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Chemical constituents from leaves and root bark of *Trichilia monadelpha* (Meliaceae)

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ABSTRACT

Two new limonoid derivatives designated, monadelphin A (**1**) and monadelphin B (**2**) and two new sesquiterpene derivatives named trichins A (**3**) and B (**4**) were isolated together with six known compounds (**5–10**) from the mixture of methylene chloride/methanol (1:1) extract of leaves and root bark of *Trichilia monadelpha* (Meliaceae) collected in Cameroon. The structures of the new compounds were unambiguously established by detailed spectroscopic analysis including 1D and 2D NMR data in conjunction with high resolution mass spectrometry data and by comparison of these data with those of related compounds described in the literature. Compounds **1–4** were screened for their cytotoxic potential. Compound **1** showed strong cytotoxicity against the mouse lymphoma L5178Y cell line with an IC_{50} value of 0.62 µg/mL. The biogenetic origin of trichin B (**4**) from trichin A (**3**) was also postulated.

1. Introduction

Trichilia, the largest genus of the Meliaceae family, consists of over 90 species which are widely distributed throughout the tropical and subtropical regions over the world (Xie et al., 1994). *Trichilia monadelpha* (Thonn) JJ De Wilde syn. *T. heudelotii* (Abbiw, 1990; Irvine, 1961), one of the thirteen species of this genus represented in Cameroon, is a towering tree with 0.4 m of diameter which grows up to 12–20 m high in the tropical rainforests in Africa (Irvine, 1961). The species of *Trichilia* genus have been used as timbers and herbal medicines by traditional healers in Cameroonian folk medicine for the treatment of various diseases such as abdominal pain, dermatitis, haemorrhoids, jaundice, gonorrhea, syphilis and skin inflammation (Pupo et al., 2002). Previous phytochemical investigations on some members of this genus reported the presence of a wide range of secondary metabolites, including phenolic acids (Aladesanmi and Odediran, 2000), terpenes (Aladesanmi and Odediran, 2000), steroids (Pupo et al., 1997) and limonoids (Adesida and Okorie, 1973; Okorie and Taylor, 1968; Tsamo et al., 2013), some of which display noteworthy biological properties, such as antimicrobial, anti-inflammatory, antiplasmodial, antioxidant, antimutagenic, cytotoxic and hepatoprotective activities (Aladesanmi and Odediran, 2000; Tsamo et al., 2016).

In the continuation of our effort in the search for bioactive secondary metabolites from Cameroonian medicinal plants (Tsamo et al., 2016, 2013), we have investigated the constituents of leaves and root bark of *T. monadelpha*. As a result, four new compounds, including two new limonoid derivatives, monadelphins A (**1**) and B (**2**), and two new sesquiterpenes, trichins A (**3**) and B (**4**), together with six known compounds (**5–10**) were isolated and structurally characterized. Herein, we describe the isolation and structure elucidation of these four new isolated compounds **1–4** as well as their cytotoxic potential. The plausible biogenetic origin of trichin B (**4**) from trichin A (**3**) was also postulated.

2. Results and discussion

The air-dried and powdered leaves (2.7 kg) and root bark (1.5 kg) of *T. monadelpha* were separately extracted by maceration at room

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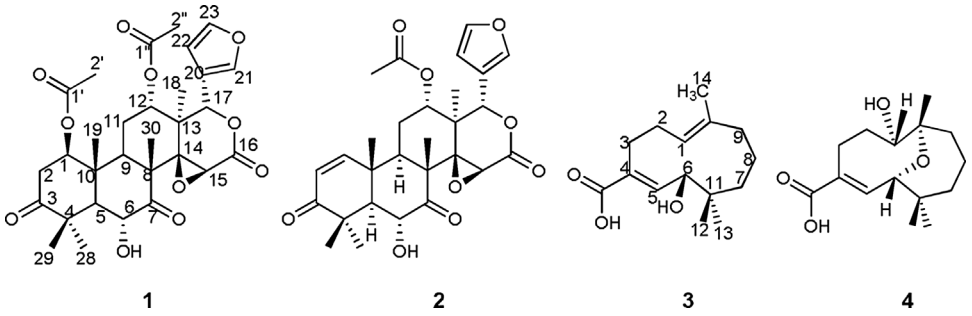

Fig. 1. Chemical structures of compounds **1–4.**

Table 1
^{1}H NMR spectroscopic data of compounds **1–4**.[a]

Position	1 [b]δ_H (m, *J*, Hz)	2 [c]δ_H (m, *J*, Hz)	3 [c]δ_H (m, *J*, Hz)	4 [c]δ_H (m, *J*, Hz)
1	4.84, dd (10.1, 1.6)	7.07, d (10.0)	5.18, t (7.6)	3.54, dd (8.9, 2.9)
2a	3.33, dd (15.3, 10.1)	5.94, d (10.0)	2.33, m	2.10, dddd (13.8, 8.9, 6.5, 4.8)
2b	2.04, dd (15.3, 1.6)	–	2.18, m	1.85, dddd (13.8, 9.5, 6.2, 2.9)
3a	–	–	2.61, m	2.71, ddd (12.7, 9.5, 6.5)
3b			2.28, m	2.54, ddd (12.7, 6.2, 4.8)
5	1.97, d (11.4)	2.09, d (12.5)	6.88, d (10.3)	7.20, d (3.2)
6	4.74, dd (11.4, 3.6)	4.96, d (12.5)	4.04, d (10.3)	4.08, d (3.2)
7a	–	–	1.26, m	1.54, m
7b			1.07, m	1.44, m
8a	–	–	1.61, m	1.73, m
8b			1.31, m	1.55, m
9a	2.33, d (11.3)	2.42, d (12.2)	2.18, m	1.81, m
9b			1.44, m	1.57, m
11a	2.02, ddd (15.7, 11.3, 5.1)	2.22, ddd (15.5, 12.2, 5.6)	–	–
11b	1.93, d (15.7)	1,97, d (15.5)	–	–
12	4.77, t (5.1)	5.05, d (5.6)	0.94, s	1.11, s
13	–	–	0.96, s	0.93, s
14	–	–	1.54, s	1.23, s
15	3.66, s	3.81, s	–	–
17	5.47, s	5.64, s		
18	1.23, s	1.29, s		
19	1.14, s	1.30, s		
20	–	–		
21	7.39, d (1.5)	7.52, dd (1.6, 0.8)		
22	6.32, dd (1.5, 0.9)	6.46, dd (1.6, 0.8)		
23	7.38, d (1.5)	7.50, d (1.6)		
28	1.34, s	1.43, s		
29	1.40, s	1.33, s		
30	1.15, s	1.23, s		
6-OH	3.67, d (3,6)	–		
2′	2.00, s	–		
2″	1.73, s	1.72, s		

[a] Chemical shifts are expressed in δ (ppm) downfield from TMS and assigned by COSY, HSQC and HMBC experiments. *J* in Hz.
[b] Recorded in $CDCl_3$.
[c] Recorded in MeOD[5].

temperature for 48 h with a mixture of CH_2Cl_2/methanol (1/1, v/v). Filtration and evaporation of each resulting solution under reduced pressure led to a dark greenish leaf extract and brown root bark extract, respectively. Since both extracts showed strong cytotoxicity when assayed against the lymphoma cell line L5178Y, each of them was further fractionated into several fractions by vacuum liquid chromatography. The different fractions were purified by combination of silica gel, reversed-phase ODS column chromatography, and semi-preparative HPLC to give four new compounds named monadelphin A (**1**), monadelphin B (**2**), trichin A (**3**) and trichin B (**4**) together with six known compounds stigmasterol (**5**), β-sistoterol (**6**), ellagic acid (**7**), protocatechuic acid (**8**), coixol (**9**) and scopoletin (**10**). The structures of new compounds (Fig. 1) were elucidated by spectroscopic analysis using HRESIMS, 1D and 2D NMR experiments.

2.1. Characterization of the new compounds

Monadelphin A (1) was isolated as colorless crystals. It reacted positively, both to Liebermann-Burchard (red purple) and Erhlich (orange) tests suggesting its limonoidic nature. It was found to possess a molecular formula of $C_{30}H_{36}O_{11}$, from the sodiated molecular ion $[M + Na]^+$ at *m/z* 595.2134 (calcd. for $C_{30}H_{36}O_{11}Na$: 595.2155) in its HRESIMS requiring 13° of unsaturation. Its IR spectrum showed absorption bands at ν_{max} 3439 (-OH), 1734 and 1710 cm^{-1}, characteristic of hydroxyl, carbonyl and furan moieties (Benjamin et al., 2003), respectively. In accordance with its molecular formula, all the 30 carbon signals were well exhibited in the ^{13}C NMR spectrum (Table 2) of compound **1**, which were further sorted by HSQC experiments as 7 methyls, 2 methylenes, 10 methines (five oxygenated and three olefinic), and 11 quaternary carbons (five carbonyls, one oxygenated and one olefinic). The ^{1}H (Table 1) and ^{13}C NMR (Table 2) data of compound **1** exhibited resonances assignable to five carbonyl groups