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Isolation of New Aliphatic Ester 8'α-Hydroxy-*n*-decanyl *n*-docosanoate from the Leaves of *Centaurothamnus maximus* Wagentz and Dittri

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Centaurothamnus maximus (Asteraceae) is a wild and one of the least explored plants of Saudi Arabia. Yellow amorphous powder compound **1** (CM-1) was obtained after eluting the ethanol extract from reverse phase column (RP-18) by chloroform eluent of mobile phase. This is a new ester of decanediol esterified with behenic acid isolated for the first time from the plant source. The chemical structure of compound (CM-1) was established as 8'α-hydroxy-*n*-decanyl *n*-docosanoate after UV, IR, ^{1}H NMR, ^{13}C NMR, COSY, HSQC, HMBC and MASS spectroscopic studies. Two known compounds *n*-hexatriacosanoic acid (CM-2) and stigmasterol (CM-3) were also isolated and identified by spectroscopic studies.

Keywords: *Centaurothamnus maximus*, Asteraceae, Isolation, Behenic acid ester.

INTRODUCTION

Centaurothamnus maximus Wagentz and Dittri belongs to family compositae includes herbs, shrubs, trees, epiphytes, vines and succulent plants having almost similar chemical profiles with respect to *Centaurea maxima* Forssk[1]. *Centaurothamnus maximus* is an indigenous leafy shrub of Saudi Arabia. It possess many branches and about 1.5 m tall[2]. *C. maximus* is found in many localities in the southern part of Saudi Arabia, on cliffs and steep hillside and its aerial parts reportedly contain sesquiterpene lactones like guainolides chlorojanerin, cynaropicrin and janerin[3]. Thirteen sesquiterpene lactones, 14 flavonoids, two lignans and one simple lactone were isolated from *Centaurea zuccariniana* DC[4]. The other species of *Centaurea* also reported to contain different phytoconstituents like *Centaurea ragusina* L. (sesquiterpenes)[5]; *Centaurea formanekii* Halacsy (hexadecanoic acid, δ-elemene and spathulenol), *C. orphanidea* Heldr. & Sart. ex Boiss. ssp. *thessala* (Hausskn.) Dostál (γ-elemene and caryophyllene oxide)[6].

The *in vitro* antimicrobial activities of sesquiterpene lactones exhibit low or moderate antibacterial, but potent antifungal activities[4]. The volatile oils from *Centaurea* spp. displayed great antibacterial potential[5]. The methanol and aqueous extracts of *Centaureapoly podiifolia* var. *pseudobehen* showed strong antioxidant activity[7]. Methanolic extract of *C. maximus* was found to possess a noteworthy growth inhibitory effect against human lung cancer (A-427), urinary bladder cancer (5637) and breast cancer (MCF-7) cell lines with IC_{50} values < 50 µg/mL and pronounced antimicrobial activity was observed only against Gram-positive bacteria among them multi resistant bacteria with inhibition zones > 15 mm and MIC values < 500 µg/mL. However *C. maximus* showed a remarkable radical scavenging effect at high concentrations[8]. Due to the significance of this plant in medicinal use we designed our study to isolate and characterize one new compound (Fig. 1) along with two known compounds from the leaves of *C. maximus*.

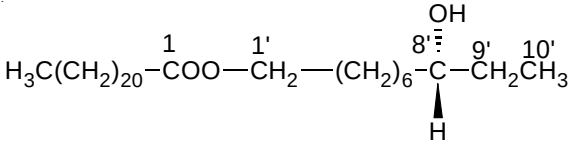


Fig. 1. Chemical structure of 8'α-hydroxy-*n*-decanyl *n*-docosanoate (CM-1)

EXPERIMENTAL

IR spectra were recorded with an ATI Mattson genesis series Fourier transform (FT-IR) spectrophotometer. UV

spectra were obtained on a Hewlett Packard 8452A diode array spectrophotometer. Optical rotations were recorded at ambient temperature using a JASCO DIP-370 digital polarimeter. Melting points were determined using a model IA9100 melting point apparatus. 1D and 2D NMR spectra for ^1H and ^{13}C were obtained on a BrukerAvance DRX 500 spectrometer. HRESIFTMS was obtained using a BrukerBioapex FT-MS in ESI mode. For TLC, glass supported silica gel plates (0.25 mm layer, F250, E. Merck) were used. Silica gel (70-230 mesh) and LiChroprep RP-18 [40-63 μm; octadecyl silica (ODS) gel] from Merck was employed for column chromatography.

All chemicals were of analytical grade. *n*-Hexane, ethyl acetate, chloroform, methanol, ethanol, water, sulphuric acid and vanillin were purchased from Faisal Zouman Al-Anazi Trading Est., Riyadh, Saudi Arabia. Thin-layer chromatography was performed on pre-coated silica gel 60 F254 plates (Merck). Visualization of the TLC plates was performed using *p*-anisaldehyde as spray reagent.

Leaves of *C. maximus* were collected in March 2006 from Aqabaat Al-Makhwah, after tunnel # 13, Kingdom of Saudi Arabia. The plant was identified by Dr. Mohammed Yousuf, Field Taxonomist, Department of Pharmacognosy, College of Pharmacy, KSU, Riyadh. A voucher specimen is deposited in herbarium (Voucher # 15024) of Pharmacognosy Department, College of Pharmacy, King Saud University, Riyadh.

Extraction and isolation: The air dried powdered leaves (1 kg) of the plant extracted exhaustively with *n*-hexane with a Soxhlet apparatus. This process was repeated, until the complete exhaustion of the plant material. The extract was concentrated under reduced pressure using rotary evaporator. Remaining marc was dried and extracted with the same apparatus till exhaustion of the drug material using dichloromethane and concentrated with rotary evaporator. The same procedure was followed for extraction with ethyl acetate and ethanol (90 %). The obtained extracts were concentrated to dryness, weighed and investigated for their phytochemical aspect.

Ethanol fraction of extract was subjected for isolation by column chromatography using LiChroprep RP-18 as stationary phase and water as eluent. CM-1 (Fig. 1) (2 g) was obtained using gradients of $CHCl_3$ and CH_3OH (90:10), CM-2 (Fig. 2b) (267 mg) with $CHCl_3$ and CH_3OH (40:60) while CM-3 (Fig. 2a) (5.8 g) was the result of elution by hexane (100 %).

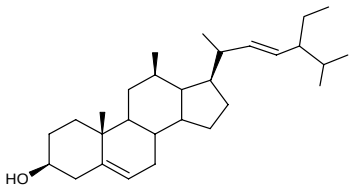
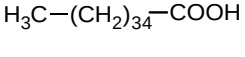


Fig. 2. (a) (CM-3) Stigmasterol



(b) (CM-2) *n*-Hexatriacosanoic acid

8'α-Hydroxy-*n*-decanylbehenate (CM-1): Yellow amorphous powder, $[\alpha]_D$: 1.6° ($CHCl_3$), R_f: 0.47 ($CHCl_3$:CH_3OH; 20:80) IR (KBr, ν_{max}, cm^{-1}): 721, 1722, 3410. ^1H NMR ($CDCl_3$): δ 4.36 (1H, d, *J* = 9.0 Hz, H_2-1'a), 4.28 (1H, d, *J* = 9.5 Hz, H_2-1'b), 3.90 (1H, brm, ω1/2 = 8.5 Hz, H-8'β), 2.30 (2H, t, *J* = 9.0 Hz, H_2-2), 1.94 (2H, m, CH_2), 1.47 (2H, m, CH_2), 1.18 (8H, brs, 4 × CH_2), 1.08 (4H, brs, 20 × CH_2), 0.88 (3H, t, *J* = 6.0 Hz, Me-22), 0.84 (3H, t, *J* = 6.1 Hz, Me-10'). ^{13}C NMR ($CDCl_3$): δ 171.16 (C-1), 63.48 (C-1'), 71.39 (C-8'), 36.81 (CH_2), 33.23 (CH_2), 31.76 (CH_2), 29.71 (10 × CH_2), 29.38 (8 × CH_2), 29.31(CH_2), 29.28 (CH_2), 28.14 (CH_2), 27.52 (CH_2), 25.62 (CH_2), 22.68 (CH_2), 14.18 (Me-22), 14.07 (Me-10'). EIMS *m/z* (rel. int.): 496 [M^+] ($C_{32}H_{64}O_3$) (6.8), 467 (14.1), 448 (18.2), 331 (2.8), 323 (13.2).

RESULTS AND DISCUSSION

Compound **1** (CM-1), an aliphatic ester, was obtained from chloroform eluents. Its IR spectrum showed absorption bands for hydroxyl group (3410 cm^{-1}), ester function (1722 cm^{-1}) and long aliphatic chain (721 cm^{-1}). Its mass spectrum displayed a molecular ion peak at *m/z* 496 corresponding to a molecular formula of a hydroxyl alkyl ester is $C_{32}H_{64}O_3$. The ion peaks generating at *m/z* 323 [CH_3 $(CH_2)_{20}CO]^+$ and 339 [CH_3 $(CH_2)_{20}COO]^+$ suggested that behenic acid was esterified with decanediol (Fig. 3). The ion fragment produced at *m/z* 467 [$M-C_2H_5]^+$ indicated the presence of the hydroxyl group at C-8' (Fig. 3). The ^1H NMR spectrum of CM-1 exhibited two one-proton doublets at δ 4.36 (*J* = 9.0 Hz) and 4.28 (*J* = 9.5 Hz) assigned to oxygenated methylene H_2-1 protons. The other methylene protons appeared from δ 2.30 to 1.08. A one-proton multiplet at δ 3.90 with half-width of 8.5 Hz was accounted to α-hydroxyl methine H-8' proton. Two three-proton triplets at δ 0.88 (*J* = 6.0 Hz) and 0.84 (*J* = 6.1 Hz) were due to terminal C-22 and C-10' primary methyl protons. The ^{13}C NMR spectrum of CM-1 showed carbon signals for ester carbon at δ 171.16 (C-1), hydroxymethine carbon at δ 71.39 (C-8'), oxygenated methylene carbon at δ 63.48 (C-1'), methylene carbons between δ 36.81-22.68 and methyl carbons at δ 14.18 (C-22) and 14.07 (C-10'). The absence of any signal beyond δ 4.36 in the ^1H NMR spectrum between δ 171.16-71.39 in the ^{13}C NMR spectrum suggested saturated nature of the molecule. The ^1H-^1H COSY spectrum of CM-1 exhibited correlations of H_2-1' with H_2-2' and H_2-3', H-8' with H_2-6', H_2-7', H_2-9' and Me-10' and Me-22 with H_2-21 and H_2-20. The HMBC spectrum of CM-1 displayed interactions of H_2-2, H_2-3 and H_2-1' with C-1; H_2-6', H_2-7' and H_2-9' with C-8'; and H_2-20, H_2-21 with H_2-22. On the basis of above discussion the structure of CM-1 has been determined (Fig. 1) as 8'α-hydroxy-*n*-decanyl *n*-docosanoate. This is a new aliphatic ester isolated for the first time in *C. maximus*.

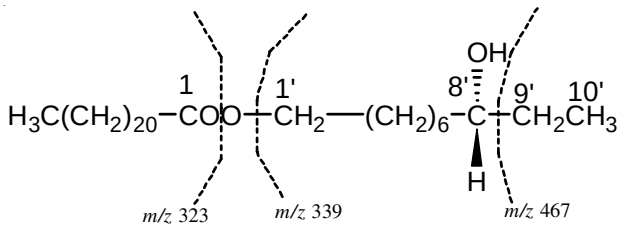


Fig. 3. Mass Fragmentation pattern of CM-1

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