学 位 論 文 の 要 旨

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学 位 論 文 名　A Phytosterol Enriched Refined Extract of Brassica Campestris L. Pollen Significantly Improves Benign Prostatic Hyperplasia (BPH) in a Rat Model as Compared to the Classical TCM Pollen Preparation Qianlie Kang Pule'an Tablets

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論 文 内 容 の 要 旨

INTRODUCTION

Benign prostate hyperplasia (BPH) is one of the most common diseases among elderly men in East Asia and exhibits gradually increasing incidence rates. In Qinghai Province, PR China, the *Brassica campestris L.* pollen preparation Qianlie Kang Pule'an Tablet (QKPT) is traditionally used for BPH therapy. QKPT is an adaptogenic traditional Chinese medicine (TCM) preparation for symptoms of weakened renal qi, commonly used in the treatment of chronic prostatitis, prostatic hyperplasia, incontinence, as well as for soreness and weakness of waist and knees. However, in QKPT the content of supposedly active phytosterols is relatively low, necessitating high doses for successful therapy. Therefore, a phytosterol enriched refined extract of *B. campestris* pollen (PE) was developed.

MATERIALS AND METHODS

The preparation method of PE is that 10kg pollen was broken down and extracted

with 95% ethanol twice, and two liquid extracts were mixed and evaporated into dry, and then yield 2.0 kg of the examined pollen extract PE. The over-all contents of phytosterolsin and β-sitosterol, which are considered as the most active compounds, were determined by the classical TCM pollen preparation. The over-all contents of phytosterolsin in QKPT and in PE were 2.59% and 4.54% respectively, and the contents of β-sitosterol were 0.101% and 0.057% respectively. In the present animal model, androgen-driven BPH was triggered by administering super-physiological testosterone-doses to castrated male rats.

In castrated rats, this main source of endogenous dihydrotestosterone (DHT) is incapacitated thus promoting prostate atrophy. Subsequent administration of exogenous testosterone lessens the effects of castration, reactivating prostate growth, and after injection of super-physiological doses leads to hyperplasia. The effect of PE on BPH rat model was compared with QKPT. Six groups of rats (n = 8 each), namely sham-operated distilled water control, castrated distilled water control, castrated QKPT 2.0 g/kg, castrated PE 0.1 g/kg, castrated PE 0.2 g/kg, and castrated PE 0.4 g/kg, were intragastrically treated with the respective daily doses. Testosterone propionate (0.3 mg/day) was administered to all castrated rats, while the sham-operated group received placebo injections. After 30 days, the animals were sacrificed and prostates as well as seminal vesicles excised and weighted in order to calculate prostate volume index (PVI) as well as prostate index (PI) and seminal vesicle index (SVI), defined as organ weight in g per 100 g body weight.

RESULTS AND DISCUSSION

Compared with sham-operated controls, PI ($p < 0.01$), PVI ($p < 0.01$), and SVI ($p < 0.01$) were all significantly increased in all castrated, testosterone treated rats. After treatment with PE at 0.4 and 0.2 g/kg or QKPT at 2.0 g/kg per day, both indices were significantly reduced ($p < 0.01$) as compared to the castrated distilled water control. For PE at 0.1 g/kg per day only PI was significantly reduced ($p < 0.05$). At the highest PE concentration of 0.4 g/kg per day both PI and SVI were also significantly reduced when compared to the QKPT group ($p < 0.05$).

In this study, a pathological classification standard for the severity of the hyperplastic state of the prostates of test animals was designed. Most of the animals in the castrated distilled water control group suffered from serious pathological changes in

their prostates. However, these symptoms were significantly reduced by treatment with PE at 0.4 and 0.2 g/kg ($p < 0.01$, $p < 0.05$). In the castrated distilled water control group, the prostatic epithelial cells proliferated to significantly higher levels than in the sham-operated distilled water control group, and the prostatic glandular cavities were also markedly enlarged. In the three PE groups and in the QKPT group both epithelial cell proliferation and glandular cavity enlargement were significantly reduced. Both maximal glandular cavity diameters and glandular epithelium height in the distilled water control group were significantly larger than those in the sham-operated distilled water control group ($p < 0.01$). In comparison with the distilled water control group, the glandular cavity diameters in the PE 0.4 and 0.2 g/kg groups as well as in the QKPT 2.0 g/kg group were significantly reduced ($p < 0.01$). A similarly significant reduction of glandular epithelium height in the PE 0.4 g/kg group was also observed ($p < 0.05$). In addition, the effects of high-dose PE (0.4 g/kg) on pathological changes of hyperplastic prostates were somewhat favourable in comparison with those of QKPT 2.0 g/kg, which contains an equivalent amount of pollen.

CONCLUSION

In conclusion, both PE and QKPT demonstrated curative effects against BPH in the applied animal model. In its highest dose at 0.4 g/kg per day, PE was clearly superior to QKPT.