INTRODUCTION

Monoamine oxidase (MAO) inhibitors were the first antidepressants introduced, but their use has dwindled because of their reported side effects, their food and drug interactions, and the introduction of other classes of agents. However, there has been renewed interest in MAO inhibitors (Wimbiscus et al., 2010). Recently, Meyer group reported the relationship between MAO-A levels and selective serotonin reuptake inhibitor (SSRI) treatment, recovery, and recurrence in major depressive disorder (MDD). They concluded that from the perspective of monoamine theory, SSRI raise serotonin levels vigorously whereas elevated MAO-A levels would be expected to metabolize serotonin, norepinephrine, and dopamine excessively. The mismatch between monoamine levels raised by treatment and monoamine levels lowered by disease processes might, at times, contribute to lack of response to SSRI treatment (Meyer et al., 2009). Consequently, a MAO-A inhibitor helps on the treatment of depression with a SSRI. On the other hand, Kitaichi group reported that the combined treatment with a MAO-A inhibitor and MAO-B inhibitor strengthens antidepressant effects because the combined treatment increases extracellular norepinephrine levels more than MAO-A inhibitor alone through increases in β-phenylethylamine (Kitaichi et al., 2010).

Angelica keiskei Koidzumi (Umbelliferae), which is growing mainly along the Pacific coast of Asia is a hardy perennial herb. It has been used traditionally as a diuretic, laxative, analeptic and galactagogue, and has recently gained attention as a health food in Korea. It has been studied for its potential health benefits, including anti-inflammatory, antioxidant, and antidiabetic effects.
ied as folklore medicine for many metabolic diseases, such as hypertension, hepatitis and neuralgia (Kim et al., 1992), and is reported to have numerous biological benefits, such as anti-hyperlipidemic activity (Park et al., 1997), lowering blood pressure (Shimizu et al., 1999), antitumor action (Oyayama et al., 1991), and suppression of gastric acid secretion (Fujita et al., 1992). Various chalcones, coumarins and flavonoids have so far been isolated and characterized from this plant (Baba et al., 1990; Park et al., 1995; Akihisa et al., 2003).

Although Ogawa group reported the dietary 4-hydroxyderricin suppresses production in the elevation of systolic blood pressure (Ogawa et al., 2005), it remains unclear whether A. keiskei affects the nervous system, such as nervous sedative effect, antidepressive, and dementia treatment, which could be controlled by MAO or DBH inhibitors.

MAO inhibitors were among the first drugs used in the treatment of depression (Quitkin et al., 1979), Parkinson’s disease (PD) (Birkmayer et al., 1983; Riederer et al., 1983; Stern et al., 1983) and schizophrenia (Rigal and Zarifian, 1983). MAO-B inhibitors have been used in the treatment of Parkinson disease. Especially, selective MAO-B inhibitor, selegiline does show success as an adjunctive treatment for Parkinson disease. Particularly, DBH inhibitors can provide the added advantage of increasing levels of dopamine (DA) with MAO-B inhibitors.

In the present study, we showed that the two prenylated chalcones, xanthoangelol and 4-hydroxyderricin isolated from A. keiskei have inhibitory activities against MAO-A and MAO-B. We also investigated the inhibitory activities of a flavonoid, cynaroside on DBH activities in in vitro assay.

**MATERIALS AND METHODS**

**Plant materials**

Fresh leaves and stems of A. keiskei were collected from Yangju, Korea, and identified by Dr. KW Park, botanist at the Korea National Arboretum. The voucher specimen (NP20-204) has been deposited in the specimen room of Duksung Women’s University, Seoul, Korea.

**Chemicals and instruments**

NMR experiments were performed on a Bruker/Advance-600 (600 MHz). The chemical shifts were reported in parts per million, and the coupling constants (J values) were in Hz. Exact masses were measured by a Hewlett Packard 5890 series II (EI-MS) or Jeol JMSAX505WA Mass spectrometer. Column chromatography was carried out on silica gel 60 (0.063-0.200 μm; Merck 7734) and Lichroprep RP-18 (particle size 40-60 μm, Merck). TLC analyses were carried out on silica gel 60 F254 (Merck 7734) and RP-18 F254s (Merck 15685) plates. In bioassay experiments, UV absorbance was measured by a UVikon XS UV/Vis spectrometer of SECOMAN. Serotonin creatinine sulfate, Iproniazid, deprenyl Tyramine-HCl, Dowex 50W 8 and Amberlite CG50 were purchased from Sigma Co., USA, and Benzylamine-HCl from Tokyo Kasei Co., Japan.

**Animals**

Male Sprague-Dawley rats weighing 180-200 g were obtained from the Orient Animal Laboratoty (Seoul, Korea) and were maintained on a 12 h light-dark cycle (light phase: 06:30-18:30) in a temperature-controlled environment (22 ± 1°C) with free access to food and water. Experiment began after 10 day period of acclimatization. All procedures were approved by the Kunkuk University Animal Care and Use Committee. They complied with the Guide for the Care and Use of Laboratory Animals, Bio-Food and Drug Research Center Kunkuk University.

**Procedures of MAO-A assay in vitro**

Rat brain mitochondrial MAO was prepared by the method of Kim et al. (2012). The activity of MAO-A was measured according to Han et al. (2001) using serotonin as the substrate. The reaction mixture containing 0.5 ml of enzyme solution in 10 mM phosphate buffered saline (pH 7.1) and 1 ml of test solution was preincubated at 37°C for 15 min, after which 0.5 ml of 1 mM solution of buffered serotonin creatinine sulfate (Sigma, USA) was added. Following incubation at 37°C for 90 min, the enzyme reaction was terminated by heating the reaction mixture for 3 min in a boiling water bath. After being centrifuged, 1.6 ml of the supernatant, was applied to an Amberlite CG50 column (0.8 i.d.×3 cm). The column was washed with 40 ml of distilled water and eluted with 3 ml of 4N acetic acid. The absorbance of the metabolite that produced after being reacted with MAO-A was measured at 277 nm. Purely isolated compounds were dissolved in DMSO and then suspended in water for testing their inhibitory activities on MAO-A. Final concentration of DMSO in enzymatic reaction mixture was below 5%. Iproniazid was used as positive control for nonselective inhibitor.

**Procedures of MAO-B assay in vitro**

Rat liver mitochondrial MAO was prepared by Zeller’s method (Kim et al., 2012). The activity of MAO-B was measured according to Han et al. (2001), using benzylamine as the substrate. The reaction mixture containing 0.5 ml of enzyme solution in 10 mM phosphate buffered saline (pH 7.1) and 1 ml of test solution was preincubated at 37°C for 15 min and then cooled in an ice bath. 0.5 ml of 4 mM benzylamine HCl (Tokyo Kasei Co., Japan) in buffer was added to it. This mixture was further incubated at 37°C for 90 min in a shaking water bath. The reaction was terminated by addition of 0.2 ml of 60% perchloric acid. After extraction with 3 ml of cyclohexane, the organic layer was taken and the absorbance of benzaldehyde produced was measured at 242 nm. Purely isolated compounds were dissolved in DMSO and then suspended in water for testing their inhibitory activities on MAO-B. Final concentration of DMSO in enzymatic reaction mixture was below 5%. Deprenyl was used as positive control for selective MAO-B inhibitor.

**Procedures of DBH assay in vitro**

The enzyme activity of DBH was determined according to Kim et al. (2012). Using tyramine as the substrate. The following were sequentially added to 0.3 ml of enzyme solution in 0.25 M sucrose: 1 ml of test solution; 0.2 ml of 3 mg/ ml catalase; 0.5 ml of 1 M acetate buffer (pH 5.0); and 0.5 ml of a reaction aid, prepared by dissolving fumaric acid, N-ethylmaleimide, iiproniazide phosphate and ascorbic acid to concentrations of 0.06, 0.06, 0.006 and 0.06 M, respectively, in distilled water. The solution was allowed to stir at 37°C for 15 min, and then 0.5 ml of 0.12 M tyramine HCl solution was added and the resulting mixture was allowed to stir for 90 min.

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Next, 0.4 ml of 3 M solution of trichloroacetic acid was added to the reaction mixture to terminate the enzyme reaction. Immediately thereafter, the solution was centrifuged and 3 ml of the supernatant was poured onto a Dowex 50 W×8 column (0.8 i.d.×3 cm, H+ form, 200-400 mesh) and the column was washed with 30 ml of distilled water. Three milliliters of 4 N NH4OH solutions were then added to the column. The eluate was collected in a test tube and 0.2 ml of 4% sodium metabisulfite solution was added. The absorbance of the resulting mixture was measured at 330 nm.

**Isolation of xanthoangelol, 4-hydroxyderricin and cynaroside from A. keiskei**

The dried aerial parts (10 kg) of *A. keiskei* were extracted three times with a mixture of methanol and distilled water (7:3, v/v: 25 L) at 80°C for 4 hr. The combined MeOH extract was concentrated in vacuo at 45°C to give 2.8 kg residue. The purification and isolation of two prenylated chalcones and a flavonoid from the EtOAc and n-BuOH extract were performed according to general chromatographic methods. Briefly, the EtOAc and BuOH extract was chromatographed on a silica gel column (Silica gel 60, 70-230 mesh: Merck Japan, Tokyo, Japan) using stepwise gradient elution with the hexane-dichloromethane (5:1), dichloromethane-methanol (30:1), dichloromethane-methanol (3:1) to yield fraction I to VI. The xanthoangelol (3.1 g, 99% purity, yellow needles) was finally purified with a LiChroprep RP-18 Lobar column (Merck, Japan) with 80% methanol from the fraction I (15 g). The 4-hydroxyderricin (400 mg, 98% purity, yellow powders) was finally purified with a LiChroprep RP-18 Lobar column with 80% methanol from the fraction II (6 g). The fraction VI (13 g) was subjected to silica gel column chromatography using dichloromethane-methanol (5:1) to afford cynaroside (300 mg, 99% purity, yellow needles). These three compounds were identified by direct comparison with an authentic sample (Park et al., 1995; Akihisa et al., 2003). The structures of the isolated compounds are given in Fig. 1.

**Xanthoangelol (1)**

Yellowish needles, EI-MS: m/z 392[M]+(C21H22O4), 1H-NMR (600MHz, DMSO d6+D2O) δ 5.04 (1H, d, J=7.5 Hz, G1), 6.44 (H, d, J=2.0 Hz, 6-H), 6.73 (1H, s, 3-H), 6.80 (1H, d, J=2.1 Hz, 8-H), 6.91 (1H, d, J=8.4 Hz, 5'-H), 6.91 (1H, d, J=8.4 Hz, 5'-H), 7.40 (1H, d, J=2.2 Hz, 2'-H), 7.45 (1H, d, J=8.4 Hz, 6'-H). 13C-NMR (150MHz, DMSO d6+D2O) δ 60.8 (G6-C), 69.8 (G4-C), 73.3 (G2-C), 76.4 (G3-C), 77.3 (G5-C), 95.3 (C-8), 99.9 (6-C), 100.2 (G1-C), 105.7 (10-C), 113.7 (2'-C), 116.3 (2-C), 116.3 (5'-C), 119.6 (6'-C), 121.7 (1'-C), 145.9 (3'-C), 150.1 (4'-C), 151.1 (5-C), 157.3 (8-C), 163.2 (7-C), 164.8 (2-C), 182.4 (4-C).

**RESULTS**

The inhibitory activities of xanthoangelol on MAOs

Each solvent fraction and isolated compounds from Fr. I to VI, concentrated EtOAc and butanol extracts of *A. keiskei* against MAO-A, MAO-B and DBH activities were examined. As shown in Table 1, total MeOH extract and each solvent fraction have inhibitory potential on MAO-A and MAO-B activities. Especially, dichloromethane and EtOAc fractions showed most potent inhibitory activities against both enzymes. BuOH fraction also shows the inhibitory activities on both enzymes. EtOAc and BuOH fractions were chosen for elucidating their active principles. Table 1 shows the inhibitory activities of each solvent fraction on MAO-A and MAO-B. The IC50 values of the dichloromethane fraction were 0.30 mg/ml for MAO-A, 0.06 mg/ml for MAO-B. The IC50 values of the EtOAc and BuOH fractions were 0.09 mg/ml and 1.3 mg/ml for MAO-A, 0.13 mg/ml and 0.33 mg/ml for MAO-B.

**Table 1.** The IC50 values of each solvent extract of *A. keiskei* against MAO-A, MAO-B and DBH activities

| Fractions | Amounts of extract (g) | IC50 values (mg/ml) |
|-----------|------------------------|---------------------|
|           |                        | MAO-A | MAO-B | DBH     |
| MeOH      | 1,000                  | 0.51   | 0.33   | 0.68    |
| Hexane    | 110                    | -      | 1.90   | -       |
| CH2Cl2    | 56                     | 0.30   | 0.06   | 0.17    |
| EtOAc     | 45                     | 0.09   | 0.13   | 0.08    |
| BuOH      | 138                    | 1.30   | 0.85   | 0.22    |
| Water     | 400                    | 2.75   | -      | -       |
lective and selective inhibitors.

Iproniazid and deprenyl were used as positive controls for nonselective MAO-A and deprenyl (selegiline) is a selective MAO-B inhibitor. Iproniazid is a nonselective inhibitor of MAOs A and B, respectively. Iproniazid is a nonselective inhibitor of MAOs A and B, respectively. Iproniazid is a nonselective inhibitor of MAOs A and B, respectively. Iproniazid and deprenyl were used as positive controls for nonselective and selective inhibitors.

The inhibitory activities of xanthoangelol on DBH

As shown in Table 1, total MeOH extract and each solvent fraction have inhibitory potential on DBH activities. Except for the hexane fraction, CH$_2$Cl$_2$, ETOAc and BuOH fractions showed lowest IC$_{50}$ values against DBH enzyme. Among them, ETOAc fraction and BuOH fraction were chosen for elucidating their active principles. Table 2 shows the inhibitory activities of the isolated compounds on DBH. Xanthoangelol exhibited the very weak inhibitory activities on DBH. The IC$_{50}$ value of xanthoangelol was 516 μM for DBH.

The inhibitory activities of 4-hydroxyderricin on MAOs

Table 2 shows the inhibitory activities of the isolated compounds on MAO-A and MAO-B. 4-hydroxyderricin exhibited the inhibitory activities on the both enzymes potently. The IC$_{50}$ value of xanthoangelol was 43.4 μM for MAO-A, 43.9 μM for MAO-B. In our examinations, the IC$_{50}$ value of the iproniazid, positive control of the nonselective MAO inhibitor was 37 μM for MAO-A and 42.5 μM for MAO-B, respectively. Iproniazid is a nonselective inhibitor of MAOs and deprenyl (selegiline) is a selective MAO-B inhibitor. Iproniazid and deprenyl were used as positive controls for nonselective and selective inhibitors.

The IC$_{50}$ values of the isolated compounds from A. keiskei against MAO-A, MAO-B and DBH activities

| Compounds         | IC$_{50}$ values (μM) |
|-------------------|-----------------------|
|                   | MAO-A     | MAO-B     | DBH      |
| Xanthoangelol     | 43.4      | 43.9      | 516      |
| 4-hydroxyderricin | 3,520     | 3.43      | 12.0     |
| Cynaroside        | 400       | 268       | 0.041    |
| Iproniazid*       | 37        | 42.5      | -        |
| Deprenyl*         | 3.3       | 0.046     | -        |

*Used as a positive control drugs for nonselective MAO inhibitor.

0.85 mg/ml for MAO-B, respectively. Table 2 shows the inhibitory activities of the isolated compounds on MAO-A and MAO-B. Xanthoangelol exhibited the inhibitory activities on both enzymes potently. The IC$_{50}$ value of xanthoangelol was 43.4 μM for MAO-A, 43.9 μM for MAO-B. In our examinations, the IC$_{50}$ value of the iproniazid, positive control of the nonselective MAO inhibitor was 37 μM for MAO-A and 42.5 μM for MAO-B, respectively. Iproniazid is a nonselective inhibitor of MAOs and deprenyl (selegiline) is a selective MAO-B inhibitor. Iproniazid and deprenyl were used as positive controls for nonselective and selective inhibitors.

The inhibitory activities of 4-hydroxyderricin on MAOs

Table 2 shows the inhibitory activities of the isolated compounds on MAO-A and MAO-B. 4-hydroxyderricin exhibited the inhibitory activities on both enzymes potently. The IC$_{50}$ value of 4-hydroxyderricin was 3.52 mM for MAO-A, 3.43 μM for MAO-B. In our examinations, the IC$_{50}$ value of the hexane fraction, CH$_2$Cl$_2$, ETOAc and BuOH fractions showed lowest IC$_{50}$ values against DBH enzyme. Among them, ETOAc fraction and BuOH fraction were chosen for elucidating their active principles. Table 2 shows the inhibitory activities of the isolated compounds on DBH. Xanthoangelol exhibited the very weak inhibitory activities on DBH. The IC$_{50}$ value of xanthoangelol was 516 μM for DBH.

The inhibitory activities of cynaroside on MAOs

As shown in Table 2, total MeOH extract and each solvent fraction have inhibitory potential on DBH activities. Except for the hexane fraction, CH$_2$Cl$_2$, ETOAc and BuOH fractions showed lowest IC$_{50}$ values against DBH enzyme. Among them, ETOAc fraction and BuOH fraction were chosen for elucidating their active principles. Table 2 shows the inhibitory activities of the isolated compounds on DBH. Xanthoangelol exhibited the very weak inhibitory activities on DBH. The IC$_{50}$ value of xanthoangelol was 516 μM for DBH.

The inhibitory activities of xanthoangelol on DBH

As shown in Table 1, total MeOH extract and each solvent fraction have inhibitory potential on DBH activities. Except for the hexane fraction, CH$_2$Cl$_2$, ETOAc and BuOH fractions showed lowest IC$_{50}$ values against DBH enzyme. Among them, ETOAc fraction and BuOH fraction were chosen for elucidating their active principles. Table 2 shows the inhibitory activities of the isolated compounds on DBH. Xanthoangelol exhibited the very weak inhibitory activities on DBH. The IC$_{50}$ value of xanthoangelol was 516 μM for DBH.

The inhibitory activities of xanthoangelol on DBH

As shown in Table 1, total MeOH extract and each solvent fraction have inhibitory potential on DBH activities. Except for the hexane fraction, CH$_2$Cl$_2$, ETOAc and BuOH fractions showed lowest IC$_{50}$ values against DBH enzyme. Among them, ETOAc fraction and BuOH fraction were chosen for elucidating their active principles. Table 2 shows the inhibitory activities of the isolated compounds on DBH. Xanthoangelol exhibited the very weak inhibitory activities on DBH. The IC$_{50}$ value of xanthoangelol was 516 μM for DBH.

The inhibitory activities of 4-hydroxyderricin on DBH

As shown in Table 1, total MeOH extract and each solvent fraction have inhibitory potential on DBH activities. Except for the hexane fraction, CH$_2$Cl$_2$, ETOAc and BuOH fractions showed lowest IC$_{50}$ values against DBH enzyme. Among them, ETOAc fraction and BuOH fraction were chosen for elucidating their active principles. Table 2 shows the inhibitory activities of the isolated compounds on DBH. Xanthoangelol exhibited the very weak inhibitory activities on DBH. The IC$_{50}$ value of xanthoangelol was 516 μM for DBH.

DISCUSSION

The activity-guided fractionation of extracts from Angelica keiskei Koidzumi led to the isolation of two prenylated chalcones, xanthoangelol and 4-hydroxyderricin and a flavonoid, cynaroside. Three compounds were exhibited the inhibitory activities against MAO-A, MAO-B and DBH respectively. A. keiskei is a major vegetable used as a fresh salad. As described in the introduction, traditional use of this plant is not well known, except for some medicinal purposes, such as hypertension, hepatitis and neuralgia (Kim et al., 1992). Reported studies about bioactivities of A. keiskei are few. There are some reports such as an anti-hyperlipidemic (Park et al., 1997), lowering blood pressure (Shimizu et al., 1999), antitumor action (Okuyama et al., 1991), and suppression of gastric acid secretion (Fujita et al., 1992). Some chalcones, coumarins and flavonoids have so far been isolated and characterized from this plant (Baba et al., 1990; Park et al., 1995; Akhisa et al., 2003). In this study, we can find out that this plant has also antidepressant effect. Each isolated compound showed different inhibitory pattern.

One of the isolated compounds, xanthoangelol was found to be nonselective MAO inhibitor, because of its inhibitory activities on MAO-A and MAO-B were very similar to iproniazid, nonselective MAO inhibitor. Although its activity was not great, xanthoangelol also inhibited the DBH activity. The other one, 4-hydroxyderricin was a potent selective MAO-B inhibitor. Its IC$_{50}$ value was higher than that of deprenyl, a selective MAO-B inhibitor used as a positive control, but this plant mainly is used as food, this value is significantly low enough. On the other hands, cynaroside showed potent inhibitory activity on DBH. This compound showed very weak inhibitory activity on MAO-A, and exhibited low activity on MAO-B.

Several reports have described the MAO-A inhibition contributes to the mechanism of antidepressant effects of MAO inhibitors more than MAO-B inhibition (Lipper et al., 1979; Mann et al., 1989). Larsen et al. (1991) reported that reversible monoamine oxidase inhibitor (RIMA) has equal antidepressant effects to those of irreversible MAO inhibitors. However,
Lotufo-Neto et al. (1999) examined antidepressant effects of MAO inhibitors in a meta-analysis and described the possibility that non-selective MAO inhibitors are more effective than RIMA. Consequently, it is likely that MAO-B inhibition also contributes to an antidepressant effects. Kitaichi et al. (2010) measured extracellular noradrenaline and serotonin levels after administration of RIMA and reversible MAO-B inhibitor in the medial prefrontal cortex of rats using the in vivo micro dialysis method. And they suggested that the combined treatment with a MAO-A inhibitor and a MAO-B inhibitor strengthens antidepressant effects because the combined treatment increases extracellular noradrenaline levels more than a MAO-A inhibitor alone through increases in β-phenylethylamine. According to the results of this study, A. keiskei is an excellent combined MAO inhibitor for treatment for depression, because its major bioactive compounds, xanthoangelol, 4-hydroxyderricin and cynaroside were selective, nonselective MAO inhibitor and DBH inhibitor, respectively. Xanthoangelol is a nonselective MAO inhibitor, 4-hydroxyderricin is a selective MAO-B inhibitor, and cynaroside is a selective DBH inhibitor.

There are more MAO-B than MAO-A in the human brain, but more MAO-A than MAO-B in the rat brain (Riederer et al., 1983). The distribution of MAO-A and MAO-B is different between the human brain and the rat brain. The role of MAO-B in antidepressant effects might be greater in human than in rat; stronger antidepressant effects of combined treatment with a MAO-A inhibitor and a MAO-B inhibitor might be likely to be induced in humans (Kitaichi et al., 2010). Results of this study suggest that xanthoangelol, as a nonselective MAO inhibitor; can be potentially used as a drug candidates against depression. 4-Hydroxyderricin, as a selective MAO-B inhibitor, can be potentially used as a drug candidate for this kind of disease. Cynaroside, as a selective DBH inhibitor, can effectively elevate the level of released dopamine (DA) by preventing DBH from converting DA to norepinephrine and being destroyed by oxidative deamination effect of MAO. Thus, that seems to be useful materials for antidepressant drug for human.

As shown in Fig. 2, the degree and the way of inhibition against each enzyme of the isolated compound was different. Xanthoangelol was nonselective between MAO-A and MAO-B. Its inhibitory potentials (IC50 value, total activity, and specific activity) on MAO-A were no less than those on MAO-B and about 10 times more than those on DBH. In addition, Its IC50 values on MAOs were at a rate comparable with those of iproniazid used as positive control. 4-Hydroxyderricin was the strongest selective MAO B inhibitor among the isolated compounds. Its specific activity on MAO-B was about 15 times more than that of xanthoangelol, about 150 times more than that of cynaroside, and about 1,000 and 5,000 times more than its own specific activity on MAO-A and DBH. In addi-

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**Fig. 2.** Inhibitory activities on MAO-A, MAO-B and DBH of the two prenylated chalcones, xanthoangelol (1) and 4-hydroxyderricin (2) and a flavonoid, cynaroside (3) isolated from Angelica keiskei. Each compound was tested at concentrations of 1-500 μg/ml to derive IC50 values, and these data obtained mean value from repeated experiments 3 to 5 times of duplicated tests. Specific activity expressed as unit/g, one unit is defined as a sample amount to give 50% inhibition against enzyme activity.
keiskei

possibility exists that these three compounds isolated from
below 0.9
It exhibited inhibitory activity against DBH at concentrations
and DBH. This result indicates that 4-hydroxyderricin is more
major active components of
results strongly suppose that the isolated compounds are the
other enzymes and the activities on DBH were lowest. These
activities. The activities on MAO-B were more than those on the
total activities of the isolated compounds (the right one). How-
left graph) were about 10 to 100 times more than accumulated
MAOs and DBH, total activities of the methanol extract (the
that on MAO-B than that on MAO-A. As Fig. 3 shows, against
MAC-A and DBH, total activities of the methanol extract (the
were about 10 to 100 times more than accumulated
total activities of the isolated compounds (the right one). How-
However, the both graphs showed similar tendency of the total ac-
tivities. The activities on MAO-B were more than those on the
other enzymes and the activities on DBH were lowest. These
results strongly suppose that the isolated compounds are the
major active components of Angelica keiskei against MAOs and
DBH. This result indicates that 4-hydroxyderricin is more
selective MAO-B inhibitor than deprenyl used as selective
MAO-B inhibitor. Cynaroside was a selective DBH inhibitor.
It exhibited inhibitory activity against DBH at concentrations
below 0.9 μM, but did not on MAO-A and MAO-B.

In conclusion, two prenylated chalcones, xanthoangelol and 4-hydroxyderricin and a flavonoid, cynaroside isolated from A. keiskei were major active principles of this plant. The possibility exists that these three compounds isolated from A. keiskei were potent candidates for development of combined antidepressant drug, and the plant A. keiskei contained xanthoangelol, 4-hydroxyderricin and cynaroside, as major active components, and will be an excellent functional food material for combined antidepressant effect.

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