THE PREVENTIVE EFFECT OF THE SAPONIN FRACTION OF *PANAX GINSENG* C.A. MEYER AGAINST ETHANOL INTOXICATION OF RAT LIVER

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ABSTRACT

Preventive effect of the saponin fraction extracted from *Panax ginseng* C.A. Meyer against ethanol intoxication of the liver has been investigated biochemically and morphologically.

Previous work in this laboratory showed that the moderate amounts of ginseng sponins stimulated several enzymes including mitochondrial dehydrogenases and transaminases so far examined *in vitro*. It was also realized that the half life of the saponin in the liver was estimated approximately five hours and the saponin concentration in the liver was around 10^{-3}% level at two hours after the saponin (1mg) administration orally. In this study, it was confirmed that ginseng saponins stimulated alcohol dehydrogenase, aldehyde dehydrogenase and microsomal ethanol oxidizing system *in vivo* as well as *in vitro*. It seemed likely that toxic aldehyde formed during ethanol oxidation in the body might be removed relatively quickly from the liver and the excess hydrogen was used for the biosynthetic work in the presence of the saponin, resulting in the liver protection from alcohol intoxication.

Electron microscopic observation demonstrated that the hepatocytes of rats doses with 12% ethanol instead of water for six days were found severely damaged while those of the ginseng saponin administered rats were not impaired suggesting that the sapcnin protected the liver against ethanol intoxication.

INTRODUCTION

Ethanol is one of the favorite mood-altering drug and its psychic effects, both pleasant and unpleasant, are well known enough but what is less known is that alcohol is a toxic drug: its overconsumption takes the body's economy, produced a number of pathological changes particularly in the liver and impairs biological functions.

Unlike carbohydrates and fats, alcohol is essentially foreign to the body and it is known that the body get rid of it by oxidizing alcohol mainly in the liver. Present knwledge on alcohol metabolism showed that over-consumption of alcohol causes cirrhosis and death not only because alcoholism promotes malnutrition but also because alcohol and its metabolic effects are reported directly linked to the first two products of its oxidation, hydrogen and acetaldehyde.

During the past two decades, physiological and biochemical approaches to elucidate the mechanism of ginseng effect on the animal body have been intensively made.

Among the properties of ginseng suggested

by results of experimental studies, such capacities as elevating non-specific resistance, detoxication of various chemicals introduced into the body, normalizing weak constitutions and promoting an early recovery from the stress following major operation were noticeable.

In the factual scene, when ginseng extract was administered to an animal following the medication of ethanol, there had been reports that the consumption rate of ethanol speed up. (Joo et al., 1977)

This paper described the effect of ginseng saponin fraction on alcohol dehydrogenase (ADH), aldehyde dehydrogenase (AlDH) and microsomal ethanol oxidizing system (MEOS) *in vitro* as well as *in vivo*. Furthermore, the preventive effect of the saponin fraction against ethanol intoxication on rat liver was demonstrated.

MATERIALS AND METHOD

Fifteen grams of ginseng saponin mixture was obtained from 300g of powered Korean white ginseng (Keumsan, 4 years, 50 pieces/300g). The chromatogram of the saponin showed that it contained several saponins with Rf values 0.66, 0.59, 0.50, 0.43, 0.33, 0.25 on silica gel thin plate using chloroform-methanol-water (14:6:1, v/v) as developing solvent. It appeared that the saponin with Rf value of 0.59 was the most abundant, the saponins with Rf values of 0.43, 0.33 were less abundant and the saponins with Rf values of 0.66, 0.25 were the least. The above saponin mixture was used without further purification in this study. Radioactive ginseng saponins were prepared as follows. 2 gram of sliced raw ginseng root (4 years, Keumsan) were incubated in the reaction mixture (3.3ml) containing 0.1M phosphate buffer (pH 6.8), 4 x 10^{-3} M $MgCl_2$, 4 x 10^{-3}M $MnCl_2$, 1.25 x 10^{-1}M sucrose, 5 x 10^{-3}M ATP, 3 x 10^{-4}M NADPH, 5 x 10^{-4}M Coenzyme A, 8 x 10^{-4}O NAD, 2.5 x 10^{-2}M glutathione, 1.2 x 10^{-3}M Na-acetate containing 1, 2-^{14}C acetate (150μCi) at 37°C for 64 hours. Following incubation, the reaction mixture was diluted with water and homogenated, followed by centrifugation to remove the insoluble pellets. The pellet was washed three times with a small volume of water. The combined soluble extract was lyophilyzed. 5ml of hot methanol were then added to the above extract and mixed sufficiently and the mixture was allowed to stand overnight in a refrigerator to precipitate the insoluble fraction. Following centrifugation to remove the insoluble fraction, the precipitate was extracted three times with a small volume of hot methanol as

Table 1. The effect of ginseng saponin on yeast alcohol dehydrogenase (E.C. 1.1.1.1). Assay mixture (3ml) contained (final concentration) 32mM sodium pyrophosphate buffer (pH 8.8), 0.8mM NAD^+, 3mM ethanol, enzyme solution (0.5ug protein) and various concentration of saponin.

Added saponin concentration(%)	Enzyme activity*	Relative activty**
0	15.1 ± 0.1	100
10-7	15.5 ± 0.1	103
10-6	15.7 ± 0.2	104
10-5	18.1 ± 0.2	120
10-4	16.7 ± 0.5	111
10-3	17.0 ± 0.5	112

* Unit of enzyme activity was defined as 0.01 increment of optical density per min. at 340nm.
** Relative activity was defined assuming control being 100.

Table 2. Radioactivity of ethanol bound to yeast alcohol dehydrogenase (E.C.1.1.1.1.) denatured by the addition of 10% TCA.
Original enzyme solution contained (final concentrations) 32mM sodium pyrophosphate buffer (pH 8.8), 0.3mM NAD^+ 3mM ethanol containing 1,2-^{14}C-ethanol (0.017μCi).

Added saponin concentration(%)	(DPM) Radioactivity	%	Relative Radioactivity
0	12655 ± 79	34	100
10^{-6}	13715 ± 95	37	108
10^{-5}	14977 ± 104	41	118
10^{-4}	13738 ± 114	37	109
10^{-3}	13924 ± 60	38	110

Table 3. The effect of ginseng saponins (Total, Diol, Triol) on Km values of horse hepatic ADH for ethanol. Km of ADH for ethanol was determined by measuring the OD increment at 340nm of the reaction mixture (3.0ml) which contained (final concentrations) glycine buffer (pH 9.6) 47mm, NAD^+ 0.4mm, various concentrations of ethanol (0.05mM-5mM) ginseng saponins (various concentrations) and ADH solution* 0.4ml.

Conc. of saponin** (%)	Km (10^{-4}M)		
	Total	Diol	Triol
Control	9.57	9.57	9.57
1.33×10^{-6}	8.96	7.62	9.07
1.33×10^{-5}	8.92	7.22	8.82
1.33×10^{-4}	8.72	6.94	8.82
1.33×10^{-3}	9.21	7.98	9.49
1.33×10^{-2}	10.10	8.62	14.7

described above. The combined methanol extract was mixed with 3 volumes of chloroform, vortexed and then centrifuged to remove the insoluble fraction (mainly sugar). The insoluble fraction was washed twice with methanol-chloroform mixture (1:3, v/v). The combined extract was then concentrated under a reduced pressure and finally dissolved in 2.0ml of methanol. The above methanolic solution was chromatographed by thin plate of silica gel (Merck nach Stahl) using chloroform-methanol-water mixture (65: 40 :9, v/v/v) as a developing solvent. The fractions corresponding to the standard saponins were scraped out and extracted with methanol. The radioactivity and Rf values of each fraction was investigated. The chromatogram of the product showed that the pattern of the radioactive saponin preparation prepared as described above was exactly the same as that of the saponin preparation from ginseng roots (4 years, Keumsan 50 pieces/300g).

Rats were fed with normal diet (Jaiilsaryo Co. product, composition; crude protein above 19.6%, crude cellulose below 7.0%, crude ash below 9.0%, Ca below 0.6%, P below 0.4%, DCP above 16.5%, TDN 7.3%, antibiotic below

Table 4. The effect of ginseng saponins (Total, Diol, Triol) on Km values of horse hepatic ADH for NAD^+. Km of ADH for NAD+ was determined by measuring the OD increment at 340nm of the reaction mixture (3.0ml) which contained (final concentrations) glycine buffer (pH 9.6) 47mM, ethanol 3mM, various concentrations of NAD^+ (0.025mM-0.2mM), ginseng saponin (various concentrations), ADH solution* 0.4ml.

Conc. of saponin** (%)	Km (10^{-5} M)		
	Total	Diol	Triol
Control	4.72	4.72	4.72
1.33×10^{-6}	4.65	4.54	4.80
1.33×10^{-5}	4.66	4.47	4.77
1.33×10^{-4}	4.41	4.23	4.64
1.33×10^{-3}	4.56	4.40	4.86
1.33×10^{-2}	4.87	4.74	5.04

Table 5. The effect of ginseng Saponin on rat hepatic mitochondrial dehydrogenase *in vitro*. Reaction mixture (3ml) contained (final concentration) 16.7mM pyrophosphate buffer (pH 9.2), acetaldehyde (various concentration), 0.3mM NAD^+, 20mM nicotinamide, saponin (various concentration) and mitochondrial preparation. Figures in bracket were relative activities assuming those of corresponding control were 100.

	Enzyme activity*					
Saponin (%)** / Substrate mM**	0	10^{-8}	10^{-7}	10^{-6}	10^{-5}	10^{-4}
1.0	0.016 (106)	0.017 (106)	0.023 (144)	0.017 (106)	0.016 (100)	0.013 (81)
2.0	0.028 (100)	0.027 (96)	0.034 (121)	0.027 (96)	0.027 (96)	0.023 (82)
5.0	0.041 (100)	0.040 (96)	0.050 (122)	0.045 (110)	0.044 (107)	0.036
Km(mM)	2.74	2.13	1.67	2.63	3.08	4.08

* Enzyme activities were shown by increase of optical density at 340nm during 9 minutes' incubation at room temperature (15°C) from 1 minute to 10 minutes after the initiation of the enzyme reactions.

** Final concentration in the assay mixture.

50ppm) until required.

Full details of experimental and analytical methods have been described by Joo et al. (1977, 1979, 1982, 1984)

RESULTS AND DISCUSSION

Previous work showed that the ginseng saponin fraction stimulates alcohol dehydro-

Table 6. The effect of ginseng saponin on partially purified rat hepatic MEOS *in vitro*.

Concentration of ginseng saponin(%)	Acetaldehyde formed (umole/15min./mg)	Relative activity
0	42.54	100
6.67×10^{-10}	44.40	104
6.67×10^{-9}	48.52	114
6.67×10^{-8}	47.93	113
6.67×10^{-7}	49.28	116
6.67×10^{-6}	59.67	140
6.67×10^{-5}	58.86	138
6.67×10^{-4}	43.28	102
6.67×10^{-3}	47.73	112

Activity of MEOS was determined as follows (Lieber et al., 1978). 0.16M phosphate buffer (pH 7.4) containing 15mM semicarbazide-HCl was placed in the center well of Warburg's manometric flask and 3ml of reaction mixture containing 1.0mM sodium EDTA, 1.0mM sodium azide, 1.14M ethanol, ginseng saponin fraction (various concentration) and MEOS preparation was placed in the main vessel. In the side arm, 70% TCA (0.6ml) was placed. After 10mins' preincubation at 37°C, NADPH was added to be 0.4mM in the reaction mixture and the flask was stoppered. After 15mins' incubation at 37°C, the reaction was terminated by adding TCA in the side arm and then the mixture was stood for 12 hours. The absorbed acetaldehyde in semicarbazide in the center well was assayed.

* The relative activities were expressed assuming the activity of control being 100.

Table 7. The effect of ginseng saponin on rat hepatic MEOS *in vitro*. The reaction mixture (final volume 3ml) contained 1.0mM Na_2-EDTA, 5.0mM $MgCl_2$, 0.1M phosphate buffer (pH 7.4),1mM sodium azide, 2mM pyrazole, 20mM nicotinamide, 5mM glucose 6-phosphate, 1M $NADP^+$, 2 units of glucose 6-phosphate dehydrogenase, various concentrations of ginseng saponin and 1ml of rat hepatic microsomal preparation. The above reaction mixture was placed in the main vessel of Warburg flask and in the center well 0.61ml of 0.16M phosphate buffer containing 0.015M semicarbazide hydrochloride. Following 10 minutes' preincubation at 37°C, ethanol containing 1-^{14}C ethanol (0.5 μCi) was added to be 50mM in the mixture and the incubation was continued for 15 minutes. At the termination of the reaction by TCA solution (5% TCA, 45mM thiourea) in the side arm, the mixture was allowed to stand overnight. The radioactivity of acetaldehyde absorbed by the semicarbazide in the center well was measured.

Conc. of ginseng saponin(w/v%)	0	10^{-2}	10^{-4}	10^{-6}	10^{-8}	10^{-10}
Acetaldehyde formed (CPM)	1013	1595	2026	3963	3357	2647
Ratio of test/control	1.00	1.58	2.00	3.91	3.31	2.61

genase (ADH) as well as aldehyde dehydrogenase (A1DH) resulting a rapid oxidation of ethanol in the body. It was also obserbed using light microscope that the hepatocytes of rats which were free access to 12% ethanol and normal diet for 14 days showed severe injury such as vacuolic degeneration, glycogen deposition and fatty degeneration but those of rats which were free access to 12% ethanol and 2% ginseng extract protected the liver from alcohol intoxication(Joo et al., 1979).

In the present study, it was confirmed that both ADH and A1DH were stimulated in the presence of moderate amounts of the saponin fraction in the reaction mixture as shown in table 1, 2 and figure 1. The Km values of horse

Table 8. The effect of ginseng saponin on ethanol oxidation in pyrazole fed rats. They were fed ginseng saponin (2mg/day/rat) for 8 weeks prior to 1 ml of 25% ethanol containing 1-^{14}C ethanol (2 μCi) by stomach tubing.

	Radioactivity (CPM)		
	Fraction / Group	Acetaldehyde	Non-volatile
Liver (CPM/g)	Control	163	383
	Test	185	416
	Ratio of test/control	1.13	1.09
Blood Serum (CPM/ml)	Control	677	166
	Test	525	158
	Ratio of test/control	0.78	0.95

Table 9. The effect of ginseng saponin on the oxidation of ethanol by rat hepatic cytosolic preparation *in vitro*.

Fraction / Condition	Acetaldehyde fraction			Non-volatile residues		
Conc. of saponin in assay mixture (%)	Radio-activity (DPM)	% of* administered incorporation	uatoms** of ^{14}C-incorporated	Radio-activity (DPM)	% of* administered isotope incorporation	uatoms** of ^{14}C-incorporated
0	39,855	1.07	0.160	42,150	1.13	0.169
1.4×10^{-4}	31,980	0.87	0.128	60,315	1.62	0.242

The assay volume was 5ml. It contained (final concentration): Glycine buffer (pH 9.0) 0.044M, NAD^+ 4.2×10^{-4}M, nicotinamide 0.028M, ethanol 3×10^{-3}M containing ethanol-1-^{14}C 1.68uCi (3.73×10^6DPM), ginseng saponin 1.4×10^{-4}% and 1ml of rat hepatic cytoplasmic preparation. After 5min. incubation at 25°C, the reaction was terminated by the addition of 1ml of 20% TCA and radioactivity of acetaldehyde and non-volatile residues were assayed.

* % of administered isotope incorporation was calculated according to the equation of (Total DPM per fraction)/$3.73\times10^6\times100$.

** No. of microatoms of ^{14}C-incorporation into the corresponding fraction was calculated according to the equation of (Ttotal DPM per fraction) ÷ ($3.73\times10^6/3\times5$)

hepatic ADH for ethanol and NAD^+ in the presence of total saponin fraction, diol saponin and triol saponin fraction were determined and realized that an adequate amounts of the saponin fraction lowered the Km (Table 3 and 4). Km of the rat hepatic mitochondrial aldehyde dehydrogenase was also lowered in the presence of the saponin fraction (10^{-7} %) (Table 5).

In addition to liver alcohol dehydrogenase, hepatic microsomal ethanol oxidizing system (MEOS), especially its capacity to increase in activity adaptively after ethanol feeding has been reported. (Lieber, 1976) Although the MEOS *in vivo* has been challenged partly because the rate of ethanol oxidation accounts for only a small fraction of ethanol metabolism *in vivo*, the MEOS may explains various effects of ethanol, inlcuding proliferation of hepatic smooth endoplasmic reticulum, induction of other hepatic microsomal drug detoxifying enzymes, and the metabolic

Table 10. The distribution of radioactivity of hepatic lipids of saponin (1.8mg/a mouse) administered mice (C-54, weighed 32g to 34g) intraperitoneally 2 hours prior to the intraperitoneal injection of 33% ethanol containing 0.26μCi of 1-^{14}C-ethanol.

	Time of continuous administration of ethanol 1-^{14}C (min)	Radioactivity of total lipid in (DPM)	% of* isotope incorporation into hepatic lipid frattion (%)	Radioactivity(DPM) in		
				Triglyceride fraction	Cholesterol fraction	Other lipid fraction
Control	50	8,650	1.51	3,058 (461)	380** (461)	4,838
Test	50	11,298	1.98	5,304	478** (525)	5,392
Test	60	14,203	2.48	7.196	720** (554)	6,037

* % of isotope incorporation into hepatic lipid fraction was calculated according to (DPM in total lipid/5.72x 10^5) x 100.

** Figures in bracket showed specific radioactivity.

Table 11. Specific radioactivity of hepatic cholesterol and fatty acids of mice (C-54, 29g-31g) administered with ginseng saponin (1.8mg/a mouse) intraperitoneally 2 hours prior to the intraperitoneal injection of 33% ethanol containing 0.2μCi of 1-^{14}C-ethanol (pulse period was 30min.).

	Specific radioactivity *CPM/mg	
	Cholesterol	fatty acids**
Control	3.5 ± 0.8	0.8 ± 0.5
Test	5.0 ± 1.2	10.3 ± 2.0

* Mean values of three mice.

** The amounts of fatty acids liberated following saponification were calculated assuming all fatty acids being stearic acid.

Table 12. The effect of ginseng saponin on ADH, ALDH, and MEOS *in vivo*.

	Alcohol Dehydrogenase		Aldehyde Dehydrogenase		MEOS	
***Group	*Activity (units/min)	**Relative activity	*Activity (units/min)	**Relative activity	Activity (μmole/15min/mg)	**Relative activity
Normal	2.12	100	9.60	100	5.41	100
Control	2.68	126	6.98	73	5.78	107
Test	2.81	133	8.13	85	8.21	152

* One unit of enzyme was defined as a density increment of 0.01 per min.

** The relative activities were expressed assuming the activity of control being 100.

*** Control group was dosed 12% ethanol instead of distilled water (free access) for 6 days and test group was dosed 0.1% ginseng sapon in 12% ethanol instead of distilled water for 6 days. Normal group was dosed distilled water freely.

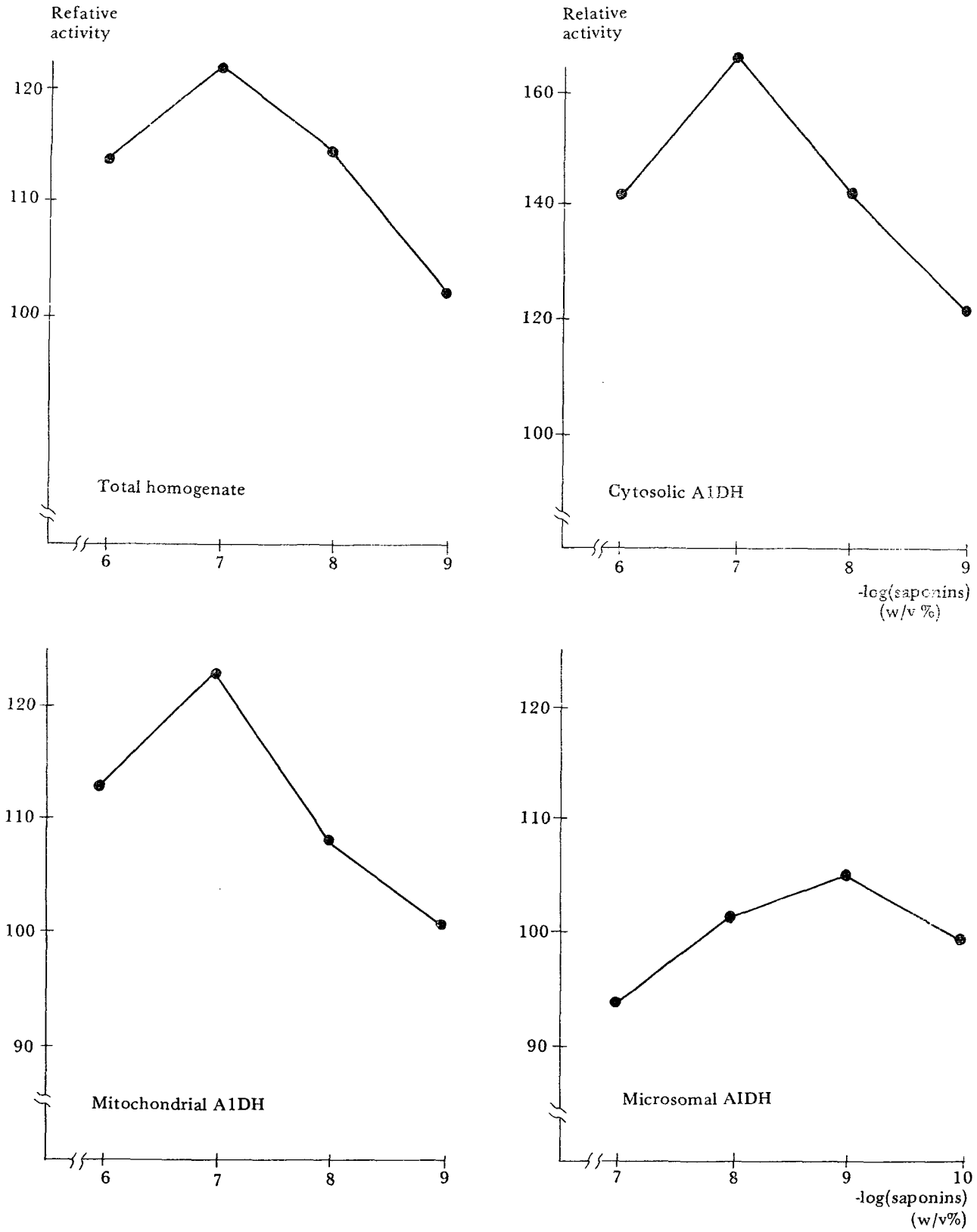

Fig. 1. The effect of ginseng saponin of rat hepatic aldehyde dehydrogenase

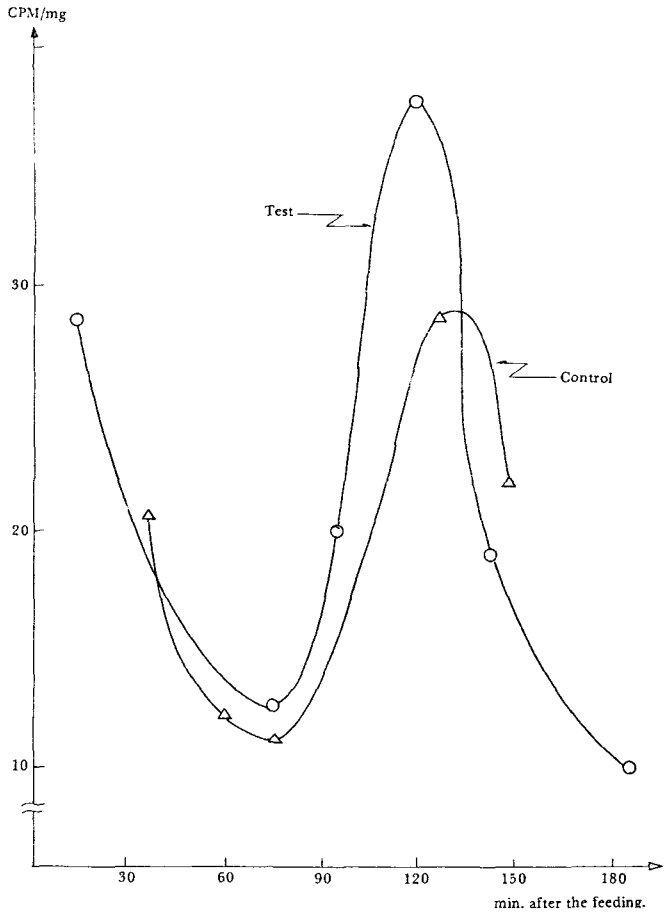

Fig. 2. Specific radioactivity of blood serum fatty acid of ginseng saponin fed rats prior to ethanol 1-1-^{14}C administration on time course after the feeding.

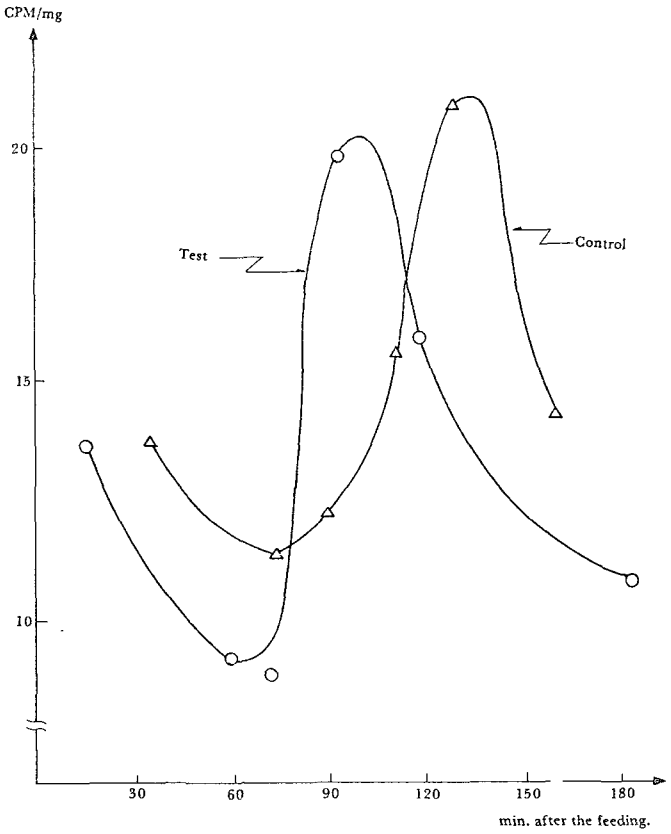

Fig. 3. Specific radioactivity of liver fatty acid of ginseng saponin fed rats prior to ethanol 1-1-^{14}C administration on time course after the feeding.

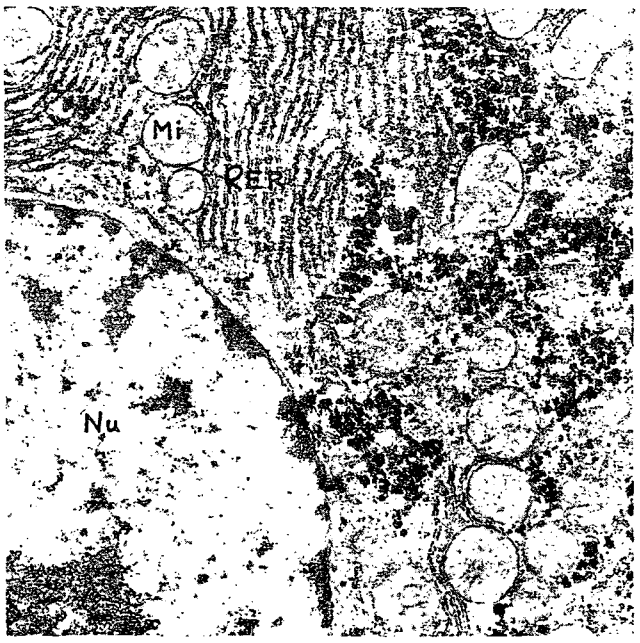

Fig. 4. Electron micrograph of the hepatocyte of rat of normal group. (X 20,000)
Nu, Mi, and RER represent nucleus, mitochondria and rough endoplasmic reticulum, respectively.

tolerance to ethanol which developes in alcoholics. Examination of the effect of ginseng saponin on rat hepatic MEOS *in vitro* as well as *in vivo* showed that the oxidation of ethanol was significantly acclerated in the presence of the saponin as shown table 6, 7 and 8.

The effect of ginseng saponin on the oxidation by rat hepatic cytosolic preparation was investigated and found that the aldehydes formed were oxidized more quickly in the presence of moderate amounts of the saponin fraction in the reaction mixture as shown table 9.

Experimental results using acetate-1, 2-^{14}C showed that the turnover rate of fatty acid and cholesterol in the liver of rat administered with ginseng saponin intraperitoneally prior to the acetate injection showed that the saponin stimulated the metabolism of lipids such as fatty acid

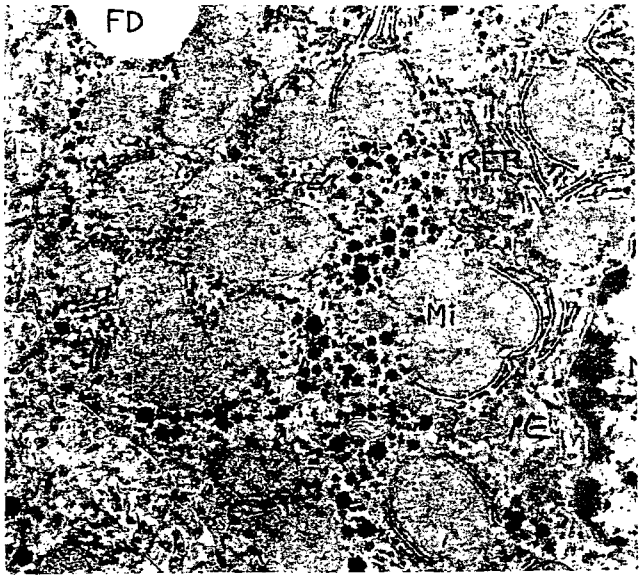

Fig. 5. Electron micrograph of the hepatocyte of rats of control group which were dosed with 12% ethanol instead of water for 6 days. Nu, Mi, RER, SER, PE and FD represent nucleus, mitochondria, rough endoplasmic reticulum, smooth endoplasmic reticulum, and Mitochondria are swollen and disrupted severly. The RER are dilated and vesiculated and the SER are proliferated.
Peroxisomes are increased in number.
Pyknosis occur and large fat droplets are seen.

and cholesterol in the body. When liver lipids of mice which had received intraperitoneal injection of ginseng saponin fraction (1.8mg) 2 hours prior to intraperitoneal injection of 0.3ml of 33% ethanol containing 1-^{14}C-ethanol was investigated at 50min. after the ethanol administration, the isotope incorporation into the hepatic lipids of the test animals were 1.98% while that of control animals was 1.51%. Radioactivities of the individual lipid fractions were also found higher in test group. Specific radioactivities of hepatic cholesterol and fatty acid of mice killed 30min. after the ethanol-1-^{14}C injection showed again that higher activities was found in test group, particularly in fatty acid fraction as shown in table 11.

When rats were dosed ginseng saponin fraction (5mg/day/rat) orally (stomach tubing) for 14 days prior to 0.5ml of 20% ethanol containing 1-^{14}C-ethanol (luCi), the radioactivity-time curves (Figure 2 and 3) of the blood serum and liver fatty acids showed that the saponin fraction stimulated the biosynthesis of fatty acids from ethanol, probably via acetate.

Based on the above experimental results, the preventive effect of ginseng saponin fraction against ethanol intoxication of the liver fed with 12% ethanol instead of water (free access) for 6 days with/without ginseng saponin was investigated and found that the activities of ADH and MEOS of both control and ginseng saponin fed group were higher than those of normal group while the activity of aldehyde dehydrogenase (AlDH) of control and test group were lower than that of normal rats. However, the AlDH activity decrease of test group was much less than that of control group (Table 12).

Electron micrograph showed that severely swollen and disrupted mitochondria and dilated and vesculated ER can be seen in control group while dilated or vesiculated ER are very few and swollen or disrupted mitochondria can not be seen in test group (Figure 4, 5 and 6).

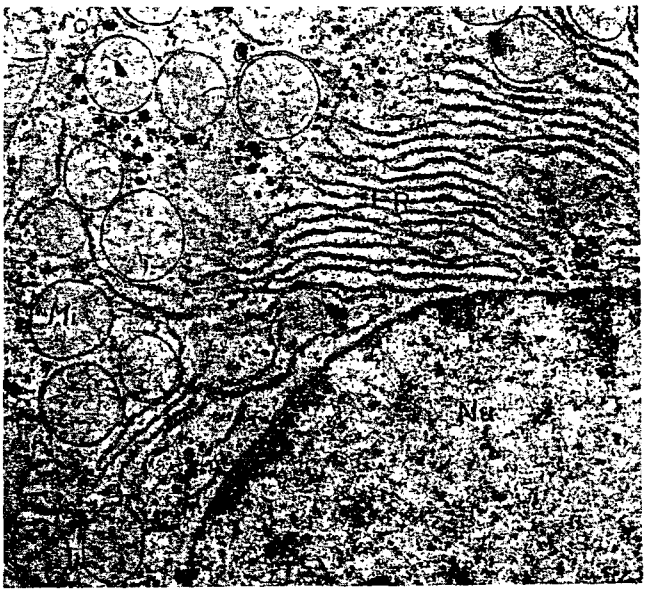

Fig. 6. Electromicroscopic photograph of rat hepatocyte of test group which were dosed with 12% ethanol containing 0.1% (w/v) ginseng saponin instead of water for 6 days. Nu, Mi, and ER represent nucleus, mitochondria, and endoplasmic reticulum, respectively. Swollen or listrupte mitochondria can not be seen.
Dilated or vesiculated ER are very few. (x 20,000)

From the above experimental results, it seems that ginseng saponin might stimulate the ethanol oxidation and the removal of acetaldehydes by rat hepatic MEOS and A1DH, respectively.

I.P. Lee: I'd like to ask you about your enzymatic activity such as alcohol dehydrogenase and aldehyde dehydrogenase that you measured for saponin treatment. Have you look at the *in-vivo* metabolism of ethanol itself or aldehyde?

Joo: It is very difficult to do *in-vivo* aldehyde experiment. The stimulation of aldehyde dehydrogenase activity can be examined only *in-vitro*.

I.P. Lee: I think, we can simply do it by using labelled aldehyde and following the disappearance of aldehyde.

Joo: Do you mean *in-vivo* experiment?

I.P. Lee: Yes, *in-vivo*.

Joo: We didn't analyze aldehyde dehydrogenase activity *in-vivo*. We checked the disappearance of the aldehyde when we fed the ^{14}C labelled alcohol, and then we found less amount of labelled aldehyde, which means ethanol converts to the end-product, acetate. It means saponin enhances the removal of aldehyde. The toxic problem is aldehyde and overproduction of NADH distrubs the balance in the body, then impairs the biochemical functions. That's why we traced the final product, not directly the aldehyde dehydrogenase activity itself *in-vivo*. We tried only the *in-vitro* approach to realize what happened with the aldehyde dehydrogenase in the presence of saponin fraction.

Cha: I'd like to make a comment. Acetaldehyde is very difficult to measure *in-vivo* because whatever it is released into the serum is all tied up with protein. So it is impossible to make an *in-vivo* measurement of acetaldehyde. Now, my question is that you have traced these animals with ginseng extract. Was it crude saponin?

Joo: We partially purified saponin fraction. We don't know yet whether it is pure saponin or contaminated with impurity. We are now under the investigation of that point.

Cha: According to Dr. Lee's results, there was much increase in the cyt. P-450 which is perhaps responsible for the microsomal ethanol oxidizing system, MEOS. Have you measured the cyt. P-450 content in your system?

Joo: Saponin fraction stimulated the MEOS very much. I recently published a paper about the concentration of cyt. P-450. Therefore if you are interested in it, I'll show you the copy.

쥐간에 미치는 ethanol 독성에 대한 한국산 인삼(Panax ginseng C.A. Meyer)의 예방적 효과

주 충 노
연세대학교 이과대학 생화학과

한국산 인삼(Panax ginseng C. A. Meyer) 뿌리에서 추출한 사포닌 분획이 쥐의 간에 미치는 에탄올 독성을 예방하는 효력이 있음을 생화학적 및 현미경적으로 관찰하였다.

본 연구실의 연구 결과에 의하면 적당량(반응액에서의 농도 : 10^{-5}%내외)의 인삼 사포닌은 여러가지 효소를 비 특이적으로 활성화하며 1mg의 사포닌 분획을 쥐에게 경구 투여하면 2시간후의 간에서의 인삼 사포닌 분획의 농도가 약 10^{-5}% 수준이고 간에서의 사포닌 분획의 반감기는 약 5시간으로 추정되었다.

본 연구에서도 인삼 사포닌 분획이 에탄올 대사에 관여하는 alcohol dehydrogenase, aldehyde dehydrogenase 그리고 microsomal ethanol oxilizing system을 시험관 내에서나 생체에서 다같이 촉진한다는 것을 알게 되었고 인삼 사포닌 분획이 에탄올 산화 과정에서 생성되는 유독한 acetadizing를 체내에서 신속히 제거하고 과량의 수소를 생합성에 효과적으로 이용함으로서 에탄올 독성으로부터 간을 보호하는 것으로 생각되었다.

전자현미경적 관찰도 물대신 12% ethanol만을 6일간 투여한 쥐의 간세포가 크게 손상되었는데 비하여 인삼 사포닌을 12%ethanol과 함께 같은 기간 투여한

쥐의 간세포는 손상되지 않았음을 나타내고 있으며, 인삼 사포닌 분획이 에탄올 독성에 예방적 효력이 있음을 확인할 수 있었다.

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