องค์ประกอบทางเคมีจากลำต้นเขยตาย

Chemical Constituents from *Glycosmis pentaphylla* Stems

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บทคัดย่อ

จากการศึกษาองค์ประกอบทางเคมีของลำต้นเขยตายสามารถแยกสารที่มีรายงานแล้วจำนวน 11 สาร ประกอบด้วย bisglybomine B (**1**), glybomine B (**2**), carbalexin C (**3**), glycoborinine (**4**), skimmianine (**5**), robustine (**6**), γ-fagarine (**7**), arborinine (**8**), *N-p-trans*-coumaroyltyramine (**9**), 2-(*N*-methyl-2-phenylacetamido)benzoic acid (**10**) และ (-)-syringa-resinol (**11**) การพิสูจน์โครงสร้างของสารทั้งหมดได้จากการวิเคราะห์ข้อมูล NMR สเปกโทรสโกปีเป็นหลัก และการเปรียบเทียบกับข้อมูลที่มีรายงานไว้แล้ว งานวิจัยนี้เป็นครั้งแรกที่สามารถแยกสารประกอบ **10** จากธรรมชาติ และเป็นครั้งแรกที่รายงานการพบสารประกอบ **10** และ **11** จากพืชในสกุล *Glycosmis* ได้ทำการศึกษาฤทธิ์ยับยั้งเอนไซม์อะเซทิลโคลีนเอสเทอเรสของสารประกอบที่แยกได้บางชนิด

ABSTRACT

Phytochemical investigation of the stems of *Glycosmis pentaphylla* led to the isolation of eleven known compounds, including bisglybomine B (**1**), glybomine B (**2**), carbalexin C (**3**), glycoborinine (**4**), skimmianine (**5**), robustine (**6**), γ-fagarine (**7**), arborinine (**8**), *N-p-trans*-coumaroyltyramine (**9**), 2-(*N*-methyl-2-phenylacetamido) benzoic acid (**10**) and (-)-syringaresinol (**11**). All structural assignments were made by comparing the NMR spectral data of the pure isolates with that published in the quoted literature. Among them, compound **10** was firstly purified as a natural product and compounds **10** and **11** were isolated from the genus *Glycosmis* for the first time. Some isolates were evaluated for anti-acetylcholinesterase activity.

คำสำคัญ: เขยตาย พืชวงศ์ส้ม แอลคาลอยด์ ลิกแนน ฤทธิ์ยับยั้งเอนไซม์อะเซทิลโคลีนเอสเทอเรส

Keywords: *Glycosmis pentaphylla*, Rutaceae, Alkaloids, Lignan, Anti-acetylcholinesterase activity

INTRODUCTION

Glycosmis is a genus of small trees of forty species from Rutaceae family commonly found in South East Asia and South China. Fourteen of these species occur in Thailand (Smitinand, 2011). Some species were traditionally used for the treatment of various diseases such as dysentery, fever cough, jaundice, rheumatism, eczema and skin diseases (Burkill, 1935; Gimlette, 1939). This genus is a rich source of various classes of compounds such as flavonoids, alkaloids and sulphur-containing amides (Greger and Zechner, 1996; Hofer et al., 2000; Rahmani et al., 2004; Wang et al., 2005b; Lukaseder et al., 2009; Rahmani et al., 2010).

Glycosmis pentaphylla, known in Thai as Khey Tay, is a small shrub which grows to a height of 5 meters and it has been used as a folk medicine in the treatment of cough, worms, jaundice, fever, inflammation, rheumatism, anaemia and vermifuge. This plant was also found to possess several pharmacological activities, such as hepatoprotective, anti-inflammatory, anti-tumor, antibacterial, anti-oxidant, anti-viral, anti-ulcer, chemo protective and antiseptic activities (Sreejith et al., 2012). Previous phytochemical studies on this plant have resulted in the isolation of alkaloids, including acridones (Ito et al., 1999), carbazoles (Bhattacharyya et al., 1985; Chowdhury et al., 1987; Kamaruzzman et al., 1989; Jash et al., 1992; Yang et al., 2012), furanopyridines (Zhang et al., 2016), quinazolines (Sarkar and Chakraborty, 1977) and quinolones (Bhattacharyya and Chowdhury, 1985), isoflavone diglycosides (Wang et al., 2006b) and hydroquinone diglycoside acyl esters (Wang et al., 2006a). In the continuing search for bioactive natural products from Thai plants, we investigated the chemical constituents of the stems of *G. pentaphylla*. As a result, eleven compounds were isolated from hexane and methanol extracts. Among them, one compound was firstly purified as a natural product, two were isolated from *G. pentaphylla* and the genus *Glycosmis* for the first time. In addition, the presence of these compounds shows the relationship between this plant and other species from the Rutaceae family.

EXPERIMENT

Plant Material

The stems of *G. pentaphylla* were purchased from Tai An Jan herbal store, Bangkok in December 2015. A voucher specimen (Thitima Rukachaisirikul, No. 010) was deposited at the Faculty of Science, Ramkhamhaeng University, Thailand.

Extraction and Isolation

The air-dried, powdered stems of *G. pentaphylla* (10 kg) were extracted successively with *n*-hexane (20L x 3) and MeOH (20L x 3) at room temperature. The hexane and MeOH extracts were filtered and concentrated to dryness under reduced pressure. The hexane extract (20.1 g) was subjected to CC using gradient solvent system of hexane, hexane-EtOAc and EtOAc to give 8 fractions (H1-H8). Fr. H5 (2.5 g) was rechromatographed on Sephadex LH-20 (40% CH_2Cl_2 in MeOH) and further resubjected to CC (5% EtOAc in hexane) to furnish compound **1** (3.2 mg). Fr. H8 (1.10 g) was fractionated on Sephadex LH-20 (20% CH_2Cl_2 in MeOH) to give 5 subfractions (H8.1-H8.5). Subfr. H8.3 (0.25 g) was further purified by CC (30% EtOAc in hexane) to afford compound **5** (59.8 mg), whereas subfr. H8.4 (54.9 mg) was separated by CC (30% EtOAc in hexane) to furnish compound **8** (31.9 mg). The MeOH extract (965 g) was subjected to CC using gradient solvent system of hexane-EtOAc, EtOAc, EtOAc-MeOH and MeOH to give 10 fractions (M1-M10). Fr. M2 (3.37 g) was rechromatographed by CC twice in

succession (4% EtOAc in hexane and 30% EtOAc in hexane) to yield compound **6** (14.6 mg). Fr. M3 (5.38 g) was separated on Sephadex LH-20 (20% CH_2Cl_2 in MeOH) to give 5 subfractions (M3.1-M3.5). Subfr. M3.3 (28.1 mg) was purified on Sephadex LH-20 (20% CH_2Cl_2 in MeOH) to obtain compound **2** (122.2 mg). Subfr. M3.4 (0.12 g) was rechromatographed on Sephadex LH-20 (MeOH) to afford compound **4** (36.8 mg), whereas subfr. M3.5 (20.4 mg) furnished compound **3** (6.5 mg). Fr. M5 (5.55 g) was subjected to CC (30% EtOAc in hexane) to furnish compound **7** (64.4 mg). Fr. M6 (16.20 g) was fractionated by CC (4% MeOH in CH_2Cl_2) to obtain 6 subfractions (M6.1-M6.6). Subfr. M6.4 (2.57 g) was rechromato-graphed by CC (hexane-EtOAc-MeOH, 60:40:3, v/v/v) to afford compound **11** (98.5 mg). Subfr. M6.5 (3.12 g) was purified by CC (3% MeOH in CH_2Cl_2) to yield compound **9** (23.7 mg). Fr. M8 (12.30 g) was further purifield by CC (5% MeOH in CH_2Cl_2) to give compound **10** (6.1 mg).

Bisglybomine B (**1**): pale yellow powder; UV λ_{max}^{MeOH} (log ε): 216 (5.33), 246 (5.32), 263 (sh), 317 (4.98), 335 (sh) nm; IR (ART): 3264, 1608, 1491, 1253, 1219, 1181, 1134, 1084, 800, 784, 733 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.99 (br s, H-4, H-4'), 7.47 (s, NH), 7.00 (d, *J* = 8.5 Hz, H-7, H-7'), 6.95 (d, *J* = 8.5 Hz, H-8, H-8'), 5.35 (t, *J* = 6.2 Hz, H-2", H-2"'), 5.24 (s, H-2, H-2'), 3.95 (d, *J* = 6.2 Hz, H-1", H-1"'), 3.85 (s, 6-OCH_3, 6'-OCH_3) , 2. 48 (s, 3-CH_3, 3'-CH_3), 1.96 (s, H-4", H-4"'), 1.73 (s, H-5", H-5"'); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 151.0 (C-2, C-2'), 150.8 (C-6, C-6'), 138.8 (C-9a, C-9a'), 134.7 (C-8a, C-8a'), 132.5 (C-3, C-3') 125.7 (C-4, C-4'), 124.2 (C-5, C-5'), 122.9 (C-4b, C-4b'), 122.2 (C-2", C-2"'), 117.2 (C-4a, C-4a'), 117.1 (C-3, C-3'), 111.0 (C-7, C-7'), 108.1 (C-8, C-8'), 98.5 (C-1, C-1'), 57.8 (6-OCH_3, 6'-OCH_3), 25.8 (C-5", C-5"'), 25.5 (C-1" , C-1"'), 18.2 (C-4", C-4"'), 16.9 (3-CH_3, 3'-CH_3); ESMS *m/z* 589.8 $[M+H]^+$.

Glybomine B (**2**): pale yellow powder; UV λ_{max}^{MeOH} (log ε): 216 (4.79), 241 (4.78), 260 (sh), 307 (4.51), 335 (sh) nm; IR (ART): 3380, 1621, 1588, 1223, 1152, 1129, 1077, 740, 716 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.79 (s, H-4), 7.71 (br s, NH), 7.02 (d, *J* = 8.4 Hz, H-8), 6.95 (d, *J* = 8.4 Hz, H-7), 6.64 (s, H-1), 5.30 (br s, H-2'), 3.90 (d, *J* = 4.8 Hz, H-1'), 3.85 (s, 6-OCH_3), 2.37 (s, 3-CH_3), 1.91 (s, H-4'), 1.66 (s, H-5'); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.0 (C-2), 150.8 (C-6), 140.6 (C-9a), 135.1 (C-8a), 132.1 (C-3'), 124.3 (C-4), 124.2 (C-5), 122.7 (C-4b), 122.4 (C-2'), 117.1 (C-4a), 116.1 (C-3), 110.9 (C-7), 107.6 (C-8), 96.1 (C-1), 58.0 (6-OCH_3), 25.67 (C-5'), 25.60 (C-1'), 18.1 (C-4'), 16.4 (3-CH_3); ESMS *m/z* 294.8 $[M-H]^-$.

Carbalexin C (**3**): pale yellow powder; UV λ_{max}^{MeOH} (log ε): 217 (4.94), 233 (4.46), 263 (sh), 312 (4.64) nm; IR (ART): 3400, 3180, 1634, 1581, 1206, 1167, 1133, 1111, 833, 808, 776 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.96 (br s, NH), 7.68 (s, H-4), 7.39 (d, *J* = 2.0 Hz, H-5), 7.18 (d, *J* = 8.8 Hz, H-8), 6.90 (dd, *J* = 8.8, 2.0 Hz, H-7), 6.74 (s, H-1), 3.87 (s, 6-OCH_3), 2.35 (s, 3-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.6 (C-6, C-2), 140.1 (C-9a), 134.3 (C-8a), 124.2 (C-4b), 121.5 (C-4), 116.8 (C-3), 116.5 (C-4a), 112.8 (C-7), 110.7 (C-8), 102.6 (C-5), 96.2 (C-1), 56.0 (6-OCH_3), 16.2 (3-CH_3); ESMS *m/z* 226.4 $[M-H]^-$.

Glycoborinine (**4**): pale yellow powder; UV λ_{max}^{MeOH} (log ε): 218 (4.39), 260 (4.04), 334 (4.04) nm; IR (ART): 3446, 3376, 1633, 1596, 1572, 1223, 1144, 1114, 1073, 802, 716 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.97 (br s, NH), 7.77 (s, H-4), 7.18 (d, *J* = 9.8 Hz, H-1'), 7.03 (d, *J* = 8.6 Hz, H-8), 6.77 (d, *J* = 8.6 Hz, H-7), 6.73 (s, H-1), 5.76 (d, *J* = 9.8 Hz, H-2'), 2.34 (s, 3-CH_3), 1.44 (s, H-4', H-5'); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 153.5 (C-2), 146.2 (C-6), 140.5 (C-9a), 134.7 (C-8a), 130.9 (C-2'), 123.6 (C-4), 120.2 (C-1'), 119.0 (C-4b), 116.7 (C-3, C-4a), 114.7 (C-5),

113.4 (C-7), 109.8 (C-8), 96.0 (C-1), 75.0 (C-3'), 27.0 (C-4', C-5'), 16.3 (3-CH_3); ESMS *m/z* 280.7 $[M+H]^+$.

Skimmianine (**5**): pale yellow powder; UV λ_{max}^{MeOH} (log £): 249 (4.33), 330 (3.33) nm; IR (ART): 1616, 1577, 1505, 1489, 1266, 1236, 1088, 1057, 771, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.99 (d, *J* = 9.4 Hz, H-5), 7.55 (br s, H-1'), 7.21 (d, *J* = 9.4 Hz, H-6), 7.01 (br s, H-2'), 4.40 (s, 4-OCH_3), 4.09 (s, 8-OCH_3), 4.00 (s, 7-OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 164.3 (C-2), 157.1 (C-4), 152.1 (C-7), 142.9 (C-1'), 141.9 (C-8), 141.4 (C-8a), 118.1 (C-5), 114.8 (C-4a), 112.0 (C-6), 104.6 (C-2'), 101.9, (C-3), 61.6 (8-OCH_3), 58.9 (4-OCH_3), 56.7 (7-OCH_3); ESMS *m/z* 260.9 $[M+H]^+$.

Robustine (**6**): pale yellow powder; UV λ_{max}^{MeOH} (log £): 245 (4.74), 329 (3.74) nm; IR (ART): 3375, 1619, 1587, 1513, 1202, 1151, 1093, 739, 712 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.70 (d, *J* = 8.0 Hz, H-5), 7.59 (d, *J* = 2.6 Hz, H-1'), 7.31 (t, *J* = 8.0 Hz, H-6), 7.15 (d, *J* = 8.0 Hz, H-7), 7.06 (d, *J* = 2.6 Hz, H-2'), 4.41 (s, 4-OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 162.4 (C-2), 157.5 (C-4), 151.0 (C-8), 143.3 (C-1'), 135.7 (C-8a), 124.2 (C-6), 118.7 (C-4a), 112.9 (C-5), 110.2 (C-7), 105.0 (C-2'), 103.9, (C-3), 59.0 (4-OCH_3); ESMS *m/z* 216.7 $[M+H]^+$.

¥-Fagarine (**7**): pale yellow powder; UV λ_{max}^{MeOH} (log £): 244 (5.09), 338 (4.04) nm; IR (ART): 1619, 1580, 1553, 1512, 1259, 1187, 1156, 1080, 978, 746, 723 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.80 (d, *J* = 8.1 Hz, H-5), 7.60 (br s, H-1'), 7.31 (t, *J* = 8.1 Hz, H-6), 7.03 (br s, H-2'), 7.02 (d, *J* = 8.1 Hz, H-7), 4.39 (s, 4-OCH_3), 4.04 (s, 8-OCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 163.1 (C-4), 156.8 (C-2), 154.5 (C-8), 143.8 (C-1'), 137.4 (C-8a), 123.3 (C-6), 119.6 (C-4a), 114.0 (C-5), 107.6 (C-7), 104.4 (C-2'), 103.8, (C-3), 58.9 (4-OCH_3), 55.9 (8-OCH_3); ESMS *m/z* 230.9 $[M+H]^+$.

Arborinine (**8**): pale yellow powder; UV λ_{max}^{MeOH} (log £): 211 (4.16), 274 (4.33) nm; IR (ART): 3311, 1637, 1589, 1555, 1508, 1250, 1182, 1138, 1105, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 14.76 (s, OH), 8.36 (d, *J* = 8.0 Hz, H-8), 7.69 (t, *J* = 8.0 Hz, H-6), 7.46 (d, *J* = 8.0 Hz, H-5), 7.25 (d, *J* = 8.0 Hz, H-7), 6.19 (s, H-4), 4.00 (s, 3-OCH_3), 3.92 (s, 2-OCH_3), 3.78 (s, NCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 180.5 (C-9), 159.1 (C-3), 155.9 (C-1), 141.7 (C-14), 140.2 (C-11), 133.8 (C-6), 129.9 (C-2), 126.3 (C-8), 121.3 (C-7), 120.4 (C-13), 114.5 (C-5), 105.5 (C-12), 86.6 (C-4), 60.7 (2-OCH_3), 55.9 (3-OCH_3), 33.9 (NCH_3); ESMS *m/z* 286.8 $[M+H]^+$.

***N-p-trans*-Coumaroyltyramine** (**9**) : white powder; UV λ_{max}^{MeOH} (log £): 224 (4.15), 300 (4.19) nm; IR (ART): 3432, 3294, 1660, 1602, 1530, 1510, 1221, 980, 828 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz): δ 7.43 (d, *J* = 16.0 Hz, H-8), 7.38 (d, *J* = 8.4 Hz, H-2, H-6), 7.04 (d, *J* = 8.6 Hz, H-2', H-6'), 6.77 (d, *J* = 8.6 Hz, H-3', H-5'), 6.70 (d, *J* = 8.4 Hz, H-3, H-5), 6.37 (d, *J* = 16.8 Hz, H-7), 3.44 (t, *J* = 7.4 Hz, H-8'), 2.73 (t, *J* = 7.4 Hz, H-7'); ^{13}C NMR (CD_3OD, 100 MHz): δ 169.2 (C-9), 160.5 (C-4), 156.9 (C-4'), 141.7 (C-7), 131.2 (C-1'), 130.7 (C-2', C-6'), 130.5 (C-2, C-6), 127.6 (C-1), 118.3 (C-8), 116.7 (C-3', C-5'), 116.2 (C-3, C-5), 42.4 (C-8'), 35.8 (C-7'); ESMS *m/z* (%) 589.4 $[2M+Na]^+$.

2-(*N*-Methyl-2-phenylacetamido) benzoic acid (**10**): pale yellow amorphous; UV λ_{max}^{MeOH} (log £): 228 (4.06), 306 (3.69) nm; IR (ART): 3698-2687, 1701, 1601, 1544, 1498, 1257, 760, 693 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 8.37 (dd, *J* = 7.8, 1.4 Hz, H-6), 7.69 (ddd, *J* = 8.0, 8.0, 1.6 Hz, H-4), 7.45 (td, *J* = 7.5, 0.6 Hz, H-5), 7.31 (m, H-3), 7.30 (s, H-2', H-3', H-5', H-6'), 7.25 (m, H-4'), 4.26 (s, H-7'), 3.60 (s, NCH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 169.0 (COOH), 162.1 (C-8'), 141.5 (C-2), 134.5 (C-1'), 133.8 (C-4), 129.1, (C-2', C-6'), 128.7 (C-6), 128.2

(C-3', C-5'), 125.9 (C-5), 127.4 (C-4'), 120.1 (C-1), 114.4 (C-3), 43.5 (C-7'), 34.8 (NCH_3); ESMS *m/z* 270.3 $[M+H]^+$.

(-)-Syrinaresinol (**11**): white powder; $[\sim]_D^{28}$-16.4° (c 0.51, $CHCl_3$) ($[\sim]_D^{24}$-32.5° (c 0.46, $CHCl_3$) (Stocklin et al., 1969)); UV λ_{max}^{MeOH} (log £): 208 (4.99), 238 (4.19), 272 (3.17) nm; IR (ART): 3422, 1608, 1517, 1199, 1105, 726 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.56 (s, H-2', H-2", H-6', H-6"), 5.49 (s, 4"-OH, 4"'-OH), 4.70 (d, *J* = 4.0 Hz, H-1, H-4), 4.26 (dd, *J* = 9.0, 6.6 Hz, H-3a, H-6a), 3.88 (s, 3'-OCH_3, 3"-OCH_3, 5'-OCH_3, 5"-OCH_3), 3.86 (overlapping signal, H-3b, H-6b), 3.07 (br s, H-2, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 147.0 (C-3', C-3", C-5', C-5"), 134.1 (C-4', C-4"), 132.0 (C-1', C-1"), 102.5 (C-2', C-2", C-6', C-6"), 86.0 (C-1, C-4), 71.7 (C-3a, C-3b, C-6a, C-6b), 56.3 (3'-OCH_3, 3"-OCH_3, 5'-OCH_3, 5"-OCH_3), 54.2 (C-2, C-5); ESMS *m/z* 859.6 $[2M+Na]^+$.

Anti-Cholinesterase Activity

Evaluation of anti-ChE activity by samples was measured by a microplate assay based on Ellman's method (Ellman et al., 1961) with modification. In brief, 140 µL of 10 mM sodium phosphate buffer (pH 8.0), 20 µL of solution of AChE (0.2 units/mL in 10 mM sodium phosphate buffer, pH 8.0) and 20 µL of test compound solution dissolved in 80% methanol (a final concen-tration of 0.1 mg/mL) were mixed in 96-well plates and the plates were immediately shaken for 10 min.

The reaction was stated by adding 20 µL of mixture solution of 5 mM 5,5′-dithiobis-(2-nitrobenzoic acid) (DTNB) in 10 mM sodium phosphate buffer (pH 8.0), containing 0.1% bovine serum albumin (BSA) and 5 mM acetylthiocholine iodide (ATCI) in 10 mM sodium phosphate buffer, pH 8.0 (5:1). The hydrolysis of acetyl-thiocholine was monitored at 405 nm after 5 minutes of incubation at room temperature. Percentage of inhibition was calculated by comparing the rate of enzymatic hydrolysis of ATCI for the sample that of blank (80% methanol in buffer). Galantamine was used as a reference standard. Every experiment was done in triplicate.

RESULTS AND DISCUSSION

The present study reported the isolation and structural elucidation of eleven known compounds from the stems of *G. pentaphylla*, identified as bisglybomine B (**1**) (Yang et al., 2012), glybomine B (**2**) (Ito et al., 2004), carbalexin C (**3**) (Pacher et al., 2001; Schmide and Knolker, 2009), glycoborinine (**4**) (Chakravarty et al., 1999), skimmianine (**5**) (Rahmani et al., 2010), robustine (**6**) (Boye et al., 2013), γ-fagarine (**7**) (Min et al., 2007), arborinine (**8**) (Rahmani et al., 2010), *N-p-trans*-coumaroyltyramine (**9**) (Mohammed Al-Taweel et al., 2012), 2-(*N*-methyl-2-phenyl-acetamido)benzoic acid (**10**) (Farooq Biabani et al., 1998) and (-)-syringaresinol (**11**) (Ragasa et al., 2015), on the basis of their ^{1}H NMR and ^{13}C NMR spectral analysis and comparison with the literature (Figure 1). The compounds may be classified as four carbazoles (**1**-**4**), three furoquinolines (**5**-**7**), one acridone (**8**), two amides (**9** and **10**) and one lignan (**11**). The isolation of compound **10** from this specie represents a new finding and this compound has not previously been reported as a natural product before. In addition, compounds **10** and **11** were isolated from the genus *Glycosmis* for the first time.

To the best of our knowledge, compounds **1** and **6** were previously reported from only one *Glycosmis* species, i.e., *G. pentaphylla* (Yang et al., 2012; Chen et al., 2015; Zhang et al., 2016). Compounds **2**-**5** and **7**-**9** were also isolated or detected in twelve species of the genus *Glycosmis*, i.e., *G. arborea* (Chakravarty et al., 1999; Ito et al., 2004), *G. bilocularis* (Bowen et al., 1978), *G. citrifolia* (Wu et al., 1995; Ito et al., 2000; Rahmani et al., 2010),

G. cochinchinensis (Sripisut et al., 2013), *G. cyanocarpa* (Greger et al., 1992), *G. elongata* (Rahmani et al., 2010), *G. macrophylla* (Cheenpracha and Laphookhieo, 2011), *G. mauritiana* (Rastogi et al., 1980), *G. montana* (Wang et al., 2005a; Zheng et al., 2013), *G. parva* (Kongsubsopa and Ruangrungsi, 2002; Chansriniyom et al., 2009), *G. parviflora* (Pacher et al., 2001) and *G. trichanthera* (Vajodaya et al., 1998), notably compound **5** widely distributed in this genus. In this study, isolation of carbazoles from *G. pentaphylla* further supports the previous opinion that the presence of carbazoles in the genus *Murraya*, *Clausena*, *Glycosmis* and *Micromelum* of Rutaceae family suggests a genetic relationship between these genus (Knolker and Reddy, 2008). In addition, this is the first report that lignan (**11**) was isolated from *G. pentaphylla* and genus *Glycosmis*. Previously, this compound was isolated from other genus in Rutaceae family, such as *Zanthoxylum ailanthoides* (Chen et al., 2013) and *Haplophyllum vulcanicum* (Gözler et al., 1996). Interesting to note is that compound **10** was isolated naturally for the first time. Therefore, it could be tentatively concluded that compounds **1**, **6**, **10** and **11** might be a useful chemotaxonomic marker of *G. pentaphylla* and could be used to differentiate *G. pentaphylla* from other species of *Glycosmis*.

Compounds **2** and **4**-**11** were evaluated for anti-acetylcholinesterase activity. Compounds **2**, **8**, and **4** exhibited anti-acetylcholinesterase activity with the IC_{50} values of 10.05, 14.99 and 32.10 μM, respectively, while the other compounds were inactive.

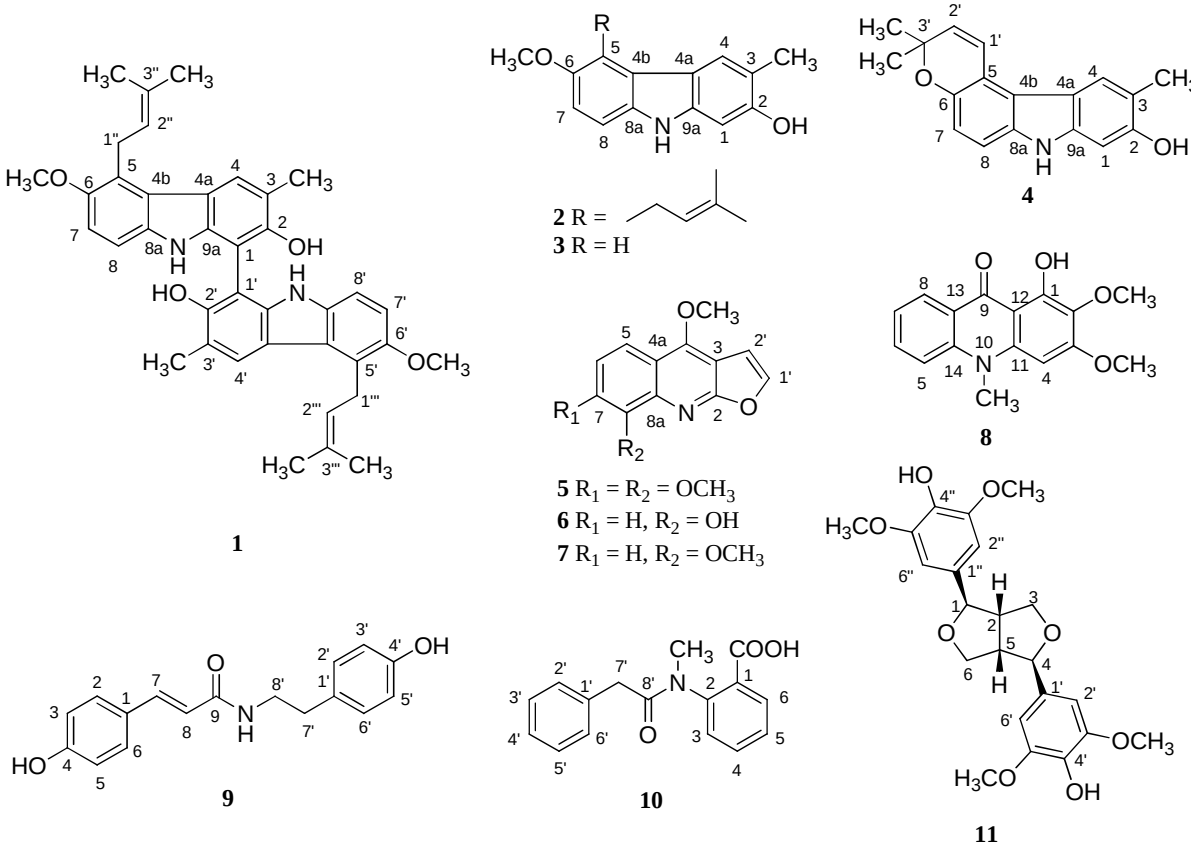

Figure 1. Structures of isolated compounds from *G. Pentaphylla*

CONCLUSION

Phytochemical investigation of *G. pentaphylla* stems led to the isolation of eleven known compounds. 2-(*N*-Methyl-2-phenyl-acetamido)benzoic acid (**10**) was firstly isolated as a natural product and compounds **10** and (-)-syringaresinol (**11**) were isolated from the genus *Glycosmis* for the first time. The co-occurrence of bisglybomine B (**1**), robustine (**6**), compounds **10** and **11** within the species *G. pentaphylla* and the genus *Glycosmis* may be chemotaxonomically important. Among the tested compounds, glybomine B (**2**) exhibited the strongest anti-acetylcholinesterase activity with the IC_{50} values of 10.05 μM.

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