

## STINGING NETTLE LEAF EXTRACT AFFECTS SMOOTH MUSCLE CONTRACTILITY IN THE ISOLATED RAT PROSTATE GLAND BY ACTING WITHIN THE PURINERGIC SYSTEM.

### Hypothesis / aims of study

*Urtica dioica* (commonly known as stinging nettle) is used worldwide as an alternative to conventional pharmacotherapies for benign prostatic hyperplasia (BPH). The root extract is commonly used in Europe, primarily in Germany, for the treatment of the symptoms associated with BPH. It is thought to alleviate lower urinary tract symptoms (LUTS) by reducing stromal proliferation and thereby decreasing the size of the prostate gland [1]. The leaf extract has been used in traditional medicine in Turkey for the relief of lower urinary tract symptoms [2], as well as in Morocco for the treatment of hypertension [3]. This hypertensive action is via a vasorelaxant mechanism which infers a relaxant effect on smooth muscle. As stinging nettle appears to be effective in treating LUTS associated with BPH and drugs which relax prostatic smooth muscle are known to be the most effective for this, it is hypothesised that commercially available stinging nettle extracts affect the prostatic smooth muscle contractility.

The objectives of this study were to investigate: (1) the smooth muscle relaxant efficacy of commercially available stinging nettle leaf and root extracts on the contractility of the rat prostate gland, (2) the pharmacological mechanism of action any smooth muscle relaxation and (3) to identify any bioactive components of these extracts.

### Study design, materials and methods

Prostates were dissected from 7-9 week old male Sprague-Dawley rats. In isolated organ bath studies, nerve terminals were stimulated using electrical field stimulation (EFS) (1 ms pulse duration, 60V, 10 pulses at 0.1 – 0.5 Hz, 10 seconds at 1.0 – 20.0 Hz) to induce prostatic contractions. MediHerb<sup>®</sup> stinging nettle leaf and root extracts (500mg dried plant material/mL in 25% ethanol) were added to the organ bath to investigate the effect that the phytotherapeutic has on prostate contractility. The mechanism of action was investigated by studying the effect of various pharmacological tools.

Liquid-liquid partitioning and reversed-phase flash column chromatography were employed to separate the extract into aqueous and organic phases and five fractions respectively as a preliminary step in the elucidation of the bioactive.

### Results

Whole leaf but not root extract attenuated EFS ( $n = 6$ ;  $P < 0.001$ ) induced contractions of the isolated rat prostate, as well as contractions elicited by exogenous administration of adenosine 5'-triphosphate (ATP) (10 nmol/L – 1 mmol/L) ( $n = 6$ ;  $P < 0.001$ ) or  $\alpha\beta$ methylene ATP (3 nmol/L – 10  $\mu$ mol/L) ( $n = 6$ ;  $P < 0.001$ ). Contractions elicited by exogenous administration of noradrenaline ( $n = 6$ ;  $P = 0.701$ ) or acetylcholine ( $n = 6$ ;  $P = 0.362$ ) were unaffected. The aqueous phase of the leaf extract demonstrated similar results, whereas the organic phase did not. Of the five fractions, only the fraction 1 elicited biological activity.

### Interpretation of results

Attenuation of contractions induced by ATP and  $\alpha\beta$ methylene ATP but not noradrenaline or acetylcholine implies that the extract engenders an effect by antagonizing P2X1-purinoreceptors or by affecting the signalling pathway activated by these receptors. The compound appears to be an aqueous-soluble, polar compound.

### Concluding message

Stinging nettle leaf extract is able to attenuate contraction of the prostate gland. It appears to be acting as an antagonist at P2X1 purinoreceptors, with the responsible compound residing in the aqueous fraction.

### References

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2. Sezik, E., et al., Traditional medicine in Turkey X. Folk medicine in Central Anatolia. *J Ethnopharmacol*, 2001. 75(2-3): p. 95-115.
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### Disclosures

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