Table 1 ED_{50} values of standard GABA-like compounds for antagonism of myoclonic seizures induced by (+)-bicuculline (0.55 mg/kg intravenously) in female CF_1 mice (20–25 g)

Compound	*Route of administration*	*Premedication time*	*ED_{50} mg/kg*	*95% Limits*
γ-Vinyl GABA	i.p.	5 h	54	(47–63)
γ-Vinyl GABA	i.v.	2 min	Not active up to 200 mg/kg	
γ-Acetylenic GABA	i.p.	5 h	26	(17–36)
γ-Acetylenic GABA	i.v.	2 min	Not active up to 200 mg/kg	
Gabaculine HCl	i.p.	5 h	Not active up to 25 mg/kg	
Isogabaculine trifluoro-methane-sulphonate	i.p.	5 h	17	(14–22)
Aminooxyacetic acid	i.p.	5 h	19	(15–23)
Sodium valproate	i.p.	30 min	120	(110–130)
Muscimol HBr	i.v.	2 min	1.8	(0.62–3.4)
THIP	i.v.	2 min	2.3	(2.2–2.4)
Diazepam	i.v.	2 min	0.038	(0.029–0.049)
Baclofen	i.v.	2 min	Not active up to 10 mg/kg	
Diaminobutyric acid	i.p.	6 h	320	(260–370)
Chlorpromazine	i.p.	30 min	0.51	(0.45–0.58)
β-Alanine	i.p.	3 h	Not active up to 500 mg/kg	

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The isolated anococcygeus muscle of the mouse

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The responses of the anococcygeus muscles of rat, cat, rabbit, and dog to drugs and nerve stimulation have already been described (Gillespie, 1972; Gillespie & McGrath, 1974; Creed, Gillespie & McCaffery, 1977; Dehpour, Khoyi, Koutcheki & Zarrindast, 1978), and marked species variations have been observed. In the present study we report initial observations on the pharmacology of the isolated anococcygeus muscle of the mouse.

Male mice (LACA; 25–35 g) were killed by stunning and exsanguination, and the anococcygeus muscles dissected as described by Gillespie (1972). The muscles were set up in series, joined at the ventral bar, in Krebs'-bicarbonate solution (37°C). A resting tension of 100 mg was placed on the tissue and changes in tension recorded isometrically. Field stimulation was applied by ring electrodes attached to a square wave pulse generator (1 ms supramaximal voltage).

The resting muscle had neither tone nor spontaneous activity and responded with slow, maintained contractions (peak rise within 3 min) to noradrenaline ($pD_2 = 6.01 \pm 0.25$; max. 564 ± 53 mg; $n = 15$) and to carbachol ($pD_2 = 5.93 \pm 0.17$; max. 417 ± 38 mg; $n = 15$). The contractions were inhibited by phentolamine ($pA_2 = 6.9$) and atropine ($pA_2 = 9.5$) respectively. Cocaine (1 μM) produced a selective leftward shift of the dose-response curve to noradrenaline ($pD_2 = 7.26 \pm 0.16$; $n = 6$). High concentrations of isoprenaline (>10 μM) produced contractions which were unaffected by propranolol but were completely blocked by phentolamine (300 nM). 5-Hydroxytryptamine (1 μM) contracted the tissue, the response being blocked by methysergide (1 μM). Histamine (1 mM)

produced a small contraction initially, which displayed rapid tachyphylaxis.

Field stimulation resulted in frequency-dependent motor responses (max. 527 ± 60 mg; $n = 6$) which were blocked by guanethidine (1 μM) and phentolamine (1 μM). Higher concentrations of guanethidine (50 μM) raised muscle tone and field stimulation now caused relaxations which were unaffected by atropine, propranolol, or hexamethonium, but were prevented by tetrodotoxin (500 ng/ml). Isoprenaline did not lower the tone of the contracted tissue, but following incubation with indomethacin (Burnstock, Cocks & Crowe, 1978) high doses of ATP (> 100 μM) produced dose-related relaxations. In some preparations high concentrations of acetylcholine (40 μM) produced relaxations of the contracted muscle which were blocked by (+)-tubocurarine (2 μM).

Thus the pharmacology of the isolated anococcygeus muscle of the mouse most closely resembles that of the rat. In particular, it will be of interest to determine whether the relaxant effects of ATP and acetylcholine are mediated directly, or indirectly by release of inhibitory transmitter (Gibson & James, 1977).

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A comparison of the effects of agonist drugs on nerve-induced contractions of the rat bisected vas deferens

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The effects of drugs on the nerve-induced contraction of vas deferens have given rise to unexpected observations difficult to reconcile with straightforward adrenergic transmission. For example, Ohlin & Stromblad (1963) commented that 'classroom experiments... had soon to be abandoned since on addition of drugs known to affect sympathetic transmission the preparation did not behave according to the classical scheme' and it has been suggested that motor transmission in the vas may not be adrenergic, the adrenergic nerves having, instead, an inhibitory function (Ambache & Zar, 1971; Ambache, Dunk, Verney & Zar, 1972).

The properties of the smooth muscle and its response to nerve stimulation, however, vary along the organ. If rat vas is bisected transversely into equal lengths then a single field stimulus will produce a biphasic contraction in each portion but the first and second components will dominate in the prostatic and epididymal ends respectively. This first component is resistant to and the second component susceptible to 'classical' pharmacological manoeuvres which modify adrenergic transmission (Booth, Connell, Docherty & McGrath, 1978; McGrath, 1978).

The present study investigates whether a variety of drugs, which are known to affect neurotransmission in other tissues, will have similar or different effects on the nerve-induced (0.5 ms field stimulus) longitudinal, isometric contractions of isolated portions from the two ends of rat vas deferens isolated in Krebs' bicarbonate saline at 37°C (see McGrath, 1978).

α-Adrenoceptor agonists produced pre-junctional α_2-mediated inhibition and post-junctional α_1-mediated excitation which acted in physiological antagonism. In the prostatic portion inhibition dominated. In the epididymal portion the inhibitory effect was accompanied by a dominant excitatory effect manifest by potentiation and prolongation of the nerve-induced response followed, at higher concentrations by drug-induced contraction (see Docherty, MacDonald & McGrath, 1979).

Catecholamines: noradrenaline, adrenaline and dopamine produced effects qualitatively similar to the other α-adrenoceptor agonists, inhibition and excitation dominating in the prostatic and epididymal portions, respectively.

β-Adrenoceptor agonists: isoprenaline and salbutamol both inhibited responses in each portion. In the