concentrations of acetylcholine and angiotensin which produced responses approximately the same size as 50% maximum acetylcholine response.

When the $Na^+$ concentration of the Tyrode solution was varied from the normal concentration of 137 mmol the responses of rat colon to acetylcholine and to angiotensin changed similarly being reduced by 12% at 120 mmol and 50% at 68.5 mmol $Na^+$ and reduced by 30% at 171 mmol and 60% at 205.5 mmol $Na^+$. At high concentrations of ouabain (1.0 mmol) there was equal reduction of responses to acetylcholine and to angiotensin of both rat colon (37%) and rat uterus (57%). After 0.1 mmol ethacrynic acid, the isometric responses of rat colon to acetylcholine were reduced by 15.4 ± 0.7% while the angiotensin response was reduced by 42.9 ± 5.3% ($n = 6$, $p$ 0.001). With rat uterus, it was necessary to record responses isotonically (1 g load), there was equal reduction (39%) of responses to acetylcholine and to angiotensin. However, with 3 g load, there was a significantly greater reduction ($n = 7$, $P$ 0.01) of the angiotensin response (60.0 ± 3.6%) compared with the acetylcholine response (35.8 ± 4.4%).

Therefore, a preferential reduction of the angiotensin response of uterus was observed only under conditions of high energy expenditure. Since it has been reported that ethacrynic acid inhibits cellular energy production (Epstein, 1972) it appears that its effect on uterus might be due to this mechanism rather than an effect on $Na^+$ movement. This conclusion is supported by the severe inhibition of all contractile responses observed during exposure of rat uterus to higher concentrations of ethacrynic acid (0.5 mmol). It is also consistent with our previous observations that the angiotensin response of these tissues involves an ATP-dependent step (Crocker & Wilson, 1975; Wilson, Crocker & Willavoys, 1974). The present findings, however, do not support a specific role for $Na^+$ in the interaction of angiotensin with these tissues.

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## A study of tetramethylenedisulphotetramine (TETS) and related compounds as antagonists of presynaptic inhibition and microiontophoretically applied γ-aminobutyric acid (GABA) and glycine in the rat cuneate nucleus


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TETS is an extremely potent convulsant that antagonizes the actions of GABA at the rat superior cervical ganglion (Bowery, Brown & Collins, 1975) and at the crustacean neuromuscular junction (Large, 1975). However, these preparations are insensitive to glycine and so give no indication of the specificity of TETS as a GABA antagonist. We have therefore examined the specificity of TETS and its effect on presynaptic inhibition in the rat cuneate nucleus. In addition, three other structurally related compounds, (Figure 1), have been examined.

Experiments were performed on 14 rats anaesthetized with urethane and prepared as described by Hill & Miller (1974). Presynaptic inhibition was estimated from the amplitude of the P-wave component of the cuneate field potential produced by stimulation of the appropriate forepaw (Anderson, Eccles, Schmidt &

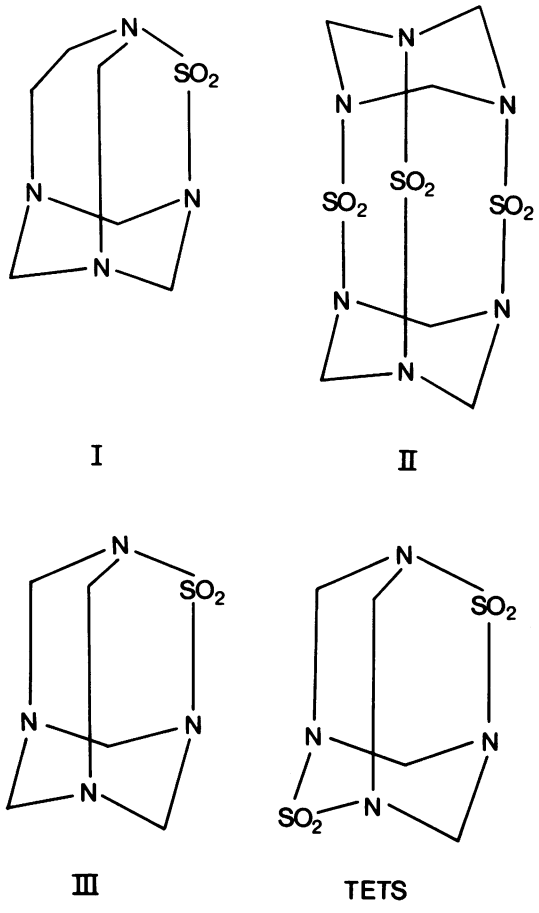


**Figure 1.**

Yokota, 1964). To examine the specificity of TETS, GABA and glycine were applied to single cuneate neurones by microiontophoresis (Hill & Simmonds, 1973) and the depression of firing so produced examined before and after the administration of TETS. Due to the low solubility of TETS (<300 μg/ml saturated aqueous solution) it was not possible to apply it by microiontophoresis.

Compounds I, II and III had no effect on presynaptic inhibition when given intravenously in doses up to 2 mg/kg or when superfused over the medulla in physiological saline (500 μg $ml^{-1}$ $h^{-1}$). However, doses of TETS as low as 20 μg/kg effectively antagonized presynaptic inhibition as measured by either test.

TETS given by intravenous infusion (100 μg $ml^{-1}$ $h^{-1}$) was found to antagonize the effect of microiontophoretically applied GABA but this was always accompanied by a parallel antagonism of glycine and so cannot be considered to be specific. However, its actions may not be completely non-specific as it does not antagonize the action of carbachol on the superior cervical ganglion (Bowery *et al.*, 1975).

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