Perfluorooctyl Bromide: A Potential Antiobesity Compound

Keyphrases □ Perfluorooctyl bromide—coated on GI tract, effect on food absorption and weight gain, rats □ Absorption, food—effect of perfluorooctyl bromide coated on GI tract, rats □ GI absorption—effect of coating with perfluorooctyl bromide, rats □ Antiobesity agents, potential—perfluorooctyl bromide, coated on GI tract, effect on food absorption and weight gain, rats

To the Editor:

Perfluorooctyl bromide (I) is a chemically and biologically inert, high molecular weight fluorocarbon used as a radiopaque contrast medium (1, 2). Although this compound is immiscible with water, its low surface tension renders it easily spreadable over mucous membranes. This property led to our investigation of its possible use in retarding food absorption and, therefore, as an agent for the treatment of obesity.

The radiopaque nature of I allowed direct observation of its transit through the GI tract using whole body X-ray imaging (Fig. 1). After administration of 2 ml of I[1] *via* an oral intubation needle to a rat weighing about 450 g, an instantaneous coating of the stomach was obtained. It took about 1.5 hr to clear the GI tract of the fluorocarbon, which uniformly coated the walls of the stomach and intestine. Since I serves as a poor solvent for most chemical structures (3), the coating of the stomach and intestines forms a temporary barrier to the absorption of ingested food.

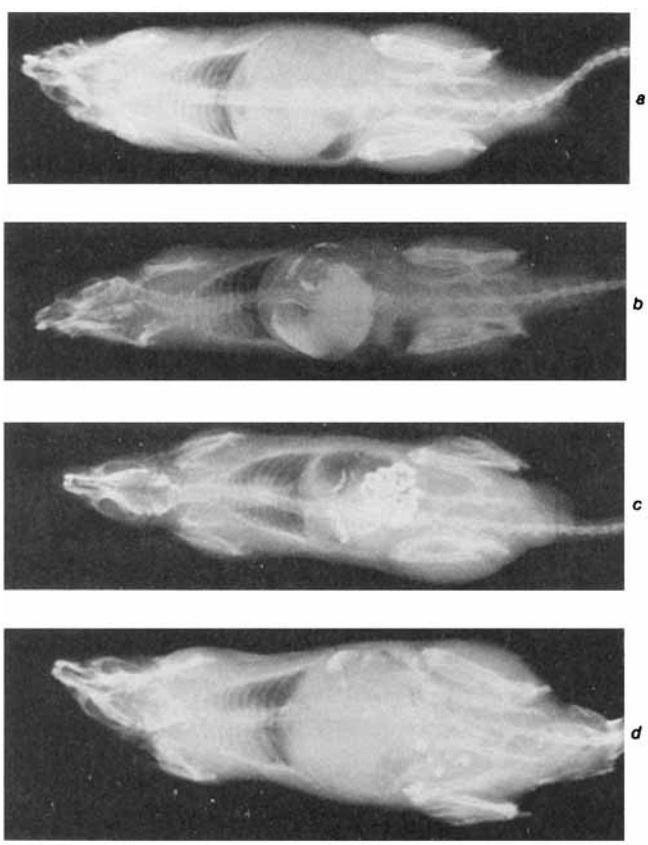

Figure 1—*Whole body X-ray images of rat before* (a) *and 7* (b), *30* (c), *and 75* (d) *min following administration of 2 ml of I.*

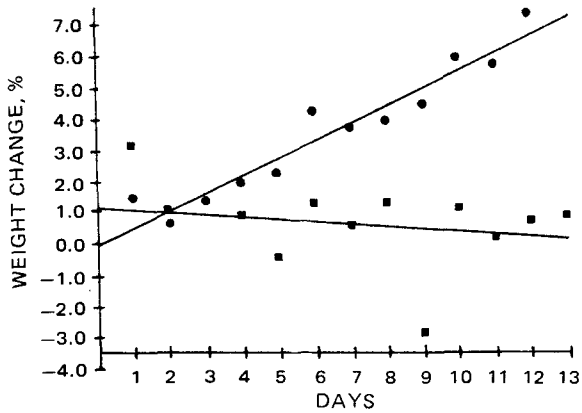

Figure 2—*Comparison of rate of growth of rats given I* (■) *and water* (●) *during their feeding cycle* (n = *19*).

To test this hypothesis, Sprague–Dawley male rats, 400–500 g, were conditioned for 2 weeks by allowing food[2] for only 3 hr/day and water for 14 hr/day, commencing with the food intake cycle. All rats were weighed before the feeding cycle. A crossover study was performed where the test group was given 1 ml of I at 1.5 and 2.0 hr of their 3-hr food intake cycle. The control group was given water instead, and the study was continued for 14 days. The control group showed a net increase in weight whereas the treated group showed a slight decrease (Fig. 2). The weight gain difference between the groups was statistically significant at the 95% confidence level, proving the definite effect of I on food absorption in rats.

The schedule of I administration was chosen to allow at least 1 hr for the coating of the stomach and almost 2 hr of residence time in the GI tract. Variations in this schedule may result in greater or lesser effects of the fluorocarbon on food absorption, and studies in this area are in progress.

The suitability of I for reducing food absorption is due to its complete inertness, lack of absorption from the GI tract, and physical properties that allow its uniform distribution throughout the GI tract. Also, the small quantity of fluorocarbon administered does not result in any apparent change in the bowel movement (diarrhea).

At present, we are designing dosage forms of I that can be tested in humans, and these findings will be reported soon.

(1) D. M. Long and M. S. Liu, *Radiology*, **10S**, 323 (1972).
(2) C. L. Clark, F. Becatlini, and S. Kaplan, *Triangle*, **2**, 115 (1972).
(3) D. M. Long, M. S. Liu, D. Dobben, P. S. Szanto, and A. S. Arambulo, in "Biochemistry Involving Carbon–Fluorine Bonds," R. Filler, Ed., American Chemical Society, Washington, D.C., 1976, pp. 171–189.

[1] Supplied by 3M Co., St. Paul, Minn.

[2] Purina rat chow.

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Cudranone: A Novel Benzophenone Derivative from *Cudrania chochinchinensis* var. *gerontogea*

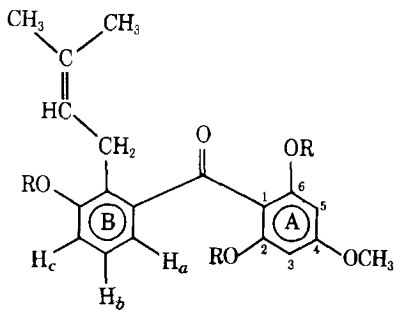
Keyphrases □ Cudranone—isolated and identified from stems and roots of *Cudrania chochinchinensis*, antimicrobial activity evaluated □ Benzophenone derivative—cudranone isolated and identified from stems and roots of *Cudrania chochinchinensis*, antimicrobial activity evaluated □ Antimicrobial agents, potential—cudranone, isolated and identified from stems and roots of *Cudrania chochinchinensis*

To the Editor:

In a largescale program for screening higher plants for antimicrobial activity, an ethanolic extract of the stems and roots of the Chinese plant[1] *Cudrania chochinchinensis* (Lour.) Kudo & Masam. var. *gerontogea* (Sieb. & Zucc.) Kudo & Masam. (Moraceae) exhibited strong activity against a wide range of microorganisms. Partitioning the alcohol extract between water and chloroform concentrated the antimicrobial activity in the chloroform phase. This fraction was then chromatographed over silica gel, using increasing amounts of ether (4–40%) in benzene as the solvent system. Several known crystalline compounds[2] were isolated from the column fractions.

The 4% ether in benzene fraction yielded, upon crystallization from *n*-hexane–ethyl acetate, a novel crystalline substance which was named cudranone (I). This new compound occurred in the form of bright-yellow needles, mp 172–173°, and had a molecular formula of $C_{19}H_{20}O_5$, as supported by elemental analysis and high-resolution mass spectral data.

The 60-MHz ^{1}H-NMR spectrum (taken in acetone-d_6 with tetramethylsilane as the internal standard) provided information on most functional groups of this compound. It revealed the presence of a β,β-dimethylallyl group (two vinylic three-proton singlets at δ 1.53 and 1.50; a broad one-proton triplet at δ 5.23, J = 8 Hz; and a two-proton doublet at δ 3.37, J = 8 Hz). It also exhibited a methoxy singlet at δ 3.83 and three exchangeable phenolic protons as a broad signal at δ 10.17. The aromatic region of the

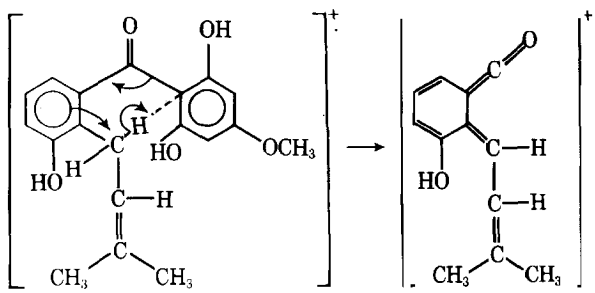


I: R = H
II: R = CH_3
III: R = CCH_3 (=O)

NMR spectrum showed a two-proton singlet at δ 6.00 and a three-proton group of signals forming a complex *ABC* system centered at δ 6.91. The IR spectrum confirmed the phenolic nature of the compound and showed a carbonyl absorption band at λ_{max} (potassium bromide) 6.06 μm, assigned to a hydrogen-bonded ketonic carbonyl function. Thus, by assuming that the compound had two aromatic rings, it was concluded that it must have a benzophenone skeleton rather than a xanthone skeleton like some reported constituents of the *Cudrania* species (1, 2).

The nature of ring A was revealed when the compound gave, in low yields, phloroglucinol monomethyl ether[3] by heating with solid potassium hydroxide at 245–250°. This finding indicated that the rest of the benzophenone moiety must be substituting ring A at C-1 rather than at C-3 or C-5 to account for the equivalency of the two aromatic protons of ring A appearing in the NMR spectrum as a sharp singlet at δ 6.00. This finding also indicated that the β,β-dimethylallyl group and the remaining hydroxyl group should be substituting ring B.

Compound I yielded the trimethyl ether (II) as white needles, mp 126–127°, by treatment with dimethyl sulfate and aqueous sodium hydroxide. The NMR spectrum of II taken in deuterochloroform still showed the complex *ABC* three-proton system in the aromatic region. However, this system was simplified and showed first-order splitting when benzene-d_6 (100%) was used as the solvent. It showed a one-proton doublet[4] at δ 7.23, J = 8 Hz; a one-proton triplet at δ 6.80, J = 8 Hz; and another one-proton doublet[4]



m/e 328 (10%) IV *m/e* 188 (100%)

Scheme I

[1] The plant material was collected in Chia-Yi, Taiwan, in 1974. Its identity was confirmed by Dr. Ping C. Cheng, Taipei Medical College. A voucher specimen is deposited in the herbarium of the Department of Pharmacognosy, School of Pharmacy, University of Mississippi.
[2] To be reported later.
[3] Characterized by direct comparison with an authentic sample (superimposable IR, NMR, and mass spectra and identical R_f values on TLC and retention times on GLC).
[4] The doublets due to H_a and H_c were slightly split (J = 2 Hz) due to *meta*-coupling to each other.