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Effect of the Saponin Fraction of *Panax ginseng* on Catecholamines in Mouse Brain

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Abstract ☐ The amount of norepinephrine and dopamine in the brain of the mouse fed with normal diet or protein deficient diet with supplement of the saponin fraction of ginseng were determined by the fluorometric method. The amount of norepinephrine in mouse brain was increased by supplement of the saponin fraction of ginseng throughout the experimental period regardless of the kind of diet. However, the enhancing efffct of the saponin fraction of ginseng on the level of norepinephrine in mouse brain was vivider in the case of protein deficiency. The increase amount of dopamine was observed only in the case of mouse fed with normal diet with supplement of the saponin fraction of ginseng for 8 weeks.

Keywords ☐ Saponin fraction of ginseng, Catecholamines, Norepinephrine, Dopamine, Normal diet, Protein deficient diet.

Ginseng, the root of *Panax ginseng C.A.Meyer* has been well known to increase arousal, stamina and resistance to stress[1~3]. These strengthening effect of central nervous system, antifatigue action and the enhancement of non-specific resistance effect of ginseng have been attributed to the saponin fraction[4~6].

Recently, it was reported that the function of nerve growth factor was markedly potentiated by the ginsenoside Rb_1[7] and the fiber outgrowth in explanted chick embryonic dorsal root ganglia was markedly induced by the saponin fraction of ginseng[8].

Catecholamines in brain have been implicated in a variety of visceral and neuroendocrine functions. Catecholamines such as norepinephrine and dopamine serve as neurotransmitters and may play a role in learning, control of mood and motor function[9]. The amounts of norepinephrine and dopamine in brain were declined by long-term stress as well as protein deficiency in prenatal stage and early in infancy[10,11].

The protein deficiency may induce the physiological and behavioral sequelae resulting from the changes in brain catecholamine metabolism[12]. The state of the depression or stress can be improved by the augmentation of the depleted catecholamines in brain[13,14].

To elucidate the effects of the saponin fraction of ginseng on the stress and the restoration from the protein malnutrition, mice were raised with normal and protein deficient diet with the supplement of saponin fraction of ginseng for 2 weeks, 4 weeks and 8 weeks, respectively. The levels of norepinephrine and dopamine in brain were determined to assess the effect of ginseng.

EXPERIMENTAL METHODS

Materials

The saponin fraction of ginseng was prepared according to the method described by Namba[15]. Norepinephrine and dopamine were purchased from Sigma Co.. All other reagents were reagent grade and used without further purification. Deionized and double-distilled water was used for the experiment. Experimental diet was pre-

Table I: Diet composition. (/kg diet)

Component	Normal Diet (18% casein)	Protein Deficient Diet (5% casein)
Corn starch	740g	870g
Casein	180g	50g
Corn oil	40g	40g
Salt mixture	40g	40g
Vitamin A, D mixture	1ml	1ml
Fat soluble vitamin mixture	2ml	2ml
Water soluble vitamin mixture	+	+

Table II: Division of experimental group.

Treatment \ Diet	Normal Diet	Protein Deficient Diet	Experimental period
Control	ND-2	PD-2	
Ginseng supplemented	NDG-2	PDG-2	2 weeks
Control	ND-4	PD-4	
Ginseng supplemented	NDG-4	PDG-4	4 weeks
Control	ND-8	PD-8	
Ginseng supplemented	NDG-8	PDG-8	8 weeks

pared as Table I.

Animals

Sixty male ICR mice weighing 20~25g were randomly divided into 12 groups as shown in Table II. The mice of each group were allowed normal diet or protein deficient diet and tap water ad. lib. for two weeks, four weeks and eight weeks, respectively. 4mg of the saponin fraction of ginseng was administered to mice by the method of oral intubation once a day until one day before sacrifice. The mice were decaptivated and the brains were excised and immediately frozen at −40°C.

Measurement of Norepinephrine and Dopamine

Norepinephrine and dopamine were extracted from mouse brain in a manner similar to that described by Ansell and Shellenberger[16,17], and the amounts of these catecholamines were determined by fluorometric methods of Martin et al.[18], and expressed as μg per g of brain weight.

RESULTS AND DISCUSSION

A significant gradual increase in the amounts of norepinephrine and dopamine in brain was noticed when the mice were fed with normal diet or protein deficient diet for 4 weeks as shown in Table III. The amounts of these catecholamines seemed to remain in normal diet fed mice for another 4 weeks thereafter. But when mice were raised with protein deficient diet for 8 weeks, the amount of norepinephrine in brain dropped significantly while the amount of dopamine showed a tendency of slight elevation compared to the amounts of these catecholamines in brains of mice fed for 4 weeks with protein deficient diet.

Growth and maturation of the brain in prenatal stage and infancy are largely affected by

Table III: Effect of the saponin fraction of *Panax ginseng* on amounts of catecholamines in mouse brain.

Group	Catecholamines(μg/g brain weight)	
	Norepinephrine	Dopamine
ND-2	0.42±0.33	0.95±0.03
NDG-2	0.48±0.06	0.97±0.07
ND-4	0.51±0.02	1.13±0.09
NDG-4	0.55±0.01*	1.13±0.09
NDG-4	0.55±0.01*	1.13±0.09
ND-8	0.49±0.04	1.19±0.03
NDG-8	0.56±0.06	1.37±0.03***
PD-2	0.43±0.04	0.96±0.04
PDG-2	0.56±0.04**	1.12±0.10*
PD-4	0.50±0.02	1.07±0.07
PDG-4	0.55±0.03*	1.10±0.08
PD-8	0.40±0.03	1.18±0.10
PDG-8	0.49±0.05*	1.13±0.03

Mean±S.E.

*; $P<0.05$ **; $P<0.01$ ***; $P<0.001$ significantly different from control

malnutrition. But the brain thereafter becomes more resistant to malnutrition such as protein deficiency than any other organ. Although the brain is preferentially protected from the effect of malnutrition, the protection is not absolute. Prolonged protein deficiency could retard the development and modify the chemical composition of brain. Therefore delay in the formation of norepinephrine synapses or inhibition on the synthesis and storage of catecholamines could be possible[19,20]. The reduction on the amount of norepinephrine in the brains of mice fed with protein deficient diet for 8 weeks seems to be attributed to the lack of tyrosine, the precursor of norepinephrine and dopamine, because of the prolonged protein deficiency.

The supplement of the saponin fraction of ginseng with normal diet or protein deficient diet appears to increase the amounts of catecholamines in mouse brain. The amount of norepinphrine in mouse brain was increased by the supplement of the saponin fraction of ginseng throughout the experimental period regardless of the kind of diet. This increasing effect of the saponin fraction of ginseng on the amount of norepinephrine in brain was more marked, showing statistically significant increase in case that mice were fed with protein deficient diet. Especially, eight week supplement of the saponin fraction of ginseng with protein deficient diet to mouse seemed to overcome the effect caused by protein deficiency and restore the amount of norepinephrine to that of the brain of mouse raised with normal diet for 8 weeks.

The effect of the saponin fraction of ginseng on the amout of norepinephrine in brain could not be observed in the case of dopamine. From the data obtained from this study, it could be concluded that the saponin fraction of ginseng might restore the impaired functions of central nervous system caused by the protein deficiency even though the biochemical mechanism of the restoration can not be explained at the present time. A study is currently in progress to determine the exact mechanism by the estimation of the level of enzymes which govern the catabolism and metabolism of catecholamines in brain.

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