FLAVONOID AGLYCONES FROM *Centaurea napifolia*

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Centaurea napifolia L. belongs to the tribe *Cynarea* of the *Asteracea*, widespread in the entire Mediterranean region. Several medicinal uses have been reported for *Centaurea* species [1, 2] but none for *C. napifolia*.

Previously isolated constituents**.** Cnicin, 4′-acetoxycnicin, melitensin, dehydromelitensin, two esters of dehydromelitensin, and lappaol; a lappaol isomer and 1,2-diacylated glucose [3].

The present study is a complete investigation of the flavonoids of *C. napifolia* .

Aerial parts, collected from El Kala (Algeria) 1992, identified by Dr. Mohamed Kaabeche from the Department of Biology (University of Setif, Algeria) on the basis of Quezel and Santa [4].

A voucher specimen has been deposited in the herbarium of the Department of Botany, University of Constantine under n° 05/1992/CCN12.

Dried powder of aerial parts from the flowering plant of *C. napifolia* was extracted with 70% MeOH. The MeOH extract was concentrated to dryness, the residue was dissolved in boiling water, and the concentrate was taken up with ethyl acetate and *n*-BuOH. The concentrated extract was evaporated and the residue was dissolved in small volumes of MeOH. The *n*-BuOH extract was applied to a column of polyamide MN SC6 and eluted with a gradient of toluene-MeOH with increasing polarity. Three flavonoides (**1-3**) contained in several fractions were isolated by preparative PC on whatman 3MM paper using 15% AcOH and BAW (*n*-BuOH-AcOH-H_2O, 4:1:5 upper phase) as solvents. The ethyl acetate extract was subjected to preparative TLC on silica gel with $CHCl_3$-acetone to yield (**4)** and (**5).** Purification of each compound for spectral analysis was carried out using MeOH over sephadex LH-20. The structures of these compounds were confirmed by UV, ^{1}H NMR, ^{13}C NMR, and MS analyses [5, 6], and all these data were in good agreement with the respective literature data. Compounds **1- 5** have been reported previously from another species of *Centaurea* [7-12], and from *C. napifolia* for the first time.

Compound 1, $C_{15}H_{10}O_7$, UV (λ_{max} , MeOH, nm): 375, 265. Characterized as quercetin.

Compound 2, $C_{16}H_{12}O_6$, M 300(100), UV (λ_{max} , MeOH, nm): 271, 336; + NaOH: 252, 274, 327, 394; +AlCl: 277, 288, 301, 360; +AlCl/HCl: 279, 285, 298, 354. Mass spectrum, *m/z*: 300 $[M]^+$, 167, 121, 118.

^{1}H NMR (CD_3OD, 300 MHz, δ, ppm): 6.55 (1H, s, H-8), 6.60 (1H, s, H-3), 7.85 (2H, d, H-2′, H-6′), 6.95 (2H, d, H-3′, H-5′), 3.90 (3H, s, 6-OMe).

The aglycone was characterized as 4′,5-dihydroxy-6-methoxyflavone (hispidulin).

Compound 3, $C_{17}H_{14}O_6$, M 314(100), UV (λ_{max}, MeOH, nm): 274, 333; +NaOH: 252, 275, 387; +AlCl: 268, 300, 361; +AlCl/HCl: 268, 299, 354.

The IR spectrum of **3** contains absorption bands of hydroxyls (3448 cm^{-1}), carbonyl of g pyrone (1651 cm^{-1}), and aromatic C–C bonds (1600, 1558, 1496 cm). Mass spectrum, *m/z*: 314 $[M]^{+\cdot}$, 299 $[M-15]^+$, 181, 153, 119.

^{1}H NMR (300 MHz, CD_3OD, δ, ppm, J/Hz): 7.958 (2H, d, J = 9, H-2′, H-6′); 6.90 (2H, d, J = 9.0, H-3′, H-5′); 6.85 (1H, d, J = 2, H-3); 6.65 (1H, d, J = 2, H-8); 3.97, 3.85 (6H, s, OCH_3).

Identified as 4′,5-dihydroxy-6,7-dimethoxyflavone (cirsimaritin).

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Compound 4, $C_{18}H_{16}O_7$, UV (λ_{max}, MeOH, nm): 275, 337; +NaOH: 265, 405; +$AlCl_3$: 281, 377; +$AICI_3$/HCI: 285, 370; +NaOAc: 265, 408; +NaOAc/H_3BO_3: 274, 341. Mass spectrum, *m/z*: 344 $[M]^+$, 329$[M-15]^+$, 315$[M-1-28]^+$, 301 $[M-15-28]^+$, 181, 153.

Identical to 4′,5-dihydroxy-3′,6,7-trimethoxyflavone (cirsilineol).

Compound 5, $C_{19}H_{18}O_7$. UV (λ_{max}, MeOH, nm): 275, 338; +NaOH: decomp., +$AlCl_3$: 269, 286, 366; +$AlCl_3$/HCI: 267, 289, 360; +NaOAc: 275, 337; +NaOAc/H_3BO_3: 274, 341. Mass spectrum, *m/z*: 360 $[M]^+$. ^{1}H-NMR (250 MHz, $CDCl_3$, d, ppm, J/Hz): 3.91 (3H, s, OMe-4′), 3.95 (3H, s, OMe-3′), 3.96 (3H, s, OMe-6), 3.99 (3H, s, OMe-7), 6.53 (1H, s, H-3), 6.58 (1H, s, H-8), 6.98 (1H, d, J = 2.5, H-5′), 7.33 (1H, d, J = 8.5, H-2′), 7.51 (1H, dd, J = 8.5; 2.5, H-6′); ^{13}C-NMR (250 MHz, $CDCl_3$, d) 56.1 (OMe-4′), 56.2 (OMe-3′), 58.5 (OMe-7), 61.0 (OMe-6), 91.0 (C-8), 104.5 (C-3), 105.5 (C-10), 110.0 (C-5′), 112.2 (C-2′), 120.1 (C-1′), 123.9 (C-6′), 133.0 (C-6), 149.5 (C-4′), 152.4 (C-3′), 153.8 (C-5), 155.0 (C-9), 159.0 (C-7), 163.0 (C-2), 182.5 (C-4). Characterized as 5-hydroxy-6,7,3′,4′-tetramethoxyflavone.

Thus, these compounds are isolated from *C. napifolia* for the first time.

The *n*-butanol extract of this species was submitted to cytotoxic tests by determination of KB cell growth inhibition. *Centaurea napifolia* extract inhibited cell growth by 9% at 10 ìg/ml and 2% at 1 ìg/ml.

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