A human plasma fraction with anti-inflammatory but without either analgesic or antipyretic properties

A fraction prepared from normal human plasma shows anti-inflammatory activity in a number of acute tests as well as in established adjuvant arthritis in the rat (Elliott, Bolam & others, 1974). When injected intravenously the fraction, 0·25 ml of the combined fractions II and IV of Ford-Hutchinson, Insley & others (1973), has now been found to inhibit the acute carrageenan-induced paw oedema reaction in the mouse (Table 1).

Table 1. *Effects of plasma fraction on carrageenan-induced acute paw oedema in the mouse.* The animals received 0·05 ml of 1·0 g/100 ml (w/v) carrageenan in the right hind foot. In the control group (16 animals) each received 0·25 ml of saline and in the experimental group (16 animals) each received 0·25 ml plasma fraction by intravenous injection into a tail vein 30 minutes before the irritant. Results given as mean ± standard error and expressed as mean percentage increases in the volume of the injected paw compared to the value at 0 h. Those marked * show a statistically significant difference ($P < 0{\cdot}01$) from the corresponding control animals.

Group	Time (h) 1	2	3
Control	28·6 ±5·6	73·1 ±9·7	101·1 ±7·1
Plasma fraction	18·3 ±3·7	14·1 ±4·5*	54·3 ±13·5*

However, in this species the fraction did not exhibit analgesic activity in either the hot plate test (Woolfe & Macdonald, 1944) in which morphine gave a positive result or in the anti-writhing test (Hendershot & Forsaith, 1959) in which phenacetin gave a positive effect.

In the rabbit intravenous administration of the plasma fraction caused a small but definite reduction in the degree of haemorrhage at the site of intradermal challenge in the reversed passive Arthus reaction and thus shows anti-inflammatory activity in this species (Bolam, Ford-Hutchinson & others, 1974). However, it did not show any antipyretic activity in rabbits in which fever was induced by the injection of proteus endotoxin and in which the administration of indomethacin caused a significant reduction in the pyrexia.

Some importance appears to be attached to the association of anti-inflammatory, analgesic and antipyretic activities both in conventional and in new non-steroidal anti-inflammatory compounds. Thus aspirin is regarded as the "ideal" drug because it inhibits inflammation, lowers fever and ameliorates pain (Glenn & Sekhar, 1971). The suggestion that there is a common mechanism, i.e. the blockade of prostaglandin biosynthesis, for this triad of pharmacological activities (Collier, 1971) infers that potentially useful drugs in this category are inhibitors of prostaglandin synthetase. The present findings show that the natural anti-inflammatory fraction present in normal human plasma possesses neither analgesic nor antipyretic activities. It is therefore suggested that the continuing search for anti-inflammatory compounds need not be conducted on the premise that substances selected for further investigation should possess analgesic and antipyretic properties as well as being active in various anti-inflammatory tests in the laboratory.

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A new source of anabasine

While investigating the chemical constituents of *Haloxylon Persicum* Boiss. (Fam. Chenopodiaceae) which grows wild in the Kingdom of Saudi Arabia we have found that anabasine is the major alkaloidal principle of this plant which causes death among grazing animals. The predominance of anabasine is in contrast to *H. salicornicum* Boiss which contains anabasine as a minor alkaloid along with many other chemically different alkaloids (Michel, Sandberg & others, 1967).

Nicotine was also identified as a minor alkaloidal component and two other alkaloids were detected in trace amounts. The powdered dried plant (1 kg) was defatted with light petroleum (b.p. 60–80°) and the defatted material exhaustively extracted with ethanol (96%). The ethanolic extract was concentrated, acidified, filtered and extracted with chloroform.

The aqueous layer was basified with ammonia and the liberated alkaloids were extracted with chloroform (yield about 57 g). Fractional distillation of the total alkaloids gave a major fraction boiling at 279–280° which was identified as anabasine (yield about 43 g) by its physical constants b.p. (279–280°); mol. wt. (162·06— by non-aqueous titration). Its infrared spectrum, R_F values on t.l.c. (Table 1) were

Table 1. *R_F values of anabasine, and nicotine on t.l.c.**

Solvent system	Anabasine		Nicotine	
	Reference	Isolated	Reference	Isolated
$CHCl_3$–MeOH (80:20)	0·23	0·22	0·55	0·53
$CHCl_3$–MeOH (33·66)	0·21	0·23	0·46	0·45
$CHCl_3$–MeOH–NH_4OH (60:10:1)	0·56	0·57	0·75	0·77
$CHCl_3$–Me OH–Ac OH (60:10:1)	0·06	0·07	0·08	0·09

* Silica gel G after Stahl (1969).