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NCX 4016, A NITRIC OXIDE-RELEASING ASPIRIN, MODULATES ADRENERGIC VASOCONSTRICTION IN THE PERFUSED RAT TAIL ARTERY

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The ability of the nitric oxide (NO)-releasing aspirin, NCX 4016, to control vasoconstrictor responses induced by electrical field stimulation (TNS) or by exogenous norepinephrine (NE) was investigated in perfused rat tail artery with intact endothelium.
NCX 4016 (25, 50 and 100 μM) dose-dependently antagonized the vasoconstriction caused by TNS (from 0.5 to 64 Hz) and by NE (from 0.01 to 10 μM). The vasorelaxant activity of NCX 4016 (100 μM) in NE-precontracted arteries was concomitant with a marked increase of tissue cyclic GMP (4.9 fold, $P < 0.001$) and was significantly antagonized by the inhibitors of soluble guanylate cyclase, methylene blue and 1H-[1,2,4]Oxadiazolo[4,3-a]quinoxalin-1-one.
In preparations perfused with N^G-monomethyl-L-arginine (10 μM), NCX 4016 prevented the rise in basal perfusion pressure and reversed the accentuation of vasoconstrictor responses caused by NO synthase inhibition.
Aspirin-moiety released by NCX 4016 inhibited the 6-keto-$PGF_{1\alpha}$ formation without interfering with the vasorelaxant activity of NCX 4016, while aspirin (100 μM) was devoid of any activity against vasoconstriction induced by both TNS and NE in perfused rat tail artery.
NCX 4016 controlled adrenergic vasoconstriction in perfused rat tail arteries by a direct donation of NO without involving the relaxant factors such as PGI_2 and NO from endothelial cells.
The results obtained with NCX 4016 in perfused rat tail artery bears some therapeutical potential in conditions associated with vascular smooth muscles hyperreactivity to adrenergic stimulation.