

97 Isosamidin, an extract of *Peucedanum japonicum*, may have pharmacological potency in the treatment of male lower urinary tract symptoms

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Introduction and Objective:

- Phytotherapy or the use of plant extracts for treatment of LUTS/BPH is common in Europe and the United States
- *Peucedanum japonicum* (PJ) is a perennial umbelliferae plant that grows naturally along southern coastal areas of Japan.
- Isosamidin is a pharmacologically active compound extracted from PJ that is classified as a coumarin and has pharmacological activities (e.g. inhibition of platelet aggregation, anti-atherosclerotic effects and vasorelaxant effects) [1]
- Isosamidin exerts concentration-dependent inhibition of phenylephrine-stimulated contractions of isolated rabbit prostate strips or acetylcholine-stimulated contractions of isolated rabbit bladder strips in vitro [2]
- In rat, it significantly decreases micturition frequency in hyperactive bladders induced by intravesical infusion of acetic acid in vivo [3]

Isosamidin has sufficient potency to treat patients not only with LUTS/BPH but also overactive bladder.



The efficacy of isosamidin on the human lower urinary tract in vitro has not been studied.



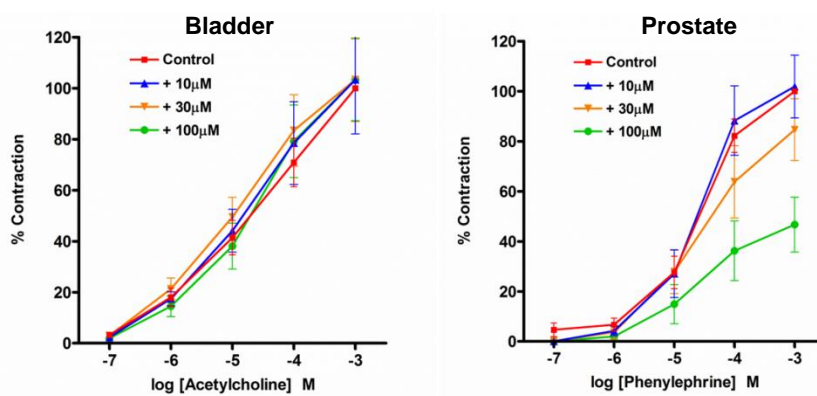
We examined whether isosamidin exerts a concentration-dependent inhibition of agonist-stimulated contraction of isolated human bladder and prostate tissue strips in vitro.

Materials and Methods:

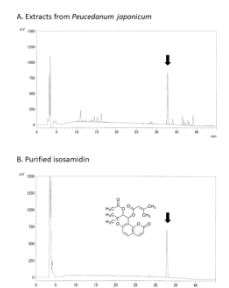
- Human bladder specimens; 9 patients (63.4 ± 10.1 years, age range: 52–84)
- Human prostatic specimens ; 10 patients (66.8 ± 10.9 years, age range: 53–84)
 - * Undergoing radical cystectomy for bladder carcinoma with no evidence of LUTS/BPH or overactive bladder
 - ** Patients with previous pelvic radiotherapy, extensive chemotherapy, or current urinary tract infection were excluded
- Peak contractions of 40 mM KCl reached 5.59 ± 0.83 g in bladder strips and 1.85 ± 0.43 g in prostate strips
- We changed from Krebs/40 mM KCl solution to simple Krebs' solution, adding isosamidin to obtain concentrations of 10, 30, and 100 µM
- Thirty min after administration of isosamidin (10, 30, and 100 µM) or vehicle (control), concentration-response curves were constructed for agonists (acetylcholine for bladder strips and phenylephrine for prostate strips) by cumulatively increasing agonist concentration (10⁻⁷-10⁻³ M) at 10 min intervals



Results:



Inhibitory effect of isosamidin on agonist (acetylcholine, phenylephrine)-stimulated contraction of isolated human bladder (a) and prostate (b).



Results of high performance liquid chromatography (HPLC) of extracts from (A) *Peucedanum japonicum* and (B) purified isosamidin. Arrows indicate isosamidin.

Discussions:

This study is the first to show that isosamidin exhibits an inhibitory effect on phenylephrine-stimulated contraction of isolated human prostate tissue strips in vitro. These results may support the potential clinical efficacy of isosamidin in the treatment of LUTS/BPH.

This study has these limitations.

- 1) We did not examine hyperplastic prostate specimens obtained from LUTS/BPH patients.
- 2) We could not examine the mechanisms of action of isosamidin using various agonists or antagonists.
- 3) To confirm whether isosamidin acts as a α_1 -adrenoceptor antagonist, the binding activity of isosamidin on α_1 -adrenoceptors should be examined.

Conclusions:

Isosamidin inhibits phenylephrine-stimulated prostate contractions in vitro and may have pharmacological potency in the treatment of male patients with LUTS/BPH. Further studies are required to determine the mechanisms underlying isosamidin action, and clinical studies are required to confirm the efficacy and safety of isosamidin in humans.

References:

- [1] Chen YC, et al. Journal of Food and Drug Analysis 16: 15–25, 2008.
- [2] Ohnogi H. Food Process and Ingredients 44: 38–40, 2009. (In Japanese)
- [3] Ito Y, et al. NeuroUrol Urodyn 32: 728–729 abstract 149, 2013.

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