Letter to the Editor

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Cornuside, identified in *Corni fructus*, suppresses melanin biosynthesis in B16/F10 melanoma cells through tyrosinase inhibition

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To the Editor

Objective section: To enhance skin whitening efficacy, tyrosinase activity and melanin biosynthesis should be inhibited in the skin. To achieve this goal, we examined the extract of *Corni fructus* (ECF), and identified cornuside, a functional metabolite in the ECF. Cornuside, identified in the ECF, effectively inhibited melanin biosynthesis in B16/F10 cells, possibly by suppressing tyrosinase activity. Therefore, this study suggests that cornuside can be used as a cosmetic ingredient for skin whitening.

Corni fructus is the fruit of *Cornus officinalis*, and has been widely used as an important herbal medicine in East Asia, including Korea. *C. fructus* has pharmacological efficacies such as cirrhosis, blood pressure strengthening, anticancer and antibacterial effects [1]. Major components of *C. fructus* are gallic acid, malic acid, tartaric acid, ursolic acid, morroniside, loganin and sweoside [2].

Melanin is a biopolymer of phenols widely distributed in nature and is a complex of black pigment and protein. Melanin, which is present in animals, plants and microorganisms, is not essential for growth and development, but is a substance that enhances the viability of any environment. Pigment accumulation in the skin such as

blemishes and freckles is due to abnormal increase of melanin pigment in the epidermis and is mainly synthesized in melanosomes of melanocytes present in the epidermis [3]. Tyrosinase, a key enzyme of melanin biosynthesis, initiates melanin biosynthesis by oxidizing tyrosine in melanosomes [4]. In order to increase skin whitening efficacy, melanin biosynthesis and tyrosinase activity need to be inhibited in the skin. In this study, we identified cornuside present in the ECF, and investigated the skin whitening effects of cornuside.

Using the UPLC-MS/MS method, we analyzed a variety of metabolites in ECF, and identified cornuside as a functional metabolite. Cornuside is included in ECF at 0.821 mg/g DW (Figure 1A). Cornuside is a metabolite of the secoiridoid glucoside family and is known to show anti-neoplastic, anti-inflammatory, hepatoprotective and anti-diabetic effects [5]. We first examined whether cornuside, identified in ECF, shows cytotoxicity in B16/F10 melanoma cells. As shown in Figure 1B, cornuside showed no cytotoxicity in B16/F10 cells. Next, we examined whether cornuside shows tyrosinase inhibition. As shown in Figure 1C, cornuside showed about 30% tyrosinase inhibition at a concentration of 50 µg/mL. In addition, cornuside inhibited melanin biosynthesis by about 75% at a concentration of 50 µg/mL (Figure 1D). These results reveal that cornuside, a functional metabolite identified in ECF, can inhibit melanin biosynthesis in B16/F10 cells by inhibiting tyrosinase activity. Therefore, this study suggests that cornuside can be used as a cosmetic ingredient to enhance skin whitening efficacy. The experimental methods used in this study are described in the supplement section.

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Figure 1: Cornuside has biological efficacies in improving skin whitening. (A) ECF contains cornuside (0.821 mg/g DW) as a functional ingredient. The UPLC-MS/MS was performed using a Waters Xevo TQ-S system (Waters, USA). (B) Cell proliferation assay was carried out using the MTS assay in B16/F10 cells. Error bars represent SD of three biological replicates. (C) Cornuside inhibits the activity of tyrosinase. 0.1 M sodium phosphate buffer and 1.5 mM tyrosine were mixed and tyrosinase (1,500–2,000 U/mL) was added sequentially. The absorbance was measured at 490 nm using an ELISA reader. Error bars represent SD of three biological replicates. (D) Cornuside inhibits melanin accumulation in B16/F10 cells. B16/F10 cells were treated with 10 µM forskolin. Absorbance was measured at 405 nm. Error bars represent SD of three biological replicates.

Ethical approval: This letter does not contain any studies with human participants or animals performed by any of the authors.

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