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Short communication

Xanthine oxidase inhibitory effects of the constituents of *Chrysanthemum morifolium* stems

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ABSTRACT

The flowers of *Chrysanthemum morifolium* Ramat. (family: Asteraceae) are used in Traditional Chinese Medicine to treat fever, cold and swelling. However the aerial part is considered as agriculture waste and the chemical and pharmacological information is scanty. From the stems of this plant, four new compounds named as morineoliganosides A (**1**), B (**2**), C (**3**) and heterophyllol-1-*O*-*β*-D-glucopyranoside A (**4**) together with 27 known isolates (**5–31**), including flavonoids and caffeoylquinic acids were isolated. Their structures were elucidated by chemical and spectroscopic methods The inhibitory effects on xanthine oxidase of these compounds have been determined. This research provided a scientific development and utilization of *C. morifolium* stems.

1. Introduction

Chrysanthemum morifolium Ramat. is a flowering perennial plant belonging to Asteraceae family, distributed from Asia to northeastern Europe. Chrysanthemum flowers are used for the treatment of fever, cold and swelling in Traditional Chinese Medicine (TCM). In some parts of Asia, chrysanthemum flowers are boiled to make tea. Pharmacological studies showed that chrysanthemum flowers exhibited antibacterial (He et al., 2013), antioxidant (Lin et al., 2010), anti-inflammatory, and heart-protective (Lii et al., 2010) activities. Caffeoylquinic acids and flavonoids have been shown to be the major bioactive constituents of *C. morifolium* (Yuan et al., 2015).

In China, the major production areas of *C. morifolium* include Henan, Anhui, Hebei and Zhejiang provinces. After separating the flowers, the medicinally useful part of the plant, the aerial part is thrown away, which may cause serious waste of *C. morifolium* resources. A study on constituents of the stems of *C. morifolium* (CMS) has been carried out and eleven known compounds, (7*S*,8*R*)-picraquassioside C, (2*R*,3*S*)-2,3-dihydro-3-hydroxymethyl-7-methoxy-2-(4′-hydroxy-3′-methoxyphenyl)-5-benzo-furanpropanol 5c-*O*-*β*-D-glucopyranoside, (+)-pinoresinol-4-*O*-*β*-D-glucoside, (+)-epipinoresinol 4-*O*-*β*-D-glucopyranoside, *O*-hydroxybenzoic acid, *p*-hydroxybenzoic acid, vanillic acid, *trans*-caffeic acid, hexacosyl (*E*)-ferulate, *trans*-syringin, and protocatechualdehyde dimer were isolated (Qu et al., 2016). Further investigation of the 70% EtOH extract of CMS resulted in the isolation of four new compounds, morineoliganosides A–C (**1–3**) and heterophyllol-1-*O*-*β*-D-glucopyranoside A (**4**) (Fig. 1), together with other 27 known ones (**5–31**) (Fig. 2). The structure elucidation and inhibitory effects on xanthine oxidase of these compounds is reported in this paper.

2. Results and discussion

The 70% EtOH extract of CMS was treated with solvent partition, chromatographic isolation, and chemical and spectral analysis. As the result, four new compounds (Fig. 1), morineoliganosides A (**1**), B (**2**), C (**3**) and heterophyllol-1-*O*-*β*-D-glucopyranoside A (**4**), together with 27 known ones (Fig. 2), 3-*O*-caffeoylquinic acid (5) (Olennikov et al., 2012), chlorogenic acid methyl ester (**6**) (Zhu et al., 2005), 4-*O*-caffeoylquinic acid (**7**) (Tatefuji et al., 1996), 1,5-di-*O*-caffeoylquinic acid (**8**) (Aboul Ela et al., 2012), 1,4-di-*O*-caffeoylquinic acid (**9**) (Aboul Ela et al., 2012), methyl 3,5-di-*O*-caffeoylquinate (**10**) (Zhang et al., 2000), 3,4-di-*O*-caffeoylquinic

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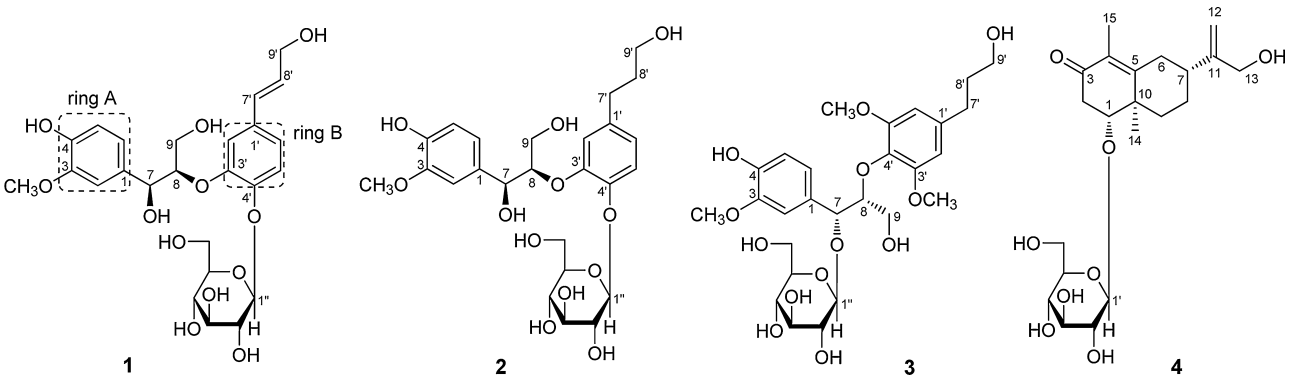
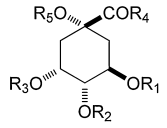
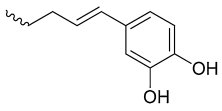


Fig. 1. Structures of new compounds (**1–4**) obtained from CMS.

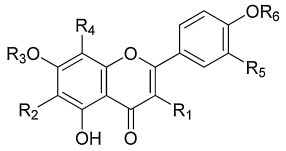


	R_1	R_2	R_3	R_4	R_5
5:	A	H	H	OH	H
6:	A	H	H	OCH_3	H
7:	H	A	H	OH	H
8:	A	H	H	OH	A
9:	H	A	H	OH	A
10:	A	H	A	OCH_3	H
11:	A	A	H	OH	H
12:	A	A	H	OCH_3	H

A:



Glc: β-D-glucopyranosyl; Rha: α-L-rhamnopyranosyl;
Glu: β-D-glucuronosyl; Xyl: β-D-xylopyranosyl;
Ara: α -L-arabinopyranosyl; B: 6-acetyl β-D-glucopyranosyl



	R_1	R_2	R_3	R_4	R_5	R_6
13:	H	H	H	H	OH	H
14:	H	H	Glu	H	OH	H
15:	H	H	Rha(1→6)Glc	H	OH	H
16:	H	H	H	H	H	CH_3
17:	H	H	Glc	H	H	CH_3
18:	H	H	B	H	H	CH_3
19:	H	H	Rha(1→6)Glc	H	H	CH_3
20:	H	H	H	H	OH	CH_3
21:	H	H	Glc	H	OH	CH_3
22:	H	OCH_3	CH_3	H	OCH_3	H
23:	OGlc(2→1)Glc	H	H	H	H	H
24:	OGlc(6→1)Rha	H	H	H	OH	H
25:	H	Ara	H	Glc	H	H
26:	H	Ara	H	Xyl	H	H
27:	H	Xyl	H	Ara	H	H
28:	H	Xyl	H	Xyl	H	H

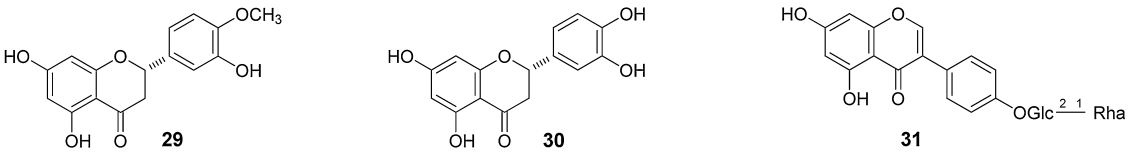


Fig. 2. Known compounds (**5–31**) obtained from CMS.

acid (**11**) (Choi et al., 2003), methyl 3,4-di-*O*-caffeoylquinate (**12**) (Basnet et al., 1996), luteolin (**13**) (Kim et al., 2004a, 2004b), luteolin-7-*O*-β-D-glucopyranoside (**14**) (Lee et al., 2002), luteolin-7-*O*-rutinoside (**15**) (Lamidi et al., 2006), acacetin (**16**) (Nawal and Atta, 2013), acacetin 7-*O*-β-D-glucopyranoside (**17**) (Zhang et al., 2010), acacetin 7-*O*-(6"-*O*-acetyl)-β-D-glucopyranoside (**18**) (Zhou et al., 2013), acacetin 7-*O*-rutinoside (**19**) (Park et al., 1995), diosmetin (**20**) (Peng, 2011), diosmetin-7-*O*-β-D-glucopyranoside (**21**) (Lee et al., 2012), cirsilineol (**22**) (Nagao et al., 2002), kaempferol-3-*O*-β-D-sophoroside (**23**) (Yoshizaki et al., 1987), rutin (**24**) (Li et al., 2008.), apigenin-6-*C*-α-L-arabinopyranosyl-8-*C*-β-D-glucopyranoside (**25**) (Xie et al., 2003), apigenin-6-*C*-α-L-arabinopyranosyl-8-*C*-β-D-xylopyranoside (**26**) (Xie et al., 2003), apigenin-6-*C*-β-D-xylopyranosyl-8-*C*-α-L-arabinopyranoside (**27**) (Xie et al., 2003), apigenin-6,8-di-*C*-β-D-xylopyranoside (**28**) (Liang, 2012), (2*S*)-hesperetin (**29**) (Chokchaisiri et al., 2009; Li, 2007), (2*S*)-eriodictyol (**30**) (Chokchaisiri et al., 2009; Huang et al., 2014), and sophorabioside (31) (Kim et al., 2004a, 2004b) were isolated and identified.

Morineoliganoside A (**1**) was obtained as a white powder with negative optical rotation ($[\alpha]_D^{25}$ −57.9° in MeOH). Its molecular formula was deduced to be $C_{25}H_{31}O_{12}$ on the basis of negative HRESI-TOF-MS at *m/z* 523.1821 $[M-H]^-$ (calcd for $C_{25}H_{31}O_{12}$, 523.1824) and NMR spectra (Table 1). The IR absorption bands in **1** suggested the presences of hydroxyl (3363 cm^{-1}), aromatic ring (1604, 1511, 1426 cm^{-1}) and *O*-glycoside bond (1072 cm^{-1}). Acid hydrolysis of **1** with 1 M HCl gave D-glucose, which was identified by HPLC analysis (Zhang et al., 2015). Its ^1H, ^{13}C NMR (Table 1) and ^1H ^1H COSY spectra displayed signals for two sets of ABX coupling phenyl [ring A: δ 6.70 (1H, d, J = 8.0 Hz, H-5), 6.80 (1H, br. d, *ca.* = 8J = 8 Hz, H-6), 7.00 (1H, br. s, H-2); ring B: 6.97 (1H, br. d, *ca.* = 8J = 8 Hz, H-6′), 6.98 (1H, d, J = 8.0 Hz, H-5′), 7.21 (1H, br. s, H-2′)];