EFFECT OF 2,4-DICHLOROPHENOXY ACETIC ACID ON RABBIT DUODENUM

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Summary: 2,4-dichlorophenoxy acetic acid (2,4-D) produces myotonia in healthy animals. The action of this drug was studied on smooth muscles *in vitro* using isolated strips of rabbit's duodenum. The drug was found to have a stimulant action on the smooth muscle. The action seems to be a direct one.

Key words: 2,4-D smooth muscle stimulant direct action

INTRODUCTION

Experimentally induced myotonia in laboratory animals is a very useful tool for the study of specific abnormalities in myotonia. Various chemical agents and drugs have been used for the induction of experimental myotonia. 2,4-dichlorophenoxyacetic acid (2, 4-D) produces in healthy animals effects which resemble myotonia (4). The drug has been used in whole animals and on isolated preparations. EMG records of myotonic discharges taken from rat muscles and intracellular records have also been studied. Since myotonia remains after curarization, it is considered to be due to changes in the excitability of the muscle fibre rather than the neuromuscular junction or nervous system and the myotonic responses can be elicited anywhere along the muscle fibre and not just at the end plate.

A variety of electrophysiological studies have been made on the myotonic muscle in man, goat, mice and rats (2,3). The studies have been mostly in the skeletal muscles. The effect of 2,4-D on the transverse tubular system of the guinea pig myocardium was studied by Preiss *et al.* (5). Bodem *et al.* (1) found that 2,4-D produced a prolonged relaxation of the isolated electrically stimulated guinea pig papillary muscle. It was thought worthwhile to study the action of the drug on smooth muscles, for the elucidation of its mode of action.

MATERIALS AND METHODS

Adult rabbits were fasted overnight and sacrificed by a blow on the head and a 2 *cm* piece of duodenum was suspended in aerated Tyrode solution at 37°C in an isolated organ bath of 25 *ml* capacity. An isotonic solution of 2,4-D was prepared and adjusted to pH 7.4, 0.5 *ml* of various doses of 2,4-D were added to the bath and the effects were noted. After noting the effects of one dose of the drug, the bath fluid was drained and the tissue washed twice with fresh Tyrode solution and a few normal contractions obtained before the addition of a second dose. In

similar preparations the effect of the drug in the presence of various spasmolytic drugs was also studied. In each case 0.5 *ml* of the spasmolytic drug and 0.5 *ml* of 2,4-D were used and the tissues washed twice in between each change of the drug.

RESULTS AND DISCUSSION

When 2,4-D was added to the bath in a concentration of 1 mM, there was slight increase in the amplitude of contractions. There was an increase in amplitude as well as tone. When a concentration of 2.5 mM was used, (Fig. 1) there was marked increase in tone and amplitude of contraction and there was slight reduction in the rate of contraction characterised by prolongation of the relaxation phase. Increasing the concentration to 3 mM and 4 mM also gave similar results and there was no further increase in response with increase in the concentration of the drug. In all these cases, phasic movements were retained.

For further experiments, the drug was used in a concentration of 2.5 mM. The increase in tone was not blocked by mepyramine maleate (Fig.2) (0.5 *ml* of M.M. 10^{-7} *g/ml*) and Atropine,

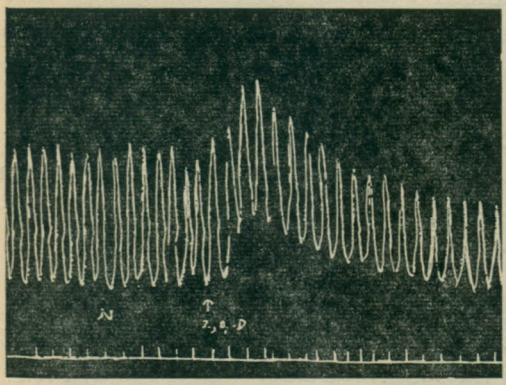

Fig. 1: Effect of 2.5 mM 2,4-D on isolated duodenum of rabbit.

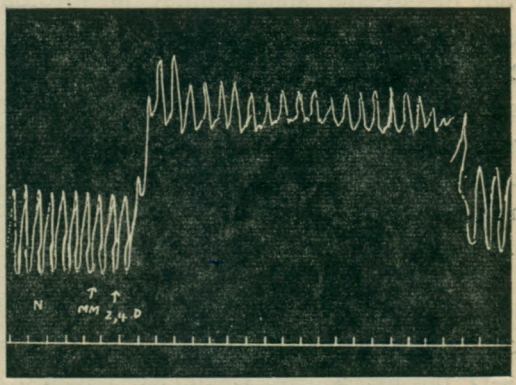

Fig. 2: Effect of 2.5 mM 2,4-D on isolated rabbit duodenum after administration of anti-histamine (0.5 *ml* of 10^{-7} *g/ml* of mepyramine maleate)

(Fig. 3) 0.5 *ml* of atropine 10^{-8} *g/ml*). 0.5 *ml* adrenaline in a concentration of 10^{-4} *g/ml* was able to block the action of 2,4-D and produce complete relaxation (Fig. 4). The effect of 2,4-D was completely blocked by papaverine 0.5 *ml* of 10^{-3} *g/ml*. These results suggest that the stimulant effect of 2,4-D on the smooth muscle of the intestine is a direct one. One interesting observation was that the stimulant action was greater with successive doses of the same concentration of the drug and the increase in tone was much higher in the presence of blocking agents like atropine and mepyramine maleate than when the drug was used alone, even though it is well known that rabbit duodenum is quite insensitive to histamine.

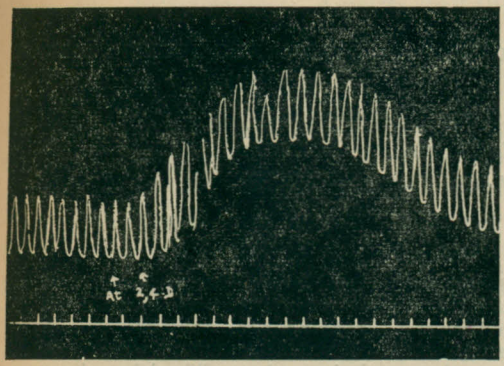

Fig. 3: Effect of 2.5 mM 2,4-D on isolated rabbit duodenum after administration of atropine (0.5 *ml* of 10^{-8} *g/ml*).

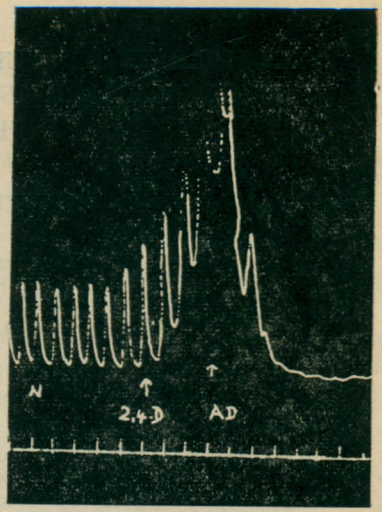

Fig. 4: Effect of 2.5 mM 2,4-D on adrenaline (0.5 *ml* of 10^{-4} *g/ml*) induced relaxation of isolated rabbit duodenum.

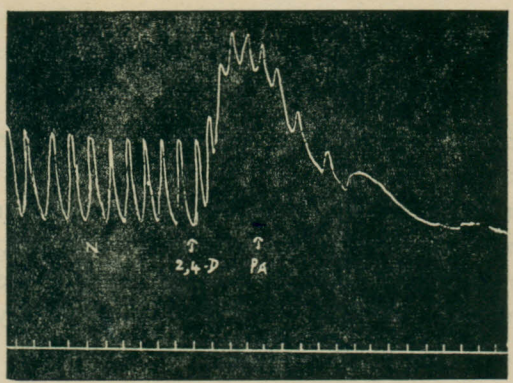

Fig. 5: Effect of Papaverine (0.5 *ml* of 10^{-3} *g/ml*) on2,4-D induced stimulation of isolated rabbit duodenum.

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