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The beneficial in vitro effects of lovastatin and chelerythrine on relaxatory response to acetylcholine in the perfused mesentric bed isolated from diabetic rats

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Abstract

View references (24)

Diabetes mellitus is associated with an increased risk of cardiovascular disease. Endothelial dysfunction (i.e. decreased endothelium-dependent vasorelaxation) plays a key role in the pathogenesis of diabetic vascular disease. The present study was undertaken to determine whether diabetes induced by streptozotocin alters mesenteric responses to vasodilators and, if so, to study the acute in vitro effects of lovastatin and chelerythrine. Endothelial function was assessed in constantly perfused preparation removed from rats, 12 weeks after treatment with either saline or streptozotocin (45 mg/kg, intraperitoneally). In pre-contracted mesenteric beds (with 100 μM phenylephrine) removed from diabetic rats, the concentration response curve to acetylcholine, but not to sodium nitroprusside, was significantly reduced. Perfusion with lovastatin (10 μM for 20 min) or chelerythrine (1 μM for 20 min) significantly improved the acetylcholine-mediated relaxation in preparations removed from diabetic but not control rats. Pre-incubation of tissue with N^G-nitro-l-argenine methyl ester hydrochloride (10 μM for 20 min) inhibited the beneficial effect of lovastatin but not chelerythrine. Pre-treatment of tissue with indomethacin (10 μM for 20 min) did not modify the effects of lovastatin or chelerythrine on acetylcholine responses. The present results demonstrate that endothelial dysfunction induced by diabetes (in a resistant vasculature, such as rat mesenteric bed) may be improved by an acute exposure to either lovastatin or chelerythrine. Furthermore, our results suggest that the beneficial effect of lovastatin is mediated via the nitric oxide pathway.

Reaxys Database Information

View Compounds |

Author keywords

Chelerythrine; Diabetes; Endothelium; Lovastatin; Rat mesenteric bed; Streptozotocin

Indexed Keywords

EMTREE drug terms: acetylcholine; chelerythrine; glucose; indometacin; mevinolin; n(g) nitroarginine methyl ester; nitroprusside sodium; phenylephrine; streptozocin

EMTREE medical terms: animal experiment; animal model; animal tissue; arterial pressure; article; body weight; controlled study; drug mechanism; endothelial dysfunction; glucose blood level; in vitro study; male; mesentery blood vessel; nonhuman; priority journal; rat; vasoconstriction; vasodilatation

MeSH: Acetylcholine; Alkaloids; Animals; Benzophenanthridines; Blood Glucose; Blood Pressure; Body Weight; Diabetes Mellitus, Experimental; Dose-Response Relationship, Drug; Enzyme Inhibitors; Hydroxymethylglutaryl-CoA Reductase Inhibitors; Lovastatin; Male; Mesenteric Arteries; Nitroprusside; Perfusion; Phenanthridines; Phenylephrine; Protein Kinase C; Rats; Rats, Wistar; Vasoconstriction; Vasoconstrictor Agents; Vasodilation; Vasodilator Agents
Medline is the source for the MeSH terms of this document.

Chemicals and CAS Registry Numbers: acetylcholine, 51-84-3, 60-31-1, 66-23-9; chelerythrine, 34316-15-9; glucose, 50-99-7, 84778-64-3; indometacin, 53-86-1, 74252-25-8, 7681-54-1;