BROOKS, C. D., SCHMID, F. R., BIUNDO, J., BLAU, S., GONZALEZ-ALCOVER, R., GOWANS, J. D. C. HURD, E., PARTRIDGE, R. E. H. & TARPLEY, E. L. (1970). *Rheumatol. Phys. Med. Suppl.*, **10**, 48–63.

GLENN, E. M. & KOOYERS, W. M. (1966). *Life Sci.*, **5**, 619–628.

KAISER, D. G. & GLENN, E. M. (1972). *J. pharm. Sci.*, **61**, 1908–1911.

METZLER, C. M. (1970). *Compilation of Symposia Papers*, p. 380. APhA Academy of Pharmaceutical Sciences.

MORTON, D. M. & CHATFIELD, D. H. (1970). *Biochem. Pharmac.*, **19**, 473–481.

QUEVAUVILLER, A., CHALCHAT, M. A., BROUILHET, H. & DELBARRE, F. (1968). *C. r. Seanc. Soc. Biol.*, **162**, 618–621.

WHITEHOUSE, M. W. & BECK, F. J. (1973). *Drug Metab. Disp.*, **1**, 251–255.

ZAK, S. B., HONC, F. & LUKAS, G. (1972). *Proc. 5th Int. Congr. Pharmacology*, 259 (abst. 1549).

1-(Hexahydroazepin-1-yl)-3-*p*-carboxyphenylsulphonylurea — a metabolite of tolazamide in man

Tolazamide [1-(hexahydroazepin-1-yl)-3-*p*-tolylsulphonylurea, I] is a potent, orally-active hypoglycaemic drug. The present communication describes the identification of a major metabolite isolated from human urine.

A 24 h urine sample (695 ml) from a normal male subject following a 2 g oral dose of the drug was adjusted to pH 1 with concentrated HCl and extracted 5 times with equal volumes of methylene chloride. Combined extracts were concentrated to dryness and the residue triturated with chloroform followed by 0·1 N HCl. The insoluble fraction was twice recrystallized from 70% ethanol to yield a product (76 mg) m.p. 180–182° (uncorrected).

Found: C, 49·4; H, 5·4; N, 12·5; O, 23·0; S, 9·3. Calculated for: $C_{14}H_{19}N_3O_5S$ C, 49·25; H, 5·6; N, 12·3; 0, 23·4; S, 9·4.

Potentiometric titration in a 60% ethanol: dimethylformamide mixture give an equivalent weight of 178 (calculated :170·7) and indicated two acidic groups with pKa′ 5·64 (characteristic of –COOH) and 7·37 (assigned to $-SO_2-NH-$; pKa′ of I under the same conditions was 7·20).

The infrared spectrum showed the characteristic absorptions of I plus the following attributed to a –COOH group: 2660 and 2540 cm^{-1}, acidic–OH; 1420 and 1278 cm^{-1}, $-COO^-$; and 960 cm^{-1}, acidic –OH deformation.

The ultraviolet spectra in acidic and alkaline ethanol showed maxima at 235 ($\epsilon = 17{,}150$) and 232 ($\epsilon = 12{,}150$) nm, respectively. The absorption of the metabolite at longer wavelengths than I (maximum in acidic ethanol, 228 nm, $\epsilon = 14\,200$) is typical of an aromatic acid (Louis, Fajans & others, 1956).

From these results it is concluded that this metabolite of I is 1-(hexahydroazepin-1-yl)-3-*p*-carboxyphenylsulphonylurea analogous to the major tolbutamide metabolite, 1-butyl-3-*p*-carboxyphenylsulphonylurea (Louis & others, 1956; Thomas & Ikeda, 1966).

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REFERENCES

LOUIS, L. H., FAJANS, S. S., CONN, J. W., STRUCK, W. A., WRIGHT, J. B. & JOHNSON, J. L. (1956). *J. Am. chem. Soc.*, **78**, 5701.

THOMAS, R. C. & IKEDA, G. J. (1966). *J. medl Chem.*, **9**, 507–510.