Hypothesis / aims of study
To assess the relaxation effect of the Korean red ginseng (KRG) on the bladder and prostatic urethra and its therapeutic potentials for benign prostatic hyperplasia (BPH)/lower urinary tract symptoms (LUTS).

Study design, materials and methods
Korean red ginseng extract derived from the root of Panax ginseng provided from the Korean Ginseng Corporation. Ginseng extract was dissolved in phosphate buffered saline (PBS) at concentration of $10^{-7}$ to $10^{-2}$ mol/L. For the in vitro study, prostatic urethra muscle strips were harvested from 18 male New Zealand rabbits. The strips were mounted in organ baths and connected to force displacement transducers. After stabilization, maximal tissue contractions were obtained by the addition of phenylepinephrine for urethra strips. When the contraction was stabilized, a dose-response curve of KRG saponin was constructed ($10^{-7}$ to $10^{-2}$). After pretreatment urethra strips with N-nitro-L-arginine methyl ester (L-NAME) which is nitric oxide blocker, a dose-response curve of Korean red ginseng was constructed. For the in vivo study, 30 adult male Sprague-Dawley rats composed of three groups: 1: normal control group, 2: partial bladder obstruction model with normal diet, 3: partial bladder obstruction model with saponin fed (dose of 50mg/Kg/day for 3 months). At 6 weeks after bladder outlet obstruction, the rats were prepared for urodynamic study. Under inhalation anaesthesia, peak vesical pressure, baseline urethral perfusion pressure during contraction, minimal urethral perfusion pressure during relaxation were measured.

Results
In the in vitro study, we observed significant relaxation effect of KRG saponin on prostatic urethra strips which were preconstricted by $10^{-4}$mol/L phenylepinephrine in a dose-dependent manner. At $10^{-5}$ M, saponin induced a significant relaxation of the urethra strips by 0.011 voltage. The relaxant effect was partially blocked after N-nitro-L-arginine methyl ester (L-NAME) pretreatment. (fig 1) In the in vivo study, baseline vesical pressure and urethral perfusion pressure during urethral relaxation and was significantly lower in KRG administration group than control group (p<0.001). (Table 1)

Interpretation of results
Korean red ginseng saponin reduces prostatic urethra pressure and has a dose-related relaxing effects on the prostatic urethra therefore might improve obstructive symptoms of BPH/LUTS and protective effect against secondary bladder deterioration due to BPH-induced BOO.

Concluding message
KRG saponin has relaxant effects on the prostatic urethral smooth muscle via NO/NOS pathway. We expect KRG could be applied as an alternative treatment for BPH/ LUTS.
Table 1. Urodynamic parameters of three rat groups. (Group 1: normal control group, group 2: PBOO (partial bladder outlet obstruction) with normal diet, group 3: PBOO group with red ginseng saponin fed group)

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
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<tbody>
<tr>
<td><strong>UPP&lt;sub&gt;basal&lt;/sub&gt;, cmH&lt;sub&gt;2&lt;/sub&gt;O</strong></td>
<td>0.907 ± 0.0112</td>
<td>0.889 ± 0.0052</td>
<td>0.905 ± 0.0188</td>
</tr>
<tr>
<td><strong>UPP&lt;sub&gt;nadir&lt;/sub&gt;, cmH&lt;sub&gt;2&lt;/sub&gt;O</strong></td>
<td>0.889 ± 0.015</td>
<td>0.880 ± 0.007</td>
<td>0.883 ± 0.0038</td>
</tr>
<tr>
<td><strong>UPP&lt;sub&gt;gap&lt;/sub&gt;, cmH&lt;sub&gt;2&lt;/sub&gt;O</strong></td>
<td>-1.178 ± 0.005</td>
<td>-0.008 ± 0.005</td>
<td>-0.022 ± 0.008</td>
</tr>
<tr>
<td><strong>P&lt;sub&gt;ves&lt;/sub&gt;, cmH&lt;sub&gt;2&lt;/sub&gt;O</strong></td>
<td>0.080 ± 0.009</td>
<td>0.114 ± 0.042</td>
<td>0.086 ± 0.015</td>
</tr>
<tr>
<td><strong>P&lt;sub&gt;pves&lt;/sub&gt;, cmH&lt;sub&gt;2&lt;/sub&gt;O</strong></td>
<td>0.103 ± 0.009</td>
<td>0.131 ± 0.039</td>
<td>0.109 ± 0.006</td>
</tr>
<tr>
<td><strong>P&lt;sub&gt;vesgap&lt;/sub&gt;, cmH&lt;sub&gt;2&lt;/sub&gt;O</strong></td>
<td>0.021 ± 0.010</td>
<td>0.016 ± 0.006</td>
<td>0.023 ± 0.016</td>
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**UPP<sub>basal</sub>** : baseline urethral perfusion pressure, **UPP<sub>nadir</sub>** : urethral perfusion pressure during relaxation, **UPP<sub>gap</sub>** : difference between UPP<sub>basal</sub> and UPP<sub>nadir</sub>, **P<sub>ves</sub>** : baseline vesical pressure, **P<sub>pves</sub>** : vesical pressure during bladder contraction, **P<sub>vesgap</sub>** : vesical pressure change between peak and baseline pressure

*Statistically significant between group 2 and 3

Specify source of funding or grant

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Is this a clinical trial?

No

What were the subjects in the study?

ANIMAL

Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?

Yes

Name of ethics committee

Korea university Institutional Animal Care and Use Committee(IACUC)