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FLAVONOID AGLYCONES FROM *Centaurea sphaerocephala*

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Centaurea sphaerocephala L. belongs to the tribe Cynarea of the Asteraceae, widespread in the entire Mediterranean region. Several medicinal uses have been reported for *Centaurea* species [1, 2] but none for *C. sphaerocephala.* Previous phytochemical studies of the species *sphaerocephala* (ssp. *sphaerocephala* and ssp. *polyacantha*) led to the isolation of sesquiterpene lactones and lignans, sesquilignans and dithienylacetylene [3, 4] respectively. Aerial parts of *Centaurea sphaerocephala* L. were collected during the flowering phase in May 2003 from El Kala (East of Algeria) and authenticated by Prof. M. Kaabeche (Biology Department, University of Setif, Algeria) on the basis of Quezel and Santa [5]. A voucher specimen (CCS13/05/03) has been deposited in the Herbarium of the Biology Department of Mentouri University of Constantine. Leaves and flowers of *Centaurea sphaerocephala* L. were dried (2170 g) and macerated at room temp. with MeOH–H_2O (80:20 v/v) for 24 hr, three times. After filtration, the filtrates were combined, concentrated at room temperature, and diluted with 850 mL H_2O. After precipitation of chlorophyll with $Pb(OAc)_4$ and filtration, the remaining yellowish aqueous solution was extracted successively with $CHCl_3$, EtOAc, and *n*-BuOH. The organic layers were dried with Na_2SO_4 giving, after removal of solvents under reduced pressure, $CHCl_3$ (2.10 g), EtOAc (10.40 g), and *n*-BuOH (35.94 g) extracts. The ethyl acetate extract of *C. sphaerocephala* was applied to a column of silica gel (230-400 mesh) and eluted with chloroform- acetone with increasing polarity to yield seventeen fractions (F_1–F_{17}). Fractions F_6 submitted to preparative TLC on silica gel GF_{254} ($CHCl_3$: MeOH, 15:1) gave **1** (12 mg) and **2** (18 mg). Fractions F_{10} submitted to preparative TLC on polyamide (toluene: methanol: methylethylketone, 4:3:3) and purified by preparative TLC on silica gel GF_{254} ($CHCl_3$:MeOH, 12:1) gave **3** (22 mg), and **4** (10 mg).

The structures of these compounds were established by UV, ^{1}H NMR, and MS analysis [6-7]. All these results were in good agreement with the respective literature data [8-14].

Compound 1: $C_{16}H_{12}O_6$, yellow powder, mp 330°C; UV (λ_{max}, MeOH, nm): 340, 272; +NaOH: 272, 348, 404; +$AlCl_3$: 276, 364; +$AlCl_3$/HCl: 276, 364; +NaOAc: 276, 348; +NaOAc/H_3BO_3: 276, 340. ^{1}H NMR (250 MHz, CD_3COCD_3, δ, ppm, J/Hz): 6.20 (1H, d, J = 2.3, H-6), 6.40 (1H, d, J = 2.3, H-8), 6.55 (1H, s, H-3), 6.80 (1H, d, J = 8.4, H-5′), 7.90 (1H, d, J = 2.3, H-2′), 7.80 (1H, dd, J = 8.4; 2.3, H-6′), 3.85 (3H, s, 3′-OMe). Mass spectrum (EI, 70 eV, *m/z,* I_{rel},%): 300 $[M]^+$ (100), 284 (22), 148(17).

The aglycone was characterized as 4′,5,7-trihydroxy-3′-methoxyflavone (chrysoeriol) [8].

Compound 2: $C_{15}H_{10}O_5$, yellow needles, mp 349°C; UV (λ_{max}, MeOH, nm): 332, 268; +NaOH: 276, 324, 392; +$AlCl_3$: 276, 348, 384; +$AlCl_3$/HCl: 276, 348, 384; +NaOAc: 272, 344; +NaOAc/H_3BO_3: 272, 348. ^{1}H NMR (250 MHz, CD_3COCD_3, δ, ppm, J/Hz): 6.28 (1H, d, J = 2.1, H-6), 6.57 (1H, d, J = 2.1, H-8), 6.64 (1H, s, H-3), 7.06 (2H, d, J = 8.9, H-3′, H-5′), 7.96 (2H, d, J = 8.9, H-2′, H-6′). Mass spectrum (EI, 70 eV, *m/z,* I_{rel},%): 270 $[M]^+$(100), 269 $[M-1]^+$ (04.2), 242 $[M-28]^+$ (13.6), 241 $[M-1-28]^+$ (04.7), 153 (17), 121 (14.8).

The aglycone was characterized as 4′,5,7-trihydroxyflavone (apigenin) [9-11].

Compound 3: $C_{16}H_{12}O_7$, yellow needles, mp 272°C; UV (λ_{max}, MeOH, nm): 352, 272; +NaOH: 272, 324, 404; +$AlCl_3$: 276, 424; +$AlCl_3$/HCl: 264, 280, 368; +NaOAc: 272, 352; +NaOAc/H_3BO_3: 264, 376. ^{1}H NMR (250 MHz, CD_3COCD_3, δ, ppm, J/Hz): 6.61 (1H, s, H-8), 6.63 (1H, s, H-3), 7.05 (1H, d, J = 8.5, H-5′), 7.50 (1H, dd, J = 8.5; 2.2, H-6′),

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7.53 (1H, d, J= 2.2, H-2′), 3.88 (3H, s, 6-OMe). Mass spectrum (EI, 70 eV, *m/z,* I_{rel},%: 316 $[M]^+$ (100), 167 (17.3), 139 (22.8), 137 (09.6), 109 (2.7).

The aglycone was characterized as 3′,4′,5,7-tetrahydroxy-6-methoxyflavone (nepetin) [12-13].

Compound 4: yellow powder, mp 330°C; UV (λ_{max}, MeOH, nm): 348, 252; +NaOH: 268, 324, 404; +$AlCl_3$: 272, 424; +$AlCl_3$/HCl: 272, 384, 388; +NaOAc: 260, 368,376; +NaOAc/H_3BO_3: 256, 360. ^{1}H NMR (250 MHz, CD_3COCD_3, δ, ppm, J/Hz): 6.27 (1H, d, J = 2.1, H-6), 6.54 (1H, d, J = 2.1, H-8), 6.61 (1H, s, H-3), 7.02 (1H, d, J = 8.1, H-5′), 7.49 (1H, dd, J = 8.1, 2.1, H-6′), 7.52 (1H, d, J = 2.1, H-2′). Mass spectrum (EI, 70 eV, *m/z,* I_{rel},%): 286 $[M]^+$ (100), 258(17.2), 153(25.4), 134(11.2).

The aglycone was characterized as 3′,4′,5,7-tetrahydroxyflavone (luteolin)[14].

All these compounds were isolated from *C. sphaerocephala* L. for the first time.

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