by the systemic injection of bicuculline (Clarke *et al.*, 1972). Further investigation of these phenomena is in progress.

The use of a small computer for on-line data analysis will also be demonstrated.

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Gas chromatography – mass spectrometry for the identification of barbiturate metabolites

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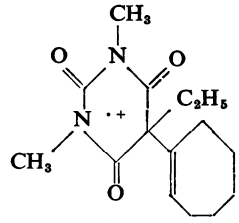
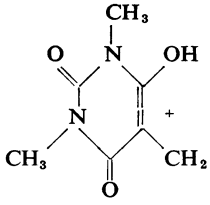
Combined gas liquid chromatography/mass spectrometry has been used previously in the study of drug metabolism (Hammer, Holmstedt, Lindgren & Tham, 1969). The sensitivity of the technique is greatly enhanced when the mass spectrometer is used as a specific detector for certain fragment ions, a procedure called mass fragmentography (Hammar, Holmstedt & Ryhage, 1968). The present demonstration makes use of this technique in the study of the metabolism of heptabarbitone in man.

A single dose of heptabarbitone (400 mg) was taken by a volunteer and urine collected in 8 h batches. Aliquot portions (100 ml) were extracted and processed by methods previously described (Gilbert, Millard, Powell, Whalley & Wilkens, 1972). The extracts from a blank urine sample and each of the 8 h samples were run on a Pye 104 gas chromatograph fitted with a flame ionization detector. The instrument was fitted with a 9 ft 1% QF1 column and was operated isothermally at 200° C for 5 min, then programmed at 6° C/min to 250° C.

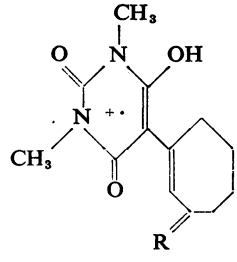
Fig. 1 Mass spectroscopic ions.



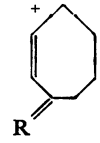
Parent methylated heptabarbitone m/e 278



Fragment ion present in all 5-ethyl substituted barbiturates m/e 169.



R=H,OH m/e 266
R=O m/e 264



R=H,OH m/e 111
R=O m/e 109

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 heptabarbitone 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.

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

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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 (0·2–0·33[μg/kg]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

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