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Article

Flavanones from aerial parts of *Cordia globosa* (Jacq.) Kunth, Boraginaceae

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RESUMO: "Flavanonas isoladas das partes aéreas de *Cordia globosa* (Jacq.) Kunth (Boraginaceae)". A análise fitoquímica das partes aéreas de *Cordia globosa*, coletadas no município de Picuí, PB, Brasil, resultou no isolamento e identificação estrutural da 7,4'-dimetilnarigenina (0,025 g) e eriodictiol (0,015 g). Estas duas flavanonas são as primeiras agliconas, desta classe, isoladas no gênero *Cordia.*

Unitermos: *Cordia globosa,* Boraginaceae, flavanonas, 7,4'-dimetilnarigenina, eriodictiol.

ABSTRACT: The phytochemical analysis of aerial parts of *Cordia globosa*, collected in the Municipality of Picuí, State of Paraíba, Brazil, resulted in the isolation and structural identification of narigenin-4',7-dimethyl ether (0.025 g) and eriodictyol (0.015 g). These compounds are the first flavanones aglycones isolated from the genus *Cordia.*

Keywords: *Cordia globosa,* Boraginaceae, flavanones, narigenin-4',7-dimethyl ether, eriodictyol.

INTRODUCTION

The Boraginaceae family comprises about 2740 species distributed in 148 genera (Stevens, 2001). The genus *Cordia* is one of the most representatives of this family and the chemical characteristic in this genus is the presence of quinones known as cordiaquinones. However, flavonoids, terpenoids, carbohydrates, lipids and phenylpropanoids are also well reported for the genus (Silva, 2004).

Cordia globosa (Jacq.) Kunth is a shrub popularly known in Northeastern Brazil as 'maria-preta'. The decoction or infusion of the leaves of *C. globosa* is used in folk medicine for the treatment of the symptoms of rheumatism, painful menstruation and dyspepsia. In Jamaica, the tea of leaves is used by women against painful menstruation (Asprey & Thornton, 1955). The leaves and the stems have spasmolytic activity on guinea pig ileum as well as on rabbit duodenum, and also was confirmed the vasodilator activity on isolated rats' hindquarter (Feng et al., 1962).

Previous studies reported the isolation of 7-methoxyflavone and 3',4',5,7-tetrahydroxy-3-methoxyflavone (Silva et al., 2004) from the aerial parts and (1aS*, 1bS*, 7aS*, 8aS*)-4,5-dimethoxy-1a,7a-dimethyl-1,1a,1b,2,7,7a,8,8a-octahydrocyclopropa [3,4] cyclopenta [1.2b] naphthalene-3,6-dione and microphyllaquinone from the roots of *C. globosa* (Menezes et al., 2005). Twenty three and twenty six volatiles compounds were identified for the essential oils obtained from fresh leaves at the flowering and fructification stages, respectively. The bicyclogermacrene (22.7-13.1%) and β-caryophyllene (11.9-11.6%) were the majority constituents (Menezes et al., 2006). In another study, a total of 38 compounds were indentified from the oils obtained from steam and leaves. The main components in the stem oil were 1-endo-bourbonanol (20.2%) and lynalyl butyrate (14.7%) and in the leaves oil, the β-caryophyllene (39.0%) and α-humulene (12.1%) were the majority (Oliveira et al., 2007).

MATERIAL AND METHODS

General

^{1}H and ^{13}C NMR (1D and 2D) were obtained on a MERCURY VARIAN spectrometer. ^{1}H and APT-^{13}C NMR spectra were recorded in a $CDCl_3$ (CG-01) or CD_3OD (CG-2) at 200 and 50 MHz, respectively. TMS was used as internal standard. TLC, on Si Gel 60 PF_{254} ART 7749 (Merck) and column chromatography with Si Gel ART 7734 (Merck) or Sephadex-LH 20 (Pharmacia) were used.

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Plant Material

The aerial parts of *Cordia globosa* (Jacq.) Kunth were collected in March 2002 in the Municipality of Picuí, State of Paraíba, Brazil. A voucher specimen (AGRA 5185) has been deposited at the Herbarium Prof. Lauro Pires Xavier (JPB) in the Universidade Federal da Paraíba.

Extraction, isolation and the structure elucidation

The fresh aerial parts were dried at 40 °C for 72 h and after were grownded in a mechanical mill. Dried and powdered aerial parts (10 kg) from *C. globosa* were extracted with EtOH at room temperature for three days, five consecutive times. The alcoholic extract was then dried and the crude extract (300 g) obtained was taken up in MeOH:H_2O (7:3) and extracted successively with hexane, chloroform, ethyl acetate and n-buthanol.

The hexane (37 g) fraction was subjected to column chromatography packed with silica gel 60 and eluted with hexane, chloroform and methanol; 286 fractions of 50 mL were collected being analyzed and joined through analytical thin-layer chromatography (TLC). The sub-fraction 102-112 (0,320 g) was submitted to column chromatography packed with silica gel 60 an eluted with hexane, ethyl acetate and methanol gradient, resulting 61 fractions of 25 mL that were analyzed and joined through analytical TLC. The sub-fraction 14-21 after being recrystallized in chloroform showed itself as an incolor solid crystalline, yielding 0.025 g of the substance CG-01.

The fraction chloroformic (31 g) was subjected to column chromatography packed with silica gel 60 and eluted with hexane, ethyl acetate and methanol, from which 185 fractions of 50 mL were collected and the analyzed and joined through analytical TLC. The sub-fraction 159-165 (158 mg) was subjected to column chromatography packed with Sephadex LH 20 and eluted with chloroform:methanol (1:1) from which 22 fractions of 20 mL were collected and then analyzed and joined through analytical TLC. The sub-fraction 16-17 (30 mg) was subjected to column chromatography packed with Sephadex LH 20 and eluted with chloroform:methanol (1:1) from which fifteen fractions of 8 mL were collected and then analyzed and joined through analytical TLC. The sub-fraction 10-11 (0.015 g), washing with acetone gave a yellow solid codified as CG-02 (0.015 g).

RESULTS AND DISCUSSION

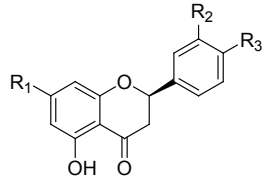
The ^{1}H NMR spectrum of compound **1** showed three protons at δ 2.76 (1H, dd, *J* = 17.3, 3.2 Hz), 3.09 (1H, dd, *J* = 17.3, 13.0 Hz) and 5.35 (1H, dd, *J* = 13.0, 3.2 Hz), typically assignable to H-3 and H-2 of a flavanone skeleton, which was indicated also in the ^{1}H NMR of CG-02 [δ 2.68 (1H, dd, *J* = 17.0, 3.0 Hz), 3.06 (1H, dd, *J* = 17.0, 12.5 Hz) and 5.26 (dd, *J* = 12.5, 3.0 Hz)]. In addition, signals for four protons at δ 6.93 (2H, d, *J* = 8.7 Hz) and 7.38 (2H, d, *J* = 8.7 Hz)] assignable to the aromatic protons of a 4-monosubstituted B-ring for **1** as well three protons at δ 6.78 (2H, s) and 6.91 (1H, sl) assignable to the aromatic protons of a 3,4-disubstituted B-ring for *2*. A downfield proton at δ 12.01 (CG-01) and δ 12.1 (CG-02, DMSO) assignable to C5-OH chelated to C-4 carbonyl, and two additional aromatic protons at δ 6.93 (1H, d, *J* = 8.7 Hz) and 7.38 (1H, d, *J* = 8.7 Hz), δ 5.87 (1H, d, *J* = 2.2 Hz) and 5.89 (1H, d, J = 2.2 Hz) were observed for **1** and **2**, respectively, could be assigned to 6 and 7 aromatics protons of the A-ring. Furthermore, two methoxy signals appeared at δ 3.78 (3H, s), 3.81 (3H, s) of compound **1**. These spectroscopic data suggested that compound **1** and **2** were 5-hydroxyflavanones substituted with two methoxy groups and three hydroxyl groups, respectively. The ^{13}C NMR spectra analysis of **1** and **2** showed signals for 17 and 15 carbons, comprising two methoxy, one methylene, seven methynes and seven non-protonated carbons to **1** and one methylene, six methynes and eight non-protonated carbons to **2**. The analysis of these data sets with the spectra of HMQC, HMBC and NOESY, as well as comparison with literature data (Agrawal, 1989), has identified **1** as 5-hydroxy-4',7-dimethoxyflavanone (narigenin-4',7-dimethyl ether) and **2** as 3',4',5,7-tetrahydroxyflavanone (eriodictyol), with yielding of 0.00025% and 0.00015%, respectively

Narigenin-4',7-dimethyl ether **(1)***:* NMR ^{1}H (200 MHz, $CDCl_3$) 2.76 (H-3a, dd, *J* = 3.2;17.3), 3.09 (H-3b, dd, *J* = 13.0; 17.3), 3.78 (OCH_3-7, s), 3.81 (OCH_3-4', s), 5.35 (H-2, dd, *J* = 3.2, 13.0), 6.02 (H-8, d, *J* = 2.3), 6.05 (H-6, d, *J* = 2.3), 6.93 (H-5', d, *J* = 8.7), 7.38 (H-6', d, J = 8.7), 12.01 (s, OH-5). NMR ^{13}C (50 MHz, $CDCl_3$): 43.2 (C-3), 55.4 (OCH_3), 55.7 (OCH_3), 79.0 (C-2), 94.2 (C-8), 95.1 (C-6), 103.1 (C-10), 114.2 (C-3', 5'), 127.7 (C-2', 6'), 130.4 (C-1'), 160.0 (C-4`), 162.9 (C-9), 164.1 (C-5), 168.0 (C-7), 196.0 (C-4).

Eriodictyol **(2):** NMR ^{1}H (200 MHz, MeOD) 2.68 (H-3a, dd, *J* = 3.0; 17.0), 3.06 (H-3b, dd, *J* = 12.5, 17.0), 5.26 (H-2, dd, *J* = 3.0, 12.5), 5.87 (H-8, d, *J* = 2.2), 5.89 (H-6, d, *J* = 2.2), 6.78 (H-5', H-6', 2H, s), 6.91 (H-2', 1H, sl). NMR ^{13}C: 44.1 (C-3), 80.5 (C-2), 96.2 (C-8), 97.0 (C-6), 103.3 (C-10), 114.7 (C-2'), 116.2 (C-5'), 119.3 (C-6'), 131.8 (C-1'), 146.5 (C-3'), 146.9 (C-4'), 164.9 (C-9), 165.4 (C-5), 168.4 (C-7), 197.8 (C-4).

The literature reports the isolation of only sixteen flavanones from Boraginaceae. The flavanones were isolated previously from genera *Heliotropium, Cordia* and *Echiochilon*. The majority of flavanones were obtained from the genus *Heliotropium,* on six species. In *Echiochilon* only *E. fruticosum* showed data from flavanones and in Cordia, two glycosides flavanones

were previously isolated. The compounds obtained in this work were reported in Boraginaceae family in only one species *H. stenophyllum*. The flavanones isolated from genera *Cordia* and *Heliotropium* are preferably 3', 4',5, 7, -tetraoxigenated (Chart 1).



(**1**) $R_1 = R_3 = OCH_3$, $R_2 = H$
(**2**) $R_1 = R_2 = R_3 = OH$

CONCLUSION

This paper indicates that in Boraginaceae family the genera *Heliotropium, Cordia* and *Echiochilon,* until the present moment, are the only ones producing flavanones as well as reports the first flavanones aglycones from *Cordia*.

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Chart 1. Distribution to flavanones in Boraginaceae family.

Compound	Specie	Reference
Hesperetin-7-*O*-α-L-rhamnoside	*Cordia obliqua*	Chauhan et al., 1978 Tiwari et al., 1979
Hesperidin	*C. francisci* *C. martinicensis* *C. myxa* *C. serratifolia*	Ficarra et al., 1995
7-hydroxy-flavanone	*Heliotropium indicum*	Singh et al., 2003
4',5-Dihydroxy-3',5',7-trimethoxyflavanone	*H. megalanthun*	Urzua et al., 2000
5-Hidroxy-3',4',5', 7-tetramethoxyflavanone	*H. megalanthum*	Urzua et al., 2000
Eriodictyol	*H. stenophyllum*	Wollenweber et al., 2002
Eriodictyol-3',7-dimethyl ether	*H. chenopodiaceum var. chenopodiaceum*	Urzua et al., 1998
Eriodictyol-7-methyl ether	*H. sinuatum*	Torres et al., 1996 Modak et al., 2005
Hesperetin	*H. sinuatum*	Torres et al., 1996 Modak et al., 2004
Pinocembrim	*H. sinuatum* *H. stenophyllum*	Torres et al., 1996 Villarroel & Urzua, 1990 Wollenweber et al., 2002
Pinocembrim-7-glycoside	*Echiochilon fruticosum*	Hammami et al., 2004
Naringenin	*H. chenopodiaceum var. chenopodiaceum* *H. chenopodiaceum var. ericoideum*	Urzua et al., 1998
	H. stenophyllum	Villarroel & Urzua, 1990 Wollenweber et al., 2002
Naringenin-5-methyl ether	*E. fruticosum*	Hammami et al., 2004
	H. indicum	Singh et al., 2003
Naringenin-7-methyl ether-4'-acetyl	*H. stenophyllum*	Wollenweber et al., 2002
Naringenin-4',7-dimethyl ether	*H. stenophyllum*	Wollenweber et al., 2002
Sakuranetin	*H. chenopodiaceum var. ericoideum*	Urzua et al., 1998
	H. stenophyllum	Wollenweber et al., 2002

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