Vasorelaxant Action of *N-p*-Nitrophenylmaleimide in the Isolated Rat Mesenteric Artery

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The vasorelaxant response of *N-p*-nitrophenylmaleimide (4-NO_2-NPM) was evaluated. The mesenteric rings (1–2 mm i.d.) were suspended by cotton thread for isometric tension recordings in a Tyrode's solution at 37 °C and gassed with a mixture of 95% O_2 and 5% CO_2, under a resting tension of 0.75 g. 4-NO_2-NPM induced relaxation in mesenteric rings pre-contracted with phenylephrine (Phe; 10 μM, pD_2 = 6.7 ± 0.3) or KCl (80 mM, pD_2 = 3.9 ± 0.2). This effect was significantly attenuated after removal of the vascular endothelium, N^G-nitro L-arginine methyl ester (L-NAME; 100 μM), atropine (1 μM), indomethacin (10 μM), L-NAME + indomethacin or 1*H*-[1,2,3]oxadiazolo[4,3-*U*]quinoxalin-1-one (ODQ; 10 μM). L-Arginine (1 mM) reversed the inhibitory effect of L-NAME. In endothelium-intact preparations pre-incubated with 20 mM KCl, tetraethylammonium bromide (TEA; 1 mM) or glibenclamide (Glib; 10 μM), the vasorelaxant effect was significantly attenuated when compared to controls (endothelium intact). In denuded rings, separate incubation with 20 mM KCl, TEA or Glib did not change the relaxation when compared with that obtained in denuded rings. 4-NO_2-NPM inhibited in a concentration-dependent and non-competitive manner the concentration-response curves induced by $CaCl_2$. In calcium-free medium, the transient contractions induced by Phe (10 μM) or caffeine (20 mM) were inhibited. The relaxant effect induced by 4-NO_2-NPM appeared to be due to endothelial muscarinic receptors activation, NO and prostacyclin release and K_{ATP} and BK_{Ca} (Ca^{2+}-activated K^+ channels) endothelium-dependent activation. Inhibition of the Ca^{2+} influx and inhibition of the Ca^{2+} release from intracellular IP_3- and caffeine-sensitive stores are also involved in the vasorelaxation.

Key words: N-p-Nitrophenylmaleimide, Endothelium-Derived Factors, Mesenteric Rings