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

Virayu Suthiphasilp a, Tharakorn Maneerat a,b, Thidarat Duangyodb c, Rawiwan Charoensup b,c, Raymond J. Andere nd, Stephen G. Pyne e, Surat Laphookhieoa,b,*

a Center of Chemical Innovation for Sustainability (CIS) and School of Science, Mae Fah Luang University, Chiang Rai, 57100, Thailand
b Medicinal Plants Innovation Center of Mae Fah Luang University, Chiang Rai, 57100, Thailand
c Center of Chemical Innovation for Sustainability (CIS) and School of Science, Mae Fah Luang University, Chiang Rai, 57100, Thailand
d Department of Chemistry and Department of Earth, Ocean & Atmospheric Sciences, University of British Columbia, 2036, Main Mall, Vancouver, BC, V6T 1Z1, Canada
e School of Chemistry and Molecular Bioscience, University of Wollongong, Wollongong, New South Wales, 2522, Australia

ABSTRACT

Phytochemical investigations from the flower and leaf extracts of *D. cochinchinensis* resulted in the isolation and structural elucidation of five new polyoxgenated seco-cyclohexene derivatives, desmoscochinhenes 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 (−)-(5R)-desmoscochinhexone B (16) inhibited α-glucosidase better than the standard control (acarbose, IC50 = 83.5 μM) with IC50 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 (Asthira and Jain, 2014), while its incapacity to regulate insulin response is called type 2 diabetes (Skyler et al., 2017). DM has also been reported to cause 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. damosus* (Roxb.) Saff., and *D. macrocarpus* Bán 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 small 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 xepinones 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 (small 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.
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 x 20 L) and EtOAc (3 x 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 (F11A-F11D). Purification of F11 (735.1 mg) was separated by Sephadex-LH20 eluting with an isocratic system of MeOH in H2O (0.7:1.3, v/v) gave compound 1 (7.1 mg, tR 146.0899). Fraction 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 C18 HPLC eluting with an isocratic system of CH3CN in H2O (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 CH2Cl2 (0:5:10, v/v) gave compounds 3 (4.1 mg) and 4 (2.1 mg). For the details of isolation procedures for known compounds, see Supplementary Material.

**Desmoscochinchenene A (1):** Colorless viscous oil; UV (MeOH) λmax (log ε) 232 (3.47) and 272 (2.81) nm, IR (neat) νmax 2944.6, 1725.8, 1452.3, 1271.9, 1112.9, 1027.3, and 713.9 cm⁻¹; 1H and 13C NMR, see Tables 1 and 2; HRESITOFMS m/z 311.0901 [M + Na]⁺ (calcd without Na ion for C16H16O5, 288.1009).

**Desmoscochinchenene B (2):** Colorless viscous oil; UV (MeOH) λmax (log ε) 233 (3.39) and 268 (2.76) nm, IR (neat) νmax 2944.7, 2755.8, 1452.3, 1271.9, 1112.9, 1027.3, and 713.0 cm⁻¹; H and 13C NMR, see Tables 1 and 2; HRESITOFMS m/z 311.0895 [M + Na]⁺ (calcd without Na ion for C16H16O5, 288.1005).

**Desmoscochinchenene C (3):** Colorless viscous oil; UV (MeOH) λmax (log ε) 232 (3.62) and 277 (2.69) nm, IR (neat) νmax 3293.1, 2873.7, 1651.0, 1413.9, and 1001.6 cm⁻¹; 1H and 13C NMR, see Tables 1 and 2; HRESITOFMS m/z 167.0690 [M + Na]⁺ (calcd without Na ion for C8H10O3, 144.0797).

**Desmoscochinchenene D (4):** Colorless viscous oil; UV (MeOH) λmax (log ε) 238 (3.30) nm, IR (neat) νmax 3429.1, 2926.8, 2702.8, 1629.9, 1270.9, 1098.5, and 713.9 cm⁻¹; H and 13C NMR, see Tables 1 and 2; HRESITOFMS m/z 209.0792 [M + Na]⁺ (calcd without Na ion for C8H10O3, 186.0899).

**Desmoscochinchenene E (5):** Colorless viscous oil; UV (MeOH) λmax (log ε) 240 (3.31) nm, IR (neat) νmax 2926.8, 1739.4, 1376.8, 1227.5, 1026.2, and 966.1 cm⁻¹; H and 13C NMR, see Tables 1 and 2; HRESITOFMS m/z 293.0999 [M + Na]⁺ (calcd without Na ion for C13H16O4, 270.1107).

**(-)-(2S)-Pinocembrin 7-O-benzoate (12):** Yellow amorphous solid; αD^20 = 117 (c 0.1, CHCl3), UV (MeOH) λmax (log ε) 328 (1.92), 290...
2.32), and 216 (2.54) nm, IR (neat)  \( \nu_{\text{max}} \) 2927, 1744, 1650, 1633, 1244, 1128, and 704 cm \(^{-1}\); ECD (5.41 \( \times \) 10\(^{-3}\) M, MeOH)  \( \lambda_{\text{max}} \) (\( \Delta \varepsilon \)) 222 (+3.96), 284 (-3.99), and 321 (+3.34) nm. 1H and 13C 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. \( \alpha \)-Glucosidase inhibitory assay

A colorimetric \( \alpha \)-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 \( \mu \)M).

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 \( \mu \)M) 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 \( \mu \)M) 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. 1H NMR spectroscopic data (mult., J in Hz, 600 MHz) of compounds 1-5.

| position | 1\(^a\) | 2\(^b\) | 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 |

| position | 3\(^a\), 7\(^a\) | 4\(^a\), 6\(^a\) | 5\(^a\) |
|----------|-----------------|-----------------|--------|
| 3\(^a\), 7\(^a\) | 8.07, d (7.4) | 8.08, d (7.8) |       |
| 4\(^a\), 6\(^a\) | 7.47, t (7.4) | 7.48, m |       |
| 5\(^a\) | 7.60, t (7.4) | 7.61, t (7.8) |       |

| 1-OCOCH\(_3\) | 2.09, s |
| 2-OCOCH\(_3\) | 2.12, s | 2.07, s |
| 3-OCOCH\(_3\) | 2.08, s | 2.06, s |

\( a \) recorded in CDCl\(_3\).

\( b \) recorded in CD\(_3\)OD.
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 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 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 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.

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 (IC₅₀ = 83.5 μM) with the half-maximal inhibitory concentration (IC₅₀) 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 IC₅₀ values of more than 100 μM. None of these compounds had NO production inhibitory or glucose uptake activities.

4. Discussion

The ¹H 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. δH 6.5–7.4 (H-3), δH 6.4–7.5 (H-4), and δH 5.6–6.2 (H-5) and one oxymethylene group at ca. δH 4.2–5.2 (H-1).

Desmoscochininone A (1) gave a molecular formula of C₁₆H₁₆O₅, as indicated by its NMR and high-resolution electrospray ionization time-of-flight mass spectrometry (HRESITOFMS) data ([M + Na]⁺ m/z 311.0901). The ¹H and ¹³C NMR spectroscopic data of 1 (Tables 1 and 2) displayed resonances typical of an of polyoxygenated seco-cyclohexene.

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

| position | 1⁷ | 2⁷ | 3³ | 4⁴ | 5⁵ |
|----------|---|---|---|---|---|
| 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 |

OBS

| 1⁷ | 166.2 |
| 2⁷ | 129.7 |
| 3, 7’ | 129.3 |
| 4, 6’ | 128.0 |
| 5⁵ | 132.8 |

3. Results

Table 4. ¹H (600 MHz) and ¹³C (150 MHz) NMR spectroscopic data of compounds 12 in CDCl₃.

| Position | ¹H (J in Hz) | ¹³C |
|----------|-------------|-----|
| 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 (IC50 (µM)) |
|-------------------|---------------------------------------------|
| 3                 | inactive                                    |
| 6                 | inactive                                    |
| 7                 | inactive                                    |
| 9                 | inactive                                    |
| 10                | inactive                                    |
| 11                | inactive                                    |
| 12                | 33.8                                        |
| 16                | 53.3                                        |
| Acarbose          | 83.5                                        |

(one benzylic unit [(δH 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 [δH 6.60 (1H, d, δC = 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 [δH 5.00 (2H, s, H-1) and 4.97 (2H, s, H-1')], and one acetoxy group [δH 2.08 (3H, s, 7-OCOCH3)], 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 δH 9.68, (1H, d, J = 7.8 Hz, H-6). The configuration of the Δ3,4 and Δ4,5 alkene units were assigned as Z (Δ3,4) and E (Δ4,5) based on the magnitude of their coupling constants (JH) of 11.5 and 15.2 Hz, respectively. The heteronuclear multiple bond connectivity (HMBC) correlations of H-6 (formyl proton) to C-5 (δC 134.2) and H-4 and H-5 to C-6 (δC 193.1) confirmed this assignment. Other HMBC correlations supporting the characterization of compound 1 was shown in Figure 3.

Desmoscochinchenines C (3), D (4), and E (5) were isolated and identified as colorless viscous oils. Their NMR spectroscopic data (Tables 1 and 2) were similar to those of desmoscochinchenine B (2) except for the lack of resonances for the benzoyl and formyl groups at C-1 and C-7, respectively. The molecular formula, C13H18O6, of compound 3 was deduced from HRESITOFMS, which showed an ion peak at m/z 209.0792 [M + Na]+. The structure of 3 is a simple polyoxygenated seco-cyclohexene containing the same substituent group, hydroxymethyl unit, on C-1 (δH 4.32/δC 56.3), C-6 (δH 4.52/δC 56.7), and C-7 (δH 4.21/δC 63.2). These assignments were supported by the HMBC correlations, as shown in Figure 2. The molecular formula of desmoscochinchenine D (4) (C13H14O5, 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 δH 2.12/δC 20.1 and δC 170.7. The HMBC correlations between methyl proton of an acetyl group (δH 2.12) and H-6 (δH 4.82) with the carbonyl carbon of the acetyl unit (δC 170.7) confirmed this assignment. The structure of 5, HRESITOFMS m/z 293.0999 [M + Na]+, corresponding to the molecular formula of C13H14O5, was closely related to that of 3. The main differences were found that all hydroxymethyl units in 3 were replaced by acetoxy units [1-OCOCH3 (δH 2.09/δC 20.4 and δC 170.4), 6-OCOCH3 (δH 2.07/δC 20.5 and δC 170.4), and 7-OCOCH3 (δH 2.06/δC 20.5 and δC 170.2)] and H-1 (δH 4.76, s), H-6 (δH 4.77, d, J = 7.0 Hz), and H-7 (δH 4.66, s) shifted to the lower field in 5. The configuration of the Δ3,4 and Δ4,5 alkene units for 3, 4, and 5 were identified according to their 2J 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 at 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.
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 a\(^{1,3}\) 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 \([\text{M}+\text{H}]^+\) corresponding to the molecular formula \(C_{22}H_{16}O_5\). The \(^1H\) and \(^{13}\)C NMR spectroscopic data (Table 3) showed the characteristic resonances for a flavanone skeleton (Hoeneisen et al., 1993); \(\delta^H/\delta^C\) 5.50 (1H, dd, \(J=13.2,3.0\) Hz, H-2)/79.3, 3.16 (1H, dd, \(J=17.2,13.2\) Hz, H-3a) and 2.91 (1H, dd, \(J=17.2,3.0\) Hz, 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\(_0\), H-3\(_0\), H-5\(_0\), and H-6\(_0\))/128.9 (\(\Delta_4\)), 7.41 (1H, m, H-4\(_0\))/H-6\(_0\), 7.52 (2H, d, \(J=7.5\) Hz, H-4\(_3\)/H-6\(_3\))/126.1), 7.66 (1H, d, \(J=7.5\) Hz, H-5\(_3\))/133.9), \(\delta^C\) 164.0 (C-1\(_3\)), and \(\delta^C\) 128.8 (C-2\(_3\)) was placed at C-7 by of the process of elimination. Full assignments of \(^1H\) and \(^{13}\)C NMR spectroscopic data are summarized in Table 3. The \((2S)\) absolute configuration of compound 12 was identified by the comparison of its electronic circular dichroism (ECD) spectrum \([222 (\pm 3.96), 284 (\pm 3.99), and 321 (\pm 3.34) \text{ nm}]\) to that of well know compound 11 \([214 (\pm 3.70), 283 (\pm 3.57), and 319 (\pm 2.98)]\), which were very similar to each other (Figure 5). Therefore, compound 12 was identified as \((-)-(2S)-\)pinocembrin 7-O-benzoate \((\alpha\overline{\alpha}23\overline{3D}/c 0.1, \text{CHCl}_3)\).

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 \(\alpha\)-glucosidase activity with the IC\(_{50}\) values of 5.7 \(\mu\)M, 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.

![Figure 4. Putative biosynthesis pathway for seco-cyclohexenes derivatives compounds 1–8 and 14–16.](image)

![Figure 5. ECD spectra of compounds 11 and 12 (MeOH).](image)
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 Charoenrus, Thidarat Duangyod: Analyzed and interpreted the data; Wrote the paper.

Funding statement
Surat Lapookhieo was supported by Thailand Science Research and Innovation (DBG62880007 & DBG6180029). Surat Lapookhieo & Virayu Suthiphasilp was supported by Thailand Research Fund (PHD/013/2559). Virayu Suthiphasilp was supported by Mae Fah Luang University.

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
Supplementary content related to this article has been published online at https://doi.org/10.1016/j.heliyon.2020.e05791.

Acknowledgements
We would like to thank Mr. Kithisak Aongyong for plant identification. Mae Fah Luang University and the University of British Columbia are also recognized for the laboratory facilities.

References
Amarin, S., Jahn, V., 2014. Advances in management of type 1 diabetes mellitus. World J. Diabetes 5, 689-696.
Ahmed, S.A., Gogal Jr., R.M., Walsh, J.E., 1994. A new rapid and simple non-radioactive assay to monitor and determine the proliferation of lymphocytes: an alternative to [3H] thymidine incorporation assay. J. Immunol. Methods 170, 211-224.
Arunriwin, C., Wongsumboon, P., Thaima, T., Rattanakit, K., Kamoonsongpaisan, S., Willis, A.C., Lapookhieo, S., Pyne, S.G., Limthanakul, T., 2019. Polyoxygenated cyclohexenes and their chlorinated derivatives from the leaves of Uvaria cherrapunji. J. Nat. Prod. 82, 101-110.
Cheng, Z., Pang, T., Gu, M., Gao, A.H., Xie, C.M., Li, J.Y., Nan, F.J., Li, J., 2006. Berberine stimulated glucose uptake in L6 myotubes involves both AMPK and p38 MAPK. Biochem. Biophys. Acta 1760, 1682-1692.
Funding statement
Surat Lapookhieo was supported by Thailand Science Research and Innovation (DBG62880007 & DBG6180029). Surat Lapookhieo & Virayu Suthiphasilp was supported by Thailand Research Fund (PHD/013/2559). Virayu Suthiphasilp was supported by Mae Fah Luang University.

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
Supplementary content related to this article has been published online at https://doi.org/10.1016/j.heliyon.2020.e05791.

Acknowledgements
We would like to thank Mr. Kithisak Aongyong for plant identification. Mae Fah Luang University and the University of British Columbia are also recognized for the laboratory facilities.

References
Amarin, S., Jahn, V., 2014. Advances in management of type 1 diabetes mellitus. World J. Diabetes 5, 689-696.
Ahmed, S.A., Gogal Jr., R.M., Walsh, J.E., 1994. A new rapid and simple non-radioactive assay to monitor and determine the proliferation of lymphocytes: an alternative to [3H] thymidine incorporation assay. J. Immunol. Methods 170, 211-224.
Arunriwin, C., Wongsumboon, P., Thaima, T., Rattanakit, K., Kamoonsongpaisan, S., Willis, A.C., Lapookhieo, S., Pyne, S.G., Limthanakul, T., 2019. Polyoxygenated cyclohexenes and their chlorinated derivatives from the leaves of Uvaria cherrapunji. J. Nat. Prod. 82, 101-110.
Cheng, Z., Pang, T., Gu, M., Gao, A.H., Xie, C.M., Li, J.Y., Nan, F.J., Li, J., 2006. Berberine stimulated glucose uptake in L6 myotubes involves both AMPK and p38 MAPK. Biochem. Biophys. Acta 1760, 1682-1692.
Drewes, S.E., van Vuuren, S.F., 2008. Antimicrobial acylphloroglucinols and dibenzyloxy flavonoids from Foeniculum damascena and their inhibitory activities against nitric oxide production. RSC Adv. 7, 17545-17550.
Meesuk, P., Pudhom, K., Pyne, S.G., Lapookhieo, S., 2017. Hybrid flavon-flavanones from Foeniculum damascena and their inhibitory activities against nitric oxide production. J. Nat. Prod. 82, 741-747.
Naing, M.Y., Choi, D.S., Lee, M.Y., Lee, H.W., Park, T.S., Kim, D.M., Chung, C.J., Kim, D.K., Kim, U.J., Jang, H.C., Park, Y.S., Kwon, H.S., Lee, S.H., Shin, H.K., 2014. Comparison of acarbose and voglibose in diabetes patients who are inadequately controlled with basal insulin treatment: randomized, parallel, open-label, active-controlled study. J. Kor. Med. Sci. 29, 90-97.
Xu, L., Li, W., Chen, Z., Guo, Q., Wang, C., Santanam, R.K., Chen, H., 2019. Inhibitory effect of epigallocatechin-3-gallate on α-glucosidase and its hypoglycemic effect via stimulation of AMPK. Biochim. Biophys. Acta 1760, 1682-1692.