Effect of two non-steroidal anti-inflammatory agents on hexosamine and sialic acid contents of inflamed tissue

SIR,—It has been shown that the levels of total mucopolysaccaride, expressed as hexosamine, and the carbohydrate moiety of glycoproteins, expressed as sialic acid, are much higher in inflamed than in normal tissue (Bolognani, Coppi & others, 1961; Delaunay & Bazin, 1965; Houck & Jacob, 1965). We have explored the effect of two non-steroidal anti-inflammatory drugs, naphthipramide (Coppi, 1966; Marazzi-Uberti & Turba, 1966; Marazzi-Uberti, Turba & Erba, 1966; Turba & Marazzi-Uberti, 1966) and phenylbutazone, on hexosamine and sialic acid contents in rat tissue inflamed by kaolin and carrageenan.

Inflammation was produced in the paws of rats (Sprague-Dawley strain; male, average weight 160 g) by injecting 0·05 ml of a 10% suspension of kaolin in water or 0·1 ml of a 1% solution of carrageenan in 0·9% cold sterile saline. Naphthipramide and phenylbutazone were administered 0, 12, 24 and 36 hr after kaolin (in doses of 100 and 50 mg/kg respectively) and 0, 2·5 and 5 hr after carrageenan (in doses of 80 and 40 mg/kg respectively). Animals were killed 48 hr after kaolin and 24 hr after carrageenan and the inflamed tissue of the paw pads was homogenized in water at +4° and freeze-dried. The freeze-dried tissue was then assayed for nitrogen according to Kjeldhal, for total hexosamine (Boas, 1953; Bolognani, Coppi & Zambotti, 1958) and for sialic acid (Svennerholm, 1958). Non-inflamed paws of treated rats were similarly assayed.

The results (Table 1) show that naphthipramide and phenylbutazone have a qualitatively similar effect, both reducing hexosamine and sialic acid contents of the inflamed tissue, with a more marked effect on kaolin than on carrageenan oedema. But phenylbutazone showed an effect quantitatively greater than that of naphthipramide on both kinds of oedema.

TABLE 1. EFFECT OF NAPHTHIPRAMIDE AND PHENYLBUTAZONE ON HEXOSAMINE AND SIALIC ACID CONTENTS OF INFLAMED TISSUE OF RATS.

Treatment	Dose of drug mg/kg (oral)	Hexosamine µg/mg N			Sialic acid µg/mg N		
		Mean ± s.e.	P*	P**	Mean ± s.e.	P*	P**
Kaolin oedema (12 animals/group)							
Normal control ..	—	118·16 ± 1·75	—	—	83·46 ± 2·33	—	—
Inflammation ..	—	194·66 ± 4·27	< 0·001	—	168·67 ± 9·82	< 0·001	—
Inflammation + naphthipramide	100 × 4	172·66 ± 4·28	< 0·001	0·001 < P < 0·01	145·61 ± 6·35	< 0·001	0·02 < P < 0·05
Inflammation + phenylbutazone ..	50 × 4	162·66 ± 7·23	< 0·001	< 0·001	129·90 ± 5·22	< 0·001	< 0·001
Carrageenan oedema (10 animals/group)							
Normal control ..	—	129·60 ± 4·76	—	—	98·60 ± 3·48	—	—
Inflammation ..	—	164·20 ± 1·55	< 0·001	—	161·20 ± 6·48	< 0·001	—
Inflammation + naphthipramide	80 × 3	159·20 + 1·89	< 0·001	> 0·05	147·50 + 4·58	< 0·001	> 0·05
Inflammation + phenilbutazone ..	40 × 3	149·20 ± 1·83	< 0·001	0·02 < P < 0·05	126·00 ± 3·32	< 0·001	< 0·001

* Statistical significance of the difference between treated and normal controls.
** Statistical significance of the difference between treated and inflamed controls.

Our results provide further evidence that anti-inflammatory agents reduce glycoprotein levels in inflamed tissue (Houck & Jacob, 1965).

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Effects of some sympathomimetic amines on the response of the rabbit isolated ear artery to noradrenaline and electrical stimulation

SIR,—The site of uptake of noradrenaline in the rabbit ear artery has been shown to be situated on the outer perimeter of the smooth muscle layer (de la Lande & Waterson, 1967). These authors have also shown that cocaine applied to the outer surface of the artery potentiated the effects of extraluminally injected noradrenaline and had little effect on the intraluminal noradrenaline. Cocaine was also shown to potentiate the electrically induced vasoconstriction (de la Lande & Rand, 1965). Since sympathomimetic amines are known to potentiate noradrenaline in other smooth muscle (Bentley, 1965) and to block the uptake of noradrenaline in heart (Burgen & Iversen, 1965), it seemed important to investigate the effects of these amines on the vascular smooth muscle in relation to the hypothesis postulated by de la Lande & Waterson (1967).

Central ear arteries, 4–5 cm long, isolated from anaesthetized (25% urethane, i.v.) rabbits weighing 1·5–2·5 kg were perfused in a 400 ml bath by the method of de la Lande & Harvey (1965) with Krebs bicarbonate solution at 37°, aerated with 95% oxygen and 5% carbon dioxide. Perfusion pressure and perfusion rate were maintained at 20–30 mm Hg and 4–5 ml/min respectively. Intraluminal injections were given through the rubber tubing at the proximal end of the artery. In some experiments a 20 ml bath was used to facilitate a quick washout. Constriction of the artery in response to noradrenaline added intra- or extraluminally was recorded with a mercury manometer on a smoked drum. A Grass model S4-D stimulator delivering pulses of 0·5 msec duration alternatively at a frequency of 5 or 10 shocks/sec for 5 sec each 2 min was used for periarterial nerve stimulation. The drugs used were: (−)-noradrenaline bitartrate (Koch-Light); (±)-amphetamine sulphate (L. Light & Co); metaraminol bitartrate (Merck Sharp & Dohme) and tyramine hydrochloride (Calbiochem).

The results showed that the artery was much less sensitive to extraluminal than to intraluminal noradrenaline, which is in agreement with the findings of Cannell, de la Lande & Waterson (1966). Of the sympathomimetic amines