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COMPOSITAE

SESQUITERPENE LACTONES OF *ARTEMISIA VERLOTORUM*

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Abstract—The plant from which vulgarin (tauremisin) was originally isolated has now been identified as *Artemisia verlotorum* Lamotte. A new collection from the original location has yielded vulgarin as the only isolable lactone. Plants designated as the same species collected in southern Germany and in Switzerland contain no vulgarin, but three other lactones.

RESULTS AND DISCUSSION

EARLIER studies on a plant identified at the time of study as *Artemisia vulgaris* L. yielded the sesquiterpene lactone vulgarin,[1] also found in *A. taurica* Willd. and named tauremisin.[2] Because at the time of the early work the plant under study was regarded by one authority as *A. verlotorum* Lamotte, a plant of the latter species, in this case unequivocally identified, was studied upon a later occasion. Specimens collected both in southern Germany and in the Tessin Alps of Switzerland yielded three new lactones—artemorin, anhydroartemorin and verlotorin—but were devoid of vulgarin.[3]

Subsequent reexamination of what was presumably the original plant, collected in Melbourne, Australia, at the site of the earlier collection, confirmed that it was indeed to be regarded as *A. verlotorum* Lamotte. However, since a period of years had elapsed between the early studies[1] and the later collection, the possibility existed that the new Australian collection was a different plant from that used earlier. Accordingly, a collection made near Melbourne in 1970 was reexamined. It was found to contain vulgarin only, and a careful examination failed to disclose the presence of artemorin, verlotorin or anhydroartemorin. The European plant, also examined with care, was found to be devoid of vulgarin.[3]

It is thus apparent that the Australian and European plants are distinct chemovars of the same species. Herbarium specimens from all three areas of collection—Germany, Switzerland and Australia—are all identifiable as *A. verlotorum* Lamotte.†

EXPERIMENTAL

Vulgarin. Dried, milled *A. verlotorum*, collected in January 1970, near Nunawading, Victoria, Australia‡ (4·6 kg) was exhaustively extracted with $CHCl_3$. The residue remaining after removal of the solvent was shaken with a mixture of 5 l. of hexane, 600 ml of methanol and 200 ml of water. The aqueous layer was washed with hexane and extracted with $CHCl_3$. Removal of the $CHCl_3$ left 42 g of a brown syrup which was chromatographed over 500 g of silica gel (Baker, AR3405). Elution was carried out with $CHCl_3$ containing increasing amounts of EtOAc and then EtOAc containing increasing amounts of acetone; twenty-three fractions of 500 ml were collected.

* Contribution No. 2686 from the Department of Chemistry, U.C.L.A., California, U.S.A.

† The vouchers, deposited in the U.C.L.A. herbarium, are identified as follows: Germany, TAG-11069-MM; Switzerland, TR-100869-TA; and Australia, CC-10170-NU.

‡ We are grateful to Dr. C. C. J. Culvenor for collecting the plant and providing herbarium vouchers for the files.

[1] T. A. GEISSMAN and G. A. ELLESTAD, *J. Org. Chem.* **27**, 1855 (1962).
[2] K. S. RYBALKO and L. DOLEJŠ, *Coll. Czech. Chem. Commun.* **26**, 2909 (1961).
[3] T. A. GEISSMAN, *Phytochem.* **9**, 2377 (1970).

Early fractions contained waxy materials which were not characterized. Eluates with $CHCl_3$–EtOAc (9:1 to 6:1) yielded crystalline residues which proved to be vulgarin. Recrystallized from CH_2Cl_2–ether, it melted at 174–175°, and was identical (m.p., i.r., NMR) with an authentic specimen of vulgarin. The yield was 3·2 g.

TLC both of the original extracts and of various column fractions, using authentic artemorin, anhydroverlotorin and verlotorin for comparison, showed that none of these compounds was present. Polar materials in later column fractions were rechromatographed but no further crystalline compounds were obtained.

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CYTOTOXIC FLAVONOLS FROM *BACCHARIS SAROTHROIDES**

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Abstract—Two cytotoxic flavonols, isolated from the leaves and twigs of *Baccharis sarothroides*, have been characterized as 3,4′-dimethoxy-3′,5,7-trihydroxyflavone and centaureidin.

INTRODUCTION

IN THE course of a continuing search for tumor inhibitors from plant origin, we found that alcoholic extracts of *Baccharis sarothroides A. Gray* (Compositae)† showed significant inhibitory activity against cells derived from human carcinoma of the nasopharynx carried in cell culture (KB).[1] We report herein the isolation and identification of cytotoxic flavonols, 3,4′-dimethoxy-3′,5,7-trihydroxyflavone (I) and centaureidin (IV)‡ from *B. sarothroides*. This appears to be the first report of the characterization of specific flavonoids from a *Baccharis* species, although flavonoids have been noted to occur in *Baccharis rosmarinifolia*.[2] In an earlier study, we have isolated two cytotoxic flavonols, eupatin and eupatoretin from *Eupatorium semiserratum* (Compositae).[3] It is noteworthy that centaureidin possesses the same oxygenation pattern as eupatin and eupatoretin.

* Part LXIII in the series "Tumor inhibitors". For part LXII, see S. M. KUPCHAN, M TAKASUGI, R. M. SMITH and P. S. STEYN, *J. Org. Chem.* in press.

† Twigs and leaves of *Baccharis sarothroides* were collected in California in May 1967. The authors acknowledge with thanks receipt of the dried plant material from Dr. Robert E. Perdue, Jr , U S. Department of Agriculture, Beltsville, Md., in accordance with the program developed with U.S.D.A. by the Cancer Chemotherapy National Service Center (C C.N S.C.).

‡ 3,4′-Dimethoxy-3′,5,7-trihydroxyflavone (I) and centaureidin (IV) showed cytoxicity (ED_{50}) against KB cell culture at 2 4 μg/ml and 2·5 μg/ml, respectively.

[1] Cytotoxicity was assayed under the auspices of the C.C.N.S.C. and the procedures were those described in *Cancer Chemotherapy Rept.* **25**, 1 (1962).

[2] E. P. BENIMELI, *Anales Fac. Quim. Farm. Univ. Chile* **16**, 133 (1964).

[3] S. M. KUPCHAN, C. W. SIGEL, J. R. KNOX and M. S. UDAYAMURTHY, *J. Org. Chem.* **34**, 1460 (1969)