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Publisher *Taylor & Francis*

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## **Nucleosides, Nucleotides and Nucleic Acids**

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597286>

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

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**To cite this Article** von Kügelgen, Ivar and Starke, Klaus(1991) 'Effects of Suramin on the ATP- and  $\alpha,\beta$ -Methylene-ATP-induced Constriction of the Rabbit Ear Artery', *Nucleosides, Nucleotides and Nucleic Acids*, 10: 5, 1181 — 1182

**To link to this Article:** DOI: 10.1080/07328319108047267

**URL:** <http://dx.doi.org/10.1080/07328319108047267>

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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.<sup>1</sup> Suramin also antagonizes the vasoconstrictor effect of  $\alpha,\beta$ -methylene-ATP (mATP) in the pithed rat.<sup>2</sup> 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.<sup>3</sup> In contrast, the whole perfused rabbit ear contains constriction-mediating  $P_{2X}$ - and dilation-mediating  $P_{2Y}$ -receptors.<sup>4</sup>

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/l), mATP (0.1 - 30  $\mu$ mol/l) and ATP (30 - 3000  $\mu$ mol/l) elicited vasoconstriction, with potency decreasing in that order. Suramin (30 - 300  $\mu$ mol/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  $\mu$ mol/l) did not attenuate the ATP-induced constriction. Suramin-resistant components of ATP-induced contractions have also been observed in the mouse vas deferens.<sup>5</sup> 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  $\mu\text{mol/l}$ . In the presence of the putative  $P_{2Y}$ -antagonist reactive blue 2 (RB2, 20 and 60  $\mu\text{mol/l}$ ), 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  $\mu\text{mol/l}$ . RB2 60  $\mu\text{mol/l}$  changed neither the vasoconstrictor effect of noradrenaline nor the subsequent vasodilator effect of adenosine 100  $\mu\text{mol/l}$ , but reversed the dilator effect of ATP 100  $\mu\text{mol/l}$  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<sup>6</sup>, 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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