Natural Product Sciences
5(4) : 155~158 (1999)

Biological Activities of the Root of *Cichorium intybus*

Chang-Geun Ki, Dong-Sool Yim and Sook-Youn Lee*

Department of Pharmacy, Sahm Yook University, Seoul 139-742, Korea

Abstract – Several biological activities of extracts from roots of *Cichorium intybus* Linne (Compositae) were studied in this paper. The antiinflammatory activity of the methanol extract of this root was investigated against carrageenin induced edema in rat's hind paw. Significant inhibitory effects were observed at the dose of 1,000 mg/kg and were compared with aspirin as a control. The hepatoprotective activities of the methanol extract, ethylacetate and butanol fraction were studied on mice whose livers are damaged by CCl_4. The serum transaminase activities (ALT, AST) were reduced at the dose of 1,000 mg/kg of the methanol extract, 500 mg/kg of ethylacetate and butanol fraction, respectively. The bile juice secretion was also increased significantly from each fraction. The antidiabetic activity was examined on streptozotocin-induced diabetic rats with methanol extract. Methanol extract gave a significant reduction of blood glucose levels in 1 week and 3 weeks.

Key words – Chicory, Compositae, Antiinflammatory Activity, Hepatoprotective Activity, Antidiabetic Activity

Introduction

Chicory, the dried or processed rhizome and roots of *Cichorium intybus* Linne (Compositae), is probably best known as an additive that enhances flavor of the bitterness, color and form of coffee (Lim, W. Getal, 1996). Leaves are used popularly as vegetables for table. The plant can grow to a height of 2 m and has a hardy, 10 to 30 cm long, thick root. The leaves are 10 to 30 cm long and 1 to 5 cm wide, obovate, oblong, shaped like a cross-cut saw or slit, with numerous stiff hairs beneath. The plant is found in Europe (Mitton, F. *et al.*, 1976, Wren, R.C. *et al.* 1975), the Near East, Africa, America, Australia and New Zealand. There are 8 species of Genus *Cichorium* in the world (Huxley, *et al.*, 1992). It is cultivated in some areas of Asia as well as Korea. The dried, aerial parts and underground parts of this plant are collected in autumn. It also has a history of use as diuretics, laxatives, tonics and a treatment of gallstone, hepatic disorders and indigestion. In animal studies a distinct reduction of pulse rate and contractility, mildly cholagogic effects, lowering of the cholesterol level and antiexudative are reported. Recently, in a report of pharmacological activities it has a inhibition effect on the free radical-mediated DNA damage in calf thymocytes (Sultana, S. *et al.*, 1995). This plant contains the bitter sesquiterpenoid lactones, lactucin and lactucopicrin (intybin) (Khalil, A.T. *et al.*, 1991) as well as cichoriin (coumarin glucoside). In the book of traditional herbal medicine you could found the effect of this plant on the liver by the channel theory and so the therapeutic activity for jaundice. Also it is widely used as thick tea for diabetics. Therefore, we undertook some biological activities-the antiinflammatory activity, the hepatoprotective activity, choleretic activity and the antidiabetic activity for proving these effects in this study.

Experimental

Plant material – The dried roots of *Chichorium intybus* L.(Compositae) were collected in In-je, Kangwon Province, Korea, at 1996 and identified specimen was deposited.

Preparation of Extract – Dried root (2 kg) were extracted with methanol under reflux (4 hrs × 3 times) and then concentrated in vacuum to get crude extract (280 g). The extract was dissolved in water and successively extracted with hexane, ethyl acetate, and butanol. For pharmacological experiments these extracts were suspended in a 1%-CMC (carboxymethyl cellulose).

Test Animals – White Albino rats (Sprague-Dawley strain) (250 ± 20 g) and ICR mice (25 ± 5 g) were

*Author for correspondence.

used for this experiment and purchased from Daehan animals Co. Ltd.. The animals were used after acclimatization period of 14 days to the laboratory environment.

Carrageenin induced rat paw edema – 1% solution/suspension of carrageenin was prepared and 0.1 ml of this solution was injected into the right hind paw of male rat (Winter *et al.*, 1962). The methanol extract was administered (1,000 mg/kg/day, *p.o.*), aspirin 200 mg/kg was injected intraperitoneally (*i.p*) 30 min. prior to the injection of carrageenin. The paw volume was measured by plethysmometer (Ugo Basil) just before and 1 to 5 hr after administration of carrageenin.

Cannulation of bile duct – The bile flow was measured as described earlier (Yim, D.S. *et al.* 1997). Briefly, the abdomen was opened with a midline incision under ether anesthesia. The common bile duct was exposed and cannulated. A small cut was made on the back of the rat to bring out polyethylene tubing which was allowed to pass below the skin. The abdominal opening was sutured. The outer end of the cannula was put into a graduated tube for collection of bile after 1 hr of the oral administration. The dose at range of methanol (1,000 mg/kg), ethylacetate (500 mg/kg) and butanol extracts (500 mg/kg) was administered orally. The bile was collected for up to intervals of 20 minutes to 240 minutes and the flow was expressed as mg/20 min.

Carbon tetrachloride induced liver injury in mice – Male ICR mice were used in these experiments. Liver damage was induced by a single administration of 0.15 ml/kg of 50% (V/V) carbon tetrachloride in cotton seed oil *via* oral route. Male mice were divided into five groups of ten, and the first group was administerd orally with 1% CMC as vehicle control. The second group was treated with a single oral dose of 0.15 ml/kg of only CCl_4. The third group was treated with CCl_4 and methanol extract, the fourth one, with CCl_4 and ethylacetate fraction, and the fifth one, CCl_4 and butanol fraction.

At fourth day, blood samples from the heart puncture were collected from mice using a disposable syringe and needle treated with heparin. Detailed processing was referred to the Scheme I.

	Control	CCl_4 only	CCl_4+ MeOH Ex	CCl_4+ EtOAc Ex.	CCl_4+BuOH Ex.
DAY1	1% CMC	1% CMC	MeOH Ex.	EtOAc Ex.	BuOH Ex.
DAY2	1% CMC	CCl_4+ 1%CMC	CCl_4+ MeOH Ex.	CCl_4+ EtOAc Ex.	CCl_4+BuOH Ex.
DAY3	1% CMC	1% CMC	MeOH Ex.	EtOAc Ex.	BuOH Ex.
DAY4	s-GPT and s-GOT checking				
Dosage	–	0.15 ml/kg	1,000 ml/kg	500 ml/kg	

Scheme I. Experimental schedule for hepatoprotective effect on CCl_4-induced toxicities in mouse.

1. Measurement of serum enzyme activity. Serum aspartate transaminase (AST) and serum alanine transaminase (ALT) were measured using the kit (A-san Pharm. Co. Ltd).

2. Measurement of liver weight. Liver weight from each group was measured after blood collecting in order to serum enzyme activity.

Streptozotocin induced diabetic rats – To evaluate the hypoglycemic activity, studies were carried out on the variation of blood glucose level after the administration of streptozotocin and then a methanol extract. The blood glucose concentration of each rat was determined on the 1st day of the experiment before administration of the extract. Owing to the instability of streptozotocin in aqueous media, the solution was made in citrate buffer (pH4.5) immediately before administration (Karunanayake *et al.*, 1974). For the induction of diabetes this streptozotocin solution was injected intravenously (*i.v*) at a dose of 45 mg/kg. Blood sugar levels of the animals were determined, 1 week after injection of streptozotocin. The extract was administered on every alternative day and blood samples were taken for glucose estimation on every 24 hr after administration of extract up to 1 week and 3 weeks of the experiment.

Statistical analysis – For this experiment, results have been expressed as mean ± SD, and the significance of the results was analyzed by student`s t-tests, comparing with control.

Results and Discussion

The inhibition effects of each fraction against carrageenin induced edema in rat paw were shown in Table 1. In the 200 mg/kg aspirin administrated group, significant inhibition effect (3 hr, $p<0.01$, 4-5 hr, $p<0.05$) was observed when it was measured after carrageenin injection. At the dose of 1,000 mg/kg (p.o) of methanol extract, significant inhibitory effects of edema (after 3 hr, $p<0.01$) were observed. These results are presumed due to sesquiterpene lactone in this plant which has generally antibacterial and antiinflammatory activity. The effect of each fraction on bile juice

Table 1. Effects of methanol extracts against carrageenin induced edema in rat paw

	Dose (mg/kg, p.o)	No. of animals	Increased percentage (M ± S.E)				
			1	2	3	4	5(hr)
Control	–	6	21.93 ± 6.95	34.50 ± 6.62	53.34 ± 6.14	66.70 ± 4.23	63.39 ± 8.06
MeOH Ex.	1,000	6	12.39 ± 2.71	17.53 ± 3.94	32.49 ± 3.26**	54.23 ± 3.06	48.75 ± 4.20
Aspirin	200	6	12.13 ± 1.68	21.58 ± 2.36	33.68 ± 4.19**	42.12 ± 6.79*	40.35 ± 5.93*

*Significantly different from the control group ($p<0.05$)
**Significantly different from the control group ($p<0.01$)

secretion was shown in Table 2. At each group treated with methanol extract, ethylacetate and butanol fractions, significant increases ($p<0.01$) of the bile juice secretion were observed. The type of the secretion pattern of bile juice was slowly decreased through whole time. Even though methanol extract in the early time has the strongest choleretic activity, after 60 minutes it was more rapidly decreased than ethyl acetate and butanol fractions. This is presumed due to coumarin which has the choleretic activity as in Artemisiae Herba (Komiya, T. *et al.*, 1976). The serum transaminase activities of mice treated with each fraction were reduced more significant than only CCl_4 treated group (Table 3). Generally, chemicals as CCl_4 induce lipid peroxidation, damage the membrane of liver cells and organelles, cause the swelling and necrosis of hepatocytes, and result in the release of cytosolic enzymes such as AST, ALT into the blood circulation. Therefore, CCl_4-induced liver injury has been used as a convenient model for investigating radical-induced

Table 2. Effects of each fraction on bile secretion of rats (n=5)

Fraction	g/20 min. (M ± S.D.)			
TIME	CONTROL	MeOH EX.	EtOAc EX.	BuOH EX.
20	0.24 ± 0.016	0.42 ± 0.012**	0.40 ± 0.014**	0.35 ± 0.013**
40	0.22 ± 0.018	0.31 ± 0.010**	0.31 ± 0.013**	0.29 ± 0.010**
60	0.21 ± 0.020	0.28 ± 0.013**	0.27 ± 0.015**	0.27 ± 0.010**
80	0.19 ± 0.021	0.24 ± 0.010**	0.24 ± 0.012**	0.26 ± 0.013**
100	0.17 ± 0.019	0.21 ± 0.014**	0.22 ± 0.011**	0.24 ± 0.012**
120	0.15 ± 0.020	0.18 ± 0.012**	0.22 ± 0.011**	0.22 ± 0.014**
140	0.13 ± 0.006	0.17 ± 0.012**	0.20 ± 0.012**	0.20 ± 0.011**
160	0.13 ± 0.007	0.16 ± 0.014**	0.20 ± 0.012**	0.20 ± 0.011**
180	0.13 ± 0.007	0.15 ± 0.010**	0.19 ± 0.014**	0.20 ± 0.008**
200	0.12 ± 0.009	0.15 ± 0.010**	0.18 ± 0.012**	0.19 ± 0.012**
220	0.12 ± 0.014	0.14 ± 0.008**	0.18 ± 0.012**	0.18 ± 0.008**
240	0.12 ± 0.014	0.14 ± 0.009*	0.17 ± 0.014**	0.16 ± 0.011**

*Significantly different from the control group ($p<0.05$)
**Significantly different from the control group ($p<0.01$)

Table 3. Effects of each fraction with CCl_4-induced toxicities of mice

Group	No. of animals	ALT (a)	AST (a)	liver weight (g)	% of gained liver weight
Control		26.3 ± 5.27	3.61±5.04	1.64	100
CCl_4 only	10	138.6 ± 8.79	198.3±7.51	2.05	125.21
MeOH+CCl_4	10	108.2 ± 8.43**	147.6±7.86**	1.95	119.14
EtOAc+CCl_4	10	101.0 ± 8.15**	128.2±8.42**	1.87	114.58
BuOH+CCl_4	10	97.9 ± 7.41**	128.1±6.31**	1.84	112.15

**Significantly different from the CCl_4 only group ($p<0.01$)
(a) These values are M ± S.D in Karmen units

Table 4. Effects of methanol extract on blood glucose level of streptozotocin-induced diabetic rats (n=5)

Duration of Administration	Blood glucose level (mg/100 ml)		
	Control (normal)	Control (streptozotocin)	MeOH Ex.
1 Time	142.8 ± 13.1	564.0 ± 62.1	530.3 ± 55.0
2 Week		560.3 ± 47.3	188.9 ± 92.9**
3 Weeks		524.1 ± 36.6	308.9 ± 45.2**

**Significantly different from the control (streptozotocin) group ($p<0.01$). These values are M ± S.D.

damage and its prevention in animal (Kiso, Y., *et al.*, 1984). Average of liver weights of control groups was 1.64 g and CCl_4 treated one was 2.05 g. After the administration of methanol extract, ethyl acetate and butanol fractions with CCl_4 liver weights were decreased to 1.95, 1.87 and 1.84 g respectively. It means that three samples made liver damage recovered significantly. Until now the barometer of hepatoprotective activities has been on bile juice secretion, measurements of serum activity and liver weight. The effects of methanol extract of *Cichorium intybus* on blood glucose levels in streptozotocin induced diabetic animals has been shown in Table 4. The blood glucose concentration of diabetic rats was significantly lowered during the 1 week, 3 weeks at a dose of 1,000 mg/kg the methanol extracts ($p<0.01$). In experiments with many animal species streptozotocin produced permanent diabetes with extrapancreatic lesions that mimic the pathological status found in human diabetes (Arison *et al.*, 1967). So streptozotocin diabetes is reproducible, convenient and induced a diabetic state of the graded severity suitable for experimental studies (Junod *et al.*, 1969).

As a conclusion, it was proved that the root of *Cichorium intybus* has the antiinflammatory activity like aspirin, the prominent hepatoprotective activity against the radical generator CCl_4 and the antidiabetic activity. However, active compounds need to be isolated from extracts or fractions and more informations have to be taken.

Acknowledgments

This study was supported by research funds from Sahm Yook University.

References

Arison, R. N., Ciaccio, E. L., Cassaro, J. A. and Pruss, M. P., Light and electron microscopy of lesions in rats rendered diabetic with streptozotocin, *Diabetes*, **16**, 51 (1967).

Huxley, A., M. G., M, L., *The New Royal Horticultural Society Dictionary of Gardening*, Vol. 4, Macmillan Publishing Company, London, 1992, p. 622.

Junod, A., Lambest, A. E., Orci, L., and Renold, A. E., Studies on the diabetogenic action of streptozotocin, *Proc. Soc. Exp. Biol. Med.*, **126**, 201 (1969).

Khalil, A. T., Adb El-Fattah, H., and Mansour, E. S., Guaianolides from Lactuca Saligna, *Planta Medica*, **57**, 190 (1991).

Kiso, Y., Tohkino, H., Hattori, M., Namba, T., *Planta Medica*, **50**, 298-302

Koniya, T., *et al.*, Yakugaku Zasshi, **96**, 841-855 (1976)

Lim, W. G., *Resources Botany*, Press of Seo il Co. 1996, p. 151.

Mitton, F., *Mitton V., Mitton's Practical Modern Herbal*, London W. Foulsham & Co. Ltd., 1976.

Sultana S., Perwaiz S., Ather M., J. Echnopharmacol (Irelcind), **45**(3), 189 (1995).

Wren, R. C., Wren, R. W., *Potter's New Cyclopaedia of Botanical Drugs and Preparations*, New ed., Hengiscote, England, Health Science Press, 1975.

Winter, C. A., Risley, E. A. and Nuss, G. W., Carrageenin induced oedema in hind paw of the rat as assay for anti-inflammatory drugs. *Proc. Soc. Exp. Biol. Med.* **111**, 544 (1962).

Yim, D. S., Yoo, S. J., Lee, S. Y., Biological activities of verbascoside from *Pedicularis resupinata var. oppositifolia, Kor. J. Pharmacogn.* **28**, 252 (1997).

(Accepted July 23, 1999)