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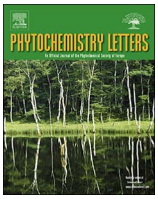

New lignan glycosides from the root barks of *Litsea glutinosa*

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ABSTRACT

An investigation on the chemical constituents in the root barks of *Litsea glutinosa* was performed for the first time. Three new lignan glycosides named Litseasins A–C (**1–3**), together with a known one (**4**), were obtained. The structures of the new compounds were established through extensive spectroscopic analyses including HR-ESI–MS, NMR, and circlar dichroism (CD). The new compounds were evaluated for their anti-inflammatory activities on lipopolysaccharide (LPS)-induce nitric oxide (NO) production in RAW264.7 murine macrophage cells. However, these compounds showed no inhibition on LPS-induced NO productions.

1. Introduction

Secondary metabolites obtained from genus *Litsea* were well documented mainly as alkaloids, lignans, flavonoids, and essential oils (Su and Ho, 2016; Wang et al., 2016). Some of them with diverse skeletons displaying potential therapeutics have attracted considerable attention from medicinal chemists and pharmacologists in recent years (Agrawal et al., 2011). *Litsea glutinosa* (Lour.) C. B. Rob., belonging to family Lauraceae, is widely distributed in subtropical and tropical regions. In China, this plant has been used as traditional medicine for treatment of many diseases mainly including diabetes, inflammation (Kong et al., 2015). Previous chemical investigations on this plant species have led to the isolation of lignans, alkaloids (Das et al., 2013). However, all previously obtained chemical constituents were from its aerial parts without any from the root barks. In present study, we investigated the chemical constituents in its root barks for the first time. Three new lignan glycosides named Litseasins A-C **(1–3)**, together with the known one, (7*R*,8*S*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9-triol 9-β-D-xylopyranoside (**4**), were isolated. Furthermore, their anti-inflammatory activities on lipopolysaccharide (LPS)-induce nitric oxide (NO) production in RAW264.7 were evaluated. However, the none of them displayed inhibition on LPS-induced NO production. This paper mainly deals with the isolation, structural characterization of the new compounds.

2. Results and discussions

Compound **1** was obtained as amorphous gum. Its molecular formula was determined to be $C_{26}H_{34}O_{11}$ by the HR-ESI–MS (*m/z* 545.2066). The ^{1}H NMR spectrum displayed signals including two benzene rings at δ_{H} 6.76 (1H, s, H-6′), 6.71 (1H, s, H-2′), 6.66 (2H, s, H-2, 6); two methines at δ_{H} 5.46 (1H, d, *J* = 6.0 Hz, H-7), 3.57 (1H, m, H-8); four methylenes at δ_{H} 3.99 (1H, dd, *J* = 12.0, 4.8 Hz, H-9a), 3.64 (1H, dd, *J* = 12.0, 1.2 Hz, H-9b), 3.41 (2H, m, H-9′), 2.54 (2H, t, *J* = 7.2 Hz, H-7′), 1.67 (2H, m, H-8′); three methoxyls at δ_{H} 3.79 (3H, s, 3′-OCH_3), 3.73 (6H, s, 3, 5-OCH_3); an anomeric proton at δ_{H} 4.23 (1H, d, *J* = 7.2 Hz, H-1″). The ^{13}C NMR spectrum confirmed the presence of two benzene rings at δ_{C} 131.8 (C-1), 104.0 (C-2, 6), 148.3 (C-3, 5), 135.7 (C-4), 135.7 (C-1′), 113.2 (C-2′), 145.9 (C-3′), 143.8 (C-4′), 128.8 (C-5′), 117.2 (C-6′); four methylenes at δ_{C} 71.0 (C-9), 60.6 (C-9′), 32.0 (C-7′), 35.1 (C-8′); two methines at δ_{C} 87.4 (C-7), 51.5 (C-8); three methoxyl groups at δ_{C} 56.5 (3, 5-OCH_3), 56.2 (3′-OCH_3). Additionally, the ^{13}C NMR spectroscopic data at δ_{C} 104.3 (C-1″), 77.1 (C-3″), 73.8 (C-2″), 70.0 (C-4″), 66.2 (C-5″) showed the presence of a xylopyranose as shown in Fig. 1. The coupling constant (*J* = 7.2 Hz) of the anomeric proton of the xylopyranose group suggested that it was a β-form. Acid hydrolysis of **1** yielded d-xylose, which was identified by Co-TLC with an authentic sample. These data suggested **1** contained a benzofuran neolignan skeleton and its NMR spectroscopic data were almost identical to those of (7*R*,8*S*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9-triol 9-β-D-xylopyranoside, which was further confirmed by its ^{1}H-^{1}H COSY and HMBC correlations as depicted in Fig. 1. Thus, **1** was considered to be an enantiomer of (7*R*,8*S*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9-triol 9-β-D-xylopyranoside. The CD spectrum of **1** showed a negative Cotton curve at 214 nm and a positive Cotton curve at 235 nm revealed its absolute configuration to be 7*S*,8*R* (Suh et al., 2015). Therefore, **1** was determined to be (7*S*,8*R*)-3,3′,5-trimethoxy-4′,7-epoxy-8,5′-neolignan-4,9,9-triol 9-β-D-xylopyranoside,

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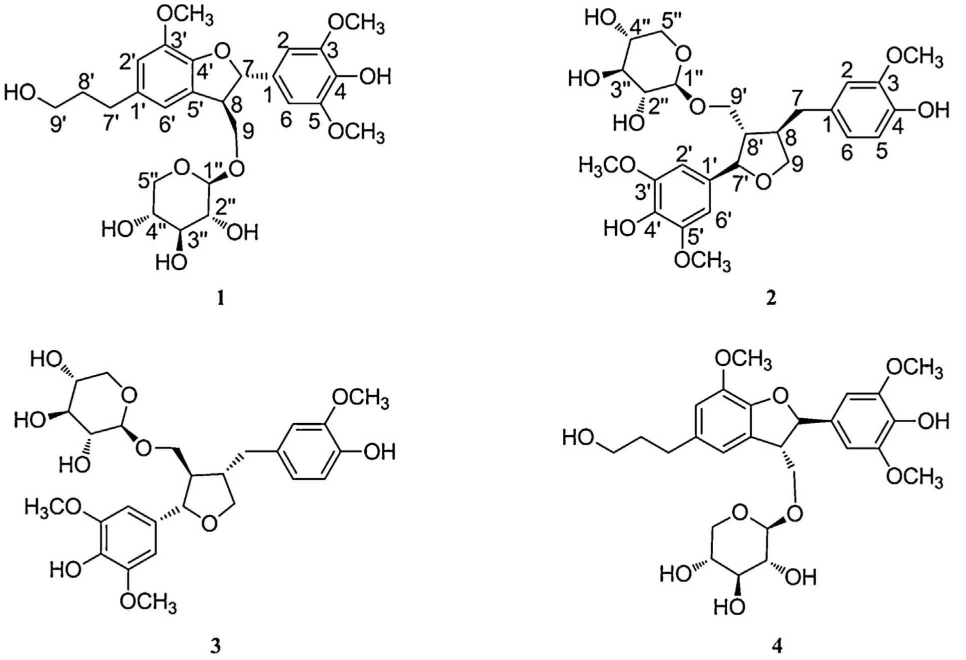

Fig. 1. Chemical structures of compounds **1**–**4**.

and named Litseasin A.

Litseasin B was obtained as a colorless powder. The molecular formula was established to be $C_{26}H_{34}O_{11}$ by HRESIMS indicating 10 ° of unsaturation. The ^{1}H NMR spectrum of **2** showed proton signals of a 1,3,4,5-tetrasubstituted aromatic ring at δ_H 6.56 (2H, s, H-2′, 6′); a 1,3,5-trisubstituted aromatic ring at δ_H 6.77 (1H, d, J = 2.4 Hz, H-2), 6.67 (1H, d, J = 8.4 Hz, H-5), 6.60 (1H, dd, J = 8.4, 2.4 Hz, H-6); two oxymethylene groups at δ_H 3.86 (1H, td, J = 8.4 Hz, H-9a), 3.54 (1H, td, J = 8.4 Hz, H-9b), 3.98 (1H, dd, J = 10.8, 8.4 Hz, H-9′a), 3.48 (1H, dd, J = 10.8, 6.0 Hz, H-9′b), 2.83 (1H, t, 12.0 Hz, H-7a), 2.41 (1H, dd, J = 12.0, 6.0 Hz, H-7b); three methines at δ_H 4.70 (1H, d, J = 6.6 Hz, H-7′), 2.61 (1H, m, H-8), 2.33 (1H, m, H-8′), an anomeric proton at δ_H 4.17 (1H, d, J = 7.2 Hz, H-1″). In the ^{13}C NMR spectrum, carbon signals observed were attributed to two aromatic rings at δ_C 133.8 (C-1′), 103.7 (C-2′, 6′), 148.1 (C-3′, 5′), 135.0 (C-4′), 132.1 (C-1), 113.2 (C-2), 147.8 (C-3), 144.9 (C-4), 121.1 (C-5), 116.7 (C-6); three methylenes at δ_C 67.1 (C-9′), 72.0 (C-9), 32.8 (C-7); and three methines at δ_C 82.3 (C-7′), 50.3 (C-8′), 42.4 (C-8). These spectroscopic data were characteristic of a 9–7′ mono-epoxy type lignan (Su et al., 1999) as shown in Fig. 1. Additionally, the ^{13}C NMR showed signal pattern of an d-xylose at δ_C 104.3 (C-1″), 77.1 (C-3″), 73.8 (C-2″), 70.0 (C-4″), 66.2 (C-5″). In the HMBC experiment, correlations from H-1″ (δ_H 4.17) to C-9′ (δ_C 67.1) indicated the links between the d-xylose and the aglycone. The connections of three methoxyl groups at C-3′, C-5′, and C-3 to the

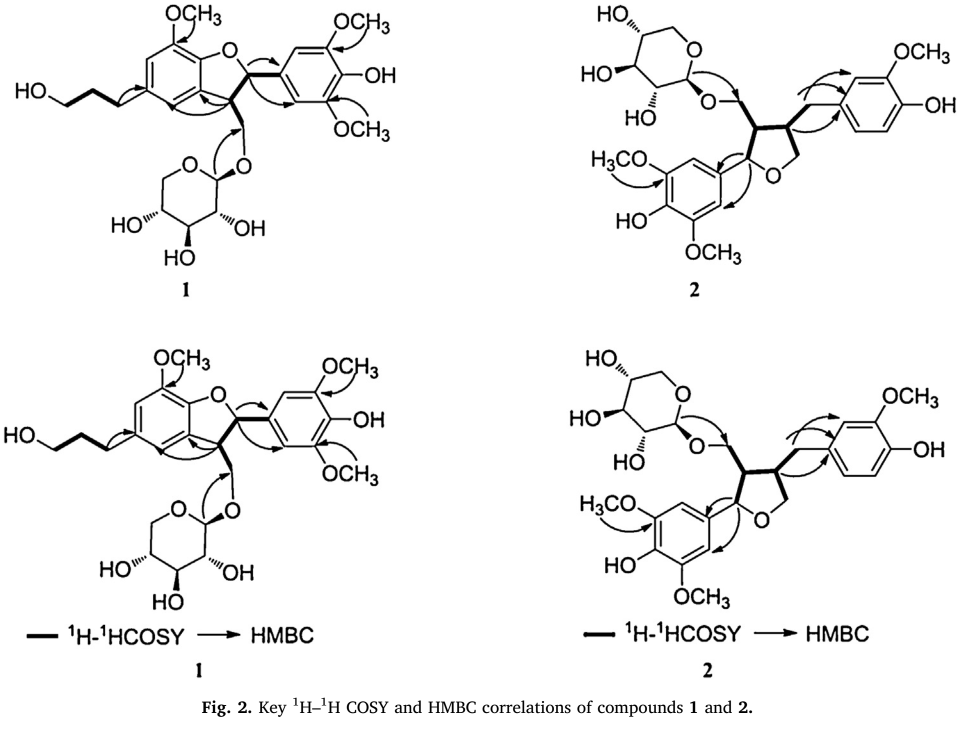

Fig. 2. Key ^{1}H–^{1}H COSY and HMBC correlations of compounds **1** and **2**.