

ESTIMATION OF DRUG ANTAGONISMS ON THE ISOLATED GUINEA-PIG VAS DEFERENS

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Received March 7, 1956

THE use of the guinea-pig vas deferens was described by Waddell¹ for studies of pilocarpine and adrenaline. Apart from this the preparation appears to have received little attention; being well adapted for drug antagonism tests it should be more widely known.

EXPERIMENTAL

Large adult male guinea-pigs were killed by a blow and bled, the vasa deferentia carefully removed, without stretching, and placed in cold aerated Tyrode's solution. A single vas deferens was suspended in a 10 ml. bath filled with Tyrode's aerated to a constant temperature. Contractions were recorded by a lightly loaded lever with a magnification of eight. The time of drug contact was one minute, followed by two washings of fresh Tyrode's to relax the preparation. Temperature variations were found to be important; thus with adrenaline the greatest contractions were observed at 32–34° C., while with acetylcholine and histamine it was 36–38° C.

RESULTS

(-)-Adrenaline, (-)-noradrenaline*, acetylcholine, and histamine, when applied to the preparation gave a contraction, and the result of increasing doses is illustrated in Figure 1. When the response of the preparation was plotted against the logarithm of the dose, a

linear form is obtained over a wide range of dose, the slope of the curve is steep, and the preparation exhibits a well defined maximum.

The regression coefficient b has been calculated for each of the dose response lines shown in Figure 1. For adrenaline b is 96.4, noradrenaline 104.7, acetylcholine 83.8, and for histamine 45.6.

* (-)-Adrenaline and (-)-noradrenaline were used throughout the work.

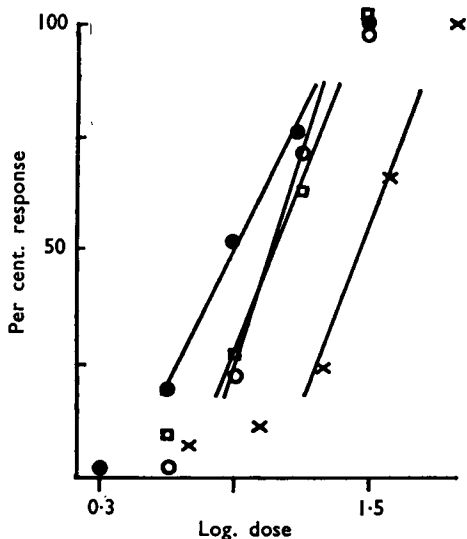


FIG. 1. Dose response curves for acetylcholine ●—●, noradrenaline ○—○, adrenaline □—□, and histamine ×—×, on the vas deferens preparation.

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All four substances give a contraction and this is useful for a study of specific antagonists, the method being illustrated in Figure 2 with 883 F. (diethylaminomethylbenzodioxane, sympatol) and noradrenaline.

Drug antagonism is conveniently studied by a modification of the method described by Schild² for the estimation of pA values. The

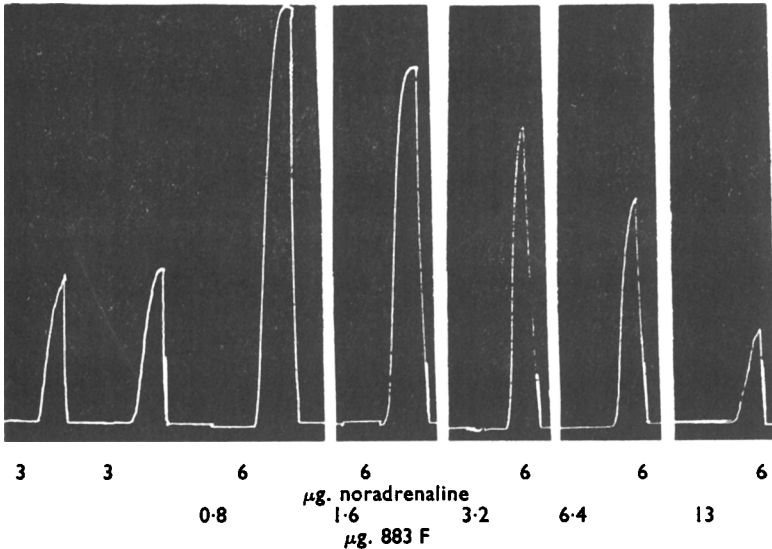


FIG. 2. Determination of antagonism of 883 F., to noradrenaline, showing decline of noradrenaline response as described in text.

preparation was first tested with a standard dose of, for example, 3 µg. of noradrenaline, to give a constant response. The antagonist was then added, e.g., 0.8 µg. of 883 F., and followed after five minutes with a double dose of the stimulating drug (6 µg. of noradrenaline). This procedure was repeated, the dose of the antagonist being doubled each time, until the contraction with the double dose of noradrenaline in the presence of the antagonist was approximately the same size as that obtained with the single dose of noradrenaline without the antagonist.

TABLE I
CONCENTRATION OF ANTAGONISTS REQUIRED TO REDUCE RESPONSES OF
(-)-ADRENALINE, (-)-NORADRENALINE AND ACETYLCHOLINE

Antagonist	Concentration of antagonist in µg./ml. required to reduce contraction		
	(-)-adrenaline	(-)-noradrenaline	Acetylcholine
Atropine	75	120	2×10^{-4}
Mepyramine	375	300	0.6
Sympatol	0.8	0.9	
Piperoxan	0.02	0.08	3.2
Yohimbine	12	24	

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Table I gives the concentration of the antagonist in $\mu\text{g./ml.}$ required to depress the contractions caused by adrenaline, noradrenaline, and acetylcholine. Noradrenaline requires more antagonist to reduce the response than does adrenaline.

The Table also shows that the antagonists of acetylcholine seem to be more specific than those of the two sympathomimetic amines used, and also that despite the large doses of stimulating agents needed to contract the preparation, it is nevertheless sensitive to small amounts of antagonist.

SUMMARY

1. The isolated vas deferens of the guinea-pig gives a contraction with (—)-adrenaline, (—)-noradrenaline, acetylcholine, and histamine, which is measured quantitatively.
2. The preparation is a convenient one for the study of drug antagonisms.

REFERENCES

1. Waddell, *J. Pharmacol.*, 1916, **8**, 551.
2. Schild, *Brit. J. Pharmacol.*, 1947, **2**, 189.