

Histomorphological changes in a rat model of polycystic ovary syndrome and the contribution of stevia leaf extract in modulating the ovarian fibrosis, VEGF, and TGF- β immunoexpressions: comparison with metformin

Ahmed A. Morsi¹, Ezat A. Mersal², Abdel Razik H. Farrag³, Ahmed M. Abdelmoneim⁴, Alshaymaa M. Abdelmenem¹, Mohamed S. Salim⁵

¹Histology and Cell Biology Department, Faculty of Medicine, Fayoum University, Fayoum, Egypt, ²Biochemistry Department, Faculty of Science, Assiut University, Assiut, Egypt, ³Department of Pathology, Medical Division Research, National Research Centre, Cairo 12622, Dokki, Egypt, ⁴Physiology Department, Faculty of Medicine, Fayoum University, Fayoum, Egypt, ⁵Research & Development Sector, The Holding Company for Biological Products and Vaccines (VACSERA), 51 Wezaret El-Zeraa St., Agouza, 22311, Giza, Egypt

Abstract

Polycystic ovary syndrome (PCOS) is a common endocrine disorder of fertile females. It has been reported that stevia leaf extract (SLE) has antidiabetic and antihyperlipidemic properties. Therefore, the current study hypothesized and investigated the role and mechanistic aspects of a natural sweetener; SLE in treating a rat model of letrozole-induced PCOS and to compare it with metformin. Thirty-five female Wistar albino rats were divided into 5 groups: control, PCOS-induced group (letrozole, 1 mg/kg/d, for 21 days), SLE, metformin, and combination-treated groups (300 mg/kg/d, for 28 days in SLE and metformin groups). Vaginal smears were done. The levels of glucose, lipid, and hormonal profiles were measured in the serum meanwhile, malonyl dialdehyde (MDA), superoxide dismutase (SOD), and tumour necrosis factor (TNF- α) were measured in the ovary. Ovarian sections were subjected to hematoxylin and eosin, Masson, and immunohistochemical identification of VEGF and TGF- β followed by morphometric analysis. PCOS rats showed altered hormonal and lipid profiles, in addition to hyperglycemia. Also, the ovarian MDA and TNF- α were elevated, and SOD was decreased. Numerous cystic follicles, decrease/absence of corpora lutea, interstitial fibrosis with positive VEGF and TGF- β immunoreactivity were evident. SLE improved all altered parameters. SLE showed potential therapeutic merits in letrozole-induced PCOS via anti-inflammatory, antioxidant, anti-fibrotic, and angiogenesis regulating mechanisms. Its effects were almost comparable to metformin, and the combination of both has no further synergistic effect.

Keywords: Letrozole-induced polycystic ovary, stevia leaf extract, angiogenesis, TGF- β immunohistochemistry, rats