

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

**Mi Hwa Chung, Ph. D.**

Division of Pharmacognosy,  
Phytochemistry and Narcotics  
National Institute of Health and Science, Japan



## Introduction and Objectives

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



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

### Tokishakuyakusan (TS)

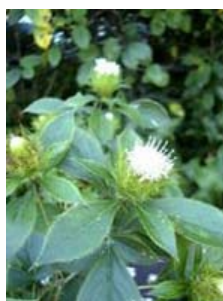
**Angelicae  
Radix**



**Paeoniae  
Radix**



**Atractylodis  
Rhizoma**



**Alismatis  
Rhizoma**



**Hoelen**



**Cnidii  
Rhizoma**



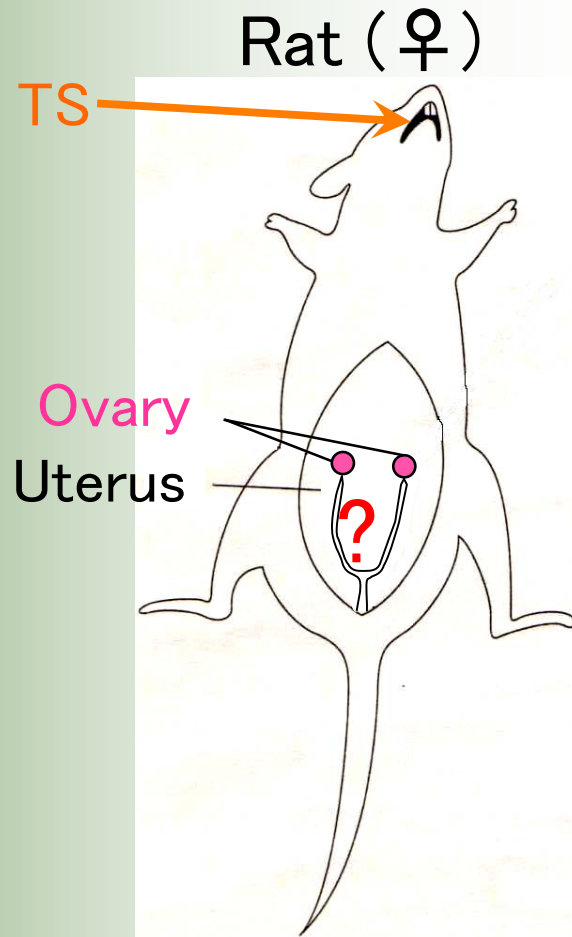
**TS** is used long time as a herbal medicine, however, its effectiveness and safety are not yet fully understood.

## Introduction and Objectives

1. The target of **TS** *in vivo*
2. What is the difference between  
**TS** and Estrogen ?
3. No side effects ?

## Methods

Animal Study; The target of **TS** *in vivo*



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

Female hormones' levels were DOWN.

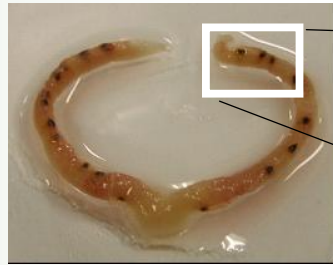
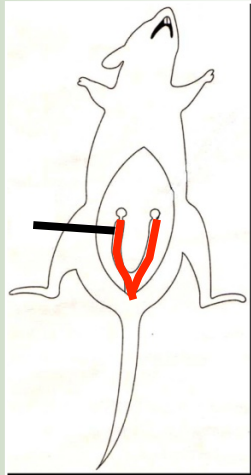
**TS** was administrated orally.

Checked the estrogenic effects.

## Results

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

uterus

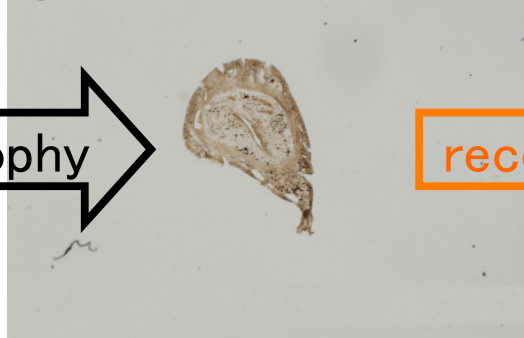


uterus

**Sham**

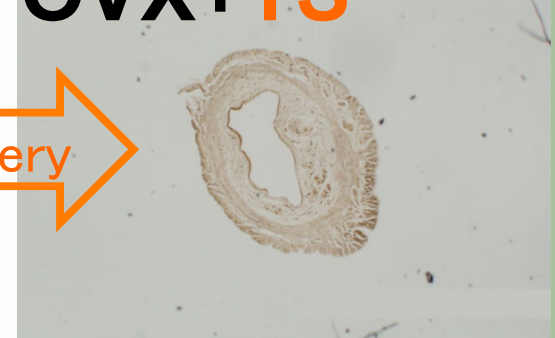


**OVX**



atrophy

**OVX+TS**



recovery

**TS** has the estrogenic effect.

## Results

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

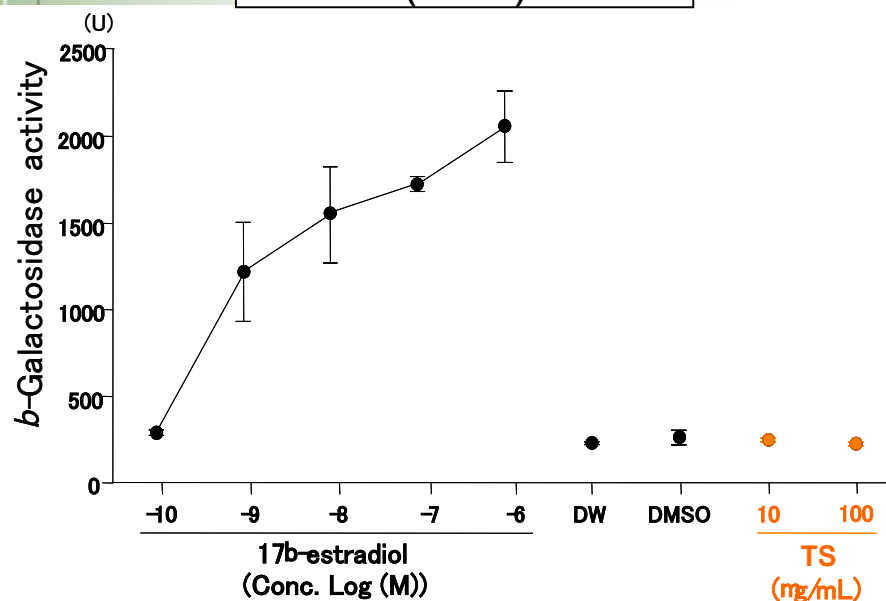
Estrogen/Estrogenic compounds usually show the estrogenic effects through binding Estrogen Receptors.



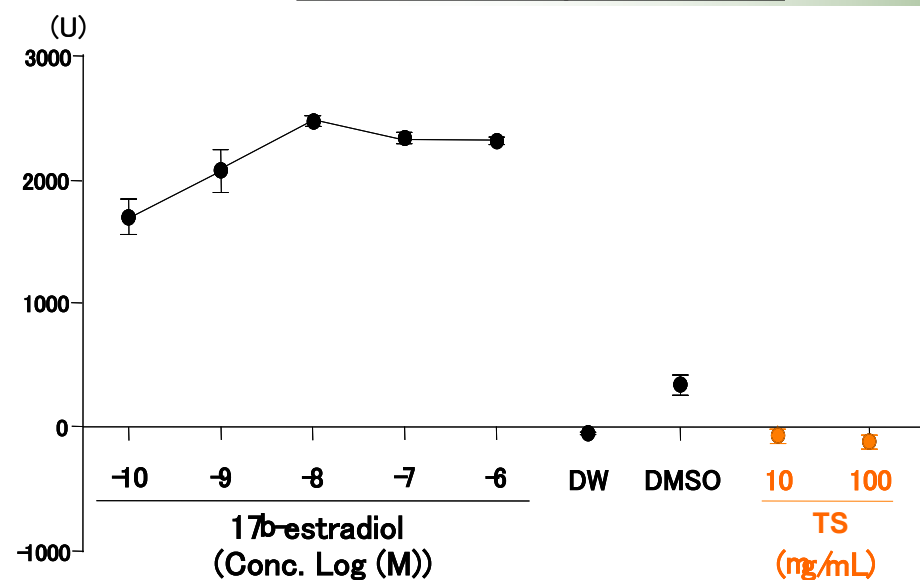
**TS** binds with Estrogen Receptor  $\alpha$  or  $\beta$  ?

### 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 $\beta$ .

## Results

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

**TS** has estrogenic effect.

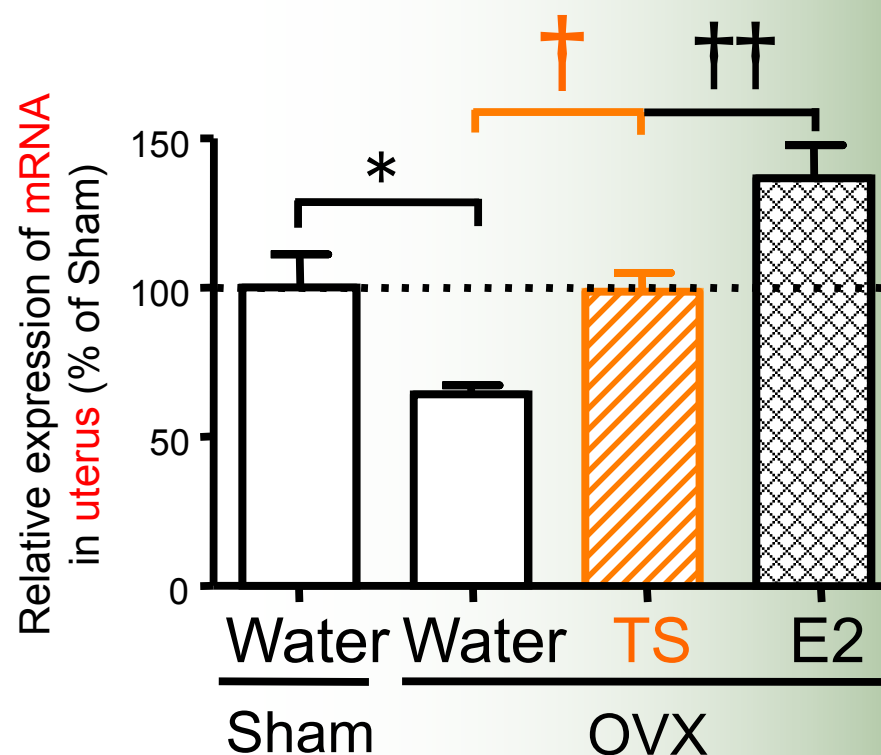


**TS** was tested by Yeast two-hybrid assay, but no activities associated with ER $\alpha$  and ER $\beta$  binding were detected.



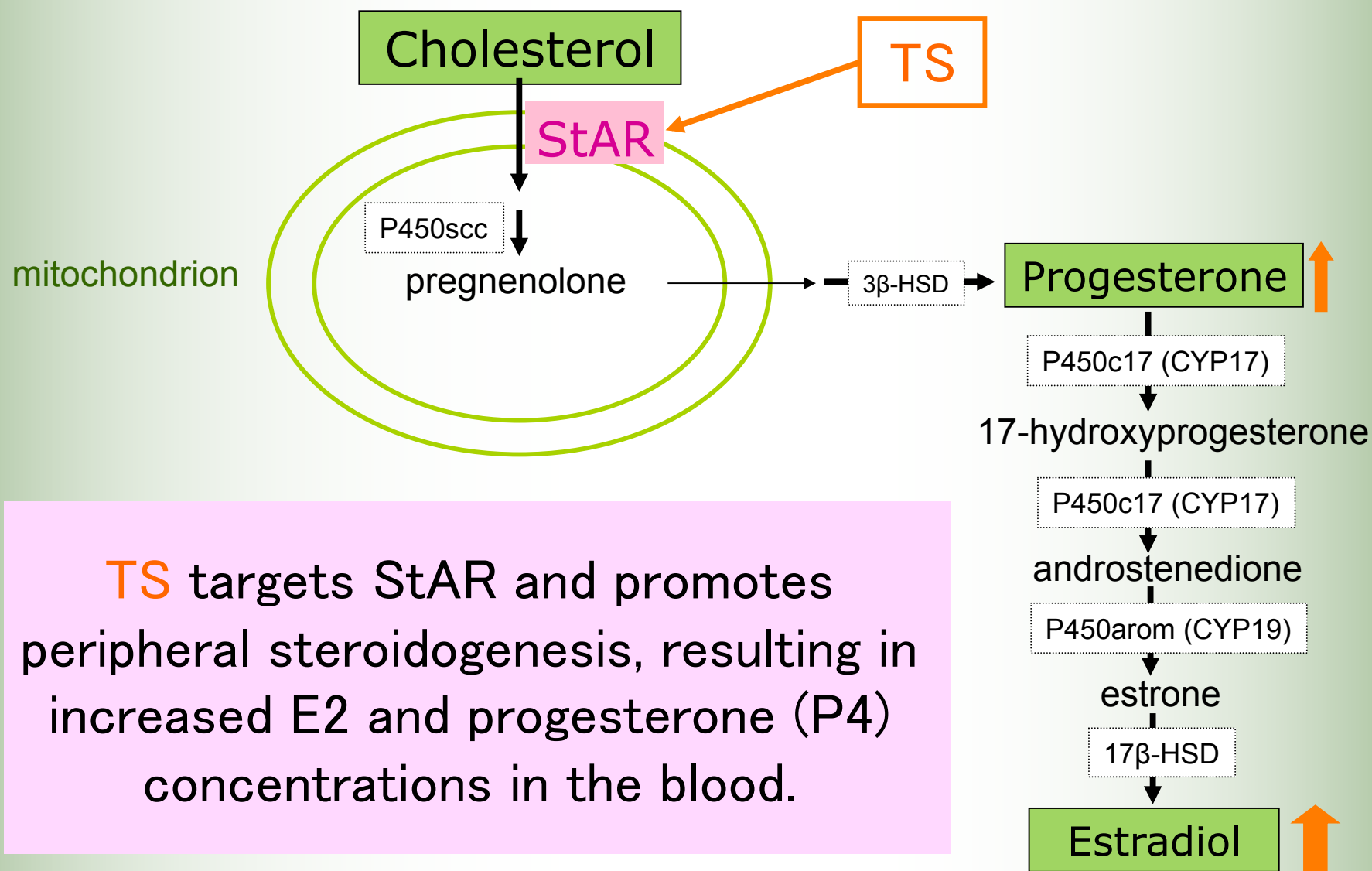
The chemical constituents of **TS** induce estrogenic effects through **other targets**.

### Steroidogenic Acute Regulatory Protein (StAR)



## Results

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

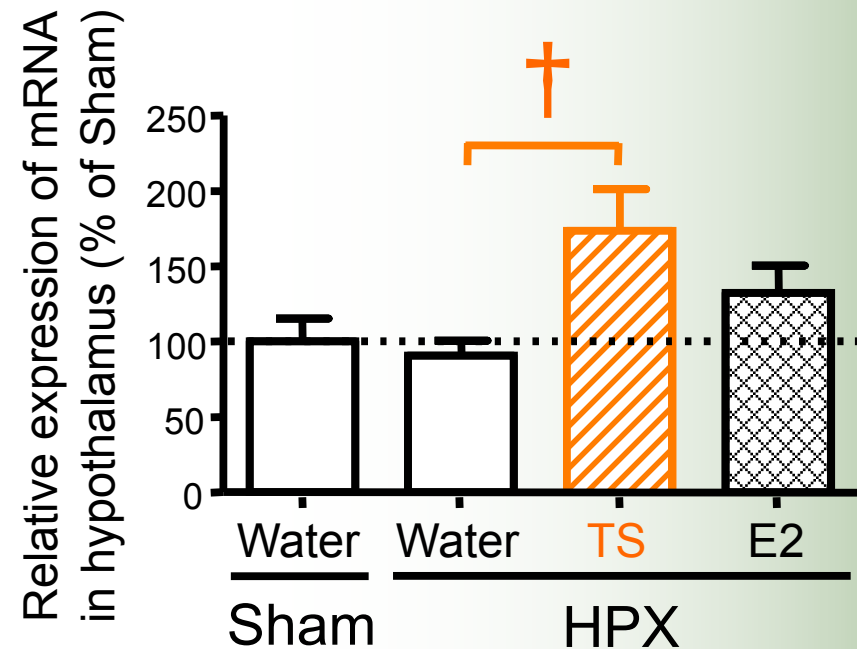
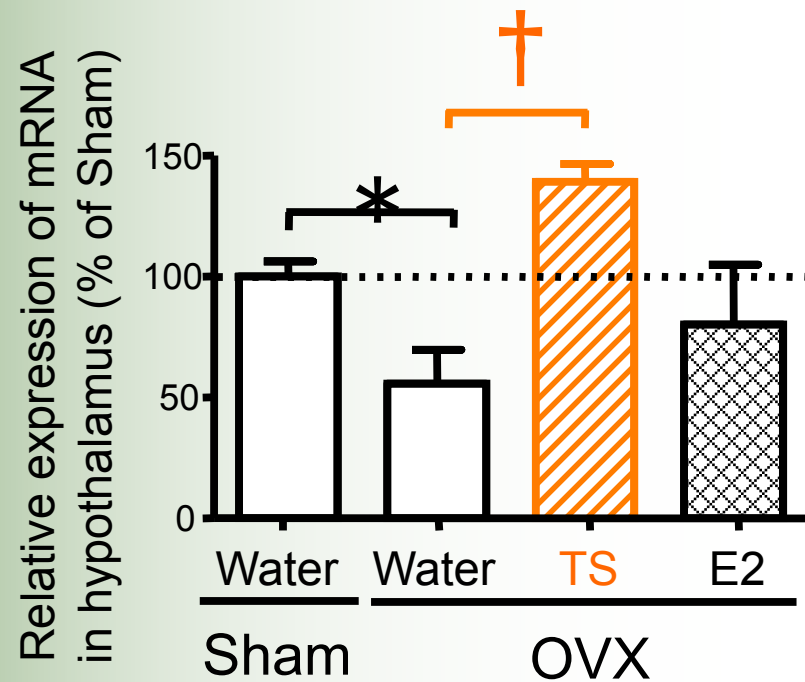


## Results

### 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.

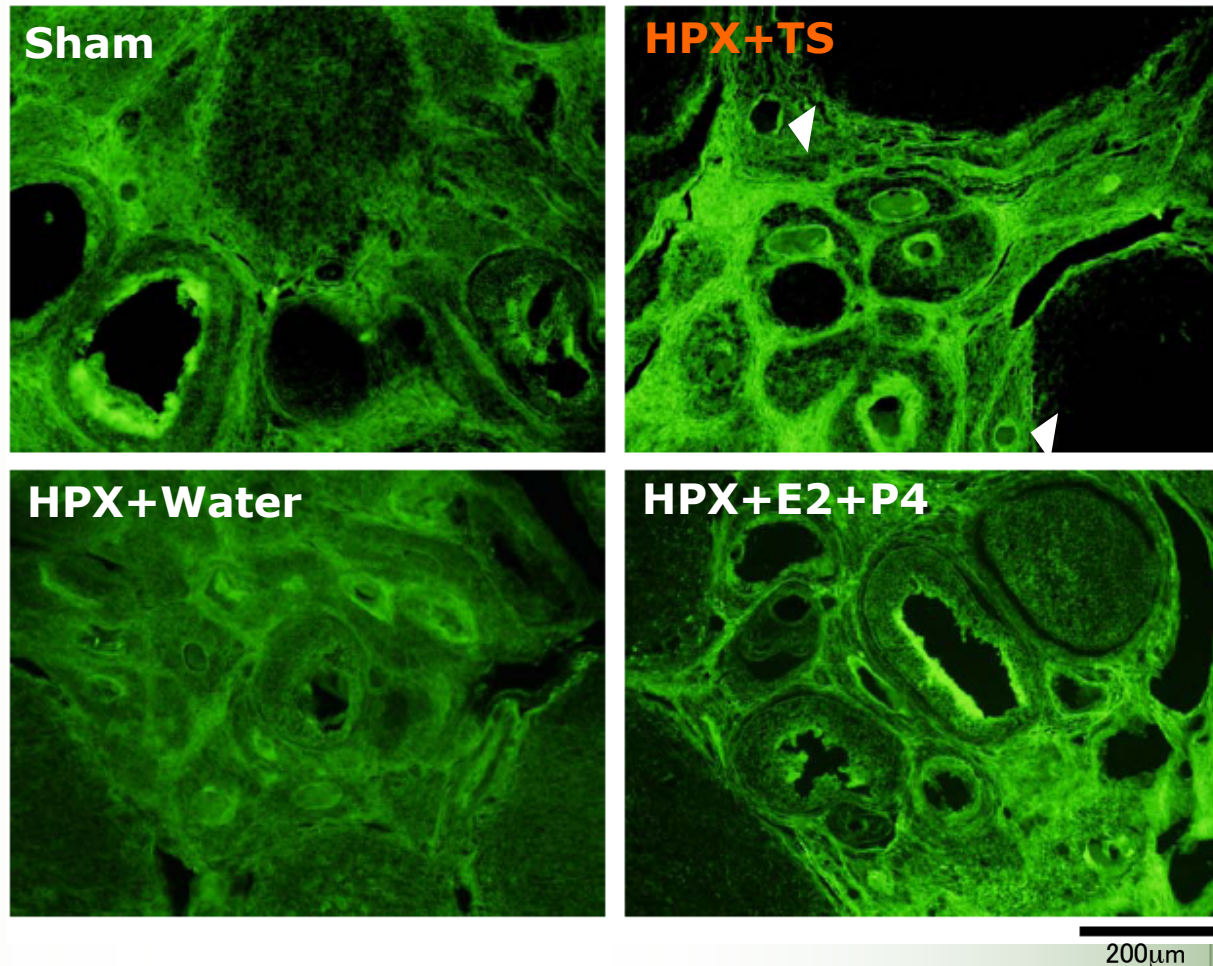
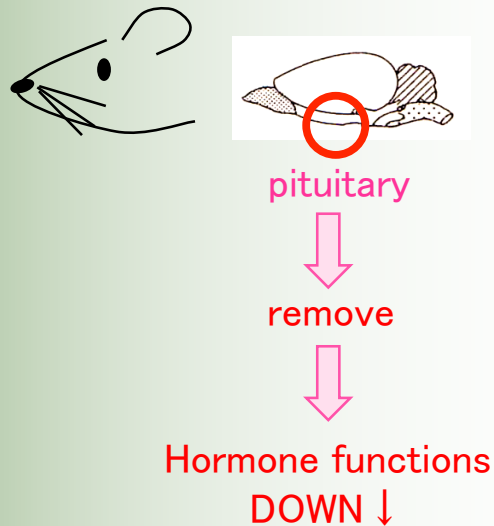
## Results

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)



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

## Results

1. The target of TS *in vivo*
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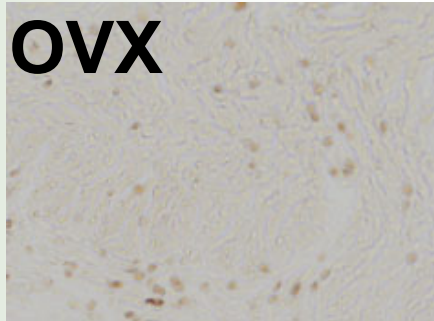
## Results

No side effects ?

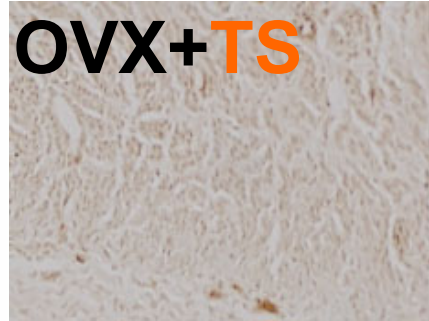
Marker of CANCER in gynecology

ER  $\alpha$

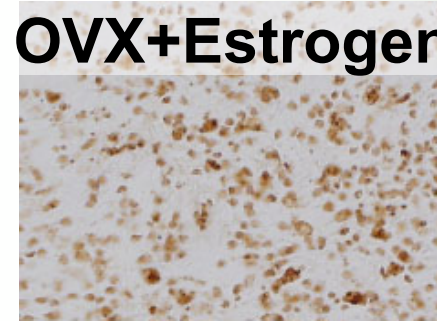
OVX



OVX+TS



OVX+Estrogen



PR

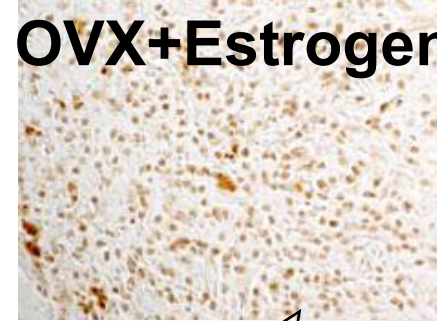
OVX



OVX+TS



OVX+Estrogen



High Risk

TS does not increase the risk for endometrial carcinogenesis.

## Summary

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

## Conclusion

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

## Introduction and Objectives

### Menoprogen (MPG)

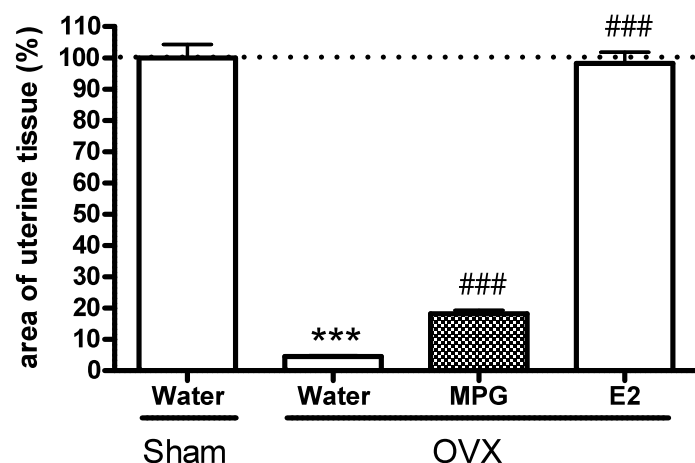
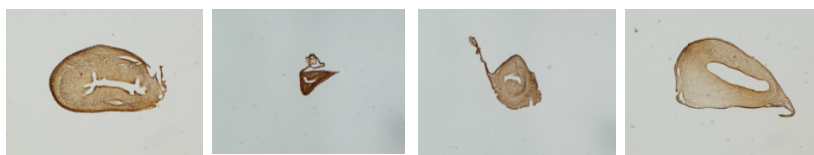
- ▪ ▪ Nanjing Mayflower Pharmaceutical Technology Corporation Ltd. (Nanjing, China)

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 as a herbal medicine, however, its effectiveness and safety are not yet fully understood.

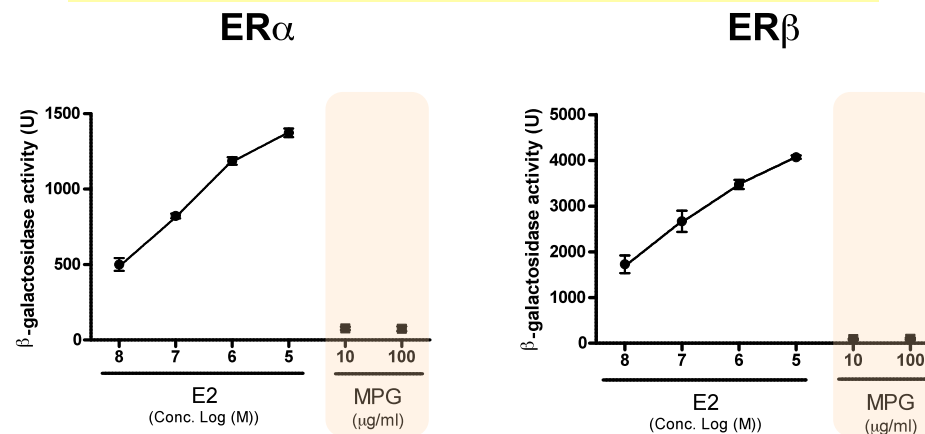
# Results



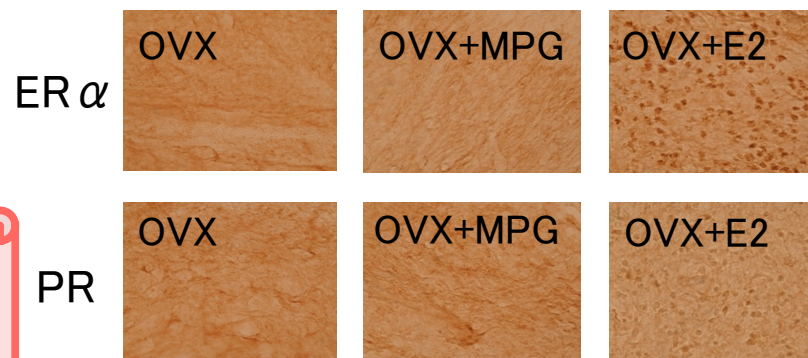
MPG has the estrogenic effect.

MPG is useful for treating women with menopausal syndromes.

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



MPG did not bind ERα and ERβ



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 (*in vivo*) and yeast two hybrid assay (*in vitro*) can evaluate the effects of herbal medicines.

Thank you very much for your attention!



## Acknowledgments

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