

Article

Analysis of Marker Compounds in *Lindera erythrocarpa* from Diverse Geographical Regions of Korea

Neil Patrick Uy ¹, Jung-Hee Kim ², Doo-Young Kim ², Jajung Ku ³ and Sanghyun Lee ^{1,4,*}

¹ Department of Plant Science and Technology, Chung-Ang University, Anseong 17546, Republic of Korea; uyneilpatrick@gmail.com

² Natural Medicine Research Center, Korea Research Institute of Bioscience and Biotechnology, Cheongju 28116, Republic of Korea; chusaa@kribb.re.kr (J.-H.K.); rose73@kribb.re.kr (D.-Y.K.)

³ Forest Bioresources Department, National Institute of Forest Science, Suwon 16631, Republic of Korea; jajungku@korea.kr

⁴ Natural Product Institute of Science and Technology, Anseong 17546, Republic of Korea

* Correspondence: slee@cau.ac.kr; Tel.: +82-31-670-4688

Abstract: *Lindera erythrocarpa* M., a medicinal plant commonly found in China, Japan, and Korea, is well known for its antioxidant, anti-inflammatory, and potential anti-cancer effects. However, data on the quantification of different marker compounds found in this species across plant parts and geographical regions remain limited. To address this gap in the literature, the marker compounds methyl lucidone (1), methyl linderone (2), and kanakugiol (3) in leaves and stems of *L. erythrocarpa* collected from five different regions in the Republic of Korea were analyzed using high-performance liquid chromatography (HPLC/UV). Among the three compounds analyzed, kanakugiol (3) was the most abundant and was predominantly found in the stem samples. Overall, stems contained higher concentrations of methyl linderone (2) and kanakugiol (3) than the leaves. These findings highlight the importance of considering regional factors and plant part selection to maximize the yield of bioactive compounds. The results support the potential of *L. erythrocarpa* as a medicinal source and contribute to the standardization and quality improvement of herbal goods, thereby enhancing consumer protection and product efficacy.

Keywords: quantitative analysis; HPLC; *Lindera erythrocarpa*; kanakugiol; phytochemicals



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1. Introduction

Lindera erythrocarpa M., a deciduous small tree or shrub belonging to the Lauraceae family, is widely found in China, Japan, and the Republic of Korea [1]. Along with other *Lindera* species, it is considered an important medicinal plant in this region [2]. Notable for its antioxidant and potential anti-cancer properties, *L. erythrocarpa* holds significant pharmacological potential [3].

This plant also contains essential oils that have previously been found to exhibit antibacterial activities against resistant skin pathogens [4] and anti-inflammatory in lipopolysaccharide-stimulated RAW264.7 cells [2]. In addition, *L. erythrocarpa* has also been found to have melanin biosynthetic inhibitory effects [5] and dermatoprotective properties against UVA-induced oxidative stress [6]. Due to these bioactive properties, many of the studies and products made from this plant have been focused on the skin care industry. The essential oils from this plant also hold potential for use in aromatherapeutic applications.

Three key marker compounds, methyl lucidone (1), methyl linderone (2), and kanakugiol (3), are identified as major contributors to its therapeutic effects [7]. These compounds exhibit various bioactive properties, including anti-inflammatory [8], juvenile hormone antagonist [7], anti-cancer, antioxidant, and antifungal activities [9–11].

Despite its widespread traditional use, scientific data on the quantification of these marker compounds in different plant parts and from various geographic locations remain

limited. There is a gap in the comprehensive chemical profiling of active components in *L. erythrocarpa* as previous research has mostly focused on the pharmacological effects of these extracts [12]. Identifying the specific plant parts and regions that contain the highest concentrations of these compounds is essential. A better understanding of the distribution and concentration of phytochemicals such as methyl lucidone (1), methyl linderone (2), and kanakugiol (3) across different plant parts and regions can enhance the standardization and quality control of herbal medicines [13].

To address this gap in the literature, this study aimed to quantify the marker compounds methyl lucidone (1), methyl linderone (2), and kanakugiol (3) in the leaves and stems of *L. erythrocarpa* collected from five different provinces in the Republic of Korea. Specifically, this study aimed to determine the concentrations of these compounds in these plant parts and compare the levels of these compounds among samples from different provinces. These compounds have potential applications in the pharmaceutical, nutraceutical, and skin care industries, pending further studies of their efficacies.

By elucidating the distribution of these key marker compounds, this study advances our understanding of the pharmacological properties of *L. erythrocarpa* and supports the plant's legitimacy as a medicinal herb [14]. The findings could improve the quality control of herbal products, thereby ensuring consumer safety and efficacy.

2. Materials and Methods

2.1. Plant Materials

Ten extracts of *L. erythrocarpa* were provided by the Republic of Korea Research Institute of Bioscience and Biotechnology (KRIBB) in Daejeon, the Republic of Korea. Additionally, two samples were collected from Gyeonggi Province and supplied by Dr. Ku of the Forest Bioresources Department, the National Institute of Forest Science, Suwon, the Republic of Korea. All samples (10 g in 200 mL MeOH) were extracted under reflux for 5 h thrice. Afterward, the extracts were filtered with Whatman qualitative filter paper 1 and concentrated in vacuo with a rotary evaporator. The samples were named according to the plant part used and the province from which they were sourced (Table 1). The Gyeonggi Province sample (GGL and GGS) and collection sites of these plants are shown in Figure 1.

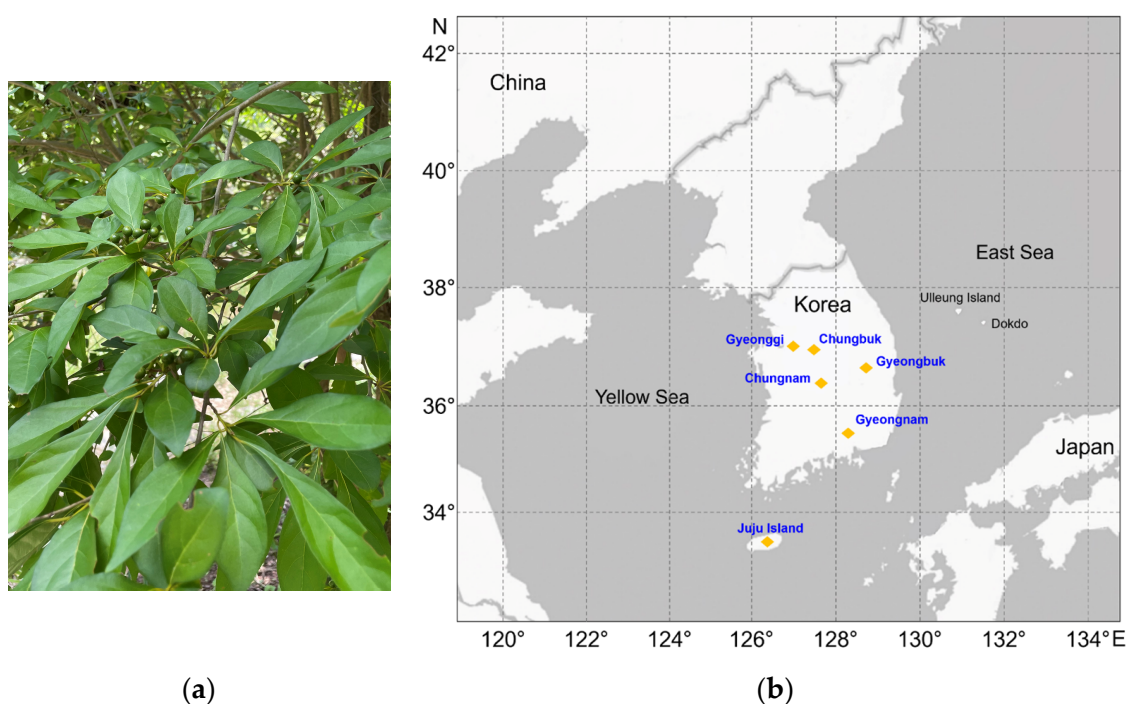


Figure 1. The Gyeonggi Province sample (a) and the collection locations (b) of the different samples of *L. erythrocarpa*.

Table 1. Information on the 12 samples of *L. erythrocarpa* used in this study.

Collection Site	Plant Part	Sample Name
Gyeonggi Province	Leaf	GGL
	Stem	GGS
Chungbuk Province	Leaf	CBL
	Stem	CBS
Chungnam Province	Leaf	CNL
	Stem	CNS
Gyeongbuk Province	Leaf	GBL
	Stem	GBS
Gyeongnam Province	Leaf	GNL
	Stem	GNS
Jeju Island	Leaf	JIL
	Stem	JIS

2.2. Instruments, Chemicals, and Reagents

Chromatographic analysis was performed using a high-performance liquid chromatography (HPLC) system (Agilent Technology 1290 Infinity II Lexington, MA, USA) equipped with a pump, an auto-sampler, and a UV detector. The solvents used for HPLC (water and acetonitrile (ACN)) were obtained from Honeywell (Burdick and Jackson, Muskegon, MI, USA), and trifluoroacetic acid (TFA) was sourced from J.T. Baker (Phillipsburg, PA, USA). The standard compounds used were methyl lucidone (1), methyl linderone (2), and kanakugiol (3) (Figure 2).

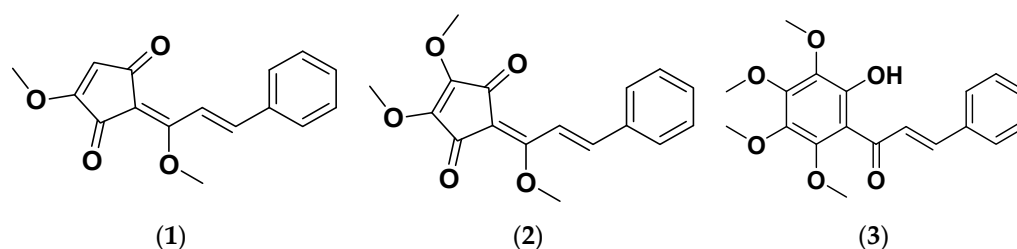


Figure 2. Chemical structures of methyl lucidone (1), methyl linderone (2), and kanakugiol (3).

2.3. HPLC Conditions and Sample Preparation

A total of 1 mg of each standard compound was dissolved in 1 mL of HPLC-grade MeOH to achieve a concentration of 1 mg/mL. In a similar manner, 30 mg of each extract was dissolved in the same solvent to achieve a final concentration of 30 mg/mL. All solutions were filtered with a 0.45 µm polyvinylidene difluoride (PVDF) filter. Quantitative analysis of the *L. erythrocarpa* extracts was conducted using a reverse-phase HPLC system equipped with an INNO C18 column (25 cm × 4.6 mm, 5 µm). The injection volume was 10 µL, and the detection was monitored at 340 nm. The column was maintained at 35 °C, and the flow rate was set at 1 mL/min. The mobile phase for the gradient elution system consisted of 0.5% TFA in water (A) and ACN (B). The elution program was as follows: 83% A at 0 min, 83% A at 10 min, 20% A at 40 min, 0% A at 41 min, 0% A at 45 min, 17% B at 50 min, and 17% B at 60 min.

2.4. Calibration Curves

The working solutions used to construct the calibration curve were prepared by serially diluting the stock solutions to the desired concentrations (0.5–0.03125 mg/mL). Similarly, the samples were dissolved in the same solvent, resulting in a final concentration of 15 mg/mL for each extract. Both the standard and sample solutions were filtered using a 0.45 µm PVDF filter before analysis. Calibration curves for the extracts of *L. erythrocarpa* were calculated based on peak areas (Y), concentrations (X, µg/10 µL), and mean values ± the standard deviation (SD) (*n* = 5).

2.5. Statistical Analysis

The results were expressed as mean $\pm$ SD, with all analyses conducted in triplicates. Data were analyzed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test. All statistical tests were generated using GraphPad Prism 8.0.2 software (GraphPad Software, Boston, MA, USA). p -values < 0.05 were considered statistically significant.

3. Results and Discussion

The present work compared the concentrations of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) in *L. erythrocarpa* grown in different provinces of Korea. HPLC analysis was performed using a reverse-phase system with a gradient elution. The calibration equations for each standard compound are presented in Table 2. The methods allowed for good separation and good retention times for the three marker compounds (Figure 3).

Table 2. Calibration data for methyl lucidone (1), methyl linderone (2), and kanakugiol (3).

Compound	t_R	Calibration Equation	Correlation Factor R^2
1	33.94	$y = 32.167x + 723.36$	0.9970
2	37.79	$y = 32.973x + 496.89$	0.9991
3	40.59	$y = 20.848x + 283.15$	0.9997

Note: t_R : retention time, Bold numbers correspond to a standard compound analyzed.

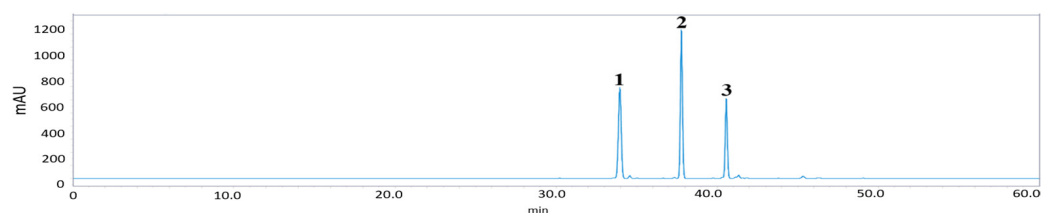


Figure 3. HPLC chromatogram showing the peaks representing the standard compounds methyl lucidone (1), methyl linderone (2), and kanakugiol (3).

The HPLC analysis of *L. erythrocarpa* samples revealed considerable variability in the concentrations of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) across different geographical locations and plant parts (Table 3). Generally, the leaf samples contained higher levels of methyl lucidone (1) than their stem counterparts. Conversely, the concentrations of methyl linderone (2) and kanakugiol (3) were found to be higher in the stem samples compared to the leaves.

Among the leaf samples, those from Gyeonggi Province (GGL) and Gyeongnam Province (GNL) exhibited particularly high total contents of 39.66 mg/g and 40.07 mg/g, respectively. The GGL sample exhibited particularly high levels of methyl lucidone (1) (9.15 mg/g) and kanakugiol (3) (21.48 mg/g). These concentrations were significantly higher compared to the leaf samples from Gyeongbuk Province (GBL), which exhibited the lowest levels of these compounds, with methyl lucidone (1) being 1.20 mg/g and kanakugiol (3) being 0.29 mg/g. This suggests that GGL and GNL are potentially more valuable sources of these marker compounds within leaf samples, as evidenced by the prominent peaks in the chromatograms (Figure 4).

Similarly, the stem samples from Gyeonggi Province (GGS) showed notably high concentrations of both methyl linderone (2) (10.03 mg/g) and kanakugiol (3) (50.10 mg/g), significantly surpassing other stem samples, such as those from Chungbuk Province (CBS) and Gyeongbuk Province (GBS), which exhibited total contents of 14.74 mg/g and 19.31 mg/g, respectively. The stem samples from Chungnam Province (CNS) also showed considerable total content of all compounds with 33.50 mg/g, driven by its high kanakugiol (3) level (23.44 mg/g). The chromatograms of the stem samples showed prominent peaks of these compounds (Figure 5).

Table 3. Quantitative analysis of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) in *L. erythrocarpa*.

Sample	Content (mg/g)			
	1	2	3	Total
GGL	9.15 ± 0.00 ^a	9.03 ± 0.00 ^c	21.48 ± 0.00 ^d	39.66 ± 0.01
GGs	2.54 ± 0.01 ^g	10.03 ± 0.04 ^b	50.10 ± 0.23 ^a	62.66 ± 0.28
CBL	4.92 ± 0.06 ^c	0.97 ± 0.02 ⁱ	5.73 ± 0.07 ^j	11.62 ± 0.15
CBS	3.14 ± 0.00 ^f	3.11 ± 0.00 ^f	8.49 ± 0.49 ^g	14.74 ± 0.50
CNL	9.08 ± 0.09 ^a	1.32 ± 0.02 ^h	7.44 ± 0.09 ^h	17.84 ± 0.20
CNS	4.85 ± 0.01 ^d	5.20 ± 0.00 ^e	23.44 ± 0.03 ^c	33.50 ± 0.05
GBL	1.20 ± 0.01 ⁱ	tr	0.29 ± 0.00 ^l	1.41 ± 0.01
GBS	0.98 ± 0.02 ^h	3.09 ± 0.03 ^f	15.24 ± 0.09 ^e	19.31 ± 0.13
GNL	8.38 ± 0.12 ^b	2.56 ± 0.04 ^g	6.92 ± 0.10 ⁱ	17.86 ± 0.26
GNS	3.03 ± 0.00 ^e	12.19 ± 0.00 ^a	24.85 ± 0.02 ^b	40.07 ± 0.03
JIL	2.57 ± 0.00 ^g	1.77 ± 0.00 ^h	4.33 ± 0.01 ^k	6.10 ± 0.01
JIS	1.33 ± 0.03 ^h	7.51 ± 0.12 ^d	13.28 ± 0.22 ^f	20.79 ± 0.34

tr: trace. All data were analyzed using one-way ANOVA, followed by Tukey's post hoc test. Values with $p < 0.05$ were considered statistically significant. Different lowercase letters following the mean ± SD values indicate significant differences.

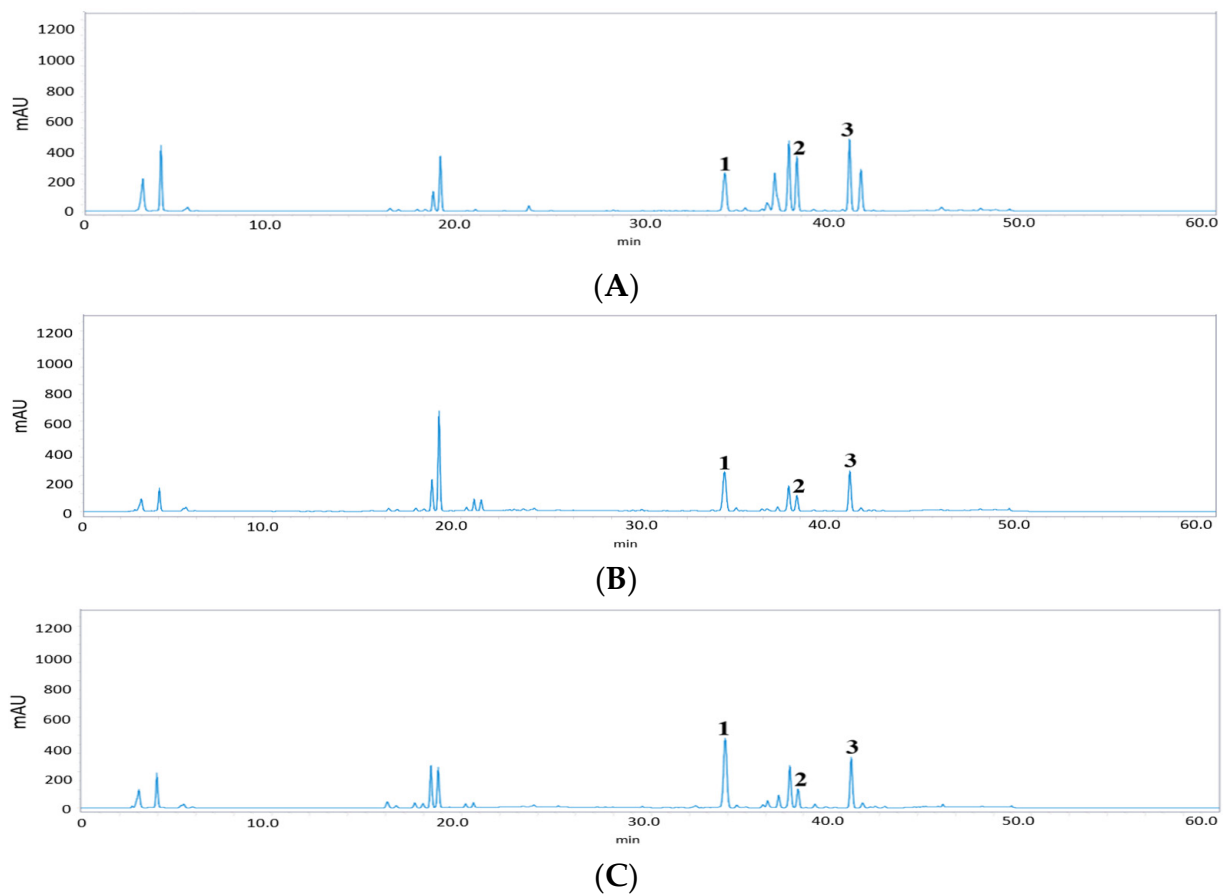


Figure 4. Cont.

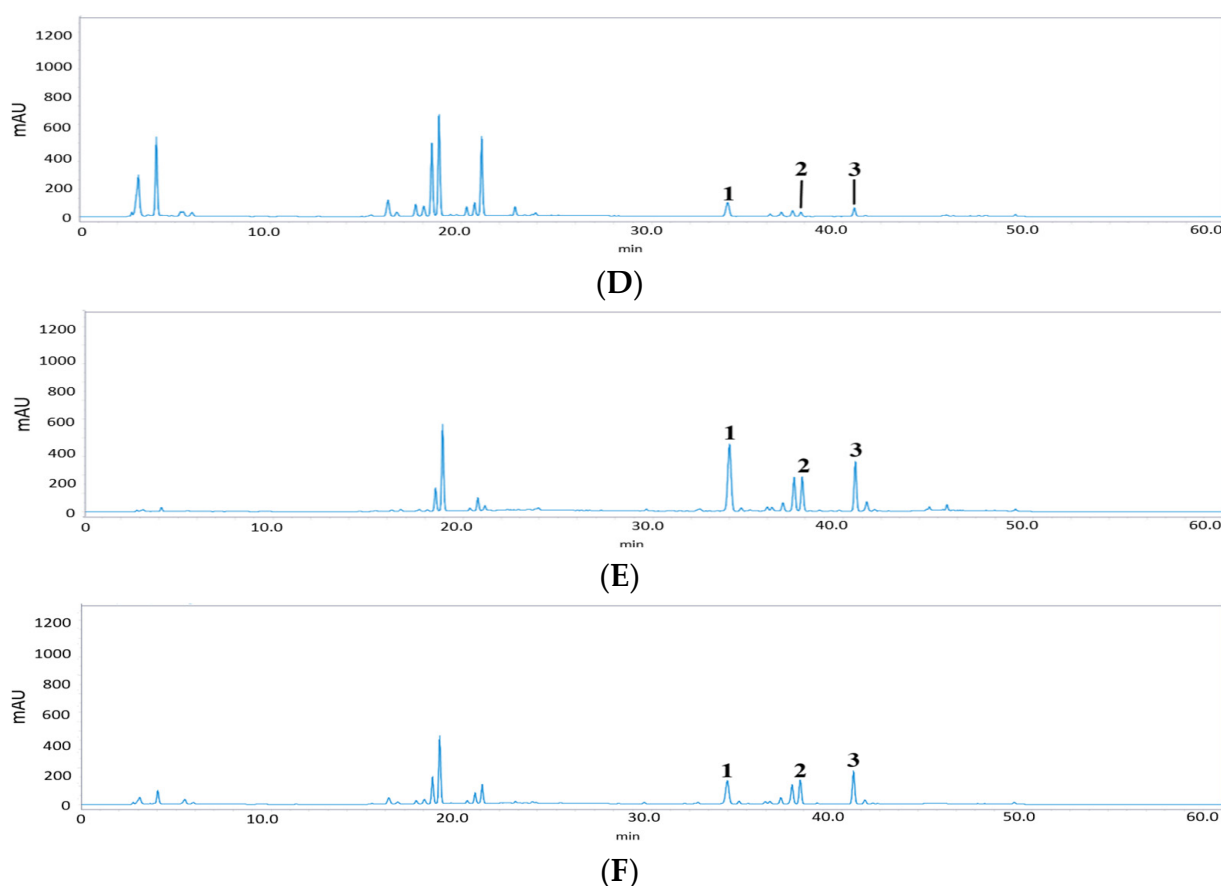


Figure 4. HPLC chromatograms of the leaf samples [GGL (A) CBL (B), CNL (C), GBL (D), GNL (E), and JIL (F); 1: methyl lucidone, 2: methyl linderone, and 3: kanakugiol].

The methyl lucidone (1) content varied among the samples, with GGL containing the highest concentrations at 9.15 mg/g and GBS containing the least at 0.98 mg/g. In contrast, methyl linderone (2) content ranged from trace amounts in GBL to a maximum of 12.19 mg/g in the stem samples from Gyeongnam Province (GNS). Leaf samples from Jeju Island (JIS) and GGL also exhibited significant concentrations of this compound, measuring 7.51 mg/g and 9.03 mg/g, respectively. Kanakugiol (3) content showed more dramatic variation, with the lowest concentration being recorded in GUL (0.29 mg/g) and the highest in stem samples from Gyeonggi Province (GGS) (50.10 mg/g). Other samples, such as CNS and GNS, exhibited notable concentrations of kanakugiol (2), measuring 23.44 mg/g and 24.85 mg/g, respectively.

The combined content of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) showed significant variation among the samples. The highest total content was found in the stem sample from the Gyeonggi Province stem sample (GGS), with 62.66 mg/g primarily attributable to its high kanakugiol (3) content (50.10 mg/g), followed by the GNS with 40.07 mg/g and GGL with 39.66 mg/g. In contrast, the lowest total content was observed in GUL, with only 1.41 mg/g, indicating significant differences between various plant parts and samples. These findings suggest that both geographical origin and plant part significantly influence the biosynthesis and accumulation of these compounds in *L. erythrocarpa* [15]. To the best of our knowledge, this is the first study that quantified these marker compounds since previous studies have focused more on their bioactivity. Additionally, studies that isolated these compounds did not perform quantification analysis.

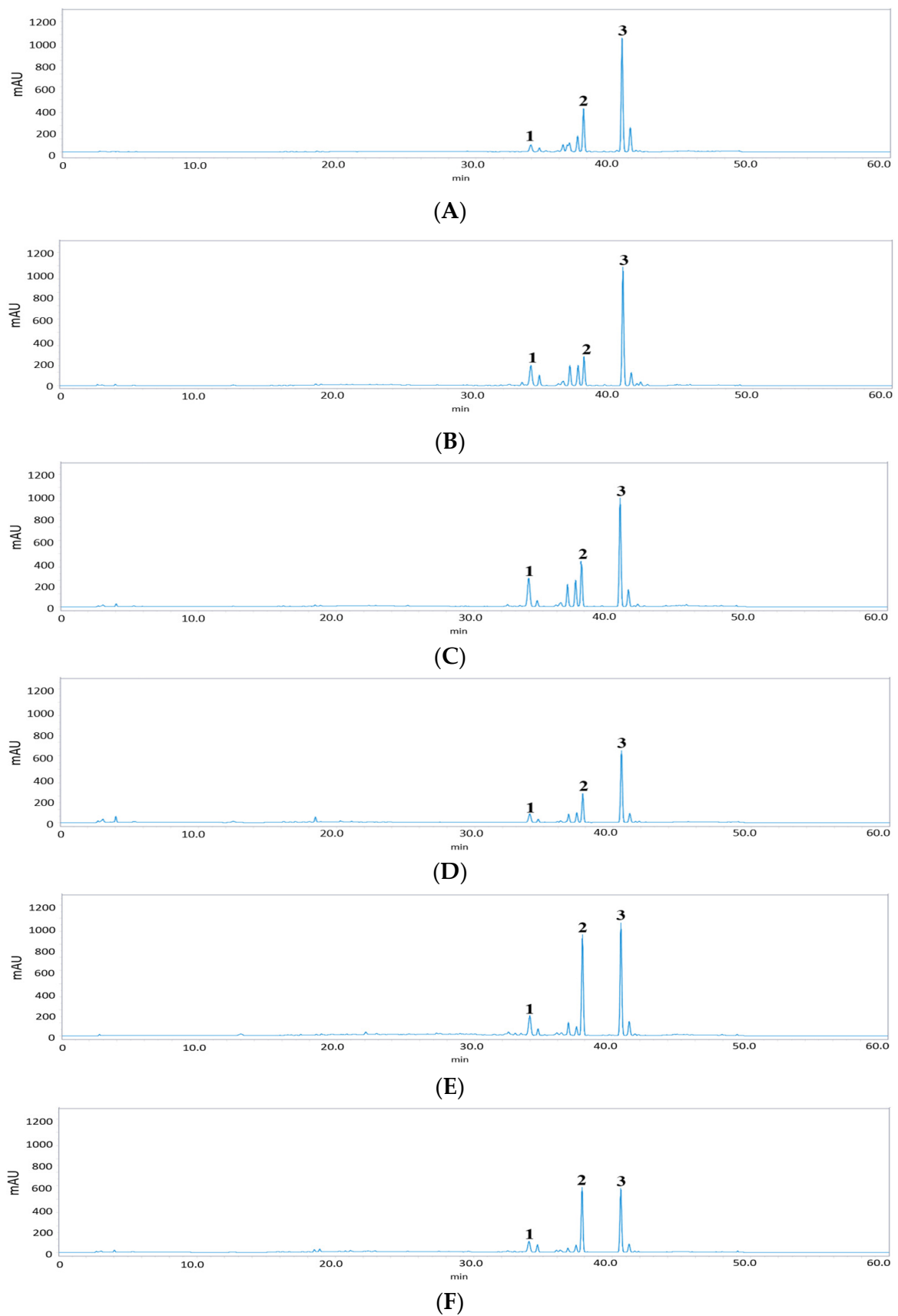


Figure 5. HPLC chromatograms of the stem samples [GGS (A), CBS (B), CNS (C), GBS (D), GNS (E), and JIS (F); 1: methyl lucidone, 2: methyl linderone, and 3: kanakugiol].

The significant differences in marker compound concentrations among the samples underscore the considerable influence of geographical factors [16]. Both samples from Gyeonggi Province (GGL and GGS) consistently exhibited high concentrations of the three compounds, suggesting that the specific environmental conditions and soil properties in this region are conducive to the biosynthesis of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) [17,18]. Environmental factors such as temperature, humidity, soil composition, and altitude may contribute to this variation [19,20]. This geographical disparity underscores the importance of selecting appropriate collection sites to achieve high concentrations of bioactive compounds.

This differential allocation of compounds within the plant may be attributable to the distinct physiological roles and metabolic processes occurring in stems versus leaves [21,22]. Such variations emphasize the importance of choosing the correct plant part for harvesting when aiming to maximize the yield of specific bioactive compounds, as phytochemical concentrations vary in different parts of a plant [23]. A previous study found that flavones, flavanols, and flavanones are concentrated in the leaves, whereas alkaloids and various types of sesquiterpenoids are concentrated in the roots of *L. aggregata*, a relative of the plant studied here [24]. The phytochemical profile of *L. erythrocarpa* has not been extensively investigated; hence, comparisons with the previous literature are primarily made with related species. Nonetheless, compounds such as methyl lucidone (1), methyl linderone (2), and kanakugiol (3) have been reported to occur naturally in different parts of this plant species [12,25].

The variability in compound concentrations has significant implications for the medicinal use of *L. erythrocarpa* [26]. Regions and specific plant parts with higher concentrations of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) could be prioritized for therapeutic applications, thereby enhancing the efficacy and potency of medicinal extracts. For instance, the high levels of these compounds in the samples from Gyeonggi Province, particularly in the stems, suggest their potential superiority for developing high-potency herbal remedies. This finding could guide future cultivation and harvesting strategies to optimize the production of bioactive compounds. For the target compound methyl linderone (2) or kanakugiol (3), it is recommended to use the stems rather than the leaves as the stems contain higher concentrations of these compounds. However, if methyl lucidone (1) is the compound of interest, the leaves should be utilized to maximize recovery, as the concentration of this compound is higher in the leaves.

Several factors could account for the observed variations in compound concentrations. Aside from environmental stressors such as light [27], temperature [28], and water availability [29], genetic factors [30] play a crucial role, as different populations may have evolved distinct metabolic pathways [31,32]. Variations in harvesting time and methods could also influence compound levels, with certain stages of plant development being more conducive to the accumulation of these compounds [33].

This study reveals significant geographical and plant part variations in the concentrations of methyl lucidone (1), methyl linderone (2), and kanakugiol (3) in *L. erythrocarpa*. The results revealed that methyl linderone (2) and kanakugiol (3) were more concentrated in the stems, whereas methyl lucidone (1) was more concentrated in the leaves of *L. erythrocarpa* regardless of the geographical origin of the plant. In addition, both the stems and leaves from Gyeonggi Province bested other samples. These findings underscore the importance of considering both geographical origin and plant part in phytochemical studies, providing valuable insights for selecting plant material for medicinal purposes. Future research should focus on elucidating the genetic and environmental factors driving these variations to optimize the cultivation and harvesting of *L. erythrocarpa* for therapeutic use. Understanding these factors is crucial for maximizing the yield and potency of bioactive compounds, thereby enhancing the medicinal value of this plant [34,35]. This study focused on quantifying and differentiating the concentrations of these compounds based on plant parts and geographical sources. Future research should explore the bioactivity of these extracts and compounds to further advance our understanding of their therapeutic potential.

Author Contributions: HPLC/UV analysis, N.P.U.; preparation of samples and compounds, J.-H.K. and D.-Y.K.; resources and experimental design, J.K.; supervision, writing—review and editing, S.L. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement: The original contributions presented in this study are included in the article; further inquiries can be directed to the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest.

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