A New Isoquinolinone Derivative with Noble Vasorelaxation Activity

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Abstract

The pharmacological effects of BDPBI (7-bromo-1,4-dihydro-2-phenyl-4,4-bis(4-pyridinylmethyl)2H-isoquinolin-3-one dihydrochloride) were tested on isolated endothelium-containing or denuded aorta of the guinea pig. BDPBI with the formula C(27)H(24)BrCl(2)N(3)O was synthesized starting with 3-isochromanone. In the endothelium-containing preparations of the aortic rings, phenylephrine (PHE; 10 micromol/l) elicited contracture and acetylcholine (ACh; 10 micromol/l) or BDPBI (0.01-10 micromol/l) elicited relaxation effects on the PHE-precontracted preparations. The BDPBI-elicited effect on the PHE-precontracted aortic rings was not altered in the presence of adrenergic blockers (propranolol or yohimbine; 1 micromol/l) or pretreated preparations with aspirin, indomethacin (10 micromol/l) or L-NAME (1 mmol/l). However, the relaxation effects of BDPBI were blocked if the preparations were pretreated with diphenhydramine (10 micromol/l) or chloropheniramine maleate (10 micromol/l). In contrast to lower concentrations of atropine (1 micromol/l), higher concentrations of atropine (30 micromol/l) did block the effects of BDPBI on the PHE-precontracted aortic rings. HTMT dimaleate (0.01-10 micromol/l), a histamine H(1) receptor agonist, also elicited relaxation effects on the PHE-precontracted preparation, and the effects were blocked if the preparations were pretreated with diphenhydramine or chloropheniramine maleate. On isolated denuded aorta of the guinea pig, BDPBI did not elicit relaxation effects on the PHE-precontracted aortic rings. These results demonstrated that the vasorelaxation effect of BDPBI on PHE-precontracted aortic rings is partly dependent on the activation of a histaminergic receptor from the vascular endothelium. We suggested that BDPBI would be an effective vasorelaxant for cardiovascular systems.