the 3PS test system is defined as an increase in the survival of treated animals over that of control animals resulting in a T/C $\geqq$ 125% (2).

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Chemical Constituents of Gentianaceae XVI: Antitubercular Activity of Xanthones of *Canscora decussata* Schult

Keyphrases □ *Canscora decussata* Schult—antitubercular activity of polyoxygenated xanthones □ Xanthones, polyoxygenated—activity against *Mycobacterium tuberculosis* □ Mangiferin—activity against *Mycobacterium tuberculosis* □ Medicinal plants—antitubercular activity of xanthones of *Canscora decussata* Schult

To the Editor:

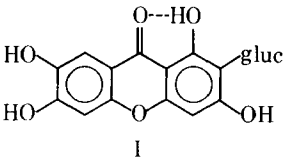
The extract of *Canscora decussata* Schult (Gentianaceae) is used in the treatment of certain mental disorders and of tuberculosis in the Indian system of medicine (1). Previously, the isolation, characterization, and pharmacological screening of about two dozen polyoxygenated xanthones of *C. decussata* were reported from this laboratory (2–5). The pharmacological profile of activities of the total xanthones (excluding mangiferin) and of the major glycoxanthone, mangiferin, was consistent with the reported uses of the plant extract in the treatment of affective disorders. We now wish to report the significant antitubercular activity of the free polyoxygenated xanthones of this medicinal plant.

After concentration, the ethanolic extract of the defatted plant material yielded mangiferin in high yield. The alcoholic mother liquor, after the separation of mangiferin, gave a syrupy mass with further concentration. The nitrogenous constituents were separated from it by aqueous acetic acid treatment in the usual way (2). The chloroform-soluble fraction of the acidic aqueous suspension gave a mixture of about a dozen polyoxygenated xanthones ("total xanthones"); their number and relative abundance were monitored by TLC and mass spectrometry of the mixture, its methyl ethers, and the acetates.

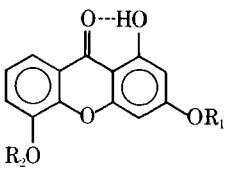
The major xanthonic constituent was mangiferin (I). The remaining total xanthones consisted of three 1,3,5-trioxygenated xanthones (II*a*–II*c*, relative proportion about 12%), four 1,3,5,6-tetraoxygenated xanthones (III*a*–III*d*, 32%), and four 1,3,5,6,7-pentaoxygenated xanthones (IV*a*–IV*d*, 56%), plus some unidentified minor xanthones. All of these compounds were screened for activity against *Mycobacterium tuberculosis* H37 RV using Youman's medium. The tube dilution method was used. The test compounds were added in different concentrations to Youman's medium tubes containing horse serum (10%). The tubes were then inoculated with the organism (about 10^6 million/ml). Thereafter, the tubes were incubated at 37° for 21 days.

After the incubation, the tubes were observed for growth of the microorganism. The minimum concentration of the compounds required for preventing the growth was recorded as the minimum inhibitory concentration (MIC). The total xanthones (II–IV) were found to be more active than mangiferin. The MIC (10 μg/ml) of the total xanthones was comparable to that of streptomycin. Mangiferin showed only weak inhibitory activity, its MIC being 200 μg/ml.

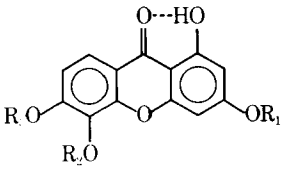
The activity of this class of compounds against *M. tuberculosis* was reported twice before in the literature. 1,3,8-Trihydroxyxanthone, a degradation product of sterigmatocystin (occurring in *Aspergillus versicolor*), was reported (6) to be active at a dilution of 1 in 80,000. Sterigmatocystin had virtually no tuberculostatic effect *per se*. Norswertianolin (3,5,8-trihydroxyxanthone-1-*O*-glucoside), occurring in a



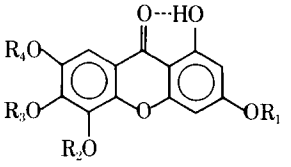
I



II*a*: $R_1 = H$, $R_2 = H$
II*b*: $R_1 = CH_3$, $R_2 = H$
II*c*: $R_1 = CH_3$, $R_2 = CH_3$



III*a*: $R_1 = H$, $R_2 = H$, $R_3 = H$
III*b*: $R_1 = H$, $R_2 = CH_3$, $R_3 = H$
III*c*: $R_1 = H$, $R_2 = H$, $R_3 = CH_3$
III*d*: $R_1 = H$, $R_2 = CH_3$, $R_3 = CH_3$



IV*a*: $R_1 = H$, $R_2 = H$, $R_3 = H$, $R_4 = H$
IV*b*: $R_1 = CH_3$, $R_2 = CH_3$, $R_3 = H$, $R_4 = H$
IV*c*: $R_1 = H$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = H$
IV*d*: $R_1 = CH_3$, $R_2 = CH_3$, $R_3 = CH_3$, $R_4 = H$

number of *Swertia* species (7), was reported to produce tuberculostatic activity, although the degree of its activity was not reported (8). The *Swertia* plant extracts are also reputed for their therapeutic uses in the treatment of tuberculosis.

The antitubercular activity of the total xanthones of *C. decussata* is particularly impressive because no adverse side effects were encountered. Also, no obvious toxicity was detected on prolonged administration of the total xanthones (50 mg/kg ip to albino rats) daily for 4 weeks.

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Improved Method for Microencapsulation of Soluble Pharmaceuticals

Keyphrases □ Nylon (formalin treated) gelatin microcapsules—preparation, physical properties □ Sulfathiazole sodium—microencapsulation, dissolution □ Microencapsulation—soluble pharmaceuticals

To the Editor:

Interest in microencapsulation technology and its application to varied problems is increasing. In addition to many nonpharmaceutical applications (1), microencapsulation has been utilized pharmaceutically to increase product stability, modify drug release, overcome drug incompatibility in formulations, and improve certain physical characteristics of formulations such as compressibility and flow (2). The technology and applications of microencapsulation have been discussed in several monographs and reviews (1–6). However, as Luzzi stated (5), much of this information is found in the patent literature and the control and testing data essential for reproducibility are frequently lacking.

Table I—Percent Sulfathiazole Sodium Released from Microcapsules[a] Prepared by the Formalin-Treated Nylon Gelatin Technique (Formula I)[b] and with Nylon Alone (Formula II)[c] in 0.1 *N* HCl and 0.1 *M* Acetate Buffer (pH 5.6)

	Recoveries[d], %			
	0.1 *N* HCl		0.1 *M* Acetate Buffer (pH 5.6)	
Minutes	Formula I	Formula II	Formula I	Formula II
2	24.5	35.7	4.3	3.8
4	36.5	56.1	11.6	6.5
8	51.5	76.1	22.3	12.5
12	62.5	87.5	29.1	17.5
16	73.0	93.3	34.1	23.4
20	80.5	96.7	37.5	26.7
30	92.0	99.0	45.1	37.4
40	95.5	100.6	51.3	46.9
50	97.5	—	57.0	54.3
60	99.0	—	60.7	59.9
120	—	—	77.3	81.5

[a] One hundred percent of unencapsulated sulfathiazole sodium passed into solution in less than 2 min in 0.1 *N* HCl and 0.1 *M* acetate buffer (pH 5.6). [b] Drug content, 21% (w/w). [c] Drug content, 49% (w/w). [d] Average of duplicate assays upon the same batches.

Of interest is the work of Chang *et al.* (7), in which enzymes in semipermeable microcapsules of nylon, collodion, and heparin-complexed collodion were prepared for potential use in enzyme replacement therapy. More recently, Luzzi *et al.* (8) used a modification of their technique (7) to encapsulate a water-soluble barbiturate in nylon. To prevent loss of the barbiturate from the nylon capsules, the microcapsules were washed in chloroform prior to drying.

The present communication outlines an improved method for microencapsulating soluble drugs. Nylon was used to coat a gelatin matrix containing the drug, and the resulting microcapsules were then hardened with formalin. Sulfathiazole sodium was used as the encapsulated drug. The concentration of reactants required to form nylon and the volume ratios of aqueous and organic solvents were the same as those reported by Chang *et al.* (7). Gelatin USP (5 g) and sulfathiazole sodium (3 g) were dissolved in 60 ml of aqueous phase prior to the encapsulation step. After the nylon-coated capsules containing gelatin and sulfathiazole sodium were formed, 20 ml of formalin (formaldehyde solution USP, 37%) was added to the total reaction volume (approximately 700 ml) and this mixture was gently stirred for an additional 10 min.

The capsules were allowed to stand at 5° for 24 hr to ensure that the hardening of the gelatin within the capsules was complete (9). The microcapsules were separated from the organic phase by vacuum filtration and were then air dried at room temperature to remove formalin vapors, organic solvents, and water. Microcapsules passing through a 100-mesh screen were assayed for sulfathiazole sodium content (21% by weight) and used for dissolution studies. As controls, nylon microcapsules containing sulfathiazole sodium without gelatin were prepared using the same procedure (assay 49% by weight).