CYTOTOXIC FLAVONOLS FROM *GUTIERREZIA MICROCEPHALA*

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Gutierrezia microcephala (DC.) Gray (Asteraceae), commonly known as broomwood, grows in arid regions of the southwestern United States. It has been reported to be toxic to range cattle (1), particularly causing abortion (2). Abortifacient and embryotoxic activities have been demonstrated with saponins obtained from extracts of *Gutierrezia* plants (3-5). Several species of *Gutierrezia* have been investigated chemically, including *G. alamanii* var. *megalocephala* (6), *G. dracunculoides* (7,8), *G. gilliesii* (9), *G. grandis* (10,11), *G. gymnospermoides* (12), *G. lucida* (13), *G. mandonii* (13), *G. microcephala* (14,15), *G. resinosa* (16,17), *G. serothrae* (13,18-20), and *G. spathulata* (9). Many of these plants are rich in flavonoids, which became a subject of chemotaxonomic studies of the *Gutierrezia-Xanthocephalum* complex (6,10,11,15).

As part of our interest in the cytotoxic activity of plant extracts, we have studied the whole plant of *G. microcephala*. We report here the isolation of two isomeric 3-methylated flavonols, namely, 3,3′-dimethylquercetin (5,7,4′-trihydroxy-3,3′-dimethoxyflavone) and 3,7-dimethylquercetin (5,3′,4′-trihydroxy-3,7-dimethoxyflavone), following bioassay-directed fractionation of a MeOH extract of the plant material. Both compounds were identified by interpretation of their spectral properties (uv with standard testing reagents, ^{1}H nmr, and ms) and by comparison with literature data (21). They showed cytotoxic activity against P-388 cells in vitro; the ED_{50}'s were 1.7 μg/ml and 3.2 μg/ml for 3,3′-dimethylquercetin and 3,7-dimethylquercetin, respectively. Neither of these flavonols has been obtained from *Gutierrezia* spp. previously.

EXPERIMENTAL

PLANT MATERIAL.—The plant material of *G. microcephala* used in this investigation was collected in Nevada in May 1981, by the USDA. An herbarium specimen has been deposited at the Morris Arboretum, Washington, DC.

EXTRACTION AND ISOLATION.—Air-dried plant material, including roots stems, and leaves, was defatted with petroleum ether, then exhaustively extracted with MeOH. The residue, after evaporation of the MeOH, was partitioned between $CHCl_3$ and H_2O. Bioassay-directed fractionation of the $CHCl_3$ fraction by repeated column chromatography over Si gel resulted in the isolation of two flavonoids, identified as 3,3′-dimethylquercetin (0.0001%) and 3,7-dimethylquercetin (0.00012%). Details of the isolation procedure and the spectral data of the isolates are available on request.

BIOLOGICAL EVALUATION.—The P-388 (9PS) cytotoxicity assay was performed according to the NIH protocol (22).

ACKNOWLEDGMENTS

This study was supported, in part, by grant CA-33047 from the National Cancer Institute. X.D. thanks the Sichuan Institute of Chinese Materia Medica, Chongqing, China, for a research fellowship.

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Received 5 September 1986