



Coumarins isolated from *Esenbeckia alata* (Rutaceae)



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1. Subject and source

The leaves, bark and wood of *Esenbeckia alata* (Karst & Triana) Tr. & Pl were collected in February of 2001 about 400 m above sea level on Cerro Vigía, Colosó, Sucre, Colombia (9° 31' 51" N, 75° 21' 12" W) during ethnobotanical field work. The species is an endangered bush that grows in tropical dry forest habitats, is known locally as "loro" ("parrot") and is used as a febrifuge and insecticide. Individuals are located very close to each other and have a very limited distribution. A voucher sample of this collection, identified by one of us (OG-B), was deposited in the National Herbarium of Colombia and coded as COL 481090.

2. Previous work

The genus *Esenbeckia* (viewed in the Englerian system as a member of the tribe Cusparieae, but closely related to *Metrodorea*, *Heliotta* and *Balfourodendron* in the "RTF" clade from Rutoideae, Toddaloideae and *Flindersia*, Groppo et al., 2008; Kubitzki et al., 2011; Groppo et al., 2012) comprises 29–30 species centred mainly in Mexico and south-eastern Brazil. At least two thirds of these have been studied chemically to varying degrees, leading to the isolation of the characteristic Rutaceous quinolone and acridone alkaloids, coumarins, limonoids and, more rarely, indole and indolopyridoquinazoline alkaloids, plus relatively common phenylpropanoids, lignoids, flavonoids, other mixed-biogenesis compounds, polyprenols and terpenoids (Vitagliano and Comin, 1970a,b; Dreyer et al., 1972; Sharma et al., 1978; Dreyer, 1980; Bévalot et al., 1984; Delle Monache et al., 1989, 1990a, b; Nakatsu et al., 1990; Rios and Delgado, 1992a,b; Guilhon et al., 1994; Oliveira et al., 1996; Mata et al., 1998; Cano et al., 2000; Torres, 2001; Rios et al., 2002a,b; Rios and Delgado, 2002; Rios and Aguilar-Guadarrama, 2002; García Beltrán and Cuca Suárez, 2003; Aguilar-Guadarrama and Rios, 2004; Barros-Filho et al., 2004; de Oliveira et al., 2004;

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Napolitano et al., 2004; Trani et al., 2004; Anaya et al., 2005; de Oliveira et al., 2005; García-Beltrán and Cuca-Suárez, 2005; Nunes et al., 2005; Simpson and Jacobs, 2005; Barros-Filho et al., 2007; Cuca Suárez and Coy Barrera, 2007; Dolabela et al., 2008; Coy Barrera, 2009; Januário et al., 2009; Cardoso-Lopes et al., 2010; Cuca-Suárez et al., 2011).

In the coumarin domain, early biogenetic precursors of the widespread furocoumarins are umbelliferone (from *Esenbeckia grandiflora*, Januário et al., 2009) and its methoxy derivative scopoletin (from *Esenbeckia pentaphylla*, Simpson and Jacobs, 2005), and the dimethylallyloxy- and geranyloxy derivatives daphnetin 7-methyl-8-(3,3-dimethylallyl) ether (from *E. grandiflora*, de Oliveira et al., 2005). Auraptin (from *Esenbeckia conspecta*, Rios et al., 2002b; from *Esenbeckia febrifuga*, Napolitano et al., 2004) appears oxygenated on the geranyl moiety as anisocoumarin H and also an unnamed isomer (in *E. grandiflora*, Trani et al., 1997). The cyclized analog rutaretin 9-methyl ether (from *Esenbeckia litoralis*, Rios et al., 2002b) represents a further step toward the biogenesis of the furocoumarins. The linear chalepin and the angular 3-(1',1'-dimethylallyl)columbianetin (from *E. grandiflora*, Oliveira et al., 1996) bear the same unusual decoration at C3 of the coumarin scaffold.

Nearly all the *Esenbeckia* furocoumarins isolated to date are linear: bergapten (from *Esenbeckia berlandieri* and *E. litoralis*, Dreyer, 1980; from *Esenbeckia ovata*, Rios and Delgado, 2002; from *E. febrifuga*, Dolabela et al., 2008), xanthotoxin (from *E. ovata*, Rios and Delgado, 2002; from *E. litoralis*, Rios et al., 2002b; from *E. grandiflora*, Trani et al., 2004), isopimpinellin (from *E. litoralis*, Dreyer, 1980; from *Esenbeckia almawillia*, Guilhon et al., 1994; from *E. ovata*, Rios and Delgado, 2002; from *E. grandiflora*, Trani et al., 2004; from *E. febrifuga*, Dolabela et al., 2008) 8-hydroxybergapten (from *E. litoralis*, Dreyer, 1980) its *O*-geranyl derivative phellopterin (from *E. litoralis*, Dreyer, 1980; from *E. ovata*, Rios and Delgado, 2002a, 2002b; from *E. conspecta*); imperatorin (from *E. litoralis*, Dreyer, 1980; from *Esenbeckia yaaxhokob* = *E. berlandieri*, Mata et al., 1998; from *E. pentaphylla*, Simpson and Jacobs, 2005) and its hydroxylated analog swietenocoumarin B (from *E. grandiflora*, de Oliveira et al., 2005), alloimperatorin, (from *E. litoralis*, Dreyer, 1980); the unusually substituted 3,8-dimethoxyfuro[3,2-*g*]coumarin (from *E. grandiflora*, Nunes et al., 2005) and the *C*-acylated furocoumarin 5-seneciolyxanthotoxin (from *E. grandiflora*, Trani et al., 2004). The only angular furocoumarins isolated from an *Esenbeckia* species are pimpinellin (from *E. grandiflora*, Trani et al., 2004) and its possibly artefactual head-to-head photodimer (also from *E. grandiflora*, de Oliveira et al., 2004). Pimpinellin is related to its biogenetic precursor columbianetin, which appears as its 3-(3',3'-dimethylallyl) derivative (in *E. grandiflora*, de Oliveira et al., 2005).

Aside from β -sitosterol, lupeol, the lignans episesamin and sesamin, the simple amide pellitorin, and 5-hydroxy-2-methylchroman-4-one, which had not been described previously as a natural product (García Beltrán and Cuca Suárez, 2003; Cuca Suárez and Coy Barrera, 2007), previous studies on *E. alata* had reported the presence of the furo- and pyranocoumarins psoralen, xanthotoxin and xanthyletin (García-Beltrán, 2004; Cuca Suárez and Coy Barrera, 2007), unsubstituted coumarin and the furocoumarin bergapten (Coy Barrera, 2009), and the 3-(1',1'-dimethylallyl)coumarins rutacultin and exo-dehydrochalepin (García-Beltrán and Cuca-Suárez, 2005).

3. Present study

The present study reports the isolation of four additional coumarins (**1–4**) (Fig. 1) from the leaves and wood of *E. alata*. Dry leaves (2.4 kg) were macerated at room temperature with 96% EtOH. Wood (3.0 kg) was macerated similarly with butanone. The concentrated leaf extracts were fractionated by treatment liquid–liquid with solvents of increasing polarity. The petroleum ether fraction was analyzed by TLC using petroleum ether:ethyl acetate (AcOEt) mixtures, increasing the system's polarity. In this way chalepensisin (**1**) (Anaya et al., 2005) and bergapten (**2**) (Steck et al., 1971; Rios et al., 2002a, b) were isolated from the leaves. Leptophyllidin (**3**) (Sharma et al., 1978) and isoangenomilin (**4**) (Bohlmann et al., 1975) were isolated from wood fractions after resolving them by preparative TLC using toluene:AcOEt mixtures of increasing polarity. The structures of the compounds were elucidated using ¹H- and ¹³C NMR, and comparison with data from the literature.

4. Chemotaxonomic significance

Esenbeckia alata, like *Esenbeckia almawillia* and *Esenbeckia grandiflora*, produce 3-(1',1'-dimethylallyl)coumarins. Therefore, the genus *Esenbeckia* is part of a small group of phylogenetically distant Rutaceae including *Ruta* and *Clausena* in which

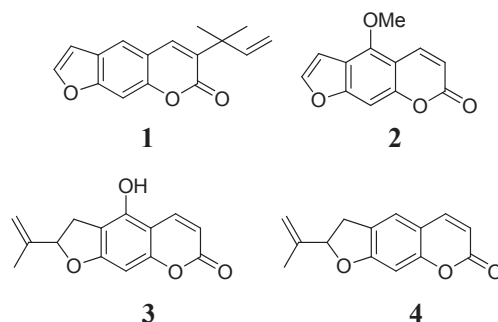


Fig. 1. Coumarins isolated from *E. alata* in the present work.

this substitution has been found (Gray and Waterman, 1978). The isopropenyldihydrofurocoumarins exo-dehydrochalepin, leptophyllidin and isoangenomalin are representatives of a rather uncommon type found in such distantly related families as Apiaceae and Goodeniaceae and might be isolation artefacts, formed by dehydration of chalepin, 5-hydroxymarmesin and marmesin, respectively, precursors of linear furocoumarins (Gray and Waterman, 1978). Overall, the occurrence in *Esenbeckia* spp. of a broad variety of coumarin-based structures common to other Rutaceae, as well as typical Rutaceous alkaloids and limonoids common to Rutaceae, Meliaceae and Simaroubaceae fails to support the chemotaxonomic utility of these compounds at the family level and immediately below. It remains to be seen if detailed metabolomic studies uncover significant variations within and among closely related genera.

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