Inhibitory Activities of Cudrania tricuspidata Leaves on Pancreatic Lipase \textit{In Vitro} and Lipolysis \textit{In Vivo}

Young Sook Kim, Youngseop Lee, Junghyun Kim, Eunjin Sohn, Chan Sik Kim, Yun Mi Lee, Kyuhyung Jo, Sodam Shin, Yoojin Song, Joo Hwan Kim, and Jin Sook Kim

1 Korean Medicine-Based Herbal Drug Research Group, Herbal Medicine Research Division, Korea Institute of Oriental Medicine (KIOM), Daejeon 305-811, Republic of Korea
2 Department of Life Science, Gachon University, Seongnam, Kyonggi-do 461-701, Republic of Korea

Correspondence should be addressed to Jin Sook Kim, jskim@kiom.re.kr

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To identify effective herb to treat obesity, we screened 115 herbal extracts for inhibition of porcine pancreatic lipase (triacylglycerol acylhydrolase, EC 3.1.1.3) activity \textit{in vitro}. Of the extracts tested, \textit{Cudrania tricuspidata} leaves exhibited the most pronounced inhibitory effect on lipase activity with an IC\textsubscript{50} value of 9.91\textmu g/mL. Antilipid absorption effects of \textit{C. tricuspidata} leaves were examined in rats after oral administration of lipid emulsions containing 50 or 250 mg \textit{C. tricuspidata}/kg body weight. Plasma triacylglycerol levels 2 h after the oral administration of emulsions containing \textit{C. tricuspidata} were significantly reduced compared to the untreated group (\(P<0.05\)). These results suggest that \textit{C. tricuspidata} leaves may be useful for the treatment of obesity.

1. Introduction

Obesity is a significant risk factor for increased morbidity and mortality from cardiovascular disease and diabetes; however, it is also associated with many other medical conditions including cancer, liver and kidney diseases, sleep apnea, and depression [1]. The recent National Health and Nutrition Examination Survey showed that 68.0\% of those studied were considered overweight (basal metabolic rate (BMI) \(\geq 25\)) and 33.8\% were obese (BMI \(\geq 30\)) [2]. The inhibition of dietary fat absorption is a logical target for managing obesity, and pancreatic lipase is a key enzyme involved in triglyceride absorption in the small intestine. It is secreted from the pancreas and hydrolyzes triglycerides into glycerol and free fatty acids. Thus, inhibitors of digestive lipases are suggested to function as antiobesity agents [3]. Orlistat, which can be found in global markets, inhibits the action of gastrointestinal lipase and thus reduces absorption of dietary fat. However, it has serious side effects, such as steatorrhea, stomach pain, irregular menstrual periods, and headaches [4]. Recently, studies have searched for new lipase inhibitors in natural resources with minimal adverse effects. In a series of investigations to evaluate potential lipase inhibitors derived from plants, researchers showed that certain plant extracts significantly inhibited porcine pancreatic lipase \textit{in vitro} [5, 6]. In this study, as a preliminary evaluation of natural antiobesity products, we tested 115 herbal extracts for inhibition of pancreatic lipase activity \textit{in vitro} and verified the suppression of lipid absorption by \textit{C. tricuspidata} leaves \textit{in vivo}. The fruits of \textit{C. tricuspidata} suppress development of atopic dermatitis in animal model and the roots of it exhibit immunomodulatory and antioxidant activities \textit{in vitro} [7, 8]. These results show that \textit{C. tricuspidata} leaves extracts have on lipase and dietary fat absorption activities and may be useful in the treatment of obesity and metabolic disease.

2. Material and Methods

2.1. Plant Materials and Chemicals. Herbs were collected from Republic of Korea from September 2005 to July 2009 and identified by Professor Kim, Division of Life Science, Gachon University, Republic of Korea. Samples
were deposited at the Herbarium of Diabetic Complication Research Team, Korea Institute of Oriental Medicine. Porcine pancreatic lipase (type II), orlistat, and p-nitrophenyl butyrate were purchased from Sigma-Aldrich (St. Louis, MO, USA). All reagents were of biochemical grade.

2.2. Animals. Male Wistar rats (6 weeks of age) were purchased from Koatech (Kyungkido, Korea) and housed for 1 week in a 12-h/12-h light/dark cycle in a temperature- and humidity-controlled room. The animals were given free access to food and water. After adaptation to these conditions for 1 week, healthy animals were used in the present study. The Animal Studies Committee of Korea Institute of Oriental Medicine approved the experimental protocol.

2.3. Preparation of Herbal Extracts. Dried and ground herbs (200 g) were extracted with 1 L of 80% EtOH 3 times by maceration. The extracts were concentrated and dried in vacuo at 40 °C. Concentrated extracts were stored at −20°C for further studies. Extracts were dissolved in dimethyl sulfoxide at concentrations that in the total volume (3%) did not affect enzyme activity.

2.4. Measurement of Porcine Pancreatic Lipase Inhibitory Activity. The ability of the herbs to inhibit pancreatic lipase was measured using the method previously reported by Kim et al. [9, 10]. Briefly, an enzyme buffer was prepared by the addition of 6 μL porcine pancreatic lipase solution (Sigma-Aldrich) in buffer containing 10 mM MOPS (morpholinepropanesulfonic acid) and 1 mM EDTA, pH 6.8, to 169 μL Tris buffer (100 mM Tris-HCl and 5 mM CaCl2, pH 7.0). Then, 20 μL of either the herbal extracts at the test concentration (0, 0.313, 0.625, 2.5, 5, 7.5, 10, 50, and 100 μg/mL) or orlistat (Roche, Basel, Switzerland) were mixed with 175 μL enzyme buffer and incubated for 15 min at 37°C with 5 μL substrate solution (10 mM p-NPB (p-nitrophenylbutyrate) in dimethyl formamide); the enzymatic reactions were allowed to proceed for 15 min at 37°C. Lipase activity was determined by measuring the hydrolysis of p-NPB to p-nitrophenol at 405 nm using an ELISA reader (BIO-TEK, Synergy HT, Winooski, VT, USA). Inhibition of lipase activity was expressed as the percentage decrease in OD when porcine pancreatic lipase was incubated with the test materials. Lipase inhibition (%) was calculated according the following formula:

\[
\text{Inhibition} \% = 100 - \left( \frac{B - b}{A - a} \times 100 \right),
\]

where A is the activity without inhibitor, a is the negative control without inhibitor, B is the activity with inhibitor, and b is the negative control with inhibitor. The results were expressed as an average (n = 3).

2.5. Estimation of Plasma Triacylglycerol after Oral Administration of Lipid Emulsion in Rats. Plasma triacylglycerol levels were estimated using the method previously reported by Kim et al. [11]. Rats (7 weeks of age, body weight 190 ~ 230 g) that had fasted overnight were orally administered 3 mL lipid emulsion consisting of corn oil (6 mL), cholic acid (80 μg), cholesteryloleate (2 g), and saline (6 mL) with or without C. tricuspidata leaves (at doses of 50 or 250 mg C. tricuspidata leaves/kg body weight). Blood was taken from the tail vein at 0, 1, 2, 3, and 4 h after oral administration of the lipid emulsion and centrifuged at 5500 × g for 5 min to obtain the plasma. Triacylglycerol levels were determined using the Cleantech TS-s kit (ASANPHARM, Seoul, Korea).

2.6. Statistical Analysis. All experiments were repeated three times, and representative data are shown. Data are expressed as the mean ± S.D. Differences between groups were analyzed using a one-way ANOVA followed by the Tukey multiple comparison test (PRISM software, Graph Pad, CA, USA). Values of P < 0.05 were considered statistically significant.

3. Results and Discussion

3.1. Pancreatic Lipase Activity of Herbal Extracts. Currently, obesity is considered a global epidemic, and many medications have been studied and developed to treat this condition. However, there is presently only one drug—orlistat—globally approved for long-term treatment of overweight patients after sibutramine was withdrawn in January 2010 from the European market [12, 13]. Although this compound strongly inhibits the activity of pancreatic lipase, which is an important enzyme associated with fat digestion, orlistat may cause serious adverse effects on the gastrointestinal, nervous, endocrine, and renal systems and interferes with the absorption and effectiveness of many drugs and vitamins [4, 14]. Therefore, researching a safe and effective natural inhibitor of pancreatic lipase has been a major target for the development of new drugs to treat obesity [15]. Among them, extracts isolated from natural sources such as Sorbus commixta, Morus bombycis, Panax ginseng, and Ginkgo biloba have been reported as potential agents in pancreatic lipase inhibition action [16–19]. Our previous studies have also identified some natural products as new pancreatic lipase inhibitors [11, 18, 19]. In this study, 115 herbal extracts were prepared from selected parts of plants and tested at various concentrations as inhibitors of pancreatic lipase. The lipase inhibitory effects of the extracts are indicated by percentage (%) and IC50 values (Table 1). Eighteen extracts had IC50 values less than 50 μg/mL, and of these extracts, three samples (i.e., the whole Solidago serotina plant, the branches and leaves of Acer mono, and the leaves of C. tricuspidata) had IC50 values less than 10 μg/mL. Notably, C. tricuspidata leaves exhibited an IC50 value of 9.91 μg/mL (Figure 1).

3.2. Inhibitory Effect of C. tricuspidata on Lipolysis In Vivo. Next, we focused on C. tricuspidata on lipolysis in vivo. C. tricuspidata has been used as an important folk medicine for the treatment of cancer in Korea and has also been used as a traditional medicine for the treatment of hypertension, neuritis, and inflammation in Asia [20–22]. To evaluate the antilipolytic effects of C. tricuspidata leaves in vivo, we analyzed plasma triacylglycerol levels after oral administration
Table 1: Lipase inhibitory activities of extracts from herbs.

| Scientific name         | Family           | Part used       | Conc. (μg/mL) | Inhibition (%) | IC₅₀ (μg/mL) |
|-------------------------|------------------|-----------------|---------------|----------------|--------------|
| Solidago serotina       | Compositae       | Whole plant     | 2.5           | 41.76 ± 2.48   | 5.16         |
|                         |                  |                 | 5             | 49.70 ± 1.44   |              |
|                         |                  |                 | 7.5           | 55.70 ± 1.81   |              |
|                         |                  |                 | 5             | 46.17 ± 3.03   |              |
| Acer mono               | Aceraceae        | Branch, leaf    | 7.5           | 48.87 ± 3.09   | 7.7          |
|                         |                  |                 | 10            | 53.16 ± 0.93   |              |
|                         |                  |                 | 5             | 26.55 ± 0.52   |              |
| Cudrania tricuspidata   | Moraceae         | Leaf            | 7.5           | 38.97 ± 2.92   | 9.91         |
|                         |                  |                 | 10            | 50.72 ± 1.05   |              |
|                         |                  |                 | 10            | 49.77 ± 1.00   |              |
| Kalopanax pictus        | Araliaceae       | Bark            | 50            | 70.52 ± 1.70   | 10.51        |
|                         |                  |                 | 100           | 76.34 ± 0.36   |              |
|                         |                  |                 | 5             | 32.34 ± 2.04   |              |
| Cudrania tricuspidata   | Moraceae         | Branch, stem    | 10            | 48.29 ± 1.19   | 13.8         |
|                         |                  |                 | 50            | 65.83 ± 0.29   |              |
|                         |                  |                 | 10            | 45.06 ± 1.81   |              |
| Oenothera odorata       | Onagraceae       | Whole plant     | 50            | 59.58 ± 0.70   | 23.34        |
|                         |                  |                 | 100           | 61.07 ± 0.63   |              |
|                         |                  |                 | 10            | 45.08 ± 4.01   |              |
| Platycarya strobilacea  | Juglandaceae     | Branch, stem    | 50            | 56.72 ± 1.74   | 25.51        |
|                         |                  |                 | 100           | 61.74 ± 1.26   |              |
|                         |                  |                 | 10            | 41.62 ± 7.54   |              |
| Actinidia arguta        | Actinidiaceae    | Fruit           | 50            | 59.30 ± 0.80   | 26.7         |
|                         |                  |                 | 100           | 67.23 ± 3.20   |              |
|                         |                  |                 | 10            | 41.72 ± 2.86   |              |
| Tilia amurensis         | Tiliaceae        | Branch, leaf    | 50            | 59.26 ± 0.55   | 28.5         |
|                         |                  |                 | 100           | 67.17 ± 1.03   |              |
|                         |                  |                 | 10            | 36.79 ± 0.82   |              |
| Actinidia arguta        | Actinidiaceae    | Stem            | 50            | 63.38 ± 2.42   | 28.51        |
|                         |                  |                 | 100           | 66.84 ± 2.70   |              |
|                         |                  |                 | 20            | 43.12 ± 4.05   |              |
| Euscaphis japonica      | Staphyleaceae    | Branch          | 30            | 50.91 ± 1.29   | 28.62        |
|                         |                  |                 | 40            | 56.29 ± 2.10   |              |
|                         |                  |                 | 10            | 34.08 ± 1.94   |              |
| Actinidia arguta        | Actinidiaceae    | Root            | 50            | 63.93 ± 1.94   | 31.34        |
|                         |                  |                 | 100           | 71.03 ± 0.89   |              |
|                         |                  |                 | 10            | 44.19 ± 3.68   |              |
| Carpinus cordata        | Betulaceae       | Branch, stem    | 50            | 54.25 ± 1.11   | 31.39        |
|                         |                  |                 | 100           | 58.91 ± 1.62   |              |
|                         |                  |                 | 10            | 41.57 ± 2.64   |              |
| Rhus sylvestris         | Anacardiaceae    | Branch, leaf    | 50            | 57.23 ± 4.33   | 32.14        |
|                         |                  |                 | 100           | 57.43 ± 2.28   |              |
| Scientific name      | Family        | Part used         | Conc. (μg/mL) | Inhibition (%) | IC<sub>50</sub> (μg/mL) |
|----------------------|---------------|-------------------|---------------|----------------|--------------------------|
| Celtis sinensis      | Ulmaceae      | Branch, stem      | 10            | 41.52 ± 1.71   | 35.89                    |
|                      |               |                   | 50            | 54.56 ± 0.52   | 42.55                    |
|                      |               |                   | 100           | 54.09 ± 3.37   | 42.58                    |
|                      |               |                   | 10            | 34.40 ± 2.70   | 42.55                    |
|                      |               |                   | 100           | 56.43 ± 3.18   | 42.58                    |
| Prunus serrulata     | Rosaceae      | Branch, leaf      | 10            | 28.48 ± 4.40   | 42.58                    |
|                      |               |                   | 100           | 61.88 ± 1.34   | 42.58                    |
| Potentilla fragarioides | Rosaceae     | Whole plant       | 10            | 32.90 ± 4.37   | 42.58                    |
| Tilia mandshurica    | Tiliaceae     | Flower, leaf      | 10            | 19.86 ± 2.15   | 48.21                    |
| Actinidia arguta     | Actinidiaceae | Stem, leaf, fruit| 10            | 51.59 ± 2.07   | 54.09                    |
|                      |               |                   | 100           | 52.74 ± 2.30   | 54.09                    |
| Hypericum ascyron    | Hypericaceae  | Whole plant       | 10            | 28.85 ± 6.19   | 56.12                    |
|                      |               |                   | 100           | 57.57 ± 3.13   | 56.12                    |
| Rhus chinensis       | Anacardiaceae | Branch, leaf      | 10            | 37.15 ± 0.50   | 56.9                     |
| Picrasma quassioides | Simaroubaceae | Branch, stem      | 10            | 23.97 ± 2.01   | 60.47                    |
|                      |               |                   | 100           | 54.89 ± 1.38   | 60.47                    |
| Prunus persica       | Rosaceae      | Branch, leaf      | 10            | 26.90 ± 1.18   | 62.12                    |
|                      |               |                   | 100           | 56.27 ± 1.46   | 62.12                    |
| Actinidia arguta     | Actinidiaceae | Root              | 10            | 12.22 ± 5.84   | 69.17                    |
|                      |               |                   | 100           | 56.48 ± 1.93   | 69.17                    |
| Spiraea pubescens    | Rosaceae      | Branch, leaf, flower | 10            | 24.96 ± 2.54   | 74.62                    |
|                      |               |                   | 100           | 52.19 ± 1.37   | 74.62                    |
| Tilia mandshurica    | Tiliaceae     | Branch, stem      | 10            | 17.77 ± 3.99   | 79.67                    |
|                      |               |                   | 100           | 54.07 ± 2.85   | 79.67                    |
| Acer ginnala         | Aceraceae     | Branch, leaf      | 10            | 17.93 ± 2.59   | 82.29                    |
|                      |               |                   | 100           | 53.89 ± 2.92   | 82.29                    |
| Elsholtzia splendens | Labiatae      | Root              | 10            | 20.95 ± 3.37   | 83.98                    |
|                      |               |                   | 100           | 52.58 ± 1.67   | 83.98                    |
| Scientific name            | Family          | Part used            | Conc. (μg/mL) | Inhibition (%)a | IC50 (μg/mL) |
|---------------------------|-----------------|----------------------|--------------|----------------|--------------|
| *Staphylea bumaalda*      | Staphyleaceae   | Branch, leaf         | 10           | 28.75 ± 5.25   | 84.28        |
|                           |                 |                      | 100          | 53.45 ± 2.55   |              |
| *Pinus densiflora*        | Pinaceae        | Stem                 | 80           | 49.17 ± 1.04   | 87.58        |
|                           |                 |                      | 100          | 52.63 ± 2.09   |              |
| *Machilus thunbergii*     | Lauraceae       | Leaf, branch         | 10           | 29.96 ± 8.94   | 67.22        |
|                           |                 |                      | 100          | 50.93 ± 0.00   |              |
| *Deutzia glabrata*        | Saxifragaceae   | Branch, leaf, flower | 10           | 27.34 ± 8.43   | 89.09        |
|                           |                 |                      | 100          | 51.51 ± 1.46   |              |
| *Indigofera kirilowii*    | Leguminosae     | Branch, leaf, flower | 10           | 22.19 ± 1.39   | 69.24        |
|                           |                 |                      | 100          | 51.24 ± 1.32   |              |
| *Opuntia ficus-indica*    | Opuntiaceae     | Stem                 | 100          | 28.17 ± 1.66   | >100         |
| *Hibiscus syriacus*       | Malvaceae       | Root                 | 100          | 13.95 ± 0.72   | >100         |
| *Actinidia arguta*        | Actinidiaceae   | Bark                 | 100          | 26.02 ± 8.63   | >100         |
| *Euonymus oxyphyllus*     | Celastraceae    | Branch               | 100          | 47.50 ± 0.76   | >100         |
| *Eucommia ulmoides*       | Eucommiaceae    | Branch, leaf         | 100          | 37.76 ± 0.89   | >100         |
| *Asarum sieboldii*        | Aristolochiace  | Root                 | 100          | 15.50 ± 5.18   | >100         |
| *Bupleurum longifolium*   | Umbelliferae    | Whole plant          | 100          | 34.69 ± 2.52   | >100         |
| *Plantago asiatica*       | Plantaginaceae  | Root                 | 100          | −14.66 ± 4.59  | >100         |
| *Alisma plantago-aquatica*| Alismataceae    | Root                 | 100          | 22.03 ± 4.65   | >100         |
| *Duchesnea chrysantha*    | Rosaceae        | Whole plant          | 100          | 36.69 ± 1.07   | >100         |
| *Cuscuta japonica*        | Convolvulaceae  | Whole plant          | 100          | 2.43 ± 1.75    | >100         |
| *Clematis apiifolia*      | Ranunculaceae   | Stem, leaf, flower   | 100          | −19.96 ± 1.10  | >100         |
| *Prunus serrulata*        | Rosaceae        | Branch               | 100          | 43.47 ± 0.18   | >100         |
| *Colocasia antiquorum*    | Araceae         | Aerial part          | 100          | −12.08 ± 3.87  | >100         |
| *Lepidoptera canadensis*  | Leguminosae     | Aerial part          | 100          | −8.62 ± 2.65   | >100         |
| *Lepidoptera canadensis*  | Leguminosae     | Root                 | 100          | −4.14 ± 1.86   | >100         |
| *Mallophus japonicas*     | Euphorbiaceae   | Aerial part          | 100          | 11.45 ± 3.84   | >100         |
| *Alisma canaliculatum*    | Alismataceae    | Aerial part          | 100          | 16.36 ± 2.85   | >100         |
| *Alisma canaliculatum*    | Alismataceae    | Root                 | 100          | 26.99 ± 0.41   | >100         |
| *Magnolia denudata*       | Magnoliaceae    | Flowers              | 100          | −5.01 ± 2.23   | >100         |
| *Scoparia japonica*       | Solanaceae      | Stem, leaf           | 100          | −10.52 ± 0.76  | >100         |
| *Scoparia japonica*       | Solanaceae      | Root                 | 100          | −18.32 ± 1.18  | >100         |
| *Chloranthus japonicus*   | Chloranthaceae  | Whole plant          | 100          | 31.04 ± 2.37   | >100         |
| *Barbara orthoceras*      | Cruciferae      | Whole plant          | 100          | −27.85 ± 2.32  | >100         |
| *Caudophyllum robustum*   | Berberidaceae   | Stem, leaf           | 100          | −4.46 ± 3.06   | >100         |
| *Caudophyllum robustum*   | Berberidaceae   | Root                 | 100          | −23.10 ± 6.27  | >100         |
| *Cardus crispus*          | Compositae      | Stem, leaf           | 100          | 30.13 ± 3.47   | >100         |
| *Cardus crispus*          | Compositae      | Flower               | 100          | 44.24 ± 2.47   | >100         |
| *Styrax japonica*         | Styracaceae     | Flower               | 100          | 31.62 ± 4.47   | >100         |
| *Cornus controversa*      | Cornaceae       | Branch, leaf         | 100          | 39.65 ± 5.62   | >100         |
| *Cornus controversa*      | Cornaceae       | Flower               | 100          | 40.45 ± 0.66   | >100         |
| *Magnolia sieboldii*      | Magnoliaceae    | Branch, leaf         | 100          | 4.84 ± 5.72    | >100         |
### Table 1: Continued.

| Scientific name           | Family            | Part used         | Conc. (µg/mL) | Inhibition (%) $^a$ | IC$_{50}$ (µg/mL) |
|---------------------------|-------------------|-------------------|---------------|---------------------|-------------------|
| Magnolia sieboldii        | Magnoliaceae      | Flower            | 100           | $-7.03 \pm 8.14$    | $>100$            |
| Prunus persica            | Rosaceae          | Fruit             | 100           | 27.35 ± 1.98        | $>100$            |
| Rhamnus yoshinai          | Rhamnaceae        | Branch, leaf      | 100           | 43.98 ± 7.76        | $>100$            |
| Erigeron annuus           | Compositae        | Whole plant       | 100           | 26.14 ± 0.86        | $>100$            |
| Styx japonica             | Styracaceae       | Branch, leaf      | 100           | 27.88 ± 0.97        | $>100$            |
| Quercus aliena            | Fagaceae          | Branch, leaf      | 100           | 45.95 ± 1.73        | $>100$            |
| Callicarpa japonica       | Verbenaceae       | Branch, leaf      | 100           | 11.36 ± 2.56        | $>100$            |
| Ligustrum obtusifolium    | Oleaceae          | Branch, leaf      | 100           | 4.18 ± 1.41         | $>100$            |
| Lindera obtusiloba        | Lauraceae         | Branch, leaf      | 100           | 41.98 ± 1.40        | $>100$            |
| Lespedeza bicolor         | Leguminosae       | Branch, leaf      | 100           | 47.02 ± 2.78        | $>100$            |
| Carpinus laxiflora        | Betulaceae        | Branch, leaf      | 100           | 39.49 ± 5.62        | $>100$            |
| Machilus thunbergii       | Lauraceae         | Bark              | 100           | 36.58 ± 3.17        | $>100$            |
| Hedera rhombea            | Araliaceae        | Whole plant       | 100           | 29.92 ± 0.78        | $>100$            |
| Aenariana serpyllifolia   | Caryophyllaceae   | Whole plant       | 100           | 13.09 ± 1.54        | $>100$            |
| Paulownia coreana         | Paulowniaceae     | Flower            | 100           | 35.25 ± 1.77        | $>100$            |
| Thlaspi arvense           | Brassicaceae      | Whole plant       | 100           | 0.32 ± 0.92         | $>100$            |
| Vicia vilosa              | Leguminosae       | Whole plant       | 100           | 28.71 ± 1.94        | $>100$            |
| Descaria jinpannna        | Brassicaceae      | Whole plant       | 100           | 7.88 ± 1.21         | $>100$            |
| Ribes fasciculatum        | Saxifragaceae     | Branch, leaf, fruit | 100 | 33.67 ± 2.10        | $>100$            |
| Corydalis speciosa        | Fumariaceae       | Whole plant       | 100           | 9.30 ± 3.47         | $>100$            |
| Clematis fusca            | Ranunculaceae     | Whole plant       | 100           | −1.24 ± 5.89        | $>100$            |
| Deutzia parviflora        | Saxifragaceae     | Branch, leaf, stem, flower | 100 | 34.77 ± 3.21        | $>100$            |
| Rosa multiflora           | Rosaceae          | Branch, leaf, stem, flower | 100 | 42.42 ± 0.26        | $>100$            |
| Parthenocissus tricuspidata | Vitaceae          | Leaf, stem        | 100           | 48.73 ± 1.62        | $>100$            |
| Chelidonium majus         | Papaveraceae      | Whole plant       | 100           | 10.93 ± 1.55        | $>100$            |
| Platycarya stobilacea     | Juglandaceae      | Leaf              | 100           | 47.97 ± 1.14        | $>100$            |
| Platycarya stobilacea     | Juglandaceae      | Flower            | 100           | 46.63 ± 0.54        | $>100$            |
| Carpinus cordata          | Betulaceae        | Leaf              | 100           | 45.84 ± 1.30        | $>100$            |
| Celtis sinensis           | Ulmaceae          | Leaf              | 100           | 40.23 ± 0.47        | $>100$            |
| Oriza japonica            | Rutaceae          | Leaf              | 100           | −0.19 ± 2.17        | $>100$            |
| Oriza japonica            | Rutaceae          | Branch, stem      | 100           | 15.79 ± 3.07        | $>100$            |
| Oriza japonica            | Rutaceae          | Fruit             | 100           | 25.89 ± 5.92        | $>100$            |
| Picrasma quassioide       | Simaroubaceae     | Leaf              | 100           | 40.51 ± 0.74        | $>100$            |
| Picrasma quassioide       | Simaroubaceae     | Fruit             | 100           | 25.21 ± 2.08        | $>100$            |
| Tilia mandshurica         | Tiliaeae          | Leaf              | 100           | 42.08 ± 1.27        | $>100$            |
| Aralial cordata           | Araliaceae        | Whole plant       | 100           | 32.27 ± 4.39        | $>100$            |
| Viburnum sargentii        | Caprifoliaceae    | Branch, leaf      | 100           | 27.00 ± 1.59        | $>100$            |
| Polygonatum odoratum      | Liliaceae         | Root              | 100           | 36.72 ± 0.40        | $>100$            |
| Astragalus membranaceus   | Leguminosae       | Root              | 100           | −4.26 ± 0.91        | $>100$            |
| Pleuropterus multiflorus  | Polygonaceae      | Root              | 100           | −17.48 ± 1.88       | $>100$            |
| Torilis japonica          | Umbelliferae      | Fruit             | 100           | −20.02 ± 4.86       | $>100$            |
| Phaseolus angularis       | Leguminosae       | Fruit             | 100           | −58.89 ± 0.70       | $>100$            |
| Phaseolus radiates        | Leguminosae       | Fruit             | 100           | −98.96 ± 9.06       | $>100$            |
| Artemisia scoparia         | Compositae        | Aerial part       | 100           | −21.76 ± 3.22       | $>100$            |
| Solanum tuberosum         | Solanaceae        | Tuber             | 100           | −38.90 ± 4.60       | $>100$            |
| Brassica juncea           | Cruciferae        | Leaf              | 100           | −34.85 ± 7.98       | $>100$            |
| Arctium lappa             | Compositae        | Root              | 100           | −38.38 ± 7.90       | $>100$            |
| Cucumis sativus           | Cucurbitaceae     | Fruit             | 100           | −138.86 ± 0.64      | $>100$            |
Table 1: Continued.

| Scientific name   | Family    | Part used | Conc. (μg/mL) | Inhibition (%)a | IC50 (μg/mL) |
|-------------------|-----------|-----------|---------------|-----------------|--------------|
| Diospyros kaki    | Ebenaceae | Fruit     | 100           | −136.26 ± 6.37  | >100         |
| Artemisia princeps| Compositae| Aerial part| 100           | 12.82 ± 2.47    | >100         |
|                   |           |           | 0.0005        | 5.53 ± 3.21     |              |
| Orlistat (positive control) | | | 0.005         | 21.40 ± 10.76  | 0.036 (0.073 μM) |
|                   |           |           | 0.05          | 63.19 ± 7.04    |              |

aResults are the mean ± SD (n = 3).

Figure 1: Inhibitory effect of Cudrania tricuspidata leaf extract on porcine pancreatic lipase. (a) Porcine pancreatic lipase activity at different concentrations of C. tricuspidata leaves. (b) Orlistat was used as a positive control. Data are the mean ± S.D. (n = 3).

Figure 2: Inhibitory effect of Cudrania tricuspidata leaves on rat plasma triacylglycerol levels. Plasma triacylglycerol levels, at the time marked by an asterisk, significantly differ between the control and C. tricuspidata (250 mg/kg body weight) groups (P < 0.05). Orlistat (a lipase inhibitor) was used as a positive control (P < 0.001 versus control).

of lipid emulsions with or without the C. tricuspidata leaves to rats. Figure 2 shows plasma triacylglycerol levels after oral administration of lipid emulsion with or without C. tricuspidata as a function of time. After oral administration, low concentrations of C. tricuspidata (50 mg/kg body weight) reduced plasma triacylglycerol levels and high concentrations of C. tricuspidata (250 mg/kg body weight) delayed lipid absorption significantly; however, these effects were weaker than that of the positive control, orlistat.

C. tricuspidata is a rich source of xanthones and flavonoids, including cudraflavone C [23]. A recent study reported that cudraflavone C from Artocarpus nitidus inhibited pancreatic lipase activity (IC50 = 17.0 ± 0.7 μM) [24]. Thus, cudraflavone C may be a potential as one of active compounds for preventing and treating obesity.

4. Conclusion

In this paper, we screened 115 herbal extracts for inhibition of porcine pancreatic lipase to identify effective herb to treat obesity. C. tricuspidata leaves show the most pronounced effect on pancreatic lipase activity and are able to suppress dietary fat absorption in vivo. Up until now, C. tricuspidata leaves extracts have not been reported on lipase and dietary fat absorption activities. Thus, it is worthwhile to further investigate these extracts for their potential pharmacological effect in antiobesity and attempt should be made to characterize phytoactive compounds to be used as safer therapeutic agents in future.
Authors’ Contribution

Y. S. Kim and Y. Lee contributed equally to this work.

Conflict of Interests

The authors declare no conflict of interests.

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