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Research article

Polyoxygenated *seco*-cyclohexenes derivatives from flower and leaf extracts of *Desmos cochinchinensis* and their α-glucosidase inhibitory activity

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ABSTRACT

Phytochemical investigations from the flower and leaf extracts of *D. cochinchinensis* resulted in the isolation and structural elucidation of five new polyoxygenated *seco*-cyclohexene derivatives, desmoscochinchinenes A-E (**1**–**5**), together with 11 known compounds (**6**–**16**). The structures on the new compounds were elucidated from their spectroscopic data, including UV, IR, NMR, and HRESITOFMS. Some of the isolated compounds were evaluated for their α-glucosidase inhibitory activities. Chrysin (**9**), pinocembrin 7-*O*-benzoate (**12**), and (−)-(5*R*)-desmoscochinoxepinone B (**16**) inhibited α-glucosidase better than the standard control (acarbose, IC_{50} = 83.5 μM) with IC_{50} values of 5.7, 33.8, 53.3 μM, respectively.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder caused by an irregular rise in plasma glucose levels due to the unbalanced development of insulin or unresponsiveness to the influence of this hormone on cellular receptor signal transduction (Stojkovic et al., 2019). There are two underlying causes of diabetes mellitus: type 1 diabetes is a chronic condition that is characterized by the body's inability to produce insulin (Aathira and Jain, 2014), while its incapacity to regulate insulin response is called type 2 diabetes (Skyler et al., 2017). DM has also been reported the cause of many serious health problems, such as eyes (retinopathy), nerves (neuropathy), heart (stroke, coronary heart disease, and peripheral artery disease), teeth and gum problems, cancer, and depression (Emerging Risk Factors Collaboration, 2011). In diabetes treatment, regulation of the absorption rate of blood sugar from the small intestine by inhibiting digestive enzymes, such as α-glucosidase, is essential (Kim et al., 2008; Holman et al., 1999). Miglitol, acarbose, and voglibose are well-known commercial drugs used as an inhibitor of α-glucosidase in DM control, particularly type 2 diabetes (Saito et al., 1998; Xu et al., 2019). However, long-term use may result in undesirable side effects (Lee et al., 2014). Therefore, it is necessary to find new α-glucosidase inhibitors to treat diabetes in the future.

Desmos (Annonaceae) genus, a shrub or climbing plant, is wildly distributed in many Asian countries, including India, Myanmar, Thailand, Philippines, and Malaysia (Kuo et al., 2015) and five species, *D. chinensis* Lour, *D. cochinchinensis* Lour, *D. crinitus* Saff., *D. dumosus* (Roxb.) Saff., and *D. macrocarpus* Bân have been found in Thailand (Forest Herbarium-BKF, 2012). *Desmos cochinchinensis* Lour is a medium-sized shrub, which is used as a traditional medicine in South China for the treatment of malaria (Liao et al., 1989; Wu et al., 1994, 1997). There are two different flower forms (large petal and slim petal) of *D. cochinchinensis* (Figure 1) have been grown in Mae Fah University (Latitude: 20°04′48″N; Longitude: 99°89′43″E). Recently, we reported many new flavonoids and oxepinones from the leaf and twig extracts of *D. cochinchinensis* (large petal). Some of them showed interesting α-glucosidase inhibitory activity (Meesakul et al., 2019). In continuation of our studies on the different forms of the flower (slim petal) of the same plant, we report herein our studies of the flower and leaf extracts, which resulted in the isolation of 16 compounds (Figure 2), including five previously undescribed compounds. Furthermore, the α-glucosidase inhibitory activities of some of the isolated compounds are also reported.

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Figure 1. Two different forms of flower of *Desmos cochinchinensis* growing in Mae Fah Luang University. (A) Slim petal of *D. cochinchinensis*. (B) large petal of *D. cochinchinensis*.

2. Materials and methods

2.1. General experimental procedures

The information on instruments and materials was the same as previous reports (Raksat et al., 2019; Phukhatmuen et al., 2020; Suthiphasilp et al., 2020). For more details, please see Supplementary Material.

2.2. Collection of plant materials

The flowers and leaves of *D. cochinchinensis* were collected in August 2015 from an authentically identified plant growing at Mae Fah Luang University Health Park, Chiang Rai Province, Thailand (GPS coordinates: 20°03′19″N 99°53′38″E). The plant was identified by Mr. Kithisak Aongyong and a voucher specimen (MFU-NPR0157) was deposited at the Natural Products Research Laboratory, School of Science, Mae Fah Luang University.

2.3. Extraction and isolation

The fresh flowers (1.72 kg) and air-dried leaves (567.4 mg) of *D. cochinchinensis* were individually extracted with MeOH (3 × 20 L) and EtOAc (3 × 10 L), respectively. The methanol extract (75.4 g) separated by quick column chromatography (QCC) over silica gel (hexanes- EtOAc, 1:0 to 0:1, *v/v*) to provide 11 fractions (F1–F11). F8 (32.7 mg) was further separated by CC eluting with ethyl acetate (EtOAc) in dichloromethane (CH_2Cl_2) (0.5:10, *v/v*) to give four fractions (F8A-F8D). Separation of F8C (10.5 mg) by reverse phase (RP) C_{18} high-performance liquid chromatography (HPLC) eluting with an isocratic system of acetonitrile (CH_3CN) in water (H_2O) (0.9:1.1, *v/v*, 2.0 mL/min) gave compounds **3** (3.1 mg, t_R 30.8 min) and **11** (4.1 mg, t_R 55.6 min). F11 (735.1 mg) was separated by Sephadex-LH20 eluting with MeOH to provide four fractions (F11A-F11D). Purification of F11C (274.1 mg) by RP C_{18} HPLC eluting with an isocratic system of MeOH in H_2O (0.7:1.3, *v/v*, 2.0 mL/min) provided seven fractions (F11CA-F11CG). Further separation of F11CC (10.5 mg) by RP C_{18} HPLC eluting with an isocratic system of MeOH in H_2O (0.7:1.3, *v/v*, 2.0 mL/min) gave compound **4** (2.3 mg, t_R 21.2 min). Compound **5** (7.1 mg, t_R 11.7 min) was obtained from F11CG (21.7 mg) by RP C_{18} HPLC eluting with an isocratic system of MeOH in H_2O (0.5:1.5, *v/v*, 2.0 mL/min). For the details of isolation procedures for known compounds, see Supplementary Material.

Similarly, the EtOAc extract (36.7 g) was separated by QCC over silica gel (hexanes in EtOAc, 1:0 to 0:1, *v/v*) to provide eight fractions (L1-L8). L4 (4.08 g) was further separated by CC eluting with EtOAc in hexanes (1:5, *v/v*) to give eight fractions (L4A-L4H). Fraction L4F (17.7 mg) by RP C_{18} HPLC eluting with an isocratic system of CH_3CN in H_2O (0.7:1.3, *v/v*, 2.0 mL/min). Fraction L4FB (3.8 mg) was further purified by PTLC eluting with EtOAc in hexanes (1:0.3, *v/v*) yielded compound **2** (1.1 mg). Fraction L4H (30.2 mg) was isolated by CC eluting with EtOAc in CH_2Cl_2 (0.5:10, *v/v*) gave compounds **1** (4.1 mg) and **4** (2.1 mg). For the details of isolation procedures for known compounds, see Supplementary Material.

Desmoscochinchinene A (***1***): Colorless viscous oil; UV (MeOH) λ_{max} (log ε) 232 (3.47) and 272 (2.81) nm, IR (neat) ν_{max} 2944.6, 1723.8, 1374.7, 1270.9, 1112.9, and 712.9 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; HRESITOFMS *m/z* 311.0901 $[M + Na]^+$ (calcd without Na ion for $C_{16}H_{16}O_5$, 288.1009).

Desmoscochinchinene B (***2***): Colorless viscous oil; UV (MeOH) λ_{max} (log ε) 233 (3.39) and 268 (2.76) nm, IR (neat) ν_{max} 2944.7, 1725.8, 1452.3, 1271.9, 1112.9, 1027.3, and 713.0 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; HRESITOFMS *m/z* 311.0895 $[M + Na]^+$ (calcd without Na ion for $C_{16}H_{16}O_5$, 288.1005).

Desmoscochinchinene C (***3***): Colorless viscous oil; UV (MeOH) λ_{max} (log ε) 232 (3.62) and 277 (2.69) nm, IR (neat) ν_{max} 3293.1, 2873.7, 1651.0, 1413.9, and 1001.6 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; HRESITOFMS *m/z* 167.0690 $[M + Na]^+$ (calcd without Na ion for $C_7H_{12}O_3$, 144.0797).

Desmoscochinchinene D (***4***): Colorless viscous oil; UV (MeOH) λ_{max} (log ε) 238 (3.30) nm, IR (neat) ν_{max} 3429.1, 2926.8, 1720.8, 1629.9, 1270.9, 1098.5, and 713.9 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; HRESITOFMS *m/z* 209.0792 $[M + Na]^+$ (calcd without Na ion for $C_9H_{14}O_4$, 186.0899).

Desmoscochinchinene E (***5***): Colorless viscous oil; UV (MeOH) λ_{max} (log ε) 240 (3.31) nm, IR (neat) ν_{max} 2926.8, 1739.4, 1376.8, 1227.5, 1026.2, and 966.1 cm^{-1}; ^1H and ^{13}C NMR, see Tables 1 and 2; HRESITOFMS *m/z* 293.0999 $[M + Na]^+$ (calcd without Na ion for $C_{13}H_{18}O_6$, 270.1107).

(−)-(2S)-Pinocembrin 7-O-benzoate (***12***): Yellow amorphous solid; $[\alpha]_D^{23}$ − 117 (*c* 0.1, $CHCl_3$), UV (MeOH) λ_{max} (log ε) 328 (1.92), 290

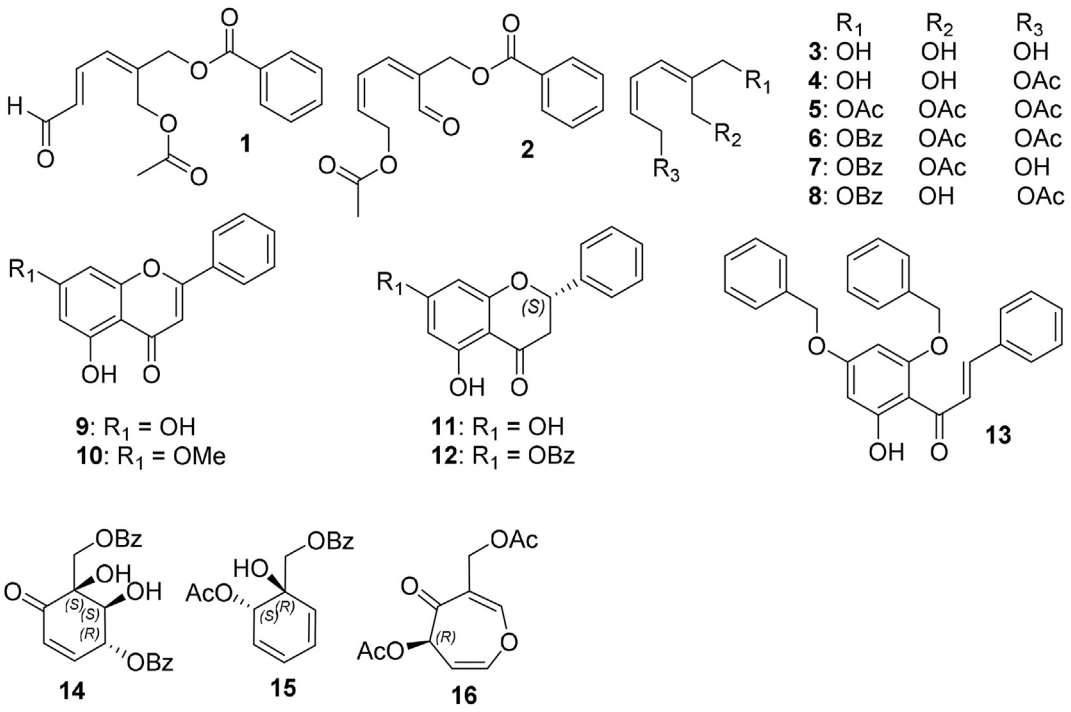

Figure 2. Compounds isolated from the flower and leaf extracts of *D. cochinchinensis*.

(2.32), and 216 (2.54) nm, IR (neat) ν_{max} 2927, 1744, 1650, 1633, 1244, 1128, and 704 cm^{-1}; ECD (5.41 × 10^{-3} M, MeOH) λ_{max} ($\Delta\varepsilon$) 222 (+3.96), 284 (-3.99) and 321 (+3.34) nm. ^{1}H and ^{13}C NMR, see Table 3; HRESITOFMS *m/z* 361.1078 $[M + H]^+$ (calcd without H ion for $C_{22}H_{16}O_5$, 360.1004).

2.4. Biological assay

2.4.1. α-Glucosidase inhibitory assay

A colorimetric α-glucosidase assay was conducted according to the previously described method (Sharma et al., 2019; Phukhatmuen et al., 2020; Suthiphasilp et al., 2020), using acarbose as a positive control (IC_{50} = 83.5 μM).

2.4.2. NO production inhibitory and cytotoxicity assays

The nitric oxide production assay (Joo et al., 2014; Suthiphasilp et al., 2020) and cytotoxicity assay (Ahmed et al., 1994) were performed according to the method described in the literature with slight modification. Indomethacin (IC_{50} value at 32.2 μM) was used as a positive control.

2.4.3. Glucose uptake assay

The glucose uptake assay was performed according to the method described in the previous reports (Sharma et al., 2019; Phukhatmuen et al., 2020; Cheng et al. (2006)) with modification. Metformin (1 mM) and insulin (1 μM) were used as positive controls in the glucose uptake assay with 1.9- and 2.07-fold induction, respectively. For more details, please see Supplementary Material.

Table 1. ^{1}H NMR spectroscopic data (mult., *J* in Hz, 600 MHz) of compounds **1-5**.

position	1[a]	2[a]	3[b]	4[a]	5[a]
1	5.00, s	5.21, s	4.28, s	4.47, s	4.76, s
3	6.60, d (11.5)	7.48, m	6.50, d (11.8)	6.51, d (11.5)	6.57, d (11.3)
4	7.52, dd (15.2, 11.5)	6.95, t (11.0)	6.46, t (11.8)	6.47, t (11.5)	6.49, t (11.3)
5	6.26, dd (15.2, 7.8)	6.21, dt (11.0, 6.8)	5.67, dt (11.8, 6.5)	5.71, dt (11.5, 7.0)	5.74, dt (11.3, 7.0)
6	9.68, d (7.8)	4.97, d (6.8)	4.32, d (6.5)	4.82, d (7.0)	4.77, d (7.0)
7	4.97, s	9.68, s	4.21, s	4.36, s	4.66, s
OBz					
3′, 7′	8.07, d (7.4)	8.08, d (7.8)			
4′, 6′	7.47, t (7.4)	7.48, m			
5′	7.60, t (7.4)	7.61, t (7.8)			
1-OCO*CH*$_3$					2.09, s
6-OCO*CH*$_3$		2.16, s		2.12, s	2.07, s
7-OCO*CH*$_3$	2.08, s				2.06, s

[a] recorded in $CDCl_3$.
[b] recorded in CD_3OD.

Table 2. ^{13}C NMR spectroscopic data (150 MHz) of compounds **1**-**5**.

position	1[a]	2[a]	3[b]	4[a]	5[a]
1	65.3	55.1	56.3	59.1	58.9
2	139.9	136.5	140.7	140.9	132.0
3	128.8	144.4	120.3	126.1	126.4
4	144.0	125.4	122.4	121.8	125.5
5	134.2	135.9	130.6	126.2	128.0
6	193.1	59.4	56.7	59.7	59.6
7	59.0	192.5	63.2	66.4	65.8
OBz					
1′	165.5	166.2			
2′	129.4	137.7			
3′, 7′	129.3	129.3			
4′, 6′	128.2	128.0			
5′	133.1	132.8			
1-OCOCH_3					170.4
1-OCOCH_3					20.4
6-OCOCH_3		170.7		170.7	170.4
6-OCOCH_3		20.4		20.1	20.5
7-OCOCH_3	170.2				170.2
7-OCOCH_3	20.3				20.5

[a] recorded in $CDCl_3$.
[b] recorded in CD_3OD.

3. Results

3.1. Structure of the isolated compounds from the flower (slim petal) and leaf extracts of D. cochinchinensis

The flower (slim petal) and leaf extracts of *D. cochinchinensis* were individually separated and purified by various chromatography techniques, which led to the isolation and identification of five new polyoxygenated *seco*-cyclohexenes (**1**–**5**), together with 11 known compounds (**6**–**16**). Two new compounds **1** and **2** were obtained from the leaf extract, while three new compounds **3–5** were obtained from the flower extract. The known compounds were characterized by the comparison of their physical properties and spectroscopic data with the previous reports and identified as flexuvarin B (**6**) (Hsu et al., 2016), flexuvarin C (**7**) (Hsu et al., 2016), flexuvarin D (**8**) (Hsu et al., 2016), chrysin (**9**) (Meesakul et al., 2017), 5-hydroxy-7-methoxyflavone (tectochrysin) (**10**) (Righi et al., 2010), pinocembrin (**11**) (Meesakul et al., 2017), pinocembrin 7-*O*-benzoate (**12**) (Hoeneisen et al., 1993), 2′-hydroxy-4′,6′-dibenzyloxychalcone (**13**) (Drewes and van Vuuren, 2008), zeylenone (**14**) (Suthiphasilp et al., 2019), 1*R*,6*S*-cherrevenol A (**15**) (Auranwiwat et al., 2019), and (−)-(5*R*)-desmoscochinoxepinone B (**16**) (Meesakul et al., 2019) (Figure 2).

3.2. α-Glucosidase inhibitory, NO production inhibitory, and glucose uptake activities of the isolated compounds from the flower (slim petal) and leaf extracts of D. cochinchinensis

Only the stable compounds of adequate amounts (**3**, **6**, **7**, **9**, **11**–**13**, and **16**) were evaluated for their α-glucosidase inhibitory, nitric oxide (NO) production inhibitory, and glucose uptake activities. Of these, compounds **9**, **12,** and **16** exhibited α-glucosidase inhibitory activity better than standard control, acarbose (IC_{50} = 83.5 μM) with the half-maximal inhibitory concentration (IC_{50}) values of 5.7, 33.8 and 53.3 μM (Table 4). In contrast, the remaining compounds were found to be inactive. It should be noted that the flavonoids **9** and **12** and the oxepinone **16** strongly inhibited α-glucosidase. While, the *seco*-cyclohexenes **3**, **6**, and **7** showed weak α-glucosidase inhibition with IC_{50} values of more than 100 μM. None of these compounds had NO production inhibitory or glucose uptake activities.

4. Discussion

The ^{1}H nuclear magnetic resonance (NMR) spectra of the new compounds **1**–**5** displayed the common characteristic resonances of a polyoxygenated *seco*-cyclohexene skeleton; including those for three olefinic protons at ca. δ_H 6.5–7.4 (H-3), δ_H 6.4–7.5 (H-4), and δ_H 5.6–6.2 (H-5) and one oxymethylene group at ca. δ_H 4.2–5.2 (H-1).

Desmoscochinchinene A (**1**) gave a molecular formula of $C_{16}H_{16}O_5$, as indicated by its NMR and high-resolution electrospray ionization time-of-flight mass spectrometry (HRESITOFMS) data ($[M + Na]^+$ *m/z* 311.0901). The ^{1}H and ^{13}C NMR spectroscopic data of **1** (Tables 1 and 2) displayed resonances typical of an of polyoxygenated *seco*-cyclohexene

Table 3. ^{1}H (600 MHz) and ^{13}C (150 MHz) NMR spectroscopic data of compounds **12** in $CDCl_3$.

Position	12	
	δ_H (mult., *J* in Hz)	δ_C
2	5.50, dd (13.2, 3.0)	79.3
3	3.16, dd (17.2, 13.2); 2.91, dd (17.2, 3.0)	43.6
4		196.9
4a		106.3
5		163.4
6	6.46, brs	103.5
7		162.3
8	6.46, brs	101.9
8a		158.7
1′		138.0
2′, 3′, 5′, 6′	7.42–7.48, m	128.9
4′	7.41, m	128.6
1″		164.0
2″		128.8
3″, 7″	8.17, d (7.5)	130.3
4″, 6″	7.52, t (7.5)	126.1
5″	7.66, t (7.5)	133.9
5-OH	11.90, s	

Table 4. α-Glucosidase inhibitory activity of some isolated compounds from flowers and leaves of *D. cochinchinensis*.

Compound	α-glucosidase inhibitory activity (IC_{50} (μM)
3	inactive
6	inactive
7	inactive
9	5.7
10	inactive
11	inactive
12	33.8
13	inactive
16	53.3
Acarbose	83.5

(one benzoyl unit [(δ_H 8.07 (2H, d, J = 7.4 Hz, H-3′ and H-7′), 7.47 (2H, t, J = 7.4 Hz, H-4′ and H-6′) 7.60, (1H, t, J = 7.4 Hz, H-5′)], three olefinic protons [δ_H 6.60 (1H, d, J = 11.5 Hz, H-3), 7.52 (1H, dd, J = 15.2, 11.5 Hz, H-4), 6.26 (1H, dd, J = 15.2, 7.8, H-5], two oxymethylene groups [δ_H 5.00 (2H, s, H-1) and 4.97 (2H, s, H-1)], and one acetoxy group [δ_H 2.08 (3H, s, 7-OCO*CH*$_3$)]), which were similar to those of flexuvarin B (**6**) previously isolated from *Uvaria flexuosa* (Hsu et al., 2016). The major difference was found that a 6-*O*-acetyl group of flexuvarin B (**6**) was replaced by an aldehyde group, which displayed the formyl proton resonance at δ_H 9.68, (1H, d, J = 7.8 Hz, H-6). The configuration of the $\Delta^{3,4}$ and $\Delta^{4,5}$ alkene units were assigned as *Z* ($\Delta^{3,4}$) and *E* ($\Delta^{4,5}$) based on the magnitude of their coupling constants (^3J) of 11.5 and 15.2 Hz, respectively. The heteronuclear multiple bond connectivity (HMBC) correlations of H-6 (formyl proton) to C-5 (δ_C 134.2) and H-4 and H-5 to C-6 (δ_C 193.1) confirmed this assignment. Other HMBC correlations supporting the characterization of compound **1** was shown in Figure 3.

Desmoscochinchinene B (**2**) gave the same molecular formula, $C_{16}H_{16}O_5$, as desmoscochinchinene A, which showed an ion peak at *m/z* 311.0895 $[M + Na]^+$ in the HRESITOFMS data. The NMR spectroscopic data (Tables 1 and 2) of compound **2** were almost identical to those of desmoscochinchinene A. The main difference is only the location of the *O*-acetyl and formyl groups. Compound **2** contained the formyl group at C-7 and *O*-acetyl group at C-6, whereas in compound **1**, these groups were at C-6 and C-7, respectively. These assignments were confirmed by the HMBC correlations between the formyl proton (δ_H 9.68) with C-1 (δ_C 55.1) and H-1 (δ_H 5.21) and H-3 (δ_H 7.48) with C-7 (δ_C 192.5), and H-6 (δ_H 4.97) and the methyl proton of acetoxy group (δ_H 2.16) with carbonyl carbon of acetoxy group (δ_C 170.7). The configuration of the $\Delta^{3,4}$ and $\Delta^{4,5}$ alkene units were assigned as *Z* based on the magnitude of the coupling constant (^3J) of 11.0 Hz. The key HMBC correlations were supported by the structural characterization of compound **2**, displayed in Figure 3.

Desmoscochinchinenes C (**3**), D (**4**), and E (**5**) were isolated as colorless viscous oils. Their NMR spectroscopic data (Tables 1 and 2) were similar to those of desmoscochinchinene B (**2**) except for the lack of resonances for the benzoyl and formyl groups at C-1 and C-7, respectively. The molecular formula, $C_7H_{12}O_3$, of compound **3** was deduced from HRESITOFMS, which showed an ion peak at *m/z* 167.0690 $[M + Na]^+$. The structure of **3** is a simple polyoxygenated *seco*-cyclohexene containing the same substituent group, hydroxymethyl unit, on C-1 (δ_H 4.28/δ_C 56.3), C-6 (δ_H 4.32/δ_C 56.7), and C-7 (δ_H 4.21/δ_C 63.2). These assignments were supported by the HMBC correlations, as shown in Figure 2. The molecular formula of desmoscochinchinene D (**4**) ($C_9H_{14}O_4$, HRESITOFMS *m/z* 209.0792 $[M + Na]^+$) indicated compound **4** contained an acetyl unit when compared to that of compound **3**. The NMR spectroscopic data of **4** (Tables 1 and 2) displayed an additional acetyl group at δ_H 2.12/δ_C 20.1 and δ_C 170.7. The HMBC correlations between methyl proton of an acetyl group (δ_H 2.12) and H-6 (δ_H 4.82) with the carbonyl carbon of the acetyl unit (δ_C 170.7) confirmed this assignment. The structure of **5**, HRESITOFMS *m/z* 293.0999 $[M + Na]^+$, corresponding to the molecular formula of $C_{13}H_{18}O_6$, was closely related to that of **3**. The main differences were found that all hydroxymethyl units in **3** were replaced by acetoxy units [1-OCOCH$_3$ (δ_H 2.09/δ_C 20.4 and δ_C 170.4), 6-OCOCH$_3$ (δ_H 2.07/δ_C 20.5 and δ_C 170.4), and 7-OCOCH$_3$ (δ_H 2.06/δ_C 20.5 and δ_C 170.2)] and H-1 (δ_H 4.76, s), H-6 (δ_H 4.77, d, J = 7.0 Hz), and H-7 (δ_H 4.66, s) shifted to the lower field in **5**. The configuration of the $\Delta^{3,4}$ and $\Delta^{4,5}$ alkene units for **3**, **4**, and **5** were identified according to their ^3J coupling constants, which were similar to those of compound **2**. All these assignments were supported by HMBC correlations, as shown in Figure 3.

The biosynthetic pathway of polyoxygenated cyclohexene and *seco*-cyclohexene were proposed from the shikimic acid pathway (Hsu et al., 2016; Macabeo et al., 2017; Suthiphasilp et al., 2019). The primary intermediate A as shown in Figure 4, is proposed as a forerunner based on our results. The enzymatic cleavage at C-6/C-7 would yield compound **3**. Selective acetylation at 6-OH of compound **3** or fully acetylation could produce compounds **4** and **5**, respectively. Benzoylation of **3** at 1-OH would produce intermediate B, which was further acetylation at 6-OH and followed by oxidation at 7-OH would provide compounds **8** and **2**,

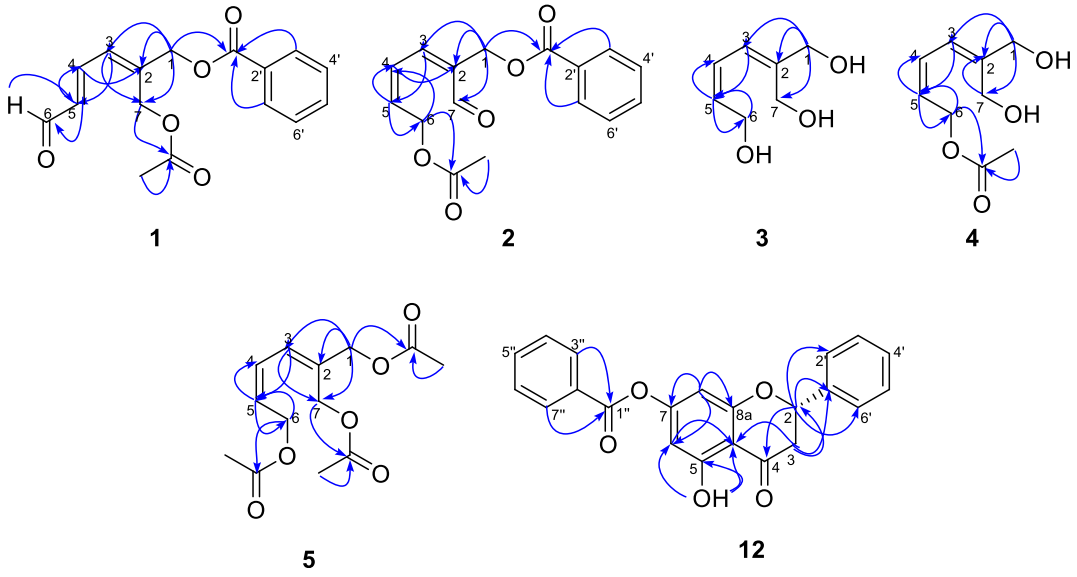

Figure 3. Selected HMBC correlations of isolated compounds **1–5** and **12**.

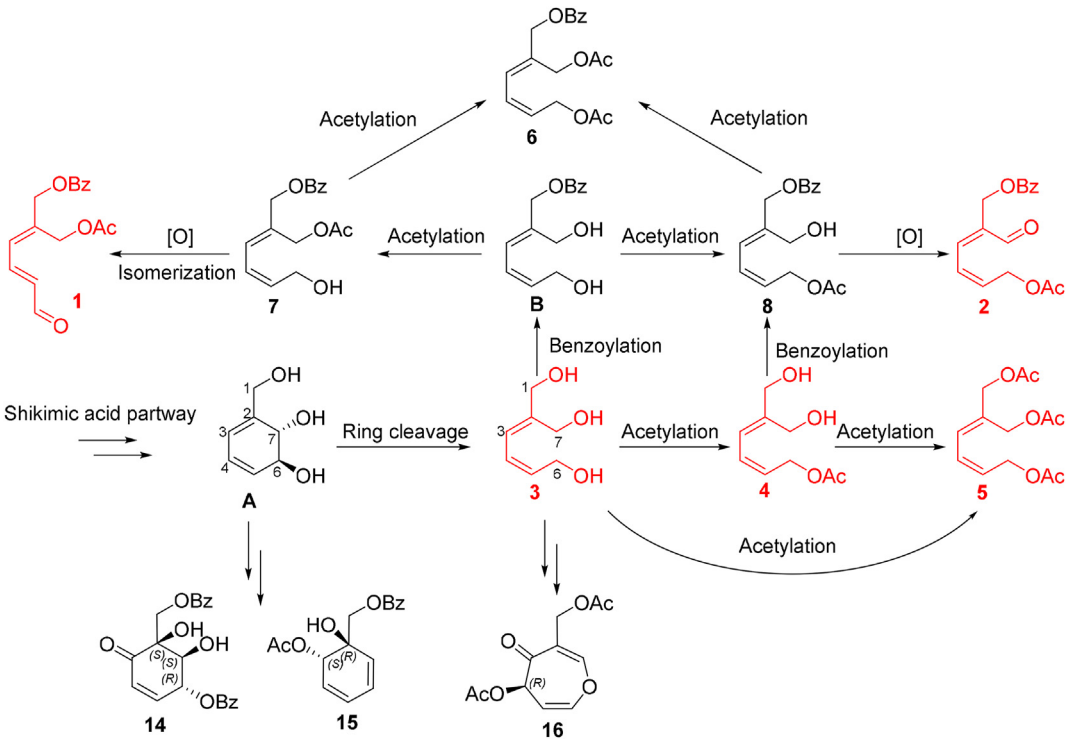

Figure 4. Putative biosynthesis pathway for *seco*-cyclohexenes derivatives compounds **1**–**8** and **14**–**16**.

respectively. On the other hand, acetylation at 7-OH and followed by oxidation at 6-OH would obtain compound **7**, and followed by isomerization at $\Delta^{4,5}$ alkene unit could give compound **1**, respectively. Multi-steps of oxidation and acylation of intermediate A would reach to compounds **14** and **15**, whereas compound **16** would obtain from compound **3** via oxidation, cyclization, and acetylation.

Compound **12**, pinocembrin 7-*O*-benzoate, was first isolated from *Pachylaena atriplicifolia* in 1993 by Hoeneisen and co-worker (Hoeneisen et al., 1993), but its ^{13}C and full 2D NMR data, specific rotation, and absolute configuration were not provided. The HRESITOFMS of pinocembrin 7-*O*-benzoate displayed an ion peak at *m/z* 361.1078 $[M + H]^+$ corresponding to the molecular formula $C_{22}H_{16}O_5$. The ^{1}H and ^{13}C NMR spectroscopic data (Table 3) showed the characteristic resonances for a flavanone skeleton (Hoeneisen et al., 1993); δ_H/δ_C 5.50 (1H, dd, J = 13.2, 3.0 Hz, H-2)/79.3, 3.16 (1H, dd, J = 17.2, 13.2, H-3a) and 2.91 (1H, dd, J = 17.2, 3.0, H-3b)/43.6), 6.46 (1H, brs, H-6)/103.5, 6.46 (1H, brs, H-8)/101.9, 7.46 (4H, m, H-2′, H-3′, H-5′, and H-6′)/128.9 (× 4), 7.41 (1H, m, H-4′)/128.6, and δ_C 138.0 (C-1′). The hydrogen bonded-hydroxy proton at δ_H 11.90 was placed at C-5 due to the HMBC correlations between this proton resonance with those of C-4a (δ_C 106.3), C-5 (δ_C 163.4), and C-6 (δ_C 103.5). Finally, the benzoyloxy group [δ_H/δ_C 8.17 (2H, d, J = 7.5 Hz, H-3″ and H-7″)/130.3), H-4″/H-6″ 7.52 (2H, d, J = 7.5 Hz, H-4″ and H-6″)/126.1), 7.66 (1H, d, J = 7.5 Hz, H-5″)/133.9), δ_C 164.0 (C-1″), and δ_C 128.8 (C-2″)] was placed at C-7 by of the process of elimination. Full assignments of ^{1}H and ^{13}C NMR spectroscopic data are summarized in Table 3. The (2*S*) absolute configuration of compound **12** was identified by the comparison of its electronic circular dichroism (ECD) spectrum [222 (+3.96), 284 (−3.99), and 321 (+3.34) nm] to that of well know compound **11** [214 (+3.70), 283 (−3.57), and 319 (+2.98)], which were very similar to each other (Figure 5). Therefore, compound **12** was identified as (−)-(2*S*)-pinocembrin 7-*O*-benzoate ($[\alpha]_D^{23}$ −117, *c* 0.1, $CHCl_3$).

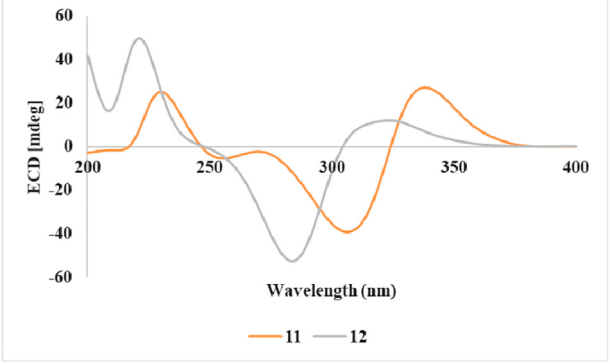

Figure 5. ECD spectra of compounds **11** and **12** (MeOH).

5. Conclusion

Phytochemical investigations of the flower and leaf extracts of the *D. cochinchinensis* resulted in the identification and elucidation of 16 compounds, five of these compounds were new polyoxygenated *seco*-cyclohexenes **1–5**. The previous investigations have been reported that flavonoids are major compounds in *Desmos* species. To the best of our knowledge, polyoxygenated *seco*-cyclohexenes **1–8** were found in the genus of *Desmos* for the first time. Chrysin (**9**) showed good α-glucosidase activity with the IC_{50} values of 5.7 μM, which could have potential as a lead compound for antidiabetic agent development.

Declarations

Author contribution statement

Surat Laphookhieo: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

Tharakorn Maneerat: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Virayu Suthiphasilp: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Raymond J. Andersen, Stephen G. Pyne, Rawiwan Charoensup, Thidarat Duangyod: Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

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