of fat in adipose tissue lipoprotein lipase is either synthesized or its activity is enhanced, which would suggest that this enzyme participates in the formation of fat depots. The finding of a reduced activity during fat mobilization must not be taken as evidence that lipoprotein lipase does not participate in this process. It is possible that during this process this enzyme is liberated by adipose tissue, just as after the administration of heparin—but much more slowly—to be transported to another site in the organism where its action is necessary.

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Metabolism of Bemegride labelled with Carbon-14

BEMEGRIDE (β-ethyl β-methyl glutarimide), labelled with carbon-14 in both the α positions, is excreted largely in the urine and to a lesser extent in the bile and fæces when administered to mice, rats and guinea pigs[1]. Chromatograms of urine and bile from these animals were developed by the ascending technique using *n*-butanol/acetic acid/water (12 : 3 : 5, v/v). Autoradiographs of chromatograms of guinea pig bile showed only one spot (R_F 0·88) which was identical in mobility to the control-labelled bemegride. The urine of rats, collected 15–120 min. after administration of labelled bemegride, revealed two spots of R_F values 0·88–0·89 and 0·77–0·81. The faster moving fraction moved as one spot when labelled bemegride was added to the urine before chromatography. The spot with the lower mobility increased in intensity over the 15–120 min. period of urine collection. Urine from mice, 15–120 min. after bemegride injection, showed two spots with R_F values similar to those of rat urine, while urine collected 8 hr. after injection revealed a third spot of R_F 0·40–0·46. This spot became progressively more intense and the faster moving fractions correspondingly less up to 24 hr.

Bemegride labelled with carbon-14 was incubated with rat liver slices in Krebs–Ringer-phosphate solution for 5 hr. at 37° C. and two radioactive spots were revealed on chromatography of the liquid medium. The R_F values, 0·88 and 0·80, corresponded to those obtained from rat urine, suggesting that the liver is the site of bemegride metabolism *in vivo*.

Partition of rat urine with ether followed by chromatography of the two layers showed that the compound of R_F 0·80 was more soluble than bemegride in the aqueous phase (the concentrations were estimated as the relative density of the spots on the autoradiographs). This partition was not changed when determined at *p*H 1 or 7, which indicates that the metabolic fraction is of a similar nature to the unchanged glutarimide. The partition between mouse urine and chloroform revealed that while the spots of R_F 0·88 and 0·79 were distributed between the two layers in a manner similar to that between rat urine and ether, the fraction of R_F 0·45 was confined to the aqueous layer. This shows that the slowest moving fraction is extremely soluble in water.

Failure to detect carbon dioxide labelled with carbon-14 in the expired air of mice receiving labelled bemegride suggests that there is no drastic degradation of the glutarimide molecule. The metabolic products of bemegride detected in the urine of the mouse and rat do not appear to be hydrolysis products of this glutarimide, for the R_F values of β-ethyl β-methyl-glutaramic acid and -glutaric acid are 0·97 and 0·99 respectively in *n*-butanol/acetic acid/water. Succinimide has been shown to be hydrolysed to succinic acid *in vivo*[2] but this metabolic pathway does not appear to be available for the glutarimides. This is supported by the finding that the imide ring of α-ethyl α-phenyl glutarimide remains intact *in vivo*[3]. It is also interesting to note that *Lactobacillus* species are unable to hydrolyse α-amino-glutarimide[4]. β-(2-hydroxyethyl) β-methyl glutarimide, isolated from the urine of a patient who received a large dose of bemegride[5], was found to have an R_F value (0·80–0·83) similar to that of the slower-moving fraction in rat urine, but results from studies in rats involving unlabelled bemegride suggest that these two fractions are not identical.

In the chromatographic location of the hydroxy derivative of bemegride use was made of the technique of Rydon and Smith[6]. This method has proved a simple and valuable means of locating glutarimides on paper chromatograms. The limit of sensitivity for detection is 20–30 μgm. of glutarimide/cm.^{2}. By using a 2 per cent starch 1 per cent potassium iodide solution a good definition of the spots is obtained.

It is clear that bemegride, while excreted partly unchanged, is metabolized *in vivo* to produce more water-soluble compounds which probably possess an intact glutarimide ring. The metabolic pathways in the rat and mouse are similar.

Work is in progress to isolate and identify these metabolic products from the urine of mice and rats receiving unlabelled bemegride.

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