A comparison of the effects of isoprenaline, WG 253 and salbutamol on the tension and rate of rabbit isolated atria

I have compared the effects of isoprenaline, WG 253 [erythro-(3,4-dihydroxyphenyl)-(2-piperdyl) methanol hydrobromide] and salbutamol on the rate and tension of isolated rabbit atria, and related these findings to the ratio for isoprenaline and salbutamol reported by Callum, Farmer & others (1969).

Pairs of atria were taken from six 500 g Dutch rabbits that had been killed by a blow on the back of the head and bled from the carotid arteries. The atria were in 70 ml of Ringer Locke solution gassed with 3% carbon dioxide in oxygen at 28°; recordings were made with isometric force-displacement transducers, Devices DC6 amplifiers and M2 recorders at a paper speed of 1 mm/s. After a control record of 30 s drug was added and the recorder was run for 120 s; the bath was then washed out three times at 3 min intervals. Intervals between doses were 15 min. Dose response curves were made for each drug using each pair of atria, a procedure followed for each of six experiments, in which drugs were added in a different order. The mean results of six experiments, in which the ratio of treated tension to control tension is plotted against the log dose, are shown in Fig. 1. The semi-log dose response

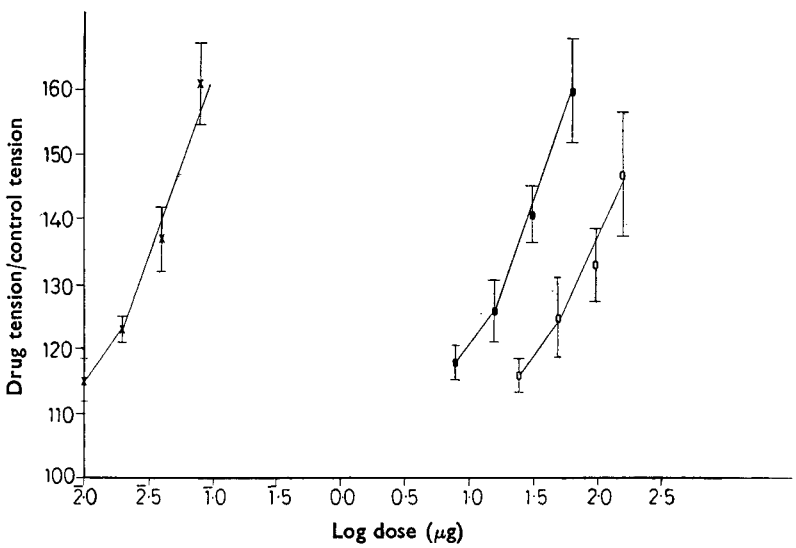

FIG. 1. Log dose-response curves to isoprenaline (×—×), WG, 253 (●—●) and salbutamol (○—○), obtained using rabbit isolated atria suspended in 70 ml, Ringer-Locke solution gassed with 97% oxygen and 3% carbon dioxide at 28°. Each point represents the mean ± standard error of six experiments.

curves are nearly parallel. From the curves, it was calculated that isoprenaline was about 720 times as potent as WG 253 and 2710 times as strong as salbutamol in its effect upon tension developed by the atria. Similar results were found when the ratio of treated rate to control rate was plotted against the log of the dose, the relative potencies being 1 to 790 to 2100. The relative potencies of isoprenaline and salbutamol compare well with those of Callum & others (1969) on guinea-pig atria tension, which were 1 to 2000.

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REFERENCE

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On the presence of histidine decarboxylase activity in rat forestomach

Recent reports on the presence of histidine decarboxylase (L-histidine-carboxy-lyase, EC 4.1.1.22) in the rat fundus (forestomach, thin membranous or ruminal portion) and the pylorus (glandular or muscular portion) have been contradictory. Radwan & West (1967) claimed preparations from the rat fundus to have many of the enzymatic properties of the specific histidine decarboxylase found in rat foetal liver and rat hepatoma; the enzymatic activity of the fundic preparations, however, was slightly inhibited by α-methyl histidine while preparations from the pylorus displayed many of the enzymatic properties of the aromatic-L-amino acid decarboxylase (EC 4.1.1.26). Håkanson & Owman (1966) and Aures, Håkanson & Schauer (1968) found that the ruminal portion had only a trace of the enzyme activity compared with the oxyntic gland area of the pyloric portion. Leinweber & Braun (1970) concluded that, in addition to the pylorus, the fundic portion also contains histidine decarboxylase activity which is resistant to most known inhibitors. The lack of response to inhibition was used to explain the failure to obtain a reduction of histamine formation *in vivo*. These authors also suggested that the activity of the fundic portion bore a striking similarity to that of the *Lactobacillus* enzyme purified by Rosenthaler, Guirard & others (1965). Kobayashi & Maudsley (1969) believed that the enzyme activity of the fundus was weak and in an insoluble form, and was present only in male rats. Isaac (1970) and Beavens, Horáková & Severs (1970) presented evidence from studies in germ-free rats that the fundus activity was of bacterial origin.

These contradictory communications prompted us to describe our early investigations on this subject which indicate that the non-enzymatic activity of the fundus offers an alternative explanation to these conflicting reports.

Adult, male Sprague-Dawley rats (CFE, Carworth Farms, New City, New York), 200 to 250 g, and fed Purina rat pellets *ad libitum* were killed by decapitation and the whole stomach immediately excised. The thin forestomach was separated from the muscular pyloric portion by cutting along the line of demarcation. Both portions were washed free of stomach contents in 0·9% cold saline and homogenized in an all-glass homogenizer with 3 volumes of cold saline. The homogenates were centrifuged at 35 000 *g* for 1 h at 4° and the resulting supernatant frozen in 2 ml aliquots at −20°, if not used immediately.

Histidine decarboxylase was assayed (Ellenbogen, Markley & Taylor, 1969). Unless otherwise noted, incubation mixtures contained 0·2 ml of 0·1M sodium phosphate buffer (pH 6·8), 0·2 ml of 1×10^{-5}M pyridoxal phosphate, 0·5 ml of enzyme, 0·1 ml of 1×10^{-2} M L-histidine-^{14}COOH (New England Nuclear or Calbiochem) and water to a final volume of 2·0 ml. After the addition of the enzyme and cofactor, the mixture was allowed to incubate for 10 min. The reaction was started by the addition of substrate, incubated at 37° for 1 h and corrected for a boiled enzyme control (boiled 30 min). All assays were made in duplicate and the results averaged.