

FLAVONOIDS AND COUMARINS FROM THE STEMS OF *Lasianthus honbaensis* V.S. Dang, Tagane & H. Toyama

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TÓM TẮT

CÁC HỢP CHẤT FLAVONOID VÀ COUMARIN TỪ PHẦN THÂN CÂY *Lasianthus honbaensis* V.S. Dang, Tagane & H. Toyama

Từ bộ phận thân cây Xú hương Hòn Bà *Lasianthus honbaensis*, được thu mẫu tại Khu bảo tồn thiên nhiên Hòn Bà, tỉnh Khánh Hoà, năm hợp chất đã được cô lập và xác định cấu trúc hoá học. Cấu trúc hoá học của năm hợp chất, trong đó bao gồm ba hợp chất flavonoid quercetin (1), kaempferol-3-O- β -D-xylopyranoside (2), và sophorin (3) cùng với hai hợp chất coumarin esculetin (4) và lasibidoupin B (5), được xác định bằng các phương pháp hoá lý hiện đại như khối phổ HR-ESI-MS, phổ cộng hưởng từ hạt nhân NMR một và hai chiều, kết hợp so sánh với dữ liệu NMR trong các tài liệu tham khảo. Các hợp chất 1-4 lần đầu tiên được tìm thấy trong chi Xú hương *Lasianthus*. Hai hợp chất esculetin (4) và lasibidoupin B (5) cho thấy có khả năng ức chế α -glucosidase với giá trị IC₅₀ (μ g/ml) lần lượt là 5,83 $\pm$ 0,50 và 4,0 $\pm$ 0,00, nhưng lại không cho hoạt tính ức chế acetylcholinesterase. Lasibidoupin B (5) cho thấy có hoạt tính ức chế yếu trên hai dòng tế bào ung thư A549 và HEK-293, trong khi esculetin (4) không cho hoạt tính trên cả ba dòng tế bào ung thư A549, HEK-293 và HepG2. Đây là lần đầu tiên loài Xú hương Hòn Bà *Lasianthus honbaensis* V. S. Dang, Tagane & H. Toyama được khảo sát về thành phần hoá học và hoạt tính sinh học.

Từ khoá: *Lasianthus honbaensis*, flavonoid, coumarin, α -glucosidase, acetylcholinesterase.

1. INTRODUCTION

The genus *Lasianthus* (Rubiaceae) consisted of more than 180 species that were widely distributed in tropical Asia forests [1]. In Vietnam, there were 40 species and one subspecies [2]. The plants belonging to this genus were garnered widespread recognition in traditional medicine due to their various pharmacological characteristics such as anti-inflammatory, antibacteria, anti-ovarian cancer, antipyretic as well as snakebites, ulcers, and anodyne treatments [3-6]. In terms of chemical composition, there were several studies conducted on *Lasianthus* plants such as *L.*

wallichii, *L. gardneri*, *L. fordii* and *L. acuminatissimus*, which determined the presence of anthraquinones, triterpenoids, benzochromenes, megastigmanes, iridoids glycosides [7-12]. More recently, several compounds, including lasibidoupin A, lasibidoupin B, 11-O-methylamnacanthol and five triterpenoids lupeol, 3-epi-betulinic acid, 3-epi-3-O-acetyl betulinic acid, 3-epi-oleanolic acid and vergatic acid were reported in the *L. bidoupensis* stems collected in Bidoup Nui Ba National Park, Lam Dong Province, Viet Nam [13,14]. The new species *Lasianthus honbaensis* V.S. Dang, Tagane & H. Toyama was

firstly discovered in Vietnam in 2019 [2]. *L. honbaensis* was not chemically and biologically studied. In this work, we examined the stems extract of *L. honbaensis* V. S. Dang, Tagane & H. Toyama collected at Hon Ba Nature Reserve and obtained five compounds. They included three flavonoids quercetin (1), kaempferol-3-*O*- β -D-xylopyranoside (2) and sophorin (3) along with two coumarins esculetin (4) and lasibidopin B (5). The chemical structures of these compounds were elucidated through extensive 1D and 2D NMR analysis as well as the comparisons of their NMR data with the literature. Among the isolated compounds, four compounds 1-4 were determined for the first time from the genus *Lasianthus*. Compounds 4 and 5 were evaluated for the acetylcholinesterase and α -glucosidase inhibition and cytotoxic activity against three cancer cell lines A549, HEK-293 and HepG2.

2. MATERIALS AND METHODS

2.1. Plant materials

The stems of *Lasianthus honbaensis* V. S. Dang, Tagane & H. Toyama were harvested in Hon Ba Nature Reserve, Khanh Hoa province, Viet Nam. The botanical names was identified by Dr. Dang Van Son, Institute of Tropical Biology, VAST.

2.2. General experimental procedures

The HR-ESI-MS was performed using an Bruker spectrometer 1100 Series LC/MSD Trap SL. NMR spectra (^1H -NMR, 500 MHz and ^{13}C -NMR, 150 MHz), HSQC and HMBC were measured on a Bruker Avance III spectrometer. All resonances were referenced to the residual signals of the deuterated solvents, and the coupling constants of protons were reported in hertz. Thin layer

chromatography (TLC) was conducted on normal phase and reversed phase silica gels (Merck, Germany). Silica gel 60 (Himedia, India) was used for column chromatography (CC).

2.3. Extraction and isolation

The powdered dry stems of *L. honbaensis* (30.5 kg) were subjected to seven repetitions of maceration in ethanol at room temperature (25 L x 7) for six days. After combining the filtrates, the ethanol was removed under reduced pressure, obtaining a crude extract (1.05 kg).

This residue was redissolved in ethanol and then suspended in water. The obtained mixture was thoroughly extracted with *n*-hexane, chloroform, and ethyl acetate. Evaporation of each organic phase yielded the corresponding extracts: 110.2 g (hexane), 50.3 g (chloroform), and 37.3 g (ethyl acetate).

The hexane extract (110.2 g) was subjected to silica gel column chromatography and eluted with hexane/ethyl acetate mixture ratios 8:2, 7:3, 5:5 and then ethyl acetate/methanol ratios 9:1, 8:2, 7:3, 6:4, 0:10 to give seven fractions (H.A-H.G). Compound 1 (46 mg) and compound 5 (1.02 g) were obtained from fraction H.B (20.5 g) by a column chromatography on silica gel eluting with hexane/chloroform (7/3, v/v). The ethyl acetate extract (37.3 g) was placed on silica gel column chromatography and eluted with ethyl acetate/methanol ratios 9:1, 8:2, 7:3, 6:4, 5:5, 1:9, 0:10 to give ten fractions (EA.A-EA.J). Fraction EA.B (1.8 g) was selected for additional processing. This material was introduced on another silica-gel column eluting a stepwise manner, using ethyl acetate/methanol ratios at 9:1, 8:2, 7:3, 6:4, 5:5 and then methanol was passed through the column to complete the procedure to give six subfractions

(EA.B1-EA.B6). Subfraction EA.B3 (0.19 g) was purified by silica gel column chromatography using chloroform-methanol (9/1, v/v) to yield compound **4** (37 mg). Compound **2** (27 mg) and compound **3** (18 mg) were obtained from fraction EA.G (1.8 g) by a column chromatography on silica gel eluting with chloroform/methanol (8/2, 7/3, v/v).

Quercetin (**1**) [15]: Yellow amorphous powder. $^1\text{H-NMR}$ (CD_3OD), δ_{H} , (J in Hz): 12.10 (1H, OH-5), 7.75 (1H, *d*, 2.0 Hz, H-2'), 7.65 (1H, *dd*, 2.0, 8.0 Hz, H-6'), 6.91 (1H, *d*, 8.0 Hz, H-5'), 6.41 (1H, *d*, 2.0 Hz, H-8), 6.21 (1H, *d*, 2.0 Hz, H-6). $^{13}\text{C-NMR}$ (CD_3OD): table 1.

Kaempferol 3-*O*- β -D-xylopyranoside (**2**) [16]: Yellow amorphous powder. HR-ESI-MS m/z 441.0715 $[\text{M}+\text{Na}]^+$. $^1\text{H-NMR}$ (CD_3OD), δ_{H} , (J in Hz): 12.14 (1H, OH-5), 8.02 (2H, *d*, 9.0 Hz, H-2', H-6'), 6.92 (2H, *d*, 9.0 Hz, H-3', H-5'), 6.44 (*d*, 2.0 Hz, H-8), 6.24 (*d*, 2.0 Hz, H-6), 5.21 (1H, *d*, 7.5 Hz, H-1''), 3.78 (1H, *dd*, 11.5, 9.5 Hz, H-5a''), 3.52 (1H, *t*, 7.5 Hz, H-2''), 3.51 (1H, *d*, 7.0 Hz, H-4''), 3.41 (1H, *dd*, 9.0, 8.5 Hz, H-3'') and 3.09 (1H, *dd*, 11.5, 9.5 Hz, H-5b''). $^{13}\text{C-NMR}$ (CD_3OD): table 1.

Sophorin (**3**) [17]: yellow amorphous powder. Yellow amorphous solid. HR-ESI-MS m/z 634.1434 $[\text{M}+\text{Na}]^+$. $^1\text{H-NMR}$ (CD_3OD), δ_{H} , (J in Hz): 12.30 (1H, OH-5), 7.69 (1H, *d*, 2.0 Hz, H-2'), 7.67 (1H, *dd*, 8.5, 2.0 Hz, H-6'), 6.90 (1H, *d*, 8.5 Hz, H-5'), 6.34 (*d*, 2.0 Hz, H-8), 6.23 (*d*, 2.0 Hz, H-6), 5.11 (1H, *d*, 7.5 Hz, H-1''), 4.55 (1H, *d*, 1.5 Hz, H-1'''), 3.68 (1H, *dd*, 3.5, 1.5 Hz, H-2'''), 3.59 (1H, *dd*, 9.5, 3.5 Hz, H-3'') and 1.15 (3H, *d*, 6.5 Hz, CH_3 -6''). $^{13}\text{C-NMR}$ (CD_3OD): table 1.

Esculetin (**4**) [18]: light yellow powder. HR-ESI-MS m/z 179.0224 $[\text{M}+\text{H}]^+$. $^1\text{H-NMR}$ (CD_3OD), δ_{H} , (J in Hz): 7.80 (1H, *d*, 9.0 Hz, H-4), 6.95 (1H, *s*, H-5), 6.77 (1H, *s*, H-8), 6.19 (1H, *d*, 9.0 Hz, H-3). $^{13}\text{C-NMR}$ (CD_3OD): table 2.

Lasibidoupin B (**5**) [13]: light yellow powder. HR-ESI-MS m/z 315.0864 $[\text{M}+\text{H}]^+$. $^1\text{H-NMR}$ (CDCl_3), δ_{H} , (J in Hz): 11.46 (1H, *s*, OH-8), 10.56 (1H, *s*, H-13), 7.97 (1H, *d*, 10.0 Hz, H-4), 7.29 (1H, *s*, H-7), 6.51 (1H, *d*, 10.0 Hz, H-3), 4.20 (3H, *s*, H-14), 3.85 (3H, *s*, H-12), 2.56 (3H, *s*, H-11). $^{13}\text{C-NMR}$ (CDCl_3): table 2.

3. RESULTS AND DISCUSSIONS

Compound **1** was yield as a yellow amorphous powder. It was identified as a flavonoid through analysing its NMR spectra. The $^1\text{H-NMR}$ spectrum of **1** exhibited the typical intramolecular proton at δ_{H} 12.10 (1H, OH-5) of the flavonoid. The $^1\text{H-NMR}$ showed two *meta*-coupled signals at δ_{H} 6.41 (1H, *d*, 2.0 Hz, H-8) and δ_{H} 6.21 (1H, *d*, 2.0 Hz, H-6), displaying the presence of a 5,7-dihydroxy A ring system in flavonol skeleton. Its also displayed the presence of three aromatic proton signals of an ABX system at δ_{H} 7.75 (1H, *d*, 2.0 Hz, H-2'), 7.65 (1H, *dd*, 2.0, 8.0 Hz, H-6') and 6.91 (1H, *d*, 8.0 Hz, H-5'), that was identified the 1',3',4'-trisubstituted benzene B ring. The $^{13}\text{C-NMR}$ spectrum exhibited 15 carbon signals in the down field of the pentahydroxyflavone, comprising a carbonyl carbon at δ_{C} 177.4 (C-4), five oxygenated aromatic carbons at δ_{C} 137.3 (C-3), 146.4 (C-3'), 148.0 (C-4'), 162.0 (C-5) and 165.4 (C-7) and nine signals from 94.4 to 158.0 ppm of the rest carbons. These spectral data revealed the presence of a flavonol quercetin. The HMBC correlations between the anomeric proton at δ_{H} 7.75 (1H, *d*, 2.0 Hz, H-2') to carbons at δ_{C} 148.6 (C-2), 148.0 (C-4') and 121.6 (C-6') demonstrated the attachment of B ring at C-2. The other cross peaks on HSQC and HMBC spectra were strongly agreed with the assignment. The comparison of NMR data of **1** with those reported in the literature revealed

the good compatibility[15], that assigned the chemical structure of **1** to be 3,3',4',5,7-pentahydroxyflavone (quercetin).

Compound **2** was also obtained as a yellow amorphous powder. The molecular formula was proved as $C_{20}H_{18}O_{10}$ by the positive HR-ESI-MS data ($[M+Na]^+$ m/z 441.0715, calcd. for $C_{20}H_{18}O_{10}Na$, 441.0707). Similar to NMR data of **1**, the 1H -NMR and ^{13}C -NMR spectra of **2** also possessed the signals of a flavonoid skeleton. However, the presence of two aromatic protons at δ_H 8.02 (2H, *d*, 9.0 Hz, H-2', H-6') and 6.92 (2H, *d*, 9.0 Hz, H-3', H-5') was the characteristic of a *para*-disubstituted benzene ring, insteads of the 1,3,4-trisubstituted as in **1**, which indicated the presence of a kaempferol skeleton. Moreover, the 1H -NMR exhibited the addition of one anomeric proton with the large coupling constant at δ_H 5.21 (1H, *d*, 7.5 Hz, H-1''). The ^{13}C -NMR was fully supported with the addition of one anomeric carbon signal at δ_C 104.5 (C-1'') and four other oxygenated carbons at δ_C 77.4 (C-3''), 75.2 (C-2''), 71.1 (C-4 and 67.3 (C-5''), which suggested the presence of one β -D-xylopyranosyl unit. The HMBC spectrum of **2** testified the correlation between the anomeric proton at δ_H 5.21 (1H, *d*, 7.5 Hz, H-1'') and carbon at δ_C 135.4 (C-3), that inferred the linking of a β -D-xylopyranosyl unit to the kaempferol skeleton at C-3. The other correlations on HSQC and HMBC spectra were fairly close to the inference. Comparison of the spectroscopic data of compound **2** with those reported showed a high degree of similarity. Consequently, the structure of **2** were defined as kaempferol 3-O- β -D-xylopyranoside[16].

Compound **3** was also yield as a yellow amorphous powder. Its molecular formula

was determined as $C_{27}H_{31}O_{16}$ by the HR-ESI-MS measurement through the ion peak at m/z 634.1434 $[M+Na]^+$ (calcd. for $C_{27}H_{31}O_{16}Na$, 634.1412). The 1H -NMR and ^{13}C -NMR spectra of **3** proved that **3** had the quercetin skeleton as **1**, except the addition of two more sugar units. The 1H -NMR exhibited the presence of two anomeric protons at δ_H 5.11 (1H, *d*, 7.5 Hz, H-1'') and 4.55 (1H, *d*, 1.5 Hz, H-1'''). The ^{13}C -NMR was fully closed with the addition of two anomeric carbons signals at δ_C 104.9 (C-1'') and δ_C 102.5 (C-1'''), which confirmed the presence of two sugar units. Their configurations were proved by the presence of the series of protons and carbons signals of two sugar moieties in the 1H - and ^{13}C -NMR spectrum. The first sugar unit was β -D-glucopyranosyl, the later one was α -L-rhamnopyranosyl. The HMBC spectrum of **3** addressed the correlations between the first anomeric proton at δ_H 5.12 (1H, *d*, 7.5 Hz, H-1'') and carbon at δ_C 135.6 (C-3), the second anomeric proton at δ_H 4.55 (1H, *d*, 1.5 Hz, H-1''') and carbon at δ_C 68.6 (C-6''), that inferred the attachment of a β -D-glucopyranosyl unit to the quercetin skeleton at C-3, α -L-rhamnopyranosyl linking to the first sugar moiety at C-6'', respectively. The remaining HSQC and HMBC data were fairly supported the elucidation. Accordingly, the chemical structure of **3** were identified as quercetin 3-rutinoside (sophorin or rutin) [17].

Compound **4** was afforded as a light yellow powder. The molecular formula of **4** was proved as $C_9H_6O_4$ by the HR-ESI-MS measurement through the positive ion peak at m/z 179.0224 $[M+H]^+$ (calcd. for $C_9H_7O_4$, 179.0244). Its NMR spectra showed signals of a coumarin skeleton. The 1H -NMR spectrum of **4** showed two *cis*-coupled signals of a typical coumarin

frame at δ_H 7.80 (1H, *d*, 9.0 Hz, H-4) and 6.19 (1H, *d*, 9.0 Hz, H-3), along with the presence of two aromatic proton signals at δ_H 6.95 (1H, *s*, H-5), and 6.77 (1H, *s*, H-8). The ^{13}C -NMR spectrum exhibited nine carbon signals in the down field of the 6,7-dihydroxycoumarin carbons from 103.6 to 164.2 ppm. The HMBC spectrum of **4** revealed the correlations between the aromatic proton at δ_H 6.95 (1H, *s*, H-5) and aromatic carbons at δ_C 151.9 (C-7), 144.5 (C-6), 112.8 (C-10), and between

the other aromatic proton at δ_H 6.77 (1H, *s*, H-8) and aromatic carbons at δ_C 151.9 (C-7), 150.5 (C-9), 144.5 (C-6), 112.8 (C-10), that confirmed the existence of two hydroxyl groups at C-6 and C-7, respectively. The other correlations on HSQC and HMBC spectra gave fully agreement with the inference. From the above analysis and comparison of NMR spectral data of **4** with those of esculetin published in the literature, compound **4** was determined as esculetin [18].

Table 1. ^{13}C -NMR spectral data of three isolated compounds **1-3** and references

C	1		2		3	
	δ_C CD ₃ OD	δ_C [15] DMSO- <i>d</i> ₆	δ_C Acetone- <i>d</i> ₆	δ_C [16] DMSO- <i>d</i> ₆	δ_C CD ₃ OD	δ_C [17] CD ₃ OD
2	148.6	147.9	158.5	158.4	159.3	159.5
3	137.3	135.8	135.4	135.3	135.6	135.7
4	177.4	176.9	179.4	179.4	179.3	179.5
5	162.0	160.8	163.1	163.0	162.8	163.2
6	99.2	98.3	100.0	99.9	99.9	100.0
7	165.4	164.1	166.1	166.0	165.9	166.2
8	94.4	93.5	94.8	94.8	94.9	95.0
9	158.0	156.3	159.0	158.9	158.4	158.5
10	104.5	103.1	105.7	105.6	105.6	105.7
1'	123.1	122.1	122.7	122.6	123.1	123.2
2'	116.0	115.2	132.2	132.2	117.7	117.8
3'	146.4	145.2	116.2	116.1	145.7	146.0
4'	148.0	146.9	161.6	161.6	149.7	150.4
5'	116.2	115.7	116.2	116.1	116.0	116.2
6'	121.6	120.1	132.2	132.2	123.6	123.7
1''			104.5	104.6	104.9	104.8
2''			75.2	75.3	75.7	75.9
3''			77.4	77.5	78.1	77.4
4''			71.1	71.0	71.4	71.5
5''			67.3	67.2	77.1	78.3
6''					68.6	68.7
1'''					102.5	102.5
2'''					72.0	72.2
3'''					72.2	72.4
4'''					73.9	74.1
5'''					69.7	69.8
6'''					17.9	18.0

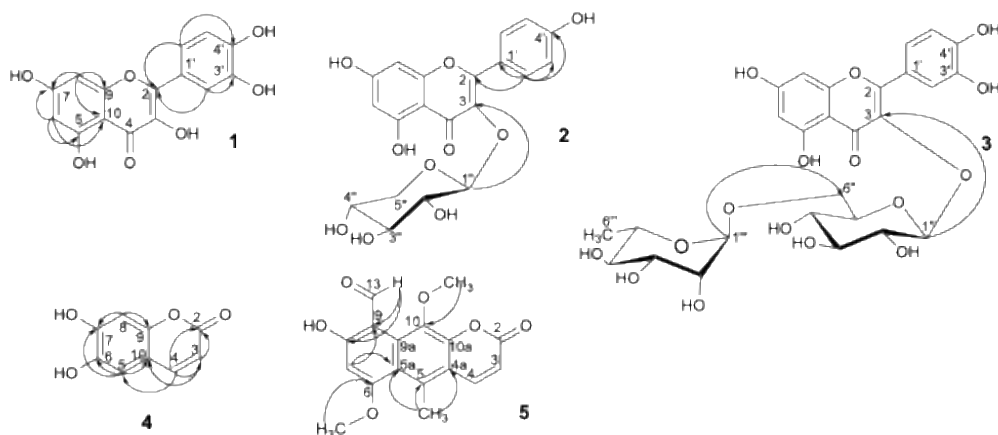


Figure 1. Key HMBC interactions of isolated compounds 1-5

Compound 5 was obtained as a yellow amorphous powder. Its molecular formula was determined as $C_{17}H_{14}O_6$ by the HR-ESI-MS data ($[M+H]^+$ m/z 315.0864, calcd. for $C_{17}H_{15}O_6$, 315.0869). Its NMR spectra showed signals of a coumarin skeleton, which was similar to 4. The NMR data of compound 5, moreover, displayed one aromatic proton signal at δ_H 7.29 (1H, s, H-7) in 1H -NMR spectrum together with four aromatic carbons signals at δ_C 160.0 (C-8), 148.9 (C-6), 115.9 (C-9) and 103.6 (C-7) in ^{13}C -NMR spectrum. Further, the aromatic proton at δ_H 7.29 (1H, s, H-7) correlated with aromatic carbons at δ_C 148.9 (C-6), 137.3 (C-5a) and 115.9 (C-9), which designed the presence of 6,7-benzocoumarin framework.

The HMBC spectrum of 5 exhibited the correlations between oxymethyl protons at δ_H 4.20 (3H, s, H-14) and carbon at δ_C 165.4 (C-10), between oxymethyl protons at δ_H 3.85 (3H, s, H-12) and carbon at δ_C 148.8 (C-6), that clarified the connection of two methoxy groups at C-10 and C-6 of 6,7-benzocoumarin frame.

The correlations between a formyl proton at δ_H 10.56 (1H, s, H-13) and aromatic carbons at δ_C 160.0 (C-8), 115.9 (C-9), 111.5 (C-9a) confirmed the attachment of one formyl function at C-9. The

correlations between methyl protons at δ_H 2.56 (3H, s, H-11) and aromatic carbons at δ_C 137.3 (C-5a), 126.5 (C-5), 113.6 (C-4a) demonstrated the attachment of one methyl group at C-5 of the frame. The other correlations on HSQC and HMBC spectra determined the elucidation. Hence, the chemical structure of 5 was evinced as lasibidoupin B [13].

Table 2. ^{13}C -NMR spectral data of two isolated compounds 4-5 and references

C	4		5	
	δ_C CD ₃ OD	δ_C [18] CD ₃ OD	δ_C CDCl ₃	δ_C [13] CD ₃ OD
2	164.2	164.6	159.9	159.9
3	112.5	112.5	114.5	114.5
4	146.0	146.2	141.1	141.1
5	113.0	113.1	126.5	126.8
6	144.5	144.6	148.9	148.9
7	151.9	152.1	103.6	103.6
8	103.6	103.7	160.0	160.1
9	150.5	150.5	115.9	115.9
10	112.8	112.8	165.4	165.3
4a			113.6	113.6
5a			137.3	137.2
9a			111.5	111.4
10a			149.6	149.6
5-CH ₃			12.0	12.0
6-OCH ₃			61.4	61.4
10-OCH ₃			66.1	66.1
9-CHO			195.5	195.3

Compounds **4** and **5** were evaluated for the inhibition of acetylcholinesterase and alpha-glucosidase. Both **4** and **5** revealed potent inhibition toward alpha-glucosidase with IC_{50} 5.83 ± 0.50 and 4.0 ± 0.00 ($\mu\text{g/mL}$), respectively, compared to the positive control, acarbose with the IC_{50} value of 166.4 ± 0.05 ($\mu\text{g/mL}$) while they failed any activity to acetylcholinesterase inhibition.

The cytotoxicity of compounds **4** and **5** against three human cancer cell lines (A549, HEK-293 and HepG2) was measured by MTT assay. As results, lasibidoupin B (**5**) showed weaker cytotoxic effect against A549 and HEK-293 with the IC_{50} values of 5.83 ± 0.50 and 13.83 ± 0.09 $\mu\text{g/mL}$, respectively, than the ellipticine positive control with the IC_{50} values of 0.41 ± 0.05 and 1.53 ± 0.12 $\mu\text{g/mL}$, respectively. Compound **5** revealed no activity against HepG2 cell line while compound **4** is inactive against all three tested cell lines A549, HEK-293, and HepG2 at the concentration 100 $\mu\text{g/mL}$.

4. CONCLUSION

In this study, three flavonoids, one flavonol quercetin (**1**), one flavonol monoglycoside kaempferol-3-*O*- β -D-xylopyranoside (**2**), one flavonol diglycoside sophorin (**3**), together with two coumarins esculetin (**4**) and lasibidoupin B (**5**) were isolated and structurally elucidated from the stems of *Lasianthus honbaensis* V. S. Dang, Tagane & H. Toyama collected at Hon Ba Nature Reserve, employing diverse chromatographic techniques and comprehensive spectroscopic analyses. This is the first time the phytochemical constituent and biological activity of the stems of *Lasianthus honbaensis* was announced. Except **5**, all remaining

compounds **1-4** were notified for the first time from the genus *Lasianthus*. Compounds **4** and **5** exhibited potential inhibition toward alpha-glucosidase while they showed no activity to acetylcholinesterase inhibition. Compound **5** displayed weak cytotoxicity against two cancer cells A549 and HEK-293.

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