Recovery of prostaglandin-like fatty acids from human allergic contact eczema using a skin perfusion method

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A method of continuous *in vivo* cutaneous perfusion using warm Tyrode solution has been developed which permits direct analysis of pharmacological agents released in inflamed human skin (Greaves & Søndergaard, 1970). Eczematous skin of sensitized patients was perfused for periods varying from 60–90 min and successive 15 min aliquots of perfusate were subjected to assay. The rate of infusion was 2 ml/min, and 40–70% of the infused Tyrode solution was recovered in the perfusate. Histamine and kinin activity were determined by bioassay and 5-hydroxytryptamine by spectrofluorometry. Using this method smooth muscle-contracting activity (SMCA), previously unrecognized in allergic eczema has been recovered (Søndergaard & Greaves, 1970). This activity, present in twenty-one of thirty patients studied, was not due to histamine, kinins, 5-hydroxytryptamine or acetylcholine. Its pharmacological properties and its solubility in ethyl acetate at pH 3 suggested that it contains fatty acid activity of the prostaglandin type. Thin-layer chromatography of the ethyl acetate extracted perfusate indicates that SMCA contains a mixture of prostaglandins.

Histamine was found in seven patients. Kinin activity was recovered in twelve of the thirty subjects but these results did not differ significantly from those obtained in the normal skin of eighteen control subjects. No 5-hydroxytryptamine, histamine or SMCA was found in the control group.

This work was supported by the Nuffield Foundation and Fisons Ltd.

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Preliminary study on the effects of fenfluramine derivative, 'S992' in man

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In rats, the fenfluramine derivative, S992 (*m*-trifluromethyl-phenyl)-1-[*β*-(benzyloxy) ethyl] amino-2-propane), exerts an anorectic effect, produces a loss of body weight and causes an elevation in free glycerol and free fatty acids (FFA) in the blood plasma (Duhault & Malen, 1970). A preliminary study was made on the effects of orally administered 'S992' in adult human volunteers eating normal diets, *ad libitum*.

Thirty subjects (88–157% of ideal body weight) completed the trial which was as follows; week 1, control; week 2, 150 mg/day; week 3, 300 mg/day; week 4, 450 mg/day; week 5, 600 mg/day; and week 6, a final control week. On the first and last days of each week, the subjects were weighed in the morning on waking, before breakfast and immediately after bladder emptying. Blood samples were obtained, with the subjects at rest, for analysis of plasma FFA, free glycerol, triglycerides, ketones, cholesterol, and glucose, by methods previously described (Pawan, 1969).

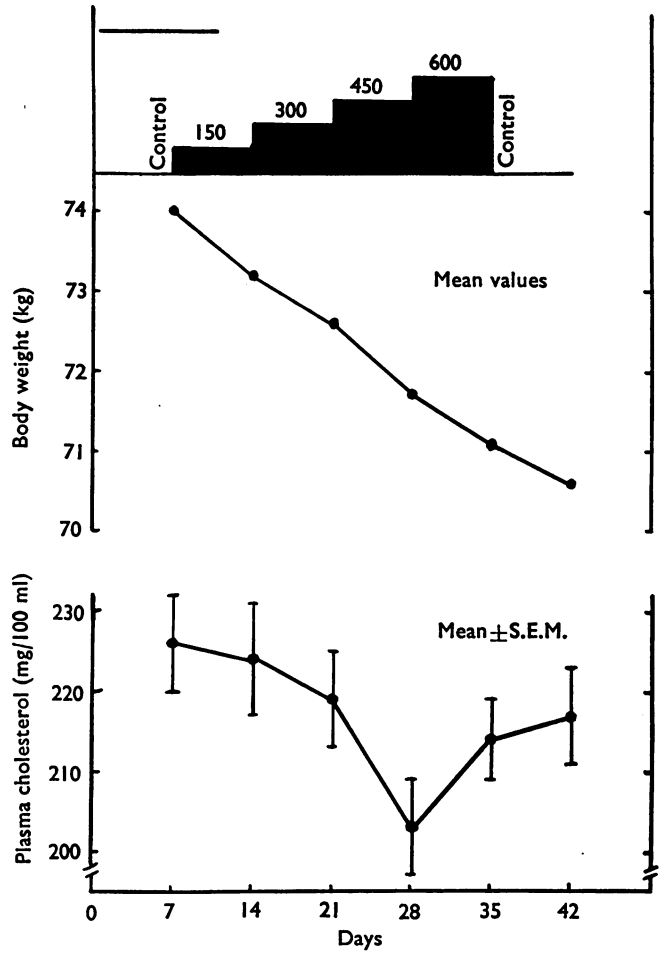

FIG. 1. The daily dose of S992 (mg) is shown at the top. Body weight (kg) and plasma cholesterol concentrations (mg/100 ml) are plotted against time (days).

There was a significant loss of body weight and fall in serum cholesterol concentration (Fig. 1). During the experiment, the following subjective effects were reported by some of the volunteers (numbers in parentheses): dry mouth and thirst (three); depression (three); irritability (five); sleepiness (thirteen); insomnia (one); reduction in cigarette consumption (seven); reduction in alcohol consumption (five).

Double-blind studies are now in progress to establish whether or not these effects were caused directly by the drug or were due to some other factor such as a change in diet.

We thank Servier Laboratories Ltd. for supplies of 'S992'.

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