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A Preliminary Study on Hypocholesterolemic and Hypoglycemic Activities of Some Medicinal Plants

Jae Sue Choi, Hae Young Chung* and Han Suk Young*

Department of Nutrition and Food Science, National Fisheries University of Pusan, Pusan 608-023
*College of Pharmacy, Pusan National University, Pusan 609-735, Korea

Abstract—Total cholesterol level in mice with hypercholesterolemia was determined after intraperitoneal administration of the methanolic extract of some medicinal plants. From the data obtained, it was suggested that the methanolic extract of *Elaeagnus crispa*, *Ixeris dentata*, *Prunus davidiana*, *Eriobotrya japonica*, *Aralia elata* and *Phragmites communis* produced a significant hypocholesterolemic effect. In the case of the extract of *Saussurea diamantiaca*, on the other hand, the total cholesterol level was markedly increased. The methanolic extract of *Ixeris dentata*, *Prunus davidiana* and *Phragmites communis* also decreased the level of blood glucose in alloxan-diabetic male albino mice while that of *Eriobotrya japonica*, *Allium tuberosum*, *Houttuynia cordata* and *Eucommia japonica* did not produce this effect.

Keywords—Hypocholesterolemic effect • hypoglycemic effect • *Elaeagnus crispa* • *Ixeris dentata* • *Prunus davidiana* • *Eriobotrya japonica* • *Aralia japonica* • *Saussurea diamantiaca* • *Phragmites communis*

Hypercholesterolemia is one of the risk factors for atherosclerosis in general and coronary heart disease in particular[1,2] and can be divided broadly into two categories: First, an exogenous hypercholesterolemia and second, an endogenous hypercholesterolemia.

These are brought about by an excessive intake of cholesterol and an excessive production of cholesterol in liver or a lowering catabolism of cholesterol, respectively.

Hypercholesterolemia in atherosclerotic patients, however, can't be adequately controlled by dietary regulation alone. Thus, many welltolerated hypocholesterolemic drugs including plant origin are widely used for the improvement of hypercholesterolemia associated atherosclerosis.[3,4] Diabetes is also known to risk factors for metabolic disease. Studies on the treatment of diabetes has centered on attempts to achieve normal blood-glucose levels by exogenous-insulin, oral-drug and dietary therapies. Although insulin has become one of the most important therapeutic agents known to medicine, the availability of an insulin substitutes from synthetic or plant sources could be of importance in the treatment of iabetes due to a) insulin has subcutaneously injected by himself several times a day and b) the patients shows a large variability in insulin absorption. To date only two groups of oral hypoglycemic agents are available for clinical use, sulphonylureas and biguanides. Over 150 plant extracts and some of their active principles are known to be used for the treatment of diabetes and information on good insulin

substitutes from plant sources is still scant.[5,6]

Hence, an investigation of hypocholesterolemic and hypoglycemic agents from plant origin used in traditional medicine seems important. In the present study, screening results for twenty widely employed Korean medicinal plants using animal experimental models with hypercholesterolemia or hyperglycemia are reported.

Dietary hypercholesterolemia was induced in mice, and screening for hypocholesterolemic effect was carried out with reference to the experimental conditions by Tensho *et al*[7]. Although mice have not been used previously in similar experiments with plant materials, they were selected as test animals because of their low food consumption, and also because of their known response to dietary cholesterol.[8]

Materials and Methods

Extraction of plant materials—Freshly collected plant materials were botanically identified and dried. A voucher specimens was deposited in the Herbarium Garden of College of Pharmacy, Pusan National University, Korea. The dried materials were coarsely crushed and extracted three times with 95% methanol at room temperature. The combined filtrate was evaporated under reduced pressure on a water bath of 40° to dryness. The dried residue was used for test.

Animals—Male and female mice of the albino (dd strain), initially weighing 20±2 g, were maintained in an air-conditioned room with lighting from 06:00 to 18:00 h. The room temperature (about 25°) and humidity (about 60%) were controlled automatically. A laboratory pellet chow (obtained from Purina Feed Ltd., Korea) and water were given freely.

Hypercholesterolemic mice—A group of mice weighing 22±2 g were placed on a diet consisting of Purina pellet supplemented with 1% cholesterol and 0.5% cholic acid. Seven days after intake of experimental diet, blood was drawn from the orbital sinus with micro-hematocrit tubes and mice with a total cholesterol level of 200 mg/dl or more used as hypercholesterolemic mice.

Alloxan-induced diabetic mice[9]—A group of mice weighing 25±2 g were made diabetic by injecting intravenously 75 mg/kg body weight of alloxan monohydrate. Six days after injection, blood was drawn from the orbital sinus with micro-hematocrit tubes and mice with a glucose level of 300 mg/dl or more were used as diabetic mice.

Treatment—The methanolic extract (40 mg/kg body weight) suspended in 5% ethanol-saline was each administered intraperitoneally to test mice, while control mice were treated with an equal volume of 5% ethanol-saline. At the 5 hrs after intraperitoneal administration of above samples, mice were killed by a sharp blow on the head and exsanguinated. Blood was collected and allowed to stand for several hours in a cold room at 4°, serum was separated by centrifugation (1,000×*g*, 10 min., 4°).

Determination of total cholesterol and glucose in serum—Total cholesterol and glucose were determined using commercial reagents obtained from Young Dong Pharmaceutical Co. Ltd., Korea.

Chemicals—Alloxan-monohydrate was purchased from Sigma Chemical Co., USA. All other reagents were of the highest grade commercially available.

Statistics—The significance of difference between the control and methanolic extract-treated groups was tested using Student's *t*-test.

Results and Discussion

The present investigation demonstrated that various methanol extracts of some medicinal

Table I. Effect of some medicinal plants on total cholesterol of hypercholesterolemic male mice

Treatment[a)]	Plant part	No. of mice	Total choleserol (mg/dl)
Control	—	7	275.71±27.37 (100)
Eucommia ulmoides	LF	8	247.09±12.78 (90)
Elaeagnus crispa	ST	7	208.20±16.39* (76)
Ixeris dentata	WP	7	184.17±11.72** (67)
Prunus davidiana	ST	5	163.42±11.15** (59)
Commelina communis	WP	6	241.28±23.61 (88)
Eriobotrya japonica	LF	6	200.68±18.69* (73)
Salvia miltiorrhiza	RZ	6	261.16±30.34 (95)

a) Mice were injected intraperitoneally once. Five hours after single administration, blood samples were obtained after decapitation of the animals. Values are mean±S.E. Figures in parenthesis are percentages of the control value.
Significantly different from the control value:* $p<0.05$, ** $p<0.01$.
Abbreviation; LF, leaf; ST, stem; WP, whole plant; RZ, rhizome.

plants affect total cholesterol and blood glucose levels in animal experimental models with hypercholesterolemia or hyperglycemia.

Table I and II shows the effect on the level of total cholesterol after a single intraperitoneal administration of the methanolic extract at 40 mg/kg in male or female hypercholesterolemic mice. The total cholesterol level was significantly decreased in the groups given extracts of ***Elaeagnus crispa***, ***Ixeris dentata***, ***Prunus davidiana***, ***Eriobotrya japonica***, ***Aralia elata*** and ***Phragmites communis***. Among them, ***Ixeris dentata*** and ***Prunus davidiana*** showed effective only in male mice. The lack of hypocholesterolemic effect of these methanol extracts in female mice may be due to hormone-dependent sensitivity of sex difference since "over-all" effect on cholesterol metabolism of sex hormones was reported

Table II. Effect of some medicinal plants on total cholesterol of hypercholesterolemic female mice

Treatment[a)]	Plant part	No. of mice	Total cholesterol (mg/dl)
Control	—	6	233.67±10.91 (100)
Capsella bursa-pastoris	WP	8	233.35±18.03 (100)
Saussurea diamantiaca	WP	7	324.59± 8.79*** (139)
Aralia elata	SP	6	200.75± 7.64* (86)
Chenopodium album	WP	8	215.44±23.14 (92)
Sedum sarmentosum	WP	7	229.57±23.91 (98)
Allium monanthum	WP	8	236.90±15.02 (101)
Allium tuberosum	LF	5	192.02±29.66 (82)
Glycine max	SD	6	266.72±36.81 (114)
Zea mays	STY	6	219.76±29.19 (94)
Cudrania tricuspidata	ST	6	236.61±29.30 (101)
Phragmites communis	RZ	6	184.86±21.40* (79)
Orostachys japonicus	WP	5	195.00±28.73 (83)
Ixeris dentata	WP	7	193.56±19.53 (83)
Prunus davidiana	ST	6	221.87±29.50 (95)

a) Mice were injected intraperitoneally once. Five hours after single administration, blood samples were obtained after decapitation of the animals. Values are mean±S.E. Figures in parenthesis are percentages of the control value.
Significantly different from the control value: *$p<0.05$, ***$p<0.001$.
Abbreviation; SD, seed; SP, sprout; STY, styles.

by Kritchevsky, D *et al.*[10] The blood cholesterol level was attributed to only two sources, either by absorption from diet or endogenous synthesis. It is lost from body by conversion into bile salts, which are slowly lost only into the feces. That is, there is a delicately regulated balance between the amount of ingested cholesterol, the amount of cholesterol synthesized in the body, and the

Table III. Dose-dependent effect of *Ixeris dentata*, *Prunus davidiana* and *Eriobotrya japonica* on total cholesterol of hypercholesterolemic male mice

Treatment[a)]	Dose (mg/kg)	No. of mice	Total cholesterol (mg/kg)
Control	—	7	249.53± 9.20 (100)
Ixeris dentata	20	6	208.08±22.41 (83)
	40	7	205.51± 7.07** (82)
	80	7	189.97±13.38** (76)
Prunus davidiana	20	7	210.23± 9.47** (84)
	40	7	212.93±16.96 (85)
	80	7	182.71±22.92* (73)
Eriobotrya japoica	20	7	228.46±18.34 (92)
	40	7	210.30±10.55** (84)
	80	6	246.05±19.18 (99)

[a)] Mice were injected intraperitoneally once. Five hours after single administration, blood samples were obtained after decapitation of the animals. Values are mean±S.E. Figures in parentheses are percentages of the control value.
Significantly different from the control value: *$p<0.05$, **$p<0.01$.

amount excreted. Among the numerous factors that regulate cholesterol metabolism, the endocrine participation may be one of the important factors. According to Kritchevsky, D. *et al*, "cholesterol was synthesized and metabolized in male rats at a much lower rate than in the castrated or in the normal female rats."

In case of the methanolic extract of *Saussurea diamantiaca*, on the other hand, the total cholesterol level was markedly increased in hypercholesterolemic female mice.

Table III shows the levels of total cholesterol in hypercholesterolemic mice given different doses of the methanol extracts of *Ixeris dentata*, *Prunus davidiana* and *Eriobotrya japonica* in comparison with control animals. Mice in the methanolic extract-treated group showed a significant decrease of total cholesterol in dose-dependent manners at 5 hr after a single intraperitoneal administration.

Table IV. Effect of some medicinal plants on blood glucose of hyperglycemic male mice

Treatment[a)]	Plant part	No. of mice	Glucose(mg/dl)
Control	—	5	664.76±65.32 (100)
Ixeris dentata	WP	5	472.98±53.28* (72)
Prunus davidiana	ST	5	444.18±42.63* (67)
Allium tuberosum	LF	5	658.32±38.43 (99)
Houttuynia cordata	WP	5	571.69±59.18 (86)
Control	—	5	626.00±29.46 (100)
Eriobotrya japonica	LF	5	539.86±90.0 (86)
Phragmites communis	RZ	5	496.58±24.05** (79)
Eucommia ulmoides	LF	5	615.44±80.5 (98)

[a)] Mice were injected intraperitonelly once. Five hours after single administration, blood samples were obtained after decapitation of the animals. Values are mean±S.E. Figures in parentheses are percentages of the control value.
Significantly different from the control value: *$p<0.05$, **$p<0.01$.

The good results observed with these methanol extracts suggest, as far as mice are concerned, that these plants deserves further phytochemical and pharmacological investigation in order to define the active constituents responsible.

The effects of some medicinal plants on the level of blood glucose after a single intraperitoneal administration are shown in Table IV. In alloxan-diabetic male mice given the methanol extracts of *Ixeris dentata*, *Prunus davidiana* and *Phragmites communis* showed a significant decrease of blood glucose; the blood glucose levels were significantly decreased by as much

as 21%, 28%, and 33% at a relatively low dose of 40 mg/kg, respectively.

The others such as *Eucommia ulmoides*, *Commelina communis*, *Salvia miltiorrhiza*, *Capsella bursa-pastrris*, *Chenopodium album*, *Sedum sarmentosum*, *Allium monanthum*, *Allium tuberosum Zea mays*, *Cudrania tricuspidata*, *Orostachys japonica*, and *Houttuynia cordata* did not show any effect on hypercholesterolemic or hyperglycemic state, which might be considered partly due either to a single administration of low dose or to the lack of effectiveness. Supplementary testing seems required before concluding that these plants are inactive on the basis of this experimental conditions.

From the present experimental results. it can be postulated that various plant drugs, when administered alone or in combination with other drug, may be used for treatment of hypercholesterolemia or hyperglycemia. Further comprehensive chemical and pharmacological investigations are thus needed to elucidate the exact mechanism of these effects and to isolate the active principles of these plants.

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Literature Cited

1. Newton, R.S. and Krause, B.R.: *Annual Reports in Medicinal Chemistry* **21**, 189 (1986).
2. Steinberg, D.: *Circulation* **76**, 502 (1987).
3. Gotto, Jr. A.M. and Jones, P.H.: *Atherosclerosis Reviews* **14**, 1 (1986).
4. Roth, B.D., Sliskovic, D.R. and Trivedi, B.K.: *Annual Reports in Medicinal Chemistry* **24**, 147 (1989).
5. Handa, S.S. and Chawla, A.S: *Fitoterapia* **LX**, 195 (1989).
6. Ivorra, M.D., Paya, M. and Villar, A.: *J. Ethnopharmacology* **27**, 243 (1989).
7. Tensho, A., Shimizu, I., Takenawa, T., Kikuchi, H., and Rokujo, T.: *Yakugaku Zasshi* **92**, 879 (1972).
8. Leveille, G.A., and Sauberlich, H.E.: *J. Nutr.* **84**, 10 (1964).
9. Lundquist, I. and Rerup, C.: *European Journal of Pharmacology* **2**, 35 (1967).
10. Kritchevsky, D., Staple, E., Rabinowitz, J.L, and Whitehouse, M.W.: *American J. Physiol.* **200**, 519 (1961).