434

Oh S. [1], Kang J. [2], Kim S. J. [3], Hong E. K. [4], Kim K. M. [1]
1. Department of Urology, Seoul National University College of Medicine, 2. Department of Urology, Eulji Medical Center, 3. Department of Physiology, School of Medicine, Sung, 4. Medvill Co., Ltd.

PHARMACOLOGICAL EFFECTS OF BERBERINE AND PALMATINE ON THE PROSTATE AND URETHRAL SMOOTH MUSCLE OF THE RABBIT

Aims of Study

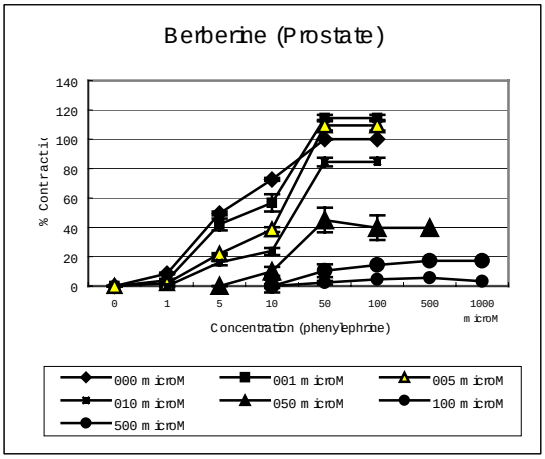
The contractile properties of the prostatic and urethral tissue are mediated primarily by alpha-adrenoreceptors. One of the major medical treatment for benign prostatic hyperplasia is targeted toward reducing bladder outlet obstruction by alpha-adrenoceptor blockade to relax the smooth muscle tone of the prostate. Alpha-adrenoceptors are also highly concentrated in the urethral smooth muscles and may play an important role in the contraction of this area [1]. Berberine (BBR) and palmatine (PMT), an isoquinoline alkaloid, derived from the Chinese herb Huanglian and many other plants, has a varied pharmacological action and have been extensively used in folk medicine. A previous large scale screening test revealed that BBR derivatives have antagonistic effects at the alpha1-adrenoceptors, although they are less potent than prazosin [2]. The aim of this study is to investigate the effect of the BBR and PMT on the contractility of the isolated prostate and urethral smooth muscle tissue of the rabbit.

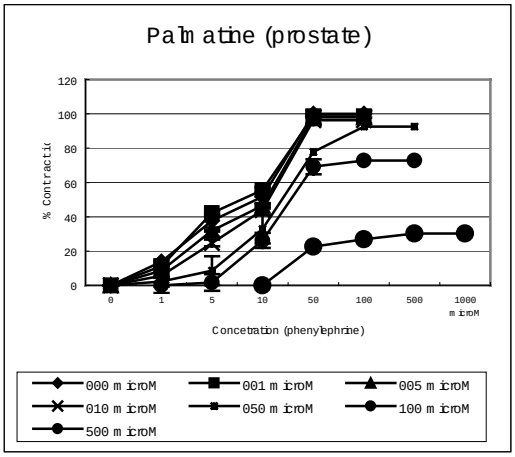
Methods

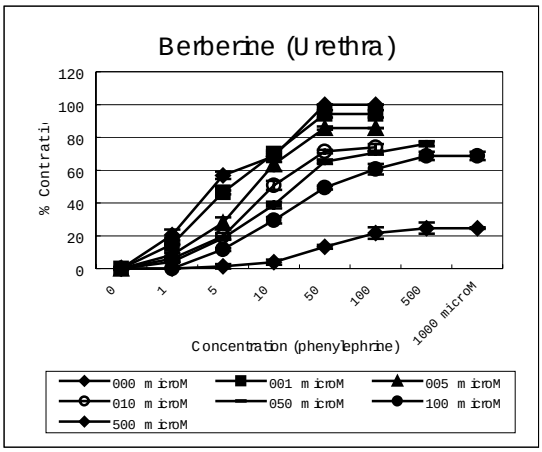
Prostate and longitudinal urethral muscle strips were obtained from 10-week-old New Zealand White rabbit. In vitro isometric contraction was measured using organ bath study. Cumulative concentrations of phenylephrine (PE) as an agonist were added to produce concentration-response relationships. BBR (1- 500μM) and PMT (1- 500μM) were added to the bath 20 min before the repeated PE-induced concentration-response curve was made. Responses of developed tension to PE were plotted as percentage of the maximal increase for each concentration-response curve in the prostate and urethral muscle strips. The pH of the bath solution was adjusted and controlled.

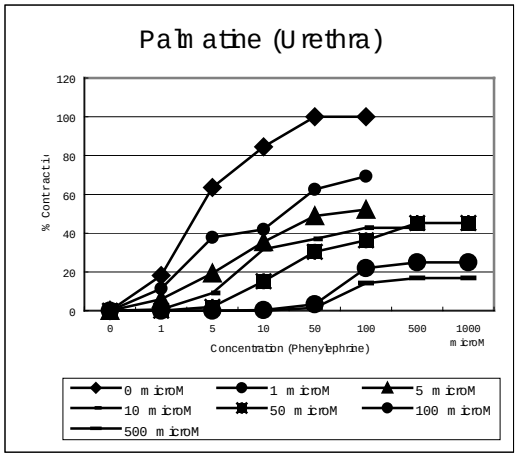
Results

PE produced concentration-dependent contractions on the rabbit prostatic and urethral preparations. BBR and PMT induced dose-dependent relaxation of the PE-induced contraction of both prostate and urethral smooth muscle. In the prostate strips, lower concentrations of BBR (1- 10μM) or PMT (1- 100μM) induced a parallel rightward shift of the dose-response curve of PE, suggesting that both agents are antagonising the actions of PE at the receptors competitively. At higher concentrations, BBR (50 - 500μM) or PMT (> 500μM) facilitated a rightward shift of the dose-response curve of PE with a reduction of maximal response, indicating that the interactions of the two agents with PE changed from competitive to noncompetitive antagonism. In the urethral tissue, both BBR (1- 500μM) and PMT (1- 500μM) reduced the maximal response to PE, showing stronger noncompetitive antagonisms rather than competitive antagonism. The rank order of potency of the antagonistic effect on prostatic alpha-adrenoceptor was BBR > PMT, while that on the urethral tissue was PMT > BBR.









Conclusions

Our results indicated that BBR or PMT might be potentially useful therapeutic agents for bladder outlet obstruction. A deeper understanding of the action mechanisms of BBR and PMT would widen our therapeutic options for voiding disorders.

References

1. BJU Int 1999 Sep;84(4):515-20
2. J Pharm Pharmacol 1996 Jun;48(6):629-34