

## Modification of the Randall-Selitto analgesic apparatus

In screening programs designed to detect analgesics, the initial testing procedure usually includes in rodents, some measurement of protection shown by a test compound against a noxious stimulus, such as chemicals (Siegmund, Cadmus & Lu, 1957), heat (Wolfe & MacDonald, 1944; Eddy & Leimbach, 1953), electricity (D'Amour & Smith, 1941) and air pressure (Randall & Selitto, 1957).

Because the air pressure method of Randall & Selitto (1957) detects antipyretic and anti-inflammatory analgesics and the more potent analgesics, its use is often preferred.

Our experience with the apparatus as modified by Winter & Flataker (1965) has been satisfactory except that, after repeated or prolonged use, the Teflon plunger sometimes becomes immobile. We now describe a simpler apparatus which has given reproducible results in our hands.

Two pieces of aluminum plate (*a*) are separated by a plexiglass tube (*b*) and "sandwiched" between the plates is a latex rubber diaphragm (*c*) which responds to externally applied low air pressure (*A*). To the diaphragm, a stainless steel rod (*e*) is attached, which in turn transmits pressure to the rat paw. The paw is placed over a positioning block similar to that described by Winter & Flataker (1965). The air pressure is regulated by a needle valve so that a rise of 10 mm/s is maintained and cut-off at 100 mm Hg. A sharp "squeak" or an escape response or both are used as an end point.

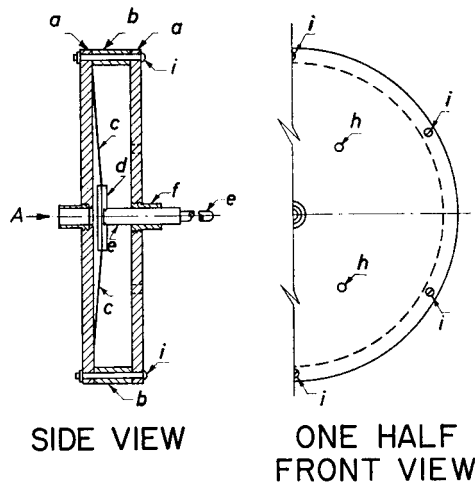


FIG. 1. *A*. Air supply. *a*. Aluminium plates— $\frac{1}{8}$  inch  $\times$  5 inch diameter. *b*. Plexiglass tube— $\frac{1}{4}$  inch  $\times$  1 inch  $\times$  5 in diameter. *c*. Latex rubber diaphragm (slightly inflated),  $\frac{1}{16}$  inch  $\times$  5 inch in diameter. *d*. Stainless steel plates— $\frac{1}{16}$  inch  $\times$  1 inch diameter. *e*. Stainless steel rod  $\frac{1}{4}$  inch tapered to 2 mm at end. *f*. Guided sleeve. *h*. Air vents. *i*. Bolts.

Female weanling Sprague-Dawley rats 40–60 g weight were fasted overnight with water *ad lib*. After pre-testing the animals for threshold responses the procedure of Winter & Flataker (1965) was followed.

The oedema and hyperesthesia, ensuing after injection of 0.1 ml of 5% yeast into the right hind paw, were allowed to develop for 2 h before drugs were administered orally. The doses were given in a volume of 1 ml/kg. The suspending agent was 0.5% carboxymethylcellulose. The thresholds to pressure were measured 1 h later.

The minimum effective dose is calculated by the dose-response curve and represents the minimum dose that produces effects statistically significantly different ( $P = 0.05$ ) from control values based on Dunnett's "t" (Dunnett, 1955).

Typical antipyretic-anti-inflammatory analgesic compounds increase only the threshold of the inflamed foot, whereas the more potent analgesics will affect both inflamed and normal foot thresholds (see also Randall & Selitto, 1957). The effect of (+)-propoxyphene at 20 mg/kg on the normal foot is just beyond significant difference and it would seem probable that a dose of 25–30 mg/kg would show significance (Table 1).

Table 1. *Effect of various drugs upon air pressure thresholds in rats*

Drugs	Oral dose** (mg/kg)	No. of rats	Thresholds* (mm pressure)		Minimum effective dose mg/kg	
			I.F.	N.F.	I.F.	N.F.
Control .. ..	CMC	25	15 ± 2.6	48 ± 1.3	—	—
Aspirin .. ..	75	10	20 ± 4.3	47 ± 0.8	100	—
	150	25	21 ± 4.3	48 ± 1.3		
	300	25	28 ± 3.9	48 ± 1.3		
Control .. ..	CMC	35	16 ± 2.2	49 ± 1.7	10	—
Phenylbutazone .. ..	10	15	21 ± 2.1	49 ± 3.2		
	20	35	29 ± 7.3	49 ± 0.9		
	40	35	32 ± 6.4	48 ± 1.3		
Control .. ..	CMC	20	14 ± 1.4	48 ± 1.7	1.4	—
Indomethacin .. ..	0.4	20	16 ± 2.1	48 ± 1.3		
	2	20	23 ± 2.6	49 ± 1.5		
Control .. ..	10	20	33 ± 2.8	50 ± 0.6	<10	16
	20	15	16 ± 2.4	50 ± 0.4		
	40	15	27 ± 2.4	51 ± 4.1		
Morphine .. ..	10	15	36 ± 7.7	55 ± 2.4	<10	16
	20	15	47 ± 6.5	61 ± 4.1		
	40	15	15 ± 3.3	50 ± 1.6		
Control .. ..	5	15	17 ± 1.6	50 ± 0.7	14	>20
	10	22	18 ± 1.5	50 ± 0.9		
	20	25	25 ± 4.5	54 ± 2.8		

CMC = carboxymethylcellulose. I.F.—inflamed foot— N.F.—normal foot.

\* Figures represent mean ± standard deviation.

\*\* Rats dosed 2 h after 0.1 ml of 5% yeast injected into subplantar tissue of hind paw. Thresholds measured 1 h after oral dosing.

The doses of compounds which show a significant difference from controls are considerably greater, especially for morphine, than those reported in the literature (Winter & Flataker, 1965, Randall & Selitto, 1957) but the animals were dosed orally rather than parenterally.

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