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Protective Effect of Several Korean Edible Plants on Galactosamine-induced Hepatic Damage in Rats

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ABSTRACT *: Hepatitis, liver cirrhosis and liver cancer caused by viral infection are among the most prevalent causes of death in Korea. Several medicines have been in use despite their nonsatisfactory effects on these disease. Some herbal medicines put to use recently have not shown beneficial effects, either. This paper evaluates the effects of extracts from 10 traditional Korean herbal medicines on rats with hepatic damage induced by galactosamine. Rubus coreanus showed an anti-inflammatory effect as shown on the data of activities of serum transaminases.*

Key Words *: Herbs, Galactosamine, Hepatitis, Rubus coreanus*

I. INTRODUCTION

Endemic viral hepatitis among inhabitants of the West Pacific regions has been a serious public health concern, the number of hepatitis B-virus (HBV) carriers exceeding 160 million(United Nation' s Demographic Year Book, 1979). The precise mode of viral pathogenesis remains unknown (Philippe *et al.*, 1984; London *et al.*, 1985). Epidemiological studies predict that a large number of patients actively infected with HBV will develop liver cirrhosis, and approximately 35% of this group will progress to primary hepatocellular carcinoma (Deodhr *et al.*, 1975). Efforts to control HBV disease have been focused on extensive vaccination of the newborn population as well as the search for therapeutic agents. Neither an antiviral approach by means of the nucleoside analogue, adenine arabinoside (Thomas *et al.*, 1988), interferon (Prrillo *et al.*, 1989; Lok *et al.*, 1988; Lai *et al.*, 1987), nor biological response modifiers (e.g. cianidanol, OK-432, BCG, leramisole) (Fattorich *et al.*, 1986; Di Bisceglie *et al.*, 1990) has demonstrated statisfactory results (Zheng *et al.*, 1990). Anti-inflammatory drugs(e.g. croticosteroids) has not been clinically effective, and may worsen the progress of the disease (Lam *et al.*, 1981).

It was found in recent years that when a human is infected with Hepatitis B virus, the hepatitis virus is found not only in hepatocytes, but also in white blood cells, kidney, bone-marrow, etc (Shen *et al.*, 1986). Accordingly, the importance of viral eradication can not be overemphasized. Equally important is a long-term administration of natural food stuff, known to be effective for protection of liver, to those with chronic carrier state of Hepatitis virus, to retard inflammatory process and to prevent hepatoma.

This study was fundamentally concentrated on the 10 kinds of herbs known to have been applied to the therapies of Jaundice and liver diseases illustrated in old oriental medicine texts (Huh *et al.*, 1613). The ten materials extracted through water were applied to liver damages of rats induced by galactosamine (Reutter *et al.*, 1975). The efficacy was determined by the changes of serum transaminases, alkaline phosphatase and bilirubin values of the experimental animals.

II. MATERIALS AND METHODS

1. Preparation of herbal medicinal plants and extraction

Between 0.5 and 1.0 kg of 10 Korean herbal medicinal plants was purchased from herbal material and media supply houses in Taegu, Korea (Table 1). The plants were washed, then dried in a

Table 1. List of 10 herbal plants used in this study

Extract No.	Scientific botanical names	Korean botanical names
1	*Sanguisorba officinalis* L.	Jiyu
2	*Terminalia chebula* R.	Kaja
3	*Rubus coreanus* M.	Bokbunja
4	*Rheum palmatum* L.	Daewhang
5	*Eugenia caryophyllata* T.	Junghyang
6	*Areca catechu* L.	Binryang
7	*Cornus officinalis* S.	Sansuyu
8	*Caesalpinia sappan* L.	Somok
9	*Ephedra sinica* S.	Mawhang
10	*Chaenomeles japonica* L.	Mokgua

convection oven at 25°C. Dried leaves, nuts and roots were chopped and grounded. 20g of each plant powder were dissolved in 1000 m*l* distilled water and extracted for 4 hours at 80°C. Aqueous extracts were centrifuged at 3,000 rpm, filtered first through Whatman No. 3 paper and then through a 0.45 μm size filter. Each filtrate was lyophilized and stored at 4°C until use.

2. Experimental animals and effects of plant extracts on galactosamine-induced hepatic damage

Male Sprague-Dawley rats weighing 200 g were divided into 11 experimental groups, each consisting of five rats. For two days prior to galactosamine treatment, every test group was given each plant extract (2% in drinking water, w/v) ad libitum. The control group (galactosamine control) was given water ad libitum. The test and control groups were treated intraperitoneally with a single dose of galactosamine (800 mg/kg body weight, Sigma Chemical. Co) (Handa and Sharma, 1990). Venous blood samples from each rat were taken from the jugular vein under ether anesthesia 48 hours prior to and 48 hours after galactosamine treatment. Serum transaminases, alkaline phosphatase, and bilirubin levels were determined. SGOT (glutamine oxaloacetic transaminase) and SGPT (glutamine pyruvic transaminase) were determined according to the method of Reitman and Frankel (Reitman *et al.*, 1957). Serum alkaline phosphate and bilirubin were measured by the methods of King (King *et al.*, 1954) and Malloy (Malloy *et al.*, 1937).

3. Effect of plant extracts on liver function parameters of normal rats (hepatotoxicity test)

Five male rats weighing approximately 200 g per each treatment group (total of 10 treatment groups) were given 2% of each plant extract (w/v) in drinking water ad libitum for 48 hours prior to sampling venous blood for liver function tests. Serum GOT, GPT, bilirubin and alkaline phosphatase levels were determined as above.

4. Statistical analysis

Data were analyzed by the *Student's t-test* using the Sigma plot software program (Conover, 1992). Statistical significance was defined as $p<0.01$-0.05 compared with the control values.

III. RESULTS AND DISCUSSION

1. Effects of 10 herbal extracts on liver function in the normal rats (hepatotoxicity test).

Ten kinds of herb extracts were administered to normal rats to see their effects on the function of the liver of the subject rats. The results, as indicated on Table 2, showed no changes in the activities of serum transaminases, alkaline phosphatase, and bilirubin pre and post administration of the extracts. None of the 10 extracts affected liver function parameters in normal rats.

2. Effects of 10 herbal extracts on liver function in the galactosamine induced hepatotoxictity in rats.

Ten kinds of herbal extracts were administered to the galactosamine induced hepatic injury in rats for tests of liver function, with the results on Table 3. The SGOT of the animals only with the galactosamine injection showed 26.5 ± 2.65, 468.2 ± 22.86 before and after the injection. The value of post-injection soard 20 times that of pre-injection. In SGPT, it jumped to 680.6 ± 24.94 from 17.2 ± 2.24. The values of bilirubin in blood were 0.2 ± 0.02 for pre-injection and 4.2 ± 0.56 for post injection.

Table 2. Effect of 10 herbal medicines on the liver function test of normal rats

Botanical names	SGOT(ku/ml)		SGPT(ku/ml)		ALP(KAU/ml)		Bilirubin(mg/dl)	
	before	after	before	after	before	after	before	after
Sanguisorba officinalis L.	38.9±2.68	48.2±2.74	15.2±2.42	14.7±2.48	97.2±4.09	74.0±4.07	0.2±0.04	0.1±0.04
Terminalia chebula R.	39.1±2.61	69.2±2.95	15.7±2.44	18.2±2.46	102.5±3.92	84.9±4.05	0.2±00.2	0.1±0.04
Rubus coreanus M.	42.3±2.24	54.5±2.46	19.6±2.47	27.2±2.36	83.2±3.75	92.3±3.12	0.1±0.02	0.1±0.04
Rheum palmatum L.	75.9±2.48	52.9±2.54	18.0±2.70	21.2±2.37	75.3±4.09	59.2±3.97	0.1±0.04	0.1±0.03
Eugenia caryophyllata T.	46.1±2.01	61.3±2.97	19.1±2.65	21.5±2.47	108.0±3.89	83.5±4.08	0.2±0.04	0.1±0.03
Areca catechu L.	76.5±2.96	116.1±2.19	21.1±2.25	33.6±2.39	102.5±3.92	97.0±4.03	0.1±0.03	-
Cornus officinalis S.	78.1±2.51	59.2±2.23	25.2±2.38	67.5±2.41	90.9±3.71	69.2±4.01	-	0.1±0.03
Caesalpinia sappan L.	53.4±2.74	75.1±2.17	20.1±2.77	18.1±2.72	89.3±3.67	81.1±3.85	0.1±0.04	-
Ephedra sinica S.	39.8±2.23	63.2±2.48	19.4±2.66	15.9±2.35	94.4±3.57	88.6±3.83	0.1±0.04	0.1±0.03
Chaenomeles japonica L.	62.4±2.18	79.2±2.53	17.6±2.09	22.8±2.82	86.8±3.87	70.4±3.79	0.2±0.02	-

Number of rats in each group=5
Data are Mean±S.D

Table 3. Effect of 10 herbal medicines on the liver function test of the galactosamine induced hepatits in rat

Botanical names	SGOT(ku/ml)		SGPT(ku/ml)		ALP(KAU/ml)		Bilirubin(mg/dl)	
	before	after	before	after	before	after	before	after
Galactosamine control	26.5±2.65	468.2±22.88	17.2±2.24	680.6±24.94	92.4±4.02	81.4±11.92	0.2±0.02	4.2±0.56
Galactosamine with								
Sanguisorba officinalis L.	38.4±2.68	510.9±23.46	16.2±2.42	680.6±24.61	97.2±4.33	73.5±12.10	0.4±0.03	4.5±0.71
Terminalia chebula R.	38.0±2.84	435.9±23.34	15.3±2.34	562.8±23.70	103.2±3.94	72.1±13.01	0.3±0.05	3.9±0.58
Rubus coreanus M.	49.2±2.46	220.1±21.48	17.5±2.37	197.2±21.55	85.6±3.27	98.7±11.72	0.2±0.05	1.6±0.54
Rheum palmatum L.	78.1±2.52	529.4±22.15	18.8±2.28	597.4±24.21	74.9±3.91	91.2±12.24	0.1±0.04	2.5±0.74
Eugenia caryophyllata T.	46.4±2.04	486.7±25.92	18.0±2.28	509.7±21.05	109.5±4.05	72.2±12.29	-	6.5±0.63
Areca catechu L.	78.6±2.35	534.1±20.98	19.2±2.45	529.6±24.10	102.5±3.69	156.8±12.43	0.3±0.05	3.6±0.52
Cornus officinalis S.	79.0±2.52	494.2±21.67	26.3±2.67	520.7±22.48	91.6±3.58	96.3±12.25	-	2.9±0.65
Caesalpinia sappan L.	43.7±2.34	614.3±20.23	18.3±2.11	427.5±20.07	88.9±3.75	103.7±13.12	0.2±0.05	3.6±0.48
Ephedra sinica S.	70.1±2.65	528.2±25.01	22.0±2.44	623.6±25.01	55.7±3.92	68.9±12.46	-	3.1±0.75
Chaenomeles japonica L.	37.2±2.01	440.6±22.5	19.5±2.33	517.9±24.81	87.4±3.79	104.2±11.96	0.3±0.05	2.9±0.73

Number of rats in each group=5
Data are Mean±S.D

Values of alkaline phosphatase, however, remained unchanged with 92.4±4.02 pre and 81.4±11.92 post-injection.

The rise in activities of serum SGOT, SGPT, serum bilirubin with the injection of galactosamine is translated mainly by necrotic changes of hepatocyte (Shearlock, 1977). On the other hand, no significant change in the value of serum alkaline phosphatase represents either no obstructive changes took place in the bile duct passage or there was a minuscule change if there was any.

Ten korean herbal extracts were applied to the treatment of the hepatocytotoxicity in the rats induced by galactosamine with the following result: The group applied with 9 kinds of the extracts excluding *Rubus coreanus* showed no changes in liver function test. That is to say, the 9 extracts were ineffective. *Rubus coreanus* when administered to animals showed a remarkably low level of rise in SGOT and SGPT following the galactosamine injection. *Rubus coreanus* appeared effective.

Rubus creanus is botanically the family of deciduous shrub and is called in Korea mountain strawberry. In a old medical literature (Huh, 1613), *Rubus coreanus* is known to be effective for blood coagulation properties, helping to facilitate blood circulation. The fruit of *Rubus coreanus* is used as a promoter for general health in Korea. The histopathological findings of galactosamine induced hepatic injury in rats are akin to those of human viral hepatitis and accordingly, this procedure may be used for screening herbs for prevention of hepatotoxicity coming from extrinsic chemicals taken or applicable for treatment of already existing hepatitis. In light of this study, a more detailed study is required on *Rubus coreanus*.

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