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Effects of Ginseng and Its Saponins on Experimental Amnesia in Mice and on Cell Cultures of Neurons

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Abstract

The present study was performed to find the effects of ginseng and its saponins, which is written in *Chung Yao Ta Tsu Tien* as anti-amnesia in its chief indication, on experimental amnesia in mice. In the step through test, ginsenoside Rb_1 (GRb_1) and GRg_1 facilitated the registration of memory and antagonized the electroconvulsive shock (ECS)-induced inhibition of the retention of memory. Moreover, GRg_1 antagonized the EtOH-induced inhibition of the retrieval of memory. In the step down test, GRb_1, GRb_2 and GRg_1 antagonized the ECS-induced inhibition of the retention of memory. Moreover, GRg_1 antagonized the EtOH-induced inhibition of the retrieval of memory and facilitated the acquisition of short term memory. In the shuttle box and lever press tests, they have no effects on acquisition and retrieval of memory, except GRb_1. GRb_1 depressed the retrieval of conditioned avoidance response in the shuttle box test. After the end of four tests, the effects of these orally administered drugs on sedative, analgesic, antipyretic and anticonvulsant actions, and on spontaneous and exploratory movements were tested in doses of less than 500mg/kg, but they had none of these effects. Present study may indicate that GRg_1 had effects on the retrieval of memory and on the acquisition process of learning response. The recent research on the role of NGF for the survival, regeneration and regulation of brain in adult animals, indicated the importance of NGF on dementia and amnesia. During our research on the specificity of the neurite out growth induced by NGF, we found that the effect of NGF was potentiated by GRb_1 in organ cultures of chick embryonic dorsal root ganglia. Then, the effect of GRb_1 on neuronal cell survivalin cell culture system was studied. GRb_1 potentiated the NGF-mediated increase of neurofilaments in cell cultures of chick embryonic sensory and sympathetic neurons. NGF with GRb_1 also showed a tendency to increase the number of surviving neurons of rat embryonic cerebral cortex. NGF increased choline acetyl transferase activity in cell cultures of rat embryonic septum area neurons, but GRb_1 did not potentiate NGF activity in cell cultures of rat embryonic septum area neurons. Present study may indicate that GRb_1 plays an important role for the survival or regeneration of neurons in the brain.

Introduction

In Chinese medicine, *Panax ginseng* which has been utilized for more than 5 thousands of years in China and is now popular in the world as natural medicine, is classified into a drug, "Bu-Chi-Yaw" which we have no alternative technical terms in modern medicine. The effect of ginseng which was expected from its chief indications written in the oldest Chinese traditional medical book, "Sheng Nung Pen Tsao Ching" and the recent Chinese medicinal plant dictionary "Chung Yao Ta Tsu Tien", gave us the suggestions on a disease of old age, especially on senile dementia.

Prof. S. Shibata and his coworkers have been determining the structure of saponins in ginseng (1) and provided us individual saponins which are specific compounds in ginseng and were found to be expected many pharmacological actions by blind and specific screenings. Both ginsenoside Rb_1 (GRb_1) and ginsenoside Rg_1 (GRg_1) are the most important pharmacological active components. Tranquilizing action of GRb_1 was confirmed with specific screenings. Conditioned avoidance response was depressed in the pole climbing and shuttle box tests in rats. Response latency (the time from the opening of the door to the start of rat) and running time (the time from the start to arrival) in the Y maze test was prolonged in the rat.

GRg_1 shortened response latency and running time in the Y maze test. Accordingly GRg_1 posseses a somewhat different CNS-stimulant action from well-known CNS-stimulants, we studied the effect of GRg_1 on learning behaviour using different types of apparatus in rat. GRg_1 accelerated the acquisition of conditioned avoidance response in the pole climbing test and the acquisition of discrimination behaviour and reversal learning in the Y-maze test (2).

The recent researches on the role of nerve growth factor (NGF) for the survival, regeneration and regulation of neurons of brain in adult animal, indicated the importance of NGF on senile dementia and amnesia. During our research on the specificity of the neurite outgrowth induced by NGF, we found that the effect of NGF was potentiated by GRb_1 in organ cultures of chick embryonic dorsal root ganglia. Then, effects of ginseng saponins on neuronal cell survival in cell culture system were studied in my laboratory.

The present study was to find out effects of ginseng and its saponins on experimental amnesia in mice, and on neuronal cell survival in cell culture system. For whole animal experiment, 4 tests, that is, step through (ST) test, step down (SD) test, shuttle box (SB) test and lever press (LP) test, were employed, and drugs were dissolved with saline and given orally.

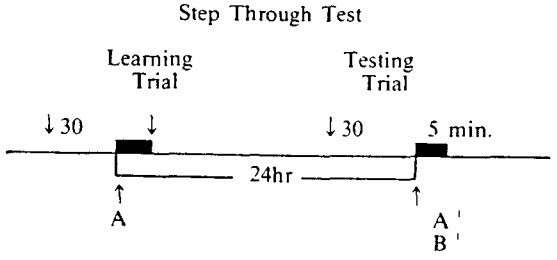
For cell culture experiment, neurons from 4 different parts of tissues (sympathetic ganglion in chick embryo, septum in rat embryo and neonate, cerebral cortex in chick and rat embryos and ventral midbrain in rat embryo) were used. The drug effect on the neuronal survival were studied in these systems.

A. Studies on Experimental Amnesia in Mice (Whole animal experiments)

1) Step Through (ST) Test

Experimental scheme for ST test is shown in Fig. 1. The mice were exposed to the apparatus for 1 min. as a learning trial. The following day the mice were exposed again for 5 min at the same time of day as a testing trial. The mice can simply learn to keep themselves in the bright compartment to avoid electric shock from the floor in the dark compartment. Step through latency in learning and testing trials, and % of animals which did not step through the opening into the dark compartment in testing trial were measured. Effects of drugs on registration, retention and retrieval of memory in normal mice were observed in Experiment 1, 2 and 3. In Experiment 1, drugs were given 30 min before learning trial, in Experiment 2, just after learning trial, and in Experiment 3, 30 min before testing trial. In Experiment 4 and 5, effect of drugs on alcohol-and scopolamine -induced inhibitions of the registration of memory were studied. Drugs were given 30 min before learning trial, and alcohol and scopolamine were given orally 20 min before learning trial. In Experiment 6, effect of drugs on the electro-convulsive shock (ECS) induced inhibition of the retention of memory was studied. Drugs were given 30 min before learning trial, and ECS, just after learning trial. In Experiment 7 and 8, effects of drugs in alcohol-and ECS-induced inhibitions of the retrieval of memory were studied. Drugs were given 40 min before testing trial and ECS and alcohol, 30 min before testing trial. For statistical analysis, one way layout ANOVAR followed by Duncan's test and Fisher's Exact Probability test were used.

Fig. 1



A : Step through latency in learning trial
A ' : Step through latency in testing trial
B ' :% of animals which did not step through the opening into the inner darkend compartment in testing trial

Effect of Drugs on

1. Registration of Memory : A A ' B '
2. Retention of Memory ; A ' B '
3. Retrieval of Memory: A ' B '
4. Registration of Memory Inhibited by Alcohol: A A ' B '
5. Registration of Memory Inhibited by Scopolamin :A A ' B '
6. Retention of Memory Inhibited by Electroshock: A A ' B '
7. Retrieval of Memory Inhibited by Alcohol : A A ' B '
8. Retrieval of Memory Inhibited by Electroshock: A A ' B '

The summary of results in ST test shown in Table 1. Upward arrows indicate significant increases of step through latency and % of animal which avoid shock, from control or conditioned control ($p<0.05$), and arrows with parenthesis, such a tendency ($p<0.10$). Downward arrows with parenthesis indicate slight decrease ($p<0.10$) of step latency in learning trial. Water extract (ext.) of ginseng, GRb_1, GRb_2, GRe and GRg_1 antagonized the ECS-induced inhibition of the retrieval of memory. GRb_1 and GRg_1 showed a tendency to increase registration and retrieval of memory. GRg_1 also showed a tendency to shorten the step through latency. Water ext. of ginseng, GRc and GRg_1 showed tendency to antagonize the ECS-induced inhibition of the retention of memory.

2) Step Down (SD) Test

Experimental scheme for step down test is shown in Fig 2. The mice were exposed the apparatus for 10 min as a learning trial. The following day the mice were exposed again for 3 min at the same time of day as a testing trial. The mice can simply learn to keep themselves on the small rubber stand to avoid electric shock from the floor. Percent of animals which avoid shocks in the second 5 min period of learning trial and in testing trial, and times which the mice stepped down on the floor in the second 5 min period of learning trial and in testing trial, were measured. Experiments were performed using normal and drug-and ECS-induced amnesia model animals. These experiments have the same schedule of drug administration as shown in the experimental scheme for ST test.

The summary of results in the SD test was shown in

Table 1

Drugs	Dose	1			2		3		4			5			6		7		8	
	(mg/kg;p.o.)	A	A '	B '	A '	B '	A '	B '	A	A '	B	A	A '	B '	A '	B '	A '	B '	A '	B '
Water ext. of	250	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(↑)
Ginseng	500	—	—	—	—	—	—	—	—	—	—	—	—	—	(↑)	(↑)	—	—	(↑)	↑
Ginsenoside Rb_1	50	—	(↑)	(↑)	—	—	(↑)	—	—	—	—	—	—	—	—	—	—	—	—	↑
Ginsenoside Rb_2	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(↑)	—	—	—	↑
Ginsenoside Rc	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ginsenoside Rd	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ginsenoside Re	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	↑
Ginsenoside Rg_1	50	(↓)	—	(↑)	—	—	(↑)	—	—	—	—	—	—	—	—	(↑)	—	—	↑	↑

↑ (increase) or ↓ (decrease): Significantly different from control or conditioned control ($p<0.05$) and parenthesis , such a tendency ($p<0.10$). — ; No effect.

Fig. 3

Shuttle Box and Lever Press Tests

1 Sessions [I.T.I=40sec. C.S.=10sec. U.S.=10sec.]

x 60 Trials/ Session/ Day

C.S. (Conditioned Stimulus): Auditory Stimulus 600HZ 60db, duration; 0.5 sec. once a second

10 Sessions U.S. (Unconditioned Stimlus): Electricshock 36 V AC (Max. 0.2 mA) with C.S.

1. Effect of Drugs on Acquisition of Memory
2. Effect of Drugs on Retrieval of Memory

Effct of Ginseng and its saponins on Acquisition and Retrieval of Memories in Shuttle Box and Lever Press Tests in mice

Compounds	Dose (mg/kg: p.o)	Shuttle Box A CAR	Shuttle Box A MA	Shuttle Box R CAR	Shuttle Box R MA	Lever Press A CAR	Lever Press A MA	Lever Press R CAR	Lever Press R MA
control		—	—	—	—	—	—	—	—
Ginseng(H_2O ext.)	500	—	—	—	—	—	—	—	(↓)
Ginsenoside Rb_1	50	—	—	↓	—	—	—	—	(↓)
Ginsenoside Rb_2	50	—	—	—	—	—	—	—	—
Ginsenoside Rd	50	—	—	—	—	—	—	—	—
Ginsenoside Rg_1	50	—	—	—	(↓)	—	—	—	—

A : *Acquisition*. R : *Retrieval*. CAR : *Conditioned Avoidance Response*. MA (Motor Activity) indicates number of spontaneous movement or Lever press without conditioned and unconditioned stimuli.
↓ (Inhibition) : Significantly different from control ($p<0.05$)

experiments. GRg_1 was supposed to have an effect on the acquisition process of learning response. Present study may also indicate that GRg_1 had an effect on the acquisition process of learning response and on the retrieval of memory.

B. Studies on Neuronal Cell Survival (Cell Culture Experiments)

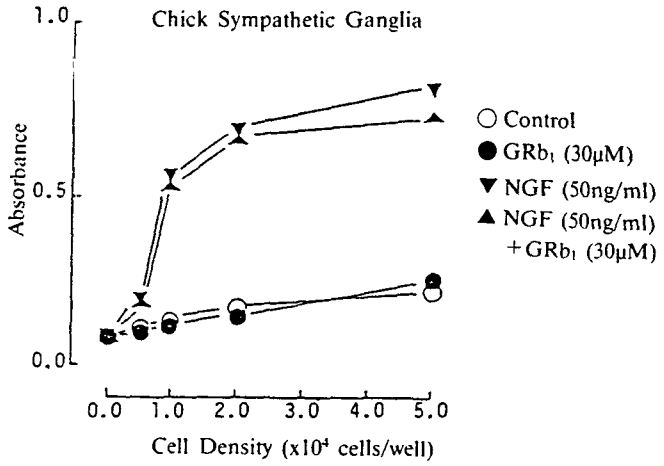
1) Embryonic Chick Sympathetic Neurons

Fig. 4 shows the effect of GRb_1 on the neuronal survivals of chick sympathetic neurons in cell cultures indicated by the neurofilament contents with enzyme-linked-immunosorbent assay (ELISA method). Horizontal axis is the cell densities before the experiment and the vertical axis is the absorbance of the product of ortho-phenylendiamine, which indicates the neurofilament contents. Ganglia were taken out from the 12-day-old chick embryos, dissociated and placed into the multiwell plates. Cells were cultured in the medium containing drugs for 72 hr. NGF showed a marked prolongation effect of neuronal survival. GRb_1 had no effect and did not potentiate the effect of NGF.

2) Embryonic and Neonatal Rat Septal Area Neurons

Fig. 5 shows the effect of GRb_1 and GRg_1 on the choline acetyltransferase (CAT) activities of rat septal area neurons in cell cultures. Septum was taken out from 16-day-old rat embryos and 13-day-old neonates, dissociated and cultured for 24 hr without drugs and cultured for another 3 or 6 days with drugs. CAT activities as the indicator of neuronal survivals were measured accordingly to Fonnum's method (3). The top figure shows the effect GRb_1 in cell cultures of 16-day-old rat embryos. NGF significantly increased CAT activities after

Fig. 4



both 3 and 6 days cultures. GRb_1 had no effects and did not potentiate the effect of NGF. The middle figure is the dose response curves of NGF. The same conditions as above (6 day culture with drugs) were used. GRb_1 and GRg_1 had no effect on CAT activities of septum area neurons in cell cultures and did not potentiate the effet of NGF. In the bottom figure, neonatal septal area cells were cultured on the feeder layer of astrocytes for 6 days with saponins. While NGF showed life-prolongation effect, GRb_1 and GRg_1 had no effect but GRg_1 showed a tendency to antagonize the effect of NGF.

3) Chick and Rat Embryonic Cerebral Cortex Neurons

Cerebral cortexes were taken out from 8-day-old chick embryos and 16-day-old rat embryos, and digested with trypsin. Cells were placed in multiwell plates and cultured. Drugs were given after 3 days preincubation and cells were cultured for another 9 day with medium change every third day. After total 12 days culture neurons were immunohistochemically stained with antineurofilament antibody.

Fig. 6 shows the effect of GRb_1 and GRg_1 on neuronal cell survival in cell cultures of chick embryonic cerebral cortex. NGF had no effect in doses of 10ng/ml -10μg/ml. GRb_1 and GRg_1 significantly prolonged neuronal survival. NGF showed a tendency to potentiate the effect of GRb_1 but not, the effect of GRg_1.

Fig. 7 shows the effect of GRb_1 and GRg_1 on neuronal survival in cell cultures of rat embryonic cerebral cortex. GRb_1 and GRg_1 also promoted significantly the neuronal survival. NGF had no effect and did not potentiate the effect of GRb_1 and GRg_1.

Fig. 8 shows rat embryonic cerebral cortex neurons after 15 days cell cultures, stained immunohistochemically with antineurofilament antibody. There were many kinds of neurons in cerebral cortex and size of the neurons were widely diverse. Compared with the cultured cells of chick ones, may non-neuronal cells remained unstained.

4) Rat Embryonic Ventral Midbrain Neurons

Effect of GRb_1 and GRg_1 on the neuronal survivals of rat embryonic ventral midbrain neurons in cell culture was studied. Ventral midbrain were dissected from 16-day-old rat embryo, dissociated, preincubated for 3 days with free medium and cultured for another 10 days with drugs. After that, cultured cells were stained with anti-tyrosine hydroxylase (TH) antibody and TH positive

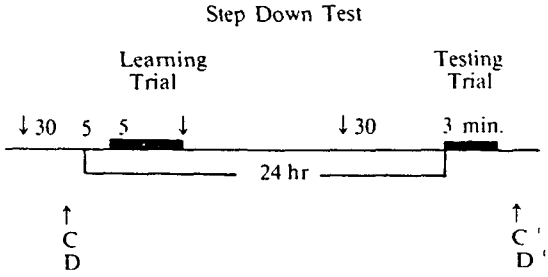
Table 2. Upward arrows indicate significant increase of % of animal which learned to avoid shock and of times which the mice stepped down on the grid floor ($p<0.05$). downward ones indicate significant decrease of them and parenthesis. such a tendency ($p<0.10$). GRg_1 increased % of animals which avoid shock in the second 5 min period of learning trial significantly and showed a tendency to decrease the time which the mice stepped down on the floor. These indicate that GRg_1 facilitated the acquisition of short term memory. GRb_1 and GRe also showed such tendencies. GRg_1 also antagonized the alcohol-induced inhibition of the retrieval of memory significantly and showed a tendency to antagonize the scopolamine-induced inhibition of the registration of memory. GRb_1, GRb_2, GRe and GRg_1 antagonized the ECS-induced inhibition of the retention of memory.

3) Shuttle Box (SB) and Lever Press (LP) Tests

Experimental scheme for SB and LP tests and the summary of results in both tests are shown in Fig. 3. The mice were exposed to the apparatus for 1 hr a day, for 10 days at the same time of day. In the SB test, the mice learn to run away from one side to avoid electric shock from the floor following signal sounds. In the LP test, the mice learn to push the lever to avoid electric shock from the floor following signal sounds. Number of conditioned avoidance response (CAR), unconditioned avoidance response (UAR) and errors in both tests, number of spontaneous movement not induced by conditioned and unconditioned stimuli in SB test, and number of lever press not induced by conditioned or unconditioned stimuli in LP test were measured. In Experiment 1, drugs were given every day 10 min before the exposure to the apparatus to study the effects of drugs on acquisition of memory. In Experiment 2, after the 9 day trainings, drugs were given to the mice which have already acquired more than 90% CAR, 10 min before the last exposure to the apparatus to study the effect of drugs on the retrieval of memory. In Experiment 1, ginseng saponins had no effect on CAR and numbers of spontaneous movement or lever press not induced by conditioned or unconditioned stimuli in both tests. That is, they have no effect on acquisition of memory in both tests. In Experiment 2, GRb_1 depressed the retrieval of CAR significantly but had no effect on the spontaneous movement in the SB test, and GRg_1 had no effect on CAR but showed a tendency to depress the number of spontaneous movement. In the LP test, they have no effect on CAR but water ext. of ginseng and GRb_1 showed a tendency to depress the number of lever press.

After the end of 4 tests, sedative, psychotropic, analgesic, antipyretic and anticonvulsant actions of these orally administered saponins were tested in doses of less than 500 mg/kg. Effect of saponins on spontaneous and exploratory movements were also tested. They did not have these actions. In our previous experiments, psychotropic actions of GRb_1 were confirmed which were not so potent as those of well-known drug, so the effect of GRb_1 on learning and memory in these experiments may result from psychotropic actions of GRb_1. In our previous

Fig. 2



C : % of animals which learned to avoid shock in the second 5 min peroid of learning trial
C ' : % of animals which learned to avoid shock in testing trial
D : Times which the mice stepped down on the grid floor in the second 5min period of learning time
D ' : Times which the mice stepped down on the grid floor in testing trial

Effect Drugs on

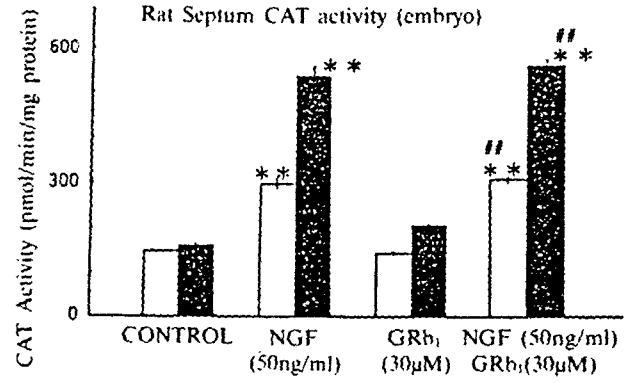
1. Registration of Memory : C C ' D D '
2. Retention of Memory : C ' D '
3. Retrieval of Memory : C ' D '
4. Registration of Memory Inhibited by Alcohol : C C ' D D '
5. Registration of Memory Inhibited by Scopolamine : C C ' DD'
6. Retention of Memory Inhibited by Electroshock : C C ' D D '
7. Retrieval of Memory Inhibited by Alcohol : C ' D '

Table 2

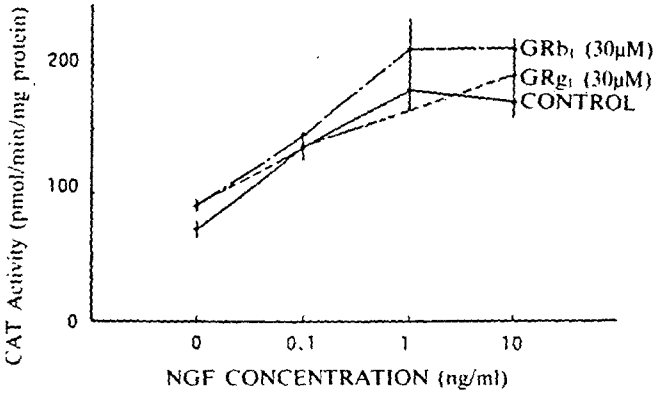
Drugs	Dose	1				2		3		4				5				6		7	
	(mg/kg;p.o.)	C	D	C '	D '	C '	D '	C '	D '	C	D	C '	D '	C	D	C '	D '	C '	D '	C '	D '
Water ext. of	250	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ginseng	500	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(↑)	(↓)	—	—
Ginsenoside Rb_1	50	(↑)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	↑	↓	↑	—
Ginsenoside Rb_2	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	↑	(↓)	↑	—
Ginsenoside Rc	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ginsenoside Rd	50	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Ginsenoside Re	50	(↑)	(↓)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	(↑)	(↓)	—	—
Ginsenoside Rg_1	50	↑	(↓)	—	—	—	—	—	—	—	—	—	—	(↑)	—	(↑)	(↓)	↑	↓	↑	—

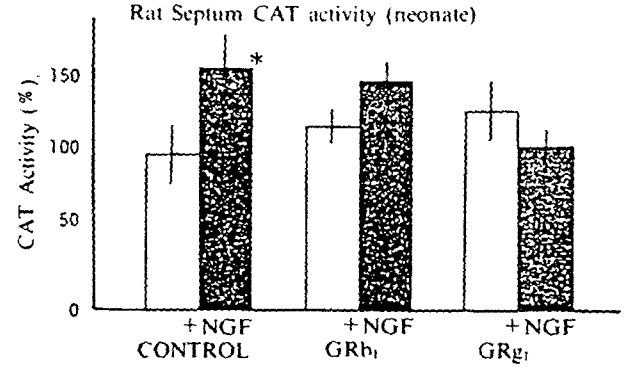
↑ (increase) or ↓ (descrease); Significantly different from control or conditioned control ($p<0.05$). and parenthesis, such a tendency ($p<0.10$). — ; No effect.

Fig. 5



Left column : 3 days cultured **p<0.01 vs. CONTROL
Right column : 6 days cultured ‡‡p<0.01 vs. GRb1



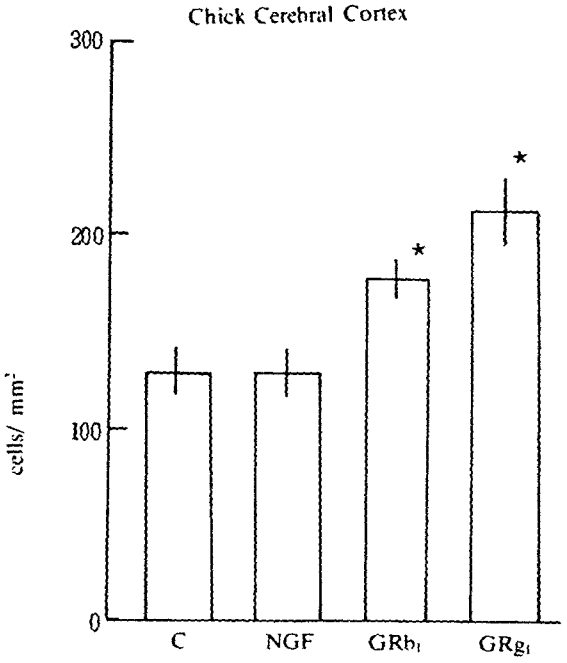


NGF : 100ng/ml GRb1, GRg1 : 30μM
*p<0.05 vs. CONTROL

neurons were counted. GRb1, GRg1 (both 30 μM) and NGF (100 ng/ml) had no effect on neuronal survivals of TH-positive neurons (data not shown).

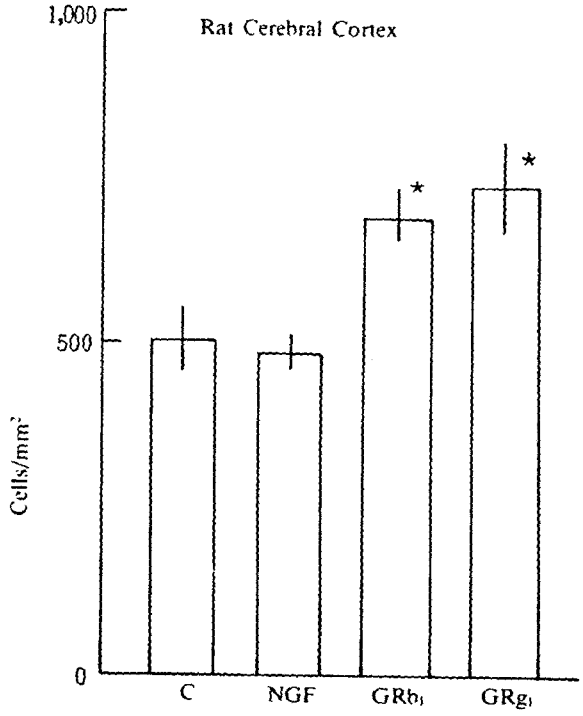
In conclusions, it is very difficult to give any definite conclusions from the results of thses experiments, but they may indicate that water extract of ginseng and some of its saponins are effective on experimental amnesia in mice. Especially GRg1 was the most effective in saponins tested. GRg1 facilitated the acquisition of short term memory, and antagonized the ECS-induced inhibition of retention of memory, the ECS-induced inhibition of retrieval of memory, and the alcohol-induced inhibition of retrieval of memory. In cell culture systems, GRg1 significantly promoted neuronal survivals of chick and

Fig. 6



C : control NGF : 100ng/ml
GRb1, GRg1 : 30μM
* p<0.05 vs. control

Fig. 7



NGF : 100ng/ml GRb1, GRg1 : 30μM
* p<0.05 vs. control (C)

rat embryonic cerebral cortex neurons in cell cultures. GRg1 may play an important role in the process of learning and memory. Though GRb1 depressed the CAR in SB test and psychotropic effect of GRb1 was indicated, GRb1 was also effective. GRb1 antagonized the ECS-

Fig. 8

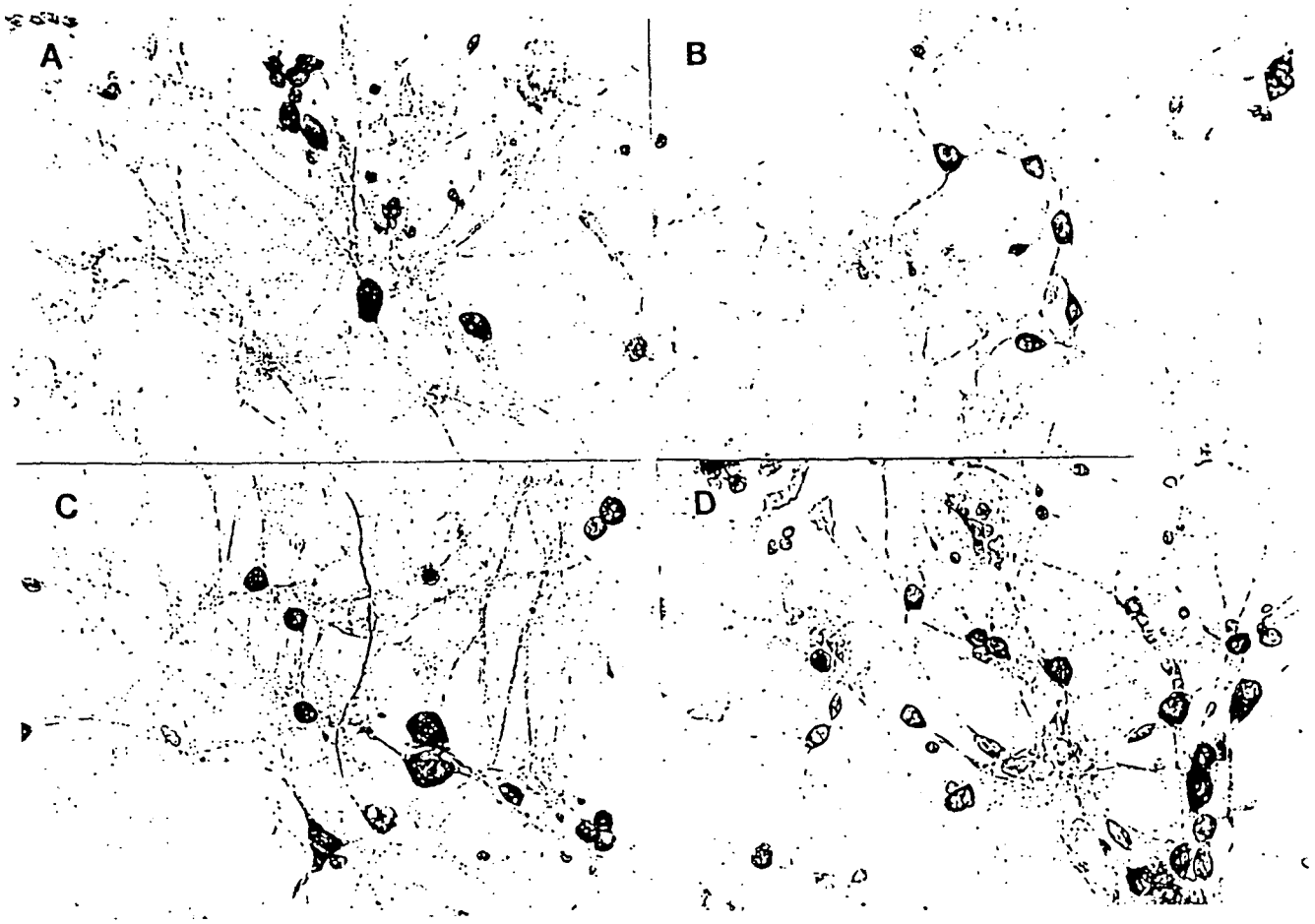


Fig. 8. Cultured rat cerebral cortex neurons immunologically stained with anti-neurofilament antibody.
A. Control, B. NGF (100 ng/ml), C. GRb (30 μM), D. GRg1 (30 μM)

induced inhibitions of retention and retrieval of memory. Moreover, in cell culture system, GRb_1 significantly promoted neuronal survivals of chick and rat embryonic cerebral cortex neurons and NGF showed a tendency to potentiate the effect of GRb_1. GRb_1 may also play an important role in the process of memory in the different way. Although GRb_1 potentiated NGF effect of neurite outgrowth in organ cultures of chick embryonic sympathetic ganglion, GRb_1 did not potentiate the neuronal survival of them. GRb_1 may not have direct effect on sympathetic neurons in cell cultures.

There are many problems left on the relationship between survival enhancing effect and the learning and memory promoting effect of ginseng saponins for us to tackle on.

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D. Mulz : Did you use 250 mg/kg body weight of fluid extract and could you comment on this ? I would like to know the actual content of substances. Or, was it a crude extract without specification?

N. Nishiyama : Yes, I used 250 and 500mg/kg body weight of mice. Its a crude extract and no specification were performed.

D. Mulz : Did you give 50 mg pure substance of saponins in your tests showing the enhancement?

N. Nishiyama : Yes, we used 50 mg/kg body weight of mice.

D. Mulz : Do you think that Rb_1 acts directly on the neuron or as well on the glial cells?

N. Nishiyama : Since we did not eliminate the glial cells in most of the culture experiment, direct target of ginsenoside is still unknown. There is possibility that ginsenosides are mainly effective on glial cells.

F. Sandberg : I am impressed by your experiments but I want to make a comment that ginsenoside do not penetrate the blood barrier. Therefore, you can not draw conclusion of any effect *in vivo* from the cell culture experiments.

N. Nishiyama : Sankawa et al. reported that a few

percent of saponins penetrate the blood brain barrier (BBB) So, the problem of BBB penetration is still open to question. Even if, however, saponin do not penetrate BBB, they can modify central nervous system indirectly via peripheral actions. Brain is, so to speak, a slave of periphery.

H. Okuda : I would like to make a comment on the problem of blood brain barrier. It is widely accepted that BBB may not be strictly constructed in the area of hypothalamus. Therefore, it seems likely that some ginsenosides could be penetrated into brain cells at least in the area of hypothalamus.

인삼 및 인삼 사포닌이 쥐의 건망증 및 신경세포배양에 미치는 영향

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본 연구는 중앙대사전에 인삼의 주 효과중 건망증 방지작용이라고 수록되어 있는 것을 확인하기 위하여 행하여졌다. Step through 시험에서 GRb_1과 GRg_1은 기억력 획득을 용이하게 하였으며 전기충격 쇼크에 의해 야기되는 기억상실 효과를 억제하였다. 게다가 Rg_1은 에타놀 야기 기억재생 저해작용을 방지하였다. Stepdown test 에 있어서 Rb_1, Rb_2, Rg_1은 전기충격쇼크에 의해 야기되는 기억보지 저해효과를 방지하였다. 또한 Rg_1은 에타놀에 의해 야기되는 기억재생 저해효과를 방지하였으며 단기적 기억력 획득을 용이케 하였다. Shuttle box와 lever press 시험에서도 Rb_1을 제외하고 나머지는 기억획득과 재생에 효과를 미치지 못했다. Rb_1은 shuttle box 시험에서 조건회피반응의 재생 (retrieval)을 억제하였다. 이와 같은 4가지 시험이 끝난후에 인삼의 구강투여가 진정, 진통, 해열, 진경효과와 자발 및 탐색활동에 미치는 영향을 500 mg/kg 투여 범위내에서 조사하였으나 아무런 반응도 관찰되지 않았다. 현재까지 연구결과는 Rg_1이 기억의 재생 및 학습반응의 획득과정에 대하여 효과가 있다는 것을 의미한다. 최근의 신경성장인자 (NGF)가 성숙동물에 있어 뇌신경세포의 생존, 재생 및 조절에 미치는 작용에 관한 연구결과는 지능장해와 건망증에 대한 신경성장인자의 중요성을 시사했다. NGF에 의해 야기된 신경세포돌기 성장의 특이성에 관한 연구결과를 병아리 배배근 신경절에 있어서 NGF의 영향은 Rb_1에 의해 증가되었다. 다음으로 Rb_1은 병아리 배의 감각 및 교감신경단위에 있어서 NGF-관련 신경섬유 증가를 강화시켰다. NGF와 Rb_1을 함께 했을 때도 역시 쥐 대뇌피질의 신경세포 생존수를 증가시키는 경향을 보였다. NGF는 쥐의 배격벽 부근의 신경세포를 배양했을 때 cholineacetyl transferase 활성을 증가시키지 않았다. 이러한 결과로 Rb_1은 뇌에 있어서 신경세포의 생존이나 재생에 중요한 역활을 한다는 것은 알 수 있었다.