

THE ANTI-INFLAMMATORY AND ANTIDIURETIC ACTIONS OF FRACTIONS OBTAINED FROM XANTHOGLABROL

BY R. BEST AND R. S. H. FINNEY

From the Biology Department, College of Technology, Leicester

Received May 23, 1961

DURING the preparation of potassium glycyrrhizinate by the method of Ruzicka and Leuenberger (1936) a yellow acidic material was isolated and named "Xanthoglabrol". In a preliminary report D'Arcy, Kellett and Somers (1957) showed that the sodium salts of this mixture had anti-inflammatory and antidiuretic activity in the rat. The separation of "Xanthoglabrol" into four fractions and an evaluation of their anti-inflammatory and antidiuretic properties is now described.

Fractionation of Xanthoglabrol. Partial evaporation of an ethereal solution of "xanthoglabrol" gave a yellowish white solid (Fraction IV). The remaining ether soluble material was recovered from the solvent and the mixture separated into three fractions on a column 11.5×3.25 cm. packed with aluminium oxide Grade I. The mixture (2 g.) was dissolved in 20 ml. of a solvent consisting of acetone (210 ml.), methanol (40 ml.) and 10 per cent aqueous sodium hydroxide (10 ml.) and placed upon the column. The same solvent was used for elution. Fraction I of the mixture was recovered from the first 260 ml. of the eluate, Fraction II from the following 325 ml. and Fraction III from the next 715 ml.

After evaporating each batch of eluate to dryness the residue was dissolved in water and the solution neutralised. The resulting precipitate was extracted with ether and recovered in the usual manner.

A total of 33 g. of crude material was chromatographed in this way yielding the following fractions: I, 7.6 g.; II, 13.2 g.; III, 9.0 g.

Anti-inflammatory activity. Cotton wool pellets were implanted subcutaneously into rats and after seven days, the pellets were removed, dried and weighed (Meier, Schuler and Desaulles, 1950). In the untreated animal the deposition of granulation tissue causes an increase in weight of the pellet. An anti-inflammatory compound depresses the production of granulation tissue. Four pellets were implanted in each rat in this way and at least five rats were used in each group.

Urine output and composition was investigated with groups of male rats starved for 18 hr. and then given 5 per cent of the body weight of distilled water by mouth as a loading-dose. Injection of the test material was made at this time, and the control animals treated with an equivalent volume of normal saline.

The urine output of each rat was noted at intervals over the next 5 hr. and the total 5 hr. urine sample of each rat was then analysed for sodium and potassium with a flame photometer. The urine volume and the sodium and potassium excretion of the test animals was compared with the controls.

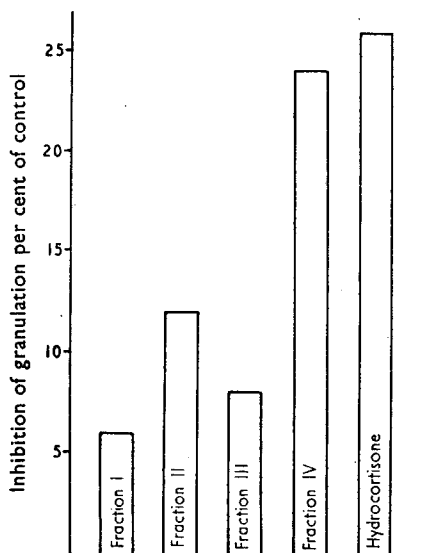


FIG. 1. The anti-inflammatory activity of "xanthoglabrol" fractions and hydrocortisone in the cotton-wool pellet test at 4 mg./rat/day.

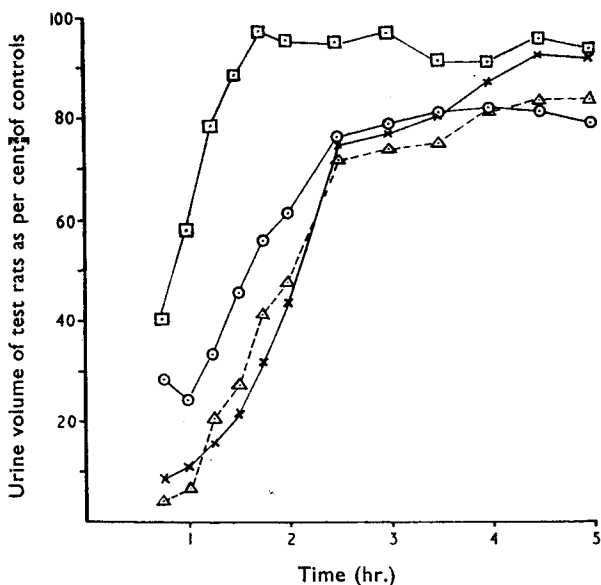


FIG. 2. The anti-diuretic action of "xanthoglabrol" fractions upon the rat at a dose of 2.5 mg./100 g. intraperitoneally.

○—○ Fraction I. △—△ Fraction II. □—□ Fraction III. X—X Fraction IV.

Each point is the mean of 10 observations.

FRACTIONS FROM XANTHOGLABROL

RESULTS

Anti-inflammatory activity. All four fractions showed a linear relation between the anti-inflammatory activity and the logarithm of the dose.

As there was some daily variation in the results of the cotton pellet test, the relative activity of each fraction and of hydrocortisone was evaluated using groups of 15 rats, all fractions being examined over the same period. At a dose level of 4 mg./rat/day, Fraction IV had a greater activity than the other fractions, being similar in potency to hydrocortisone (Fig. 1).

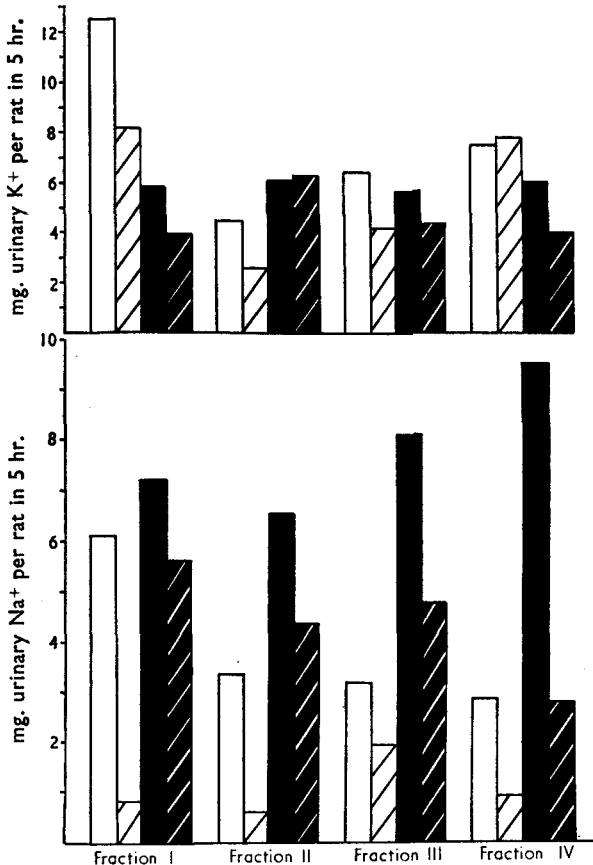


FIG. 3. Upper graph. The effect of "xanthoglabrol" fractions on urine potassium levels at a dose of 2.5 mg./100 g. sub-cutaneously to normal and adrenalectomised rats.

Lower graph. The effect of Xanthoglabrol fractions on urine sodium levels at a dose of 2.5 mg./100 g. sub-cutaneously to normal and adrenalectomised rats.

Unshaded column, normal control (10 rats).

Hatched column, normal test (10 rats).

Solid column, adrenalectomised control (16 rats).

Striped column, adrenalectomised test (16 rats).

Antidiuretic activity. With all fractions, an intraperitoneal injection of 2.5 mg./100 g. weight gave a strong antidiuretic effect (Fig. 2). This was accompanied by a reduction in the amount of sodium being excreted although the potassium excretion was only slightly affected. The same dose subcutaneously did not give the antidiuretic action, but examination of the urine showed a fall in sodium excretion, with a varying fall in potassium excretion.

Sodium excretion also fell in adrenalectomised rats similarly treated (Fig. 3).

These results are in sharp contrast to those obtained after deoxycorticosterone where a fall in sodium excretion occurred with an increase in urinary potassium levels (Marcus, Romanoff and Pincus, 1952), and it is suggested that the action of "Xanthoglabrol" upon urine electrolyte concentration is not mediated through the adrenal glands.

Acknowledgements. The authors wish to express their thanks to Professor E. E. Turner, F.R.S., Mr. D. E. M. Wotton, and Dr. S. Gottfried, of Biorex Laboratories Limited, London, E.C.1, for their advice, criticism and generous supply of materials, and Mr. H. S. Grainger of Westminster Hospital for the preparation of "xanthoglabrol".

REFERENCES

- D'Arcy, P. F., Kellett, D. N. and Somers, G. F. (1957). British Pharmacological Society Oxford Meeting.
Meier, R., Schuler, W. and Desaulles, P. (1950). *Experientia*, **6**, 469.
Marcus, F., Romanoff, L. P. and Pincus, G. (1952). *Endocrinology*, **50**, 286-293.
Ruzicka, L. and Leuenberger, H. (1936). *Helv. Chim. Acta*, **19**, 1402-1406.

The paper was presented by MR. BEST.