

SHORT COMMUNICATION

**EFFECT OF SOME DRUGS ON HUMAN APPENDIX *IN VITRO***

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**Summary:** Muscarinic action of acetylcholine was demonstrated in the human isolated appendix. Histamine-induced contractions seemed to be mediated by H<sub>1</sub> receptors. Nicotine and DMPP-induced contractions were mediated through their action on ganglion cells. Experiments with adrenergic drugs suggested the presence of beta receptors.

**Key words:** human isolated appendix    acetylcholine    histamine    adrenergic drugs

INTRODUCTION

An attempt has been made in this study to delineate the general pattern of receptor population in human appendices obtained from patients undergoing appendicectomy, at Civil Hospital and Cancer Hospital, Ahmedabad. The work was undertaken to confirm and extend the report on the pharmacological responses of drugs on human appendix (1).

MATERIALS AND METHODS

Appendices were obtained from patients scheduled for appendicectomy, under general anaesthesia with ether or halothane. Pre-anaesthetic medication, consisted of hyoscine or atropine and morphine or pethidine.

The whole appendix was mounted in a 30 ml bath containing Krebs Hansleit solution gassed with carbogen. The contractions were recorded with frontal writing lever, under a load of 1 g and six times magnification. Contact time for the agonists was about 2 min, and that for the antagonists 15 min.

Drugs used were acetylcholine hydrochloride (Ach), adrenaline hydrochloride, nor-adrenaline hydrochloride, isoprenaline sulphate, atropine sulphate, hexamethonium bromide, histamine acid phosphate, 5-hydroxytryptamine creatinine sulphate (5-HT), nicotine acid

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tartrate, phenoxybenzamine, tolazoline hydrochloride, antazoline methane sulfonate (antistine), propranolol hydrochloride and dimethylphenylpiperazinium (DMPP).

The concentrations of drugs are expressed as  $\mu\text{g/ml}$  of the salts.

## RESULTS AND DISCUSSION

A slow spontaneous activity seen in some preparations did not interfere with the responses to the drugs used.

*Effect of Ach* : Ach induced a dose related ( $0.05 - 1 \mu\text{g/ml}$ ;  $n=3$ ), contraction. The contractions were completely abolished by  $0.5 \mu\text{g/ml}$  of atropine (Fig.1). Hexamethonium ( $50 \mu\text{g/ml}$ ) or antazoline ( $3 \mu\text{g/ml}$ ), failed to block the Ach-induced contractions indicating the involvement of muscarinic receptors.

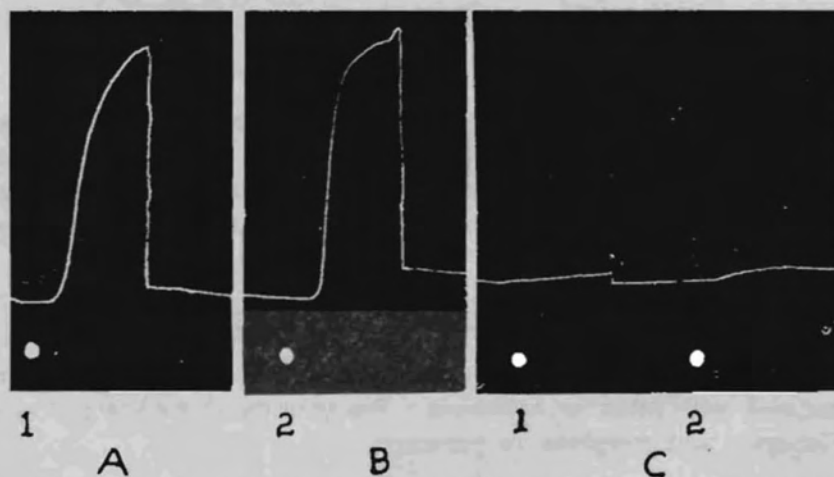


Fig. 1: Human appendix. Responses to acetylcholine ( $1 \mu\text{g/ml}$ ) at 1 and 2 (white dots) in A and B. In C, the same doses of acetylcholine were repeated at 1 and 2 in presence of atropine ( $0.5 \mu\text{g/ml}$ ).

*Effect of histamine* : Histamine induced dose-related ( $1.5 \mu\text{g/ml}$ ;  $n=4$ ), contractile responses which were effectively blocked by  $3 \mu\text{g/ml}$  of antazoline but were unaffected by  $1 \mu\text{g/ml}$  of metiamide (Fig.2), suggesting a preponderance of  $H_1$  receptors in the human appendix. Neither atropine ( $0.5 \mu\text{g/ml}$ ) nor hexamethonium ( $50 \mu\text{g/ml}$ ), affected the histamine-induced contractions.

*Effect of 5-HT*: Contractile responses to 0.5  $\mu\text{g/ml}$  of 5-HT were effectively blocked by 10  $\mu\text{g/ml}$  of cyproheptadine ( $n=3$ , Fig.3), but were unaffected by atropine (0.5  $\mu\text{g/ml}$ ,  $n=3$ ) or hexamethonium (50  $\mu\text{g/ml}$ ,  $n=4$ ). It is known that 5-HT acts directly on receptors as well as indirectly by stimulating nerve fibers of guinea-pig ileum (2). The present experiments suggest a direct mode of action for 5-HT-induced contraction on human appendix, as it remained unaffected by atropine or hexamethonium, but was completely antagonised by cyproheptadine.

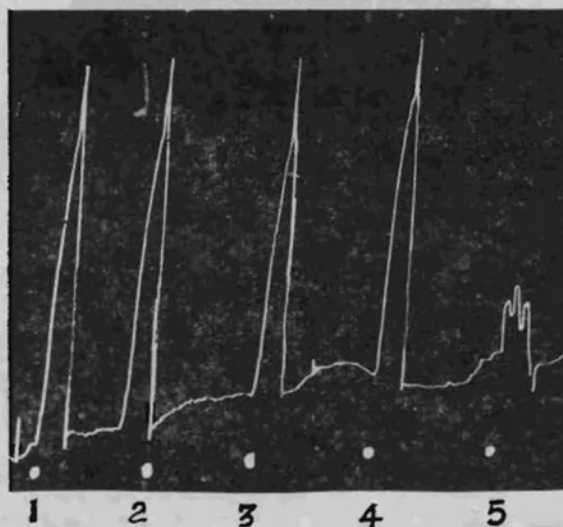


Fig. 2: Human appendix. Responses to histamine (1  $\mu\text{g/ml}$ ) at 1 and 2 (white dots). At 3 and 4, the same dose of histamine was repeated in the presence of metiamide (1  $\mu\text{g/ml}$ ). The response 5 shows the effect of histamine (1  $\mu\text{g/ml}$ ) in the presence of antazoline (3  $\mu\text{g/ml}$ ).

*Effect of DMPP*: Both nicotine (2-10  $\mu\text{g/ml}$ ,  $n=3$ ), and DMPP (2-10  $\mu\text{g/ml}$ ,  $n=3$ ) provoked dose-related contractile responses, which were antagonised by atropine (0.5  $\mu\text{g/ml}$ ,  $n=3$ ), as well as by hexamethonium (50  $\mu\text{g/ml}$ ,  $n=4$ , Fig.4). These findings are not in agreement with those of Atanakovic *et al.* (1), who found that hexamethonium did not affect the response to nicotine, suggesting the absence of ganglion cells in the appendix. The present study suggests the possibility of the presence of ganglion cells.

*Effect of adrenergic drugs*: Adrenaline, noradrenaline and isoprenaline, used in the concentration range of 0.01 to 1  $\mu\text{g/ml}$ , produced relaxation of the tissue, but the responses were not dose-related. Tolazoline (10-50  $\mu\text{g/ml}$ ) or phenoxybenzamine (10-50  $\mu\text{g/ml}$ ) failed to block the relaxant responses. However, propranolol (15-30  $\mu\text{g/ml}$ , exposure

5 min) almost completely abolished these in 70% of the experiments, ( $n=5$ , Fig. 5.). These findings are at variance with those reported by Atanackovic *et al.* (1). They reported

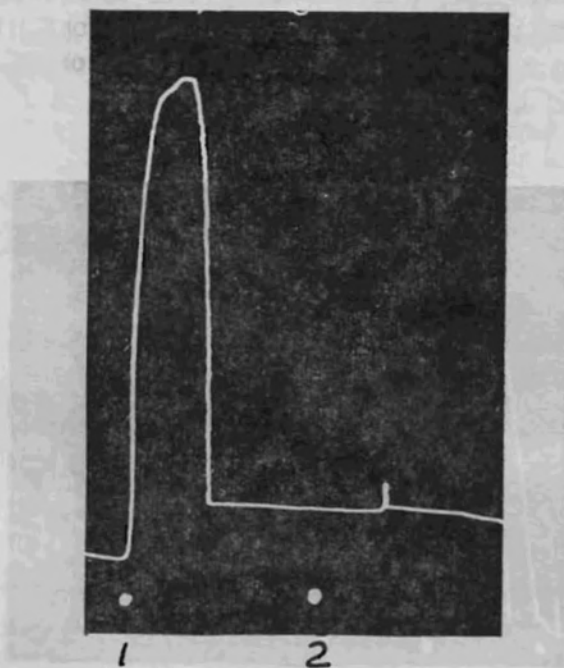


Fig. 3: Human appendix. Response to 5-HT ( $0.5 \mu\text{g/ml}$ ) at 1. At 2, the same dose was repeated in presence of cyproheptadine ( $10 \mu\text{g/ml}$ ).

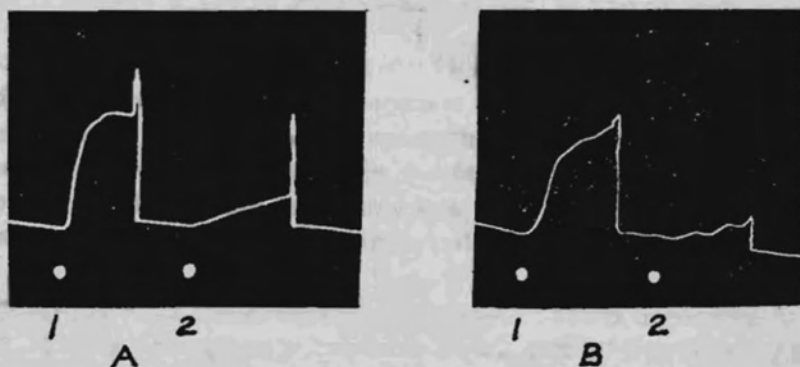


Fig. 4: Human appendix. Responses to nicotine ( $4 \mu\text{g/ml}$ ) and DMPP ( $4 \mu\text{g/ml}$ ) at 1 and 2 respectively in both panels A and B. Control responses are at 1; at 2, the same drugs were repeated in the presence of hexamethonium ( $50 \mu\text{g/ml}$ ) in both the panels.

absence of antagonism with either alpha or beta-blocking agents and proposed non-specific adrenergic relaxation.

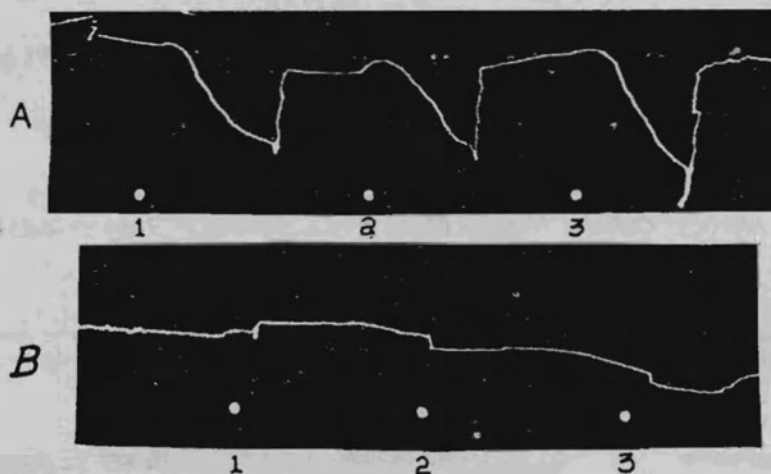


Fig. 5: Human appendix. Responses to adrenaline ( $1 \mu\text{g/ml}$ ) at 1, noradrenaline ( $1 \mu\text{g/ml}$ ) at 2 and isoprenaline ( $1 \mu\text{g/ml}$ ) at 3. Panel A shows control responses. In panel B, the responses were elicited in the presence of propranolol ( $20 \mu\text{g/ml}$ ).

Preanaesthetic medication with atropine apparently did not affect the responses to any of the agonists used.

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