Biochemical Pharmacology, Vol. 18, pp. 531–532. Pergamon Press. 1969. Printed in Great Britain

SHORT COMMUNICATIONS

Effect of anti-inflammatory drugs on plasma corticosterone level in albino rats

(*Received* 25 *April* 1968; *accepted* 5 *July* 1968)

THE ANTI-INFLAMMATORY action of several drugs is said to be mediated through the pituitary adrenal axis. Salicylates repeatedly have been found to cause a marked reduction in ascorbic acid and cholesterol contents of adrenals in experimental animals.[1,2] Done *et al.*[3] have demonstrated marked elevation of the concentration of circulating 17-hydroxycorticosteroids throughout the period of salicylate administration and concluded that their anti-rheumatic effect is mediated through the pituitary adrenal system. In the present study, the effect of newer anti-inflammatory agents viz. indomethacin,[4] oxyphenbutazone[5,6] and β-glycyrrhetinic acid[7,8] on plasma corticosterone level and adrenal weight has been studied in albino rats.

Plasma corticosterone was estimated by the method of Zenker and Bernstein[9] involving the double extraction technique of Silber and Porter[10] and a modification of the fluorescence technique described by Sweat.[11] Adult rats of either sex weighing between 130 and 170 g were divided into groups of five animals each. One group of animals served as control and the other groups received the drugs i.p. daily for 6 days from the commencement of experiment. Plasma was obtained after decapitation of rats on the 7th day. Extraction and washing were done with chloroform (45 ml) and sodium hydroxide (0·1 N, 4·5 ml) respectively. The fluorescence was measured by the Aminco Bowman Spectrophotofluorometer at excitation and emission wavelengths of 450 and 520 mμ respectively.

The effect of indomethacin, oxyphenbutazone and β-glycerrhetinic acid on plasma corticosterone level and adrenal weight is shown in Table 1. The dose of each anti-inflammatory drug employed was twice its ED50 determined earlier by the cotton pellet implantation method of Meier *et al.*[12]

TABLE 1. EFFECT OF ANTI-INFLAMMATORY DRUGS ON ADRENAL WEIGHT AND PLASMA CORTICOSTERONE LEVEL IN RATS

Drug	Dose in mg/100 gm i.p.	Mean adrenal wt. in mg ± S.E.	Corticosterone in μg/100 ml on plasma ± S.E.	't'	P
Normal saline (Control)	1 ml	33·8 ± 1·0	33·5 ± 1·2	—	—
Indomethacin	0·6	34·6 ± 2·0	35·1 ± 1·4	0·84	>0·05
Oxyphenbutazone	20	35·7 ± 1·2	30·4 ± 1·1	1·8	>0·05
β-glycyrrhetinic acid	10	34·8 ± 1·6	29·3 ± 1·1	2·33	<0·05

Indomethacin (0·6 mg/100 g) did not alter the plasma corticosterone level and adrenal weight significantly. This shows that indomethacin is not acting through pituitary adrenal axis and supports the findings of Hart *et al.*,[13] who reported that indomethacin was active as an anti-inflammatory agent even in adrenalectomized animals. Similarly, oxyphenbutazone (20 mg/100 g) did not produce any significant change in plasma corticosterone level and adrenal weight. This is in agreement with the findings of Domenjoz[5] who reported that oxyphenbutazone is equally active in adrenalectomized and hypophysectomized animals.

It is interesting to observe that β-glycyrrhetinic acid (10 mg/100 g) caused a significant decrease in the plasma corticosterone level ($P - < 0.05$) without altering the mean adrenal weight. The lowering of plasma corticosterone level by β-glycyrrhetinic acid is not consistent with its anti-inflammatory activity. The supression of adrenal cortical secretion by the drug is unlikely in view of the fact that

the adrenal weight is not altered. Furthermore, glycyrrhizin was found effective as an anti-inflammatory agent in adrenalectomized animals.[14] Thus, it may be concluded that the anti-inflammatory action of β-glycyrrhetinic acid is independent of the pituitary adrenal axis.

Acknowledgement—The authors are grateful to the Indian Council of Medical Research, New Delhi (India) for providing financial assistance.

Department of Pharmacology and Therapeutics,
K.G.'s Medical College, Lucknow University,
Lucknow—3, India.

M. B. GUPTA
G. P. GUPTA
K. K. TANGRI
K. P. BHARGAVA

REFERENCES

1. H. V. COUWENBERG, *Lancet* ii, 374 (1954).
2. G. C. FEENEY, P. E. CARLS and K. P. SMITH, *J. Pharmac. exp. Ther.* **114**, 99 (1955).
3. A. K. DONE, R. S. FLY and V. C. KELLEY, *Metabolism* **7**, 52 (1958).
4. C. A. WINTER, E. A. RISLEY and G. W. NUSS, *J. Pharmac. exp. Ther.* **141**, 369 (1963).
5. R. DOMENJOZ, *Ann. N.Y. Acad. Sci.* **86**, 253 (1960).
6. J. J. BURN, T. F. YU, P. G. DAYTON, A. B. GUTMAN and B. A. BRODIE, *Ann. N.Y. Acad. Sci.* **86**, 259 (1960).
7. R. S. H. FINNEY and G. F. SOMER, *J. Pharm. Pharmac.* **10**, 613 (1948).
8. M. L. GUJRAL, K. N. SAREEN, K. K. TANGRI, A. K. ROY, G. P. GUPTA and M. K. P. AMMA, *Ind. J. Physiol. Pharmac.* **3**, 39 (1959).
9. N. ZENKER and D. E. BERNSTEIN, *J. biol. Chem.* **231**, 695 (1958).
10. H. SILBER and C. C. PORTER, *J. biol. Chem.* **210**, 923 (1954).
11. M. L. SWEAT, *Analyt. Chem.* **26**, 773 (1954).
12. R. MEIER, W. SCHULER and P. DESANLLES, *Experientia* **6**, 965 (1963).
13. F. D. HART and P. L. BOARDMAN, *Br. Med. J.* **2**, 965 (1963).
14. M. L. GUJRAL, K. N. SAREEN, D. P. PHUKAN and M. K. P. AMMA, *Ind. J. Med. Sci.* **15**, 625 (1961).

Biochemical Pharmacology, Vol. 18, pp. 532–534. Pergamon Press. 1969. Printed in Great Britain

Norepinephrine turnover and brain monoamine levels in aggressive mouse-killing rats

(*Received* 9 *April* 1968; *accepted* 5 *July* 1968)

KARLI[1] and Karli and Vergnes[2] reported that some laboratory rats will spontaneously attack and kill a mouse when presented. Horovitz *et al.*[3,4] showed that this response, which they called "muricide," could be selectively blocked by certain classes of drugs such as antidepressants and stimulants. Karli[1] reported that the muricidal response could be exacerbated by lesioning of the septal area, but that it could not be induced in normal nonkilling rats. Additionally, Horovitz *et al.*[4] reported that lesions of the amygdala blocked this response, as did interruption of the amygdala-hypothalamic routes.[5] Since the initial report of Yen *et al.*,[6] several investigators have studied the aggressive behavior in mice induced by prolonged isolation. Valzelli[7] showed that serotonin synthesis occurs at a slower rate in aggressive mice. In his recent review on drugs in various aggressive states, Valzelli[8] reported that blockade of catecholamine synthesis results in a faster decline in brain norepinephrine levels in aggressive than in normal mice.

This communication reports our findings on the levels of brain serotonin and norepinephrine and the turnover rate of norepinephrine in aggressive mouse-killing rats. Male Long–Evans rats weighing