.* except that this study used ginseng saponin instead of its extract, that the sample was administered subcutaneously instead of oral route, and that the doses were a little different although they are not directly comparable. Therefore it is not clear at the present whether ginseng let the animal eat much more feeds by making it sleep less in normal *ad lib.* situation, or whether by reducing the rearing of the animal. By combining the results of this and the previous studies it is clear that the long-term administration of ginseng has no significant effects on the diurnal cycle of normal behaviors of rats. Therefore it can be stated that the long-term administration of ginseng causes no side effect on the rhythm of the normal general behaviors. On the other hand the general behaviors such as locomotive activity and standing, increased and the inactivity decreased in the two ginseng groups in the hunger situation. And these facts suggest that ginseng may increase the resistance against a severe biological stress such as food deprivation. Wald and Jackson[12] reported that general behaviors increased in the slight deprivation of food in rats, that the increase meant an enhancement of searching activity for food, and that a severe food deprivation harmful to health strongly decreased general behavioral activities. Therefore the change of behavioral activities elicited in the food deprivation may reflect the physiological condition of the animal itself. The increase in the general behaviors of the ginseng group in the severe deprivation of food suggests a greater physiological response against the food deprivation than that of the control group. On the other hand, three animals of the control group died during the 86-120 hours period of food deprivation, whereas only one animal of the 10mg/kg ginseng group among 20 animals of the two ginseng

groups died. Since the death rate was lower in the ginseng groups, it can be related with the so-called tonic action of ginseng, a protective action against diseases. This is supported by Karzel's report that ginseng increased the basic metabolic activity of humans in a severe hunger situation

2. Conditioned Avoidance Response

In experiment 2 of this study, ginseng saponins in doses of 2.5mg/kg exhibited a significantly increased CR in total avoidance trials as compared with the control. Other dose groups of ginseng saponins showed no significant difference from the control although it tended to increase slightly in CR in the ginseng groups. However, this tendency agrees with the results of the previous two studies by the authors (Hong *et al.*,[3] and Chang,[2]). It suggests therefore that ginseng may stimulate learning activity. The reports that ginseng enhanced varius performances related to learning activities agree with the reports of Petkov[9] and Sandberg[10]. Petkov(1961) reported that ginseng extract stimulated a positive conditioned defensive reflex(i. e., conditioned avoidance response), and this result is very similar to the results of the two reports by the authors's study, university students given with "Ginseng Geriatric Pharmaton" and "Gerikamplex vitamex", two capsules a day for 33 days, made significantly less errors in both spiral maze test and letter cancellation test and this suggests that ginseng stimulated the learning performance. Nabata *et al.*[13] reported that the administration of neutral ginseng saponin in a dose of 30mg/kg blocked CR of the already tranined rats in the conditioned avoidance response and that the administration in doses over 200mg/kg blocked both CR and UR, suggesting that ginseng might block selectively the conditioned response like chlorpromazine. His result does not agree with the results of our present study in which ginseng was administered from the initial stage of training for conditioned avoidance. Although the data were not shown in the tables in the present study, 50% of CR was blocked when it was observed in 30 minutes after injecting a single dose of 100mg/kg ginseng saponin to the experimental animals which had previously shown 80% CR without administering ginseng saponin, and this result is similar to that of Nabata's study. Even though it is not clear at the present what this fact means in concrete detail, it is assumed that different psychopharmacological actions may be elicited by short-term and long-term administration of ginseng saponins.

3. Aggressive Emotional Response

In the third experiment of this study, the occurrence of aggressive behavior after the onset of an electric shock significantly decreased in the 400 mg/kg ginseng

mice group, but there was no difference between the 100mg/kg ginseng group and the control group. Nabata *et al.*[13] reported that the occurrence of reflexive fighting induced by an electric shock significantly decreased in the 400mg/kg ginseng saponin mice group as compared with the 4 mg/kg chlorpromazine mice group. However, over 70% of the mice died in a day after 400 mg/kg ginseng or 4 mg/kg chlorpromazine were given to them in the present study. The different result of this experiment from that of Nabata *et al.*[13] may be due to the fact that the genetically different mice strains were used in the two experiments. Therefore the result of this experiment does not warrant any theory or suggestion as to the effect of ginseng on the aggressive behaviors of mice.

Conclusion

As a continuation of series of works on the pharmacological actions of *Panax ginseng*, three kinds of behavioral experiments were carried out using rats and mice.

1) General behavior analysis

The occurrence of component patterns of general behavioral activity in rat was examined by visual scanning using the time sample method in the *ad lib.* and the hunger deprivated situation.

In normal *ad lib.* situation, the eating behavior of rat treated with 100mg/kg of ginseng saponin was signigicantly more frequent than that of saline control rat at night and throughout the 24hr period. But grooming was less frequent than the control at the same period.

In the hunger situation followed by 96~120hrs of food deprivation, the locomotive activity and rearing were significantly more often and sleeping was less frequent in the two dosage groups of ginseng saponin (10 and 100 mg/kg) than in the saline group throughout the observation period.

2) Shuttle avoidance response

Training of avoidance conditioning in rats was done in a two-way shuttle box. the number of conditioned response(CR) in which the animal avoided successfully an electric shock by running into the other compartment of the box was regarded as an index of learning performance.

Ginseng saponin in doses of 2.5 mg/kg produced a significantly increased CR in total avoidance trials compared with the control. Although other dosage groups of ginseng saponin (5.0, 50 mg and 100 mg/kg) showed no significant statistical difference from the normal control, it tended to increase in CR in the ginseng groups than in the control.

3) Aggressive behavior

An aggressive behavior in mice was observed in a shock-generating fighting box. The occurrence of reflexive fighting between two animals induced by an electric shock applied to the feet was checked as an index of aggression.

The occurrences of reciprocal fighting episode immediately after the onset of the shock was significantly decreased in the dosage group of 400 mg/kg ginseng saponin, but it did not differ in the 100mg/kg group of ginseng saponin from the control group. The dose, 400 mg/kg of ginseng saponin, inhibited fighting behavior in more than 80% of the pairs, but 100 mg/kg of ginseng did inhibit it in less than 20% of the pairs.

Acknowledgment

This work was supported by the research grant of the Central Research Institute, Office of Monopoly, Seoul, Korea.

Literature Cited

1. Shim, S. C., and Oh, J. S.: Effect of ginseng saponin on the general behavior in rats. *Korean J. Pharmacol.* **9**, 9~16 (1973).
2. Chang, H. K.: Effect of ginseng glycosides on the maze learning and the emotional behavior in mice. *Korean J. Psychology* **1**, 178~185 (1971).
3. Hong, S. A., Oh, J. S., Park, C. W., Chang, H. K., and Kim, E. C: Effects of *Panax ginseng* on the central nervous system. Effects of *Panax ginseng* on the conditioned avoidance response in the rats. *Korean J. Pharmacol.* **6**, 1~9 (1970).
4. Hong, S. A., Chang, H. K., and Hong, S. K.: Effects of *Panax ginseng* on the general behavioral activity and survival time of food deprivation in rats. *Choesin Uihak* **15**, 87~91 (1972).
5. Hong, S. A., Park, C. W., Kim, J. H., Chang, H. K., Hong, S. K., and Kim, M. S.: The effects of ginseng saponin on animal behavior. *Korean J. Pharmacol.* **10**, 1~11 (1974).
6. Bindra, D.: Components of general activity and the analysis of behavior. *Psychol. Rev.* **68**, 205~212 (1961).
7. Karzel, K. : Pharmacological aspects of ginseng, *Proceedings of International Ginseng Symposium*, p. 49~55 Seoul, Korea. Sep. 26~30, 1974.
8. Kim, C., Choi, H., Chang, H. K., and Park, R. S: General behavioral activity and its in hippo-campectomized rats. *Brain Research* **19**, 379~394 (1970).
9. Petkov, W: Über der Wirkungsmechanismus ces Panax Ginseng, C. A. May, zur Firage einer Pharmakologie der Reactivittät. *Arzneimittel-Forschung* **3**, 288, (1961).
10. Sandberg, F: Clinical effects of ginseng preparation. *Proceedings of International Ginseng Symposium* p. 65~67 Seoul, Korea, Sep. 26~30, (1974).
11. Tedechi, P., Fowler, P., Miller, R., and Macko, E.: Pharmacological analysis of food shock-induced fighting behavior, In Gurattini, S. and Sigg, E. C., Eds., Aggressive Behavior. New York, John Wiley and Sons, (1969).

12. Wall. G., and Zackson; B.: Activity and Nutritonal deprivation, *Proc. Nat. Acad. Sci.*, **30**, 255~263 (1944).

13. Nobata, Jo, Sato, H., and, Takagi, K.: Pharmacological studies of neutral saponins(GNS) of *Panax ginseng* root. *Jap. J. Pharmacol.* **23**, 29~41. [*C.A.* **78**, 143761 V, (1973)]

〈Received 29 April 1976〉

인삼의 향정신작용에 관한 연구

洪 思 岳·金 明 石
서울대학교 의과대학 약리학교실

張 鉉 甲
서울대학교 사회과학대학 심리학과

초 록

인삼이 중추신경계에 대한 작용을 검토하기 위한 일련의 연구로 본 연구에서는 흰쥐와 마우스를 사용하여 다음과 같은 몇가지 행동연구를 행하였다.

1) 수면과 일반행동 분석

흰쥐를 사용하여 음식물이 충분한 정상상태와 96~120시간 굶주린 절식상태에서 나타내는 일반행동을 분석하였다. 정상상태에서 100mg/kg 인삼투여군은 대조군에 비해 음식먹는 회수가 유의성있게 증가하였고, 반면 몸치장활동이 유의성있게 감소되었다.

96~120시간의 절식상황에서는 두 인삼투여군 모두 대조군에 비해 이동행동, 탐색행동과 같은 활동성이 유의성있게 많고 잠자기와 같은 무활동성은 유의성있게 감소되었다.

2) 조건 회피 반응

흰쥐를 사용하여 왕복회피형 shuttle box에서 전기충격(VS)을 받지 않고 불빛(CS)에 의해 회피한 조건반응(CR)의 수를 학습의 지표로 삼아, 인삼 사포닌 2.5, 5.0, 50 및 100 mg/kg 투여군과 식염수군간에 성적을 비교하였다.

모든 인삼 사포닌투여군의 성적이 식염수 대조군에 비해 앞서는 경향이 뚜렷하지만 통계적으로 유의성있는 경우는 2.5 mg/kg경우 뿐이었다.

3) 공격적 정서반응

전기충격을 마우스의 발바닥에 가해 일어난 싸움에 인삼 사포닌이 어떠한 영향을 미치는가를 알아 보았다.

인삼 사포닌을 400 mg/kg로 투여하면 chlorpromazine 2 mg/kg로 투여한 동물처럼 공격적 행동이 유의성있게 감소되었다. 그러나 100 mg/kg의 경우에는 이렇다할 변화를 초래하지 못하였다.