Metabolism and incorporation in the tissues of arachidonic acid in normal and essential fatty acid deficient rats

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The metabolism of arachidonic acid (AA) was studied after i.v. injection of [1-^{14}C]-AA into rats. The urinary excretion of radioactive material was determined in both normal and essential fatty acid (EFA) deficient rats. The highest amounts were excreted on the first day. After 15 days there was still a certain amount of radioactivity present in the urine. The overall excretion of radioactivity was considerably lower in EFA-deficient rats. There was a difference between normal and EFA-deficient rats in the time in which the excretion of the radioactivity was reduced to 50% in both the period of 1–4 and 5–15 days.

Radioactive metabolites were isolated from the urine by Amberlite chromatography and TLC. $^{14}CO_2$ production was measured in normal animals. Highest formation occurs in the first hour. At the end of the second hour, the amount of $^{14}CO_2$ rapidly diminishes. Incorporation of AA in the tissues was determined after the injection of 92.5 μg AA containing 18.5 μCi [1-^{14}C]-AA into normal and EFA-deficient rats. At different times, the animals were sacrificed and ultra-thin total body slices were prepared. Of the latter, autoradiograms were made by long-term exposure. After 5 min, the highest level of radioactivity is seen in the following organs:

Normal: brown fat, perispinal fat, liver, heart muscle, kidney, adrenal. The distribution in the liver was not uniform.
EFA-deficient: similar

After 30 min
Normal: liver
EFA-deficient: same as 5 min;

After 24 h
Normal: radioactivity had nearly disappeared, small amount present in liver
EFA-deficient: same as 30 min, small decrease.

These results indicate that EFA-deficient rats retain the injected AA longer than normal animals. In how far a relationship exists between the rapidity of incorporation of AA and prostaglandin metabolism in the tissues is unknown. A higher sensitivity of EFA-deficient rats to certain effects of prostaglandins has been reported (Bonta & Parnham, 1979). This fact may eventually establish a link with the enhanced incorporation of AA into certain tissues.

Reference

BONTA, I.L. & PARNHAM, M.J. (1979). Time-dependent stimulatory and inhibitory effects of prostaglandin E_1 on exudative and tissue components of granulomatous inflammation in rats. *Br. J. Pharmac.*, **65**, 465–472.

Effects of exogenous arachidonic acid on the anti-inflammatory actions of dexamethasone in the rat

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It has been postulated that the anti-inflammatory action of steroids may be due to inhibition of arachidonic acid production from phospholipids (Hong & Levine, 1976). As arachidonic acid is the precursor not only of the proinflammatory prostaglandins but also of the chemotactic lipid 12-L-hydroxy-5, 8, 10, 14-eicosa-tetraenoic acid (Turner, Tainer & Lynn, 1975) the proposal offers an explanation for the effects of anti-inflammatory steroids on the cellular as well as the exudative phase of inflammation. We have tested this hypothesis by investigating the effects of exogenous arachidonic acid on the inhibition by dexamethasone of carrageenin-induced oedema and carboxymethylcellulose-induced cell emigration in the rat.

Oedema was produced in the left hind paw of female PVG/c rats by subplantar injection of 0.1 ml 1% (w/v) carrageenin in saline. Arachidonic acid was given with the carrageenin. Paw volumes were measured by mercury displacement. Cell emigration was induced in male PVG/c rats by injecting 5 ml of 2% (w/v) carboxymethylcellulose into a dorsal air pouch (Ishikawa, Mori & Tsurufuji, 1969). Exudate fluid was diluted with heparin-saline and cells (predominantly polymorphs) were counted using a haemocytometer. Dexamethasone was given orally 1 h (cell emigration) or 2.5 h (oedema) before induction of inflammation.

Arachidonic acid (1 mg/kg) increased carrageenin