Alteration of pharmacologically relevant bladder receptors in cyclophosphamide-induced cystitis rats and effects of plant extracts

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Interstitial cystitis (IC) is a chronic, abacterial inflammatory disease of the bladder characterized by urinary frequency, urgency and suprapubic pain associated with bladder filling and relieved by voiding, but its exact etiology and pathogenesis remain unclear and effective treatment is not established. Currently, there are increasing evidences to suggest the idea that the abnormality of muscarinic receptors in the bladder is implicated in the development of IC (Kageyama et al.,2008). The present study was aimed to characterize the pharmacologically relevant receptor in the pathophysiology of IC and the effects of plant extracts (Saw palmetto extract: SPE, Gosha jinki gan: GJG, Eviprostat: EVI), by measuring muscarinic receptors in the bladder and submaxillary gland of rats with cystitis induced by cyclophosphamide (CYP).

Cystitis model was induced by injecting CYP (150mg/kg, i.p.) in female Sprague-Dawley rats (9 weeks old). Rats were divided into sham group, CYP-treated group, CYP+drug-treated group. SPE (60 mg/kg), GJG (1000 mg/kg), and EVI (18 mg/kg) were administered orally for 7 days. On the last day of treatment, the tissue muscarinic receptor was measured by radioligand binding assay using [^{3}H]NMS, and binding parameters of apparent dissociation constant (K_d) and maximal number of binding sites (B_{max}) were estimated by nonlinear regression analysis using Graph Pad Prism.

The B_{max} for specific [^{3}H]NMS binding was significantly decreased in the bladder of CYP treated rats compared with sham rats. Thus, CYP treatment was shown to cause down-regulation of muscarinic receptors in the bladder of rats. There was significant increase in the Bmax for [^{3}H]NMS in the bladder of rats treated with CYP+SPE, CYP+GJG, and CYP+EVI, compared with CYP treated bladder. On the other hand, the B_{max} for [^{3}H]NMS in the submaxillary gland was not altered by the CYP treatment. In conclusion, the current study indicates that SPE, GJG, and EVI attenuate down-regulation of muscarinic receptors in the bladder of rats with CYP-induced cystitis, suggesting pharmacological usefulness.