

Effects of dietary probiotic supplementation on the serum reproductive hormone levels of rats subjected to high-fat diet- and letrozole-induced experimental polycystic ovary syndrome

Bassam Hasan, Aymen A. Bash, and Lena Fadhil Hamza

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The polycystic ovary syndrome (PCOS) is a complicated endocrine disease that occurs in women of reproductive age and that is marked by hyperandrogenism, ovulation disorders, and multiple ovarian cysts. Other related symptoms include insulin resistance, hirsutism, and obesity, while the biguanide metformin is the most appropriate drug for the treatment of PCOS. Intestinal microbiota plays a role in maintaining metabolic and hormonal health, while dysbiosis disrupts the regulation of reproductive hormones, leading to increased intestinal permeability, intestinal microbiota imbalance, and – finally – to PCOS development. This aim of this study was to examine the impact of probiotic supplementation (mostly of *Lactobacillus* and *Bifidobacterium*) on the serum levels of testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) in female rats undergoing an experimental simulation of PCOS with the use of high-fat diet (HFD) and letrozole. To this end, 28 female Wistar rats were randomly assigned into four groups (n=7 each): a control group, a PCOS group, a metformin-treated PCOS group, and a probiotic-receiving PCOS group. The HFD that was used in this study was a commercial product obtained from Research Diets, Inc. (USA) with a total kcal value

of 4.73 kcal/g; this HFD was coupled with letrozole (given orally, *via* gavage, at a dose of 1 mg/kg/day) in order to induce PCOS. After 21 days of stimulation, the PCOS rats were returned to a normal diet (like the one fed to the control group). Metformin was then administered at a dose of 300 mg/kg/day in distilled water, while probiotic supplementation with a combination of *Bifidobacterium* and *Lactobacillus* bacteria (using a commercial product obtained from Medwise Healthcare Limited, UK) took place at a dose of 1×10^9 CFU/day for 28 days. Daily vaginal swabs were obtained throughout the induction period in order to determine the oestrous cycle irregularity and to confirm PCOS. Subsequently, cardiac puncture was used in rats anesthetized with diethyl ether in order to obtain blood samples, and serum hormone levels were measured with ELISA. Rat serum testosterone and LH levels were found to be significantly increased by 72.11% ($p=0.003$) and 89.25% ($p=0.001$), respectively, in the PCOS group, while the serum FSH levels were found to be significantly decreased by 38.02% ($p<0.001$) in the same group when compared to those of the control group. The metformin-treated PCOS group exhibited a decrease by 35.09% ($p>0.05$) in its serum LH levels when compared

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to those of the PCOS group. Finally, the herein employed probiotic supplementation led to a moderate reduction of the serum testosterone and LH levels by 15.31% ($p>0.05$) and 23.73% ($p>0.05$), respectively, when compared to those of the PCOS group. The serum FSH levels were found to be significantly lower (by 30.67%; $p=0.004$) in the probiotic-receiving PCOS group when compared to those of the control group. Our findings indicate that despite the fact that probiotic supplementation has an impact on the reproductive axis, it cannot be used as the only intervention for the restoration of hormonal balance in female rats undergoing an experimental simulation of PCOS.

Keywords

letrozole; metformin; PCOS; probiotics; testosterone

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Conflicts of interest statement

None to declare.

Affiliation(s)

College of Pharmacy, University of Babylon, Hillah, Iraq (BH) ▪ Department of Pharmacology, College of Pharmacy, University of Babylon, Hillah, Iraq (AAB) ▪ Department of Clinical Laboratory Sciences, College of Pharmacy, University of Babylon, Hillah, Iraq (LFH)

Correspondence

Bassam Hasan
College of Pharmacy
University of Babylon
Hillah, Iraq
pha386.bssam.hasan@student.uobabylon.edu.iq