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PHYTOCHEMICAL CONSTITUENTS FROM THE AERIAL PARTS OF *LACTUCA INDICA*

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Summary

Phytochemical Constituents from the Aerial Parts of *Lactuca indica*

From the ethyl acetate-soluble fraction of the aerial parts of *Lactuca indica* L., seven compounds, including three sesquiterpene lactones (**1**, **6**, and **7**), two phenylpropanoids (**2** and **3**), and two quinic acid derivatives (**4** and **5**) were isolated by using chromatographic methods (TLC and CC). The structures of compounds (**1-7**) were elucidated as lactuside B (**1**), caffeic acid (**2**), caffeic acid methyl ester (**3**), 3,4-di-*O*-caffeoylquinic acid methyl ester (**4**), 3,5-di-*O*-caffeoylquinic acid methyl ester (**5**), 11β,13-dihydrolactucin (**6**), and cichorioside B (**7**) by spectroscopic data (^{1}H- and ^{13}C-NMR and ESI-MS). This is the first report on the occurrence of **4** and **5** in the *Lactuca* genus and **1-3** in *L. indica*.

Keywords: *Lactuca indica, Sesquiterpene lactones, Phenylpropanoids, Quinic acid derivatives.*

1. Introduction

Lactuca indica L. (Asteraceae) is an edible wild vegetable mainly distributed in Asia [1]. This plant has been used as a fork remedy in antibacterial and anti-inflammatory applications and the treatment of intestinal disorders [1],[2],[3],[4]. In Vietnam, *L. indica* leaves are a vital drug in traditional medicine for the management of colic and stomach aches. Previous phytochemical studies on *L. indica* have resulted in the isolation of flavonoids, terpenoids, phenolic compounds, and quinic acid derivatives, which exhibit antioxidant, antidiabetic, anticholesterolemic, and hepatoprotective activities [5]. In a previous study conducted on the aerial part of *L. indica* harvested in Vietnam [6], luteolin, luteolin-7-*O*-β- D-glucopyranose, 11β,13-dihydrolactucin, cichorioside B were isolated and structurally identified. Finding chemical constituents from plants that can be used as food materials and medicine encourages us to conduct a phytochemical investigation on *L. indica*. The present study reported the isolation and identification of three sesquiterpene lactones (**1**, **6**, and **7**), two phenyl propanoids (**2** and **3**), and two quinic acid derivatives (**4** and **5**).

2. Materials and methods

2.1. Plant materials

The aerial parts of *L. indica* L. was collected in August 2022 in Thanh Tri, Hanoi, Vietnam, and was identified by Dr. Do Van Truong, Center for Life Science, Vietnam National Museum of Nature and Prof.Dr. Phuong Thien Thuong, Biotechnology Division, Vietnam - Korea Institute of Science and Technology (VKIST), Hanoi, Vietnam. The voucher specimen (BCA-2022) was kept in the Herbarium of the Division of Biotechnology, VKIST.

2.2. General experimental procedures

NMR spectra were measured on a Bruker Avance III 600 spectrometer (^{1}H at 600 MHz and ^{13}C at 150 MHz) with tetramethylsilane as the internal standard. ESI-MS analyses were conducted on a Shimadzu Triple Quadrupole LC-MS 8045 system equipped with a DAD detector. Column chromatography (CC) was carried out on *silica gel* 60 (60-200 µm, Merck), and YMC RP-18 (120 Å, 150 µm), and thin layer chromatography (TLC) on *silica gel* 60 F254 and RP-18 F254s (Merck) [7].

2.3. Extraction and isolation

The dried aerial parts of *L. indica* (5.0 kg) was extracted with EtOH 80% (20L) under reflux (70ºC, 3h, 3 times). The extracts were filtered and concentrated under reduced pressure to obtain a crude ethanol extract (400.0 g), which was suspended in water (1L) and partitioned with *n*-hexane, methylene chloride (MC), and ethyl acetate (EtOAc) (3L x 3, each). After the evaporation of EtOAc under reduced pressure, a brown extract was yielded. The EtOAc-soluble fraction (15.0 g) was subjected to *silica gel* CC, eluting with a gradient of MC: MeOH (20:1 - 0:1, v/v) to afford five fractions (LI-1A - LI-1E). Fraction LI-1B (1.3 g) was separated by RP-18 gel CC, eluting with MeOH: H_2O (1:1 - 3:1, v/v) to obtain compound **6** (10.2 mg). Fraction LI-1C (6.3 g) was chromatographed by *silica gel* CC, eluting with MC: MeOH (10:1 - 7:3, v/v) to give seven fractions (LI-2A - LI-2F). Fraction LI-2F

(3.0 g) was applied to RP-18 gel CC, eluting with MeOH: H_2O (1:1, v/v) to yield five fractions (LI-3A - LI-3E). Fraction LI-3D (840.3 mg) was purified by *silica gel* CC, eluting with an isocratic solvent system of MC:MeOH: H_2O (5:1:0.1, v/v/v) to give compounds **7** (7.3 mg) and **1** (6.4 mg). Compounds **4** (8.8 mg) and **5** (5.6 mg) were isolated from fraction LI-3B (1.4 g) by using RP-18 gel CC and eluting with MeOH: H_2O (1:1, v/v). In the same way, compounds **2** (5.2 mg) and **3** (4.0 mg) were afforded from fraction LI-2B (978.3 mg).

Lactuside B (**1**): White amorphous powder; $[\alpha]_D^{25}$ – 34 (c 0.05, MeOH); ^{1}H-NMR (600 MHz, CD_3OD) δ: 5.08 (1H, d, J = 11.4, 5.4 Hz, H-1), 2.44 (2H, dd, J = 11.4, 6.6 Hz, H-2), 4.59 (1H, dd, J = 9.6, 6.6 Hz, H-3), 5.01 (1H, d, J = 10.2 Hz, H-5), 4.84 (1H, t, J = 10.2 Hz, H-6), 1.92 (2H, m, ovelapped, H-7, H-8a), 1.79 (2H, m, overlapped, H-8b, H-9a), 2.85 (1H, m, H-9b), 2.50 (1H, dd, J = 11.4, 7.2 Hz, H-11), 1.28 (3H, d, J = 7.2 Hz, H-13), 1.73 (3H, s, H-14), 3.73 (1H, dd, J = 12.0, 6.0 Hz, H-15a), 3.94 (1H, dd, J = 12.0, 2.4 Hz, H-15b), 4.27 (1H, d, J = 7.8 Hz, H-1'), 3.20 - 3.90 (6H, m, H-2' - 2H-6'); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 427 $[M-H]^-$.

Caffeic acid (**2**): Colorless oil; ^{1}H-NMR (600 MHz, CD_3OD) δ: 7.03 (1H, d, J = 2.4 Hz, H-2), 6.83 (1H, d, J = 8.4 Hz, H-5), 6.99 (1H, d, J = 8.4, 2.4 Hz, H-6), 7.60 (1H, d, J = 16.0 Hz, H-7), 6.31 (1H, d, J = 16.0 Hz, H-8); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 179 $[M-H]^-$.

Caffeic acid methyl ester (**3**): yellow powder; ^{1}H-NMR (600 MHz, CD_3OD) δ: 7.09 (1H, d, J = 2.4 Hz, H-2), 6.78 (1H, d, J = 8.4 Hz, H-5), 6.93 (1H, d, J = 8.4, 2.4 Hz, H-6), 7.53 (1H, d, J = 16.0 Hz, H-7), 6.21 (1H, d, J = 16.0 Hz, H-8), 3.81 (3H, s, 9-OCH_3); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 193 $[M-H]^-$.

3,4-di-*O*-Caffeoylquinic acid methyl ester (**4**): Colorless gum; $[\alpha]_D^{25}$ – 15.2 (c 0.05, MeOH); ^{1}H-NMR (600 MHz, CD_3OD) δ: 2.38 (2H, m, H-2), 5.38 (1H, d, J = 3.6 Hz, H-3), 4.04 (1H, dd, J = 6.6, 3.2 Hz, H-4), 5.46 (1H, m, H-5), 2.23 (2H, m, H-6), 3.75 (3H, s, 1-OCH_3), 7.12 (1H, d, J = 2.4 Hz, H-2'), 6.85 (1H, d, J = 8.4 Hz, H-5'), 7.02 (1H, dd, J = 8.4, 2.4 Hz, H-6'), 7.18 (1H, d, J = 16.0 Hz, H-7'), 6.40 (1H, d, J = 16.0 Hz, H-8'), 7.12 (1H, d, J = 2.4 Hz, H-2'', 6.84 (1H, d, J = 8.4 Hz, H-5'', 7.02 (1H, d, J = 8.4, 2.4 Hz, H-6'', 7.60 (1H, d, J = 16.0 Hz, H-7'', 6.28 (1H, d, J = 16.0 Hz, H-8''); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 529 $[M-H]^-$.

3,5-di-*O*-Caffeoylquinic acid methyl ester (**5**): Colorless gum; $[\alpha]_D^{25}$ – 17.8 (c 0.05, MeOH); ^{1}H-NMR (600 MHz, CD_3OD) δ: 2.15 (1H, dd, J = 13.8, 6.6 Hz, H-2a), 2.38 (1H, dd, J = 13.8, 3.6 Hz, H-2b), 4.41 (1H, dt, J = 6.6, 3.6 Hz, H-3), 5.17 (1H, dd, J = 8.4, 3.6 Hz, H-4), 5.61 (1H, td, J = 8.4, 5.2 Hz, H-5), 2.31 (2H, m, H-6), 3.78 (3H, s, 1-OCH_3), 7.09 (1H, d, J = 2.4 Hz, H-2'), 6.82 (1H, d, J = 8.4 Hz, H-5', 6.98 (1H, dd, J = 8.4, 2.4 Hz, H-6'), 7.66 (1H, d, J = 16.0 Hz, H-7'), 6.35 (1H, d, J = 16.0 Hz, H-8'), 7.07 (1H, d, J = 2.4 Hz, H-2''), 6.82 (1H, d, J = 8.4 Hz, H-5''), 6.98 (1H, d, J = 8.4, 2.4 Hz, H-6"), 7.56 (1H, d, J = 16.0 Hz, H-7''), 6.23 (1H, d, J = 16.0 Hz, H-8"); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 529 $[M-H]^-$.

11β,13-Dihydrolactucin (**6**): Amophour powder; ^{1}H-NMR (600 MHz, CD_3OD) δ: 6.39 (1H, d, J = 1.2 Hz, H-3), 3.68 (1H, d, J = 10.2 Hz, H-5), 3.62 (1H, dd, J = 10.2, 1.8 Hz, H-6), 2.15 (1H, dd, J = 12.0, 10.2 Hz, H-7), 3.66 (1H, m, overlapped, H-8), 2.37 (1H, dd, J = 13.8, 2.4 Hz, H-9a), 2.80 (1H, dd, J = 13.8, 10.2 Hz, H-9b), 2.64 (1H, dd, J = 12.0, 7.2 Hz, H-11), 1.37 (3H, d, J = 7.2 Hz, H-13), 2.41 (3H, s, H-14), 4.39 (1H, dd, J = 18.6, 1.8 Hz, H-15a), 4.82 (1H, dd, J = 18.6, 1.8 Hz, H-15b); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 277 $[M-H]^-$.

Cichorioside B (**7**): Colorless oil; ^{1}H-NMR (600 MHz, CD_3OD) δ: 6.62 (1H, d, J = 1.2 Hz, H-3), 3.72 (2H, m, overlapped, H-5, H-6), 2.20 (1H, ddd, J = 12.0, 10.2, 9.6 Hz, H-7), 3.81 (1H, m, H-8), 2.45 (1H, dd, J = 13.8, 2.4 Hz, H-9a), 2.88 (1H, dd, J = 13.8, 10.8 Hz, H-9b), 2.71 (1H, dd, J = 12.0, 7.2 Hz, H-11), 1.44 (1H, d, J = 7.2 Hz, H-13), 2.48 (3H, s, H-14), 4.82 (1H, d, J = 17.4 Hz, H-15a), 4.94 (1H, d, J = 17.4 Hz, H-15b), 4.44 (1H, d, J = 7.8 Hz, H-1'), 3.31 (1H, dd, J = 9.0, 7.8 Hz, H-2'), 3.43 (1H, m, H-3'), 3.36 (1H, m, H-4'), 3.44 (1H, m, H-5'), 3.78 (1H, m, overlapped, H-6'a), 3.94 (1H, dd, J = 12.0, 2.4 Hz, H-6'b); ^{13}C-NMR (150 MHz, CD_3OD): see Table 1; ESI-MS: *m/z* 439 $[M-H]^-$.

3. Results and discussion

The ethyl acetate extract of the aerial parts of *L. indica* was repeatedly chromatographed to reveal the presence of seven compounds as lactuside B (**1**), caffeic acid (**2**), caffeic acid methyl ester (**3**), 3,4-di-*O*-caffeoylquinic acid methyl ester (**4**), 3,5-di-*O*-caffeoylquinic acid methyl ester (**5**), 11β,13-dihydrolactucin (**6**), and cichorioside B (**7**) (Fig. 1). The structures of compounds **1-7** were elucidated by spectroscopic data analyses and comparison with the published results in the literature.

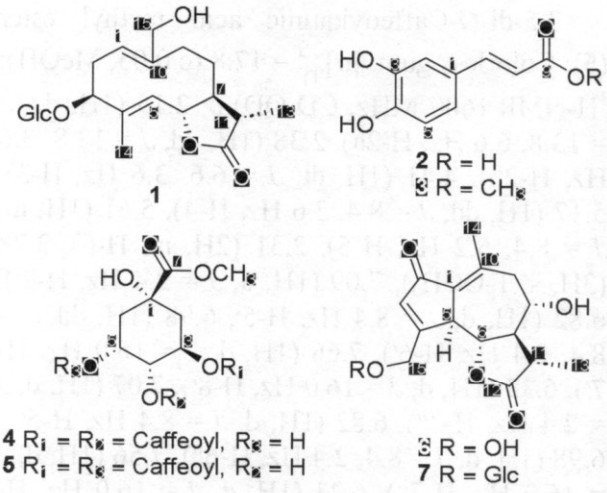

Fig. 1. Chemical structures of isolated compounds **1** - **7** from *L. indica*

Compound **1** was afforded as a white amorphous powder, and a molecular formula of $C_{21}H_{32}O_9$ was assigned by the ESI-MS spectrum at *m/z* 427 $[M-H]^-$. Analysis of the ^{1}H- and ^{13}C-NMR of **1** suggested that 1 had the skeleton of a sesquiterpene lactone glycoside. The ^{1}H-NMR data of **1** showed signals of two olefinic protons at δ_H 5.08 (1H, dd, J = 11.4, 5.4 Hz, H-1), 5.01 (1H, d, J = 10.2 Hz, H-5), two oxygenated methines at δ_H 4.84 (1H, d, J = 10.2 Hz, H-6), 4.59 (1H, d, J = 9.6, 6.6 Hz, H-3), an oxygenated methylene at δ_H 3.73 (1H, dd, J = 12.0, 6.0 Hz, H-15a), 3.94 (1H, dd, J = 12.0, 2.4 Hz, H-15b), and two methyls at δ_H 1.28 (3H, d, J = 7.2 Hz, H-13), and 1.73 (3H, s, H-14). In addition, the β-D-glucopyranoside moiety was recognized by an aromatic proton signal at δ_H 4.27 (1H, d, J = 7.8 Hz, H-1') in the ^{1}H-NMR spectrum as well as at δ_C 102.4 (C-1'), 75.1 (C-2'), 78.1 (C-3'), 71.8 (C-4'), 77.9 (C-5'), 62.8 (C-6') in the ^{13}C-NMR spectrum of **1**. The remaining carbon signals belonged to the aglycone part, including two double bonds at δ_C 128.7 (C-1), 141.4 (C-4), 128.4 (C-5), 142.0 (C-10), a γ-lactone moiety at δ_C 82.5 (C-6), 55.5 (C-7), 43.3 (C-11), 181.3 (C-12), 13.3 (C-13), an oxygenated methine at δ_C 84.0 (C-3), four methylenes at δ_C 33.3 (C-2), 29.4 (C-8), 37.0 (C-9), 58.8 (C-15), and a tertiary methyl at δ_C 11.7 (C-14) (Table 1). The planar structure of **1** was further confirmed by the COSY and HMBC correlations (Fig. 2). The [4,4]-bicyclodecane system containing two double bonds inferred from the ^{1}H-^{1}H COSY spectrum of H-1/H-2/H-3 and of H-5/H-6/H-7/H-8/H-9 as well as the HMBC correlations between H-1 and C-9, between H-14 and C-3/C-4/C-5. The presence of γ-lactone at C-6 and C-7 was demonstrated by the COSY linkgates of H-6/H-7/H-11/H-13 together with the HMBC cross-peaks of H-13 and C-7/C-11/C-12, of H-6 and C-12. Finally, the locations of oxymethylene and β-glucosyl moiety at C-3 and C-10, respectively, were determined by the HMBC correlations from H-1' to C-3 and from H-15 to C-10. The α-configuration of H-3 was established on the basis of its chemical shift observed in the ^{1}H-NMR spectrum at δ_H 4.59 (1H, dd, J = 9.7, 6.8 Hz) [8]. The configuration of H-6β, H-7α, H-11β, and H-13α was determined based on the large coupling constants of $J_{6,7}$ = 10.1 Hz and $J_{7,11}$ = 11.3 Hz, which deduced *trans*-diaxial configuration of these protons [8]. From this evidence, compound **1** was determined as lactuside B [9]. Lactuside B (**1**) was detected in *L. laciniata* roots and *L. serriola* aerial parts, however, this compound was isolated from *L. indica* for the first time [5].

Compound **2** was isolated as a yellow oil. The ^{1}H-NMR data of **2** showed signals for an ABX system at δ_H 7.03 (1H, d, J = 2.4 Hz, H-2), 6.83 (1H, d, J = 8.4 Hz, H-5), 6.99 (1H, d, J = 8.4, 2.4 Hz, H-6), a *trans*-double bond at δ_H 7.60 (1H, d, J = 16.0 Hz, H-7), 6.31 (1H, d, J = 16.0 Hz, H-8). The ^{13}C-NMR revealed signals of nine carbons, including a carbonyl, six aromatic carbons, and two *trans*-olefinic carbons (Table 1). The NMR data of **2** were completely consistent with those of caffeic acid [10]. Thus, compound **2** was identified as caffeic acid. Caffeic acid (**2**) has been reported from L. viminea, L. sativa, and L. tuberosa, however, this is the first time caffeic acid was isolated from L. indica [5].

Compound **3** was obtained as a yellow powder. Its ^{1}H- and ^{13}C-NMR spectra of **3** were similar to those of **2**, except for the addition of a methoxy group at δ_H 3.81 (3H, s, 9-OCH$_3$), δ_C 52.0. The upfield chemical shifts of the methoxy group (δ_C 52.0) and C-9 (δ_C 169.8) demonstrated that the methoxy group was located in C-9. In combination with the published data, compound **3** was identified as caffeic acid methyl ester [11]. Similar to **2**, compound **3** was detected in *L. indica* for the first time [5].

Compound **4** was obtained as colorless gum, and its molecular formula was determined as $C_{26}H_{26}O_{12}$ by the ESI-MS spectrum at *m/z* 529 $[M-H]^-$. The 1D-NMR data of **4** suggested that the structure of **4** was comprised of a quinic acid with a methoxy group and two caffeoyl units. The ^{1}H-NMR spectrum of **4** showed signals of two methylenes at δ_H 2.38 (2H, m, H-2), 2.23 (2H, m, H-6), three oxygenated methines at δ_H 5.38 (1H, d, J = 3.6 Hz, H-3), 4.04 (1H, dd, J =

6.6, 3.2 Hz, H-4), 5.46 (1H, m, H-5), which implied the presence of a quinic acid moiety. In addition, six aromatic protons at δ_H 7.12 (2H, d, J = 2.4 Hz, H-2', H-2"), 6.85 (1H, d, J = 8.4 Hz, H-5'), 6.84 (1H, d, J = 8.4 Hz, H-5'), 7.02 (2H, dd, J = 8.4, 2.4 Hz, H-6', H-6") together with four *trans*-olefinic protons at δ_H 7.18 (1H, d, J = 16.0 Hz, H-7'), 6.40 (1H, d, J = 16.0 Hz, H-8'), 7.60 (1H, d, J = 16.0 Hz, H-7"), 6.28 (1H, d, J = 16.0 Hz, H-8") were observed in the ^{1}H-NMR spectrum, which indicated the presence of two *trans*-caffeoyl moieties in **4**. The location of two caffeoyl moieties at C-3 and C-4 was confirmed by the HMBC correlations between H-3, H-4, and C-9', C-9", respectively. Furthermore, the position of the methoxy group (δ_H 3.75, δ_C 53.0) at C-7 was determined by the HMBC correlation between a methoxy group and C-7 (Fig. 2). Based on the above analysis and comparison of NMR data of **4** with those previously reported, the structure of **4** was elucidated as 3,4-di-*O*-caffeoylquinic acid methyl ester [12].

Compound **5** was isolated as a colorless gum. The molecular formula of **5** was determined to be $C_{26}H_{26}O_{12}$ by the ESI-MS spectrum at *m/z* 529 $[M-H]^-$, and the same with that of **4**. The NMR spectra of **5** were closely related to compound **4**, except for the chemical shifts of H-4, H-5, C-3, C-4, and C-5 in the ^{1}H- and ^{13}C-NMR spectra. The signals of H-4 and C-4 in **5** were shifted downfield from those of **4**, where H-5, C-3, and C-5 were shifted upfield, suggesting that two caffeoyl moieties were attached to C-3 and C-5 (Table 2). The locations of these moieties at C-3 and C-5 were also supported by the HMBC correlations from H-3 to C-9' and from H-5 to C-9" (Fig. 2). From the above evidence, the structure of **5** was determined as 3,5-di-*O*-caffeoylquinic acid methyl ester [12]. It is the first time compounds **4** and **5** were isolated from the *Lactuca* genus [5].

Compounds **6** and **7** were determined as 11β,13-dihydrolactucin (**6**), cichorioside B (**7**), respectively based on the consistency of their NMR data with those of the previous publications of *L. indica* in Vietnam [6].

Table 1. ^{13}C-NMR spectroscopic data of **1-5**

	1	2	3	4	5
1	128.7	127.8	127.7	74.6	74.9
2	33.3	115.5	115.1	35.6	38.4
3	84.0	147.0	146.8	72.2	69.1
4	141.4	149.9	149.6	69.8	75.8
5	128.4	116.1	116.5	72.0	68.6
6	82.5	122.8	122.9	37.1	38.4
7	55.5	115.1	146.9	175.6	175.2
8	29.4	147.0	114.9		
9	37.0	171.0	169.8		
10	142.0				
11	43.3				
12	181.3				
13	13.3				
14	11.7				
15	58.8				
OCH_3			52.0	53.0	53.1
1'/1"	102.1			127.7/127.6	127.7/127.6
2'/2"	75.1			115.2/115.0	115.2
3'/3"	78.1			147.4/146.7	146.8
4'/4"	71.8			149.7/149.5	149.8/149.7
5'/5"	77.9			116.6/116.5	116.5
6'/6"	62.8			123.1/123.0	123.1
7'/7"				147.4/147.1	147.7
8'/8"				115.4/114.9	114.7/114.6
9'/9"				168.7/168.6	168.5/167.9

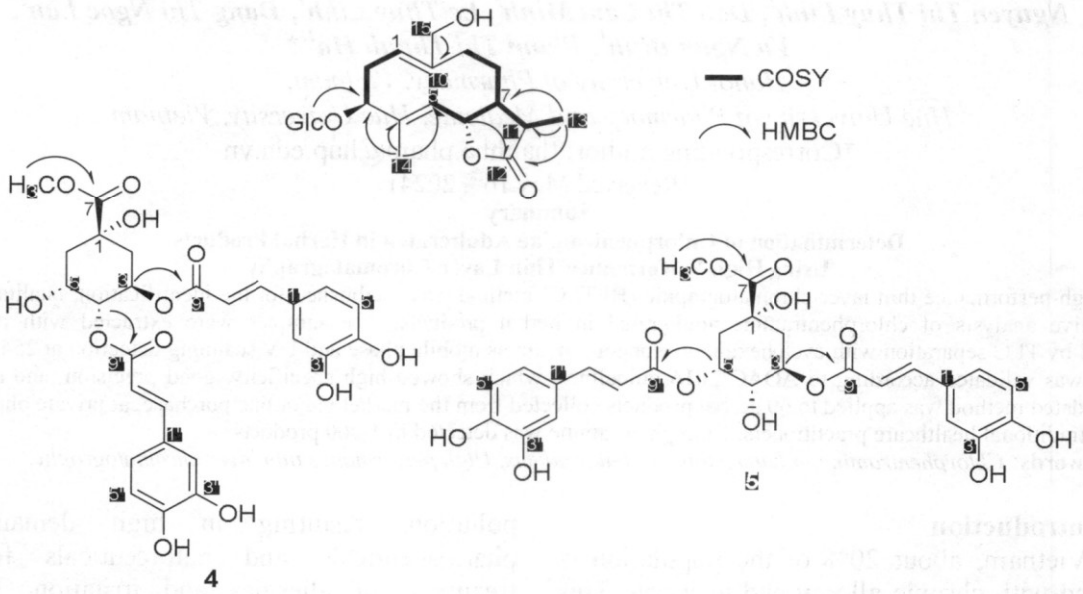

Fig. 2. Key HMBC correlations of compounds **4** and **5**

4. Conclusion

Phytochemical investigation of the aerial parts of *L. indica* has resulted in the isolation of three sesquiterpene lactones, lactuside B (**1**), 11β,13-dihydrolactucin (**6**), cichorioside B (**7**); two phenylpropanoids, caffeic acid (**2**), caffeic acid methyl ester (**3**); and two quinic acid derivatives, 3,4-di-*O*-caffeoylquinic acid methyl ester (**4**), 3,5-di-*O*-caffeoylquinic acid methyl ester (**5**). To the best of our knowledge, this study was the first to isolate compounds **1-3** from *L. indica*, and compounds **4** and **5** from the *Lactuca* genus.

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DETERMINATION OF CHLORPHENIRAMINE ADULTERATED IN HERBAL PRODUCTS USING HIGH PERFORMANCE THIN LAYER CHROMATOGRAPHY

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Summary

Determination of Chlorpheniramine Adulterated in Herbal Products Using High Performance Thin Layer Chromatography

A high-performance thin layer chromatographic (HPTLC) method was established for the identification, qualitative, and quantitative analysis of chlorpheniramine adulterated in herbal products. The samples were extracted with methanol, followed by TLC separation with cyclohexane-acetone-ammonia as mobile phase and UV scanning detection at 254 nm. The method was validated according to AOAC 2016 guidelines, which showed high specificity, good precision, and accuracy. The validated method was applied to 60 herbal products collected from the market via online purchase, at private pharmacies, or from traditional healthcare practitioners. Chlorpheniramine was detected in 18/60 products.

Keywords: *Chlorpheniramine, Adulteration, Herbal products, High performance thin layer chromatography.*

1. Introduction

In Vietnam, about 20% of the population is involved with chronic allergy and urticaria. This percentage kept increasing due to environmental pollution, resulting in high demand for pharmaceuticals and nutraceuticals for the treatment of allergies and irritation. Besides chemical drugs, people with allergies often prefer