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A new lignan glycoside from the stems of *Zanthoxylum armatum* DC

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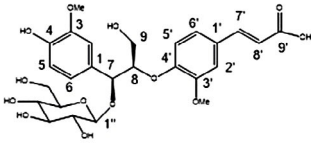
ABSTRACT

A new lignan glycoside, (*7S*,*8R*)-guaiacylglycerol-ferulic acid ether-7-O-*β*-D-glucopyranoside (**1**), along with five known phenylpropanoids (**2**–**6**) and seven phenylpropanoid glycosides (**7**–**13**), were isolated from the stems of *Zanthoxylum armatum* DC. Their structures were elucidated by spectroscopic analysis. Compounds **2**–**8** and **11**–**13** were first isolated from Rutaceae and the others were isolated for the first time from *Z. armatum*.



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KEYWORDS
Zanthoxylum armatum; Rutaceae; lignan glycoside; phenylpropanoid; phenylpropanoid glycoside

1. Introduction

The genus *Zanthoxylum* (Rutaceae) comprises 250 species distributed in the tropical and subtropical zones of Asia, Africa, America and Oceania, and there are 39 species and 14 varieties in China. *Z. armatum* DC is a wild shrub distributed mainly in southeast Asia, the Himalayas and China. It has a long history to be used in folk medicines to treat abdominal pain, cold and cough, tonsillitis, fever, altitude sickness, diarrhoea and dysentery. Recent studies have demonstrated the extract of *Z. armatum* possesses anti-proliferative (Kumar & Müller 1999), anti-inflammatory (Bhatt & Upadhyaya 2010), antioxidant (Kanwal et al. 2015; Zhang et al. 2015), hepatoprotective (Verma & Khosa 2010), antinociceptive (Guo et al. 2011; Ibrar et al. 2012), antidiabetic (Karki et al. 2014) and larvicidal activities (Kumar et al. 2016). The essential oil of *Z. armatum* exhibited good antimicrobial and anthelmintic activities (Barkatullah et al. 2013). Several kinds of compounds, including lignan, alkaloid, enoic acid, flavonoid, coumarin and amide have been isolated from the plant (Ahmad et al. 2004;

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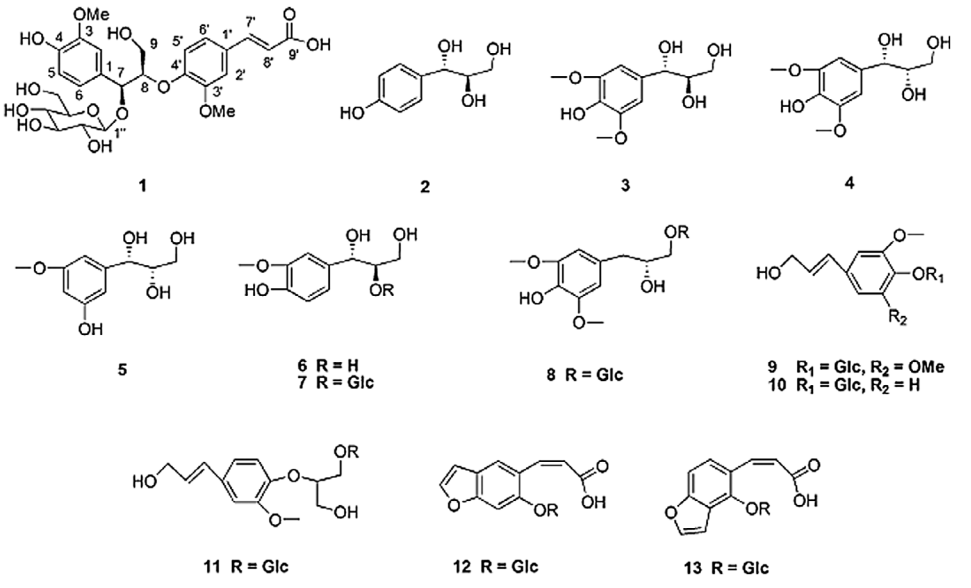

Figure 1. Chemical structures of compounds **1**–**13** isolated from the stems of *Z. armatum*.

Li et al. 1996; Kalia et al. 1999; Li et al. 2006; Singh & Singh 2011; Guo et al. 2012; Mehta et al. 2012; Devkota et al. 2013; Samad et al. 2014, 2015). However, the hydrophilic fraction of *Z. armatum* was rarely reported.

As a part of our systematic investigation on chemical constituents of *Z. armatum*, a new lignan glycoside, (*7S,8R*)-guaiacylglycerol-ferulic acid ether-7-O-*β*-D-glucopyranoside (**1**), along with five known phenylpropanoids (**2**–**6**) and seven phenylpropanoid glycosides (**7**–**13**), were isolated from the stems of *Z. armatum* (Figure 1). Their structures were elucidated by spectroscopic analysis.

2. Result and discussion

Compound **1** was obtained as colourless oil. Its molecular formula was determined as $C_{26}H_{32}O_{13}$ by HR-ESI-MS at *m/z* 575.1739 $[M + Na]^+$, possessing 11° of unsaturation. The ^1H NMR spectrum of **1** (Table S1) showed six aromatic protons of two ABX type [*δ* 7.01 (1H, d, *J* = 1.7 Hz, H-2), 6.91 (1H, dd, *J* = 8.8, 1.7 Hz, H-6), 6.82 (1H, d, *J* = 8.8 Hz, H-5), 7.17 (1H, d, *J* = 1.7 Hz, H-2′), 6.99 (1H, dd, *J* = 8.8, 1.7 Hz, H-6′), 6.81 (1H, d, *J* = 8.8 Hz, H-5′)] in the low field. Two olefin protons [*δ* 7.25 (1H, d, *J* = 16 Hz, H-7′), 6.35 (1H, d, *J* = 16 Hz, H-8′)] indicated the presence of *trans* double bond. There are one methylene proton [*δ* 3.68 (2H, m)], two methine protons [*δ* 5.03 (1H, d, *J* = 4.5 Hz), 3.86 (1H, m)] and one glucopyranosyl anomeric proton [*δ* 4.61 (1H, d, *J* = 7.6 Hz)]. In the ^{13}C NMR spectrum, the presence of two C_6–C_3 units arising from lignan and a glucopyranose was suggested. The proton and carbon signals were assigned with the ^1H–^1H COSY, HMBC and HMQC. The correlation site between the guaiacylglycerol and the ferulic acid moiety was established by a HMBC experiment (Figure S1) in which the long-range correlation between H-8 (*δ* 3.86) and C-4′ (*δ* 147.5) was observed. Acid hydrolysis of **1** with 5% HCl afforded D-glucose, which compared with authentic samples. The stereochemistry of the anomeric carbon of glucose was determined as *β* according to

the coupling constant of the anomeric proton and the chemical shift of C-1″ (102.3). The glycosidic site was unambiguously established by a HMBC experiment in which the long-range correlation between H-1″ (δ 4.61) and C-7 (δ 79.7) was observed. The small coupling constant ($J_{7,8}$ = 4.5 Hz) in the ^{1}H NMR spectrum indicated a erythro configuration between H-7 and H-8. The CD spectrum of **1** showed a negative Cotton effect at 238 nm, together with the clear NOESY correlations between H-8/H-2 and H-8/H-6 (Figure S1), indicated the *7S,8R*-configuration (Matsuda & Kikuchi 1996; Hu et al. 2012). Finally, structure of **1** was defined as (*7S,8R*)-guaiacylglycerol-*β*-ferulic acid ether-7-O-*β*-D-glucopyranoside.

Twelve known compounds were identified as *erythro*-1-(4-hydroxyphenyl) glycerol (**2**) (Lundgren et al. 1985), *thero*-syringylglycerol (**3**) (Otsuka et al. 1989), *erythro*-syringylglycerol (**4**) (Lin et al. 2007), 7-(3-hydroxy-5-methoxyphenyl) propane-7,8,9-triol (**5**) (Zeng et al. 2012), *threo*-guaiacylglycerol (**6**) (Okyuama et al. 1998), (-)-(*7R,8S*)-guaiacylglycerol 8-O-*β*-D-glucopyranoside (**7**) (Ishimaru et al. 1987), xylocoside A (**8**) (Zheng et al. 2008), syringin (**9**) (Calis et al. 1993), coniferin (**10**) (Calis et al. 1993), 3-hydroxy-2-{4-[(1E)-3-hydroxyprop-1-en-1-yl] -2-methoxyphenoxy}propyl-D-glucopyranoside (**11**) (Liu et al. 2009), psoralenoside (**12**) (Qiao et al. 2006) and isopsoralenoside (**13**) (Qiao et al. 2006). Their structures were established on the basis of spectral and chemical evidence, which were in good agreement with those reported in the literature. Among that, compounds **2**–**8** and **11**–**13** were first isolated from Rutaceae and others were isolated for the first time from *Z. armatum*.

3. Experimental

3.1. General experimental producers

Optical rotation data were obtained on a Perkin-Elmer 241 automatic digital polarimeter. UV spectral data were measured on a Shimadzu UV-260 instrument. Optical rotations were measured on a JASCO P-1020 spectropolarimeter (JASCO, Tokyo, Japan). ^{1}H, ^{13}C NMR, ^{1}H–^{1}H COSY, HMQC, HMBC and NOESY spectra were recorded on a Bruker DRX-400 spectrometer (^{1}H 400 MHz and ^{13}C 100 MHz). The carbon multiplicities were obtained by DEPT experiment. HR-ESI-MS data were measured on Bruker APEX 7.0 TESLA FT-MS apparatus (Bruker, Axs Gmbh, Switzerland). Reversed-phase chromatography utilised TSK gel Toyopearl HW-40F (30–60 μm, Toso Co., Ltd.), MCI gel CHP 20P (75–150 μm, Mitsubishi Chemical Industries Co., Ltd.) and Cosmosil 75 C_{18}-OPN (42–105 μm, Nacalai Tesque Inc.) columns. TLC was performed using precoated silica gel 60 F_{254} plates (0.2 mm, Merck).

3.2. Plant materials

The stems of *Z. armatum* DC. was collected from Nanning of Guangxi Province, China in September 2014, and identified by associate professor Ze-hao Huang, and a voucher specimen of the plant (#Z140934) was deposited in school of life science and engineering, Lanzhou University of Technology, Gansu, China.

3.3. Extraction and isolation

The air-dried stems of *Z. armatum* fruits (20 kg) were extracted three times with 40 L of 95% ethanol at room temperature, each for 4 days. The solvent was concentrated under reduced pressure to give a residue. The residue was suspended in water (2 L) and extracted with

petroleum ether, EtOAc and *n*-BuOH, successively. The water soluble fraction (83 g) dissolved in 300 mL water was subjected to MCI gel CHP 20P (8 × 60 cm) and eluted with MeOH/H_2O to obtain fraction 1 [1.0 L, H_2O], fraction 2 [0.6 L, MeOH/H_2O (10 : 90)], fraction 3 [0.6 L, MeOH/H_2O (30 : 70)], fraction 4 [0.6 L, MeOH/H_2O (50 : 50)], fraction 5 [0.6 L, MeOH/H_2O (70 : 30)], fraction 6 [1.0 L, MeOH]. Fraction 2 (12.9 g) was chromatographed on Toyopearl HW-40F (6 × 60 cm) using H_2O obtained fractions 2A–2E. Fraction 2B (0.9 g) was further purified by Cosmosil 75 C_{18}-OPN (4 × 30 cm, eluted with H_2O → 10% MeOH) and MCI gel CHP 20P (5 × 40 cm, eluted with H_2O → 10% MeOH) to yield **7** (63.0 mg) and **6** (143.3 mg). Fraction 2C (0.3 g) was subjected to MCI gel CHP 20P (5 × 40 cm, eluted with H_2O → 10% MeOH), then separated by Toyopearl HW-40F (6 × 60 cm, eluted with H_2O) to give **5** (53.9 mg) and **2** (9.2 mg). Fraction 3 (8.9 g) was subjected to Toyopearl HW-40F (6 × 60 cm, eluted with H_2O) to obtained fraction 3A–3D. Fraction 3B (0.3 g) was further purified by MCI gel CHP 20P (5 × 40 cm, eluted with H_2O-20% MeOH) and Cosmosil 75 C_{18}-OPN (4 × 30 cm, eluted with H_2O → 20% MeOH) to give **4** (6.5 mg) and **8** (10.2 mg). Fraction 3C (0.2 g) was chromatographed on MCI gel CHP 20P (5 × 40 cm, eluted with H_2O → 20% MeOH) to yield **3** (23.2 mg). Fraction 4 (9.4 g) was chromatographed on Toyopearl HW-40F (6 × 60 cm, eluted with H_2O) to yield six fractions 4A–4F. Fraction 4C (0.2 g) was further purified by MCI gel CHP 20P (5 × 40 cm, eluted with 30–50% MeOH) and Cosmosil 75 C_{18}-OPN (4 × 30 cm, eluted with 30 → 50% MeOH) to give **9** (6.2 mg) and **11** (5 mg). Fraction 4D (0.1 g) was further purified by Cosmosil 75 C_{18}-OPN (4 × 30 cm, eluted with 30 → 50% MeOH) and Toyopearl HW-40F (6 × 60 cm, eluted with H_2O) to give **10** (6.5 mg). Fraction 5 (5.8 g) was separated by Toyopearl HW-40F (6 × 60 cm) using H_2O as eluent to obtained fractions 5A–5C. Fraction 5B (0.3 g) was further purified by Cosmosil 75 C_{18}-OPN (4 × 30 cm, eluted with 40% → 70% MeOH) and Toyopearl HW-40F (6 × 60 cm, eluted with H_2O) to yield **12** (18.9 mg), **13** (7.4 mg) and **1** (13.2 mg).

Compound **1**: colourless oil. $[\alpha]_D^{20}$ − 69.3° (*c* 0.10, H_2O); HR-ESI-MS *m/z* 575.1739 $[M + Na]^+$ (Calcd for $C_{26}H_{32}O_{13}Na$, 575.1741); ^1H and ^{13}C NMR: see Table S**1**.

3.4. Acid hydrolysis of 1

A solution of compounds **1** (1 mg) in 5% HCl (0.5 mL) was heated (90 °C) for 2 h. After removing HCl by evaporation in vacuum, the mixture was diluted with H_2O and extracted with EtOAc. The aqueous layer was neutralised with 0.1 M NaOH and glucose was detected by TLC analysis with authentic sugars: $CHCl_3$–MeOH–H_2O (14 : 6 : 1), Rf 0.13 (glucose); *n*-BuOH-pyridine-H_2O (6 : 4 : 3), Rf 0.37 (glucose).

4. Conclusion

The Z. *armatum* (Rutaceae) is widely distributed in China, which has been used as Traditional Chinese Medicine. Chemical study on the stems of Z. *armatum* has resulted in the isolation of a new phenylpropanoid glycoside, (*7S,8R*)-guaiacylglycerol-β-ferulic acid ether-7-O-β-D-glucopyranoside (**1**), along with 12 known compounds. Compounds **2**–**8** and **11**–**13** were first isolated from Rutaceae and others were isolated for the first time from *Z. armatum*.

Supplementary material

Supplementary material relating to this article is available online, alongside Tables S1 and Figures S1–S5.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

Ahmad A, Misra LN, Gupta MM. 2004. Hydroxyalk-(4Z)-enoic acids and volatile components from the seeds of *Zanthoxylum armatum*. J Nat Prod. 56:456–460.

Barkatullah, Ibrar M, Muhammad N, Innayat-Ur-Rehman, Mujeeb-Ur-Rehman, Khan A. 2013. Chemical composition and biological screening of essential oils of *Zanthoxylum armatum* DC leaves. J Clin Toxicol. 3:1–6.

Bhatt N, Upadhyaya K. 2010. Anti inflammatory activity of ethanolic extract of bark of *Zanthoxylum armatum* D.C. Pharmacol Online. 2:123–132.

Calis I, Saracoglu I, Basaran AA, Sticher O. 1993. Two phenethyl alcohol glycosides from *Scutellaria orientalis* subsp. *Pinnatifida*. Phytochemistry. 32:1621–1623.

Devkota KP, Wilson J, Henrich CJ, McMahon JB, Reilly KM, Beutler JA. 2013. Isobutylhydroxyamides from the pericarp of Nepalese *Zanthoxylum armatum* inhibit NF1-Defective tumor cell line growth. J Nat Prod. 76:59–63.

Guo T, Deng Y.X, Xie H, Yao CY. Cai CC, Pan SL, Wang YL. 2011. Antinociceptive and anti-inflammatory activities of ethyl acetate fraction from *Zanthoxylum armatum* in mice. Fitoterapia. 82:347–351.

Guo T, Xie H, Deng YX, Pan SL. 2012. A new lignan and other constituents from *Zanthoxylum armatum* DC. Nat Prod Res. 26:859–864.

Hu J, Shi XD, Chen JG, Li CS. 2012. Two new rhamnopyranosides of neolignans from *Sanguisorba officinalis*. J Asian Nat Prod Res. 14:171–175.

Ibrar M, Muhammad N, Barkatullah Khan H, Jahan F, Ashraf N. 2012. Antinociceptive and anticonvulsant activities of essential oils of *Zanthoxylum armatum*. Phytopharmacology. 3:191–198.

Ishimaru K, Nonaka G, Nishioka I. 1987. Phenolic glucoside gallates from *quercus mongolica* and *q. acutissima*. Phytochemistry. 26:1147–1152.

Kalia NK, Singh B, Sood RP. 1999. A new amide from *Zanthoxylum armatum*. J Nat Prod. 62:311–312.

Kanwal R, Arshad M, Bibi Y, Asif S, Chaudhari SK. 2015. Evaluation of ethnopharmacological and antioxidant potential of *Zanthoxylum armatum* DC. J Chem. 2015:1–8.

Karki H, Upadhayay K, Pal H, Singh R. 2014. Antidiabetic potential of *Zanthoxylum armatum* bark extract on streptozotocin-induced diabetic rats. Int J Green Pharm. 8:77–83.

Kumar S, Müller K. 1999. Inhibition of keratinocyte growth by different *Nepalese zanthoxylum* species. Phytother Res. 13:214–217.

Kumar V, Reddy SGE, Chauhan U, Kumar N, Singh B. 2016. Chemical composition and larvicidal activity of *Zanthoxylum armatum* against diamondback moth, *Plutella xylostella*. Nat Prod Res. 30:689–692.

Li X, Li Z, Zheng Q, Cui T, Zhu W, Tu Z. 1996. Studies on the chemical constituents of *Zanthoxylum armatum* DC. Tianran Chanwu Yanjiu Yu Kaifa. 8:24–27.

Li H, Li P, Zhu L, Xie M, Wu Z. 2006. Chemical constituents of *Zanthoxylum armatum* DC. Zhongguo Yaofang. 17:1035–1037.
Lin S, Wang S, Liu M, Gan M, Li S, Yang Y, Wang Y, He W, Shi J. 2007. Glycosides from the stem bark of *Fraxinus sieboldiana*. J Nat Prod. 70:817–823.
Liu SS, Zhou T, Zhang SW, Xuan LJ. 2009. Chemical constituents from *Clerodendrum bungei* and their cytotoxic activities. Helv Chim Acta. 92:1070–1079.
Lundgren LN, Shen ZB, Theander O. 1985. The constituents of conifer needles. Dilignol glycosides from *Pinus massoniana lamb*. Acta Chem Scand. 39:241–248.
Matsuda N, Kikuchi M. 1996. Studies on the constituents of *Lonicera species*. X. neolignan glycosides from the leaves of *Lonicera gracilipes* var. glandulosa Maxim. Chem Pharm Bull. 44:1676–1679.
Mehta DK, Bhandari A, Satti NK, Singh S, Das R, Suri KA. 2012. Isolation and characterization of a glycoside 1-methoxy-2-methyl-3,6,-dihydroxy anthraquinone from *Zanthoxylum armatum* D.C. J Pharm Res. 5:5155–5156.
Okyuama E, Fujimori S, Yamazaki M, Deyama T. 1998. Pharmacologically active components of *viticis fructus* (Vitex rotundifolia).II. The components having analgesic effects. Chem Pharm Bull. 46:655–662.
Otsuka H, Takeuchi M, Inoshiri S, Sato T, Yamasaki K. 1989. Phenolic compounds from *Coix lachryma-jobi* var. *Ma-yuen*. Phytochemistry. 28:883–886.
Qiao CF, Han QB, Mo SF, Song JZ, Xu LJ, Chen SL, Yang DJ, Kong LD, Kung HF, Xu HX. 2006. Psoralenoside and isopsoralenoside, two new benzofuran glycosides from *Psoralea corylifolia*. Chem Pharm Bull. 54:714–716.
Samad A, Adeel M, Khan D, Badshah S, Muhammad Z, Khan S, Han J. 2015. Two new bioactive furoquinoline alkaloids from *Zanthoxylum armatum*. Asian J Chem. 27:2468–2472.
Samad A, Badshah S, Khan D, Ali F, Amanullah M, Hanrahan J. 2014. New prenylated carbazole alkaloids from *Zanthoxylum armatum*. J Asian Nat Prod Res. 16:1126–1131.
Singh TP, Singh OM. 2011. Phytochemical and pharmacological profile of *Zanthoxylum armatum* DC.–An overview. Indian J Nat Prod Resour. 2:275–285.
Verma N, Khosa RL. 2010. Hepatoprotective activity of leaves of *Zanthoxylum armatum* DC in CCl_4 produced hepatotoxicity in rats. Indian J Biochem Biophys. 47:124–127.
Zeng Q, Cheng XR, Qin JJ, Guan B, Chang RJ, Yan SK, Jin HZ, Zhang WD. 2012. Norlignans and phenylpropanoids from *Metasequoia glyptostroboides* Hu et Cheng. Helv Chim Acta. 95:606–612.
Zhang YJ, Luo ZW, Wang DM. 2015. Efficient quantification of the phenolic profiles of *Zanthoxylum bungeanum* leaves and correlation between chromatographic fingerprint and antioxidant activity. Nat Prod Res. 29:2024–2029.
Zheng RX, Chai XY, Bai CC, Ren HY, Lu YN, Shi HM, Tu PF. 2008. Xylocosides A–G, phenolic glucosides from the stems of *Xylosma controversum*. Helv Chim Acta. 91:1346–1354.