# Liver Protective Activities of Korean Medicinal Plants

## ——Pharmacology of Plantago Semen——

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Plantago semen, the seeds of plantago species, have long been used for medicinal purposes for controlling various liver diseases. In addition, they have been used as anti-inflammatory, antitussive, obstipant and diuretic agents for treating various alimentary, respiratory and renal disorders.[1-5]

On the course of our preliminary screening tests for hepatotonic plant materials as shown on Table I, several of the plant materials including plantago semen were found to exert potent liver protective activities against carbon tetrachloride intoxication in mice, [6,7] The biochemical and pharmacological examinations on the anti-hepatotoxic effects of plantago semen have been undertaken.

Reports have been indicated that rat liver intoxication with halogenated hydrocarbons, especially, carbon tetrachloride caused structural and metabolic changes in hepatic tissues and cells, with distinctive changes of endoplasmic reticulum and marked depression in microsomal enzymatic activities and hepatic protein syntheses.[8,10] Following such disturbances, liver necrosis is usually accompanied.[11] The chosen dose schedule of carbon tetrachloride in our experiments could induce histological changes in appearance of liver closely equivalent to diffused hepatitis in men.[12,13]

Table II shows the dose schedule of carbon tetrachloride and test samples against carbon tetrachloride intoxication. Each mice was treated for four days with saline, $CCl_4$ and test samples

**Table 1.** List of medicinal plants and their liver protective activities.[6]

| Family name | Scientific name | Parts of plants | Activities[a] |
|---|---|---|---|
| Lardizabalaceae | *Akebia quinata* | vi | Toxic |
| Alismataceae | *Alisma orientale* | tu | ## |
| Umbelliferae | *Angelica gigas* | ra | + |
| Compositae | *Artemisia Messer-Schmidtiana var. viridis f. typica* | ha | — |
| Aristolochiaceae | *Asiasarum sieboldii* | wp | Toxic |
| Liliaceae | *Asparagus cochinchinensis* | tu | ## |
| Leguminosae | *Astragalus membranaceus* | ra | 0 |
| Compositae | *Atractylodes japonica* | rh | Toxic |
| Compositae | *Atractylodes japonica* | rh (alba) | ## |
| Umbelliferae | *Bupleurum falcatum* | ra | — |
| Umbelliferae | *Bupleurum longeradiatum* | ra | Toxic |
| Compositae | *Carduus crispus* | ha | 0 |
| Leguminosae | *Cassia tora* | sm | ## |
| Amarantaceae | *Celosia argentea* | sm | -- |
| Papaveraceae | *Chelidonium majus* | ha | — |
| Cyatheaceae | *Cibotium barometz* | rh | ## |
| Compositae | *Cirsium pendulum* | ha | — |
| Rutaceae | *Citrus aurantium* | fs | 0 |
| Cornaceae | *Cornus officinalis* | fr | 0 |
| Rosaceae | *Crataegus pinnatifida* | fr | + |
| Cyperaceae | *Cyperus rotundus* | tu | ## |
| Equisetaceae | *Equisetum hyemale var. japonicum* | ha | ## |
| Rutaceae | *Evodia rutaecarpa* | fr | ## |
| Gentianaceae | *Gentiana scabra* | ra | ## |

| | | | |
|---|---|---|---|
| Leguminosae | *Glycyrrhiza uralensis* | ra | ++ |
| Solanaceae | *Lycium chinense* | fr | + |
| Polyporaceae | *Pachyma hoelen* | sc | ++ |
| Ranunculaceae | *Paeonia albiflora var. trichocarpa* | ra | ++ |
| Araliaceae | *Panax ginseng* | ra | ++ |
| Scrophulariaceae | *Picrorrhiza kurroa* | rh | ++ |
| Araceae | *Pinellia ternata* | tu | 0 |
| Plantaginaceae | *Plantago asiatica* | sm | +++ |
| Liliaceae | *Polygonatum japonicum* | rh | +++ |
| Polygonaceae | *Polygonum multiflorum* | ra | -- |
| Rutaceae | *Poncirus trifoliata* | fs | ++ |
| Labiatae | *Prunella vulgaris* | ha | — |
| Rosaceae | *Prunus persica* | sm | ++ |
| Scrophulariaceae | *Rehmania glutionosa* | ra | ++ |
| Rhamnaceae | *Rhamnus crenatus* | b | ++ |
| Polygonaceae | *Rheum undulatum* | rh | ++ |
| Labiatae | *Salvia multicorrhiza* | ra | + |
| Labiatae | *Scutellaria baicalensis* | ra | + |
| Menispermaceae | *Sinomenium acutum* | ra | + |
| Compositae | *Taraxacum platycarpum* | wp | — |

a: activities counteracting carbon tetrachloride intoxication measured with the duration of sleeping time after injection of hexobarbital.

b: bark fr: fruit skin ha: herba ra: radix rh: rhizome sc: sclerotium sm: semen tu: tuber vi: vine wp: whole plant

as indicated and pharmacological and biochemical evaluations were undertaken on the fifth day.

**Table 2.** Schedule of treatment of mice with carbon tetrachloride and test samples.

| | Days | | | | |
|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 |
| Control | Sal. | Sal. | Sal. | Sal. | Biochemical or pharmacological measurements were undertaken |
| $CCl_4$ | Sal. | $CCl_4$ | $CCl_4$ | Sal. | |
| Test samples | T.S. | T.S. + $CCl_4$ | T.S. + $CCl_4$ | T.S. | |

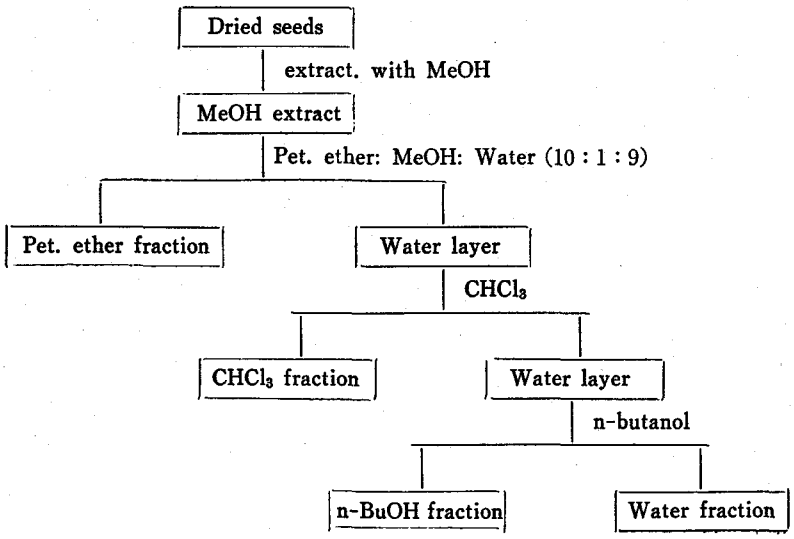
Sal.: 0.9% physiological saline, T.S.: Test sample in saline

Sample preparations were made with plantago semen for hepatotonic activity tests as described in chart I. Total methanol extract was first prepared from plantago semen and fractionated into four different solvent fractions; petroleum ether, chloroform, n-butanol and water fractions. Methaol extract and each fraction was subjected to pharmacological and biochemical evaluations.

### 1) Effects on the duration of sleeping time induced by hexobarbital:

The duration of sleeping time was measured

**Chart I.** Fractionation of methanol extract of Plantago semen.



following hexobarbital injection [14] on the fifth day of experimental schedule as appeared in Table II. Carbon tetrachloride intoxication caused elongation of sleeping time comparing with that of control group which could be explained by the reduction of enzymatic metabolism of hexobarbital in liver. Table III shows the favorable effects of methanol extract, water and chloroform fractions of plantago semen counteracting carbon tetrachloride intoxication.

Especially, the effect of water fraction restored the sleeping time to nearly normal state. However, the duration of sleeping became longer with butanol and petroleum fractions.

**Table 3.** Effects of plantago semen on duration of sleeping time induced by hexobarbital.

| | duration of sleep |
|---|---|
| Control | 13 |
| $CCl_4$ | 21 |
| MeOH ext.+$CCl_4$ | 16 |
| $H_2O$ fr.+$CCl_4$ | 14 |
| n-BuOH fr.+$CCl_4$ | 27 |
| $CHCl_3$ fr.+$CCl_4$ | 18 |
| Pet, Ether fr.+$CCl_4$ | 73 |

### 2) Effects on serum transaminase activities:

The elevation of serum glutamate-oxaloacetate transaminase (S-GOT, EC. 2, 6, 1, 1) and serum glutamate-pyruvate transaminase (S-GPT, EC. 2, 6, 1, 2) activities have very close relationships. [15,16] On the fifth day of experiment following four-days of treatment of mice as on Table II, blood samples were collected and the enzymatic activities were assayed.[14] As the fig. I and II show, both S-GOT and S-GPT activities were markedly increased with $CCl_4$ intoxication comparing with the control. Methanol extract, water and chloroform fraction treated group of mice showed S-GOT and S-GPT activities comparable with that of control group while petroleum and butanol fractions rather elevated S-GOT and S-GPT levels. These biochemical data appeared to be correlated with

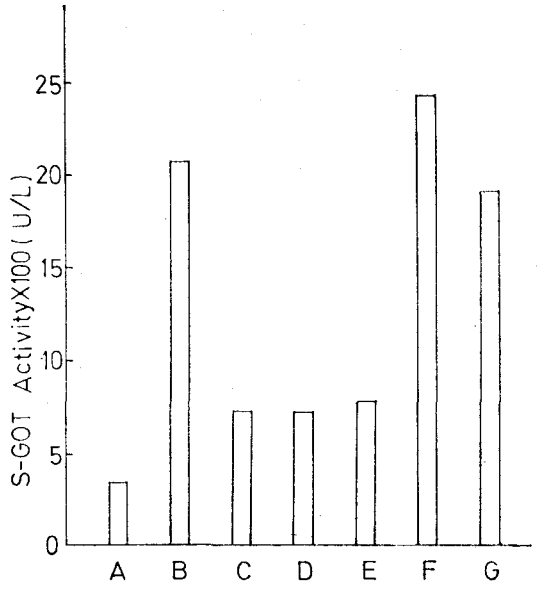


**Fig. 1.** S-GOT activities

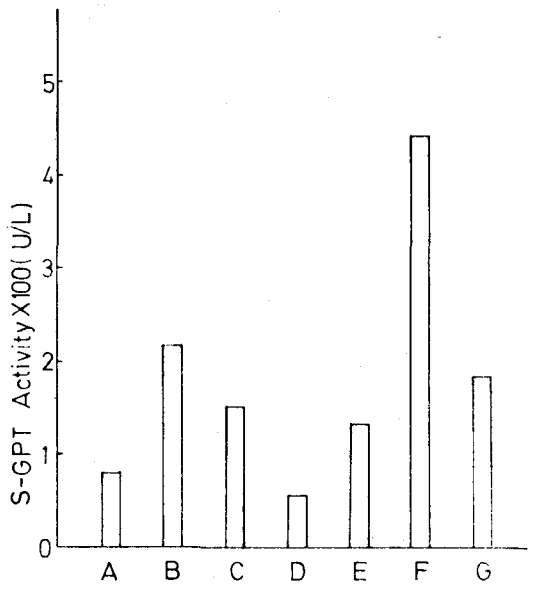


**Fig. 2.** S-GPT activities

A: Control, B: $CCl_4$, C: Methanol extract+$CCl_4$, D: $H_2O$ fraction+$CCl_4$, E: $CHCl_3$ fraction+$CCl_4$, F: Pet. ether fraction+$CCl_4$, G: n-BuOH fraction+$CCl_4$

the pharmacological evaluation that methanol extract, water and chloroform fractions of plantago semen have counteracting effects against $CCl_4$ intoxication.

### 3) Histological observation of liver tissue:

On the day of five, after treating mice as the schedule on Table II, liver slices were prepared with each mice for direct microscopic observations. The biopsy data confirmed the previous pharmacological and biochemical evaluations.[17] With the administration of $CCl_4$, liver showed typical hepatic symptoms especially around portal area. Treatment with methanol extract, water or chloroform fraction of plantago semen together with $CCl_4$ reduced the hepatotoxic effects of $CCl_4$ restoring the overall condition near normal state. Butanol and petroleum ether fraction showed rather toxicity. The overall histological observation appeared to be coincide with the results obtained from measurement of the duration of sleeping time induced by hexobarbital and serum transaminase activities that the whole methanol extract, water and chloroform fraction had liver protective effects and that especially the hepatotonic effect of water fraction was significant.

The water fraction of plantago semen contain various mono-, di-, tri- and poly-saccharides and the presence of aucubin was confirmed. The chemical and biological mechanism of active constituents from plantago semen should next be investigated.

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