SHORT COMMUNICATION

ANTIMUSCARINIC ACTIVITY OF NICOTINE

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Summary: On the isolated rabbit ileum nicotine and DMPP blocked the contractile effect of muscarine and shifted the muscarine dose-response curve to the right without affecting the maximum response indicating that both the agents acted competitively.

Key words: rabbit ileum muscarine nicotine DMPP competition

INTRODUCTION

Nicotine and dimethyl-phenylpiperazinium (DMPP) are commonly used as agonists for studying the mechanism of ganglionic blocking action of ganglion blockers. On the other hand, it is interesting to note that Barlow and Franks (2) have reported an atropine-like action for DMPP on the gunea pig ileum. Therefore, experiments were conducted to see if nicotine too possesses an atropine-like action.

MATERIALS AND METHODS

About 3 cm long terminal portions of rabbit ileum were suspended in 33 *ml* organ bath containing Tyrode solution of pH 7.5. Two preparations from the same ileum were set up simultaneously and were maintained at 37°C±1°C and bubbled with air. The contractions were recorded on smoked kymograph paper with an auxotonic lever which gave 10-fold magnification and was initially under 1 *g* tension. The preparations were equilibrated for 20-30 min before adding drugs. The preparations were washed every 8 min except during exposure to the blocker i.e. the agonist response—wash cycle without the blocker was 8 min. After eliciting control dose-response curve with (±)—muscarine iodide (contact time 30 sec), the tissue was exposed to DMPP iodide or nicotine (base) for 15 min and a response to muscarine was re-elicited. A washout was then given. Fifteen min later, response to a higher dose of muscarine in the presence of the same dose of the blocker (contact time 15 min) was elicited. This was repeated till a full muscarine dose-response curve in the presence of a dose of blocker was obtained. The procedure was repeated with a higher dose of the blocker. Not more than two doses of a blocker were tested in one preparation. Since two preparations from the same ileum were set up simultaneously, it was possible to test 3-4 doses of a blocker on the same ileum. Three pairs of preparations were employed for each dose. Muscarine dose-reponse curves were constructed by plotting the log dose on the abscissa and per centage of the maximum contraction on the ordinate.

Dose-ratio which is the ratio of the equiactive doses of the agonist after and before the antagonist (3) was determined from the horizontal distance between the parallel lines. The method of Arunlakshana and Schild (1) was used for constructing pA_x plots. For this purpose log (dose ratio-1) was plotted on the ordinate against the negative log of the molar concentration of the antagonist on the abscissa. The intercept of the regression line with the abscissa (at zero level) gave pA_2 value. Antagonism was considered as competitive if the slope value (b) of the regression line was significantly ($P<0.05$) different from the theoretical value of slope of -1 for competitive antagonism.

RESULTS AND DISCUSSION

Both DMPP (5.2×10^{-5} — 5.2×10^{-6} M) and nicotine (2×10^{-5}—6.4×10^{-4} M) blocked responses of the rabbit ileum to muscarine (4.6×10^{-8}—2×10^{-6} M) and brought about a para-

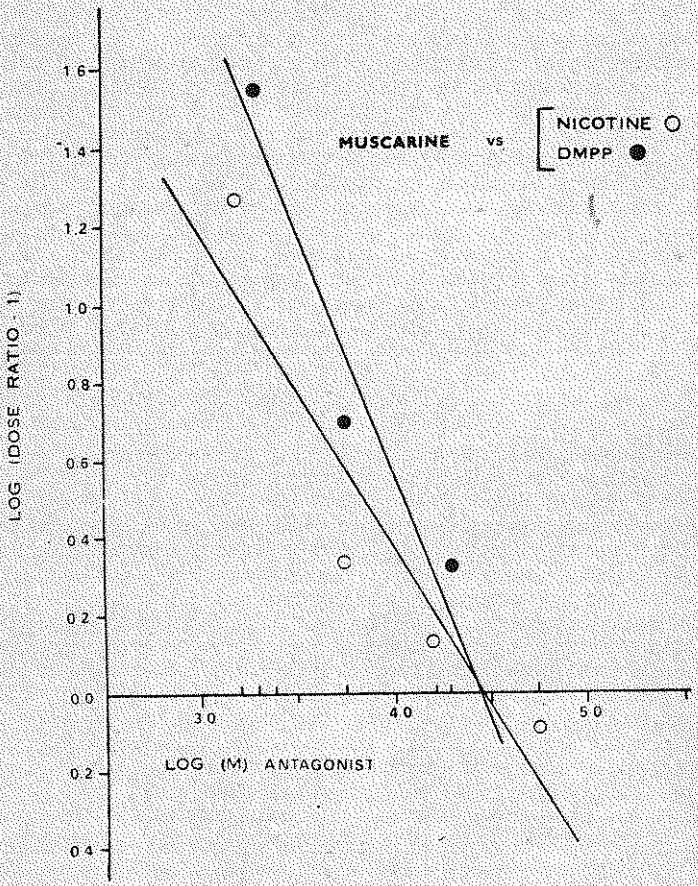

Fig. 1: pA_x regression lines plotted according to the method of Arunlakshana and Schild (1) for the antagonistic effects of DMPP and nicotine against muscarine on the rabbit ileum (auxotonic lever). The best fitting lines hrough the plotted points were determined by regression analysis (method of least squares). They wore significantly ($P<0.05$) different from zero. The PA_2 and slope values for nicotine were 4.46 and 0.87 ± 0.07 respecuively and those for DMPP were 4.43 and 1.3 ± 0.4 respectively.

llel shift of its dose-response curve to the right. The slope values of pA_x regression lines of nicotine and DMPP determined by the method of least squares (5) were -0.87±0.07 and -1.3 ±0.4 respectively. The respective pA_2 valeus were 4.46 and 4.43 (Fig. 1). The slope values are not significantly different ($P>0.05$) from the theoretical value of unity for competitive antagonism. This coupled with the parallel shifts of muscarine dose-response lines both by DMPP and nicotine suggests a competitive mode of action for both the agents. The antimuscarinic pA_2 value of DMPP obtained in the present study agrees with the value of 4.575 reported by Barlow and Franks (2).

Barlow and Franks (2) did not investigate the antimuscarinic action of nicotine but suggested on the basis of indirect evidence a muscarinic action for nicotine. The reason for the discrepancy between our finding the anti-muscarinic activity of nicotine and the muscarinic activity suggested for nicotine by Barlow and Franks (2) may be accounted for by species difference. On the basis of results of Barlow and Franks (2), the muscarinic action of nicotine would add to its ganglionic agonistic action and the anti-muscarinic action of DMPP would have the opposite effect. However using DMPP and nicotine as the agonists, Sethi and Gulati (4) obtained approximately identical pA_2 values of hexamethonium or TEA with both the guinea pig iluem and the rabbit ileum.

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