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Three new resin glycosides compounds from *Argyreia acuta* and their α-glucosidase inhibitory activity

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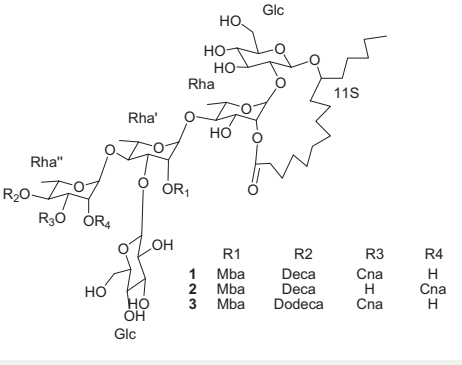
ABSTRACT

Three new phenolic compounds, acutacoside C (**1**), acutacoside D (**2**) and acutacoside E (**3**) were isolated from the aerial part of *Argyreia acuta*. The oligosaccharide chain was composed of two glucoses and three rhamnoses, and the aglycone was (11*S*)-hydroxyhexadecanoic acid (jalapinolic acid). The core of the three compounds was operculinic acid B, which was rare in resin glycosides. Their structures were established by a combination of spectroscopic and chemical methods. Compounds **1-3** have been evaluated for inhibitory activity against α-glucosidase, which all showed weak inhibitory activities.



From the aerial parts of *Argyreia acuta*, three new pentasaccharide compounds were isolated, identified and evaluated for their *a*-glucosidase inhibition activity.

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KEYWORDS
Argyreia acuta; resin glycosides; structural identification; α-glucosidase

1. Introduction

In recent years, with the development of social economy and the improvement of living standards of people in the world, the prevalence rate of diabetes has reached 6.4% in 2010 and it will probably reach to 7.7% in 2030 (Nolan et al. 2011). Diabetes is the third most

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serious threat to human health, at present, the cause of T2DM (type 2 diabetes mellitus) is complicated and lack of early preventive medicine (Wang et al. 2015). The mechanism of *α*-glucosidase inhibitor is the inhibition of the enzyme activity, which was at the top part of small intestine to blocking carbohydrates break down into individual glucose. The next to small intestine, and make these parts of the alpha-enzyme activity increased, the decomposition of carbohydrates into a single glucose and absorbed into the blood, so they can make blood sugar stable and slow to maintain at a certain level, to prevent postprandial hyperglycemia and rapid elevation of blood glucose. So, we have chosen *α*-glucosidase as target to express the activities of compounds **1**-**3**.

Argyreia acuta which belongs to Convolvulaceae family, is a climbing shrub and grows in Guangdong and Guangxi of China. Tender tip and leaves of *A. acuta* are considered as a vegetable in the Deang nationality of China (Xu 2001). Previous studies have shown that *A. acuta* contains diverse range of bioactive phytochemicals, including saponins, steroids, fatty acids (Zeng 2013), flavonoids, coumarins, cardiac glycosides and phenolics (Zeng et al. 2015). We have reported that some resin glycoside showed the *α*-glucosidase inhibitory activity of which were evaluated (Pan et al. 2015) in our preliminary studies. An investigation of the chemical constituents in the bioactive extract led to the isolation of three new resin glycosides, which were evaluated as the *α*-glucosidase inhibitory activity. Herein, the separation process as well as the structural elucidation of these compounds were described.

2. Results and discussion

Chloroform ($CHCl_3$) extract from 95% EtOH extract of the dried aerial parts of *A. acuta* was separated with several different chromatographic methods to afford compounds **1**–**3.**

Acutacoside C (**1**): white amorphous powder. Its molecular formula was determined to be $C_{70}H_{112}O_{27}Na$ on the basis of HRTOFMS analysis of the pseudomolecular ion peak at *m/z* 1407.7385 $[M + Na]^+$ (calculated as 1407.7289). The UV spectrum of compound **1** revealed a strong absorption band at 280 nm. The IR spectrum displayed strong absorption bands at 3439, 2929, 1726 and 1056 cm^{-1}, corresponding to hydroxyl, alkyl, carbonyl and ether groups, respectively. The ^1H NMR and ^{13}C NMR spectra of compound **1** revealed the presence of one benzene ring, one *trans*-olefinic bond and five sugar unit in the molecule. Analysis of the totalcorrelation spectroscopy (TCOSY), heteronuclear singular quantum correlation (HSQC) and heteronuclear multiple-bond correlation (HMBC) spectra of compound **1** allowed for the complete assignment of the ^1H and ^{13}C NMR spectral data (Table S1). The shifts of four ester carbonyl carbons were at δ_C 175.8, 175.4, 173.0 and 166.2 and five carbon signals of saccharide anomeric were at δ_C 104.2, 98.3, 100.0, 103.2 and 105.3. By the HSQC spectrum data, the linking anomeric protons in each saccharide unit were easy to be assigned at 5.03 (1H, d, $J = 7.5$ Hz), 5.72 (1H, br s), 5.99 (1H, br s), 6.41 (1H, br s) and 5.24 (1H, d, $J = 7.2$ Hz), respectively. Then each sugar unit was established by TOCSY experiments, and the correlative carbons were assigned by HSQC spectrum data, which gave one glucopyranosyl unit and four rhamnopyranosyl units in **1**. HMBC analysis of compound **1** displayed several key correlations, which can assign the correlation sites between sugar and sugar, sugars and fatty acids. The HMBC correlations between H-1 of *β*-Glc and C-11 of the 11-hydroxyhexadecanoyl moiety (aglycone), H-1 of Rha to C-2 of Glc, H-1 of Rha′ to C-4 of Rha, H-1 of *α*-Rha″ to C-4 of Rha′ and H-1 of Glc′ to C-3 of Rha′ provide the proof that the sequence of the sugar moiety

glucosyl-(1→3)-[rhamnosyl-(1→4)]-rhamnosyl-(1→4)-rhamnosyl-(1→2)-glucosyl by HMBC experiment, see Figure S1. In addition, the positions of esterification were inferred from the correlations: H-2 of Rha′ to C-1 of Mba, H-3 of Rha″ to C-1 of Cna and H-4 of Rha″ to C-1 of Deca, respectively. The C-2 (Rha) site of lactonisation was corroborated by the correlation between C-1 of aglycone. The anomeric configuration of the pyranosyl sugar unit was identified as a *β*-glucopyranosyl group on the basis of the coupling constant 7.5 and 7.2 Hz and *α*-rhamnopyranosyl from the C-5 chemical shift (Sang et al. 2000). Compound **1** was alkaline hydrolysed, then organic layer was methylated and identified by gas chromatography–mass spectrometry (GC–MS) analysis. 2-Methylbutyric acid methyl ester (t_R 4.39 min) *m/z* $[M + H]^+$ 117 (5), 101 (23), 88 (96), 57 (100), 41 (55), 29 (45), 27 (19) and *trans*-cinnamic acid methyl ester (t_R 13.29 min) *m/z* $[M]^+$ *m/z*162 (40), 131 (100), 103 (66), 77 (32), *n*-decanoic acid methyl ester (t_R 12.37 min) were identified. The 2-methylbutyric acid was proved to have an *S* configuration by comparing the specific rotation with that of authentic 2S-methylbutanoic acid (Yin et al. 2008). The glycosidic acid was operculinic acid B (Ono et al.1991) (**4**) (4 mg, from alkaline hydrolysis) was methylated and acid hydrolysed afford the methylated aglycone(11-hydroxyhexadecanoic acid methyl ester) (Yin et al. 2008) and sugar mixture, which allowed the identification of the components of the mixture of sugars as L-rhamnose and D-glucose by comparison their derivatives with those of authentic L-rhamnose (t_R 30.14 min) and D-glucose (t_R 31.65 min) derivatives prepared in the same way by GC–MS, respectively. Consequently, the structure of compound 1 was determined to be (*S*)-jalapinolic acid 11-*O*-*β*-D-glucopyranosyl-(1→3)-*O*-[3-*O*-*trans*-cinnamoyl-4-*O*-*n*-decanoyl-α-L-rhamnopyranosyl-(1→4)]-*O*-[2-*O*-(*S*)-2-meth-ylbutyryl]-α-L-rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-*β*-D-glucopyranoside, intramolecular 1,2″-ester (Figure 1).

Compounds **2** and **3** were isolated as white amorphous powder. The molecular formula were both determined to be $C_{72}H_{116}O_{27}Na$ on the basis of HRTOFMS analysis of the pseudomolecular ion peaks at *m/z* 1435.7733 $[M + Na]^+$ (calculated as 1435.7602) and *m/z* 1435.7692 $[M + Na]^+$ (calculated as 1435.7602). The UV spectrum of compounds **2** and **3**

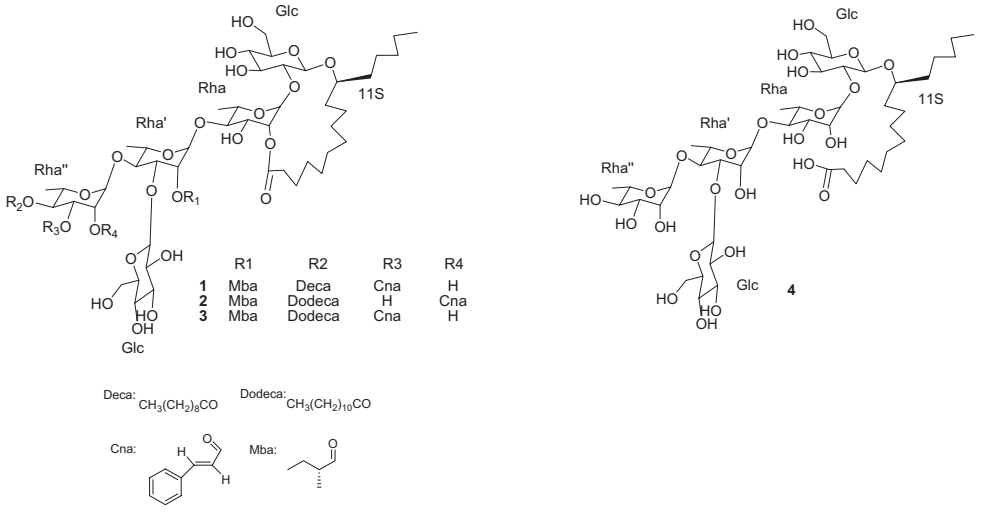

Figure 1. Structures of compounds **1**–**4**.

revealed strong absorption band at 280 nm. The IR spectrum of compound **2** displayed strong absorption bands at 3445, 2929, 1731 and 1070 cm^{-1} and compound **3** displayed strong absorption bands at 3444, 2930, 1726 and 1072 cm^{-1}. Independent alkaline hydrolysis of **2** and **3** afforded the same products as a mixture of and a glycosidic acid. The organic acids were composed of 2*S*-Methylbutyric acid, *n*-dodecanoic acid and a *trans*-cinnamoic acid by GC–MS experiment. The ^{1}H NMR and ^{13}C NMR spectra of compounds **2** and **3** revealed the presence of one *trans*-cinnamoyl group, and five sugar unit in the molecule. Analysis of the TCOSY, HSQC and HMBC spectra of compounds **2** and **3**, suggested that compounds **2** and **3** and compound **1** were just connected to different groups or different esterification positions. For complete assignments of the ^{1}H and ^{13}C NMR spectral data, see Table S1. The key HMBC correlations confirmed the esterification positions of the acyl residues in the oligosaccharide core, thus a *2S*-methylbutanoyl group was located at C-2 of Rha′ and *n*-dodeca was located at C-4 of Rha″ in **2** and **3**, a *trans*-cinnamoyl group was located at C-2 of Rha″ in **2** and at C-3 of Rha″ in **3**, respectively. The structure of compound **2** was determined to be (*S*)-jalapinolic acid 11-*O*-*β*-D-glucopyranosyl-(1→3)-*O*-[2-*O*-*trans*-cinnamoyl-4-*O*-(*S*)-*n*-dode-canoyl-α-L-rhamnopyranosyl(1→4)]-*O*-[2-*O*-(*S*)-2-methylbutyryl]-α-L-rhamnopyranosyl-(1→4)-*O*-α-L-rhamnopyr-anosyl-(1→2)-*O*-β-D-glucopyranoside, intramolecular 1,2″-ester and thestructureofcompound**3**wassuggestedas(*S*)-jalapinolicacid11-*O*-*β*-D-glucopyranosyl-(1→3)-*O*-[3-*O*-*trans*-cinnamoyl-4-*O*-*n*-dodecanoyl-α-L-rhamnopyranosyl-(1→4)]-*O*-[2-*O*-(*S*)-2-methyl-butyryl]-α-L-rhamnopyrano-syl-(1→4)-*O*-α-L-rhamnopyranosyl-(1→2)-*O*-*β*-D-glucopyranoside, intramolecular 1,2″-ester (Figure 1).

Some resin glycosides have been reported to exert anti-diabetes activities or potent *α*-glucosidase inhibitory activities (Pan et al. 2015), so compounds **1**–**3** have been evaluated for inhibitory activities against *α*-glucosidase. As shown in Table S2, new compounds **1**–**3** exhibited weak *α*-glucosidase inhibitory activities.

3. Experimental

3.1. General

UV spectra were recorded on Shimadzu UV-2550 spectrophotometer. IR spectra were taken from KBr discs on a Shimadzu FT-IR spectrophotometer. All of the ^{1}H and ^{13}C NMR spectra were recorded on INOVA 500 spectrometer, using tetramethylsilane as an internal standard. Two-dimensional NMR spectra include TCOSY, HSQC and HMBC. The chemical shifts in the NMR spectra were recorded as δ values. HR-TOF-MS experiments were performed on AB SCIEX Triple TOF 5600 plus MS spectrometer. Preparative high-performance liquid chromatography was performed using a Shimadzu LC-6ADseries instrument equipped with a UV detector at 280 nm and Shim-Park RP-C_{18} column (20 × 200 mm i.d.). GC–MS experiments were performed on a TRACE GC ULTRA DSQ II instrument. Optical rotations were measured with an Anton Paar-MCP600 polarimeter in MeOH solution. The centrifugation was applied with D05 (Hunan Hexi Instrument Co., Ltd, Changsha, China). *α*-Glucosidase was monitored continuously with an auto multi-functional microplate reader ELX800 (BioTek Instruments, Inc., Winooski, VT, USA). Adsorbents for column chromatography (CC) were silica gel (200–300 μm, Qingdao Marine Chemical Co., Ltd., China), Sephadex LH-20 (75–150 μm, Pharmacia, Sweden), ODS (40–63 μm, Fuji, Japan).

3.2. Plant material

The aerial parts of *A. acuta* L. were collected in April 2014 from the Yulin city of the Guangxi Province, China, and identified by associate Prof. Hongyan Ma. A voucher specimen (no. 2014-4) is deposited at Department of Traditional Chinese Medicinal Chemistry, Guangdong Pharmaceutical University.

3.3. Extraction and isolation

Dried aerial parts (30 kg) of *A. acuta* were cut to small pieces and were extracted two times with 95% EtOH under reflux for 2 h. The resulting solution was then filtered, and the filtrate was combined and concentrated under vacuum at 60 °C until approximately 90% of the solvent had been evaporated. The remaining solution was then extracted three times sequentially with equal volumes of petroleum ether (MSO) and $CHCl_3$. The $CHCl_3$ extract (0.56 kg) (150 g) was separated into five fractions (A–E) by normal-phase silica gel CC (3.0 kg of silica gel, 200–300 mesh) using a stepwise gradient elution of $CHCl_3$/MeOH (from 100:0 to 0:100, v/v). Fracton D (5 g) was separated into three subfractions (D-1, D-2 and D-3) on a normal-phase silica gel column using a stepwise gradient elution of petroleum ether/acetone (from 98:2 to 50:50, v/v). Fraction D-1 was then passed through a Sephadex LH-20 column with a MeOH eluent to yield three subfractions (D-1-1 and D-1-2), subfraction the D-1-2 was purified by a reverse-phase HPLC system (10 mL/min, 280 nm), eluted with MeOH/H_2O (98:2, v/v) to afford **1** (35 mg), **2** (23 mg), **3** (28 mg).

3.4. Spectral data

*Acutacoside C (**1**)*: white amorphous powder; $[\alpha]_D^{25}$ −4.5° (*c* 0.11, MeOH); UV (MeOH) λ_{max} 217 (0.52), 280 (0.65) nm; IR (KBr) ν_{max}: 3439, 2929, 1726 and 1056 cm^{-1}, ^1H NMR and ^{13}C NMR data, see Table S1; HR-TOF-MS *m/z* 1407.7385 $[M + Na]^+$ (calcd for $C_{70}H_{112}O_{26}Na$: 1407.7289).

*Acutacoside D (**2**)*: white amorphous powder; $[\alpha]_D^{25}$ −16° (*c* 0.10, MeOH); UV (MeOH) λ_{max} 218 (0.32), 281 (0.41) nm; IR (KBr) ν_{max}: 3445, 2929, 1731 and 1070 cm^{-1}, ^1H NMR and ^{13}C NMR data, see Table S1; HR-TOF-MS *m/z* 1435.7733 $[M + Na]^+$ (calcd for $C_{72}H_{116}O_{26}Na$: 1435.7602).

*Acutacoside E (**3**)*: white amorphous powder; $[\alpha]_D^{25}$ −17.0° (*c* 0.14, MeOH); UV (MeOH) λ_{max} 217 (0.50), 280 (0.63) nm; IR (KBr) ν_{max}: 3444, 2930, 1726 and 1072 cm^{-1}, ^1H NMR and ^{13}C NMR data, see Table S1; HR-TOF-MS *m/z* 1435.7692 $[M + Na]^+$ (calcd for $C_{72}H_{116}O_{26}Na$: 1435.7602).

3.5. Hydrolysis

In order to measure the kinds of organic acid groups, sugar and the absolute configuration of aglycone, compounds **1**-**3** were hydrolysed , including alkaline hydrolysis and acid hydrolysis. The procedures were performed as described earlier (Yin et al. 2016).

3.6. α-Glucosidase enzyme inhibition activity

The α-glucosidase inhibition assay was performed according to a slightly modified method of Pierre et al **(**Sang et al. 2000**)** and the method was performed as described earlier (She 2004).

4. Conclusion

In conclusion, investigation of the aerial parts of *A. acuta* afforded three new compounds, which had weak α-glucosidase inhibitory activities.

Supplementary material

Supplementary material relating to this article is available online, alongside Figures S1–S22.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

Nolan CJ, Damm P, Prentki M. 2011. Type 2 diabetes across generations: from pathophysiology to prevention and management. Lancet. 378:169–181.

Ono M, Kawasaki T, Miyahara K. 1991. Resin glycosides. XI. Operculins III, IV, IX, X, XVI, XVII and XVIII, new ether-soluble resin glycosides of rhizoma jalapae braziliensis (root of *Ipomoea operculata*). Chem Pharm Bull. 39:2534–2539.

Pan JT, Yu BW, Yin YQ, Li JH, Wang L, Guo LB, Shen ZB. 2015. Four new pentasaccharide resin glycosides from *Ipomoea cairica* with strong α-glucosidase inhibitory activity. Molecules. 20:6601–6610.

Sang SM, Lao AN, Leng Y, Gu ZP, Chen ZL, Uzawa J, Fujimoto Y. 2000. Segetoside F a new triterpenoid saponin with inhibition of luteal cell from the seeds of *Vaccaria segetalis*. Tetrahedron Lett. 41:9205–9207.

She ZH. 2004. Oil fatty acid derivatization method and choose in gas chromatography. Grain Process. 29:64–66.

Wang C, Zhou J, Li MX, Jia ZP, Zhang RX. 2015. Research on progress of traditional Chinese medicine treatment of type 2 diabetes mellitus. Clin J Chin Med. 7:96–97, 106.

Xu BH. 2001. The medicinal vegetables of *Argyreia acuta*. J Plant. 28:19.

Yin YQ, Huang XF, Kong LY, Niwa M. 2008. Three new pentasaccharide resin glycosides from the roots of sweet potato (*Ipomoea batatas*). Chem Pharm Bull. 56:1670–1674.

Yin YQ, Pan JT, Yu BW, Cui HH, Yan YS, Chen YF. 2016. Two pentasaccharide resin glycosides from *Argyreia acuta*. Nat Prod Res. 30:20–24.

Zeng FL. 2013. Studies on chemical xonstituents of *Argyreia acuta* Lour. Asia-Pacific Traitional Med. 9:31–32.

Zeng FL, Shen YF, Zhang XJ. 2015. Pre-experiment of chemical composition from *Argyreia acuta*. Guide Chin Med. 13:49–50.