

## EFFECTS OF LUTEOLIN AND LUTEOLIN-7-METHYL ETHER ON ESTROUS CYCLE AND INSULIN LEVEL IN PCOS MICE

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**Relevance:** Polycystic ovary syndrome (PCOS) is one of the most common reproductive and endocrine disorders, accompanied by metabolic disturbances such as insulin resistance, hyperandrogenism, and infertility. Despite the wide spectrum of clinical manifestations, the exact etiology of PCOS remains unclear and involves genetic, environmental, and hormonal factors. Current therapies (oral contraceptives, insulin sensitizers, letrozole) primarily target symptoms, but their long-term application is limited by side effects and insufficient efficacy. Therefore, the search for alternative therapeutic agents is of particular importance. Recent studies indicate that flavonoids, such as luteolin, may exert beneficial effects on glucose and lipid metabolism, hormone regulation, and ovarian function.

**Materials and Methods.** A PCOS model was induced in female C57BL/6J mice by daily subcutaneous injections of dehydroepiandrosterone (DHEA, 60 mg/kg) combined with a high-fat diet for one month. Control animals received vehicle injections and a standard diet. After successful model establishment, luteolin at different doses and letrozole were administered. Physiological and biochemical parameters were monitored: body and ovarian weight, estrous cycle regularity (vaginal smear), serum insulin, and testosterone levels.

**Results.** PCOS mice developed increased body and ovarian weight, disrupted estrous cycles, and elevated fasting insulin, confirming the model. Luteolin significantly reduced body and ovarian weight, restored estrous cycle regularity, and decreased fasting insulin levels in a dose-dependent manner. Luteolin-7-methyl ether produced similar effects. Importantly, luteolin lowered serum testosterone, reduced the number of polycystic follicles, and promoted ovulation. While letrozole improved ovulation, it had no significant effect on androgen reduction.

**Discussion.** Insulin resistance is a central feature of PCOS, contributing to hyperinsulinemia, hyperandrogenism, and metabolic imbalance. Existing therapies such as metformin and letrozole are insufficient to fully correct these dysfunctions and may lead to adverse effects. The present study demonstrates that luteolin and luteolin-7-methyl ether not only improve insulin sensitivity but also restore reproductive parameters and reduce androgen excess, offering broader therapeutic benefits compared to standard treatment.

**Conclusion.** Luteolin and luteolin-7-methyl ether effectively alleviate metabolic and reproductive abnormalities in PCOS mice, including weight gain, estrous cycle irregularities, insulin resistance, and hyperandrogenism. These findings suggest that luteolin may serve as a promising candidate for the development of new therapeutic strategies targeting both metabolic and endocrine aspects of PCOS.