Norbornide: a Calcium Entry Blocker with Selective Vasoconstrictor Activity in Rat Peripheral Arteries

Sergio Bova, Lorenzo Cima, *Vera Golovina, Sisto Luciani, Gabriella Cargnelli

Department of Pharmacology and Anesthesiology, University of Padova, Italy; *Department of Physiology, University of Maryland School of Medicine, Baltimore, MD USA

Key Words: Calcium entry blockers—Norbornide—PLC—Rat—Selective vasoconstriction.

ABSTRACT

Norbornide is a unique vasoactive substance endowed with species- and tissue-specific, endothelium independent, vasoconstrictor activity that is restricted to the peripheral arteries of rat. In rat aorta and in all tested arteries of other species norbornide exhibits vasorelaxant property presumably due to the blockade of calcium channels. A calcium entry blocker effect of norbornide has also been described in isolated, perfused guinea pig hearts. In these preparations norbornide produced coronary vasodilator, as well as negative inotropic and dromotropic effects. In single ventricular myocytes of guinea pigs norbornide reduces L-type calcium current. The mechanism underlying the selective vasoconstrictor effect of norbornide is unknown. In rat caudal artery, a vessel contracted by norbornide, the drug activates phospholipase C (PLC) signal cascade which is the biochemical pathway involved in the contractile effect triggered by most receptor-activating vasoactive agents. Therefore, norbornide-induced contraction of rat peripheral vessels is likely to be due to the activation of a PLC-coupled receptor abundantly or selectively expressed in vascular smooth muscle cells. The identification of this putative receptor could facilitate the development of tissue-selective pharmacological agents.