



## Abietane diterpenes from *Hyptis carvalhoi* Harley

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### 1. Subject and source

Aerial parts of *Hyptis carvalhoi* Harley were collected in Jacobina County (Bahia State, northeast of Brazil). Voucher specimens (#95146/95112) were deposited at the Herbário Alexandre Leal Costa (ALCB), Universidade Federal da Bahia, Bahia, Brazil, and identified by M.Sc. Maria Lenise Silva Guedes, from the Instituto de Biologia, Departamento de Botânica, Universidade Federal da Bahia, Bahia, Brazil.

### 2. Previous work

*Hyptis* is the largest genus of the neotropical sub-tribe Hyptidinae [(Lamiaceae) tribe Ocimeae] with over 300 species (Raymond and Harley, 1988). Many of its reported species are known for their medicinal use as indigenous drugs (Kuhnt et al., 1994; Almtorp et al., 1991; Raja Rao et al., 1990), however a literature survey revealed that phytochemical analysis of plants belonging to this genus has been limited to a few species. Previous chemical reports include the isolation of a range of triterpenes (Lee et al., 1988; Yamagishi et al., 1998; Almtorp et al., 1991; Deng et al., 2009; Pereda-Miranda and Delgado, 1990; Pereda-Miranda and Gascon-Figueroa, 1988; Mukherjee et al., 1984), flavonoids (Almtorp et al., 1991; Deng et al., 2009; Takahiko et al., 2006; Lin et al., 1993; Romo de Vivar et al., 1991; Pereda-Miranda and Delgado, 1990; Messana et al., 1990) lignans (Indane and Chaturvedi, 2007), lactones (Romo de Vivar et al., 1991; Pereda-Miranda and Delgado, 1990; Deng et al., 2009; Fragoso-Serrano et al., 1999; Boalino et al., 2003) and diterpenes, especially of the labdane and abietane-type (Bakir et al., 2006; Lin et al., 1993; Chukwujekwu et al., 2005; Araujo et al., 2004, 2005, 2006; Porter Roy et al., 2009; Urones et al., 1998). *H. carvalhoi* is a subshrub growing to 1 m high, endemic to Bahia that grows in the cerrado region of Central Brazil, and no phytochemical investigation on this species has so far been reported.

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### 3. Present study

Ground dried aerial parts of *H. carvalhoi* (1.54 kg) were extracted with ethanol at room temperature (3 × 6 l). Evaporation of the solvent under vacuum yielded the ethanol extract (170.0 g).

Part of the EtOH extract (67.0 g) was redissolved in a mixture of MeOH:H<sub>2</sub>O (1:1 v/v) and filtrated to removal of chlorophyll. Evaporation of the mother liquor yielded a brown viscous residue. The residue (13.0 g) was further purified by flash chromatography after elution with mixtures of hexane, CH<sub>2</sub>Cl<sub>2</sub> and MeOH to give thirty sub-fractions. Flash chromatography of sub-fraction F-2 (0.32 g) using the solvents CHCl<sub>3</sub> and MeOH as binary mixtures of increasing polarity afforded 65 fractions (5 ml each) that were pooled together to 5 fractions, after TLC comparison. The sub-fraction F-2 (5) was further purified by HPLC using a mixture of hexane/EtOAc (75/25 v/v) as eluent with flow rate of 3.0 ml/min to yield 7 $\alpha$ -ethoxyrosmanol (14.0 mg), 7 $\alpha$ -methoxyrosmanol (32.0 mg) and galdosol (11.0 mg). The sub-fraction F-3 (260.0 mg) yielded small crystals, which were collected by removal of the supernatant liquid and recrystallized from CHCl<sub>3</sub> yielding *epi*-isosrosmanol (34.0 mg). Sub-fraction F-4 (352.0 mg) was submitted to semi-preparative HPLC using a mixture of hexane:EtOAc (6:4) as eluent and flow rate 3.0 ml/min, to obtain both rosmanol (15.0 mg) and 7 $\beta$ -methoxyrosmanol (7.0 mg).

### 4. Chemotaxonomic significance

Abietane-type diterpenoids, and their rearranged carbon skeletons covering a wide range of different structures, are natural products well distributed in the Lamiaceae family, particularly in the genera *Hyptis* (Araujo et al., 2004, 2005, 2006; Porter Roy et al., 2009; Urones et al., 1998; Chukwujekwu et al., 2005) *Lycopus* (Radulovic et al., 2010), *Clerodendrum* (Maschumi et al., 2010; Ali et al., 2010), *Plectranthus* (Alabashi and Melzig, 2010), *Sphacele* (Areche et al., 2009); *Salvia* (Kolak et al., 2009), *Isodon* (Lee et al., 2008), *Fuerstia* (Koch et al., 2006), *Schnabelia* (Dou et al., 2003) and *Aegiphila* (Costa-Lotufo et al., 2004).

In *Hyptis*, this class of diterpenes is well represented in the species *Hyptis martiusii*, *Hyptis rhomboides*, *Hyptis platanifolia*, *Hyptis suaveolens* and *Hyptis dilatata* as highly oxygenated compounds containing the C-ring saturated, unsaturated, aromatic, and as *ortho* or *para*-naphthoquinones. The chemical investigation of *H. carvalhoi* yielded abietane diterpenes with an aromatic C-ring, and agrees with the distribution pattern of these compounds in the Lamiaceae. Rosmanol, and 7 $\alpha$  and 7 $\beta$ -methoxyrosmanol were reported to *H. dilatata* (Urones et al., 1998) and *H. martiusii* (Araujo et al., 2005). On the other hand, the 7 $\alpha$ -ethoxyrosmanol, galdosol and *epi*-isosrosmanol have their occurrence reported to the Lamiaceae family only to species of the genera *Rosmarinus* and *Salvia* (González et al., 1989; Urones et al., 1998; Marrero et al., 2002). Thus, this is the first report of the presence of the later compounds in *Hyptis*, what is in agreement with the abietane diterpenes as chemomarkers for the Lamiaceae family, particularly to that genus.

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