LETTER TO THE EDITOR

ACTIVITY OF SOME ANTI-INFLAMMATORY AGENTS AGAINST CARRAGEENIN-INDUCED PEDAL OEDEMA IN MICE*

Sir,

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Carrageenin-induced oedema of the paw is a well established model for testing anti-inflammatory drug potency in rats (4). Attempts have been made to test anti-inflammatory compounds by measuring the paw volume of mice also (3) employing plethysmometer but such work becomes difficult due to small volume of the mouse hind paw. Srimal and Dhawan (2) employed the method of weighing the severed hind limbs of the mice rather than plethysmography for assessing the oedema. We used their method in our laboratory to study the action of some steroidal and non-steroidal anti-inflammatory drugs but found the mouse model to be less sensitive particularly for evaluating non-steroidal anti-inflammatory agents.

The experiments were conducted on Swiss strain of male albino mice (20–22 g) and Wistar strain of male albino rats (140–160 g) in an air-conditioned room (ambient temperature, 23±0.5°C). Animals were fed Gold Mohur Hind Lever diet and water *ad libitum*. Each group consisted of 6 mice or rat. Carrageenin (0.03 *ml* of 1% suspension in normal saline) was injected in plantar aponeurosis of right hind limb of each mouse, while the other limb served as control. A group each was sacrificed with chloroform at the end of 1, 2, 3, 4. 5 and 6 hrs, both hind limbs were cut identically at lower end of the tibia, weighed and mean oedema weight was calculated from the differences in their weights. Experiments were also performed using the standard method of carrageenin-induced oedema (4) in rats. In these experiments volume of carrageenin-suspension injected was 0.1 *ml*. Oedema was calculated plethysmographically from paw volume at a given time and immediately after carrageenin injection. Drugs studied included hydrocortisone hemisuccinate, betamethasone disodium phosphate, indomethacin, aspirin and phenylbutazone; the drugs were suspended in 2% gum acacia and given po in animals fasted overnight (water *ad libitum*), 1 hr before administration of the phlogistic agent. Control animals were given vehicle alone. ED_{50} values were calculated according to the method of Litchfield and Wilcoxon (1) and student's 't' test was used to assess difference between the groups.

Carrageenin produced paw oedema in mice, the mean oedema weight (*mg*, mean ±S.E.M.) being 51.3±6.1, 59.6±5.8, 64.1±6.9, 72.7±5.7, 59.2±4.3and 71.3±8.4 at

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1, 2, 3, 4, 5 and 6 hrs, respectively. In rats respective oedema volumes (*ml*, mean±S.E.M. were 0.37±0.05, 0.81±0.09, 1.04±0.10, 0.88±0.07, 1.03±0.06 and 0.82±0.07. It is evident that carrageenin produced a biphasic pattern of swelling in both mouse-and rat-foot, peak effects being observed in mouse at 4 and 6 hrs and in rat at 3 and 5 hrs.

TABLE I : Effect of anti-inflammatory agents on carrageenin-induced pedal oedema in mice and rats.

	Treatment	Dose mg/kg po	Mice		Rats	
			Mean oedema weight in mg ±S.E.M.	ED_{50} (mg/kg) and confidence limits (in parenthesis)	Mean oedema volume in ml ±S.E.M.	ED_{50} (mg/kg) and confidence limits (in parenthesis)
I	Vehicle (controls)	—	54.2±5.4		0.89±0.09	
	Hydrocortisone	10	30.2±3.3**	28.0	0.51±0.02**	14.0
		20	28.7±3.8**	(15.1 – 51.8)	0.34±0.01***	(5.4 – 36.4)
		40	24.2±3.4***		0.24±0.01***	
II	Vehicle (controls)	—	61.7±5.9		0.93±0.13	
	Betamethasone	0.5	34.5±2.9**	1.5	0.50±0.03**	0.7
		1.0	32.5±3.5***	(0.6 – 3.6)	0.42±0.02**	(0.3 – 1.7)
		2.0	28.8±3.2***		0.27±0.01***	
III	Vehicle (controls)	—	55.3±4.5		1.00±0.15	
	Indomethacin	2	33.2±3.3**	6.0	0.57±0.02*	2.9
		4	30.8±2.5***	(2.8 – 12.6)	0.34±0.01**	(1.6 – 5.4)
		8	26.0±1.6***		0.11±0.01***	
		16	23.8±2.1***		—	
IV	Vehicle (controls)	—	70.7±7.9		0.99±0.11	
	Aspirin	100	62.2±6.4		0.55±0.03**	
		200	52.8±6.2	>400	0.41±0.01***	175.0
		400	42.2±5.0*		0.29±0.02***	(100 – 306)
V	Vehicle (controls)	—	56.7±5.1		0.94±0.12	
	Phenylbutazone	20	51.1±5.6		0.66±0.04*	
		40	44.8±7.3		0.52±0.02**	
		80	42.5±4.2	>320	0.30±0.01**	45.0
		160	40.5±5.8		—	(17.3 – 117.0)
		320	35.8±5.5*		—	

Oedema values are based on difference in weight (*mg*) in mice and volume (*ml*) in rats. There were 6 animals in each treatment group. All drugs were given po as aqueous suspension in 2% gum acacia 1 hr before carrageenin injection. Values differ significantly (*$P<0.05$, **$P<0.01$, ***$P<0.001$ from their respective controls).

As evident from Table I which is based on oedema values seen at 4 hr in mice and 3 hr in rats, hydrocortisone, betamethasone and indomethacin produced dose-dependent inhibition of oedema in mice but the drugs were less effective in mice since ED_{50} values in mice are almost double of those in rats. Aspirin and phenylbutazone produced a dose-dependent and significant inhibition of carrageenin-induced oedema in rats at all the doses. However, in mice significant inhibition was observed only at highest doses used (Table I) and even these doses did not result in 50% inhibition of paw oedema, whereas in rat the ED_{50} values for these two agents were 175 *mg/kg* and 45 *mg/kg*, respectively.

It is concluded that the mouse-carrageenin-oedema-model is not sensitive enough for screening anti-inflammatory potency, particularly of non-steroidal anti-inflammatory agents.

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