Table 1 A comparison of the antagonist affinity constants for the adrenal medulla and those values reported for the guinea pig ileum

Antagonist	*Mean dose ratio*	*Adrenomedullary affinity constant (K_B medulla)*	*Reported ileum affinity constant (K_B ileum)*	$\frac{K_B \text{ ileum}}{K_B \text{ medulla}}$
Atropine sulphate, 10^{-6} m, $n=3$	7.36 (6.99–7.80)	6.36×10^{6}	10^{9}*	157
Oxyphenonium bromide, 2×10^{-7} m, $n=3$	18.38 (9.17–34.20)	8.69×10^{7}	5.98×10^{9}*	69
Oxyphenonium bromide, 2×10^{-2} m, $n=3$	77.06 (54.7–116.6)	3.80×10^{7}	5.98×10^{9}*	157
Methylhyoscinium iodide, 2×10^{-7} m, $n=3$	10.42 (5.18–17.69)	4.71×10^{7}	5.03×10^{9}†	107

* Abramson, Barlow, Mustafa & Stephenson, 1969.
† Barlow, Franks & Pearson, 1973.

flow of 2 ml/minute. The effluent was collected for 30 s periods and the catecholamine content assayed by the trihydroxyindole method (Vendsalü, 1960). The glands were stimulated by two low and two high doses of the specific muscarinic agonist acetyl beta methylcholine ($10^{-8} \rightarrow 10^{-6}$ M) prior to a 90 min equilibration with perfusate containing the antagonist. The response to the agonist was defined as the increment of catecholamine output expressed as a percentage of the resting output. Further higher doses of agonist, in the presence of antagonist, were administered to produce similar responses to those previously obtained enabling the affinity constant of the antagonist to be calculated from the Gaddum/Schild equation (Table 1).

We conclude that in the canine adrenal medulla there exists a population of muscarinic receptors for which the muscarinic antagonists tested showed an affinity two orders lower than that reported for the guinea-pig ileum receptors and this may prove to be a true case of muscarinic receptor heterogeneity.

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Muscarinic agonists and sympathetic ganglia

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Muscarinic agonists can depolarize sympathetic ganglion cells (see Volle, 1966) but quantitative measurements of their potencies are sparse. We have made some potency measurements on the isolated desheathed rat superior cervical ganglion, superfused with Krebs solution at 25°C bubbled with 95% oxygen/5% carbon dioxide (Brown & Marsh, 1975).

Muscarinic agonists produced a delayed, sustained depolarization of maximum amplitude 0.5–1 mV with extracellular recording (about 20% of a maximal 'nicotinic' depolarization). Comparable responses to carbachol or bethanechol were obtained after suppressing nicotinic depolarization with 2.5 mM hexamethonium. (Hexamethonium reduced the effect

Table 1 Potencies of muscarinic agonists as depolarizing agents on isolated rat ganglia

Agonist	[1] EC_{50} (μM)	[2] *Hyoscine* K_I (nM)
DL-Muscarine	0.35	0.49
Methylfurmethide	0.11	0.39
Furmethide	1.9	0.54
Pilocarpine	6.4	0.74
[3] AHR-602	11	0.15
DL-Muscarine*	2.6	5.3
Bethanechol*	68	7.4
Methacholine*	94	2.9

[1] Estimated from mean cumulative concentration—response curves from at least 3 experiments.
[2] Estimated from cumulative concentration—response curves for agonist in the presence of 3 nM hyoscine.
[3] *N*-benzyl-3-pyrrolidyl acetate methobromide (Franko, Ward & Alphin, 1963).
* Measured in the presence of 2.5 mM hexamethonium.

of DL-muscarine ten-fold). EC_{50} values for the agonists used lay within the range 0.1–10 μM (Table 1).

Hyoscine inhibited all agonists tested, with an apparent dissociation constant (K_I) around 0.5 nM (5 nM in hexamethonium solution). K_I for atropine and lachesine against DL-muscarine were 0.19 and 0.12 nM respectively.

Fair comparability—but not identity—with smooth muscle receptors is apparent.

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