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Chemical constituents from the roots of *Elephantopus scaber* L.

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ABSTRACT

A chemical investigation of the roots of *Elephantopus scaber* L. led to the isolation of thirteen compounds, including four sesquiterpenoids (**5**, **6**, **7**, **8**), two phenols (**1**, **2**), three triterpenoids (**9**, **10**, **11**), two caffeoylquinic acids (**3**, **4**), one alkaloid (**12**), and one sterol (**13**). Among these molecules, compound **2** (2-butenoic acid, 3-methyl-[4-(1,5-dimethyl-4-hexenyl)-3-hydroxyphenyl] methyl ester) was identified for the first time from this species, while compounds **1** (curcuphenol) and **12** (patriscabratine) were isolated for the first time from the genus *Elephantopus*.

1. Subject and source

The genus *Elephantopus* (Asteraceae) is widely distributed in America and partly in Africa, Asia, and Oceania. Two species are grown in China, *Elephantopus scaber* L. and *Elephantopus mollis* (Wang et al., 2013). *E. scaber* is used as folk medicine for treating the common cold, pertussis, and inflammation in South China (Mohan et al., 2010), and *E. mollis* is a common medicine in Hong Kong and Taiwan (Li et al., 2013). The *E. scaber* L. plant is known as “Didancao” in Chinese medicine. Material was collected at Zhanjiang, Guangdong Province, China, in August 2012. A voucher specimen (ES-20120308) was identified by Dr. Chunyan Han from the Kunming Institute of Botany and deposited at the Small Molecular Repository Center, School of Pharmaceutical Sciences, SunYat-sen University.

2. Previous work

The genus *Elephantopus* is characterized by the occurrence of sesquiterpene lactones, such as elephantin and elephantopin from *E. scaber* L. (Govindachari et al., 1970) and molephantinin and phantomolin from *E. mollis* (Lee, 2010). Previous phytochemical investigations on *Elephantopus* have also resulted in the isolation of flavonoids (Wang et al., 2013), triterpenoids (Liang et al., 2007), caffeic acids (Fumihiro et al., 2005), and sterols (Zhao et al., 2000). Among these compounds, sesquiterpene lactone is regarded as a chemotaxonomic marker for the genus *Elephantopus* (Mei et al., 2012).

3. Present study

Dried and powdered roots of *E. scaber* L. (3.2 kg) were extracted with 95% EtOH (32 L) at room temperature for 3 × 48 h. The 95% EtOH extract was evaporated under reduced pressure to yield a dark brown residue (105 g). The residue was then

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suspended in water (500 mL) and partitioned successively with EtOAc (4 × 500 mL) and *n*-BuOH (4 × 500 mL) to afford an EtOAc fraction (49 g) and a *n*-BuOH fraction (21 g). The EtOAc-soluble fraction (49 g) was chromatographed on a silica gel column (200–300 mesh), eluting with petroleum ether (PE)-EtOAc (100:0, 95:5, 9:1, 4:1, 3:2, 1:1, 0:1) to give ten fractions (Fr. 1-Fr. 10). Fr. 3 (7.9 g) was subjected to silica gel column chromatography (CC), eluting with PE-EtOAc (95:5, 70:30) to yield six subfractions (Fr. 3.1-Fr. 3.6). Fr. 3.1 was further subjected to silica gel CC, eluting with PE-EtOAc (50:1) to afford compound **11** (200 mg). Fr. 3.2 was recrystallized using CH_2Cl_2–MeOH mixtures to give compound **13** (80 mg). Fr. 3.4 and Fr. 3.5 were chromatographed on two silica gel columns with PE-CH_2Cl_2 (70:30) and PE-EtOAc successively (9:1) to yield compounds **1** (27 mg), **2** (8 mg), and **9** (30 mg). Fr. 3.6 was recrystallized using CH_2Cl_2–MeOH mixtures to afford compound **10** (12 mg). Fr. 7 was chromatographed on a MCI gel column, eluting with a CH_3OH–H_2O gradient of increasing polarity, and then further purified using semi-preparative HPLC (ODS, MeOH–H_2O, 70:30) to yield compounds **5** (30 mg), **6** (35 mg), **7** (4 mg), **8** (22 mg), and **12** (18 mg). Fr. 9 was separated using MCI gel CC, eluting with CH_3OH–H_2O (20:80, 40:60, 50:50, 60:40, 80:20, 90:10) to give five subfractions (Fr. 9.1-Fr. 9.5). Fr. 9.3 was purified via semi-preparative RP-HPLC using a mobile phase of MeOH–H_2O (72:28) to give compounds **3** (8 mg) and **4** (13 mg).

The known compounds (Fig. 1) were identified as curcuphenol (**1**) (Joseph-Nathan et al., 1988), 2-butenoic acid, 3-methyl-[4-(1,5-dimethyl-4-hexenyl)-3-hydroxyphenyl] methyl ester (**2**) (Bohlmann and Zdero, 1976), methyl 3,5-di-*O*-caffeoyl quinate (**3**) (Sang et al., 2003), 3,4-di-*O*-caffeoylquinic acid methyl ester (**4**) (Fumihiro et al., 2005), isodeoxyelephantopin (**5**) (Liang et al., 2008), isoscabertopin (**6**) (Than et al., 2005), scabertopin (**7**) (Than et al., 2005), deoxyelephantopin (**8**) (Than et al., 2005), lupeol (**9**) (Jean et al., 2006), lupeol acetate (**10**) (Stefano and Pitonzo, 2012), ursa-12-en-3β-heptadecanoate (**11**) (Liang et al., 2007), patriscabratine (**12**) (Li et al., 2011), and β-sitosterol (**13**) (Zhao et al., 2000), by spectroscopic analyses and comparisons of the obtained data with literature values.

4. Chemotaxonomic significance

The genus *Elephantopus* is known to be an abundant source of sesquiterpene lactones (Mei et al., 2012), which are considered as taxonomic markers of the family Asteraceae. Sesquiterpene lactones exhibit many biological activities and

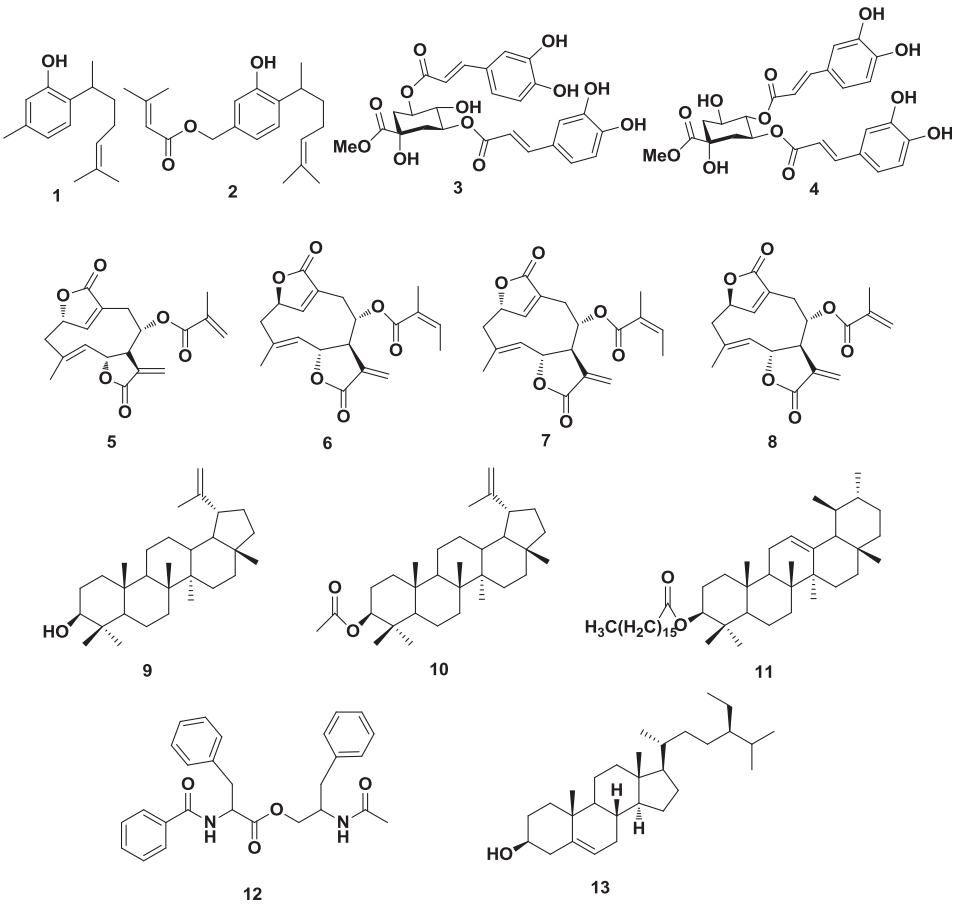

Fig. 1. Chemical structures of compounds **1**–**13** from *Elephantopus scaber*.

possess commercial as well as ecological value (Seaman, 1982; Zdero and Bohlmann, 1990). In this study, four sesquiterpene lactones (**5**–**8**), two phenols (**1**–**2**), three triterpenoids (**9**–**11**), two caffeoylquinic acids (**3**–**4**), one dipeptide (**12**), and one steroid (**13**) were separated from the roots of *E. scaber* L. Compounds **5**–**8** [isodeoxy-elephantopin (**5**), isoscabertopin (**6**), scabertopin (**7**), deoxyelephantopin (**8**)] are germacranolide-type sesquiterpenoids, which further confirmed that this plant biogenetically belongs to the Asteraceae family. This report is the first to identify curcuphenol (**1**) from the genus *Elephantopus*. Although compound **2** has been previously isolated from *E. mollis* (Bohlmann and Zdero, 1976), this paper is the first to extract it from *E. scaber*. Curcuphenol (**1**) has previously been isolated from the marine sponge *Didiscus flavus* (Wright et al., 1987) and from the terrestrial plant *Lasianthaea podocephala* (Ghisalberti et al., 1979). Compounds **1** and **2** have the same sesquiterpene phenol scaffold, suggesting that this scaffold type might be a useful chemotaxonomic marker for *E. scaber* and *E. mollis*. However, their presence in other species of *Elephantous* must be evaluated. Compound **12**, a rare dipeptide containing the phenylalanine moiety, was characterized for the first time from the genus *Elephantopus*. Compounds **1**, **2**, **3**, **4**, **9**, **10**, and **13** were isolated from *E. scaber* and *E. mollis*. Twelve compounds were also identified from the PE-soluble extract of *E. scaber* and *E. mollis* using a GC–MS (Wang et al., 2012). *E. scaber* is closely related to *E. mollis* by DNA fingerprinting analyses (Cao and Bi, 1999). These results may illustrate why these two species are mainly distributed in South China.

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