Vascular activity of (-)-anonaine, (-)-roemerine and (-)-pukateine, three natural 6a(R)-1,2-methylenedioxyaporphines with different affinities for ?1-adrenoceptor subtypes

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We have studied the mechanism of action of three 6a(R)-1,2- methylenedioxyaporphines as vasorelaxant compounds. The alkaloids assayed showed different affinities for the three human cloned ?1- adrenoceptor (AR) subtypes stably expressed in rat-1 fibroblasts, showing lower affinity for ?1B-AR with regard to the ?1A- or ?1D-subtypes. These three natural compounds are more potent inhibitors of [3H]-prazosin binding than of [3H]-diltiazem binding to rat cerebral cortical membranes. As all these alkaloids inhibited noradrenaline (NA)-induced [3H]-inositol phosphate formation in cerebral cortex and rat tail artery, they may be safely viewed as ?1-AR antagonists, as is demonstrated by the vasorelaxant responses observed in isolated rat tail artery and/or aorta precontracted with NA. The alkaloids also inhibited the contractile response evoked by KCl (80 mM) but with a lower potency than that shown against NA-induced contraction. We have also examined their ability to inhibit the different for