Evaluation of Herbal Medicines on Gynecology Diseases Using Ovariectomized and Hypophysectomized Rats

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The Ministry of Health, Labour and Welfare in Japan has approved Herbal Medicines.

Tokishakuyakusan (TS) is one of herbal medicines, mainly used by gynecology. TS consists of 6 crude drugs.

**Tokishakuyakusan (TS)**

<table>
<thead>
<tr>
<th>Angelicae Radix</th>
<th>Paeoniae Radix</th>
<th>Atractylodis Rhizoma</th>
<th>Alismatis Rhizoma</th>
<th>Hoelen</th>
<th>Cnidii Rhizoma</th>
</tr>
</thead>
</table>

TS is used long time as a herbal medicine, however, its effectiveness and safety are not yet fully understood.
1. The target of TS in vivo
2. What is the difference between TS and Estrogen?
3. No side effects?
Animal Study: The target of TS in vivo

Rats were bilaterally ovariectomized (OVX) or Sham-operated (Sham).

Female hormones’ levels were DOWN.

TS was administrated orally.

Checked the estrogenic effects.

The target of TS in vivo

TS has the estrogenic effect.

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Results

The target of TS in vivo

Estrogen/Estrogenic compounds usually show the estrogenic effects through binding Estrogen Receptors.

TS binds with Estrogen Receptor $\alpha$ or $\beta$?

Yeast Two-Hybrid Assay System (in vitro)

Estrogen Receptor $\alpha$ (ER$\alpha$)    Estrogen Receptor $\beta$ (ER$\beta$)

*TS did not bind ER$\alpha$ and ER$\beta$.*


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The target of TS in vivo

**TS** has estrogenic effect.

**TS** was tested by Yeast two-hybrid assay, but no activities associated with ERα and ERβ binding were detected.

The chemical constituents of **TS** induce estrogenic effects through other targets.

TS targets StAR and promotes peripheral steroidogenesis, resulting in increased E2 and progesterone (P4) concentrations in the blood.
**Results**

The target of **TS** *in vivo*

**Pituitary adenylate cyclase-activating polypeptide (PACAP)**
- controlling the ovulation in the brain

**TS** is able to stimulate the central nervous system through the reproductive pathway.

Results

1. The target of TS *in vivo*

2. What is the difference between **TS** and Estrogen?

3. No side effects?
Results

What is the difference between TS and Estrogen?

Hypophysectomized Rat (HPX)

- Sham
- HPX+TS
- HPX+Water
- HPX+E2+P4

TS complements the function of the pituitary and/or supports the process of ovulation.

1. The target of TS \textit{in vivo}

2. What is the difference between TS and Estrogen?

3. No side effects?
Results

Marker of CANCER in gynecology

ERα

OVX

OVX+TS

OVX+Estrogen

PR

OVX

OVX+TS

OVX+Estrogen

TS does not increase the risk for endometrial carcinogenesis.


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Summary

1. TS targets StAR and PACAP through different pathways than estrogen.
2. But TS does not stimulate the cell to cancreration.

Conclusion

TS is beneficial and safe for the treatment of menopausal syndrome in women.
Introduction and Objectives

Menoprogen (MPG)
  Nanjing Mayflower Pharmaceutical Technology Corporation Ltd. (Nanjing, China)

Lycii fructus
Rehmanniae radix
Mori fructus
Carthami flos

MPG clinically elevates blood estrogen levels and is regarded as useful for improving menopausal symptoms.

MPG is used a herbal medicine, however, its effectiveness and safety are not yet fully understood.
**Results**

**Yeast Two-Hybrid Assay System (in vitro)**

**ERα**

**ERβ**

**MPG** did not bind ERα and ERβ.

**MPG** has the estrogenic effect.

**MPG** is useful for treating women with menopausal syndromes.

**MPG** does not increase the risk for endometrial carcinogenesis.

The experimental results suggest that these herbal medicines are beneficial and safe for the treatment of menopausal syndrome in women.

Animal study (\textit{in vivo}) and yeast two hybrid assay (\textit{in vitro}) can evaluate the effects of herbal medicines.

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