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COUMARINS AND CINNAMIC ACID FROM *GYMNOPHYTON ISATIDICARPUM*

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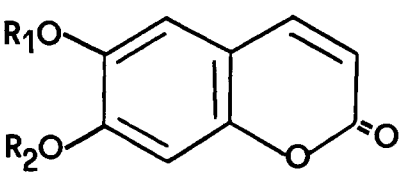
The Umbelliferae family is one of the best known sources of coumarins (1). Lately, the antimicrobial activity of coumarins has been attracting interest because of the possible activity of these compounds as phytoalexins (2–5).

In the course of a systematic investigation of Chilean plants, we examined *Gymnophyton isatidicarpum*, which grows in the vicinity of Santiago, Chile. In screening for antimicrobial activity, a 50% ethanol extract of that species showed activity against *Sarcina lutea*, *Staphylococcus aureus* and *E. coli* (6).

From the petroleum ether extract, a considerable quantity of 6-methoxy-7-geranyloxycoumarin (**1**), an unusual coumarin, was isolated. This was isolated for the first time by Larsen and Sandberg from the roots of *Thapsia garganica*, another Umbelliferae species (7) and, then, from four other Rutaceous plants: *Feronia elephantum* (8), *Haplophyllum hispanicum* (9), *H. pedicellatum* (10), and *Poncirus trifoliata* (11, 12), always in small quantities.

From the methanol extract, two common coumarins, scopoletin (**2**) and esculetin (**3**) and their biogenetic precursor, cinnamic acid, were isolated. The bactericidal activity of *Gymnophyton* is due principally to esculetin. This coumarin has been shown in a previous report to be more bacteriostatic than simple phenols (5). In our assays, 6-methoxy-7-geranyl-oxycoumarin was not active against *Staphylococcus pyogenes*, *E. coli*, *Pseudomonas pyogenes*, *Candida albicans*, *Streptococcus pyogenes* and *Diplococcus pneumoniae*. The substance was tested in multistage assays which are convenient to demonstrate insect growth regulatory and insecticidal effects on three species: a bug (*Dysdercus cingulatus*), a mosquito (*Culex pipiens*)



	R_1	R_2
1	CH_3	Geranyl
2	CH_3	H
3	H	H

and a butterfly (*Adoxophyes orana*). The results show a low insecticide activity on *A. orana* and no insect growth regulatory effect.

EXPERIMENTAL[2]

PLANT MATERIAL.—*Gymnophyton isatidicarpum* (Presl. ex DC) Mathias Constance was collected in December (summer) 1976 in San José dei Maipo near Santiago (prov. Santiago, Region Metropolitana, Chile). A

[1]Fellowship from IILA/CNR. On leave from Facultad de Ciencias Universidad Técnica del Estado, Santiago, Chile.

[2]Melting points were obtained in a Kofler apparatus and are uncorrected; uv spectra were recorded on a Beckman model Acta III spectrophotometer; pmr spectra were determined on a Varian model EM 360 instrument, using TMS as internal standard; mass spectra were run on an LKB-9000 S mass spectrometer.

voucher specimen is kept in the Herbarium of the Museo Nacional de Historia Natural, Santiago, Chile.

EXTRACTION AND FRACTIONATION.—Finely ground aerial parts (5.5 kg) of *G. isatidicarpum* were extracted with petroleum ether and then with methanol in a Soxhlet apparatus. The petroleum ether extract (10 liters) was concentrated to 2.5 liters and let stand at 0° for 48 h. A whitish yellow solid was obtained (solid A, 67.5 g). The methanolic extract (10 liters) was concentrated to 1 liter and 4 liters of water were added.

The mixture was let stand at 0° for 24 h. The solution was filtered and extracted with chloroform. When the chloroform layers were washed with water, dried with anhydrous Na_2SO_4, filtered, and concentrated to dryness, a brownish residue (residue B, 30 g) resulted.

CHARACTERIZATION OF 6-METHOXY-7-GERANYLOXYCOUMARIN (**1**).—Tlc showed just one fluorescent spot for residue A (1 g) which was purified by means of column chromatography (20 g, silica gel) prepared in benzene. Elution with chloroform afforded 750 mg of a white solid which crystallized from ethanol. It gave the following physical properties: mp 88–89° (lit. (8) mp 88–89°); uv, λmax (log ε) (EtOH), 229, 295 and 345 nm (4.17, 4.56 and 4.50); ir, νmax (KBr), 1715, 1610, 1560 cm^{-1}; pmr ($CDCl_3$) δ 1.61 (d, 3H, J=1 Hz), 1.65 (d, 3H, J=1 Hz), 1.76 (d, 3H, J=1 Hz), 2.0–2.25 (m, 4H), 3.83 (s, 3H), 4.85–5.32 (m, 1H), 4.71 (d, 2H, J=6.5 Hz), 5.47 (m, 1H, J=6.5 Hz and J=1 Hz), 6.26 (d, 1H, J=9 Hz), 6.82 (s, 1H), 6.85 (s, 1H), 7.63 (d, 1H, J=9.5 Hz); ms, *m/e* 328·1667 (M^+, calculated for $C_{20}H_{24}O_4$, 328·1674 (11), 259 (10), 193 (22), 192 (100), 191 (15), 177 (12), 164 (6), 149 (5), 136 (16), 93 (10).

These spectral data were identical with those already reported (8). Acid hydrolysis in 2N-methanolic HCl produced scopoletin, mp 204–205°, identical in all respects with an authentic sample.

SEPARATION OF COMPOUNDS OF METHANOLIC EXTRACT.—Residue B (3 g), which showed three principal spots in tlc, was separated by column chromatography. The column was prepared with 300 g of silica gel with benzene and was eluted with benzene, benzene-chloroform mixture, chloroform and chloroform-methanol mixtures.

SCOPOLETIN (**2**).—Elution with benzene-chloroform (1:1) yielded 550 mg of a white solid which crystallized from chloroform. It had a mp 204–205°. The physical and spectral data were identical with an authentic sample.

CINNAMIC ACID.—Further elution with chloroform gave a white solid crystallized from chloroform, mp 133°. Physical and spectral data of the acid and its methyl ester were identical with those of authentic samples.

ESCULETIN (**3**).—Elution with chloroform yielded 60 mg of a solid which was crystallized from chloroform, mp 265–66°. Spectral data were identical with those of an authentic sample.

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