Research Article

Skin-Related Properties and Constituents from the Aerial Parts Extract of *Persicaria senticosa*

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Abstract

In the course of screening for cosmetic ingredients by measuring antioxidant and antiwrinkle and whitening and anti-inflammatory activities, skin-related activity was tested using 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical scavenging, elastase inhibition, tyrosinase inhibition, and nitric oxide assay. Several Polygonaseae extracts were found to show potent activity. The results showed that the *Persicaria senticosa* methanolic extract has the 1,1-diphenyl-2-picrylhydrazyl (DPPH) and ABTS radical scavenging activities (IC₅₀ 61.0 and 17.5 μg/mL). In the elastase inhibition assay and nitric oxide assay, the IC₅₀ of methanolic extract of *Persicaria senticosa* was 739.7 μg/mL and 71.8 μg/mL. The *Persicaria senticosa* 70% ethanolic extract partitioned with n-hexane, CH₂Cl₂, EtOAc, n-BuOH, and aqueous fractions. The purification of EtOAc soluble layer was by column chromatography separation and MPLC analysis of Compounds 1-7. It was identified as loliolide (1), quercetin-3-O-glucoside (2), quercetin-3-O-glucuronide (3), 4-methoxy caftraric acid (4), kaempferol-3-(6-methylglucuronide) (5), quercetin-3-(6-methylglucuronide) (6), and quercetin (7). Structure was elucidated by a combination of 1D and 2D NMR and MS spectrometry as well as comparison with reported literatures. Radical scavenging effect on DPPH, tyrosinase inhibition, and nitric oxide assay on several compounds from *Persicaria senticosa* was found to show potent activity. The results showed that Compound 7 has the NO assay (IC₅₀ 29.7 μM). For DPPH, the IC₅₀ of Compounds 2, 3, 5, and 7 was 39.6, 31.2, 37.0, and 22.7 μM. In tyrosinase inhibitory activity, the IC₅₀ of Compound 7 was 14.3 μM.

1. Introduction

*Persicaria senticosa* is an annual plant in the family Polygonaseae, which is distributed in the whole of Korea. Since early times, this plant has been used as folk medicine with beneficial effects for the treatment of various diseases such as removing the swelling parts of the wound or carbuncles and cellulitis and circulating blood and removing blood stagnation. Recent studies have shown that *Persicaria senticosa* had anti-inflammatory effects [1]; however, this plant has not been reported as bioactive cosmetic ingredients. And previous phytochemical studies on the flowers, stem, and roots of the genus Polygonum have revealed that various flavonoids and phenolic compounds such as hydroxybenzoic acid, rutin, quercetin-3-O-glucuronide, quercetin-3-O-glucoside, and luteolin-7-O-rutinoside were considered the major active components [2, 3]. These active compounds exhibit diverse pharmacological effects, such as anti-inflammatory, antiulcer, antihypertensive, and anticancer effects [4]. During the screening for cosmetic ingredients by measuring the radical scavenging effect on 1,1-diphenyl-2-picrylhydrazyl (DPPH), ABTS radical scavenging, elastase inhibition, tyrosinase inhibition and nitric oxide assay, several Polygonum extracts were found to show potent activity.
2. Materials and Methods

2.1. Plant Materials and General Procedures of Natural Products. *Persicaria senticosa* was collected from Seo-meoyeon, Chuncheon-si, Gangwon-do, Korea, in 2016 (GPS: N 37° 55′ 30.1″, E 127° 37′ 57.0″, altitude: 434 m). Voucher specimens (G071) were authenticated by Dr. Chun Whan Choi. *Persicaria senticosa* were deposited at the herbarium of Biocenter, Gyeonggido Business & Science Accelerator, Suwon, South Korea (Fig. S3). The 99.9% methanol extract of thirty-four Polygonum was obtained from the Korea Plant Extract Bank at the Korea Research Institute of Bioscience and Biotechnology (Daejeon, Korea). 1H and 13C NMR experiments were performed on a Bruker Ascend 700 MHz spectrometer with tetramethylsilane (TMS). LC-ESI-MS was obtained on a Triple TOF 5600+ instrument (AB SCIX, USA) and HRESI-MS on a LTQ Orbitrap XL instrument (Thermo, USA). Thin-layer chromatography (TLC) was conducted on Silica gel 60 F254 (Merck, Germany) and Silica gel 60 RP-18 F254S (Merck, Germany) plates. Column chromatography (CC) was performed using Silica gel 60 (70–230 mesh, Merck, Germany), ODS-A (12 nm S-7 μm, YMC GEL, Japan), and preparative HPLC was performed on LC-8A (Shimadzu, Japan).

2.2. NO Assay. RAW 264.7 cells were seeded in 96-well plates (5 × 10^4 cells/well) and were treated with sample for 1 h prior to LPS (1 μg/mL) stimulation for 24 h. The negative control was treated with serum-free media. The amount of nitrite, a stable metabolite of NO, was measured by using Griess reagent (1% sulfanilamide and 0.1% naphthylethylenediamine dihydrochloride in 2.5% phosphoric acid). Absorbance was subsequently measured at 540 nm using an ELISA reader. The quantity of nitrite was determined from a standard curve for sodium nitrite [5–7].

2.3. Cell Cytotoxicity Assay. RAW 264.7 cells were plated at a density of 5 × 10^4 cells/well in 96-well plates. Cells were treated with samples for 1 h prior to LPS (1 μg/mL) stimulation for 24 h. MTT (5 mg/mL in PBS) was added to each well and incubated for 2 hr. The medium was removed from the wells by aspiration, DMSO was added to each well, and the plate was shaken. The absorbance of each well was measured at a wavelength of 540 nm using an ELISA reader. Data are presented as the mean ± SD of three replicates.

2.4. DPPH Radical Scavenging Activity Assay. DPPH radical scavenging activity was measured by using the method described by Blois [8] and Ozgen et al. [9]. DPPH solution dissolved in methanol was added to the sample, which was diluted to the required concentration, and the reaction was carried out at room temperature for 30 min. Absorbance was measured at 517 nm using an ELISA reader. The antioxidant butylated hydroxyanisole (BHA) was used as a positive control, and the IC_{50} value of the sample was determined.

2.5. ABTS Radical Scavenging Activity. ABTS radical scavenging activity was measured by using a previously described method [10, 11]. ABTS+ was formed by mixing 7 mM ABTS solution and 2.45 mM potassium persulfate (K₂S₂O₈) solution with ABTS: K₂S₂O₈ (2:1 ratio) for 12–16 h to form a cation (ABTS+). The absorbance was measured at 734 nm using an ELISA reader. BHA, an antioxidant, was used as the positive control.

2.6. Tyrosinase Inhibition Assay. Tyrosinase inhibitory activity was measured by using the method described by Yagi et al. [12]. The reaction was carried out in 0.1 M potassium phosphate buffer (pH 6.5) containing 1.5 mM L-tyrosine and 1250 units/mL mushroom tyrosinase. The reaction mixture was incubated at 37°C for 20 min. The test samples were assayed for tyrosinase inhibition by measuring its effect on tyrosinase activity using SpectraMax 190PC microplate ELISA reader at 490 nm. Arbutin and kojic acid were used as a positive control, and the IC_{50} value of the sample was determined.

2.7. Elastase Inhibition Assay. The reaction was carried out in 0.5 mM Tris buffer (pH 8.5) containing 1 mg/mL N-succinyl-(Ala)₃-p-nitroanilide and 0.6 unit/mL elastase. The reaction mixture was incubated at 25°C for 10 min. The test samples were assayed for elastase inhibition by measuring its effect on elastase activity using an ELISA reader at 405 nm. Ursolic acid was used as a positive control, and the IC_{50} value of the sample was determined [13].

2.8. Statistical Analysis. Statistical analysis of the data was performed by PRIZM5 software (GraphPad, CA, USA), and data are presented as mean ± SD. One-tailed Student’s t-test was used for analyzing the significance of difference between groups, and P < 0.05 was considered statistically significant.

3. Results and Discussion

3.1. Skin-Related Properties of Plants Extracts in the Family Polygonaceae. Radical scavenging effect on DPPH, ABTS radical scavenging, elastase inhibition, tyrosinase inhibition, and nitric oxide assay on several Polygonum extracts were found to show potent activity. The results showed that the *Persicaria japonica* and *Rheum longifolius* has the NO assay (IC₅₀ 45.3 and under 25.0 μg/mL). For DPPH, the IC₅₀ of methanolic extract of *Polygonum ciliinerve* was 36.9, 15.4, and 19.2 μg/mL, respectively. In the ABTS radical scavenging activity, the IC₅₀ of methanolic extract of *Polygonum cuspidata* and *Polygonum alpinum* was 5.2 and 5.3 μg/mL, respectively. In tyrosinase inhibitory activity, the IC₅₀ of methanolic extract of *Polygonum sachalinensis* root and *Polygonum cuspidata* was 289.0 and 483.9 μg/mL, respectively. In the elastase inhibition assay, the IC₅₀ of methanolic extract of *Polygonum sachalinensis* was 5.2 and 5.3 μg/mL, respectively. In tyrosinase inhibitory activity, the IC₅₀ of methanolic extract of *Polygonum cuspidata* and *Polygonum alpinum* was under 100 μg/mL (Table 1).

3.2. Skin-Related Properties of *Persicaria senticosa* Fractions. Radical scavenging effect on 1,1-diphenyl-2-picrylhydrazyl (DPPH), ABTS radical scavenging, elastase inhibition, and nitric oxide assay on several *Persicaria senticosa* fractions was found to show potent activity. The results showed that...
Table 1: Skin-related properties of plants extracts in the family Polygonaceae.

| No. | Name                  | Parts                  | Anti-inflammatory | Antioxidant | Whitening | Anti-wrinkle |
|-----|-----------------------|------------------------|-------------------|-------------|-----------|--------------|
|     |                       |                        | NO (μg/mL)        | DPPH (μg/mL) | ABTS (μg/mL) | Elastase assay (μg/mL) |
| 1   | *Polygonum sachalinense* | Fruits            | 71.1 ± 6.9        | 98.5 ± 2.4   | 6.0 ± 0.1  | 308.8 ± 9.2  | <100          |
|     |                       | Root                 | >100              | >100         | >100       | >100         | <100          |
| 2   | *Rumex japonicus*     | Whole plants         | >100              | >100         | >100       | >100         | 400.6 ± 4.3  |
| 3   | *Polygonum ciliinerve* | Whole plants         | >100              | >100         | >100       | >100         | 216.0 ± 5.0  |
| 4   | *Polygonum manshuriense* | Whole plants     | >100              | >100         | >100       | >100         | 564.0 ± 9.3  |
| 5   | *Persicaria cuspidaatum* | Whole plants     | >100              | >100         | >100       | >100         | <100          |
| 6   | *Persicaria hydropiper* | Whole plants         | >100              | >100         | >100       | >100         | <100          |
| 7   | *Polygonum senticosum* | Aerial parts         | 71.8 ± 3.7        | 61.0 ± 0.6   | 17.5 ± 0.1 | >100         | 739.7 ± 6.5  |
| 8   | *Persicaria sieboldi*  | Whole plants         | >100              | >100         | >100       | >100         | <100          |
| 9   | *Polygonum orientale*  | Fruits               | 54.5 ± 2.3        | 50.6 ± 3.3   | 14.4 ± 0.1 | 445.4 ± 5.3  | <100          |
| 10  | *Polygonum cuspidata*  | Whole plants         | >100              | >100         | >100       | >100         | 263.9 ± 3.8  |
| 11  | *Persicaria tinctoria* | Aerial parts         | >100              | >100         | >100       | >100         | <100          |
| 12  | *Rumex conglomeratus*  | Root                 | 48.2 ± 1.6        | 18.9 ± 0.2   | >100       | >100         | 536.9 ± 2.9  |
| 13  | *Persicaria lapathifolia* | Whole plants   | >100              | >100         | >100       | >100         | 348.0 ± 7.3  |
| 14  | *Persicaria dissitiflora* | Whole plants     | >100              | >100         | >100       | >100         | <100          |
| 15  | *Persicaria thunbergii* | Aerial parts         | 65.7 ± 12.3       | >100         | >100       | >100         | >100          |
| 16  | *Polygonum aviculare*  | Whole plants         | 74.5 ± 4.2        | >100         | >100       | >100         | >100          |
| 17  | *Polygonum emarginatum* | Whole plants     | 79.3 ± 1.3        | >100         | >100       | >100         | 832.9 ± 9.8  |
| 18  | *Rumex obtusifolius*  | Aerial parts         | >100              | >100         | >100       | >100         | 348.8 ± 4.7  |
| 19  | *Rumex acetosella*     | Root                 | >100              | >100         | >100       | >100         | 438.1 ± 9.8  |
| 20  | *Rumex crispus*        | Aerial parts         | 90.4 ± 4.3        | >100         | >100       | >100         | 318.1 ± 7.6  |

1: Skin-related properties of plants extracts in the family Polygonaceae.
Table 1: Continued.

| No. | Name               | Parts        | Anti-inflammatory | Antioxidant | Whitening | Anti-wrinkle |
|-----|--------------------|--------------|------------------|-------------|-----------|--------------|
|     |                    |              | NO (μg/mL) | MTT (μg/mL) | DPPH (μg/mL) | ABTS (μg/mL) | Tyrosinase assay | Elastase assay |
| 21  | *Persicaria nepalensis* | Whole plants | 90.8 ± 3.1 | >100        | 50.3 ± 0.2  | 17.2 ± 0.1  | >1000          | >1000         |
|     |                    | Aerial parts | 83.3 ± 6.8 | >100        | 28.3 ± 0.3  | 9.8 ± 0.1   | >1000          | <100          |
| 22  | *Polygonum alpinum* | Aerial parts | 71.6 ± 7.9 | >100        | 15.4 ± 0.5  | 5.3 ± 0.1   | 564.8 ± 4.7    | <100          |
|     |                    | Whole plants | 72.1 ± 5.3 | >100        | 22.2 ± 0.1  | 9.0 ± 0.2   | >1000          | <100          |
| 23  | *Persicaria longiseta* | Whole plants | >100       | >100        | 44.9 ± 0.4  | 12.2 ± 0.1  | >1000          | <100          |
| 24  | *Persicaria chinensis* | Whole plants | 72.1 ± 9.3 | >100        | 19.2 ± 0.5  | 7.2 ± 0.0   | 726.4 ± 6.9    | <100          |
|     |                    | Whole plants | 45.3 ± 5.5 | >100        | 24.4 ± 0.7  | 9.4 ± 0.1   | 431.1 ± 7.8    | <100          |
| 25  | *Persicaria japonica* | Leaf, stem | >100        | >100        | 26.4 ± 1.0  | 10.7 ± 0.3  | >1000          | <100          |
| 26  | *Persicaria viscofera* | Whole plants | 86.5 ± 2.7 | >100        | 39.1 ± 0.6  | 11.4 ± 0.0  | 694.9 ± 6.8    | <100          |
| 27  | *Rumex longifolius* | Aerial parts | <25         | >100        | >100        | 78.2 ± 0.2  | >1000          | >1000         |
|     |                    | Aerial parts | 82.4 ± 5.8 | >100        | >100        | 82.0 ± 1.1  | >1000          | >1000         |
| 28  | *Persicaria conspicua* | Whole plants | >100       | >100        | 48.1 ± 0.6  | 16.8 ± 0.2  | >1000          | <100          |
| 29  | *Persicaria sieboldi* | Whole plants | >100       | >100        | 80.3 ± 0.8  | 21.9 ± 0.4  | >1000          | 406.2 ± 7.4   |
| 30  | *Persicaria perfoliata* | Aerial parts | 52.2 ± 6.4 | >100        | 68.8 ± 0.5  | 17.4 ± 0.4  | >1000          | 352.1 ± 3.2   |
|     |                    | Whole plants | >100       | >100        | 50.4 ± 2.4  | 15.4 ± 0.1  | >1000          | 164.0 ± 4.1   |
| 31  | *Rheum palmatum*    | Whole plants | 71.8 ± 6.8 | >100        | 27.3 ± 0.8  | 8.6 ± 0.2   | >1000          | <100          |
| 32  | *Rumex acetosa*     | Whole plants | >100       | >100        | >100        | 59.8 ± 1.2  | >1000          | >1000         |
| 33  | *Polygonum multiflorum* | Whole plants | >100       | >100        | 51.7 ± 0.9  | 16.1 ± 0.1  | >1000          | 647.4 ± 7.4   |
| 34  | *Persicaria lapathifolia* | Whole plants | 86.9 ± 5.2 | >100        | 24.5 ± 0.8  | 11.1 ± 0.1  | >1000          | <100          |

P.C. | L-NMMA 36.3 ± 6.1 μM | L-NMMA >100 μM | BHA 15.6 ± 0.2 | BHA 2.9 ± 0.1 | Arbutin 135.0 ± 19.9 | Ursolic acid 53.2 ± 6.1 |

the CH₂Cl₂ and EtOAc fractions have the NO assay (under 25 and 44.64 μg/mL, respectively). The DPPH and ABTS radical scavenging activities of EtOAc fractions were 13.7 and 5.0 μg/mL, respectively. In the elastase inhibition assay, the IC₅₀ of these compounds were under 100 μg/mL (Table 2).

3.3. Isolation and Determination of Compounds from *Persicaria senticosa* Extract. *Persicaria senticosa* aerial parts (1.4 kg), dried in the shade and powdered, were added to 40 L of 70% ethanol (HPLC grade) and two times at room temperature (each time for 2 days) and were concentrated in vacuum at 40°C to yield 180.4 g of extracts. The extracts were suspended in distilled water and then partitioned with n-hexane (4.0 L × 3), CH₂Cl₂ (4.0 L × 3), EtOAc (4.0 L × 3), and n-butanol (4.0 L × 3) to give n-hexane (11.7 g), CH₂Cl₂ (7.4 g), EtOAc (21.7 g), n-butanol (22.5 g), and water-soluble fractions (110.1 g) (Scheme 1). The fraction of EtOAc (21.7 g) was separated by MPLC that used gradient mixtures as eluents (F001-003).
Compounds 1 (3.2 mg) and 5 (3.9 mg) were isolated from F002 that used by prep-HPLC. The fraction F001 was separated by MPLC that used gradient mixtures as eluents (F011-F018). Compound 6 (1.5 mg) was isolated from F016 that used by preparative HPLC. Compound 7 (2.7 mg) was isolated from F017 that was used by preparative HPLC. F012 was separated by using MPLC which used gradient mixtures as eluents (F121-F124). Compound 4 (10.8 mg) was isolated from F124 that used by preparative HPLC. In addition, F014 was separated by preparative HPLC using gradient mixtures as eluents (F141-F143). Compound 3 (2.3 mg) was isolated from F141 using preparative HPLC. Compound 2 (4.8 mg) was isolated from F142 using semipreparative HPLC. The purification of the EtOAc soluble layer was performed by column chromatography separation and MPLC analysis to Compounds 1-7. It was identified as loliolide (1) [14], quercetin-3-O-glucoside (2) [15], quercetin-3-O-glucuronide (3) [16], 4-methoxy caftraric acid (4) [17], kaempferol-3-(6-methylglucuronide) (5) [18], quercetin-3-(6-methylglucuronide) (6) [19, 20], and quercetin (7) [21]. Structure was elucidated by a combination of 1D and 2D NMR and MS spectrometry as well as comparison with reported literatures (Figure 1).
3.4. Skin-Related Properties of Compounds from *Persicaria senticosa*. Radical scavenging effect on DPPH, tyrosinase inhibition, and nitric oxide assay on several compounds from *Persicaria senticosa* was found to show potent activity (Fig. S4–7). The results showed that Compound 7 has the NO assay (IC$_{50}$ 29.7 $\mu$g/mL). For DPPH, the IC$_{50}$ of Compounds 2, 3, 5, and 7 was 39.6, 31.2, 37.0, and 22.7 $\mu$g/mL, respectively. In tyrosinase inhibitory activity, the IC$_{50}$ of Compound 7 was 14.3 $\mu$g/mL (Table 3).

### 4. Conclusions

*Persicaria senticosa* is an annual plant in the family Polygonaceae which is distributed in whole Korea. Since early times, this plant has been used as folk medicine with beneficial effects for the treatment of various diseases. This study evaluated skin-related properties and constituents from the aerial part extract of *Persicaria senticosa* and thirty-four Polygonaceae plants. In the course of screening for cosmetic ingredients by measuring the radical scavenging effect on DPPH, ABTS radical scavenging, antiwrinkle was evaluated using elastase inhibition, whitening was studied by tyrosinase inhibition, and anti-inflammatory was tested on nitric oxide assay. Several Polygonum extracts were found to show potent activity. The results showed that the *Persicaria senticosa* methanolic extract has the DPPH and ABTS radical scavenging activities (IC$_{50}$ 61.0 and 17.5 $\mu$g/mL). In the elastase inhibition assay and nitric oxide assay, the IC$_{50}$ of methanolic extract of *Persicaria senticosa* was 241.5 $\mu$g/mL and 71.8 $\mu$g/mL, respectively. The *Persicaria senticosa* 70% ethanolic extract was partitioned with n-hexane, CH$_2$Cl$_2$, EtOAc, n-BuOH, and aqueous fractions.

EtOAc soluble fraction showed a potent skin-related activity (Figure 2 and Table 3). These results suggested that
active components in *Persicaria senticosa* responsible for the skin-related activity were concentrated in the EtOAc soluble fraction of *Persicaria senticosa* (Scheme 1). On the other hand, the n-hexane, dichloromethane soluble fraction, and the BuOH soluble fraction derived from the extract of *Persicaria senticosa* showed equipotent activity on nitric oxide assay, DPPH, and ABTS radical scavenging activity, whereas remaining water fraction demonstrated poor inhibitory effects (Table 2).

Thus, bioassay-guided purification of three active fractions, i.e., the EtOAc soluble fraction of *Persicaria senticosa* was conducted to purify the active principles responsible for the skin-related activity followed by the process described in Scheme 1, respectively.
The purification of the EtOAc soluble layer from *Persicaria senticosa* 70% ethanolic extract was performed by column chromatography separation and MPLC analysis to Compounds 1-7. It was identified as lolilolide (1), quercetin-3-O-glucoside (2), quercetin-3-O-glucuronide (3), 4-methoxy caftraric acid (4), kaempferol-3-(6-methylglucuronide) (5), quercetin-3-(6-methylglucuronide) (6), and quercetin (7). Structure was elucidated by a combination of 1D and 2D NMR and MS spectrometry as well as comparison with reported literatures (Fig. S2). Radical scavenging effect on 1,1-diphenyl-2-picrylhydrazyl (DPPH), tyrosinase inhibition, and nitric oxide assay on several compounds from *Persicaria senticosa* was found to show potent activity. The results showed that Compound 7 has the NO assay (IC_{50} 29.7 μM). For DPPH, the IC_{50} of Compounds 2, 3, 5, and 7 was 39.4, 32.1, 37.0, and 22.7 μM, respectively. In tyrosinase inhibitory activity, the IC_{50} of Compound 7 was 14.3 μM. As shown in Figure 3, Compounds 2 and 5 are the main compounds in the EtOAc soluble fraction of *Persicaria senticosa*(Fig. S1). And Compounds 2 and 5 showed excellent antioxidant activity(Figure 4), which is consistent with previous studies [18, 22].

This present study demonstrated that *Persicaria senticosa* and Polygonasæae contain chemical compounds with good skin-related activities and could be interesting as a novel source of bioactive agents for cosmetic industries.

**Data Availability**

The data used to support the findings of this study are included in the Supplemental Information File.

**Conflicts of Interest**

The authors have no conflicts of interest to declare.

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**Supplementary Materials**

Attached is the NMR as supplementary data for this research work (Supplementary Materials). Figure S1: specimen photo of *Persicaria sentiecosa*. Figure S2: DPPH radical scavenging activity assay data of isolated compounds from *Persicaria sentiecosa*. Figure S3: tyrosinase inhibition assay data of isolated compounds from *Persicaria sentiecosa*. Figure S4: NO assay data of isolated compounds from *Persicaria sentiecosa*. Figure S5: cell cytotoxicity assay data of isolated compounds from *Persicaria sentiecosa*. Figure S6: spectral data of isolated compounds *Persicaria sentiecosa* (Compounds 1-7). Figure S7: high-performance liquid chromatography (HPLC) condition and profile of EtOAc fraction of *Persicaria sentiecosa*. (Supplementary Materials)

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