Pharmacological efficacy of the traditional Chinese medicinal formula Kun-Tai-1A in the treatment of letrozole-induced polycystic ovary syndrome

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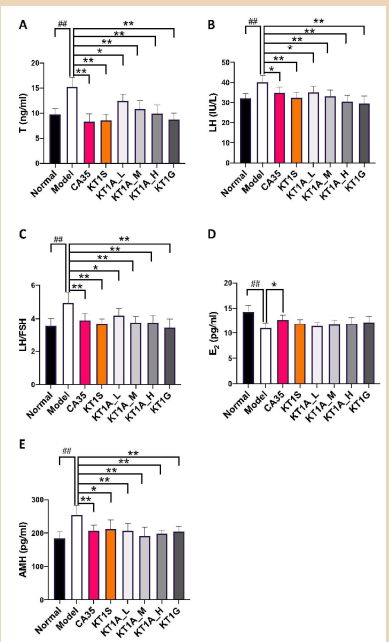
ABSTRACT

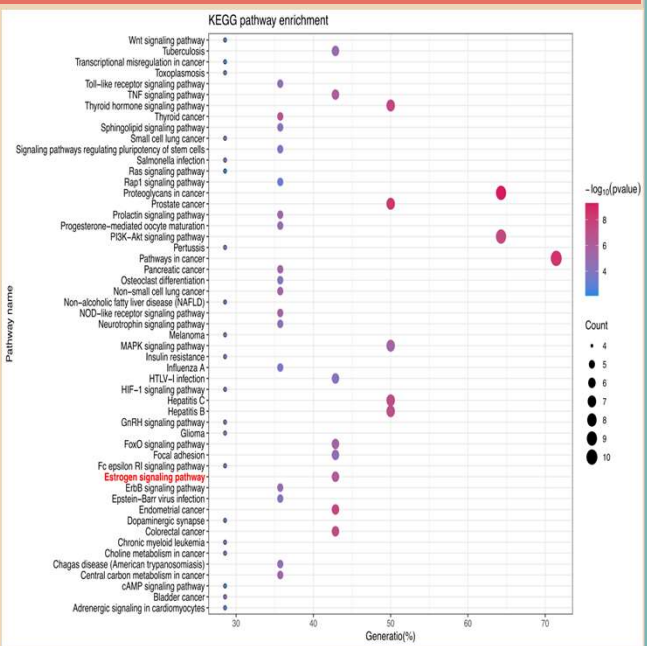
Background: **Polycystic ovary syndrome (PCOS)** is an endocrine disorder that occurs in women of child-bearing age. Moreover, PCOS patients have decreased pregnancy rates and clomiphene citrate resistance. The traditional Chinese medicine formula **Kun-Tai-1S (KT1S)**, consisting of the seahorse species hippocampus, has been reported to elicit therapeutic effects in patients with PCOS. However, given the limited resources and global demand for wild hippocampus, whether KT1S with or without hippocampus can elicit similar therapeutic effects has not been confirmed. **Methods:** KT1S and **Kun-Tai-1A (KT1A, KT1S without dry hippocampus)** were used to treat a letrozole-induced rat model of PCOS with an established disease. The serum levels of testosterone, luteinizing hormone, anti-Müllerian hormone, and estradiol were determined, the luteinizing hormone/follicle-stimulating hormone ratio was determined, and the ovarian pathology was evaluated. **Results:** Similar to the therapeutic effects of cyproterone acetate, both the KT1S and KT1A treatments reduced the body weight and ovarian and uterine indices in the rats with PCOS. The serum levels of testosterone, anti-Müllerian hormone, and luteinizing hormone and the luteinizing hormone/follicle-stimulating hormone ratio were significantly lower in the KT1S and KT1A treatment groups compared to the model group ($P < 0.01$ and $P < 0.05$, respectively). Moreover, the histopathological assessment results suggested that both the KT1S and KT1A treatments significantly ameliorated the PCOS pathology in the rats with an established disease, with a reduced number of cystic and atretic follicles and an increased number of corpora lutea being observed in the ovaries. Notably, there was no obvious difference in the disease outcomes between the KT1S- and KT1A-treated groups. Network pharmacology analysis revealed that 4',7-dihydroxyflavanone, sinpemine A, quercetin, 8-isopentenyl-kaempferol, and luteolin in KT1A may promote estrogen signaling; furthermore, the nitric oxide regulation pathway is also closely involved. **Conclusion:** KT1A and KT1S treatments both significantly ameliorated the PCOS-related pathology in rats, suggesting that the hippocampus component is dispensable for KT1S-mediated amelioration.

RESULTS



- KT1A treatment reduced body and ovary weights in PCOS rats
- KT1A treatment reduced ovarian and uterine index values in PCOS rats
- KT1A treatment modulated serum hormone levels in PCOS model rats
- KT1A treatment ameliorated ovarian pathology in PCOS rats
- Network pharmacology analysis of KT1A against PCOS

Fig. 1 (Left). Effects of KT1A, KT1G, KT1S and CA35 on serum hormone levels. Serum (A) T, (B) LH, (C) LH/FSH, (D) E2 and (E) AMH levels were determined after treatment with KT1A_L (0.75 g/kg KT1A in solution), KT1A_M (1.50 g/kg), KTA1_H (3.00 g/kg), KT1G (granule form of Kun-Tai-1A), KT1S (Kun-Tai-1S) and CA35 (cyproterone acetate 35, positive control). T, testosterone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; E2, estradiol; AMH, anti-Müllerian hormone. **Fig. 2 (Right).** Scatter plot of KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway analysis suggested that estrogen signaling was involved in KT1A-mediated therapeutic effects.



CONCLUSION

Given the limited resources and global demand for wild hippocampus for use in complementary medicines, our findings may help conserve this species. Together, our results suggest that KT1A is a promising approach for treating PCOS.

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