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Investigación

Terpenoids and Flavones from *Achillea falcata* (Asteraceae)

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Dedicated to Professor Alfonso Romo de Vivar, a valued collaborator during the early stages of his career

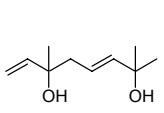
Abstract. Aerial parts of *Achillea falcata* L. furnished the monoterpenes 3,7-dihydroxy-3,7-dimethyl-1,5-octadiene and 3,6-dihydroxy-3,7-dimethyl-1,7-octadiene, the sesquiterpene lactone sintenin and the flavonoids 5-hydroxy-6,7,3', 4'-tetramethoxyflavone (6-hydroxyluteolin-6,7,3',4'-tetramethyl ether) and 5-hydroxy-6,7,8,3',4'-pentamethoxyflavone (desmethoxynobiletin).
Keywords: *Achillea falcata*, Asteraceae, monoterpenes, sesquiterpene lactone, sintenin, flavonoids.

Resumen. El análisis químico de las partes aéreas de *Achillea falcata* permitió la caracterización de los monoterpenos 3,7-dihidroxi-3,7-dimetil-1,5-octadieno y 3,6-dihidroxi-3,7-dimetil-1,7-octadieno, la lactona sesquiterpénica sintenina y los flavonoides 5-hidroxi-6,7,3',4'-tetrametoxi-flavona (6,7,3',4'-tetrametil éter de 6-hidroxi-luteolina) y 5-hidroxi-6,7,8,3',4'-pentametoxiflavona (desmetoxinobiletina).
Palabras clave: *Achillea falcata*, asteraceae, monoterpenos, lactona sesquiterpénica, sintenina, flavonas.

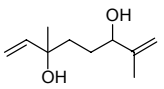
Our groups have previously described the chemistry of two *Achillea* species, *A. ligustica* All. from Sicily [1] and *A. cretica* L. from Cyprus [2]. We now report the results of our study of *Achillea falcata* L. from Lebanon.

Aerial parts of *A. falcata* L. (syns. *A. damascene* DC, *A. sulfurea* Boiss.) were extracted at room temperature with acetone; the extract was purified by silica gel chromatography and radial chromatography to afford five compounds. Of these, 5-hydroxy-6,7,3',4'-tetramethoxyflavone(6-hydroxyluteolin-6,7,3',4'-tetramethyl ether) and 5-hydroxy-6,7,8,3'4'-pentamethoxyflavone (desmethoxynobiletin) were identified by MS and comparison of their ^{1}H-NMR spectra with spectra in our files. Two others, the monoterpenes 3,7-dihydroxy-3,7-dimethyl-1,5-octadiene (**1**) and its isomer 3,6-dihydroxy-3,7-dimethyl-1,7-octadiene (**2**), have been previously reported from *Cinnamum camphora* [3]; diene **1** has also been isolated in our laboratories from *Achillea ligustica* All. [1] where its high resolution ^{1}H NMR spectrum was reported. Doubling of the signals of H-1a, H-1b and H-2 in our 500 MHz ^{1}H NMR spectrum of **2** (see Experimental section) indicated that it was a 1:1 mixture of C-3 epimers. The remaining constituent was the germacradienolide sintenin (**3**) first reported with incorrect C-9 stereochemistry from *Achillea sintenisii* Hub.-Mor. [4], a matter subsequently corrected with material from *Achillea biebersteinii* Afran (as *A. micrantha* Willd.) [5].

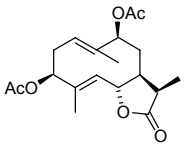
Sintenin has also been isolated from the near Eastern species *A. aleppica* DC. and *pseudoaleppica* Hub. Mor. [6], *A. cucullata* (Haussk.) Bornm., *A. goniocephala* Boiss. *et* Bal. and *A. vermicularis* Trin. [7] as well as from *A. teretifolia* Willd. [8], all, like *A. sintenisii*, *A. biebersteinii* and now *A. falcata*, members of *Achillea* sect. Santolinoidea C. Koch [9] which suggests that sintenin might be a marker for the section. An exception is the Balkan species *A. crithmifolia* Waldst. *et* Kit. several collections of which [10-13] yielded a variety of sesquiterpene lactone types among which sintenin appeared only once [12].



1



2



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Experimental section

General experimental procedures. Column chromatography was performed using Merck Si gel (No. 7734). ^{1}H NMR spectra were obtained on a Varian Inova 500 MHz NMR spectrometer in $CDCl_3$, whereas ^{13}C NMR spectra were run on an IBM/Bruker WP27OSY NMR spectrometer at 67.5 MHz in $CDCl_3$. Mass spectra were acquired on a JEOL MS Route 600 H instrument.

Plant material. Aerial parts of *Achillea falcata* L. were collected at Jab. Kneissé, Lebanon at 1700 m s / l in July 2000.

A voucher specimen (leg., det. and confirmed by N. Arnold *s.n.* is deposited in the herbarium of the Botanical Garden and the Botanische Museum, Freie Universität Berlin, Germany.

Extraction and isolation. Dried and powdered aerial parts (750 g) were extracted with acetone (3 × 5 l) at room temperature for one week each time. The extracts were combined and evaporated at reduced pressure and low temperature (35 °C) to give 58 g of residue. The residue was subjected to dry column chromatography over Si gel with a solvent gradient ranging from petroleum ether (bp 50-70 °C) to EtOAc (100 %) and finally with EtOAc-MeOH (19:1 and 9:1). The fraction eluted with petroleum ether-EtOAc (2:3) was resubmitted to chromatography using petroleum ether-EtOAc (4:1, 3:7 and 1:1) as eluent to afford several subfractions. The subfraction eluted with petroleum ether-EtOAc (3:70 weighing 250 mg was subjected to radial chromatography using CH_2Cl_2-MeOH (99:1) as eluent to afford, in order of increasing polarity, desmethokynobiletin (20 mg) identified by MS and ^{1}H NMR spectrometry, sintenin (10 mg), identified by MS, ^{1}H and ^{13}C NMR spectrometry [5], and 10 mg of **2**. The subfraction eluted with petroleum ether-ethyl acetate (1:1) weighing 200 mg was subjected to radial chromatography using CH_2Cl_2-MeOH (49:1) as eluent to afford in order of increasing polarity 60 mg of 5-hydroxy-6,7,3',4'-tetramethoxyflavone and 45 mg of **1**.

3,7-Dihydroxy-3,7-dimethyl-1,5-octadiene (1): Mass and ^{1}H NMR spectra corresponded to data reported earlier.

3,6-Dihydroxy-3,7-dimethyl-1,7-octadiene (2): 1:1 mixture of C-3 epimers; oil, MS CI (isobutene) 153.1279 (25), 135.1174 (21.9); calcd for $C_{10}H_{18}\text{-}O_2H_2O$ + H 153.1279; for $C_{10}H_{18}O_2\text{-}$ $2H_2O$ + H, 135.1174; ^{1}H NMR ($CDCl_3$) δ 5.89 and 5.88 (both *dd*, J = 17.3, 10.8 Hz, H-2 of epimers A and B), 5.22 and 5.21 (both *dd*, J = 17.3, 1.4 Hz, H-1a of epimers A and B), 4.94 and 4.93 (both q, *J* = 4, 1 Hz, H-8a of both epimers), 4.83 and 4.82 (both *q*, 4 Hz, H-8b of both epimers), 4.04 (*brq*, 6.3 Hz, H-6 of both epimers, 1.70 (*brs*, 3H, H-8), 1.64-1.53 (c, 4H, H-4a,b H-5a,b), 1.28 *s* (3H, H-10).

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