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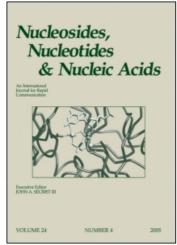
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# Effects of Suramin on the ATP- and $\alpha$ , $\beta$ -Methylene-ATP-induced Constriction of the Rabbit Ear Artery

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## EFFECTS OF SURAMIN ON THE ATP- and $\alpha$ , $\beta$ -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. Suramin also antagonizes the vasoconstrictor effect of  $\alpha$ ,  $\beta$ -methylene-ATP (mATP) in the pithed rat. 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. In contrast, the whole perfused rabbit ear contains constriction-mediating  $P_{2X}$ - and dilation-mediating  $P_{2Y}$ -receptors.  $P_{2X}$ - and dilation-mediating  $P_{2Y}$ -receptors.

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  $\mu$ mol/1), mATP (0.1 - 30  $\mu$ mol/1) and ATP (30 - 3000  $\mu$ mol/1) elicited vasoconstriction, with potency decreasing in that order. Suramin (30 - 300  $\mu$ mol/1) 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  $\mu$ mol/1) did not attenuate the ATP-induced constriction. Suramin-resistant components of ATP-induced contractions have also been observed in the mouse vas deferens. 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  $\mu$ mol/l. In the presence of the putative  $P_{2Y}$ -antagonist reactive blue 2 (RB2, 20 and 60  $\mu$ mol/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  $\mu$ mol/l. RB2 60  $\mu$ mol/l changed neither the vasoconstrictor effect of noradrenaline nor the subsequent vasodilator effect of adenosine 100  $\mu$ mol/l, but reversed the dilator effect of ATP 100  $\mu$ mol/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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