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Plants with Liver Protective Activities (I)

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强肝劑로 使用된 生藥의 調査研究(I)

肝炎에 미치는 効果에 關하여

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Literature survey was undertaken to investigate what medicinal plants have been used as hepatotonic or for treatment of various liver diseases in far eastern asian countries. Total 59 plants were found to be described in the literatures. And 9 plants among them were studied on their hepatotonic activities against animal model of hepatitis. Several plants appeared to exhibit profound activities on the hepatitis model employed.

It was reported that high incidence of diseases related to liver occurred in Korea[1~3]. One survey indicated that the occurrence rates of hepatitis in Korea appeared to be ten times higher than in Japan and even three times higher than average rates of other Asian endemic areas. It is well known that chronic active hepatitis can lead to liver cirrhosis, and often be complicated with other diseases such as glomerular damage, skin manifestations, endocrine abnomalities and diabetes mellitus[4]. In addition, it seems to be no effective therapeutic agents available for hepatitis and liver cirrhosis at present time, although many efforts have been made to develope effective methods and remedies for protecting liver from damage or for the treatment of liver diseases.

This study aimed to investigate plausible liver protecting agents through literature survey and to evaluate the potential agents and plants in animal model of hepatitis.

Literature Survey

The literature survey so far of the oriental old medicinal books and folkloric remedies revealed that numerous plant preparations have been used for the purpose of liver protection or for the treatment of liver diseases.

As the table I shows, total 59 plants were found to be effective, of which 37 plants were described to be used as hepatotonic, 27 plants for unspecified liver diseases, 5 plants for hepatitis and 2 plants for cirrhosis.

And 12 plants were multipurposely used for both liver protection and the treatment of liver diseases, though it is uncertain that the pathological contexts described in old literature are indeed coincided with the modern medical terms in present time.

Table I. Plants Used for Liver Protective Activities.

Plant Names	Family Names	生藥名	Part in use	Purpose of use	References
Allium bakeri	Liliaceae	韮 菜	s	P	6,8
Allium fistulosum	Liliaceae	葱 白	rt	D	8
Aloe sp.	Liliaceae	蘆 薈	ext	P	5,6,13
Amaranthus ascendus	Amaranthaceae	莧	s	D	8
Asparagus cochinchinensis	Liliaceae	天門冬	rh	P	4,5,8
Asiasarum heterotropoides var. seoulense	Aristorochiaceae	細 辛	rt	P	5,6,8
Begonia crassiostus	Begoniaceae	秋海棠	s	H	7
Benincosa cerifera	Cucurbitaceae	冬 瓜	fr	D,P	6,9
Buddeia officinalis	Loganiaceae	蜜蒙花	fl	P	5,6
Bupleurum falcatum	Umbelliferae	柴 胡	rt	D,P	6,8,9,13
Capsella bursa-pastoris	Cruciferae	薺 菜	wp, s	D,P	6,8
Cassia Tora	Leguminosae	決明子	s	D,P	5,7,8
Celosia argentea	Amarantaceae	青箱子	s	D	5,7,8
Chaenomeles sinensis	Rosaceae	木 瓜	fr	P	6,8
Chelidonium sinense	Papaveraceae	白屈菜	wp	C,D	6,9,11
Chrysanthenum sibiricum	Compositae	九折草	wp	D	11
Cibotium barometz	Cyatheaceae	狗 背	rh	P	5,6,13
Cinnamomum cassia	Lauraceae	桂 皮	b	P	1,6,8
Citrus unshiu	Rutaceae	青 皮	p	D	5,6,8
Cnidium officinale	Umbelliferae	川 芎	rh	P	5,8
Codonopsis lanceolata	Campanulaceae	沙 蔘	rt	P	8
Coptis japonica	Ranunculaceae	黃 連	rh	P	5,8
Cucurbita moschata	Cucurbitaceae	南 瓜	fr	P	6,8
Cyperus rotundus	Cyperaceae	香附子	rh	P	6,9,10
Dioscorea Tokoro	Dioscoreaceae	薥 蘞	rh	P	5,6
Equisetum hiemale var. japonicum	Equsetaceae	木 賊	h	D	5,9,13
Evodia rutaecarpa	Rutaceae	吳茱萸	fr	H,P	6,9,10
Fraxinus rhynchophylla	Oleaceae	秦 皮	b	D,H	5,7
Gentiana scabra var. buergeri	Gentianaceae	龍 膽	rt	D	5,6,8
Gledtisia japonica var. koraiensis	Leguminosae	皂 莢	fr	D	5
Leonurus sibiricus	Labiatae	益母草	wp	D	7
Liqustrum lucidum	Oleaceae	女貞實	fr	P	7
Lysium chinense	Solanaceae	枸杞子	fr	D,P	5,9
Macrocarpium officinale	Cornaceae	山茱萸	fr	P	6,8
Paeonia albiflora var. tricocarpa	Ranunculaceae	芍 藥	rt	D,P	6,7,8
Panax ginseng	Araliaceae	人 蔘	rt,l	P	5,6,12,13
Perilla frutescens var. japonica	Labiatae	荏 子	s	P	8
Plantago asiatica	Plantaginaceae	車前子	s	D,P	5,6,8
Picrorrhiza kurroa	Scrophulariaceae	胡黃連	rh	P	6,8

Plant Names	Family Names	生藥名	Part in use	Purpose of use	References
Polygonatum japonicum	Lilaceae	黃 精	rh	P	5, 6, 11
Polygonum multiflorum	Polygonaceae	何首烏	rt	D, P	6, 7, 9, 11, 13
Polygonum orientale	Polygonaceae	萚 實	s	H	7
Polygonum tinctorium	Polygonaceae	藍 實	s	P	6, 8
Prunella asiatica	Labiatae	夏枯草	wp	P	6, 7
Prunus persica	Rosaceae	桃 仁	s	P	6, 8, 13
Prunus salicina	Rosaceae	李桃仁	s	D	6, 8
Rehmannia glutinosa var. lutea	Scrophulariaceae	地 黃	rh	D	5, 6, 7
Rhamnus crenatus	Rhamnaceae	山 黃	b	C, H	7
Rheum undulatum	Polygonaceae	大 黃	rh	P	6, 7
Rubus coreanus	Rosaceae	覆盆子	fr	P	6, 8
Scutellaria baicalensis	Labiatae	黃 芩	rt	D	5
Silybum marianum	Compositae	薊	s	D	7
Sophora angustifolia	Leguminosae	苦 蔘	rt	P	8, 11
Taraxacum platycarpum	Compositae	蒲公英	wp	D	7, 11
Tribulus terrestris	Zygophyllaceae	蒺 莉	s	D	5, 7
Triticum sativum	Gramineae	小 麥	s	P	5, 6, 8
Uncaria rhynchophylla	Rubiaceae	鈎藤鈎	sp	D	7
Xanthium chinensis	Compositae	蒼耳子	s, fr	D	8
Zizyphus vulgaris var. spinosus	Rhamnaceae	酸棗仁	s	P	5, 6, 8

b; bark, ext; extract, fl; flower, fr; fruit, p; pericarp, rh; rhizome, rt; root, s; seed, sp; spina, wp; whole plant C; Liver cirrhosis, D; Unspesified Liver Desease, H: Hepatitis, P; Protection of Liver (Hepatotonic)

Pharmacological Evaluations

In order to evaluate the hepatotonic activities of the medicinal plants shown in table I, 9 plants which are well known as tonic folklore were selected. Then crude methanol extracts of those plants were prepared. One of animal models of hepatitis which could be produced by damaging mouse liver with carbon tetrachloride administration were chosen for evaluation system.

Animal and plant samples: Most of plant samples were purchased from the local herb drug dealers except Rhamnus crenatus which was collected from Keum Gok, Kyung Gi Do, Korea. They were identified taxonomically by specialist in the Natural Products Research Institute, Seoul National University, Seoul(110), Korea. Silymarin was purchased from the Laboratory Oftalmiso S.L. (Spain). Mice, Swiss albino, were supplied by the Animal Care House of Seoul National University.

Preparations of plants extracts: The air-dried plant samples were placed in 10 L flask and were refluxed with 90% methanol for 6 hrs. Then it was filtered off and the filtrates were concentrated under reduced pressure into complete dryness. In order to extract the residual components as much as possible, the extraction procedures were repeated for two times. The plant extracts were dissolved in 0.9% saline and were subjected to oral administration. In case of insoluble plant extracts in saline, few drops of Tween 80 were added into saline and the plants extracts were homoginized to form suspension.

Table II. Hepatotonic Activities of Plants.

	Days					Duration of sleep (min.)
	1	2	3	4	5	
Control	Vehicle				Hexobarbital	23.5
CCl_4	Vehicle	CCl_4		Vehicle		39.3
Silymarin	Silymarin	Silymarin+CCl_4		Silymarin		15
Polygonatum japonicum	Extract	Extract+CCl_4		Extract		14.6
Cyperus rotundus						15
Polygonum multiflorum						16.3
Rehmannia glutinosa var. lutea						19
Asparagus cochinchinensis						24.9
Cassia Tora						22
Plantago asiatica						12.8
Rhamnus davurica						18.7
Panax ginseng						18

* each group consists of 5 mice.

Animal model of hepatitis: The procedure in detail was reported previously else where[14]. It was slightly modified in this experiment as the followings; On day 1, each mouse, male, weighing 30 g in the control group, CCl_4 group, silymarin group and the test group received orally saline, saline, silymarin (25mg/kg) and the plants extracts (670mg/kg), respectively. On day 2 and 3, CCl_4 group mouse was administered orally with CCl_4 (0.13ml/kg/day). Each mouse in silymarin group received orally 25mg/kg/day of silymarin together with CCl_4 (0.13ml/kg/day) and other test group mouse was fed with 670mg/kg/day of plants extracts together with CCl_4 (0.13ml/kg/day). Each mouse in the control group received orally saline as a vehicle. On day 4, each mouse in both control and CCl_4 groups was administered orally with vehicle only. The silymarin group and the test group was each fed same doses of silymarin and plants extracts as those of day 1, respectively. On day 5, each mouse in all groups was injected intraperitoneally with hexobarbital sodium, 25mg/kg. Then the duration of sleep was measured. The duration of sleep was taken as the time from the end of hexobarbital injection to the point at which the animal first stood up and made coordinated forward movement.

Results and Discussion

Regarding the animal model of hepatitis in the experiment, the chosen dose of CCl_4 could induce histological changes in liver closely equivalent to diffuse hepatitis in man[14]. As the data shown in table 2, silymarin which is a principal component contained in *Silybum marianum* is currently on market as a hepatotonic agent. Therefore, it was used as a positive control in the experiments.

As the data showed, CCl_4 group animals exhibited increased duration of sleep in comparison with those of the control group animals. The mice received silymarin together with CCl_4 exhibited marked reduction of the duration of sleeping time compared with those of CCl_4 group, and even shorter than those of the

control group. Although the results imply that the plant extracts so far tested appear to exhibit potential hepatotonic activities, of great importance is the fact that the hepatitis model system employed in the experiments may not be a sufficient measure for the purposes of evaluation. In addition, it is well known that certain chemicals and drugs are able to cause the increase of liver microsomal enzymes responsible for the oxidative metabolism of hexobarbital,[15,16] they are not hepatotonic agents, though. With respect such facts, the results obtained from the studies with hepatitis model system can only be used as an indication for the purpose of preliminary screening of hepatotonic activities. Nonetheless, it is belived that present works warrant for further studies.

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