

derivatives obtained from isolated electrically driven ventricle strips of guinea pigs were analysed with regard to the force of contraction, time to peak tension and of relaxation, velocity of tension development and of relaxation.

Histamine stimulates cardiac contraction more effectively than noradrenaline, leaving unchanged the relaxation time which was strongly diminished by noradrenaline. The histamine effects were antagonized by burimamide and metiamide, which produced a dose-related displacement of the cumulative dose-response curves to histamine, without significantly affecting their slope or maximum. The dissociation constants were 2.1 and 4.2 respectively.

Both drugs in concentrations up to  $10^{-4}$ M, failed to displace the dose-response curves to noradrenaline significantly.

Other antihistamines, such as triprolidine, shifted the cumulative dose-response curves to histamine in a non-competitive way.

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### The pharmacological effects of imidazole and some of its derivatives on neuromuscular transmission

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The pharmacological activity of imidazole, 2-methyl-imidazole, *N*-methyl-imidazole and *N*-butyl-imidazole, has been studied using striated neuromuscular preparations *in vivo* and *in vitro*.

The results obtained suggest that imidazole and 2-methyl-imidazole increase *per se* neuromuscular contraction, while *N*-methyl-imidazole and *N*-butyl-imidazole are devoid of any pharmacological activity. *In vivo* experiments show that the effect of 2-methyl-imidazole is more potent and longer lasting than that of imidazole itself in potentiating the contractions of the *tibialis anterior* muscle of the cat, evoked by electrical stimulation of the sciatic nerve.

The pharmacological analysis performed in order to clarify the mechanism of actions of different imidazoles, show that these compounds exert a pronounced and long-lasting antagonism against paralysis induced by *d*-tubocurarine.

These imidazoles, on the other hand, do not show any activity against succinylcholine induced

blockade of neuromuscular transmission.

The adrenergic receptors involved in striated neuromuscular transmission (Bowman & Raper, 1967; Bowman & Nott, 1969), do not seem to be relevant to the imidazole activity.

Since exogenous cyclic AMP has been demonstrated to increase the frequency but not the amplitude of the spontaneous m.e.p.p. and the number of the transmitter packets in response to nerve stimulation (Goldberg & Singer, 1969), imidazole, which has been shown to activate phosphodiesterase activity in rabbit skeletal muscle (Huang & Kemp, 1971), does not seem to exert its pharmacological action through the cyclic AMP system. A possible mechanism of action of these compounds was discussed.

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