level of these substances was concurrently determined in the blood. Moreover, the above mentioned determinations were extended to urine and blood samples obtained from animals treated with insulin.

The results of the *in vitro* and *in vivo* experiments indicated that there is a significant difference in the rate of phenylbutazone metabolism in the normal and alloxan diabetic rats and rabbits, being slower in the alloxan-treated group. Because NADPH is involved in drug metabolism by microsomes it was speculated that the nucleotide may be deficient in the diabetic anaimals. To probe this possibility a specific micro assay procedure for NADPH in biological material was developed and applied to livers of normal and alloxan diabetic animals. The results indicated a very sharp drop in hepatic NADPH in the latter group as compared to the controls.

Metabolism of 5,8,11,14-eicosatetraynoic acid in the rat

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Administration of 5,8,11,14-eicosatetraynoic acid (I) (2g/day for 3 to 4 months) to patients suffering from acne decreased sebum production by up to 40% over control values (Strauss, Pochi & Whitman, 1967), indicating a potential use as an anti-acne agent. The metabolism of this compound is not known, but the disubstituted acetylene group in a number of drugs is apparently biologically stable.

$$CH_3{\cdot}(CH_2)_4{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}CH_2{\cdot}C{\equiv}C{\cdot}(CH_2)_3{\cdot}COOH....I$$

Intravenous administration (0·7 mg/kg) of Δ^{5-6}-^{14}C–I to the rat resulted in an initial rapid concentration of radioactivity in the liver (maximum of 40% of dose at 15 min to 1 h). This activity was excreted almost exclusively as metabolized drug via the bile to give about 60% of the radioactivity in the intestinal contents in 6 h. However it was only after 4 to 5 days that this amount of activity was excreted in faeces following i.p. administration of a similar quantity of radiolabelled I. Also, in the bile-duct-cannulated rat about 90% of administered activity was secreted in bile in 24 h, while in the intact animal only 40% appeared in faeces and 3% in urine in 18 h. Thus extensive reabsorption and entrohepatic cycling of this material was occurring. Within 5 days of an i.p. injection most of the radioactivity had been excreted with 65–68% in faeces, 8–17% in urine and 2–3% expired as $^{14}CO_2$. The latter would indicate a minor metabolic route by oxidative attack on the Δ^{5-6}-acetylene bond, probably following initial β-oxidation. The activity remaining in the body at 5 days (14–22%) was concentrated mainly in skeletal muscle (7·7%), skin (4·3%) and fat (3·8%).

Analysis of bile by radio-t.l.c. indicated exclusive incorporation of the radiolabel in phospholipids. Hydrolysis released a dicarboxylic fatty acid fraction as the main radioactive area. Further analysis indicated the presence of two non-endogenous compounds corresponding (by carbon number correlation on g.l.c.) to C-18 and C-16 dicarboxylic acids. In addition, examination of urine and faeces also indicated the presence of [^{14}C]dicarboxylic fatty acids. The finding of these products would suggest that both β- and ω-oxidative processes are important in the metabolism of I. Corroboration of the β-oxidation pathway was obtained from a similar study with 1-^{14}C-I. Within 5 days of an i.p. injection, 40% of the radioactivity was expired as $^{14}CO_2$ and the activity secreted in bile was associated mainly with the sterol/bile acid fraction, little remaining in the fatty acids.

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REFERENCE

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