Hypothesis / aims of study
Phytotherapeutic agents, including Saw palmetto extract (SPE), are popular in many European countries as herbal remedies representing up to 80% of all drugs prescribed for benign prostatic hyperplasia (BPH) and associated lower urinary tract symptoms (LUTS). However, the mechanism of pharmacological action of SPE is not fully elucidated. Animal experiments with SPE have demonstrated antiandrogen activity and inhibition of 5\'-reductase, the enzyme that converts testosterone to its active metabolite, dihydrotestosterone [1]. Recently, we have demonstrated that SPE alleviates significantly urodynamic symptoms in acetic acid-induced hyperactive rat bladders by increasing bladder capacity and subsequently prolonging the micturition interval. 1-Adrenoceptor antagonists and muscarinic cholinceptor antagonists are commonly used in the treatment of men with voiding symptoms (urinary obstruction, pollakiuria and urinary incontinence) secondary to BPH. Thus, such improvement of voiding symptoms by SPE might be expected to result from its significant antagonism of autonomic receptors in the lower urinary tract because SPE contains many constituents. In fact, Goepel et al. [2] have shown that SPE has 1-adrenoceptor inhibitory property. Thus, we examined the binding activities of SPE and its crude fractions to several receptors (1-adrenoceptors, muscarinic cholinceptors, 1,4-dihydropyridine calcium channel antagonist receptors and P2X receptors) in the prostate and bladder of rats.

Study design, materials and methods
The rat bladder and prostate were excised and the homogenates were used for the radioligand binding assays of each receptor. Muscarinic cholinceptors, 1,4-dihydropyridine calcium channel antagonist receptors and P2X receptors in the rat bladder and 1-adrenoceptors in the prostate were measured by radioligand binding assays of [3H]N-methylscopolamine (NMS), (+)[3H]PN 200-110, [3H]-MeATP and [3H]prazosin, respectively.

Results
Relatively low concentrations (10-1000 g/mL) of SPE inhibited specific binding of [3H]NMS and (+)[3H]PN 200-110 (rat bladder) and [3H]prazosin (prostate) in a concentration dependent manner, and their IC50 values were 40.0, 93.7 and 169 g/mL, respectively. Furthermore, SPE (0.1-1000 g/mL) did not inhibited specific binding of [3H]-MeATP in the rat bladder. n-Hexane fraction and diethyl ether fraction of SPE (10-500 g/mL) inhibited specific binding of [3H]NMS and (+)[3H]PN 200-110 in the rat bladder and [3H]prazosin in the prostate in a concentration dependent manner. The IC50 values of n-hexane fraction and diethyl ether fraction of SPE were 67.9 and 57.7 g/mL for [3H]NMS, 31.0 and 37.5 g/mL for (+)[3H]PN 200-110, 195 and 208 g/mL for [3H]prazosin, respectively. SPE ([3H]NMS: 50 g/mL, (+)[3H]PN 200-110: 100 g/mL, [3H]prazosin: 150 g/mL) brought about a significant (30.2-66.6%) decrease of maximal number of binding sites for [3H]NMS and (+)[3H]PN 200-110 in the rat bladder and for [3H]prazosin in the prostate, respectively.

Interpretation of results
These data suggest that SPE exerts significant binding activities of autonomic and calcium channel antagonist receptors in the prostate and bladder, targeting sites of drugs used clinically in the treatment of BPH and LUTS. Moreover, the n-hexane and diethyl ether fractions of SPE may contain active constituents for these receptors.

Concluding message
The present study has first shown that SPE may act as relatively potent agonists and/or antagonists of muscarinic cholinceptors, 1-adrenoceptors and 1,4-dihydropyridine calcium channel antagonist receptors in the lower urinary tract.
References: