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Study on Animal Liver Excretion Function Affected by Administration of Korean Ginseng Glycoside

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Research findings and accomplishments in the study of Ginseng constituents and its physiological activity doned uring the past decade, have far surpassed the research achievements attained during the preceding 100 years. As we all know, there are numerous reports on the efficacy of *Panax shinseng* and its physiological activities by such renowned scholars in the field of phytochemistry, pharmacology and gerontology[1~5].

Since the Three kingdoms period (57 B.C.-668 A.D.), Ginseng has been used for both tonic and medicinal purposes.

There are many legendary stories about the effectiveness of *Panax shinseng*. Getting a hunch from one of them, for the object of detoxication after heavy drinks, it was widely used among the Korean people from the imperial time.

Lee and Shin and others conducted the research on the influence of alcoholic extract of Ginseng on the liver functions[6,7].

Kim reported that ether extract and petroleum-ether extract of Ginseng do not have any effect but alcoholic extract and watery extract of Ginseng do have effective influence on the liver functions[8]. For the purpose of investigating the influence of Ginseng (*Panax shinseng*) glycosides (hereafter referred to as PSG) on the liver function, was applied the biochemical method to measure serum glutamic oxaloacetic transaminase (S-GPT) activity, serum glutamic pyruvic transaminase (S-GPT) activity and bromsulphophthalein retention rate. Along with this method, also was conducted the histochemical observation on the effect of Ginseng glycosides to the thioacetamide intoxicated rats. With the results of these two approaches, was examined the effect of Ginseng glycosides on the protection of the induced liver damage.

Biochemical survey. Measuring S-GOT and S-GPT activity : 95% carbon tetrachloride (0.1 ml/kg) was injected to the muscle, and PSG was orally administered to the intoxicated rabbit. To investigate any resultant change in the liver functions, S-GOT and S-GPT activity in the rabbit serum was measured. At the same time the bromsulphophthalein retention rate was also measured.

As for S-GOT and S-GPT activity, 1, 2, 3, 4, and 5 days after the injection of carbon tetrachloride the blood taken by the heart puncture was tested. S-GOT activity increases created by the injection of carbon tetrachloride were 322.8±14, 305.2±10.3, 213.2±13.7, 164.8±11.1, and 110.4±13.9 unit, respectively. Four hrs. after the injection, 50 mg/kg/day of PSG was orally administered to the test group, and S-GOT activities measured were at 316±11.2, 258±11.8, 146±7.6, 103±7.5 and 72±12.1 unit, respectively.

Except the data of the first day of the test, S-GOT activities were remarkably decreased (Table I).

Table I—The effect of the PSG on the S-GOT activity of rabbits treated with carbon tetrachloride

Day after intoxication	Carbon tetrachloride in control	Carbon tetrachloride with PSG administration
	M±SD(unit)	M±SD(unit)
1st day	322.8±14	316±11.2
2nd day	305.2±10.3	258±11.8
3rd day	213.2±13.7	146± 7.6
4th day	164.8±11.1	103± 7.5
5th day	110.4±13.9	72±12.1

On the other hand S-GPT activities of the control group intoxicated with carbon tetrachloride were 325.2±14.9, 352±8.1, 300±9.1, 260.4±7.5, and 224.4±21.2 unit, respectively. In the case of the PSG-administered group, they were 316.8±7.9, 275.4±10.8, 217±7.2, 209±12.8, and 188.2±9.6 unit, respectively.

The activities were clearly reduced with the exception of the 1st day group(Table II).

BSP retention rate: BSP retention rates of the rabbit intoxicated with carbon tetrachloride and the PSG-administered group 2 days after the start of the test method described above were 82.5% and 21.5%, respectively, clearly indicating the effect of PSG in lowering the BSP retention rate(Table III).

From the foregoing biochemical assay, it is found simultaneously that PSG dose have effect on the recovery of the liver functions damaged by carbon tetrachloride.

To validate the data obtained through this biochemical assay, a histochemical survey was conducted.

Histochemical survey—Two groups of healthy rats were used in this survey. 25 mg of thioacetamide was injected into the first group (control group), and PSG was orally administered to the second group (test group). At the intervals of 6, 12, and 24 hrs after the administration of these agents into the control group and the test group, the liver was ectomized for the histochemical survey. The following were findings from this histochemical survey.

Rat liver histochemical changes 3 hrs after single dose (25 mg) of thioacetamide showed moderately distorted hepatic cell cords with slightly swollen parenchymal cells, bearing

Table II—The effect of the PSG on the S-GPT activity of rabbits treated with carbon tetrachloride

Day after intoxication	Carbon tetrachloride in control M±SD(unit)	Carbon tetrachloride with the PSG M±SD(unit)
1 st day	325.2±14.9	316.8±7.9
2 nd day	322±8.1	275.4±10.8
3 rd day	300±9.1	247±7.2
4 th day	260.4±7.5	209±12.8
5 th day	224.4±21.2	188.2±9.6

Table III—BSP retention equivalents(%) at the time of 30 min. after BSP injection

Animal group	Control group	Thioacetamide 25 mg single dose	PSG and thioacetamide simultaneous dose
BSP retention equivalent (%)	18.00±4.90	82.5±7.36	21.5±2.05

acidophilic cytoplasm. Central vein is congested moderately. There is no evidence of Kupffer cell proliferation in the sinusoidal wall. Portal fibrous tissue remains normal.

In the case of 6hrs after thioacetamide dose Parenchymal cell swelling is more prominent in the centri lobular zone and mid zone. Cells in these areas showed fine granularity of the cytoplasm, and swollen, enlarged and smudged nuclei. Other findings are almost similar with those of the above results. PAS stain showed negative finding in the cytoplasm.

In Fig. 1 normal rat liver pattern and in Fig. 2 the case of 24hrs of thioacetamide single dose are shown.

There is noted extensive necrotic changes of the parenchymal cells around the central vein. In this area, cells exhibited vacuolization, balloon formation and necrosis with marked hemorrhage. Dark hypertrophied and binucleated cells are presented between necrotic centrilobular area and relatively preserved mid zone. Portal area remains normal. PAS stain showed positive tinctorial reaction in the necrotic cells.

Rat liver histochemical pattern 6 hours after simultaneous dose of thioacetamide (25 mg) and PSG (25 mg) showed congestion of the central vein, and dilated sinusoids. Hepatic cells are rather swollen. However, cell cords remain normal architecture. No significant change is seen in the nucleus. PAS stain showed weak positive reaction in the parenchymal cells (Fig. 3).

The pattern 12 hours after a simultaneous dose of thioacetamide and PSG showed swelling of the hepatic cells with fine granular cytoplasm with slight basophilia. There is no evidence of cytoplasmic vacuolization or cell necrosis. No significant nuclear change is seen. PAS stain showed positive tinctorial reaction around the portal cells.

The pattern 24 hours after a simultaneous dose of thioacetamide and PSG showed moderately distorted hepatic architecture and hemorrhage around the central vein. Cytoplasmic

degeneration is seen, however, no vacuolization or balloon cell formation is encountered. Portal area showed well preserved hepatic cells without evidence of cytoplasmic degeneration. PAS Stain reveals complete absence of the positive material, but weak positive findings in the parenohymal cells ofthe portal area.

The pattern 24 hrs after administration of PSG at the beginning of the test and 4 hrs after thioacetamide showed extensive cytoplasmic degeneration with vacuolization hemorrhage and necrotic change around the centrilobular parenchymal cells. Periportal parenchymal cells are relatively well preserved but occasionally showed basophilic cytoplasm. Mild degree of chronic inflammatory cell infiltration is seen in the portal fibrous tissue. PAS stain showed complete negative findings in the entire zone of the hepatic lobules. Changes are very pronounced, but milder than that 24 hrs after thioacetamide (25 mg) and that of the following case.

The pattern 24 hrs after a thioacetamide administered at the beginning of the test and 4 hrs after PSG showed more extensive cellular destruction and hemorrhage around the centrilobular parenchymal cells. Periportal parenchymal cells exhibited basophilic degeneration. Cytoplasmic change is extended to the mid zone of the lovules and more pronounced than that of the above case. PAS stain reveals complete absence in the entire zone of thelobules. Chronic inflammatory cells are presented in the portal fibrous tissue. Changes are more prominent than that of the for mer case but milder than that of 24 hrs after thioacetamide.

The pattern 24 hrs after PSG and thioacetamide administered at beginning of the test and 6 hrs after PSG showed very mild cellular change around the centrilobular area. No vacuolization, cytoplasmic degeneration or necrotic change is seen. Periportal parenchymal cells are relatively well preserved. Chronic inflammatory cell infiltration is seen in the portal cells.

Significant histologic change is seen from 6 hrs after the thioacetamide injection. Changes are more prominent in Fig .s 2 and 5 in which necrotic change is seen in the centrilobular area. On the other hand, PSG and thioacetamide injection groups showed mild changes compared with the group injected thioacetamide alone. Generally 24 hrs groups showed significant changes in the order of Figs. 2, 7, 5, 6 and 8.

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Fig. 1—Normal rat liver histological pattern.

Fig. 2—The pattern 24 hrs. after single dose of thioacetamide.

Fig. 3—The pattern 6 hrs. after simultaneous dose of thioacetamide (25 mg) and PSG (25 mg).

Fig. 4—The pattern 12 hrs. after doses of thioacetamide and PSG.

Fig. 5—The pattern 24 hrs. after doses of thioacetamide and PSG.

Fig. 6—The pattern 24 hrs. after dose of PSG at the beginning of the test and 4 hrs. after thioacetamide.

Fig. 7—The pattern 24 hrs. after thioaceramide administered at the begginning of the test and 4 hrs. after PSG.

Fig. 8—The pattern 24 hrs. after PSG and thioacetamide administered at the beginning of the test and 6 hrs. after PSG.

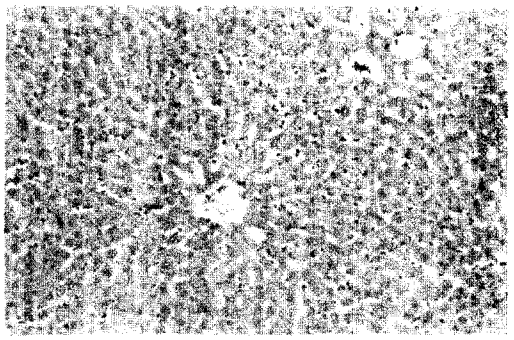


Fig. 1

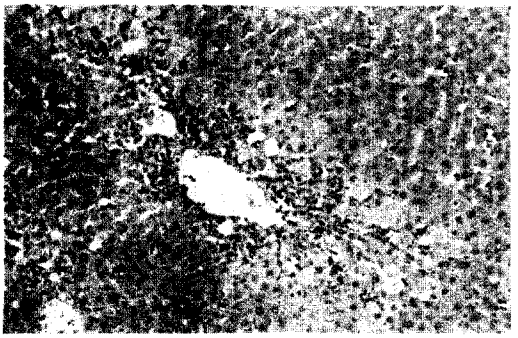
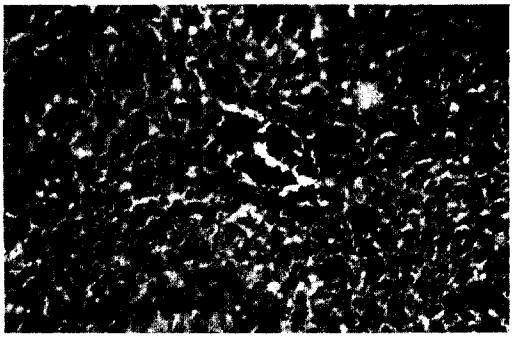


Fig. 2



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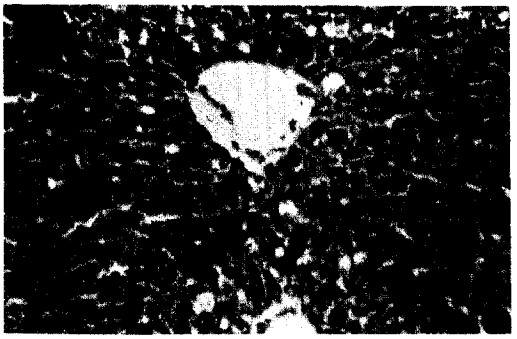
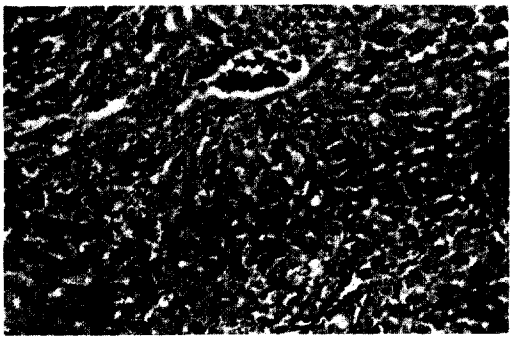


Fig. 4



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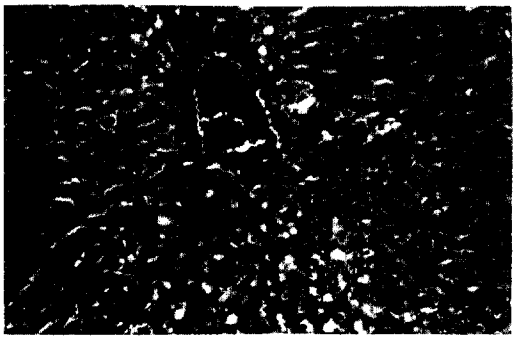

Fig. 6

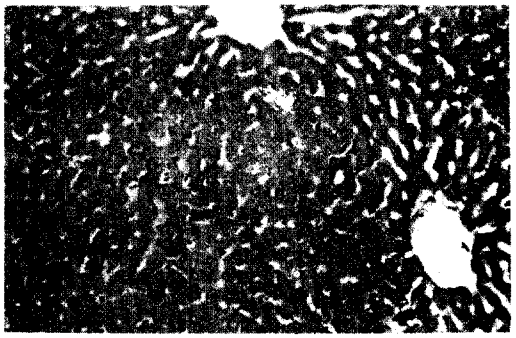

Fig. 7

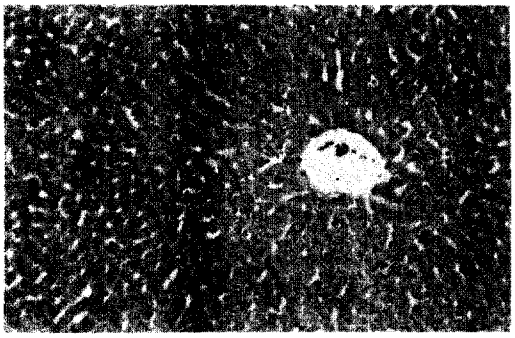

Fig. 8