RELAXANT EFFECT OF NORBORMIDE, A SELECTIVE VASOCONSTRICTOR AGENT FOR THE RAT PERIPHERAL VESSELS, ON RAT TRACHEAL, URINARY BLADDER, AND INTESTINAL SMOOTH MUSCLES

Cavalli M., 1° anno di corso del Dottorato in Farmacologia Molecolare e Cellulare, II ciclo. Durata del Dottorato in anni: 3. Sede diservizio: Dipartimento di Farmacologia ed Anestesiologia, Università di Padova.

Introduction. Norbormide, 5-(α-hydroxy-α-2-pyridylbenzil)-7-(α-2-pyridylbenzilidene) -5-norbormene-2,3-dicarboximide, has been shown to be a selective vasoconstrictor agent for the rat peripheral arteries and to induce a vasorelaxant effect in rat aorta as well as in small and large arteries of non rat species. In this study it has been investigated the effect of norbormide on rat non-vascular smooth muscles, namely tracheal (TR), duodenal (DUO) and urinary bladder (UB) smooth muscles.
Methods: Rat UB, TR and DUO were extracted, cleaned of connective tissue and cut into rings of 2 mm length. Tissue rings were vertically suspended between 100 OD tungsten wires in organ baths filled with a physiological salt solution. Tension was recorded on a pen recorder via an isometric force displacement transducer. Rings were stretched passively to impose a resting tension of 1-2 gr. Before starting the experimental procedure, rings were allowed to equilibrate for 60 min. and then repeatedly stimulated with carbamylcholine (10μM) until reproducible contractile responses were obtained.
Results. Norbormide, at a concentration that induces the maximal contractile effect in rat peripheral arteries, does not contract rat TR, DUO, and UB smooth muscle rings. In all these preparations, concentration-response curve for KCl (30-60-90 mM) were shifted to the right dose-dependently by norbormide (5 and 50 μM) with a maximal inhibitory effect that was of 74%, 68% and 56% in DUO, UB, and TR, respectively. Similarly, norbormide, at the same concentrations, shifted to the right the concentration-response curve for carbachol, a muscarinic receptor agonist, in UB and TR rings, with a maximum inhibitory effect of 42% and 10%, respectively. Qualitatively same results were obtained by using verapamil, a well known inhibitor of L-type Ca2+ channels, instead of norbormide.
Conclusions. Our results strongly support the hypothesis that norbormide contractile effect is selective for rat peripheral arteries and indicate that in rat non vascular smooth muscle this compound elicits a relaxing action presumably mediated by a block of L-type Ca2+ current.