THE EFFECTS OF GINSENG SAPONIN ON ANIMAL BEHAVIOR

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I. Introduction

It is well known that Panax ginseng has widely been used in various parts of the Oriental world for many centuries, either as a single medical substance or in combination with other substances. It is also true that numerous researchers have published results of studies on its pharmacological actions as well as on its composition.

The Department of Pharmacology, Seoul National University's College of Medicine, in its earlier attempts for uncovering the basis for the alleged tonic actions of Panax ginseng, departed from the assumption that the said actions of ginseng might be stemming from its effects on central nervous system, rather than from some independent actions on various organs. It was assumed, thus, that the major site of its action would be located within the central nervous system.

Accordingly, most of our research efforts were directed to the effects of Panax ginseng on central nervous system.

Kim (1966) reported that alcohol extract of Panax ginseng itself did not display any noticeable effect on the body temperature of rat but interfaced with the effect of nembutal and chlorpromazine, in lowering the body temperature he also reported that his observation on the possible effect of the alcohol extract of Panax ginseng on histamine and serotonin liberation did not disclose any tangible relationship. He observed, however, that alcohol extract of Panax ginseng did prolong the sleep induced by nembutal and that it increased the lethal dose of picrotoxin and strychnine in mouse. These findings, together with other studies, were construed as pointing to the possibility of ginseng's effect on central nervous system.

Oh and others (1969), observed the individual effects of the alcohol extract, saponin fraction, essential oil fraction and fat oil fraction of Panax ginseng in mouse. These fractions themselves did not produce any noticeable effect on the normal sleep of mice.

Administration of saponin in small dosage, however, shortened the duration of sleep induced by nembutal, while administration in a large dose prolonged the sleep. It was also observed that administration of ginseng saponin in large dosage decreased the amphetamine toxicity in mice.

They also reported that administration of ginseng saponin in large amount prolonged duration of convulsion induced by metrazole and cocaine and prolonged the time leading to the death of the experimental animals owing to the administration of the above drugs.

Hong and others (1969) also measured the decline in body temperature effected by various frac-

tions of ginseng extract administered in conjunction with the administration of nembutal, chlorpormazine and reserpine. They reported that alcohol extract and saponin fraction appeared to accelerate decline of body temperature resulting from the use of reserpine, but that they inhibited the temperature decline effected by chlorpormazine. They also reported that a diphenhydramine premedication prevented all the effects of ginseng saponin. Based on the above findings, it was assumed that the saponin fraction might be the principal agent within alcohol extract of Panax ginseng, which may be related to the histamine and serotonin liberation rather closely.

After observing the conditioned avoidance response brought about collectively by all ingredients of Panax ginseng in rat, Hong's group in 1970 reported that the group of experimental animals treated with ginseng acquired a significantly higher degree of conditioned avoidance response than the control group, while treatment of rat with Panax ginseng resulted in somewhat slowing down the extinction of conditioned avoidance response. These findings appeared to indicate the possibility of ginseng influence of animal behavior, especially on the learning process and emotional pattern.

Considering the conditioned and unconditioned stimuli give to experimental animals, however, it appeared rather difficult to isolate the effects from a simple learning process.

Chang in 1971 observed rats in their learning in a maze and their exploratory behavior in the open field. In this experiment, ginseng saponin appeared to accelerate learning in a maze, which in turn, seemed to be suggesting the possibility of its stimulating effect on central nervous system. The study, however, concluded that the direct effect of ginseng saponin on the learning process itself had to be carefully reviewed in the light of the findings presented by other researchers. They observed a decrease in the span of motion following the administration of ginseng saponin and assumed that this might be associated with the inhibition of sedative effect on animals. This finding, in turn, appeared to suggest varying of Panax ginseng depending dosage and method of experiment employed.

Kim and others (1971) observed the span of motion and analysed behavior of rats in an open field with a purpose of measuring the effect of ginseng on the emotional manifestations of experimental animals. This experiment revealed that administration of ginseng increased exploratory behaviors and motility, decreased total excretions in an open field observation, which might be interpreted as phenomena a resulting from ginseng's inhibitory actions CNS.

The above series of experiments appeared to suggest that analysis of general activity of experimental animals might form the basis for further studies in the effect of Panax ginseng on the central nervous system.

In 1972 Hong and others observed that administration of alcohol extract of ginseng decreased the total sleeping hours of rats during 24 hours of unit observation time and that it increased general activity as well as feed intake, suggesting a stimulating effect on central nervous system.

In 1973 Shim and others also reported results suggesting that saponin fraction of Panax ginseng might have a stimulating effect on the central nervous system.

Others including Kim, Chin, and Oh (1973) observed that while ginseng increased spontaneous motility of rats in the open field, it decreased such motility in mouse, and that it did increase exploratory behavior of mice. These findings appeared to suggest complexity of the mechanism of ginseng action.

This paper reports our recent findings on the effects of ginseng saponin on the general activity, exploratory behavior in an open field and spontaneous behavior of these experimental animals.

II. Experimental Method and Meterials

A. Materials

Ethanol extract of ginseng is resolved in absolute alcohol and sediments are obtained by adding ether to this solution three times. The sediment is resolved in water, to which an equal amount of n-Butanol is added. The extract obtained three times from this solution is then distilled on 37°C water bath under decreased pressure to obtain ginseng saponin (G. S.).

B. Measurement of spontaneous motor activity

1. Spontaneous motor activity of mice.

Male albino mice with body weight of about 20 gm each were raised in the laboratory without limitation of feed and water supply. They were fed in groups of five per cage for one week's period. The main apparatus of experiment, the beam cutting apparatus consist of a box of 35 cm by 17 cm by 18 cm. The light source was set up about 2 cm above the longest inner surface. A phototube was placed on the opposite wall of the box, so that blocking of light passage resulting from movement of experimental animals could be automatically counted and registered. The ceiling as well as floor of the box was of metal (iron) net, and all the inner surface of the box were painted black.

Method of observation: The experimental animals were separated into five groups by using the random selection technique, namely, those groups for administration of saline, G. S. 100.0 mg/kg, G. S. 50 mg/kg, G. S. 5.0 mg/kg and G. S. 2.5 mg/kg. Each dose of administration consisted of 0.5 cc per 10 gm. body weight solutions of various dose, to be injected intraperitoneally. Immediately after the injection, each animal was placed into separate apparatus so that the frequency of blocking the passage of light could be recorded at an interval of five minutes. Total length of observation time was two hours. The whole experiment was conducted in a dark room.

2. Spontaneous motor activity of rats

Male white rats of 200 gm body weight were used. Other procedures were identical with those in the case of mice. Each dose of administration consisted of 0.5 cc per 100 gm body weight.

C. Analysis of general behavior

1. General behavior of mice

For experiment, male albino mice of body weight 15 — 25 gm were selected. The experimental apparatus consisted of a box of size 14 × 14 × 14 cm, which housed one mouse for each and served the dual purposes of cage and observation apparatus. The floor and ceiling as well as two opposite walls of the box made of wire netting, while the remaining two walls consisted of metal plates. One unit comprised 5 such boxes, and all the units were arrayed in 2 rows on a shelf of three steps, to facilitate observation. The laboratory was a room of temperatures 25° — 27°C under natural lighting conditions, segregated from outside. No limit was posed on the amount of feed and drinking water supply.

Method observation: Ten experimental animals formed one unit group for observation. The animals were grouped into five, namely for administration of saline, G. S. 100.0 gm/kg, G. S. 50.0 mg/kg, G. S. 5.0 mg/kg, and G. S. 2.5 mg/kg. Each group of experimental animals were allowed one week's period within the apparatus for adaptation. Each dose of 0.5 cc per 10 gm body weight, to be injected intraperitoneally. Following the injection, a 10 minute pause was allowed before commercing observations. The first step of observation begins with inspecting experimental animals place on the upper-most shelf, moving the eyes from the right to the left until they reach the 10th animal of the shelf. Any movement or behavior of the animals are recorded. The observer repeats the same procedure on the animals placed on the 2nd and 3rd shelf, consuming about 2 minutes, in completing observation of 30 animals.

The above procedure is repeated by 10 times. Another round of observation takes place following a 10 minutes' recess. Thus, within a span of 2 hours 4 rounds of observations are carried out, thus recording a total of 40 separate behaviors.

Inspection of animal behaviors began at 12:00 o'clock noon each day and was closed at 6:00 p.m. The recording of the behaviors of experimental animals were carried out in the following categories;

a. Sleeping
b. Lying
c. Rearing
d. Walking
e. Eating or drinking
f. Grooming

2. General behavior of rats

Rats belonging to Sprague Dowley family, of body weight 250 gm were selected as subjects of experiment. The experimental apparatus consisted

of a box of size 30 × 30 × 30 cm, each of which housed one animal. Two opposite walls of the box were of metal plates, while the rest of the walls as well as the ceiling and floor consisted of wire netting.

One unit comprised 4 cages, all cages were arrayed on 2 rows spread through 3 steps or shelves. Procedure for obtaining various doses was identical with that in the case of mouse. Each dose of administration amounted to 0.5 cc/100 gm.

D. Open-field exploratory behavior

1. Experiment with mice.

Experimental animals were selected according to the procedure described above. A box containing two smaller boxes (departure box and selection box), a discrimination maze, was remodelled to serve as an open-field. The entire floor of the apparatus was divided into blocks of sizes 15 cm by 12 cm. Metallic objects were placed on the floor at regular intervals, as objects for exploration. A fluorescent lamp was hung about 2 m above the floor, so that the illumination over the entire field was somewhat homogenous.

Method of observation: All experimental animals were divided into separate groups for administration of saline, G. S. 100.0 mg/kg, G. S. 50.0 mg/kg, G. S. 5.0 gm/kg and G. S. 2.5 mg/kg. Each dose was injected intraperitoneally in the amount of 0.5 cc per 10 gm body weight, 30 minutes prior to placing the experimental animals in the field of observation.

During the 10 minutes period that followed, two observers followed up the behavior of animals. One observer counted the frequency of blocks on the floor trodden by animals during each of one minute's time that followed. The other recorded at an interval of every 10 seconds animal behavior classified into the following categories;

a. Walking
b. Lying
c. Grooming
d. Rearing
e. Exploration
f. Other

2. Experiment with rats.

Experimental animals were selected according to the same procedure described above.

The apparatus for experiment consisted of a wooden box of size 2.2 m by 2.2 m by 0.9 m. The open-field or the floor of the box was marked in blocks of 15 cm by 15 cm, on which were arrayed metallic objects at regular distances for detecting exploratory behaviors of animals. Other procedures of experiment were similar to that in the case of mouse, except that each dose of administration of various doses was set at 0.5 cc per 100 gm body weight.

The results obtained through the above procedures were subjected to Mann-Whitney's "U-Test" for determining the level of significance, employing the saline administered animals as the control group.

III. Results of Experiment

A. Spontaneous motor activity

1. Spontaneous motor activity in mouse.

Motility of mice was observed by measuring the frequency of interrupting the flow of beams within the beam cutting apparatus, to assess the effects of

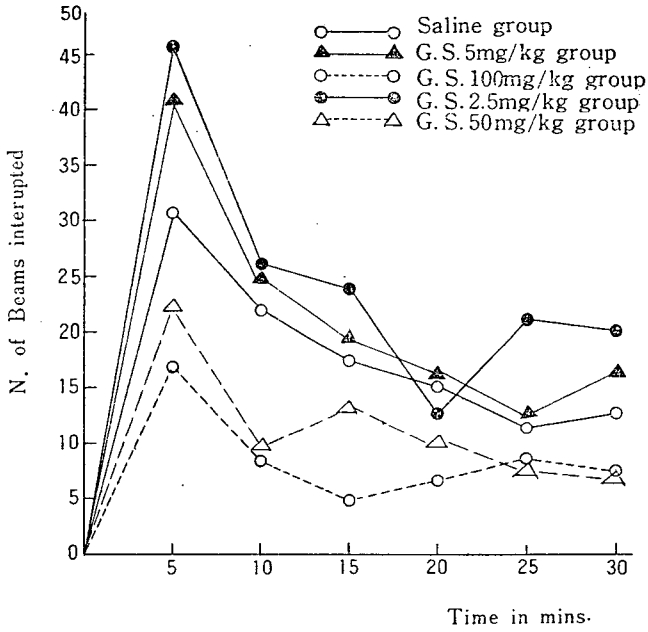

Fig. 1. The effects of Ginseng saponin on spontaneous motor activity in mice during first 30 mins term.

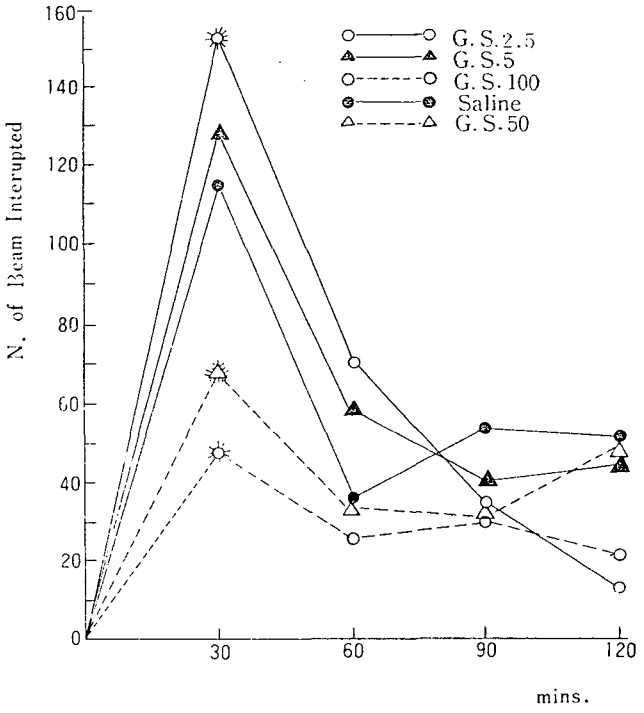

Fig. 2. Mean number of beam interruption during 2 hr observation in mice.

ginseng saponin upon spontaneous motor activity.

As seen in Fig. 1, the groups of mice given 2.5 mg/kg and 5.0 mg/kg body weight of ginseng saponin demonstrated within 30 minutes of administration of the said drug a higher activity than the control group while the experimental groups administered with ginseng saponin in the doses of 50.0 mg and 100.0 mg per kilogram body weight demonstrated a lower activity compared with the physiologic saline group.

Fig. 2 gives an illustration of change in the activity during the entire period of observation of 2 hours. Both the 2.5 mg and 5.0 mg per kilogram body weight groups appeared to be more active, first 30 minutes observation than the saline group. But their activities appeared to decline with the passing of time and towards the closure of observation period or 2 hours, their activities came down to the level of that of the saline group.

In the case of both the 50.0 mg and 100.0 mg per kilogram body weight groups, highest activity was noted 30 minutes following the administration of the drugs but their activities turned out to be significantly low compared with the saline group. After two hours, however, their activity slowed down to reach the level of the saline or control group.

By and large, a two hour observation revealed that the group of mice given 2.5 mg per kilogram body weight of ginseng saponin demonstrated a notably higher activity than the control or saline group ($p < 0.05$) during the first 30 minutes, while the activities of both the 50.0 mg and 100.0 mg per kilogram body weight groups diminished significantly ($p < 0.02$ and $p < 0.001$, respectively).

2. Spontaneous motor activity in rats.

By counting the total frequencies of beam cutting, both the groups given 2.5 mg and 5.0 mg 50.0 mg per kilogram body weight were found to demonstrate a higher activity than the control or saline group, while the 100.0 mg/kg group showed a lower activity during the first 5 minutes' period.

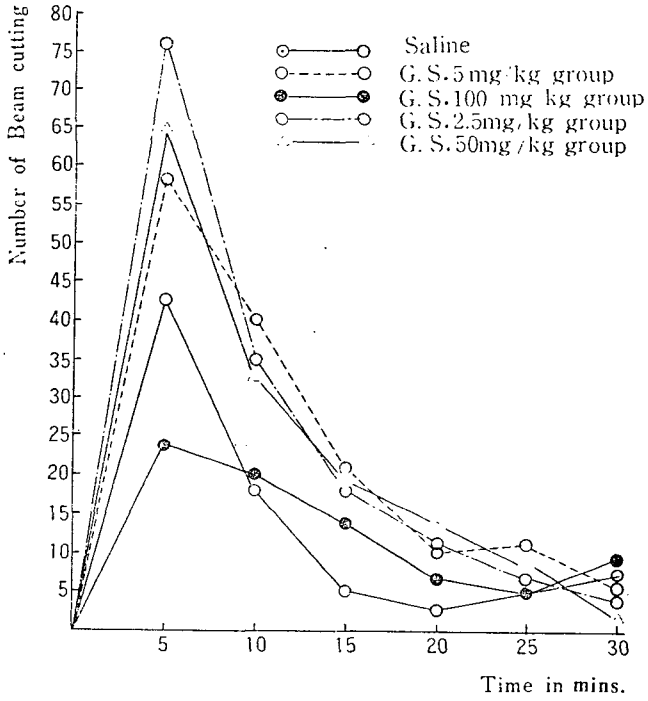

Fig. 3. The effects of Ginseng saponin on spontaneous motor activity in rats during first 30 mins term.

Summarizing the results of observations over the entire observation period or 2 hours, the groups of animals who were given either 2.5 mg, 5.0 mg, or 50.0 mg of ginseng saponin per kilogram body weight demonstrated an increased activity compared with the control group.

Table 1. Mean number of beam interruption for each 30 mins term during 2 hr observation in mice. Mean ± (S.D.)

Drug \ Mins	30	60	90	120	Total
Saline	114.1	35.7	52.2	51.9	254.1
(Control)	54.6	27.4	47.9	43.9	110.9
G.S.P.	154.7	68.7	34.3	12.9	270.9
2.5 mg/kg	43.8	61.2	34.3	24.2	121.2
	(<.05)			(<.01)	
G.S.P.	128.3	59.0	38.1	45.6	270.9
5 mg/kg	41.7	46.0	40.5	41.9	120.9
G.S.P.	68.1	33.8	30.8	47.5	180.1
50 mg/kg	34.4	30.9	38.4	49.9	104.8
	(<.02)				(<.05)
G.S.P.	48.1	26.0	28.5	21.6	124.2
100 mg/kg	27.9	33.4	34.4	47.1	96.1
	(<.001)				(<.01)

The figures in the parenthesis represent p value compared with saline treated group

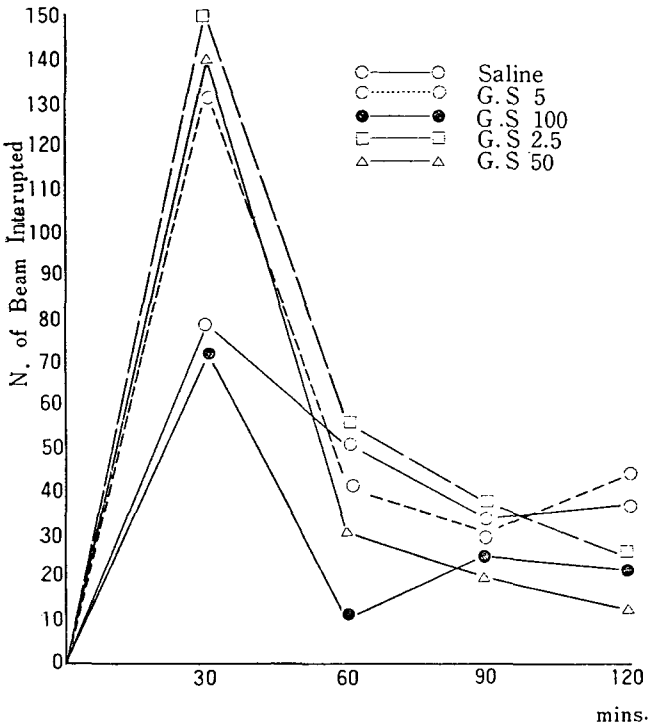

Fig. 4. Mean number of beam interruption during 2 hr observation in rats.

Their activity decreased in the period that followed and both the 2.5 mg and 5.0 mg per kilogram body weight groups approached the level of saline group. The groups of experimental animals given 50.0 mg and 100.0 mg per kilogram body weight, however, began to demonstrate even lower activities than the control group, as seen in Fig. 4.

Total count of frequencies of beams cut by animal activity during the 2 hour period indicates that the groups who were administered 2.5 mg and 5.0 mg per kilogram body weight have demonstrated significantly higher activities ($p < 0.02$ and $p < 0.05$, respectively) than the saline group, while the 50.0 mg/kg group has been found on a lower level of activity, though this difference was found statistically insignificant (See Table 2). The group who were administered 100.0 mg/kg showed a marked decrease in activity ($p < 0.01$).

B. General behavior analysis.

1. General behavior of mice.

In this experiment, general behavior of mice was observed after they underwent a certain period of adaptation in the observation-cumfeeding apparatus. It was found that the sleeping component decreased among the group of mice treated with different doses of ginseng saponin, compared with the

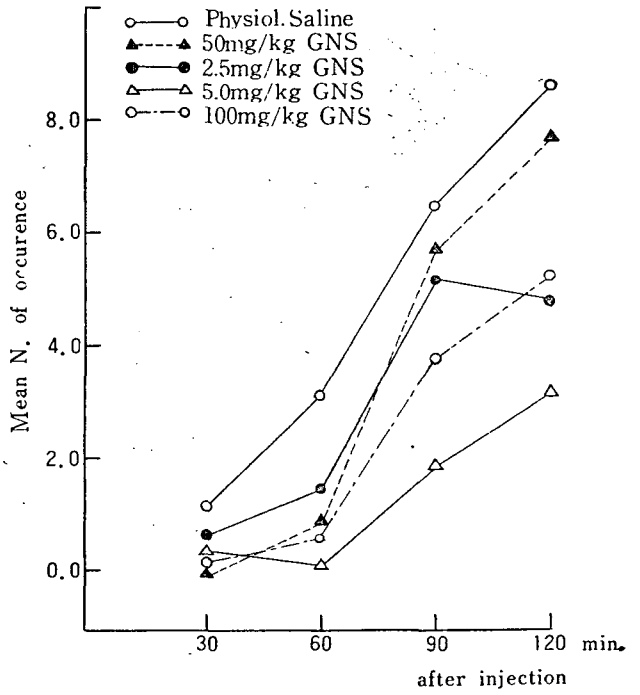

Fig. 5. Effect of ginseng saponin on sleeping component of general behavior in mouse for each 30 mins term.

group treated with physiologic saline, and the 5.0 mg/kg and 100.0 mg/kg groups were located at particularly low level, as shown by Fig. 5.

In contrast, all groups who were administered ginseng saponin demonstrated an increase initially in the walking and rearing components, the effect of drug gradually diminish with the progress of time after administration of drugs, with the exception of the 5.0 mg/kg group which demonstrated a high level of activities throughout the entire period of observation (Fig. 6).

The observation of average behavior during the 2 hours of observation disclosed that only the ginseng saponin 5.0 mg/kg group presented a significant difference from the control group, where the sleeping component of the saline group was counted at 17.6 ± 6.3, while that of ginseng saponin group turned

Table 2. Mean number of beam interruption for each 30 mins term during 2 hr observation in rats. Mean ± (S.D.)

Drug \ Mins	30	60	90	120	Total
Saline (Control)	76.7 31.9	50.8 62.0	33.3 25.2	34.9 22.8	195.7 80.0
GSP 2.5 mg/kg	149.5 64.4 (<0.001)	54.1 32.2	37.6 35.4	22.8 27.2	259.0 121.2 (<0.02)
GSP 5 mg/kg	138.7 54.7 (<0.001)	39.2 43.5	31.5 38.9	40.1 51.9	249.6 130.2 (<0.05)
GSP 50 mg/kg	141.7 52.3 (<.001)	30.5 39.6	19.4 28.5	10.1 22.1 (<0.05)	201.7 89.6
GSP 100 mg/kg	73.8 35.6	10.6 9.0 (<0.05)	21.1 13.2	19.9 21.2	125.4 45.7 (<0.01)

The figures in the parenthesis represent p value compared with saline treated group.

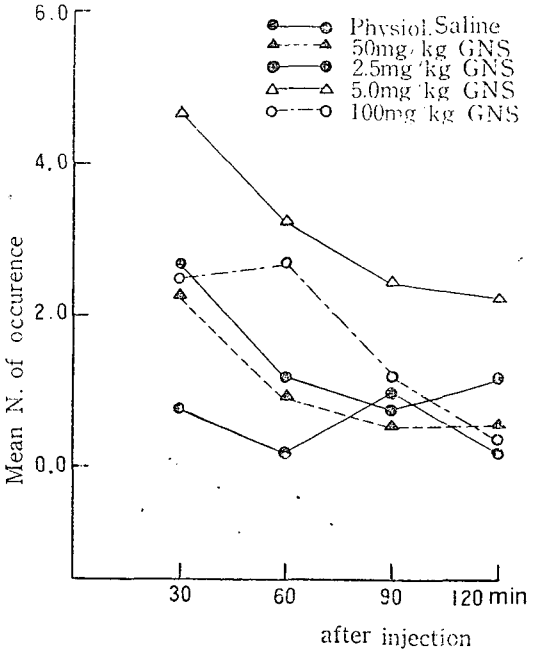

Fig. 6. Effect of Ginseng saponin on walking & rearing component of general behavior in mouse for each 30 mins term.

Table 3. Mean number of 7 component pattern of general behavioral activity in the home cage of mice during 2hrs-observation. (Mean ± S.E.)

Group \ behaviors	Sleeping	Lying	Locomotion	Rearing	Eating & Drinking	Grooming	Lying & Sniffing
Saline	M = 17.6 S.E = ±6.3	14.1 ± 6.9	2.1 ± 1.8	0.1 ± 0.3	0.7 ± 0.6	3.4 ± 9.2	2.0 ± 3.6
GSP 2.5 mg/kg	12.0 ± 6.1 p < .05	13.0 ± 4.3	4.3 ± 4.3 0 < .05	0.9 ± 3.6 p < .01	2.0 ± 3.2	3.3 ± 7.9	4.5 ± 7.5 p < .01
GSP 5.0 mg/kg	5.1 ± 3 p < .001	9.3 ± 6.2 p < .01	8.4 ± 4.6 p < .001	4.4 ± 4.0 p < .001	3.2 ± 4.1 p < .001	4.0 ± 2.4	5.9 ± 8.1 p < .05
GSP 50 mg/kg	13.9 ± 6.1	14.9 ± 5.9	2.9 ± 3.5	1.1 ± 5.3	0.3 ± 3.1	4.0 ± 9.5	2.9 ± 8.5
GSP 100 mg/kg	9.9 ± 6.2 p < .01	15.5 ± 5.0	5.1 ± 6.1	1.5 ± 6.6	1.1 ± 4.9	2.9 ± 9.6	4.0 ± 3.7

out to be 5.1 ± 3.0, implying a marked decrease ($p < 0.001$). In this experiment the walking and rearing components were measured at 2.1 ± 1.8 and 0.1 ± 0.3 respectively with the saline group, which are distinctly lower than those with the ginseng saponin group, or 8.4 ± 4.6 and 4.4 ± 4.0, respectively, as seen in Table 3.

2. General behavior of rats.

Table 4 gives an illustration of the effect of ginseng saponin upon general behavior of rats. Our overall finding is that sleeping component is markedly decreased with the ginseng saponin treated group compared with the saline group, while the activities of the former were located on a higher level.

In other words, the sleeping components of the groups given 2.5 mg, 5.0 mg, 50.0 mg and 100.0 mg of ginseng saponin per kilogram body weight demonstrated a statistically significant decrease ($p < 0.005$-$p < 0.001$) compared with those of the control group, while the walking and rearing components of the groups treated with 2.5 mg, 50.0 mg and 100.0 mg of ginseng saponin per kilogram body weight showed a marked increase ($p < 0.05$-$p < 0.001$) over the control group. In all of the experimental groups treated with ginseng saponin the lying and grooming components were on higher levels ($p < 0.001$).

C. Open-field exploratory behavior.

1. Exploratory behavior of mice.

Movement of a mouse treated only with saline in an open field was recorded to be 359.2 ± 69.0 on the average during 10 minutes, while that of those treated with 2.5 mg of ginseng saponin per kilogram body weight turned out to be 333.5 ± 106.3 during the period of observation of same length, showing no visible difference from the former or the control group.

The 5.0 mg/kg, 50.0 mg/kg and 100.0 mg/kg groups, however, recorded average of 271.2 ± 123.9, 273.0 ± 104.0 and 182.0 ± 143.1 respectively, implying a lower level of movement signified within a limit of 5% compared with the control group. (Table 4)

The movement of the experimental animals

Table 4. Patterns of general behavioral component in the home cage of rat during 2hr-session. (Mean ± S.E.)

behaviors	Sleeping	Lying & Grooming	Walking & Rearing	Eating & Drinking
Control	28.7 ± 6.6	7.9 ± 4.3	1.8± 1.7	1.7 ± 2.3
GSP 2.5 mg/kg	8.4 ± 4.9 P < .001	20.9 ± 5.9 P < .001	4.0 ± 2.9 P = .05	6.8 ± 3.2 P < .002
GSP 5 mg/kg	17.8 ± 7.4 P < .005	14.8 ± 5.2 P < .05	0.8 ± 1.0	5.8 ± 3.6 P < .02
GSP 50 mg/bg	15.8 ± 6.9 P < .001	14.6 ± 3.5 P < .001	7.8 ± 4.5 P < .001	1.9 ± 1.5
GSP 100 mg/bg	15.5 ± 5.1 P < .001	15.6 ± 3.8 P < .001	8.6 ± 2.0 P < .001	0.9 ± 0.8 P < .005

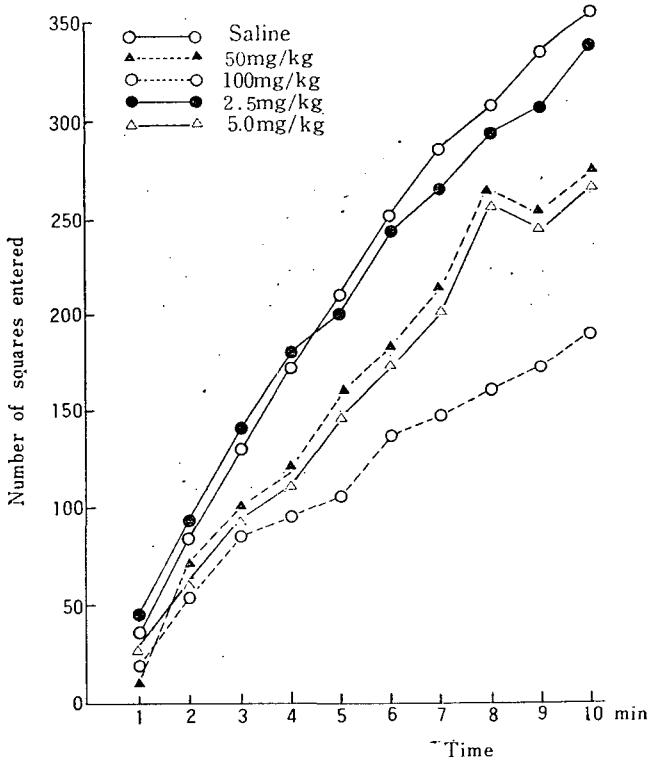

Fig. 7. Effect of Ginseng saponin on the open-field exploratory behavior in mouse.

in an open-field illustrated in Fig. 7 indicate that all ginseng saponin treated groups demonstrated lower levels of movement than the control group.

Table 5 further illustrates the behavior of mice within the experimental open-field. In general, a

Table 5. Open-field cross checking, mean number of squares entered in each one minute in open field & total mean number in mouse.

min / group	1	2	3	4	5	6	7	8	9	10	Total
Saline	36.3 (±15.2)	46.4 (±18.6)	43.8 (±9.1)	43.5 (±7.0)	35.6 (±16.8)	38.4 (±11.1)	32.2 (±14.2)	28.0 (±5.8)	26.3 (±8.5)	28.8 (±7.2)	359.2 (±69.0)
GSP 2.5 mg/kg	44.8 (±8.6)	50.9 (±12.5)	43.4 (±13.3)	33.7 (±14.0)	31.6 (±15.5)	35.8 (±17.9)	24.5 (±16.7)	24.4 (±16.7)	19.7 (±14.8)	23.1 (±15.5)	333.5 (±106.3)
GSP 5 mg/kg	27.5 (±10.5)	32.8 (±17.5)	28.3 (±19.2) $p < .05$	34.0 (±19.4)	26.4 (±14.6)	28.8 (±14.2)	22.8 (±12.7)	25.9 (±16.4)	24.6 (±15.7)	18.3 (±12.8)	271.2 (±123.9) $p < .05$
GSP 50 mg/kg	25.8 (±7.7)	35.9 (±12.2)	35.2 (±15.2)	30.7 (±15.2) $p < .02$	31.0 (±11.9)	24.9 (±10.2)	20.9 (±10.6)	24.2 (±12.7)	23.9 (±14.6)	19.8 (±10.7)	273.2 (±104.0) $p < .05$
GSP 100 mg/kg	27.1 (±19.5)	28.4 (±23.0)	20.6 (±19.0) $p < .01$	22.8 (±16.5) $p < .001$	20.3 (±18.1)	17.5 (± 9.2) $p < .001$	13.3 (±16.5) $p < .01$	14.1 (±17.4) $p < .02$	7.8 (±11.8) $p < .001$	10.9 (±16.1) $p < .01$	182 (±143.1) $p < .01$

Table 6. Patterns of behavioral component in the open-field in mouse during 10 min.

Behavior / group	Walking	Rearing	Grooming	Explor.	Lying	Micellaneous
Saline control	20.2 (±6.0)	20.2 (±3.9)	2.2 (±2.03)	12.9 (±3.8)	3.3 (±1.7)	1.1 (±1.7)
GSP 2.5 mg/kg	15.3 (±4.5) $p < .05$	13.5 (±5.5) $p < .01$	6.0 (±5.1) $p < .05$	19.8 (±5.7) $p < .01$	3.9 (±3.9)	1.3 (±3.8)
GSP 5 mg/kg	19.8 (±5.1)	13.0 (±7.4) $p < .01$	2.5 (±2.5)	18.8 (±4.2) $p < .001$	6.2 (±9.2)	0.3 (±0.62)
GSP 50 mg/kg	21.2 (±4.97)	11.9 (±7.2) $p < .01$	2.0 (±2.19)	16.9 (±5.3) $p < .05$	7.4 (±7.0) $p < .05$	0.4 (±0.64)
GSP 100 mg/kg	14.7 (±7.1)	6.7 (±6.8) $p < .001$	3.1 (±3.3)	15.6 (±5.0)	19.7 (±15.7) $p < .01$	0.3 (±1.8)

markedly lower level of walking component, compared with the saline group was observed with the ginseng saponin administered groups, and difference appeared to be great particularly with those treated with 2.5 mg of ginseng saponin per kilogram body weight ($p < 0.05$).

Also noticed was that a marked decrease in the rearing component and increase in exploratory behavior were recorded with all the ginseng saponin treated groups.

2. Exploratory behavior of rats.

Movement of rats per minute within the experimental open-field is summarized in Table 6. Both the control group and ginseng saponin treated groups showed a tendency of being better adjusted to the experimental conditions with the progress of time.

Table 7. Open-field cross checking mean number of squares entered in each minute and total mean number in rat.

	1	2	3	4	5	6	7	8	9	10	Total
Control	20.16	17.94	17.35	12.81	8.23	5.45	4.58	5.84	4.35	5.81	102.71
	2.72	2.72	3.03	2.41	2.01	1.88	1.58	1.61	1.33	2.09	13.75
G.S	21.67	19.27	13.8	13.47	8.73	11.47	7.73	8.07	5.87	6.27	118.73
2.5 mg	3.77	3.87	4.30	3.69	3.13	4.46	3.16	3.50	2.70	3.37	2.78
					$0.1 < p < 0.2$						
G.S	25.79	24.29	18.93	20.29	13.29	16.21	8.21	8.43	7	6.64	148.21
5mg	6.65	9.67	7.41	6.07	3.45	3.25	2.99	2.93	2.16	2.00	24.44
						$0.01 < p < 0.001$				$0.1 < p < 0.2$	
G.S	18.47	13.93	10.33	11.67	7.33	3.67	5.47	6.0	2.4	2.4	81.67
50mg	3.49	3.49	3.49	3.63	2.97	2.13	2.46	2.77	1.79	2.32	19.69
			$0.1 < p < 0.2$								
G.S	16.36	15.5	13.43	13.57	4.86	8.14	2.43	3.43	1.86	2.93	85.86
100 mg	3.74	4.44	4.00	3.64	1.99	3.48	1.36	1.53	1.19	1.96	20.8
								$0.1 < p < 0.2$			

Table 8. Patterns of behavioral component in open-field in mouse during 10 min.

	Walking	Grooming	Rearing	Explor.	Lying	Faces
Control	3.23	7.54	9.27	39.85	9.35	2.06
	0.49	2.42	1.69	2.68	2.06	0.35
G.S	1.73	13.67	8.2	35.13	0.6	1.47
2.5 mg	0.57	3.88	2.52	3.27	0.16	0.28
	$0.05 < p < 0.1$	$0.1 < p < 0.2$			$p < 0.001$	$0.1 < p < 0.2$
G.S	2.64	11.14	5.36	38.64	2.14	2.14
5 mg	0.46	2.48	0.55	2.80	2.07	0.32
			$0.02 < p < 0.05$		$0.01 < p < 0.02$	
G.S	2.13	15.87	3.2	31.93	6.8	0.2
50 mg	0.55	2.76	1.13	2.74	2.71	0.14
	$0.1 < p < 0.2$	$0.02 < p < 0.05$	$0.001 < p < 0.01$	$0.02 < p < 0.05$		$p < 0.001$
G.S	2.43	16.62	5	33.36	3.5	2.21
100 mg	0.77	3.00	1.27	3.38	1.98	0.76
		$0.02 < p < 0.05$	$0.05 < p < 0.1$	$0.1 < p < 0.2$	$0.05 < p < 0.1$	

The movement, however, of the groups of animals given 2.5 mg/kg and 5.0 mg/kg of ginseng saponin was recorded on a higher level than the saline treated group. Especially, the ginseng saponin 5.0 mg/kg group demonstrated a significantly higher level of movement in the period following 6 minutes after the administration of the above dosage, while the 50.0 mg/kg and 100.0 mg/kg groups showed a low level of movement, if not statistically significant, compared with the saline group. (Fig. 8)

In general, the grooming component of rat behavior within the open-field can be placed on significantly higher levels with those treated with ginseng saponin, than the control group, while other behaviors of the former also suggested lower levels than the latter, though the latter data appeared to be beyond the limit of statistical significance.

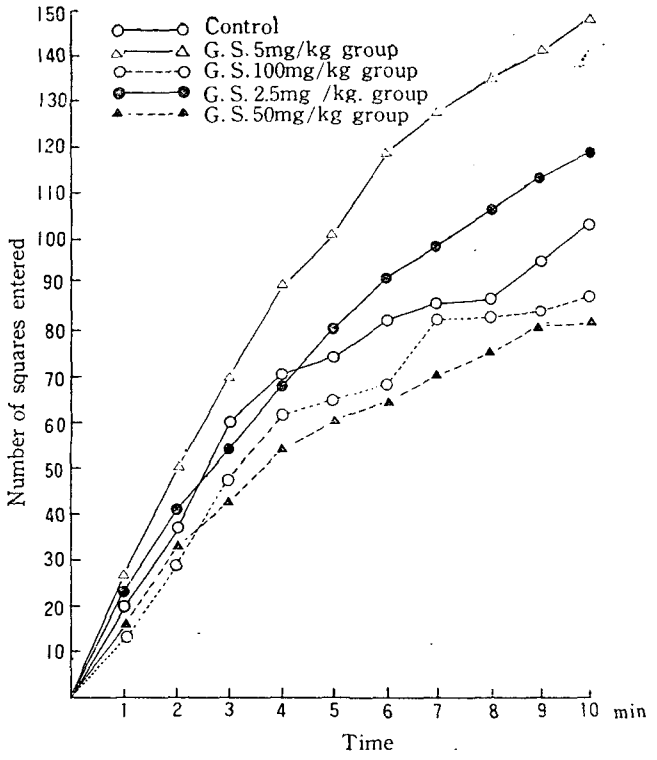

Fig. 8. Effect of Ginseng saponin on the open-field exploratory behavior in rat.

IV. Discussion

Through a series of pharmacological experiments with rats and mice conducted to observe possible effect of ginseng saponin upon the behavior, the authors have obtained the following results:

1. Ginseng saponin appears to increase the activity of experimental animals in a limited space with no external stimuli, when they are given small doses (2.5 mg/kg or 5.0 mg/kg), but their activity decreased with administration in large doses (50.0 mg/kg or more). Thus, it is construed that ginseng saponin does not have a singular stimulative or inhibitory effect on the central nervous system. Instead, this drug appears to have a stimulatory effect in small dose, while it gives an inhibitory effect in large doses. This finding conforms in general the results obtained in our previous studies at the Department of Pharmacology, Seoul National University, College of Medicine. Noted here are published reports of researchers observing the increase in spontaneous motor activity, when small dosage of ginseng saponin is administered and suggesting a stimulative actions of ginseng saponin on the central nervous system as well as the possibility of the nerve stimulating action reflected in the increase in the stimulativeness of various behaviors (Petkov 1963, Brekhman and Dardymov 1969, and Hong et al. 1970).

Nabata in 1973 reported that neutral saponin of ginseng increased the spontaneous motor activity in mice, but the effect was rather insignificant when administered in small doses, which might will be construed as similar to the findings obtained by us, following the administration in large doses. Takagi, however, reported in 1972 that administration of ginseng saponin G. No. 4 in divided small doses (5–10 mg/kg) resulted in the increase of the level of awareness to loud sounds and an increase in the spontaneous motor activity as well as in the apperance of startle responses which can be regarded as phenomenon implying a central nervous system stimulating effect.

We interpret that the actions of G. No. 4 have led to the findings similar to our results obtained from use of ginseng saponin.

2. Analysis of the general behavior of experimental animals within the cages has led to the finding that adminsitration of ginseng saponin in varying doses generally decreased the sleeping component of animal behavior while it increased all behaviors when the animals were awake. This further led us to suspect that the major action of ginseng saponin might be that of a stimulant to the central nervous system.

Observing the results obtained from our most recent study just as they are, and ruling out other possible conditions affecting the outcome of the experiment and considering the general property of central nerve stimulants causing depression following stimulation or causing stimulation at small dosage and depression at large dosage, it is well assumed that ginseng saponin might fall in the general category of central nerve stimulant.

In the case of the spontaneous motor activity, considering that the experimental animals had to leave their cages to be subjected to a series of experiment in a strange surrounding, where each animal

was segregated from others, their behavior within the experimental apparatus could not be regarded as being under identical conditions at their cages, which, in turn, is believed to account for the differences in the effects of ginseng saponin accruing from the different surroundings.

It is also believed that administration of ginseng saponin in large doses exercises an inhibitory action upon the central nervous system.

3. Some differences in the exploratory behaviors were noted between mice and rats in this experiment conducted under environment strange to the animals with placement of strange objects. The rats demonstrated an increased movement at administration of ginseng saponin in small doses, while their activity appeared to be inhibited at large doses. On the contrary, only the inhibitory actions were observed in the rats.

In the open-field experiments, increase in the exploratory behavior as well as in frequency of grooming was noted in mice, while with rats, increase was noted only in the grooming component but a decrease in other components of animal behavior.

The animal behavior within the open-field, by and large, appeared be similar to the trends observed with the spontaneous motor activity, which is construed as resulting from a general increase in the emotionality of animals.

Also, it is believed that there were slight, if not large, differences in the susceptibility of animals to drugs, and possibly some difference in the animal reaction to drugs, accruing from difference in species. The scope and intensity of this experiment, however, are believed to be inadequate for measuring these differentials.

In this experiment, the lowest limit of dosage of ginseng saponin was fixed at 2.5 mg/kg, which in turn is based on the daily dose of ginseng prescribed by the traditional or herb medicine.

The "large" doses of ginseng saponin was calculated on the basis of average lethal dose (LD_{50}) for mouse (C_3HF) being 791 mg/kg, and on the observation that convulsions were induced within 10 minutes following the administration of ginseng saponin in the doses of 1,000–2,000 mg/kg, which led the animal to an instantaneous death. Considering these findings the upper limit for dosage was set at 50–100 mg/kg.

Based on the above set of findings, we are inclined to believe that a small dose of ginseng saponin might act as a stimulant to the central nervous system, while a large dose exercises a depressive effect. Whether this can be interpreted as an nonspecific action on the overall central nervous system or as a reflection of a specific psychopharmacologic action remains to be subject to further studies.

References*

*This article is the English translation of the original report written in Korean, references will be found in the original report published in
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