

An appropriate extract was then injected into a Finnigan Model 1015 G.L.C.-Mass Spectrometer fitted with a four channel peak selector, using similar chromatographic conditions. Fragment ions having m/e 169, 109, 111 and 266 were monitored and the results displayed on a pen recorder. These fragment ions are characteristic of metabolites possessing the structures shown in Fig. 1 below. The ion at m/e 169 is associated with all likely heptabarbitalone metabolites; modification of the cycloheptenyl substituent is indicated by peaks at m/e 264 or 266 and m/e 109 or 111.

With this technique it is possible to detect nanogram amounts of material in a highly specific manner. The second 8 h urine extract shows a complete absence of unchanged drug and the presence of three barbiturate metabolites. One is the 3'-hydroxylated derivative; another the 3'-oxo derivative (confirmed by comparison with authentic samples); the third is an as yet unidentified metabolite.

REFERENCES

- GILBERT, J. N. T., MILLARD, B. J., POWELL, J. W., WHALLEY, W. B. & WILKENS, B. J. (1972). Drug metabolism—Nealbarbitone. *J. Pharm. Pharmacol.* (in the press).
 HAMMAR, C. G., HOLMSTEDT, B., LINDGREN, J. E. & THAM, R. (1969). The combination of gas chromatography and mass spectrometry in the identification of drugs and metabolites. *Adv. Pharmacol. Chemother.*, **7**, 53–89.
 HAMMAR, C. G., HOLMSTEDT, B. & RYHAGE, R. (1968). Mass fragmentography. Identification of chlorpromazine metabolites in human blood by a new method. *Anal. Biochem.*, **25**, 532–548.

Effects of indomethacin on rat gastric acid secretion and mucosal blood flow

I. H. M. MAIN and B. J. R. WHITTLE

Department of Pharmacology, The School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX

Simultaneous measurement of gastric mucosal blood flow (MBF) and acid secretion may help to elucidate the mechanism of action of drugs which affect gastric function. The ^{14}C -aniline clearance technique for measuring MBF in the anaesthetized rat (Main & Whittle, 1972), which provides a convenient means of studying these parameters, will be demonstrated.

We have used this technique to study the acute effects of indomethacin, a potent inhibitor of prostaglandin synthesis (Vane, 1971), which causes gastric mucosal erosions. During the steady submaximal secretory response to pentagastrin ($0.2\text{--}0.33[\mu\text{g}/\text{kg}]\text{min}$), indomethacin, injected intravenously in doses of 20 to 40 mg/kg, caused an increase in acid secretion (by a mean of $120\% \pm$ standard error of the mean 49% in 5 experiments, 2 h following injection) accompanied by a rise in MBF. These effects were usually followed by the appearance of blood in the gastric perfusate, and mucosal erosions were observed post mortem. During basal conditions, indomethacin had no effect on acid secretion but reduced MBF (by $45.2 \pm 9.3\%$, mean, S.E. of mean; $n=4$).

Although these results indicate that indomethacin can alter acid secretion and MBF in the rat, it is not yet clear whether these effects are causally related to the development of mucosal erosions. The extent to which these findings can be attributed to inhibition of prostaglandin synthesis is not known. However, our results are compatible with the hypothesis that endogenous prostaglandins have a role as inhibitors of acid secretion and as vasodilators in the rat gastric mucosa.

B.J.R.W. is an M.R.C. Scholar

REFERENCES

- MAIN, I. H. M. & WHITTLE, B. J. R. (1972). Effects of prostaglandin E_2 on rat gastric mucosal blood flow, as determined by ^{14}C -aniline clearance. *Br. J. Pharmacol.*, **44**, 331–332P.
 VANE, J. R. (1971). Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature, New Biol.*, **231**, 232–235.