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SHORT COMMUNICATION

THE IDENTITY OF CIRANTIN, A REPORTED ANTIFERTILITY AGENT, WITH HESPERIDIN

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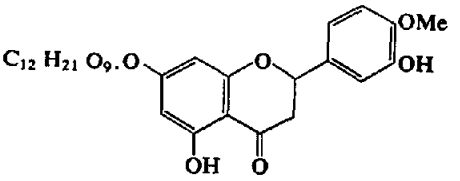
Abstract—Cirantin, a compound isolated from *Citrus aurantium* peel and reported to have oral contraceptive properties in animals, is identical with hesperidin (I).

IN 1955 Ghosh and co-workers[1] isolated from *Citrus aurantium* peel a compound, believed to be a new pyrone, which they called cirantin. Preliminary studies[1] on rabbits indicated its possible efficacy as an oral contraceptive. Ghosh[2] demonstrated that a water-soluble phosphorylated derivative of cirantin was an inhibitor of hyaluronidase *in vitro*. Subsequently, Ghosh and Bose[3] found the water-soluble sodium salt of sulphonated cirantin to be considerably more effective than cirantin itself in preventing pregnancy when administered orally to rats and mice. In view of the need, in both veterinary and, in certain areas, clinical practice, for a fertility control agent which is readily available even if not absolutely effective, we have investigated the constitution of cirantin. We are indebted to Mr. S. K. Datta Roy, of Gluconate Limited, Calcutta, India, for a generous sample of authentic cirantin.

The u.v. spectrum of cirantin (in EtOH) showed λ_{max} 285 nm, λ_{inflex} 225 and 325 nm ($\log \epsilon$ 4·27, 4·38 and 3·59) unaffected by the addition of NaOAc, but altered to λ_{max} 243, 287 and 360 nm ($\log \epsilon$ 4·27, 4·21 and 3·84) on the addition of alkali, and to λ_{max} 306 and 378 nm in the presence of $AlCl_3$. These spectra are typical of a 7-alkoxyflavanone carrying a 5-hydroxyl group.[4] In agreement, the i.r. spectrum of cirantin (in Nujol) shows a hydrogen-bonded aromatic ketone band at 1649 cm^{-1}, together with free and hydrogen-bonded hydroxyl absorption between 3640 and 2540 cm^{-1}. The melting point, 259–264° (reported[1] 250–252°), and optical rotation $[\alpha]_D^{27} - 77{\cdot}4°$ (*c* 0·0086 per cent in pyridine) indicated that cirantin could be identical with hesperidin (I), hesperetin 7-rutinoside, m.p. 261–262°, $[\alpha]_D^{20} - 76{\cdot}1$ (in pyridine).[5] This was confirmed by determination of mixed m.p. with authentic hesperidin, and by direct comparison of i.r. and u.v. spectra and thin-layer chromatographic behaviour. *C. aurantium* is known to be a source of hesperidin.[6]

[1] B. P. GHOSH, A. K. MUKHERJEE and S. BANERJEE, *Naturwissenschaften* **42**, 77 (1955).
[2] B. P. GHOSH, *Indian J. Med. Sci.* **12** (12), 991 (1958).
[3] B. P. GHOSH and S. N. BOSE, *Med. Exptl* **5**, 130 (1961).
[4] R. M. HOROWITZ and L. JURD, *J. Org. Chem.* **26**, 2446 (1961).
[5] G. ZEMPLEN and R. BOGNAR, *Chem. Ber.* **76**, 773 (1943).
[6] M. SHIMOKORIYAMA, in *The Chemistry of Flavonoid Compounds* (edited by T. A. GEISSMAN), p. 286, Pergamon Press, New York (1962), and refs. therein.



(I)

In view of the identity of cirantin with hesperidin, the reports[1–3] on the fertility control properties of cirantin and its derivatives must be compared with data on hesperidin. Phosphorylated hesperidin, known to be a potent hyaluronidase inhibitor,[7] initially showed effective oral contraceptive action not only in rats[8] and mice[9] but also in humans.[9] Later experiments with phosphorylated hesperidin, deposited into the Fallopian tubes of rabbits[10] or administered either orally or intraperitoneally to rats[10–12] and mice,[11–13] failed to reveal any such activity. Negative results were also obtained using hesperidin itself[14] and a hesperidin complex from citrus pulp[15] in rabbits and rats respectively. These results of animal tests contrast with the marked effectiveness of phosphorylated hesperidin as an oral contraceptive in a clinical trial.[9]

[7] J. M. BEILER and G. J. MARTIN, *J. Biol. Chem.* **174**, 31 (1948).
[8] G. J. MARTIN and J. M. BEILER, *Science* **115**, 402 (1952).
[9] B. F. SIEVE, *Science* **116**, 373 (1952).
[10] M. C. CHANG and G. PINCUS, *Science* **117**, 274 (1953).
[11] G. J. MARTIN, *Science* **117**, 363 (1953).
[12] N. MILLMAN and F. ROSEN, *Science* **118**, 212 (1953).
[13] R. Q. THOMPSON, M. STURTEVANT and O. D. BIRD, *Science* **118**, 657 (1953).
[14] M. FRIZ, *Zentr. Gynaekol.* **81**, 1635 (1959).
[15] N. A. FRANK, W. D. POUNDEN and J. W. KESTERSON, *Citrus Ind.* **44**, 9 (1963).