671 Efficacy of Canephron® N against bacterial adhesion, inflammation and bladder hyperactivity

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Künstle G., Brenneis C., Haunschild J.

Bionorica SE, Preclinical and Project Management, Neumarkt, Germany

INTRODUCTION & OBJECTIVES: Canephron® N, a herbal drug combination which contains dried and pulverized *Rosmarini folium*, *Levistici radix* and *Centaurii herba* (1:1:1), is used since decades against urinary tract infections (UTI). During UTI mostly E. coli adhere to the bladder urothelium were they cause inflammatory reactions. As a result, the bladder gets hyperactive and patients suffer from increased micturition frequency and pain. To investigate whether orally applied Canephron® N possesses relevant pharmacological activities we characterized its anti-adhesive and anti-inflammatory activity and its potency to treatoveractive bladder and to ease bladder functions in a rat model of cyclophosphamide (CYP)-induced cystitis.

MATERIAL & METHODS: Anti-adhesive effects were investigated by *in vitro* inhibition of the adhesion of E. coli (DSM-10777) to human bladder cells. Anti-inflammatory effects were analyzed by *in vitro* inhibition of the activity of recombinant human 5-lipoxygenase (5-LO), zymosan-induced interleukin 1-beta (IL-1β) release from splenic monocytes and efficacy against carrageenan-induced paw edema formation after oral administration of Canephron® N in rats. To investigate bladder hyperactivity, interstitial cystitis was experimentally induced in female rats by cyclophosphamide (CYP, 150 mg/kg) injection (i.p) and urodynamic parameters characterized by cystomanometric measurements. Canephron® N was orally applied twice per day by gavage.

RESULTS: Canephron® N concentration-dependently inhibited the adhesion of E. coli to bladder cells for up to 61% at 100 µg/ml. 5-LO activity was concentration-dependently inhibited by Canephron® N for up to 100% by 100 µg/ml (IC_{50} = 8.4 µg/ml) and IL1β release to 96 % at 400 µg/ml (IC_{50} = 218 µg/ml). *In vivo*, Canephron N significantly attenuated carrageenan-induced paw edema formation at 250 mg/kg and higher. CYP injection caused a strongly reduced bladder capacity (BC) which was significantly and dose-dependently increased by oral Canephron® N treatment in doses of up to 666 mg/kg reaching baseline levels.

CONCLUSIONS: The experiments show that Canephron® N potentially acted against the adhesion of uropathogenic bacteria to bladder urothelium and that it attenuated inflammatory reactions *in vitro* and *in vivo* after oral application. Finally, we found that orally applied Canephron® N was able to reverse bladder hyperactivity in a model of interstitial cystitis. In summary, the anti-adhesive and anti-inflammatory as well as the positive effects on bladder hyperactivity *in vivo* gives a strong indication that the pharmacological activities of Canephron® N are multifactorial and appears to be tailored for the treatment of urinary tract infections.