

Original Article

Antioxidant and Lipid-lowering Effects of *Artemisia capillaris* on a Rat Model of Hyperlipidemia

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Objectives: This study was designed to evaluate lipid-lowering and antioxidant effects of *Artemisia capillaris*(*A. capillaris*) using a model of hyperlipidemic rats induced by poloxamer-407.

Methods: Rats were previously treated by *A. capillaris* water extract, and intraperitoneally injected by poloxamer-407 to induce hyperlipidemia. Parameters of serum lipid and oxidative stress biomarkers were determined.

Results:

1. *A. capillaris* ameliorated the elevation of serum total cholesterol, triglyceride, LDL-cholesterol and MDA level.

2. *A. capillaris* ameliorated the reduction of serum TAC and SOD activities.

3. *A. capillaris* ameliorated the reduction of serum GSH and GSH-reductase level.

Conclusions: According to these results, *A. capillaris* can be used to treat hyperlipidemia or as basis for making new drugs for treating hyperlipidemia in the future.

Key Words : *Artemisia capillaris*, hyperlipidemia, oxidative stress

Introduction

Hyperlipidemia, also known as hyperlipoproteinemia, refers to the excess status of fatty substances including cholesterol, triglycerides or lipoproteins in the bloodstream^{1,2)}.

Hyperlipidemia is an important risk factor in developing heart disease and stroke which are leading causes of death in most developed countries, including Korea^{3,4)}. Accordingly, the appropriate control of lipid levels in the bloodstream is a standard strategy to prevent the development of vascular disease⁵⁾. There are four classes of lipid lowering drugs: 3-hydroxy-3-methylglutaryl coenzyme A(HMG-

CoA) reductase inhibitors commonly referred to as statins, bile acid sequestrants, nicotinic acid, and fibric acids^{6,7)}. These hypolipidemic agents lower lipid levels somewhat, but have a limitation due to lack of final clinical outcome in prevention of heart disease and stroke, and often adverse effects such as hepatotoxicity, myopathy or noncardiovascular death^{8,9)}.

On the other hand, oxidative stress has been linked to the pathological process of hyperlipidemia¹⁰⁻¹²⁾. Many studies have paid attention to natural products as candidates of hypolipidemics which are antioxidant but have no side effects^{13,14)}. These candidates are supposed to improve quality of life which can be impaired by western hypolipidemic agents. Accordingly,

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traditional herbal formulae or medicinal plants would be valuable as new drugs for patients suffering from blood lipid disorders.

Traditionally, many Korean patients with stroke or problems with blood circulation prefer to take oriental medicines. Hyperlipidemia is regarded as status of spleen-deficiency and phlegm-stagnation, accumulation and stasis of damp-heat, and *qi* and blood stagnation in traditional Korean medicine^{15,16}.

Artemisia capillaris(*A. capillaris*) is an herbal medicine which has been prescribed for patients with phlegm-stagnation or heating damp in the digestive system including liver. *A. capillaris* has mainly treated jaundice and liver diseases as a herb component in poly-herb formulae¹⁷. Several studies have reported the pharmaceutical properties of *A. capillaris* on hyperlipidemia using animal models¹⁸⁻²⁰. One group presented the antioxidant effect of *A. capillaris*²¹. Thus it is proposed that *A. capillaris* could be developed in hypolipidemics which guarantee both improving blood lipidemic levels and reducing complications. However, there was no study to simultaneously determine the hypolipidemic effect and antioxidant activity in hyperlipidemia animal models.

The present study aimed to evaluate the effects of *A. capillaris* on serum lipid levels, and oxidative stress-related biomarkers.

Materials and Methods

1. Preparation of *A. capillaris* water extract

A. capillaris was purchased from Jeongseong Herbal Company(Daejeon, Korea). After a multiple cleaning process and drying, 500g of sliced *A. capillaris* was mixed with 5 L of distilled water and boiled for 2 hrs. The decoction was filtered and then centrifuged at 2,000 rpm for 20 mins to remove the unsolved and coarse materials. After evaporation (Rotary evaporator, Buchi B-480, Switzerland), the

decoction was freeze-dried(Freeze dryer, Eyela FDU-540, Japan). Finally 14.1 g of *A. capillaris* dried extract was obtained, and the yield was 2.82%(w/w). The extract was stored in a deep freezer(-70°C for experimental use.

2. High performance–thin layer chromatography (HP–TLC)–based fingerprinting

In order to produce the fingerprint of *A. capillaris*, a HP-TLC procedure was adapted using the CAMAG application system(Muttenez, Switzerland). Aqueous extracts of *A. capillaris* and its main compositional ingredient, 6,7-dimethoxycoumarin(Sigma Chemical Co., St. Louis, MO, USA) as standard, were dissolved in HPLC-grade methanol and applied to pre-washed 60 F254 HP-TLC plates(silica gel thickness 2mm, from Merck, Darmstadt, Germany) with an automated applicator(Linomat IV; CAMAG). *A. capillaris* and 6,7-dimethoxycoumarin were separated(migration distance 75mm) using HPLC-grade 2-methylpropanoic acid (C₄H₈O₂) : acetic acid(CH₃CO₂H) : acetic acid(C₂H₄O₂) : water(H₂O)=79 : 1 : 5 and then were visualized under UV of wavelength 366nm. Thereafter photos were taken using Reprostar 3 with a digital camera (CAMAG).

3. Total antioxidant capacity (TAC) of *A. capillaris*

To 90μL of 10mM phosphate-buffered saline (pH7.2), 50μL of myoglobin solution(45μM), 20μL of 3mM ABTS solution, and serially diluted *A. capillaris* extract(from 5μg to 1,000μg/mL) sample were added to 96-well microplates and mixed thoroughly at 25°C. Then 20μL of H₂O₂ was added to each well, and incubated for 5 mins. The absorbance was read using a plate reader at 600nm(Molecular Device Corp., USA). Gallic acid was used as control and antioxidant activity was expressed as gallic equivalent antioxidant capacity (GEAC).

4. Animal and experimental design

Seven-week-old male Sprague-Dawley rats were purchased from a commercial animal breeder(Dae-hanBioLink, Korea). After one week of acclimation, rats were used in this experiment. The rats were housed in an environmentally controlled room at 22±2°C relative humidity at 55±10% and 12hrs light/dark and fed with commercial pellets (Samyang Feed Co, Korea) and tap water ad libitum.

Forty rats were divided into 5 groups of 8 animals each. Hyperlipidemia was induced by 30% poloxamer-407(Sigma Chemical Co., St. Louis, MO, USA) injection. Rats were pre-treated with *A. capillaris*(50 or 100mg/kg body weight), Lipitor(Pfizer, USA, 10mg/kg body weight) or distilled water by oral administration for seven days. The rats were intraperitoneally injected with 2mL of poloxamer-407, and then orally fed with *A. capillaris*, Lipitor or distilled water respectively once again at 12 hrs after poloxamer-407 injection. On 24 hr-time point of poloxamer-407 injection as status of 12 hrs fasting, animals were sacrificed by whole blood collection from abdominal aorta under ether anesthesia. The experimental procedure is summarized in Fig. 1.

5. Measurement of serum cholesterol and triglycerides

The levels of serum total cholesterol, high density lipoprotein(HDL)-cholesterol, low density lipoprotein (LDL)-cholesterol, and triglycerides were determined using Olympus optical reply(Olympus, Japan).

6. Measurement of serum oxidative stress parameters

1) Determination of malondialdehyde(MDA) level

The concentration of thiobarbituric acid reactive substances(TBARS) was expressed as MDA $\mu\text{M}/\mu\text{L}$ serum. 250 μL of serum or standard solution was added to 2.5mL of 20% trichloroacetic acid(TCA). Next, it was mixed with 1 mL of 0.67% thiobarbituric acid(TBA) and heated at 100°C for 30 mins, followed by cooling on the ice and vigorous vortexing with 4mL *n*-butanol. After centrifugation at 3000 \times g for 20 mins, the absorbance upper organic layer was measured at 535nm with a spectrophotometer and compared with 1,1,3,3-tetraethoxypropane (TEP) standard curve.

2) Determination of total antioxidant capacity (TAC) level

90 μL of 10 mM phosphate-buffered saline(pH7.2), 50 μL of myoglobin solution(45 μM), 20 μL of 3mM ABTS solution, 20 μL of diluted serum sample, and gallic acid were added to 96-well microplate and mixed thoroughly at 25°C. Then 20 μL of H₂O₂ was added to each well, and incubated for 5 mins. The absorbance was read using a plate reader at 600 nm (Molecular Device Corp., USA). The level of TAC was expressed as gallic equivalent antioxidant capacity(GEAC).

3) Determination of superoxide dismutase (SOD) level

SOD activity in the serum was determined using a SOD assay kit(Dojindo Laboratories, Kumamoto, Japan). Bovine erythrocyte SOD (Sigma, USA) was diluted

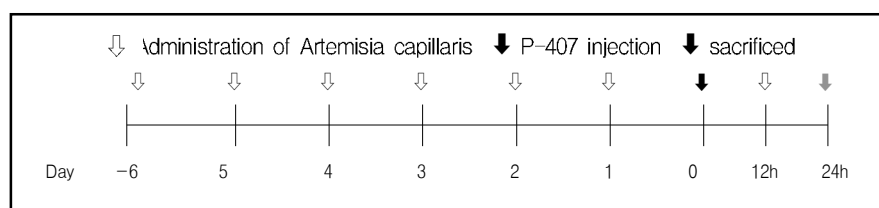


Fig. 1. Scheme of Procedure for Animal Experiment

serially from 100 to 0.001 U/mL and used as a standard.

4) Determination of total glutathione (GSH) content level

50 μ L of diluted serum(in PBS 10 mM, pH7.2) or glutathione standard was combined with 80 μ L of DTNB/NADPH mixture(10 μ L of 4 mM DTNB and 70 μ L of 0.3mM NADPH) in a 96-well micro plate. Next, 20 μ L(0.06 U) of glutathione reductase solution was added to each well and the absorbance was measured using a plate reader at 405 nm(Molecular Devices, Sunnyvale, CA).

5) Determination of glutathione reductase (GSH-Rd) level

150 μ L of GSSG with 30 μ L of GSH-reductase assay buffer(100mM potassium phosphate buffer, pH 7.5, with 1mM EDTA) was added to 30 μ L of serum sample and diluted with GSH-reductase dilution buffer(100mM potassium phosphate buffer, pH 7.5, with 1mM EDTA and 1 mg/kg bovine serum albumin). 75 μ L of DTNB and 2mM NADPH were added and an absorbance was read at 412 nm. The enzyme activity was represented as unit (mmol/mL/min) by calculation with the following formula:

$$\text{Units/mL} = \{(\Delta A \text{ sample} - \Delta A \text{ blank}) \times (\text{dilution factor})\} / \{\epsilon \text{mM} \times (\text{volume of sample in mL})\}$$

ϵ mM was according 14.15 mM⁻¹cm⁻¹.

7. Statistical analysis

Results were expressed as the mean \pm standard deviation. Statistical analysis of the data was carried out by Student's t-test. A difference from the respective control data at the levels of P<0.05 and P<0.01 were regarded as statistically significant.

Results

1. Fingerprint of *A. capillaris*

The fingerprint of *A. capillaris* with 6,7-dimethoxycoumarin as a reference component was produced using HP-TLC system(Fig. 2). The semi-quantity of 6,7-dimethoxycoumarin was approximately 3.15% of *A. capillaris* extract used in the present study.

2. Total antioxidant capacity (TAC) of *A. capillaris*

In order to examine the antioxidant capacity of *A. capillaris* itself, total antioxidant capacity(TAC) was determined using *in vitro* assay. When the value was expressed as gallic equivalent antioxidant capacity (GEAC), the capacity of *A. capillaris* showed a very high GEAC value from the lowest volume 5 μ g(62.1 μ M GEAC) to the high volume 1,000 μ g(452.1 μ M GEAC) of *A. capillaris* respectively (Fig. 3).

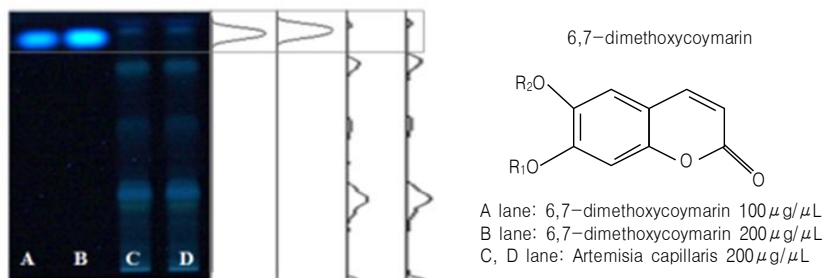


Fig. 2. HP-TLC-based Fingerprint for *Artemisia capillaris*

HP-TLC analysis was performed to produce the fingerprint of *A. capillaris*. 2 μ L of the *A. capillaris* extract and 6, 7-dimethoxycoumarin as a reference component were subjected to HP-TLC.

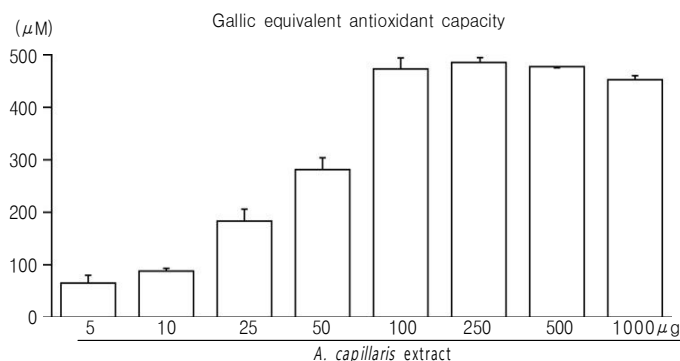


Fig. 3. Total Antioxidant Capacity of *Artemisia capillaris*.

Total antioxidant capacity of *A. capillaris* itself was determined using *in vitro* assay, and expressed as GEAC.

3. Comparison of body and liver weight

On the last day of the experiment, the removed liver weight was compared among groups. The Poloxamer-407 induced group showed a slight increase of body weight and absolute liver weight without statistical significance. *A. capillaris* pre-treatment (50, 100mg) and Lipitor groups ameliorated these changes. *A. capillaris* pre-treatment(50mg) and Lipitor groups showed the significant decrease of comparative liver weight as $P<0.05$ (Table 1, Fig. 4).

4. The effect on serum cholesterol and triglyceride level

On the last day of experiment, the serum levels of lipid parameters were compared among groups. Poloxamer-407 injection induced severe elevation of total cholesterol by about 3 fold and especially triglyceride by about 20 fold. Accordingly, LDL-cholesterol was elevated by about 10 fold. Low-dose

of *A. capillaris*(50mg/kg) lowered triglyceride significantly while high-dose of *A. capillaris*(100mg/kg) specifically lowered total cholesterol and LDL-cholesterol $P<0.05$ (Fig 5-1~5-4). The Lipitor group showed a positive trend, but not significant (Table 2).

5. The effect on serum malondialdehyde (MDA) level

On the last day of experiment, the serum MDA levels were compared among groups. Poloxamer-407 injection elevated serum MDA level by 2 fold, and then pre-treatment with *A. capillaris* 50 mg/kg and 100 mg/kg ameliorated this elevation by 80% and 64% respectively compared to induced groups while Lipitor also inhibited the elevation of MDA level by 39%(Fig. 6).

6. The effect on serum total antioxidant capacity(TAC) level

On the last day of experiment, the serum TAC

Table 1. Comparison of Body and Liver Weight

Group	Normal	Induced	50 mg/kg 100 mg/kg		Lipitor
			<i>A. capillaris</i>		
Body weight(g)	268.4 ± 3.3	273.9 ± 14.4	273.1 ± 7.8	272.8 ± 10.6	272.6 ± 9.6
Absolute weight(g)	10.90 ± 0.38	11.17 ± 0.85	10.51 ± 0.58	11.00 ± .661	10.53 ± 0.33
Comparative weight(%)	4.06 ± 0.30	4.08 ± 0.20	3.84 ± 0.15*	4.03 ± 0.02	3.86 ± 0.13*

Data are expressed as mean±standard deviation.

*: $P<0.05$, significant differences compared with the induced group.

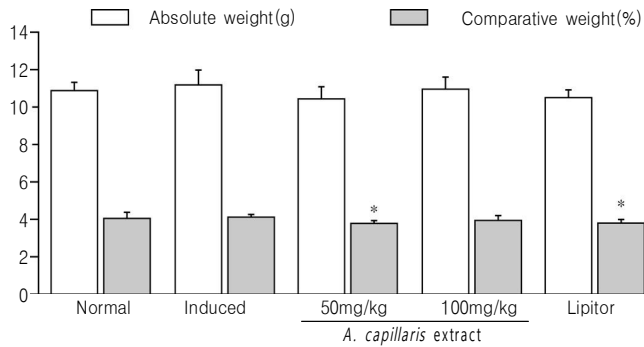


Fig. 4. Comparison of Liver Weight. On the last day of experiment, absolute and comparative liver weight was compared among groups. Data are expressed as mean±standard deviation. *: $P < 0.05$, significant differences compared with the induced group.

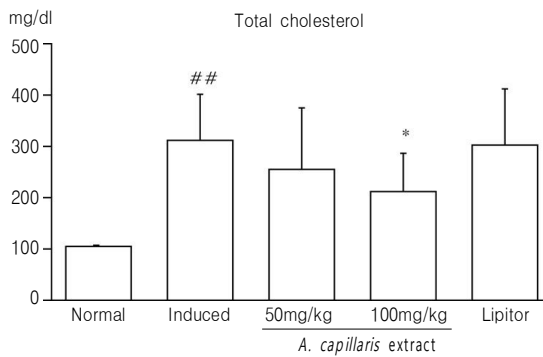


Fig. 5-1. The Effect on Serum Total Cholesterol Level. Rats were pre-treated with water, *A. capillaris*(50, 100mg/kg) or Lipitor(10mg/kg) before poloxamer-407 injection. On the last day of experiment, serum total cholesterol was determined. Data are expressed as mean±standard deviation. ##: $P < 0.01$, significant differences compared with the normal group. *: $P < 0.05$, significant differences compared with the induced group.

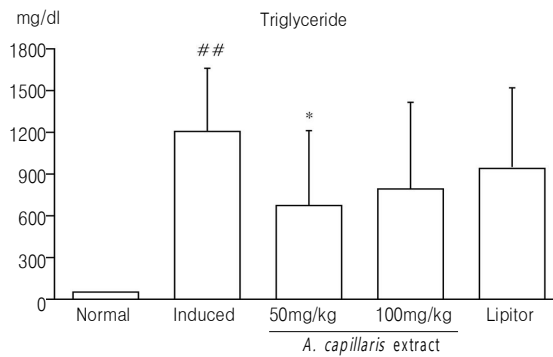


Fig. 5-2. The Effect on Serum Triglyceride Level. Rats were pre-treated with water, *A. capillaris*(50, 100mg/kg) or Lipitor(10mg/kg) before poloxamer-407 injection. On the last day of experiment, serum triglyceride level was determined. Data are expressed as mean±standard deviation. ##: $P < 0.01$, significant differences compared with the normal group. *: $P < 0.05$, significant differences compared with the induced group.

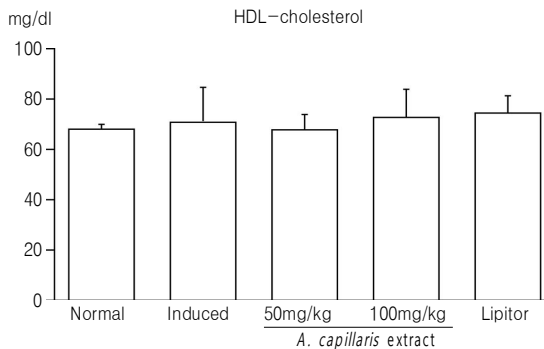


Fig. 5-3. The Effect on Serum HDL-cholesterol Level. Rats were pre-treated with water, *A. capillaris*(50, 100mg/kg) or Lipitor (10 mg/kg) before poloxamer-407 injection. On the last day of experiment, serum HDL-cholesterol level was determined. Data are expressed as mean±standard deviation.

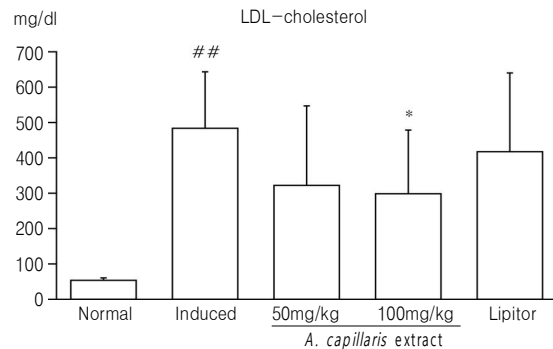


Fig. 5-4. The Effect on Serum LDL-cholesterol Level. Rats were pre-treated with water, *A. capillaris*(50, 100mg/kg) or Lipitor(10mg/kg) before poloxamer-407 injection. On the last day of experiment, serum LDL-cholesterol level was determined. Data are expressed as mean±standard deviation. ##: $P < 0.01$, significant differences compared with the normal group. *: $P < 0.05$, significant differences compared with the induced group.

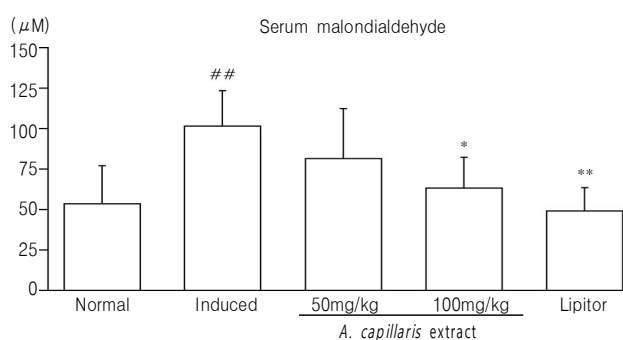
Table 2. Comparison of Serum Cholesterol and Triglyceride Level

Group	Normal	Induced	50 mg/kg 100 mg/kg <i>A. capillaris</i>		Lipitor
Total cholesterol(mg/dL)	108.5± 3.8	312.9± 91.5 ^{###}	258.4± 120.1	214.5± 76.7*	305.9± 110.2
Triglyceride(mg/dL)	66.3± 4.6	1208.8± 442.0 ^{###}	673.9± 533.0*	793.0± 627.1	934.6± 573.8
HDL-cholesterol(mg/dL)	68.4± 1.9	71.1± 13.7	68.1± 5.4	72.6± 9.1	74.0± 7.8
LDL-cholesterol(mg/dL)	53.3± 2.2	483.5± 161.3 ^{###}	325.1± 222.9	300.5± 177.8*	418.8± 224.4

Data are expressed as mean±standard deviation.

###: P<0.01, significant differences compared with the normal group.

*: P<0.05, significant differences compared with the induced group.


Fig. 6. The Effect on Serum MDA Level

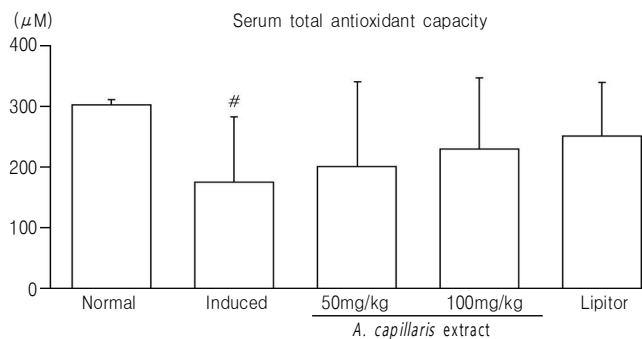
Rats were pre-treated with water, *A. capillaris* (50, 100 mg/kg) or Lipitor (10 mg/kg) before poloxamer-407 injection. On the last day of experiment, serum MDA level was determined. Data are expressed as mean±standard deviation.

###: P<0.01, significant differences compared with the normal group.

*: P<0.05 and **: P<0.01, significant differences compared with the induced group.

levels as gallic equivalent antioxidant capacity (GEAC) were compared among groups. Poloxamer-407 injection significantly depleted serum TAC level by

60% of normal level. *A. capillaris* 50 mg/kg and 100 mg/kg ameliorated this depletion slightly, but didn't reach to statistical significance (Fig. 7).


Fig. 7. The Effect on Serum TAC Level

Rats were pre-treated with water, *A. capillaris* (50, 100 mg/kg) or Lipitor (10 mg/kg) before poloxamer-407 injection. On the last day of experiment, serum TAC level as GEAC was determined. Data are expressed as mean±standard deviation.

#: P<0.05, significant differences compared with the normal group.

7. The effect on serum superoxide dismutase (SOD) level

On the last day of experiment, the serum SOD levels were compared among groups. Poloxamer-407 injection depleted serum SOD level by 18% of normal level. *A. capillaris* ameliorated significantly this depletion especially in the 100 mg/kg group, but Lipitor didn't show any change (Fig. 8).

8. The effect on serum total glutathione(GSH) content level

On the last day of experiment, the serum GSH

content levels were compared among groups. Poloxamer-407 injection depleted serum GSH content level by 6% of normal level. *A. capillaris* and Lipitor treatment significantly ameliorated this depletion (Fig. 9).

9. The effect on serum total glutathione reductase(GSH-Rd) level

On the last day of experiment, the serum GSH-Rd levels were compared among groups. Poloxamer-407 injection slightly reduced serum GSH-Rd level. *A. capillaris* completely ameliorated significantly this decrease, especially in the 100 mg/kg group(Fig. 10).

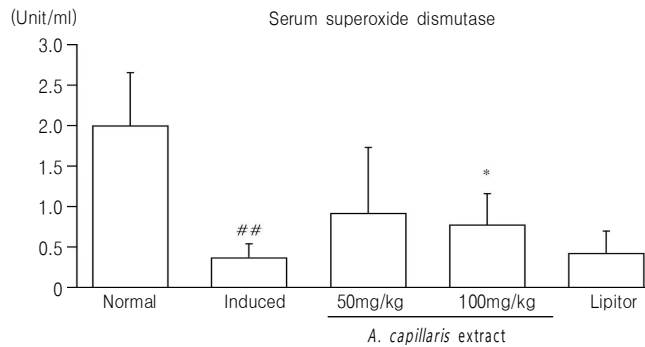


Fig. 8. The Effect on Serum SOD Level

Rats were pre-treated with water, *A. capillaris*(50,100mg/kg) or Lipitor(10mg/kg) before poloxamer-407 injection. On the last day of experiment, serum SOD level was determined. Data are expressed as mean±standard deviation. ##: $P<0.01$, significant differences compared with the normal group.

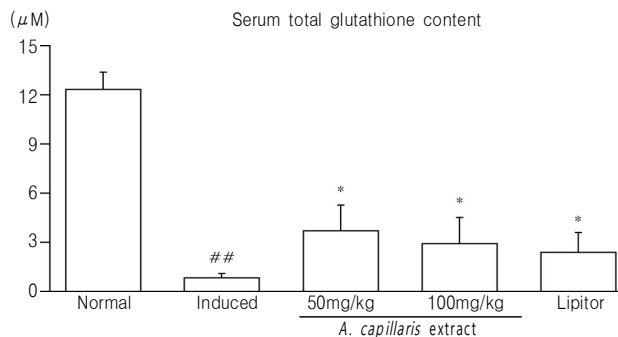


Fig. 9. The Effect on Serum Total GSH Content Level

Rats were pre-treated with water, *A. capillaris*(50, 100mg/kg) or Lipitor (10mg/kg) before poloxamer-407 injection. On the last day of experiment, serum GSH content was determined. Data are expressed as mean±standard deviation.

##: $P<0.01$, significant differences compared with the normal group.

*: $P<0.05$, significant differences compared with the induced group.

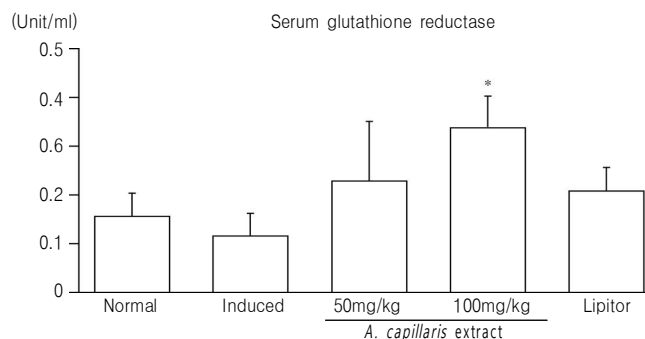


Fig. 10. The Effect on Serum Total GSH-Rd Level

Rats were pre-treated with water, *A. capillaris* (50, 100mg/kg) or Lipitor (10mg/kg) before poloxamer-407 injection. On the last day of experiment, serum GSH-Rd was determined. Data are expressed as mean±standard deviation.

*: $P < 0.05$, significant differences compared with the induced group.

Discussion

The supply of animal body lipids is originated from both the diet and endogenous fatty acid synthesis, or each of them, primarily in the liver²². For traveling via the bloodstream, the lipids should be combined with apoprotein resulting in forming one of the lipoproteins: chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low-density lipoproteins (LDL), or high-density lipoproteins (HDL)^{22,23}. Cholesterol is an essential element of human cell membranes and a structural component of steroid hormones while triglycerides play an important role as energy sources and transporters of dietary fat^{24,25}.

Recently metabolic syndrome, a combination of hyperlipidemia, hypertension, obesity, and diabetes mellitus, is increasing even in younger people^{26,27}. Among those disorders, hyperlipidemia is well known to be a risk factor for cardiovascular and cerebrovascular diseases which are the second and third causes of death in Korea²⁸⁻³⁰. Hyperlipidemia presents two different aspects of pathologic disorders: quantitative overload of lipid and qualitative unbalance of lipoproteins and ratio of HDL-cholesterol and LDL-cholesterol levels³¹. It is evidenced that lack of physical activity and intensive emotional and environ-

mental stress induce the unbalance between HDL-cholesterol and LDL-cholesterol, which is associated with the ischemic disorders in the heart, brain and elsewhere³².

Therefore, appropriate control of blood lipid levels is fundamental to reduce the risk of arteriosclerosis, and many hypolipidemic agents have been developed such as statins, bile acid sequestrants, nicotinic acid, and fibric acids^{6,33,34}. However, current lipid-lowering drugs don't satisfy the clinical goal, reduction of cardiovascular and cerebrovascular disorders. Moreover those drugs often cause adverse effects associated with impaired quality of life. For example, statins, 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, are the most potent lipid-lowering agents currently available, but may induce myopathy and elevation of liver enzyme levels⁷. The bile acid sequestrants, nicotinic acid, and fibric acids would also induce gastrointestinal distress, constipation, flushing, hyperglycemia, hyperuricemia, or hepatotoxicity³⁵.

Ideal anti-lipidemic drugs would improve quality of life of patients while lowering blood lipid levels³⁶. So far, many groups have researched herbal medicines for development of anti-lipidemic drugs. There have been many experimental studies of herbal medicine, such as *Phyllostachys folium*, *Melandry-*

ifirmiherba, *Leonuriherba*, *Cynanchiwilfordii radix*, *Saliaemiltiorrhizae radix*, *Crataegifructus*. The subjects of these studies were hyperlipidemia induced by alcohol and effects on the liver, but there was no study about both lipid-lowering and antioxidant effect. Traditionally, many patients in Korea with stroke or problems in blood circulation prefer to visit an oriental hospital¹⁶. In traditional Korean medicine, herbal drugs for hyperlipidemia improve spleen-deficiency and eliminate phlegm-stagnation, accumulation of damp-heat, or blood stagnation in the body^{15,16}. From this point of view, it is believed that traditional herbal drugs would be good resource for hypolipidemia.

The present study investigated the possibility of *A. capillaris* as a candidate for hypolipidemics, based on its traditional applications. The main herbal pharmaceutical property is to treat the disorders by phlegm-stagnation or heating damp, especially in the liver, the primary center for lipid metabolism and endogenous lipid synthesis¹⁷.

In order to induce hyperlipidemia animal model, poloxamer-407 was injected to Sprague-Dawley rats. Poloxamer-407 is known as a general lipase inhibitor by altering the normal elimination of lipids in bile³⁷. In this experiment, a single injection with poloxamer-407 drastically elevated lipid levels, total cholesterol, LDL-cholesterol, and triglyceride by about 3 fold, 10 fold, and 20 fold respectively. However, pre-treatment with *A. capillaris* significantly attenuated the abnormality of all those lipid parameters. A low-dose of *A. capillaris*(50mg/kg) significantly lowered triglycerides while a high dose of *A. capillaris*(100mg/kg) specifically lowered total cholesterol and LDL-cholesterol (Fig. 5-1~5-4).

Lipitor, trade name of atorvastatin (INN), is a member of statins, and has been the top-selling branded pharmaceutical in the world³⁸. This experimental result showed better efficacy than Lipitor. This result is in accordance with other reports using different animal models^{18,39,40}.

In addition, pre-treatment with *A. capillaris* improved

the status of oxidative stress-related parameters. The link between oxidative stress and the excess consumption of fat is well known⁴¹. In this model poloxamer-407 induced hyperlipidemia produced intensive oxidative stress, evidenced by high level of serum MDA and depletion of TAC, SOD activity, and GSH system. Oxidative stress represents an imbalance between the production of reactive oxygen species(ROS) and ability to readily detoxify the reactive intermediates, and then this is generally defended by various antioxidant systems including catalase, SOD, and the glutathione oxidation/reduction system⁴²⁻⁴⁴. MDA is a quantitative marker of lipid peroxidation by ROS. In this study, MDA level was attenuated significantly on 100 mg/kg, SOD on 50, 100 mg/kg, GSH content on 50, 100 mg/kg, and GSH-Rd on 100mg/kg of *A. capillaris*(Fig. 6~10).

The co-effectiveness of *A. capillaris* on hyperlipidemia and oxidative stress indicates a strong point of this medicinal plant. Oxidative stress is an early event in the evolution of hyperlipidemia, and affects the development of arteriosclerosis and myocardial infarction^{45,46}.

Currently, the prevention of hyperlipidemia-associated complications and improving quality of life are the main goals of management of patients with lipid disorders and drug developments. This study explored the hypolipidemic effect and antioxidant activity of *A. capillaris* in an animal model.

Taken together, this study produced a scientific basis for clinical application and anti-lipidemic drug development using *A. capillaris*.

Conclusion

This study investigated the hypolipidemic and antioxidant effects of *A. capillaris* using rat model induced by poloxamer-407 injection. Serum lipid

parameters and oxidative stress-associated biomarkers were determined.

1. Poloxamer-407 injection elevated serum cholesterol level by about 3 fold, and then pre-treatment with *A. capillaris* 100mg/kg ameliorated this elevation as 83% and 68% of induced group, respectively.
2. Poloxamer-407 injection elevated serum triglyceride level by 20 fold, and then pre-treatment with *A. capillaris* 50mg/kg ameliorated this elevation by 56% and 66% of induced group, respectively.
3. Poloxamer-407 injection elevated serum LDL-cholesterol level by 9 fold, and then pre-treatment with *A. capillaris* 100mg/kg ameliorated this elevation by 67% and 62% of induced group, respectively.
4. Poloxamer-407 injection elevated serum MDA level by 2 fold, and then pre-treatment with *A. capillaris* 100 mg/kg ameliorated this elevation by 80% and 64% of induced group, respectively.
5. Poloxamer-407 injection reduced serum TAC level by 60% of normal, and then pre-treatment with *A. capillaris* 50mg/kg and 100mg/kg slightly ameliorated this reduction.
6. Poloxamer-407 injection reduced serum SOD level by 18% of normal level, and then pre-treatment with *A. capillaris* significantly ameliorated this reduction, especially in the 100 mg/kg group.
7. Poloxamer-407 injection reduced serum GSH level by 6% of normal level, and then pre-treatment with *A. capillaris* 50 mg/kg and 100mg/kg treatment significantly ameliorated this reduction.
8. Poloxamer-407 injection moderately reduced serum GSH-reductase level, and then *A. capillaris*

100mg/kg treatment significantly ameliorated this reduction.

From these results, the hypolipidemic and antioxidant properties of *A. capillaris* are evidenced. This study provides a scientific basis for the clinical application and development of hypolipidemics using of *A. capillaris* in the future.

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