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Pharmacological Differentiation of Presynaptic M_1 Muscarinic Receptors Modulating Acetylcholine Release from Postsynaptic Muscarinic Receptors in Guinea-Pig Ileum*

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1. Effects of three muscarinic antagonists on electrically evoked ACh release and contractile response were investigated in longitudinal muscle strips of guinea-pig ileum suspended in an organ-bath and superfused with Krebs solution. ACh release was determined by a specific radioimmunoassay.

2. Telenzepine, a selective M_1, muscarinic antagonist, increased the ACh release at a concentration of 100-fold less than that inhibiting the contractile response (10 vs 1000 nM).

3. AF-DX 116, a cardioselective M_2, muscarinic antagonist, inhibited the contractile response at 10 μM, but did not affect the ACh release at this concentration.

4. (−)*N*-Methylscopolamine (NMS) did not affect the ACh release, but inhibited the contractile response at all concentrations tested (1-1000 nM), indicating (−) NMS can be used as an ileal specific postsynaptic muscarinic antagonist.

5. These data demonstrate that presynaptic muscarinic receptors modulating ACh release are distinct from postsynaptic ones involved in the contractile response and can be classified as M_1 subtype.

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