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Analysis of essential oils by GC/MS and tilianin by HPLC/UV of the aerial parts of *Agastache rugosa*

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Abstract

Agastache rugosa is an edible plant belonging to the Lamiaceae family and has different names including Korean Mint, purple giant hyssop, Indiana mint, and wrinkled giant hyssop. *A. rugosa* is renowned as a vegetable and herbal medicine in conventional therapy. Many compounds of *A. rugosa* were detected by instruments for industrial use. To examine various compounds in *A. rugosa*, gas chromatography-mass spectrometry (GC/MS) and high-performance liquid chromatography coupled with an ultraviolet-visible method (HPLC/UV) was developed. Essential oils including those used to treat diseases were extracted by a steam distillation method and characterized using the GC/MS method. Tilianin, a polyphenol compound possessing antioxidant capacity, was then analyzed by the HPLC/UV method. The six compounds of *A. rugosa* essential oil were identified as 1-heptanol, N,N-dimethylvinylamine, limonene, isomenthone, 4-allylanisole, and pulegone. Among these, the most abundant component was 4-allylanisole, accounting for 90.4% of the compounds. The tilianin content from aerial parts of *A. rugosa* was 9.58 $mg \cdot g^{-1}$ extract. Tilianin thus may serve as a marker compound for evaluating the bioactivity and determining the therapeutic efficacy of this plant. *A. rugosa* containing these bioactive compounds is expected to be a beneficial resource for expanding industrial applications in the future.

Key words: *Agastache rugosa*, essential oil, quantitative analysis, steam distillation, tilianin

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Introduction

Agastache rugosa is an edible plant belonging to the Lamiaceae family (Kim et al., 2017; Do et al., 2020). This plant also has different names including Korean Mint, purple giant hyssop, Indiana

mint, and the wrinkled giant hyssop. *A. rugosa* is renowned as a vegetable and herbal medicine in conventional treatment. It is broadly cultivated in China for treating diseases such as anxiety, nausea, and bacterial infections (Gong et al., 2017; Kim et al., 2018). Previous studies showed that constituents of *A. rugosa* have many pharmacological activities, including antioxidant and anti-HIV integrase actions (Kim et al., 1999; Shin, 2004). Additionally, *A. rugosa* has demonstrated antifungal, antibacterial, carminative, and antipyretic activities (Hong et al., 2001; Oh et al., 2006; Kim, 2008; Haiyan et al., 2016). Some research on its chemical composition revealed that this plant contains an abundance of essential oils. Gas chromatography/mass spectrometry (GC/MS) analysis of *A. rugosa* determined 43 constituents present in the essential oils, 34 of which are commonly found in both the flowers and leaves. There was a large amount of methyl-chavicol and 2-phenyl-propionaldehyde in the leaves, whereas L-limonene, *trans*-caryophyllene, and 2-ethyl-2,5-dimethylpentane were prevalent in the flower (Lim et al., 2013).

Essential oils are natural products, extracted from fragrant plants, historically used throughout the world as anti-inflammatory, soothing, and stimulating agents. They have potential use in the modern application of experimental medicine. Essential oils are generally utilized and produced in the cosmetic, food, and medicinal industries as natural alternatives to synthetic products for preventing and treating infectious diseases. Traditional usage of essential oils includes treating diseases in the digestive, and nervous systems, respiratory tract, and skin (Chung et al., 2003; Firenzuoli et al., 2014; Park et al., 2016; Liu et al., 2019; Hong et al., 2020; Park et al., 2020a; Choi et al., 2021; Jung and Jung, 2022; Yuk, 2022). Various methods of obtaining essential oils from plant resources include steam distillation, expression, solution extraction, cold enfleurage, and supercritical extraction. Each process has its strengths and weaknesses, and from an economic perspective, the steam distillation method is the most appropriate for many production purposes. The content and yield in the steam distillation process depend on the component acquisition and the extraction method (Lee, 2015; Seify et al., 2018; Song et al., 2020).

Tilianin is a polyphenol compound possessing antioxidant capacity (Park et al., 2020a; 2020b). It is also well-known for its health benefits such as modulating oxidative stress-related inflammation (Nam et al., 2006; Hernández-Abreu et al., 2009) and apoptosis and cardio-protective and anti-hypertensive behaviors (Dauer and Przedborski, 2003; Gálvez et al., 2015; Wang et al., 2017; Zeng et al., 2018; Hwang et al., 2021).

This research aimed to examine the essential oils in *A. rugosa* by using GC/MS method and tilianin through high-performance liquid chromatography (HPLC) via the ultraviolet-visible (UV) method.

Materials and Methods

Plant materials

The leaves and stems of *A. rugosa* which were cultivated at Eumseong, Korea. An authenticated voucher specimen (MPS006452) was deposited at the Herbarium of the Department of Herbal Crop Research, National Institute of Horticultural and Herbal Science, Eumseong 27709, Korea.

Instruments and reagents

Analysis was conducted by an HPLC instrument (Agilent 1260 Infinity II Quat Pump, CA, USA) equipped with a diode array detector (DAD WR detector, CA, USA), pump, and auto-sampler with an INNO C18 column. HPLC-grade solvents

such as water, acetonitrile, and methanol were purchased from J. T. Baker, (Philipsburg, Pennsylvania). Ethanol (EtOH) and acetic acid were purchased from Samchun Chemicals, (Pyeongtaek, Korea). GC/MS analysis was conducted using a 7890BGC/7010QQQ MS instrument (Agilent, Palo Alto, CA, USA) and a DB5-MS capillary column (30 m × 0.25 mm, film thickness 0.25 μm). Tilianin was obtained from the Natural Product Institute of Science and Technology (Anseong, Korea).

Essential oil by steam distillation and GC/MS conditions

The *A. rugosa* aerial parts (2.58 kg) were collected (Fig. 1A) and subjected to conventional steam distillation to extract the essential oil. Boiling distilled water crosses the plant to produce vapor, which is then charged with essential oil and passed through the condenser to a receiving flask (Fig. 1B and C). In the separation funnel, the essential oil will float on top of the hydrosol (distilled water component) for separation. The tap was then unlocked so that the water layer slowly ran out of the funnel to retain the oil (Fig. 1D).

GC/MS analysis was conducted using a 7890BGC/7010QQQ MS instrument (Agilent, Palo Alto, CA, USA) and a DB5-MS capillary column (30 m × 0.25 mm, film thickness 0.25 μm). Helium was used as a carrier gas at a flow rate of 1 $mL \cdot min^{-1}$. The injector port, ion source, and interface temperatures were 300, 230, and 300°C, respectively. The GC oven was set up as follows: 40°C for 3 min, 40 - 230°C at $2°C \cdot min^{-1}$, 230 - 300°C at $5°C \cdot min^{-1}$, and 300°C for 15 min. The split ratio was 1 : 10. Masses were scanned from *m/z* 50 to 800.

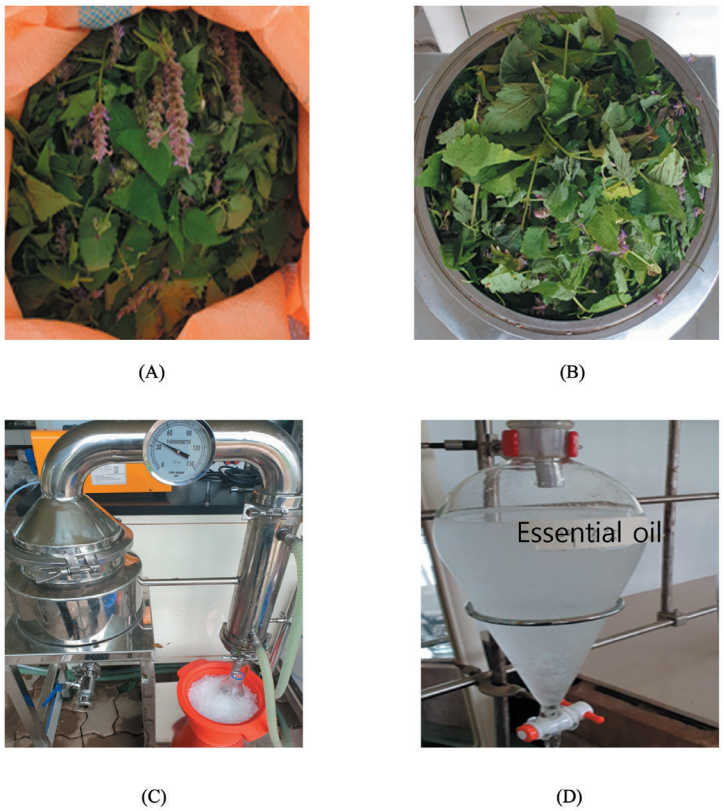

Fig. 1. Extraction procedure of collection of *Agastache rugosa* (A), extraction mantle of *A. rugosa* (B), steam distillation (C), and essential oil and hydrosol (D).

Sample preparation and HPLC conditions

Dried *A. rugosa* (10 g) was extracted in EtOH under reflux for three hours, a process that was repeated three times, and then a vacuum concentrator was used to dry the sample for 2.0 g of extract. For quantitative evaluation of the extract, *A. rugosa* extract was dissolved in methanol (MeOH) and sonicated for 30 min. Next, the sample was filtered using a 0.45 μm polyvinylidene fluoride (PVDF) membrane filter. A stock solution was also prepared. The composite content of all samples was calculated by the calibration curves.

Tilianin was conducted for quantitative analysis using a reverse-phase HPLC system. Chromatographic separation was carried out using an INNO C18 column (25 cm × 4.6 mm, 5 μm). This analysis was performed by a gradient elution system which used a mobile phase composed of 0.5% acetic acid in water (A) and acetonitrile (B). The elution conditions were 75% A at 0 min until 5 min, 30% A at 20 min, 0% A at 30 min, 0% A at 40 min, 75% A at 41 min, and 75% A at 50 min. The column temperature was retained at 20℃. The injection volume was 10 μL and the flow rate was set at 1.0 $mL \cdot min^{-1}$.

Calibration curve

Next, the compound was dissolved in MeOH (1.0 $mg \cdot mL^{-1}$) to obtain the standard stock solution of tilianin. The stock solutions were serially diluted to the desired concentrations to prepare the working solutions used to construct the calibration curve. The samples were dissolved in MeOH (32 $mg \cdot mL^{-1}$). Then, both the standard and sample solutions were filtered using a 0.45-μm PVDF filter before use. From the corresponding calibration curves, the analysis content was determined. The calibration function of tilianin is measured with peak area (Y), concentration (X, $\mu g \cdot mL^{-1}$), and mean values (n = 3) ± standard deviation.

Results and Discussion

Conventional steam distillation was used to extract the essential oils in the aerial parts of *A. rugosa* (Fig. 1). The yield was 0.35% ($v \cdot w^{-1}$) and the leaf oil gave off a strong fragrant odor and brilliant yellow color. After extraction, the essential oil was analyzed by GC/MS, and a total of six major compounds were identified (Figs. 2 - 4), where all components were organized corresponding to their elution on the DB5-MS capillary column. The primary compounds of *A. rugosa* oil were 4-allylanisole (90.4%), followed by N,N-dimethylvinylamine (3.2%) and limonene (2.2%), and the minor components were isomenthone (2.0%), 1-heptanol (1.2%), and pulegone (1.0%) (Table 1). 4-Allylanisole is a natural product that can be found in the essential oils of many plants. 4-Allylanisole possesses many pharmacological and biological activities, including antioxidant, antimicrobial, and anti-inflammatory properties, and its flavors can be also used in the pharmaceutical, cosmetic, and antimicrobial fields for food preservation (Silva-Alves et al., 2013).

Methyl chavicol (80.24%), also known as 4-allylanisole (Kim, 2008), is the primary component of the essential oil from *A. rugosa* leaf extract. In addition, 31 compounds were determined from this plant (Kim, 2008), while only six compounds were characterized in this study. Another study was conducted on the dried flower and leaf of *A. rugosa* with a similar method and illustrated 21 components in the flower oil, representing 99.7% of the total oil (Gong et al., 2012). The major constituents were oxygenated terpenes (35.4%), such as pulegone (34.1%), 4-allylanisole (29.5%), *p*-menthan-3-one (19.2%), and monoterpenes (8.8%). Meanwhile, 26 compounds (99.6%) in leaf oil were identified, *p*-menthan-3-one (48.8%) being

the main component, and the others were 4-allylanisole (20.8%), monoterpenes (8.3%), and oxygenated terpenes (5.6%). The aerial parts of this plant were identified, and the essential oil was quantified by GC/MS analysis, which showed a total of 37 major components (Li et al., 2013). The principal constituents were methyleugenol (50.51%), estragole (8.55%), and eugenol (7.54%), and others present in lower amounts included thymol (3.62%), pulegone (2.56%), limonene (2.49%), and caryophyllene (2.38%). The research above exhibited a variety of essential oils in *A. rugosa*, whereas this study determined only six compounds. This trend can be caused by differences in growing location, collecting period, and plant location.

Table 1. Chemical composition of *Agastache rugosa* essential oil.

Compound	Area (%)	RI	
		Observed[y]	Literature[z]
1-Heptanol	1.2	691	969
N,N-dimethylvinylamine	3.2	700	604
Limonene	2.2	1,024	1,031
Isomenthone	2.0	1,158	1,149
4-Allylanisole	90.4	1,192	1,195
Pulegone	1.0	1,230	1,209

RI, retention index.

[y] Retention index on column.

[z] Retention index relative to literature value.

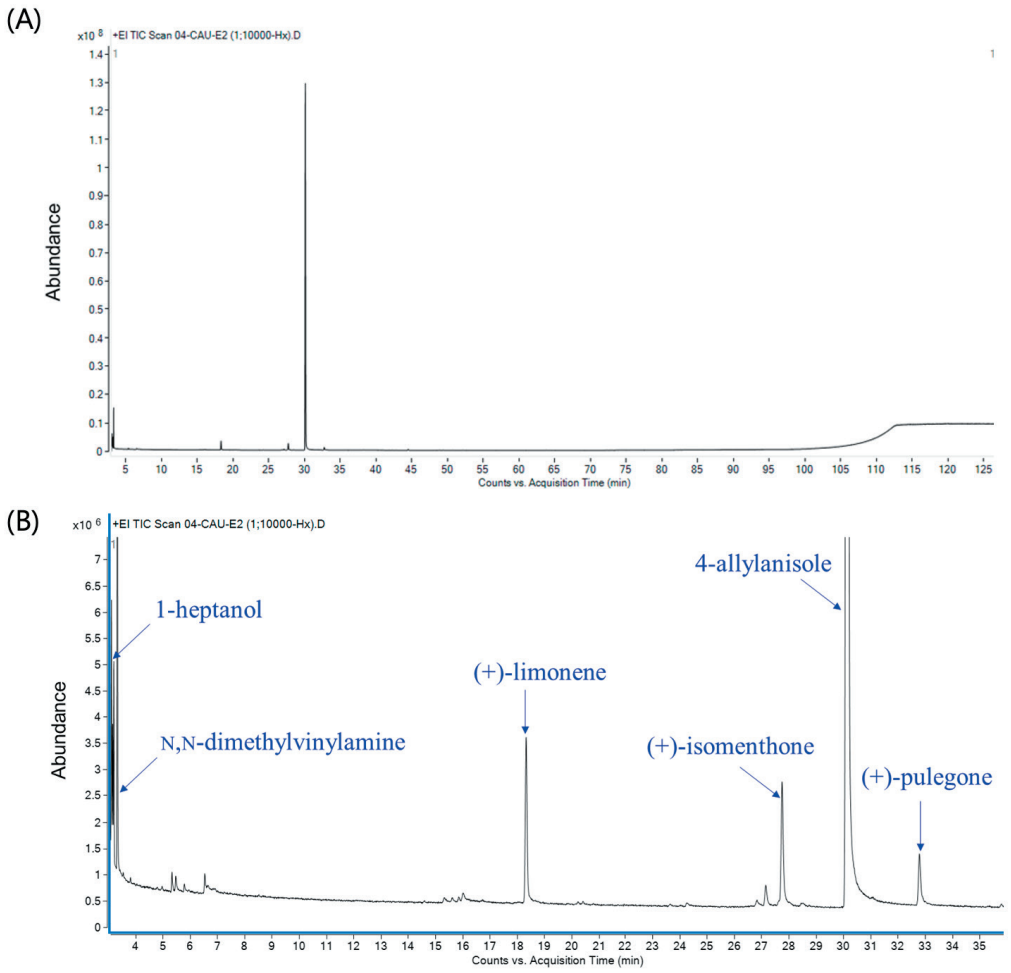

Fig. 2. GC/MS chromatograms of essential oils from *Agastache rugosa* (A) and expanded chromatogram (B).

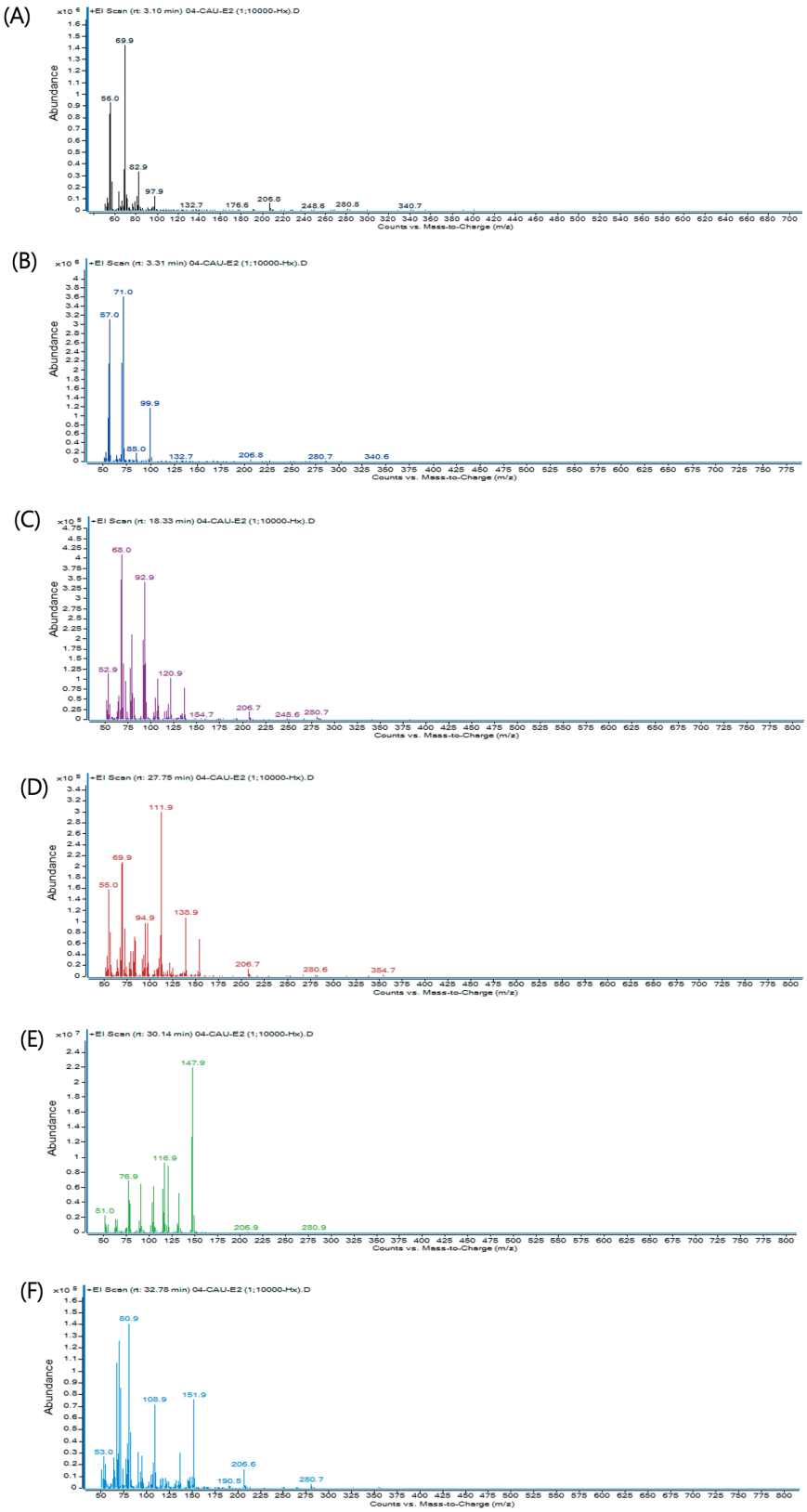

Fig. 3. Gas chromatography-mass spectrometry (GC/MS) data of essential oils (1-heptanol [A], N,N-dimethylvinylamine [B], limonene [C], isomenthone [D], 4-allylanisole [E], and pulegone [F]) from *Agastache rugosa*.

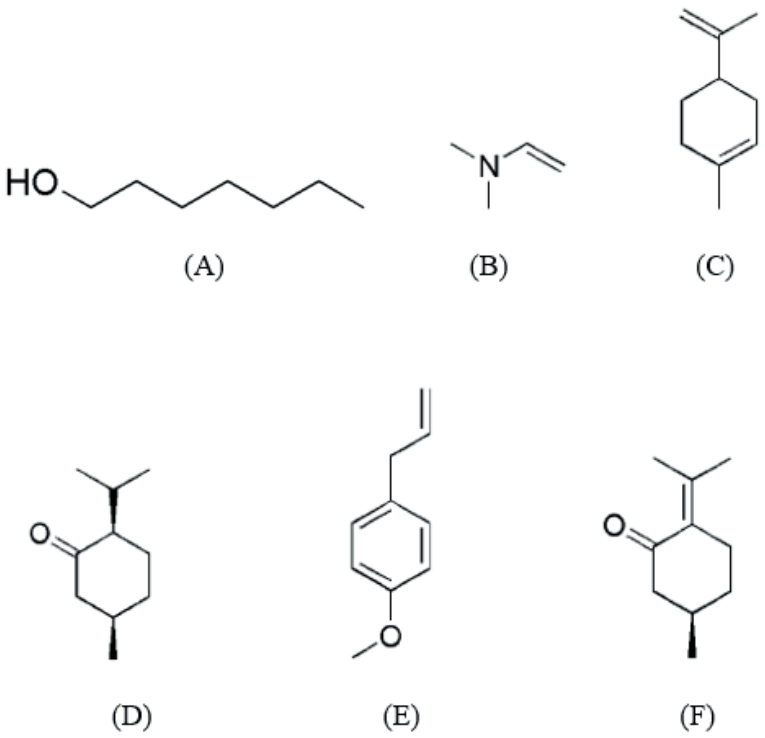

Fig. 4. Chemical structures of 1-heptanol (A), N,N-dimethylvinylamine (B), limonene (C), somenthone (D), 4-allylanisole (E), and pulegone (F).

Tilianin (Fig. 5) is a flavonoid glycoside found in a wide range of herbal plants such as *A. mexicana, A. rugosa, Dracocephalum moldavica, D. tanguticum, D. moldavica, Lygodium japonicum,* and *Discocleidion rufescens* (Hernandez-Abreu et al., 2013; Wei et al., 2016; Wang et al., 2018). Tilianin has various biological and therapeutic impacts (Nam et al., 2005). There are various mechanisms contributing to the protective activity of tilianin such as free radical scavenging and inflammation modulation. Tilianin is used to treat a variety of ailments, and to modulate health and longevity. It is a potential treatment for many different diseases via several therapeutic pathways (Akanda et al., 2019).

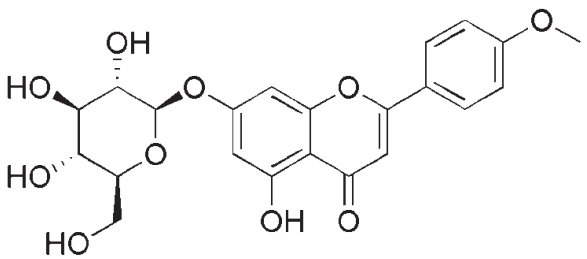

Fig. 5. Chemical structures of tilianin.

To determine the amount of tilianin in aerial parts of *A. rugosa*, different amounts of tilianin were dissolved in MeOH to obtain stock solutions. The calibration curve for tilianin shown in Table 2 has good linearity. The calibration equation was Y = 25.468X + 579 and the correlation factor was 0.9981. HPLC/UV analysis was then carried out to examine the amount of tilianin in the aerial parts of *A. rugosa*. Fig. 6 described the standard tilianin and *A. rugosa* extract. The retention

time of tilianin was 13.2 min, indicating an excellent separation. A wavelength of 333 nm provided the most efficient response for tilianin quantification in a single run, comprising all impurities. Co-eluted peaks were not observed during tilianin quantification, demonstrating that this method is reliable. The tilianin content was examined as 9.58 mg·g^{-1} (Table 3). Another investigation showed that the tilianin content of *A. rugosa* leaf extract was 21.14 mg·g^{-1} (Hwang et al., 2021). Thus far research has explored four parts (flower, leaf, stem, and root) of *A. foeniculum*, belonging to the same family as *A. rugosa* (Park et al., 2014). The results indicate that flowers of *A. foeniculum* contained 1.0 mg·g^{-1} tilianin, and the leaves 0.5 mg·g^{-1}. Tilianin was not identified in the stem of *A. foeniculum* and the root only presented a small amount. We found the content of tilianin to be lower than the two articles above, but higher than that of other plants in its family. This may be because tilianin content could vary depending on solvent extraction or drying temperature. Nevertheless, tilianin could contribute to the antioxidant capacities of *A. rugosa* and the plant's biological and pharmaceutical functions.

Table 2. Calibration curve of tilianin in *Agastache rugosa*.

Compound	t_R	Calibration equation[y]	Correlation factor, r^{2z}
Tilianin	13.4	Y = 25.468X + 579	0.9981

t_R, retention time.

[y] Y = peak area, X = concentration of standards (μg·mL^{-1}).

[z] r^2 = correlation coefficient based on three data points in the calibration curves.

Table 3. Content of tilianin in *Agastache rugosa* extract.

Compound	Content (mg·g^{-1} extract)
Tilianin	9.58 ± 0.01

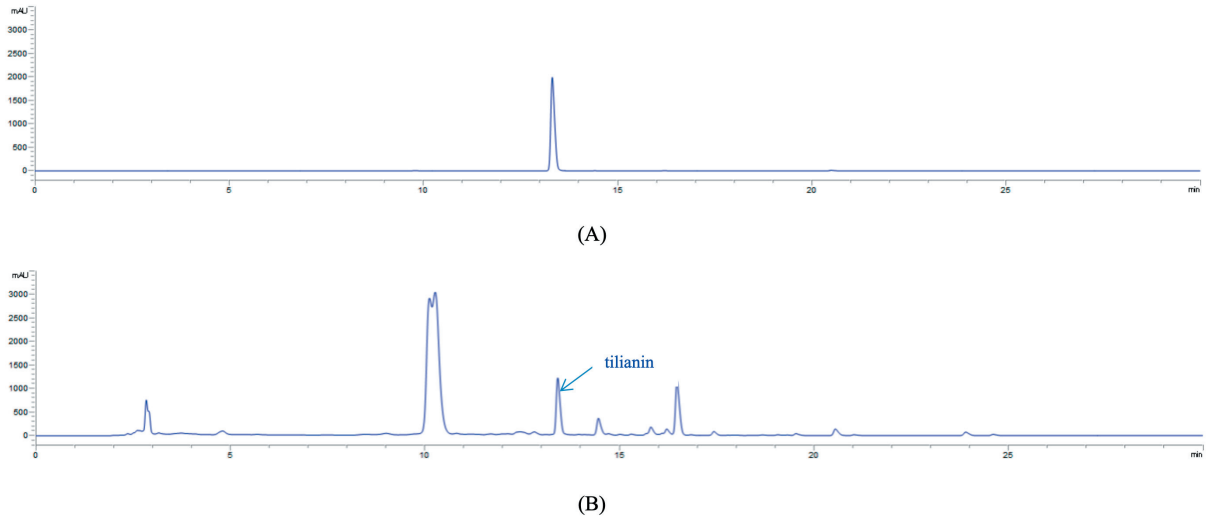

Fig. 6. High-performance liquid chromatography (HPLC) chromatograms of tilianin (A) and the MeOH extract of *Agastache rugosa* (B).

In conclusion, the aerial parts of *A. rugosa* were extracted with ethanol and subjected to conventional steam distillation to obtain the essential oil. After analysis by the GC/MS method, six components were identified: 1-heptanol, N,N-dimethylvinylamine, limonene, isomenthone, 4-allylanisole, and pulegone. Among these six compounds, the most prevalent was 4-allylanisole, while the least prevalent was pulegone. Furthermore, the tilianin content was examined by HPLC analysis, and 9.58 $mg \cdot g^{-1}$ extract of tilianin was found in the aerial parts of *A. rugosa.* Through GC/MS and HPLC analysis, two main compounds namely 4-allylanisole and tilianin were obtained from *A. rugosa.* They may serve as a marker compound for evaluating the bioactivity and determining the therapeutic efficacy of this plant.

Conflict of Interests

No potential conflict of interest relevant to this article was reported.

Authors' Contributions

G. H. Tran, J. Choi, H.-D. Lee: HPLC analysis, Y. Lee: sampling and experimental design, J. S. Hwang, D. Y. Kim: steam distillation, H. M. Lee: data analysis and data curation, and S. Lee: experimental design and writing.

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