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Original article

Antidiabetic properties of garciniacowone L, a new xanthone with an unusual 5,5,8a-trimethyloctahydro-2*H*-1-benzopyran moiety, and other xanthones from the twig extract of *Garcinia cowa* Roxb. ex Choisy

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ABSTRACT

The aims of this study are to investigate chemical compounds from *Garcinia cowa* Roxb. ex Choisy and evaluate their antidiabetic activities, including α-glucosidase inhibitory, α-amylase inhibitory, glycation, glucose consumption, and glucose uptake. The EtOAc extract of the twigs of *Garcinia cowa* Roxb. ex Choisy were separated and purified by chromatographic techniques to give eight compounds (**1**–**8**). Of these, a xanthone with 5,5,8a-trimethyloctahydro-2*H*-1-benzopyran moiety, garciniacowone L (**1**), was isolated as a new compound, which was characterized by extensive spectroscopic data and high-resolution mass spectrometry. The known compounds were characterized by NMR spectroscopy techniques, and by comparisons of these data with those reported. All isolated compounds except β-mangostin (**4**) were evaluated for antidiabetic activities. Forbexanthone (**8**) exhibited good α-glucosidase inhibitory activity with an IC_{50} value of 85.1 ± 0.3 μM. 1-Hydroxy-7-methoxyxanthone (**7**) inhibited the highest glycation activity with the IC_{50} value of 170.3 ± 0.9 μM. From cell-based assays, mangostinone (**3**) showed glucose consumption and glucose uptake with the IC_{50} value of 18.3 ± 0.5 μM and 2.9-fold, respectively. This study revealed that some xanthones isolated from *Garcinia cowa* Roxb. ex Choisy might be interesting for further evaluation as a new drug candidate for diabetes mellitus.

1. Introduction

Xanthones, known as 9H-xanthen-9-one, are one of the most important classes in natural products, as they exhibit a variety of pharmacological and health benefits (Ritthiwigrom et al., 2013; Rukachaisirikul et al., 2005; Mahabusarakam et al., 2005; Rukachaisirikul et al., 2006; Trisuwan and Ritthiwigrom, 2012; Sriyatep et al., 2015; Phukhatmuen et al., 2020; Raksat et al., 2020). Some of them have been reported to have promising antidiabetic bioactivities. α-Mangostin, the best-known xanthone from *Garcinia mangostana*, has several antidiabetic activities, including inhibition of insulin secretion and inhibition of protein expression of insulin signaling pathways (Lee et al., 2018), and inhibition of α-glucosidase (Sriyatep et al., 2015). In addition, mangiferin was shown to reduce blood glucose levels of KK-Ay mice after oral administration by decreasing insulin resistance (Miura et al., 2001), while γ-mangostin and smeathxanthone A displayed potent α-glucosidase inhibitory with IC_{50} values of 1.5 and 6.9 μM, respectively (Ryu et al., 2011). Therefore, identifying new natural products in this structural family might lead to the discovery of bioactive compounds for diabetes mellitus (DM) treatment.

Garcinia cowa Roxb. ex Choisy belonging to the Clusiaceae family have been demonstrated to be rich sources of xanthones with therapeutic properties (Santo et al., 2020). This genus contains over 300 species often distributed in tropical and subtropical countries (Raksat et al., 2019). In previous phytochemical investigations of *G. cowa*, a number of new xanthones were isolated and identified (Ritthiwigrom et al., 2013; Sriyatep et al., 2015; Phukhatmuen

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et al., 2020; Raksat et al., 2020). The different parts of the plant and the different areas of plant collection are produced the diverse structures of new xanthones. In this study, the twigs of *G. cowa* were collected from Chiang Rai Province, Thailand. The EtOAc extract showed good α-glucosidase inhibitory activity with an IC_{50} values of 23.5 ± 0.2 μg/mL. This prompted us to further investigate their phytochemicals and antidiabetic properties. This report describes the isolation and structure elucidation of a new xanthone, garciniacowone L (**1**), and seven known compounds, including 2-geranyl-1,3,7-trihydroxy-4-(3,3-dimethylallyl)-xanthone (**2**), mangostinone (**3**), β-mangostin (**4**), cochinchinone G (**5**), 1,7-dihydroxyxanthone (**6**), 1-hydroxy-7-methoxy xanthone (**7**), and forbexanthone (**8**). The anti-diabetes activities, including α-glucosidase inhibition, α-amylase inhibition, glycation, glucose consumption, and glucose uptake are also reported.

2. Materials and methods

2.1. Materials and instruments

Materials for chromatography and instruments were the same as in previous reports (Phukhatmuen et al., 2020; Raksat et al., 2020; Raksat et al., 2019).

2.2. Extraction and isolation

The twigs of *G. cowa* were collected in January 2019 from Chiang Rai Province, Thailand. Herbarium specimen number MFU-NPR0186 was deposited at the Natural Products Research Laboratory, School of Science, Mae Fah Luang University.

Air-dried twigs of *G. cowa* (3.8 kg) were extracted with EtOAc for 3 days at room temperature and concentrated under reduced pressure to give the EtOAc extract (103.6 g). This extract was subjected to QCC over silica gel and eluted with a gradient of hexanes-acetone (100% hexanes to 100% acetone) to obtain eight fractions (GCT1-GCT8). Fraction GCT5 (1.1 g) was isolated by CC over silica gel (1:9 *v*/*v*, acetone-hexanes) to give compounds **2** (9.5 mg) and **5** (12.4 mg). Fraction GCT6 (2.3 g) was further purified by CC over silica gel (3:17 *v*/*v*, EtOAc-hexanes) to obtain compounds **1** (2.8 mg) and **7** (3.7 mg). Compounds **4** (1.3 mg) and **8** (2.6 mg) were afforded from fraction GCT7 (3.3 g) by repeated CC over silica gel (1:9 *v*/*v*, acetone-hexanes). Fraction GCT8 (4.13 g) was purified by CC over silica gel (1:4 *v*/*v*, acetone-hexanes) yielded compounds **3** (4.6 mg) and **6** (4.5 mg).

*Garciniacowone L (**1**).* Light yellow viscous oil. $[\alpha]_D^{25}$ + 9 (*c* 0.1, MeOH); UV λ_{max} (log ε): 212 (2.94), 242 (3.46), 259 (3.61), 286 (2.90), 318 (3.55), and 368 (3.38) nm; IR (KBr) ν_{max}: 3354, 2932, 2162, 1712, 1478, 1285, and 1173 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HRESITOFMS *m*/*z* 411.1785, $[M + H]^+$ (calcd for $C_{24}H_{26}O_6$,411.1802).

2.3. α-Glucosidase inhibitory assay

The α-glucosidase inhibitory assay was performed in triplicate using the previous reports (Phukhatmuen et al., 2020; Raksat et al., 2020). Positive controls were acarbose, voglibose, and quercetin.

2.4. α-Amylase inhibitory assay

The α-amylase inhibitory assay was performed in triplicate using a modified previous report (Kusano et al., 2011).

2.5. Glycation inhibitory assay

The glycation inhibition assay was performed in triplicate using the same procedure as in the previous report (Justino et al., 2016). The standard control was quercetin. The procedure for the glycation inhibition assay was performed.

2.6. Glucose uptake assay

The glucose uptake assay was carried out in triplicate using the same procedure as in the previous report with slight alteration (Phukhatmuen et al., 2020), and metformin was used as the standard control.

2.7. Glucose consumption assay

The glucose consumption assay was performed in triplicate, using the same procedure as in our previous report (Phukhatmuen et al., 2020), and metformin was used as standard control. Cell viability was carried out by MTT assay, as previously described (Phukhatmuen et al., 2020).

3. Results and discussion

3.1. Isolation and structure elucidation

Phytochemical investigation of the EtOAc extract of *G. cowa* twigs led to the isolation and identification of a new xanthone, garciniacowone L (**1**), together with seven known xanthones (Fig. 1). The known xanthones were identified 2-geranyl-1,3,7-tri hydroxy-4-(3,3-dimethylallyl)-xanthone (**2**) (Bennett et al., 1993), mangostinone (**3**) (Asai et al., 1995), β-mangostin (**4**) (Trisuwan and Ritthiwigrom, 2012), cochinchinone G (**5**) (Boonnak et al., 2009), 1,7-dihydroxyxanthone (**6**) (Mak et al., 1999), 1-hydroxy-7-methoxy xanthone (**7**) (Dharmaratne et al., 2009), and forbexanthone (**8**) (Harrison et al., 1993) by comparisons made with the literature reported spectroscopic data.

Compound **1** was obtained as a light-yellow viscous oil. The molecular formula of $C_{24}H_{26}O_6$ was deduced from HRESITOFMS data, which showed a $[M+H]^+$ ion peak at *m*/*z* 411.1785, (calcd 411.1802). The IR spectrum showed the hydroxy and carbonyl functionalities at 3354 and 1712 cm^1, respectively, while the UV spectrum showed absorption bands at λ_{max} 212, 242, 259, 286, 318, and 368 nm. The ^{13}C NMR and DEPT spectroscopic data (Table 1) displayed resonances for 24 carbons, including four methyls (δ_C 19.9, 20.6, 32.1, and 56.5), four methylenes (δ_C 17.1, 19.7, 39.7, and 41.4), four methines (δ_C 94.7, 102.7, 104.5, and 47.7), and 12 quaternary carbons (δ_C 33.6, 79.4, 103.6, 105.5, 113.3, 144.2, 152.4, 152.7, 155.7, 160.1, 160.5, and 180.0). The ^1H NMR spectroscopic data (Table 1) indicated that this compound showed the characteristics of a xanthone (Trinh et al., 2017) with a hydrogen-bonded hydroxy proton [δ_H 13.39 (1H, s, OH-1)], three singlet aromatic protons [δ_H 6.31 (1H, s, H-4), 6.93 (1H, s, H-5), and 7.59 (1H, s, H-8)], and a methoxy group [δ_H 4.01 (3H, s, OMe-7)]. The methoxy group was placed at C-7 due to the HMBC correlation (Fig. 2) between H-8 (δ_H 7.59), H-5 (δ_H 6.93), and methoxy protons (δ_H 4.01) with C-7 (δ_C 144.2). The methoxy at C-7 (δ_C 144.2) was also confirmed by the NOESY cross peak between H-8 (δ_H 7.59) and 7-OMe (δ_H 4.01). The low field ^{13}C NMR resonance of C-6 (δ_C 152.7) suggested that a hydroxy group was attached to this carbon. Furthermore, the main interest of this molecule is a cyclization of the geranyl side chain and cowaxanthone (**i**) was proposed as a precursor. The concerted cyclization of the geranyl side chain of cowaxanthone (**i**) would give the 5,5,8a-trimethyloctahydro-2*H*-1-benzopyran moiety of compound **1** (Fig. 2), which showed the

Table 1
NMR Spectroscopic data of compound **1** in $CDCl_3$, 500 MHz.

Position	δ_C	Carbon type	δ_H (mult *J* in Hz)	HMBC
1	160.5	C	–	–
2	105.5	C	–	–
3	160.1	C	–	–
4	94.7	CH	6.31 (s)	C-1, C-3, C-4a, C9a
4a	155.7	C	–	–
5	102.7	CH	6.93 (s)	C-6, C-7, C-10a
6	152.7	C	–	–
7	144.2	C	–	–
8	104.5	CH	7.59 (s)	C-7, C-8a, C-9, C10a
8a	113.3	C	–	–
9	180.0	C	–	–
9a	103.6	C	–	–
10a	152.4	C	–	–
1′	17.1	CH_2	2.85 (dd, 16.5, 4.9);2.36 (dd, 16.6, 13.4)	C-1, C-2, C-2′, C-3′
2′	47.4	CH	1.68 (m)	C-1′, C-3′, C-7′, C-8′, C-9′
3′	79.4	C	–	–
4′	39.7	CH_2	2.01 (dd, 10.7, 2.4);1.65 (m)	C-2′, C-3′, C-5′, C-7′
5′	19.7	CH_2	1.67 (m)	C-4′, C-6′, C-7′
6′	41.4	CH_2	1.52, 1.33 (m)	C-5′, C-7′
7′	33.6	C	–	–
8′	20.6	CH_3	0.96 (s)	C-2′, C-6′, C-7′, C-9′
9′	32.1	CH_3	1.06 (s)	C-2′, C-6′, C-7′, C-8′
10′	19.9	CH_3	1.26 (s)	C-2′, C-3′, C-4′
1-OH	–	–	13.39 (brs)	–
7-OMe	56.5	CH_3	4.01 (s)	C-7

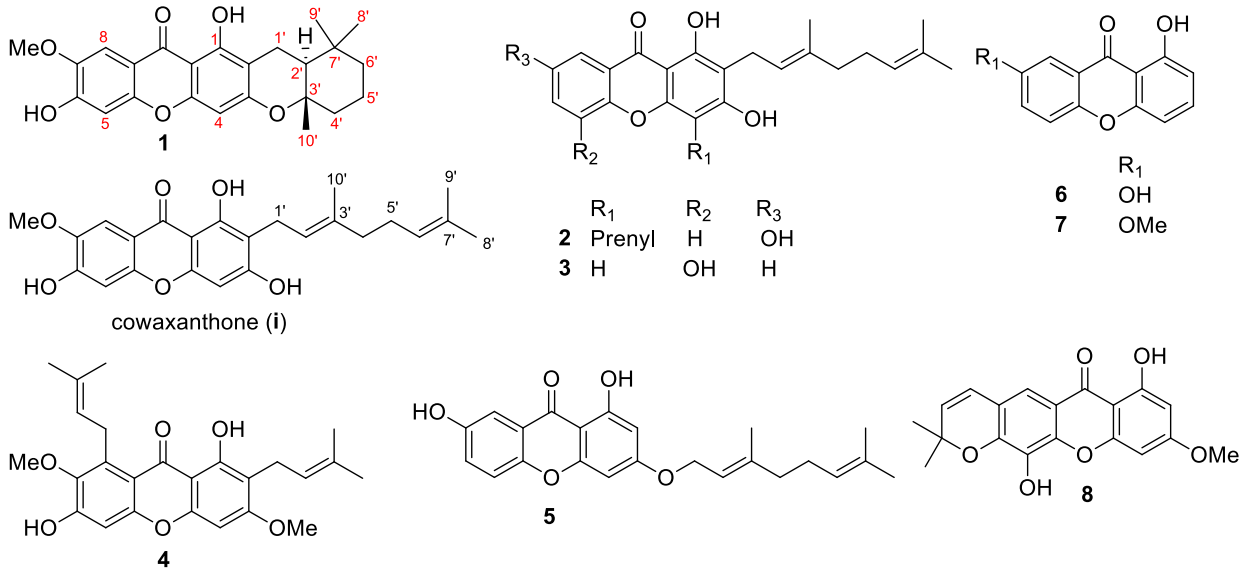

Fig. 1. Isolated compounds from the twigs extract of *G. cowa*.

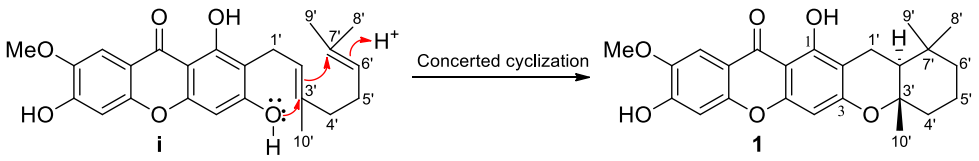

Fig. 2. The propose of concerted cyclization of garciniacowone L (**1**) from cowaxanthone (**i**).

^1H and ^{13}C resonances at δ_H 2.85 (dd, 16.5, 4.9 Hz, H-1′)/δ_C 17.1, 2.36 (dd, 16.6, 4.8 Hz, H-1′)/δ_C 17.1, 1.68 (1H, m, H-2′)/δ_C 47.4, 2.01 (1H, dd, 10.7, 2.4, H-4′)/δ_C 39.7, 1.65 (2H, m, H-4′)/δ_C 39.7, 1.67 (1H, m, H-5′)/δ_C 19.7, 1.52, 1.33 (2H, m, H-6′)/δ_C 41.4, 1.26 (3H, s, H-10′)/δ_C 19.9, 0.96 (3H, s, H-8′)/δ_C 20.6, 1.06 (3H, s, H-9′)/δ_C 32.1, δ_C 79.4 (C-3′), and δ_C 33.6 (C-7′). The ^{13}C NMR resonances of the geminal dimethyl group [C-8′ (δ_C 20.6) and C-9′ (δ_C 32.1)] on C-7 were different because they were diastereotropic methyl

groups. The following HMBC correlations (Fig. 3, Supplementary Material, Fig. S5 and Fig. S6) supported the 5,5,8a-trimethyloctahydro-2*H*-1-benzopyran moiety: H-1′ (δ_H 2.85 and 2.36) with C-2′ (δ_C 47.4), C-3′ (δ_C 79.4), and C-7′ (δ_C 33.6); H-2′ (δ_H 1.68) with C-1′ (δ_C 17.1), C-3′ (δ_C 79.4), and C-7′ (δ_C 33.6); Me-8′ (δ_H 0.96) and Me-9′ (δ_H 1.06) with C-2′ (δ_C 47.4), C-6′ (δ_C 41.4), and C-7′ (δ_C 33.6), and Me-10′ (δ_H 1.26) with C-2′ (δ_C 47.4), C-3′ (δ_C 79.4), and C-4′ (δ_C 39.7). In addition, the ^{1}H–^{1}H COSY correlations between H-1′ (δ_H 2.85 and 2.36) with H-1′ (δ_H 2.85 and 2.36) with H-2′ (δ_H 1.68) and H-4′ (δ_H 1.33) with H-5′ (δ_H 1.67) and H-5′ (δ_H 1.67) with H-6′ (δ_H 1.33) supported the connections of C-1′–C-2′ and C-4′–C-5′–C-6′, respectively (Fig. 3). The ring junction at C-2′/C-3′ was proposed to be a *trans*-ring junction because there is no NOESY cross peak between H-2′ (δ_H 1.68) and Me-10′ (δ_H 1.26) (Supplementary Material, Fig. S7). The 5,5,8a-trimethyloctahydro-2*H*-1-benzopyran moiety was placed at C-2/C-3 due to HMBC correlations between H-1′ (δ_H 2.85 and 2.36) with C-2 (δ_C 105.5). Finally, the C-3 of the xanthone skeleton was an oxygenated carbon due to the low field ^{13}C NMR resonance of this carbon (δ_H 160.1). Accordingly, compound **1** was characterized as garciniacowone L. The full assignments of ^{1}H and ^{13}C NMR spectroscopic data were shown in Table 1.

The known xanthones (**2**–**8**) displayed a resonance of a hydrogen-bonded hydroxy proton (ca. δ_H 13.7–12.6) at C-1 (Figs. S9–S15, Supplementary Material). Compounds **2** (2-geranyl-1,3,7-trihydroxy-4-(3,3-dimethylallyl)-xanthone) and **3** (mangostinone) contained a geranyl group at C-2. These two compounds have differed in the substituent groups of R_1, R_2, and R_3 at C-4, C-5, and C-7, respectively. Compound **2** displayed an isoprenyl unit, a hydrogen atom, and a hydroxy group at R_1, R_2, and R_3, respectively, whereas compound **3** was two hydrogen atoms at R_1 and R_3 and a hydroxy group at R_2. Compound **4** (β-mangostin) was identified as a tetraoxygenated xanthone containing two isoprenyl groups at C-2 and C-8, two methoxy groups at C-3 and C-7, and a hydroxy group at C-6. In the case of compound **5** (cochinchinone G), an oxygeranyl unit and a hydroxy group were observed at C-3 and C-7, respectively. Compounds **6** (1,7-dihydroxyxanthone) and **7** (1-hydroxy-7-methoxy xanthone) were the simplest xanthone, which containing a hydroxy group (**6**) or a methoxy group (**7**) at C-7. In contrast, compound **8** (forbexanthone) displayed a chromene ring, a methoxy group, and a hydroxy group at C-6/C-7, C-3, and C-5, respectively.

Xanthones are the principal chemotaxonomic markers in *Garcinia* genus (Ritthiwigrom et al., 2013; Rukachaisirikul et al., 2005; Mahabusarakam et al., 2005; Rukachaisirikul et al., 2006; Trisuwan and Ritthiwigrom, 2012; Sriyatep et al., 2015; Phukhatmuen et al., 2020; Raksat et al., 2020). Xanthones **2**, **5**, **7**, and **8** were found in *G. cowa* for the first time. However, they have been reported from other *Garcinia* species and the related Clusiaceae family. 2-Geranyl-1,3,7-trihydroxy-4-(3,3-dimethylallyl)-xanthone (**2**) was previously isolated from two species of *Cratoxylum* genus (Hypericaceae): *C. cochinchinense* (Bennett et al., 1993) and *C. formasum* (Chailap and Nuanyai, 2019), while mangostinone (**3**) widely distributed in several *Garcinia* species: *G. cowa* (Mahabusarakam et al., 2005; Raksat et al., 2020), *G. parvifolia* (Rukachaisirikul et al., 2006), *G. mangostana* (Asai et al., 1995), and *G. xipshuanbannaensis* (Na and Xu, 2010). β-Mangostin (**4**) and 1,7-dihydroxyxanthone (**6**) were also found in various *Garcinia* species, including *G. cowa* (Phukhatmuen et al., 2020), *G. malaccensis* (Taher et al., 2012), *Garcinia sp.* (Siridechakorn et al., 2014), *G. schomburgkiana* (Vo et al., 2012), *G. dulcis* (Likhitwitayawuid et al., 1998), and *G. griffithii* (Nguyen et al., 2005) and *Cratoxylum* species, including *C. glaucum* (Sim et al., 2011), *C. arborescens* (Syam et al., 2014). Cochinchinone G (**5**), 1-hydroxy-7-methoxy xanthone (**7**), and forbexanthone (**8**) are commonly found in other Clusiaceae genus and another family related to the Clusiaceae, including *C. cochinchinense* (Hypericaceae) (Boonnak et al., 2009), *C. formasum* (Hypericaceae) (Duan et al., 2011), *Hypericum laricifolium* (Hypericaceae) (Ramírez-González et al., 2013), *H. petiolulatum* (Hypericaceae) (Rui et al., 2017), *H. przewalskii* (Hypericaceae) (Zhang et al., 2021), *Allanblackia gabonensis* (Clusiaceae) (Azebaze et al., 2008), *G. edulis* (Magadula, 2010), *G. vieillardii* (Hay et al., 2004), *G. nigrolineata* (Rukachaisirikul et al., 2005).

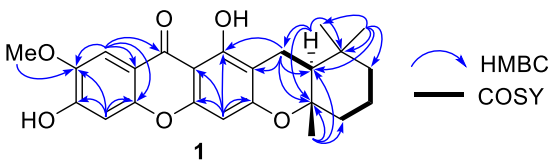

Fig. 3. ^{1}H–^{1}H COSY and selected HMBC correlations of garciniacowone L (**1**).

3.2. Antidiabetic activities

3.2.1. α-Glucosidase inhibition activity

All isolated compounds, except compound **4**, were further evaluated for their α-glucosidase inhibition activity. Compound **8** displayed moderated inhibitory effect with an IC_{50} value of 85.1 ± 0.3 μM, which is better than that of the voglibose (127.4 ± 1.2 μM). However, it was less active than those of acarbose (76.7 ± 1.4 μM) and quercetin (30.6 ± 0.9 μM). Other compounds were found to have weak α-glucosidase inhibition activity or inactive. This study is the first report of the α-glucosidase inhibitory activity of compounds **2**, **5**, and **8**. The IC_{50} values of compounds **3** (188.8 ± 0.6 μM) and **7** (156.9 ± 1.4 μM) were consistent with the previous study, which had been reported their IC_{50} values of > 100 μM (Phukhatmuen et al., 2020; Raksat et al., 2020). In 2011, Ryu and co-workers have reported the α-glucosidase inhibitory activity of β-mangostin (**4**) with the IC_{50} value of 14.4 ± 0.1 μM. In this study, the α-glucosidase inhibitory activity of β-mangostin (**4**) was not evaluated due to the small isolation of β-mangostin (**4**).

3.2.2. α-Amylase inhibition activity

The inhibition of carbohydrate hydrolyzing enzymes (α-amylase) can be a practical therapeutic approach for diabetes by preventing the breakdown of long-chain polysaccharides to glucose and decreasing high blood glucose levels (Ojah et al., 2020). The isolated xanthones (**1**–**8**) were assayed for inhibition of α-amylase as indicated in Table 2. Unfortunately, they showed no α-amylase inhibition activity at 100 μg/mL.

Table 2
α-Glucosidase, α-amylase, and glycation inhibition activities of compounds 1–8.

Compounds	α-Glucosidase inhibition	α-Amylase inhibition	Glycation inhibition
	IC_{50}, μM		
1	117.2 ± 1.5	Inactive	Inactive
2	111.7 ± 0.1	Inactive	Inactive
3	188.8 ± 0.6	Inactive	Inactive
5	162.6 ± 0.3	Inactive	Inactive
6	Inactive	Inactive	Inactive
7	156.9 ± 1.4	Inactive	170.3 ± 0.9
8	85.1 ± 0.3	Inactive	Inactive
Acarbose	76.7 ± 1.4	105.8 ± 1.1	Not tested
Voglibose	127.4 ± 1.2	198.3 ± 0.8	Not tested
Quercetin	30.6 ± 0.9	180.1 ± 1.4	62.4 ± 1.5

Inactive at >200 μM.

Table 3
Glucose consumption and glucose uptake activities of compounds **3**, **6**, and **7**.

Compounds	Glucose consumption (IC_{50}, μM)	Glucose uptake (fold)
3	18.3 ± 0.5	2.9
6	57.5 ± 1.3	1.2
7	25.3 ± 0.7	1.6
Metformin	50.3 ± 0.9	3.8

3.2.3. Glycation inhibition activity

The formation of advanced glycation end products (AGEs) contributes to the development and progression of diabetic complications, including nephropathy, retinopathy, and neuropathy (Singh et al., 2014). Xanthones have been reported to have the ability to inhibit the formation of AGEs (Abdallah et al., 2017). The inhibition of glycation by xanthones **1**–**8** is summarized in Table 2. Only xanthone **7** displayed glycation inhibition activity with the IC_{50} value of 170.3 ± 0.9 μM, which was less active than that of the positive control (quercetin, IC_{50} value of 62.4 ± 1.5 μM). All remaining tested compounds were inactive. These findings may lead to further investigation and clarification of other mechanisms of AGEs properties of xanthones.

3.2.4. Glucose consumption and glucose uptake activities

It has been reported that xanthones from *Garcinia* species displayed glucose consumption and glucose uptake activities (Li et al., 2017). Xanthones **1**–**8** were evaluated for their glucose consumption in 3T3-L1 cells. Of these, xanthones **3**, **6**, and **7** displayed glucose consumption (Table 3) with IC_{50} values in the range of 18.3–57.5 μM. Xanthones **3** and **7** showed the glucose consumption activity better than that of positive control (metformin, IC_{50} = 50.3 ± 0.9) with the IC_{50} values of 18.3 ± 0.5 and 25.3 ± 0.7 μM. To confirm the glucose consumption activity, xanthones **3**, **6**, and **7** were further evaluated for glucose uptake induced by L6 myotube cells. As summarized in Table 3, xanthones **3**, **6**, and **7** enhanced the glucose uptake stimulation in adipocyte L6 myotube cells by 2.9, 1.2, and 1.6-fold, respectively, compared to the positive control (metformin, 3.8-fold). This information suggested that xanthones **3** showed potential glucose transportation into cells and provide energy in adenosine triphosphate (ATP) and play a crucial part in other cellular operations.

4. Conclusions

The chemical investigation of *G. cowa* twigs led to the isolation and identification of a new xanthone, garciniacowone L (**1**), together with seven known xanthones. Xanthone **8** exhibited moderate α-glucosidase inhibitory activity, while xanthones **1**–**8** showed no α-amylase inhibitory activity. Xanthone 7 showed the best inhibition of glycation activity, whereas xanthone 3 displayed the best glucose consumption and glucose uptake activities without cell toxicity. Based on these findings, xanthone derivatives from various species of Garcinia genus might be interesting lead compounds for developing drug candidates with therapeutic potential for the treatment of diabetes mellitus.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jksus.2022.102201.

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