

PROCEEDINGS ABSTRACT

## Critical serum cytokine levels of rats subjected to high-fat diet- and letrozole-induced experimental model of the polycystic ovary syndrome: modulation by dietary probiotic supplementation

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

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The polycystic ovary syndrome (PCOS) is an endocrine and metabolic disease, and a major cause of anovulatory infertility in women worldwide. The most commonly used drug for the treatment of PCOS is metformin, which enhances insulin sensitivity and glucose uptake into the peripheral tissue, and decreases glucose production by the liver. According to recent research, microbial imbalances may increase intestinal permeability resulting in the release of endotoxins into the bloodstream; these endotoxins can trigger low-grade systemic inflammation with high levels of tumor necrosis factor alpha (TNF- $\alpha$ ) and low levels of interleukin-10 (IL-10), thereby contributing to the development of insulin resistance and ovarian dysfunction. The aim of this study was to determine whether a dietary supplementation with probiotics could reduce the inflammatory response (by restoring the serum levels of TNF- $\alpha$  and IL-10 to normal ones) in a high-fat diet- and letrozole-induced model of PCOS in rats. To this end, a total of 28 female Wistar rats were randomly assigned into four groups (n=7 each): a control group, a PCOS (positive control) group, a metformin-treated PCOS group, and a probiotic-receiving PCOS group. Letrozole (an aromatase inhibitor) was administered orally (*via* gavage) at a

dose of 1 mg/kg/day along with a high-fat diet (with a total kcal value of 4.73 kcal/g) that was obtained from Research Diets, Inc. (USA). The PCOS-undergoing rats were returned into the same diet as the control group after 21 days of stimulation and the letrozole administration was then also stopped. The metformin-treated PCOS group was treated with 300 mg/kg/day of metformin in distilled water, while the rats in the probiotic-receiving PCOS group were fed with commercially available probiotics obtained from Medwise Healthcare Limited (UK), at a dose of  $1 \times 10^9$  CFU/day for 28 days. The measurement of the serum IL-10 and TNF- $\alpha$  levels was performed after 28 days of treatment. Our findings revealed that the experimental simulation of PCOS in rats significantly increased the TNF- $\alpha$  levels by 46.33% ( $p < 0.001$ ) and significantly decreased those of IL-10 by 32.98% ( $p < 0.001$ ) compared to the respective TNF- $\alpha$  and IL-10 levels of the control group, thereby highlighting the existence of low-grade systemic inflammation in the PCOS group. In the rats of the metformin-treated PCOS group, a significant increase in their IL-10 levels (+36.88%;  $p < 0.001$ ) and a moderate decrease in their TNF- $\alpha$  levels (-7.71%;  $p > 0.05$ ) were observed as compared to those of the PCOS group. The serum levels of

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IL-10 were also found to be significantly increased by 27.51% ( $p<0.001$ ) in the probiotic-receiving PCOS group when compared with those of the PCOS group, and significantly decreased by 14.54% ( $p=0.003$ ) when compared with those of the control group. Finally, the serum TNF- $\alpha$  levels were found to be slightly decreased by 4.69% ( $p>0.05$ ) in the rats of the probiotic-receiving PCOS group when compared with those of the PCOS group, and significantly increased by 39.46% ( $p=0.001$ ) when compared with those of the control group. Therefore, our findings suggest that a supplementation with probiotics is not enough in order to achieve normal serum IL-10 and TNF- $\alpha$  levels in an experimental model of PCOS in rats.

### Keywords

inflammation; letrozole; metformin; PCOS; probiotics

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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