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Dissertations-Kurzfassung

The relaxant effects of the L- and T- type calcium antagonists on contractions of isolated porcine and human detrusor muscle *in vitro*

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In the present study, the *in vitro* influence of L- and T- type calcium antagonists on contractility and contractions of isolated porcine and human detrusor muscle was investigated. Muscle strips were mounted in an organ bath to record isometric contractions induced by K^+, electrical field stimulation (EFS) and carbachol. The effects of all 3 subgroups of the L-type calcium antagonists and the selective T-type calcium antagonist mibefradil were investigated.

1. All L-type calcium antagonists significantly suppress the maximum contraction of porcine detrusor induced by high-concentrated potassium solution. Nifedipine significantly reduced the maximum contraction to 89%, 60%, 21%, 8% and 4% (10^{-9} M to 10^{-5} M, respectively), verapamil to 64%, 30% and 5% (10^{-7} M to 10^{-5} M, resp.), diltiazem to 79%, 27%, 7% und 1% (10^{-7} M to 10^{-4} M, resp.).
2. The effects of 5 calcium antagonists at different concentrations on the concentration-response curves for carbachol were investigated in human detrusor muscle. The concentration-relaxation experiments resulted in the following pD2 values and maximum relaxations of nifedipine, nimodipine, verapamil and diltiazem, respectively: 6.23, 6.37, 5.66, 5.81 and 85%, 83%, 82%, 90%. The lowest concentration for which a significant difference was found was 10^{-10} M for nimodipine, 10^{-9} M for nifedipine, 10^{-7} M for diltiazem, $10^{-6,5}$ M for verapamil and 10^{-4} M for mibefradil.
3. EFS was performed in porcine detrusor. Nifedipine significantly reduced the electrically generated contraction to 55%, 36%, 34% and 25% at 10^{-7} M to 10^{-4} M, resp., verapamil to 71%, 32% and 2% (10^{-6} M to 10^{-4} M, resp.), diltiazem to 96%, 78%, 38% and 5% (10^{-7} M to 10^{-4} M, resp.).
4. The concentration-response curve of carbachol after pretreatment with different calcium antagonists was investigated.
   - Human: nifedipine significantly reduced the maximum contraction to 75% and 44%, verapamil to 75% and 67% at concentrations of 10^{-7} M and 10^{-6} M, respectively. Diltiazem insignificantly reduced it to 96% and 71%, resp. Mibefradil up to 10^{-5} M did not significantly suppress the mean concentration-response curve of carbachol.
   - Porcine: nifedipine, nimodipine, verapamil and diltiazem significantly suppress the mean concentration-response curve of carbachol at 10^{-7} M. Nifedipine at a concentration of 10^{-6} M suppress the contraction almost completely. Mibefradil showed only a significant effect at a concentration = 10^{-5} M.
5. The study demonstrates strong inhibitory effects of L-type calcium antagonists on the contraction of human and porcine detrusor muscle. It suggests that these substances may be useful therapeutic agents for the treatment of bladder hyperactivity. The small differences between human and porcine urinary bladder`s smooth muscle show that the pig is a good experimental model for human bladder research.