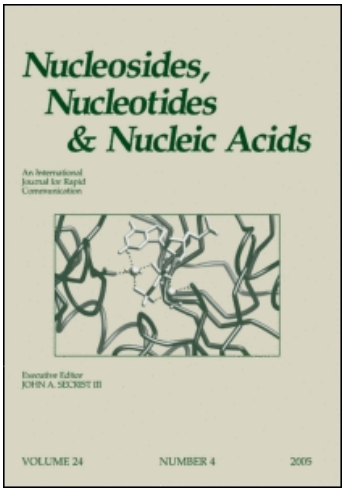

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Effects of Suramin on the ATP- and α,β-Methylene-ATP-induced Constriction of the Rabbit Ear Artery

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EFFECTS OF SURAMIN ON THE ATP- and α,ß-METHYLENE-ATP-INDUCED CONSTRICTION OF THE RABBIT EAR ARTERY

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Abstract. The isolated rabbit ear artery contains both dilation-mediating P_{2Y}-receptors and constriction-mediating P_{2X}-receptors. Suramin antagonizes the effects of ATP at either receptor.

The trypanocide suramin has been described as a P_{2X}-antagonist in the mouse vas deferens.[1] Suramin also antagonizes the vasoconstrictor effect of α,ß-methylene-ATP (mATP) in the pithed rat.[2] We examined the interaction of suramin with ATP and mATP in an isolated blood vessel, the ear artery of the rabbit, which has been reported to possess only vasoconstriction-mediating P_2-receptors.[3] In contrast, the whole perfused rabbit ear contains constriction-mediating P_{2X}- and dilation-mediating P_{2Y}-receptors.[4]

The ear arteries were simultaneously incubated and perfused (2.7 ml/min). Non-cumulative concentration-response curves of agonists were determined by addition to the bath fluid at increasing concentrations. Noradrenaline (0.1 - 30 µmol/l), mATP (0.1 - 30 µmol/l) and ATP (30 - 3000 µmol/l) elicited vasoconstriction, with potency decreasing in that order. Suramin (30 - 300 µmol/l) did not alter the basal perfusion pressure and the response to noradrenaline. Increasing concentrations of suramin shifted the concentration-response curve for mATP increasingly to the right. In contrast to its effect against mATP, suramin (30 - 300 µmol/l) did not attenuate the ATP-induced constriction. Suramin-resistant components of ATP-induced contractions have also been observed in the mouse vas deferens.[5] The lack of antagonism of suramin against ATP was not due to a simultaneous

blockade by suramin of a vasodilatory P_1-receptor since suramin also failed to antagonize ATP in the presence of 8-(p-sulphophenyl)-theophylline 100 μmol/l. In the presence of the putative P_{2Y}-antagonist reactive blue 2 (RB2, 20 and 60 μmol/l), however, responses to ATP were enhanced, and increasing concentrations of suramin now shifted the concentration-response curve for ATP increasingly to the right. In additional experiments, vasodilator effects of adenosine and ATP were studied after pre-contraction by noradrenaline 0.3 μmol/l. RB2 60 μmol/l changed neither the vasoconstrictor effect of noradrenaline nor the subsequent vasodilator effect of adenosine 100 μmol/l, but reversed the dilator effect of ATP 100 μmol/l to an additional contraction.

The increase in constrictor responses to ATP in the presence of RB2 and the inhibition of the ATP- but not the adenosine-induced dilation by RB2 indicate that ATP activates relaxation-mediating P_{2Y}-receptors in addition to the constriction-mediating P_{2X}-receptors in the isolated rabbit ear artery. The inhibition of the constrictor effect of the P_{2X}-selective agonist mATP by suramin confirms the idea that suramin has antagonist properties at the P_{2X}-receptor. Moreover, suramin also blocks dilatory P_{2Y}-receptors[6], since a concentration-dependent shift by suramin to the right of the ATP concentration-response curve by suramin was observed only in the presence of RB2.

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