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N-hexacosanol prevents diabetes-induced rat ileal dysfunction without qualitative alteration of the muscarinic receptor system

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ABSTRACT

We evaluated the effects of N-hexacosanol, a cyclohexenonic long-chain fatty alcohol, on muscarinic receptors in diabetic rat ileal dysfunction. Eight-week-old male SD rats were divided into four groups. After induction of diabetes (streptozotocin 50 mg/kg, i.p.), three groups were maintained for eight weeks with treatment by N-hexacosanol (0, 2 or 8 mg/kg, s.c. every day). Ileum function was investigated by organ bath studies using carbachol and KCl, and the expression levels of muscarinic M_2 and M_3 receptors were investigated by real-time polymerase chain reaction. Various concentrations of subtype-selective muscarinic antagonists, *i.e.*, atropine (non-selective), pirenzepine (M_1 selective), methoctramine (M_2 selective), and 4-diphenylacetoxy-N-methylpiperidine methiodide (4-DAMP, M_1/M_3 selective), were used in this study. In the presence and absence of these antagonists, contractile response curves to increasing concentrations of carbachol were investigated. Treatment with N-hexacosanol did not alter the diabetic status of the rats, but did significantly prevent the carbachol-induced hypercontractility in diabetic rat ileum. Estimation of the pA_2 values for atropine, pirenzepine, methoctramine, and 4-DAMP indicated that the carbacholinduced contractile response in the ileum is mainly mediated through the muscarinic M_3 receptor subtype in all groups. Furthermore, N-hexacosanol significantly prevented the diabetes-induced up-regulation of intestinal muscarinic M_2 and M_3 receptor

mRNAs in streptozotocin-diabetic rats. Our data indicated that N-hexacosanol exerts preventive effects with respect to carbachol-induced hypercontractility in the diabetic rat ileum without qualitative alteration of the muscarinic receptor system.

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