Phytochemistry 101 (2014) 91–100

Contents lists available at ScienceDirect

Phytochemistry

journal homepage: www.elsevier.com/locate/phytochem

Monoterpene glycosides, phenylpropanoids, and acacetin glycosides from *Dracocephalum foetidum*

Erdenechimeg Selenge [a], Toshihiro Murata [a,*], Shiho Tanaka [a], Kenroh Sasaki [a], Javzan Batkhuu [b], Fumihiko Yoshizaki [a]

[a] Department of Pharmacognosy, Tohoku Pharmaceutical University, 4-1 Komatsushima 4-chome Aoba-ku, Sendai 981-8558, Japan
[b] School of Biology and Biotechnology, National University of Mongolia, PO Box 617, Ulaanbaatar 46A, Mongolia

ARTICLE INFO

Article history:
Received 23 August 2013
Received in revised form 15 November 2013
Available online 28 February 2014

Keywords:
Dracocephalum foetidum
Lamiaceae
Limonene glycoside
Phenylpropanoid
Hyaluronidase inhibitory activity
DPPH radical scavenging activity

ABSTRACT

Chemical investigation of the acetone extract from the aerial parts of the Mongolian medicinal plant *Dracocephalum foetidum* resulted in the isolation of three limonene glycosides, a caffeic acid trimer, four rosmarinic acid glucosides, and five acacetin acyl glycosides, together with 13 known natural products. The chemical structures of all of the compounds were determined by spectroscopic analyses. Among these compounds three showed hyaluronidase inhibitory activity. In addition, one other compound showed stronger 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity than the positive control Trolox, whereas three other compounds demonstrated a similar activity to that of Trolox.

Introduction

The genus *Dracocephalum*, belonging to the Lamiaceae family, is characterized as containing perennial herbs with purple flowers that are widely distributed in Northeast Asia, including Japan, Korea, China, and Mongolia. There are 17 species of *Dracocephalum* in Mongolia (Ligaa, 2005). Recently, attention has been paid to *Dracocephalum* species and their chemical constituents because of their diverse biological effects, such as antioxidant, anti-inflammatory, antihypoxic, and immunomodulatory activities. The plants of this genus typically contain terpenoids and flavonoids (Zeng et al., 2010). A recent study investigated *Dracocephalum* species, namely are of *D. ruyschiana* and various chemical constituents were reported (Selenge et al., 2013a).

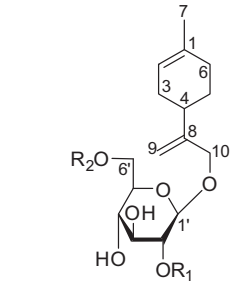
Dracocephalum foetidum Bunge is an herbaceous plant that grows on the Mongolian steppes. It has been used for treatment of various inflammatory conditions, such as oral cavity diseases, rheumatic edema, and wounds. In addition, leaves and flowers of *D. foetidum* are used as a traditional medicine among Mongolian nomads to wash their faces and hands to prevent bacterial and fungal infections (Shatar and Altantsetseg, 2000). Flowers of the plant are also used to treat fever and suppurative diseases (Batkhuu et al., 2005). There have been few studies on *D. foetidum*, and the only report on the chemical constituents of *D. foetidum* focused on the essential oil components that are effective against bacteria (Lee et al., 2007). Therefore, it is important to study the specific chemical characteristics and physiological roles of the constituents of *D. foetidum*.

Hyaluronidase has been recognized as a modulator in numerous physiological and pathological processes, such as inflammation and allergies (Girish and Kemparaju, 2007; Kakegawa et al., 1992). Some anti-allergenic drugs have antioxidant actions due to scavenging superoxide radicals or to inhibition of superoxide production (Yoshikawa et al., 1989). Therefore, it is important to identify hyaluronidase inhibitors and antioxidants from natural resources for medicinal use to prevent and treat various inflammatory conditions.

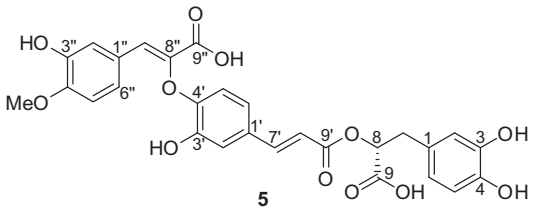
Taking into consideration all of these aspects, the present study was undertaken to evaluate hyaluronidase inhibitory effects and the antioxidant activity of compounds isolated from *D. foetidum*. Herein, isolation of three limonene glycosides (**1–3**), a caffeic acid trimer (**5**), four rosmarinic acid glucosides (**8–10**, **12**), and five acacetin acyl glycosides (**13–17**), along with 13 known compounds (**4**, **6–7**, **11**, **18–26**) from *D. foetidum* (Fig. 1) are described. Hyaluronidase inhibitory and antioxidative activities of all fractions and isolated compounds were evaluated *in vitro*.

* Corresponding author. Tel./fax: +81 22 727 0220.
E-mail address: murata-t@tohoku-pharm.ac.jp (T. Murata).

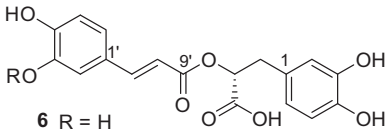
http://dx.doi.org/10.1016/j.phytochem.2014.02.007
0031-9422/



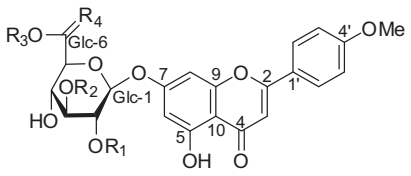
1 R_1 = 6-malonyl-β-D-glucopyranosyl, R_2 = malonyl
2 R_1 = β-D-glucopyranosyl, R_2 = malonyl
3 R_1 = 6-malonyl-β-D-glucopyranosyl, R_2 = H
4 R_1 = H, R_2 = H



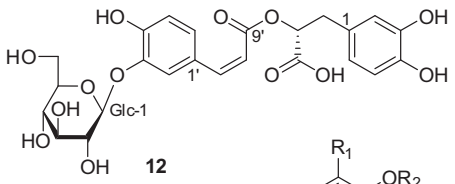
5



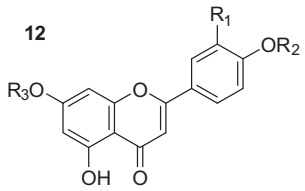
6 R = H
7 R = Me
8 R = 6-malonyl-β-D-glucopyranosyl
9 R = 6-feruloyl-β-D-glucopyranosyl
10 R = 6-synapoyl-β-D-glucopyranosyl
11 R = β-D-glucopyranosyl



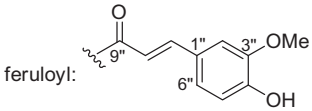
13 R_1 = H, R_2 = malonyl, R_3 = H, R_4 = H_2
14 R_1 = H, R_2 = malonyl, R_3 = malonyl, R_4 = H_2
15 R_1 = acetyl, R_2 = H, R_3 = H, R_4 = O
16 R_1 = malonyl, R_2 = H, R_3 = H, R_4 = O
17 R_1 = H, R_2 = malonyl, R_3 = H, R_4 = O
18 R_1 = H, R_2 = H, R_3 = H, R_4 = H_2
19 R_1 = H, R_2 = H, R_3 = malonyl, R_4 = H_2
20 R_1 = H, R_2 = H, R_3 = α-L-rhamnopyranosyl, R_4 = H_2
21 R_1 = H, R_2 = H, R_3 = H, R_4 = O

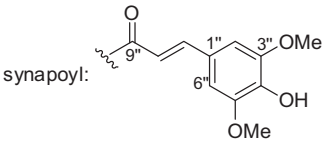


12



22 R_1 = H, R_2 = H, R_3 = 6-malonyl-β-D-glucopyranosyl
23 R_1 = H, R_2 = H, R_3 = β-D-glucuronopyranosyl
24 R_1 = OH, R_2 = H, R_3 = β-D-glucuronopyranosyl
25 R_1 = OH, R_2 = Me, R_3 = β-D-glucuronopyranosyl
26 R_1 = H, R_2 = H, R_3 = H





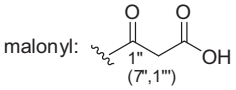


Fig. 1. Structures of **1**–**26**.

Results and discussion

Aerial parts of *D. foetidum*, including flowers, were extracted with acetone–H_2O (8:2), and the extract was partitioned between H_2O and diethyl ether. The H_2O fraction was then subjected to various chromatographic purification procedures to obtain four limonene glycosides (**1–4**), eight rosmarinic acid derivatives (**5–12**), and 14 flavones (**13–26**). (Fig. 1).

The present study identified the following known compounds by comparison of their spectroscopic data with those reported in the literature: limonene-10-ol 10-*O*-*β*-D-glucopyranoside (**4**) (Saeidnia et al., 2004), rosmarinic acid (**6**) (Dapkevicius et al., 2002), 3′-*O*-methyl-rosmarinic acid (**7**) (Murata et al., 2012), rosmarinic acid-3-*O*-β-D-glucopyranoside (**11**) (Tezuka et al., 1998), acacetin-7-*O*-β-D-glucopyranoside (**18**) (Li et al., 2008), acacetin-7-*O*-(6″-malonyl)-β-D-glucopyranoside (**19**) (Sugawara and Igarashi, 2009), acacetin-7-*O*-α-L-rhamnopyranosyl-(1–6)-β-D-glucopyranoside (**20**) (Piao et al., 2003), acacetin-7-*O*-β-D-glucuronide (**21**) (Kartnig et al., 1993; Lee et al., 2002), apigenin-7-*O*-(6″-malonyl)-β-D-glucopyranoside (**22**) (Svehlikova et al., 2004), apigenin-7-*O*-β-D-glucuronide (**23**) (Flamini et al., 2001; Vanhoenacker et al., 2002), luteolin-7-*O*-β-D-glucuronide (**24**) (Vanhoenacker et al., 2002), diosmetin-7-*O*-β-D-glucuronide (**25**) (Murata et al., 2010a), and apigenin (**26**) (Ha et al., 2012), respectively. These known compounds were isolated from *D. foetidum* for the first time. Limonene glycosides, a number of flavones and their glycosides, and rosmarinic acid have already been isolated from various species of *Dracocephalum* (Zeng et al., 2010).

Limonene glycosides **1–3** were isolated as colorless gums; ^{1}H- and ^{13}C-NMR spectroscopic data (measured in CD_3OD at 30 °C) are shown in Table 1. The NMR resonances of **1–3** were similar to compound **4** and limonene-10-ol 10-*O*-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside (Saeidnia et al., 2004).

Compound **1** was deduced to have the molecular formula $C_{28}H_{40}O_{17}$ based on HRFABMS (*m*/*z* 671.2162, calcd for $C_{28}H_{40}O_{17}Na$, 671.2162). Its molecular formula had an additional $C_6H_4O_6$ compared to limonene-10-ol 10-*O*-β-D-glucopyranosyl-(1→2)-β-D-glucopyranoside. It was considered that this $C_6H_4O_6$ corresponded