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Interactions between Carbon Monoxide Releasing Molecules and Nitric Oxide Donors in Vascular Tissue

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SUMMARY

Carbon monoxide (CO) is a weak sGC stimulator, leading to transient increases in cGMP and vasodilation. Transition metal carbonyls liberate CO in a controlled fashion and function as CO-releasing molecules (CORMs). The aim of the present work was to test the ability of a number of CORMs to modulate basal and nitric oxide (NO)-induced cGMP formation and vasorelaxation. cGMP accumulation was measured in rat aortic smooth muscle cells in the presence of CORMs and/or nitric oxide (NO) donors using ELISA. Basal and nitric oxide-stimulated sGC activity was determined using purified rat recombinant sGC. Vasodilation was determined using pre-contracted rat aortic rings after incubation with a CORM, in the presence or absence of S-nitroso N-acetylpenicillamine. Incubation of cells with some, but not all of the CORMs caused a minor increase in cGMP levels. Concentration-response curves were bell-shaped for most of the CORMs studied. Although exposure of cells to CORM-2 or ALF157 enhanced cGMP formation we observed that both compounds inhibited NO-stimulated cGMP accumulation in cells and NO-stimulated sGC activity that could be reversed by superoxide anion scavengers. Superoxide anion generation from both CORM-2 and ALF157 was confirmed using luminol-induced chemiluminescence. Furthermore, we observed that NO is scavenged by CORM-2. When used alone CORM-2 relaxed vessels through a cGMP-mediated pathway, but attenuates NO donor-stimulated vasorelaxation. We conclude that CORMs have variable, context-dependent effects on vessel tone as they can directly dilate blood vessels and also block NO-induced vasorelaxation.