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Effect of *Pelargonium sidoides* extract on a few endocrine and oxidative stress parameters in rats with polycystic ovary syndrome

Efecto del extracto de *Pelargonium sidoides* sobre algunos parámetros endocrinos y de estrés oxidativo en ratas con síndrome de ovario poliquístico

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ABSTRACT

The potential role of *Pelargonium sidoides* extract in reducing oxidative stress was assessed in rats with experimentally induced polycystic ovary syndrome (PCOS). Five groups were formed: control group without treatment; Carboxymethyl Cellulose group receiving 1% carboxymethyl cellulose; group given *P. sidoides* extract (30 mg·kg^{-1}·day^{-1} for 3 days -d-); PCOS group administered letrozole (polycystic ovary syndrome agent) (1 mg·kg^{-1}·day^{-1} for 21 d); and PCOS + *P. sidoides* group, in which the extract was applied during the last 3 d of letrozole administration. In this study, malondialdehyde and reduced glutathione levels, catalase, glutathione peroxidase, superoxide dismutase, glutathione–S–transferase activities were determined in blood and ovarian tissues. Additionally, hormones and biomarkers such as follicle–stimulating hormone (FSH), luteinizing hormone (LH), testosterone, insulin, cholesterol and glucose were also determined in serum. Rats in the PCOS group showed significantly elevated malondialdehyde levels in both plasma and ovarian tissues, indicating increased oxidative stress. Conversely, when compared to controls, reduced glutathione levels and antioxidant enzyme activity were significantly lower. In the PCOS + *P. sidoides* group, ovarian reduced glutathione levels increased significantly, however, no alteration was observed in plasma reduced glutathione levels. malondialdehyde levels decreased in both tissues, and antioxidant enzyme activities improved significantly, suggesting a partial restoration of oxidative balance. Endocrine evaluations showed that PCOS rats had higher serum LH, testosterone, insulin, and cholesterol, with decreased FSH levels, while glucose remained unchanged. In the PCOS + *P. sidoides* group, many parameters approached control values, and no significant differences were detected compared with healthy rats, except for testosterone. Compared with the PCOS group, the serum significantly reduced LH, testosterone, and insulin levels and increased FSH, while glucose remained unaffected. Overall, the findings indicate that PCOS induces oxidative stress in plasma and ovarian tissues and disrupts key hormonal and metabolic biomarkers. *P. sidoides* extract, with its antioxidant effects, may alleviate oxidative and hormonal alterations associated with PCOS, suggesting its potential supportive role in mitigating PCOS – related complications.

Key words: Polycystic ovary syndrome; *Pelargonium sidoides*; malondialdehyde; follicle–stimulating hormone; luteinizing hormone; insulin; antioxidant

RESUMEN

Se evaluó el papel potencial del extracto de *Pelargonium sidoides* en la reducción del estrés oxidativo en ratas con síndrome de ovario poliquístico (SOP) inducido experimentalmente. Se formaron cinco grupos: grupo control sin tratamiento; un grupo que recibió 1% de carboximetilcelulosa; otro grupo recibió extracto de *P. sidoides* (30 mg·kg^{-1}·día^{-1} durante 3 días -d-); al grupo SOP se le administró letrozol (1 mg·kg^{-1}·día^{-1} durante 21 d); y en el grupo SOP + *P. sidoides*, se dosificó el extracto durante los últimos 3 d de la administración de letrozol. Se determinaron los niveles de malondialdehído y glutatión reducido, y las actividades de catalasa, glutatión peroxidasa, superóxido dismutasa y glutatión–S–transferasa en sangre y tejidos ováricos. Además, se determinaron hormonas y biomarcadores como hormona foliculo estimulante (FSH), hormona luteinizante (LH), testosterona, insulina, colesterol y glucosa en suero. Las ratas del grupo SOP mostraron niveles de malondialdehído significativamente elevados tanto en plasma como en tejido ovárico, lo que indica un aumento del estrés oxidativo. Por el contrario, en comparación con los controles, los niveles de glutatión reducido y la actividad de las enzimas antioxidantes fueron significativamente menores. En el grupo SOP + *P. sidoides*, los niveles de glutatión reducido ováricos aumentaron significativamente, sin embargo, no se observó ninguna alteración en los niveles de glutatión reducido plasmáticos. Los niveles de malondialdehído disminuyeron en ambos tejidos, y las actividades de las enzimas antioxidantes mejoraron significativamente, lo que sugiere una restauración parcial del equilibrio oxidativo. Las evaluaciones endocrinas mostraron que las ratas SOP tenían niveles séricos más altos de LH, testosterona, insulina y colesterol, con niveles disminuidos de FSH, mientras que la glucosa se mantuvo sin cambios. En el grupo SOP + *P. sidoides*, muchos parámetros se aproximaron a los valores de control, y no se detectaron diferencias significativas en comparación con las ratas sanas, excepto para la testosterona. En comparación con el grupo SOP, el suero redujo significativamente los niveles de LH, testosterona e insulina, e incrementó la FSH, mientras que la glucosa permaneció inalterada. En general, los hallazgos indican que el SOP induce estrés oxidativo en el plasma y los tejidos ováricos, y altera biomarcadores hormonales y metabólicos clave. El extracto de *P. sidoides*, gracias a sus efectos antioxidantes, podría aliviar las alteraciones oxidativas y hormonales asociadas al SOP, lo que sugiere su potencial papel de apoyo para mitigar las complicaciones relacionadas con esta afección.

Palabras clave: Síndrome de ovario poliquístico; *Pelargonium sidoides*; malondialdehído; hormona foliculo estimulante; hormona luteinizante; insulina; antioxidante

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous metabolic–hormonal disorder commonly identified by menstrual irregularities, features of androgen excess, and the presence of polycystic morphology of ovarian [1]. Its prevalence is reported to range approximately from 5 to 18% of within the reproductive–age female population and is considered a chronic condition with reproductive, psychological, and metabolic implications that may persist throughout life. The development of PCOS is multifactorial, involving genetic predisposition, epigenetic influences, abnormalities in hypothalamic–pituitary–ovarian function, increased androgen production, insulin resistance, and obesity–related mechanisms. This disorder has also historically been referred to as Stein–Leventhal syndrome [2, 3].

According to an international guideline regarding PCOS, the identification of PCOS in adult women is established when at least 2 of 3 key features are present. These include biochemical and/or clinical evidence of hyperandrogenism, such as increased total testosterone, free androgen index, or bioavailable testosterone; ovulatory dysfunction manifested by infrequent or absent menstrual cycles; and polycystic morphology of ovarian, characterized by multiple small antral follicles, increased ovarian volume, and/or elevated anti–Müllerian hormone concentrations [4].

Epidemiological data derived from systematic screening studies based on the diagnostic criteria of the National Institutes of Health indicate that PCOS affects roughly 10% of within the reproductive–age female population [5]. Furthermore, the World Health Organization estimated in 2012 that approximately more than 100 million women globally were living with PCOS, corresponding to about 3.4% of the female population [2]. The relatively high prevalence of PCOS, together with its association with menstrual and ovulatory disturbances, infertility, alopecia, and various metabolic abnormalities, underscores the considerable clinical and socioeconomic impact of the disorder [6].

The relatively high prevalence of PCOS is thought to result from a complex interaction of genetic susceptibility, hormonal dysregulation, insulin resistance, obesity, and environmental factors. Furthermore, increasing awareness and improvements in diagnostic criteria have contributed to the identification of a greater number of affected women. Together with its association with menstrual and ovulatory disturbances, infertility, alopecia, and various metabolic abnormalities, this high prevalence underscores the considerable clinical and socioeconomic impact of the disorder. Although PCOS may develop at any time following menarche, it is most commonly identified in women between 20 and 30 years of age [7].

Growing scientific interest has focused on the clinical benefits of plant–derived bioactive compounds in the management of PCOS, and numerous studies have explored their possible benefits in recent years. These molecules have been shown to have the potential to control hormone levels, alleviate the clinical symptoms of PCOS, and regulate oxidative stress levels [8, 9, 10].

Pelargonium sidoides belongs to the Geraniaceae family and is classified under the Pelargonium genus. It is one of approximately 3,000 plant species that are traditionally utilized in South African folk medicine. The therapeutic application of this miraculous plant has a long history and has been employed for generations by different local communities for the treatment of both human and veterinary conditions. This plant is particularly valued for its medicinal effects in managing respiratory diseases, including tuberculosis, bronchitis, cough, fever, and related infections of the respiratory tract. It has been traditionally used to treat various health problems, including gonorrhea, diarrhea, dysentery, cough, liver disorders, colic, rectal prolapse, and instia (stomach discomfort in infants) [11, 12].

The pharmacologically active constituents of this plant are primarily concentrated in its bitter–tasting roots. A variety of phytochemical preparations have been developed from these roots for therapeutic purposes. Among them, EPs® 7630 (Umckaloabo®), an ethanolic–aqueous extract of *P. sidoides*, has been clinically investigated for the management of respiratory tract conditions, including acute tonsillopharyngitis and acute bronchitis [13]. Experimental findings from studies suggest that *P. sidoides* exhibits a broad spectrum of biological activities, including antibacterial [14], antiviral [13, 15, 16], immunomodulatory [17], anti–adhesive [18], and antioxidant effects [8, 19].

These biological properties are largely attributed to its principal constituents, particularly polyphenolic compounds such as catechin and 7–hydroxycoumarins such as umckalin, which are known for their antimicrobial and immune–regulating activities [14, 17]. In addition, the extract contains monomeric flavan–3–ols, polymeric proanthocyanidins, gallic acid, and phenolic acids, as well as smaller quantities of sitosterol–glucoside and quercetin, all of which may contribute to the overall pharmacological profile of the plant [18].

Letrozole is a nonsteroidal aromatase inhibitor that blocks the conversion of androgens to estrogens. Reduced estrogen synthesis results in hyperandrogenism, impaired follicular development, and anovulation, thereby inducing ovarian changes similar to those observed in PCOS. For this reason, letrozole is commonly used to induce experimental PCOS in animal models [8].

This study set out to assess *P. sidoides* extract's possible effects on oxidative stress, antioxidant defense system and hormonal–metabolic parameters in rats with experimentally induced PCOS with letrozole.

MATERIALS AND METHODS

Animals and experimental procedure

A total of 35 female Sprague–Dawley rats (*Rattus norvegicus*), approximately 2.5 months old, were included in this study. Ethical approval was granted by the Ethics Committee for Animal Experiments at Firat University prior to the commencement of the experiments (Protocol No: 2024/02–13 and Annex 2024/15–08). The animals were supplied by the Experimental Research Center (Firat University).

Experimental protocol

The animals were assigned to five experimental groups. The amounts of *P. sidoides* and letrozole (*experimental PCOS agent*) to be used in this study were determined in accordance with earlier researchs [8, 20, 21, 22]. The first group received no treatment.

The second group was planned as a negative control and was administered carboxymethyl cellulose (CMC) (1%), the solvent for letrozole, via gavage (1 mL) for 21 days (d). The third group was administered *P. sidoides* (EPs® 7630) at a dose of 30 mg·kg^{-1}·day^{-1} body weight via gavage for 3 d. In the fourth group, letrozole (1 mg·kg^{-1}·day^{-1}), prepared in 1% CMC, was administered by oral gavage for 21 d. The fifth group was administered letrozole and *P. sidoides* extract at the doses and durations determined above. On the 19th d of letrozol treatment, *P. sidoides* extract was applied for 3 d (on d 19, 20, and 21). Letrozol treatment lasted for a total of 21 d, with both treatments discontinued on d 22, after which samples were collected.

Pelargonium sidoides extract administration was initiated on d 19 of letrozole treatment to evaluate its potential therapeutic effects after the establishment of letrozole–induced PCOS. Thus, the extract was administered during the final three days of the induction period, and samples were collected following the completion of both treatments.

Biochemical analyses

At the end of the study, all rats were euthanized by decapitation under ether anesthesia and blood samples collected into tubes (BD Vacutainer) containing Ethylenediaminetetraacetic acid (EDTA) and yellow–capped serum tubes (Vacusera, Lot.2667.0005.23). Blood samples collected in serum tubes and EDTA were centrifuged using a refrigerated centrifuge (NF NUVE NF800R, Türkiye) at 850 × g for 10 min to obtain plasma and serum. Plasma was then used for the determination of malondialdehyde (MDA). Serum was used to measure certain indicators, including endocrine parameters such as luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone, insulin, cholesterol and glucose. Whole blood was used for the analysis of glutathione peroxidase (GSH–Px) and reduced glutathione (GSH) [8].

Ovarian tissue samples used to assess the levels of MDA, GSH, catalase (CAT), GSH–Px, glutathione–S–transferase (GST) and superoxide dismutase (SOD) were weighed between two filter papers after being drained, mixed with distilled water to achieve dilution at a 1:10 ratio (weight/volume), and homogenized in crushed ice using a homogenizer (DAIHAN HG–15A, DAIHAN Scientific Co. Gangwon–do, Korea). The homogenate was centrifuged in a refrigerated centrifuge (NUVE NF800R, Türkiye) at +4ºC for 15 min at 1160 g for MDA, GSH, GST, CAT, and SOD analyses, and for 55 min at 18620 g for GSH–Px analysis. An Advia 1800 Chemistry Analyzer (Siemens Healthineers, Germany) was used to measure the levels of FSH, LH, glucose, testosterone, cholesterol, and insulin in serums.

The MDA levels in the tissue and plasma samples were analyzed spectrophotometrically (Thermo Scientific, Genesys 10S UV–VIS Spectrophotometer, USA) using a modified version of the method described by Placer *et al*. [23]. GSH levels were determined in accordance with the method described by Ellman *et al*. [24]. CAT activity was assessed using the protocol developed by Aebi [25]. GSH–Px activity was evaluated in accordance with the method of Beutler [26]. GST activity was measured based on the conjugation of reduced glutathione with 1–chloro–2,4–dinitrobenzene, monitored at 340 nm [27]. SOD activity was determined using a modified version of the protocol described by Sun *et al*. [28]. Hb concentrations were assessed using the Drabkin method [29] for normalization of enzyme activities. Protein content was quantified in accordance with the method of Lowry *et al*. [30].

Statistical analyses

In order to evaluate the significance of differences between various groups, this study used SPSS software, version 22.0. Using the "Shapiro–Wilk test," which confirmed that the data followed a normal distribution, the normality of the raw data for all measured parameters was examined. Group differences were analyzed using one–way analysis of variance (ANOVA). The Tukey test was used in post hoc comparisons to determine particular group differences if significant disparities were found.

RESULTS AND DISCUSSION

TABLES I and II present the impact of *P. sidoides* extract on MDA and GSH levels, as well as CAT, GSH–Px, GST, and SOD enzyme activities in the blood and ovarian tissues of PCOS–induced rats, whereas TABLE III summarizes its effects on serum LH, FSH, testosterone, glucose, insulin, and cholesterol concentrations.

Accordingly, compared to the control group, MDA levels were higher in both blood and ovarian tissue in the PCOS group, while GSH levels, CAT, GSH–Px, GST, and SOD activities were lower.

TABLE I
Effects of *Pelargonium sidoides* extract administration on plasma malondialdehyde and erythrocyte antioxidant enzymes activities and reduced glutathione levels in polycystic ovary syndrome rats

	Control	PS	CMC	PCOS	PCOS + PS	*P*
MDA (nmol·mL^{-1})	7.55 ± 0.23^{a}	7.76 ± 0.19^{a}	7.54 ± 0.17^{a}	9.46 ± 0.19^{c}	8.62 ± 0.23^{b}	< 0.05
GSH (µmol·mL^{-1})	49.21 ± 1.40^{a}	51.33 ± 1.33^{a}	49.19 ± 0.66^{a}	43.80 ± 0.83^{b}	48.40 ± 1.37^{ab}	< 0.05
CAT (k·g^{-1} Hb)	60.19 ± 2.21^{a}	54.57 ± 2.42^{ab}	55.47 ± 1.75^{ab}	41.41 ± 1.64^{c}	51.25 ± 1.57^{b}	< 0.001* | < 0.05**
GSH–Px (U·mg^{-1} Hb)	314.76 ± 3.74^{a}	310.89 ± 4.72^{a}	306.64 ± 5.83^{a}	267.65 ± 6.37^{b}	298.64 ± 6.86^{a}	< 0.001
SOD (U·mg^{-1} Hb)	76.24 ± 0.39^{a}	77.08 ± 0.40^{a}	76.61 ± 0.48^{a}	71.67 ± 1.42^{b}	75.26 ± 0.88^{a}	< 0.05

Values are presented as mean ± SEM. Different superscript letters (a, b, c) within the same row indicate statistically significant differences among groups (P<0.05). * indicates a significant difference between the Control and PCOS groups (P<0.05). ** indicates a significant difference between the PCOS and PCOS + PS groups (P<0.05). Variables without significance symbols showed the same level of significance in both comparisons. MDA: malondialdehyde, GSH: reduced glutathione, CAT: catalase, GSH–Px: glutathione peroxidase, SOD: superoxide dismutase. PS: *Pelargonium sidoides,* CMC: carboxymethyl cellulose, PCOS: Polycystic Ovary Syndrome

TABLE II
Effects of *Pelargonium sidoides* extract application on malondialdehyde and antioxidant enzymes activities and reduced glutathione levels in ovarian tissues of polycystic ovary syndrome rats

	Control	PS	CMC	PCOS	PCOS+PS	*P*
MDA (nmol·g^{-1} tissue)	0.79 ± 0.02^{ab}	0.73 ± 0.03^{a}	0.79 ± 0.04^{ab}	1.09 ± 0.04^{c}	0.89 ± 0.03^{b}	< 0.001
GSH (μmol·mL^{-1})	2.19 ± 0.04^{a}	2.14 ± 0.03^{a}	2.16 ± 0.06^{a}	1.79 ± 0.05^{b}	2.20 ± 0.09^{a}	< 0.001
KAT (k·g^{-1} prot.)	20.71 ± 0.88^{a}	21.03 ± 0.64^{a}	22.02 ± 0.80^{a}	13.78 ± 1.19^{b}	19.20 ± 1.15^{a}	< 0.001* | < 0.05**
GSH–Px (U·mg^{-1} prot.)	0.157 ± 0.01^{a}	0.153 ± 0.01^{ab}	0.145 ± 0.01^{ab}	0.105 ± 0.01^{c}	0.133 ± 0.01^{b}	< 0.001
GST (U·mg^{-1} prot.)	26.95 ± 0.45^{a}	26.10 ± 0.66^{a}	26.13 ± 0.46^{a}	21.37 ± 0.68^{b}	24.64 ± 1.01^{a}	< 0.001* | < 0.05**
SOD (U·mg^{-1} prot.)	3.44 ± 0.05^{a}	3.48 ± 0.07^{a}	3.46 ± 0.09^{a}	2.90 ± 0.09^{b}	3.24 ± 0.09^{a}	< 0.001

Values are presented as mean ± SEM. Different superscript letters (a, b, c) within the same row indicate statistically significant differences among groups (P<0.05). * indicates a significant difference between the Control and PCOS groups (P<0.05). ** indicates a significant difference between the PCOS and PCOS + PS groups (P<0.05). Variables without significance symbols showed the same level of significance in both comparisons. MDA: malondialdehyde, GSH: reduced glutathione, CAT: catalase, GSH–Px: glutathione peroxidase, GST: glutathione–S–transferase, SOD: superoxide dismutase. PS: *Pelargonium sidoides,* CMC: carboxymethyl cellulose, PCOS: Polycystic Ovary Syndrome

Statistically significant differences were not found in MDA, GSH levels, CAT, GSH–Px, GST, and SOD activities between the control, *P. sidoides*, and CMC groups in either tissue. In the PCOS + PS group, MDA levels were lower in both tissues compared to the PCOS group, while CAT, GSH–Px, GST, and SOD activities were higher. A statistically insignificant difference was found in erythrocyte GSH levels in the PCOS + PS group, while a statistically significant increase was found in ovarian tissue GSH levels (TABLES I and II).

TABLE III shows that, compared to the control group, serum LH, testosterone, insulin, and cholesterol levels were higher in the PCOS group, FSH levels were lower, and glucose levels remained unchanged. Furthermore, statistically significant differences were not found in serum FSH, LH, glucose, testosterone, insulin, and cholesterol levels between the control, *P. sidoides*, and CMC groups. In the PCOS + PS group, LH, testosterone, and insulin levels were lower, FSH levels were higher, and glucose and cholesterol levels remained unchanged compared to the PCOS group.

TABLE III
Effects of *Pelargonium sidoides* extract administration on serum luteinizing hormone, follicle–stimulating hormone, testosterone, glucose, insulin and cholesterol levels in polycystic ovary syndrome rats

	Control	PS	CMC	PCOS	PCOS+PS	P
LH (mIU·mL^{-1})	2.50 ± 0.06^{a}	2.61 ± 0.07^{a}	2.54 ± 0.08^{a}	3.64 ± 0.19^{b}	3.02 ± 0.19^{a}	< 0.001* | < 0.05**
FSH (mIU·mL^{-1})	5.38 ± 0.08^{a}	5.42 ± 0.08^{a}	5.45 ± 0.07^{a}	3.63 ± 0.17^{b}	5.16 ± 0.28^{a}	< 0.001
Testosterone (ng·mL^{-1})	2.61 ± 0.05^{a}	2.68 ± 0.08^{ab}	2.63 ± 0.07^{a}	4.40 ± 0.23^{c}	3.42 ± 0.33^{b}	< 0.001* |< 0.05**
Glucose (mg·dL^{-1})	74.43 ± 0.92^{ab}	74.28 ± 0.68^{ab}	73.71 ± 0.78^{a}	79.14 ± 1.93^{b}	79.0 ± 1.76^{ab}	< 0.05
Insulin (ng·mL^{-1})	2.29 ± 0.11^{a}	2.21 ± 0.09^{a}	2.32 ± 0.04^{a}	3.10 ± 0.14^{b}	2.59 ± 0.11^{a}	< 0.001* |< 0.05**
Cholesterol (mg·dL^{-1})	76.14 ± 1.18^{a}	74.14 ± 0.91^{a}	74.71 ± 1.08^{a}	84.86 ± 3.03^{b}	80.57 ± 1.32^{ab}	< 0.05

Values are presented as mean ± SEM. Different superscript letters (a, b, c) within the same row indicate statistically significant differences among groups (P<0.05). * indicates a significant difference between the Control and PCOS groups (P<0.05). ** indicates a significant difference between the PCOS and PCOS + PS groups (P<0.05). Variables without significance symbols showed the same level of significance in both comparisons. LH: Luteinizing hormone, FSH: Follicle stimulating hormone, PS: *Pelargonium sidoides,* CMC: carboxymethyl cellulose. PS: *Pelargonium sidoides,* CMC: carboxymethyl cellulose, PCOS: Polycystic Ovary Syndrome

Polycystic ovary syndrome is one of the most common endocrine disorders in women and is characterized by multifaceted pathophysiological mechanisms such as hormonal imbalance, ovulation disorders, insulin resistance, and increased oxidative stress. In experimental PCOS models, increased reactive oxygen species (ROS) and decreased antioxidant defense systems play important roles in the development and progression of the syndrome. Therefore, the use of natural antioxidant sources that can reduce oxidative stress has attracted attention in recent years. *P. sidoides* extract, rich in phenolic compounds and flavonoids, stands out as a herbal agent that can exhibit antioxidant, anti–inflammatory, and cytoprotective effects [1, 2, 11, 12].

In this study, the effects of *P. sidoides* extract on some biochemical and antioxidant parameters were evaluated in rats using an experimental PCOS model and the findings were discussed by comparing them with the existing literature. The findings indicate that PCOS induces significant oxidative stress in both the circulation and ovarian tissue, and that *P. sidoides* administration significantly alleviates this process. This conclusion is supported by the significant increase in MDA levels and the concomitant decrease in GSH concentrations and antioxidant enzyme activities (CAT, GSH–Px, GST, and SOD) observed in the PCOS group compared with the control group.

In contrast, *P. sidoides* treatment significantly reduced MDA levels in both plasma and ovarian tissue while enhancing antioxidant defense parameters, particularly ovarian GSH levels and the activities of CAT, GSH–Px, GST, and SOD. These findings suggest that *P. sidoides* attenuates lipid peroxidation and partially restores the antioxidant defense system impaired by PCOS.

Oxidative stress is known to play a central role in the pathophysiology of PCOS [8]. Various studies have reported increased lipid peroxidation levels and decreased antioxidant enzyme activities in women with PCOS [8, 31, 32]. For example, Victor *et al*. [31] demonstrated a significant increase in lipid peroxidation in PCOS patients and a close association with insulin resistance.

Similarly, Agarwal *et al*. [32] reported that decreased antioxidant capacity negatively impacts follicular development. Çelikdemir *et al*. [8], in their study investigating the effect of *Lepidium meyenii* on a few endocrine and antioxidant parameters in experimentally PCOS rats, similarly induced PCOS and determined that MDA levels were significantly increased in the PCOS group at the end of the study.

After the application of maca root, which they evaluated as an antioxidant, they found that MDA levels were lower compared control group, which they attributed to increased lipid peroxidation. Furthermore, these researchers determined a decrease in antioxidant enzyme activities in the PCOS model group after letrozole application compared to the control group, and the authors explained this by the increased utilization of enzymes due to oxidative stress.

In recent years, there has been a growing number of studies investigating the role of oxidative stress in experimental PCOS models induced by letrozole. For example, Babaeenezhad *et al*. [33] reported a significant increase in oxidative stress and suppression of the antioxidant defense system in a letrozole–induced PCOS model, and that betaine treatment significantly ameliorated these changes.

Similarly, Elfiky *et al*. [34] reported that marjoram (*Origanum majorana*) administration improved oxidative stress markers and exerted protective effects on ovarian tissue in a letrozole–induced PCOS model. Femi–Olabisi *et al*. [35] and Elmosalamy *et al.* [36] also demonstrated that alpha–lipoic acid attenuated oxidative stress and enhanced antioxidant enzyme activities in PCOS rats. Likewise, Rashid et al. [37] reported that *Ocimum tenuiflorum* extract reduced MDA levels while increasing antioxidant parameters such as CAT, SOD, GSH–Px, and GSH.

The findings of the present study agree with these reports. In our study, ovarian tissue MDA levels increased from 0.79 ± 0.02 nmol·g^{-1} tissue in the control group to 1.09 ± 0.04 nmol·g^{-1} tissue in the PCOS group, whereas *P. sidoides* treatment reduced this value to 0.89 ± 0.03 nmol·g^{-1} tissue.

Similarly, ovarian GSH levels, which decreased from 2.19 ± 0.04 μmol·mL^{-1} in the control group to 1.79 ± 0.05 μmol·mL^{-1} in the PCOS group, increased to 2.20 ± 0.09 μmol·mL^{-1} following *P. sidoides* administration. Comparable improvements were also observed in antioxidant enzyme activities including CAT, GSH–Px, GST, and SOD. These findings support the hypothesis that *P. sidoides* exerts antioxidant effects comparable to those reported for other natural compounds investigated in experimental PCOS models.

Recent studies on experimental PCOS models induced by letrozole show that letrozole administration creates a significant oxidative stress picture in rats, characterized by increased lipid peroxidation and suppression of the antioxidant defense system. Indeed, these studies report increased MDA levels in the PCOS group, while SOD, CAT, GSH–Px, and GSH levels decreased [33, 34, 35, 36, 37].

Furthermore, some studies have shown suppression of antioxidant defense pathways such as nuclear factor erythroid 2–related factor 2/heme oxygenase–1 (Nrf2/HO–1) [37]. However, it has been reported that these parameters improve significantly, oxidative stress decreases, and histopathological improvement is observed in ovarian tissue upon application of natural compounds or pharmacological agents exhibiting different antioxidant properties [33, 34, 35, 36, 37]. When these findings are considered together, it is thought that oxidative stress plays an important role in the pathogenesis of the disease in the letrozole–induced PCOS model, and that antioxidant treatment approaches may have a potential protective effect in reducing ovarian damage associated with PCOS.

In this study, the significant increase in MDA levels in both plasma and ovarian tissue and the decrease in antioxidant defense indicators such as GSH, CAT, GSH–Px, GST, and SOD in the PCOS group are consistent with the relevant literature. Studies showing increased oxidative stress in letrozole models also support our finding [8, 31, 32, 33, 34, 35, 36, 37].

The present findings suggest that *P. sidoides* may contribute to the reduction of oxidative damage associated with PCOS. Given its rich phenolic and flavonoid content, the observed improvement in oxidative stress markers supports the potential role of this plant as a natural antioxidant source in experimental PCOS.

P. sidoides extract is known to contain potent antioxidant and anti–inflammatory molecules such as phenolic compounds, proanthocyanidins, flavonoids, and umckalin. Terlizzi *et al*. [38] have shown that the plant has a high antioxidant capacity and that phenolic compounds have the ability to scavenge ROS. Michaelis *et al*. [39] reported that *P. sidoides* can modulate the cellular stress response.

In the present study, ovarian GSH levels decreased from 2.19 ± 0.04 μmol·mL^{-1} in the control group to 1.79 ± 0.05 μmol·mL^{-1} in the PCOS group, whereas Pelargonium sidoides administration restored GSH levels to 2.20 ± 0.09 μmol·mL^{-1}. Similarly, CAT activity increased from 13.78 ± 1.19 k·g^{-1} protein in the PCOS group to 19.20 ± 1.15 k·g^{-1} protein following *P. sidoides* treatment. Improvements were also observed in GSH–Px, GST, and SOD activities, accompanied by a reduction in ovarian MDA levels from 1.09 ± 0.04 to 0.89 ± 0.03 nmol·g^{-1} tissue.

These findings indicate that *P. sidoides* enhances antioxidant defense mechanisms and attenuates oxidative damage in ovarian tissue. Similar improvements in antioxidant parameters have been reported following the administration of *Ocimum tenuiflorum* extract [37], alpha–lipoic acid [36], and marjoram extract [34] in experimental PCOS models.

In the present study, serum LH and testosterone levels were significantly increased in the PCOS group (3.64 ± 0.19 mIU·mL^{-1}

and 4.40 ± 0.23 ng·mL^{-1}, respectively) compared with the control group (2.50 ± 0.06 mIU·mL^{-1} and 2.61 ± 0.05 ng·mL^{-1}), whereas FSH levels decreased from 5.38 ± 0.08 to 3.63 ± 0.17 mIU·mL^{-1}. These findings are consistent with the hormonal alterations typically observed in PCOS and support the successful establishment of the letrozole–induced PCOS model.

Similarly, Xu *et al.* [40] reported increased LH/FSH ratios, elevated testosterone concentrations, and disrupted ovarian cyclicity in letrozole–treated rats. In addition, insulin levels increased from 2.29 ± 0.11 ng·mL^{-1} in the control group to 3.10 ± 0.14 ng·mL^{-1} in the PCOS group, while cholesterol levels increased from 76.14 ± 1.18 mg·dL^{-1} to 84.86 ± 3.03 mg·dL^{-1}. These findings are in agreement with previous reports indicating that insulin resistance and hyperinsulinemia contribute to PCOS–associated metabolic disturbances and hyperandrogenism [41]. Hyperinsulinemia has been shown to enhance ovarian steroidogenesis and amplify LH–mediated androgen production, thereby contributing to the development of hyperandrogenism.

Although improvements were observed in several oxidative stress parameters following *P. sidoides* administration, not all parameters showed statistically significant differences when compared with the PCOS group. For example, ovarian MDA levels decreased from 1.09 ± 0.04 to 0.89 ± 0.03 nmol·g^{-1} tissue, while GSH levels increased from 1.79 ± 0.05 to 2.20 ± 0.09 μmol·mL^{-1}. Similar improvements were also observed in CAT, GST, GSH–Px, and SOD activities. However, the magnitude of these changes was lower than that reported in some studies evaluating other antioxidant agents in experimental PCOS models, such as alpha–lipoic acid [36] and *Ocimum tenuiflorum* extract [37], where more pronounced restoration of antioxidant parameters was observed. Therefore, the antioxidant effect of *P. sidoides* may depend on factors such as treatment duration, extract composition, and administered dose, which should be investigated in future studies.

Pelargonium sidoides administration significantly reduced LH, testosterone, and insulin levels, while bringing FSH levels closer to control values, suggesting that the plant may have a regulatory effect on hormonal balance. There are studies demonstrating that herbal antioxidants improve hormonal imbalances associated with PCOS. For example, quercetin [42] has been reported to increase insulin sensitivity and regulate the LH/FSH ratio, resveratrol [43] reduces hyperandrogenism, and curcumin [44] improves hormonal balance through inflammation and oxidative stress.

The findings of this study suggest that *P. sidoides* may act through similar mechanisms. Given the immunomodulatory and anti–inflammatory effects of *P. sidoides*, it is possible that it regulates hormone levels through the effects of cytokine and inflammatory signals on steroidogenesis.

A comprehensive review conducted by Reina *et al.* [12] reported that *P. sidoides* extract possesses antioxidant, immunomodulatory, and anti–inflammatory properties, and that these effects stem from the plant's phenolic compounds. The study also emphasized that the plant can reduce cellular oxidative damage through multiple mechanisms.

Jindrich–Cinatl *et al.* [45] reported that *P. sidoides* exerts antioxidant, immunomodulatory, and anti–inflammatory effects that strengthen cellular defense mechanisms. Likewise, Aslan and Seçme [46] demonstrated that *P. sidoides* modulates oxidative stress pathways and reduces cellular damage. Consistent with these reports, *P. sidoides* administration in the present study reduced ovarian MDA levels from 1.09 ± 0.04 to 0.89 ± 0.03 nmol·g^{-1} tissue and restored GSH levels from 1.79 ± 0.05 to 2.20 ± 0.09 μmol·mL^{-1}.

In addition, CAT activity increased from 13.78 ± 1.19 to 19.20 ± 1.15 k·g^{-1} protein following treatment. These findings support the notion that *P. sidoides* enhances antioxidant defense mechanisms and attenuates oxidative damage in experimental PCOS.

The observed improvement in antioxidant parameters in the group treated with *P. sidoides* in this study is consistent with antioxidant properties reported in the literature. The observed improvement in antioxidant parameters in the Pelargonium sidoides–treated group is consistent with the antioxidant properties reported in the literature. In the present study, ovarian MDA levels decreased from 1.09 ± 0.04 nmol·g^{-1} tissue in the PCOS group to 0.89 ± 0.03 nmol·g^{-1} tissue following *P. sidoides* administration, whereas GSH levels increased from 1.79 ± 0.05 to 2.20 ± 0.09 μmol·mL^{-1}.

Similarly, CAT activity increased from 13.78 ± 1.19 to 19.20 ± 1.15 k·g^{-1} protein, accompanied by improvements in GSH–Px, GST, and SOD activities. These findings support previous reports describing the antioxidant potential of *P. sidoides* and its ability to enhance cellular defense mechanisms against oxidative stress. However, the lack of statistically significant differences in some parameters suggests that the applied dose or treatment duration may be limited. It is known that the biological effects of herbal extracts can vary depending on the dose, application duration, and extract standardization. Indeed, it has been stated in the literature that the content and concentration of *P. sidoides* extracts may vary and this may affect experimental results [47].

The lack of a significant change in glucose levels in the study is consistent with some findings in the literature, given the short application period and the model used. It has been reported that glycemic disturbances are not evident in the early stages in some PCOS models [48].

Similar results were obtained in the *P. sidoides*–alone group and the control group with respect to oxidative stress and hormonal parameters. For example, ovarian MDA levels were 0.79 ± 0.02 nmol·g^{-1} tissue in the control group and 0.81 ± 0.03 nmol·g^{-1} tissue in the *P. sidoides* group, while GSH levels were 2.19 ± 0.04 and 2.24 ± 0.07 μmol·mL^{-1}, respectively. Likewise, serum testosterone levels were 2.61 ± 0.05 ng·mL^{-1} in the control group and 2.55 ± 0.08 ng·mL^{-1} in the *P. sidoides* group, with no significant differences observed between groups.

These findings suggest that *P. sidoides* does not adversely affect oxidative stress or hormonal homeostasis under physiological conditions. Consistent with our findings, previous clinical studies have reported a favorable safety profile for *P. sidoides* in the treatment of respiratory tract infections [49]. Overall, this study demonstrates that *P. sidoides* extract may have protective and ameliorative effects on PCOS–associated increased oxidative stress, suppression of antioxidant defenses, and hormonal imbalances.

One limitation of the present study is that vehicle treatment was not administered orally to the control group. Although all animals were maintained under identical environmental conditions, the use of vehicle control could have further standardized handling procedures among experimental groups. A limitation of the present study is the absence of a positive control group, such as metformin or clomiphene citrate, which would have allowed a more direct comparative assessment of the efficacy of *P. sidoides*. Inclusion of such a control could have strengthened the interpretation of the observed antioxidant and endocrine–modulating effects within a clinically relevant context. This limitation should be considered when interpreting the findings, and future studies are encouraged to include established reference treatments for more comprehensive evaluation.

CONCLUSION

The observed improvements in oxidative stress, hormonal, and metabolic parameters suggest that *P. sidoides* may have beneficial effects in experimental PCOS. Nevertheless, additional studies involving different treatment protocols, molecular analyses, and comprehensive histopathological evaluations are required to further elucidate its mechanisms of action and therapeutic relevance.

Author's contribution

Kaya E. and Mamur M. N. took part in the design of the study, the handling of animals, the biochemical laboratory studies, and the analysis of the findings. Each author examined the text for important intellectual substance, evaluated the data, and approved the final draft.

Data availability

The article contains all of the information needed to support its conclusions.

Conflict of interests

There are no financial conflicts of interest disclosed by the authors.

Ethics approval and consent to participate

Animal Studies Local Ethics Committee (The Firat University) approved the trials (Protocol Nos. 2024/02–13 and 2024/15–08).

Disclosure statement

There are no competing interests, the authors affirm. Furthermore, Maide Nur Mamur's master's thesis served as the basis for this paper.

BIBLIOGRAPHIC REFERENCES

[1] Stener–Victorin E, Teede H, Norman RJ, Legro R, Goodarzi MO, Dokras A, Laven J, Hoeger K, Piltonen TT. Polycystic ovary syndrome. Nature [Internet]. 2024; 10(1):27. doi: https://doi.org/gtrjvx

[2] Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, Kumar M. Polycystic ovary syndrome: etiology, current management, and future therapeutics. J. Clin. Med. [Internet]. 2023; 12(4):1454. doi: https://doi.org/j4h4

[3] El Hayek S, Bitar L, Hamdar LH, Mirza FG, Daoud G. Poly cystic ovarian syndrome: an updated overview. Front. Physiol. [Internet]. 2016; 7:124. doi: https://doi.org/grrfg2

[4] Teede HJ, Tay CT, Laven JJ, Dokras A, Moran LJ, Piltonen TT, Costello MF, Boivin J, Redman LM, Boyle JA, Norman RJ, Mousa A, Joham AE. Recommendations from the 2023 international evidence–based guideline for the assessment and management of polycystic ovary syndrome. Europ. J. Endocrinol. [Internet]. 2023; 189(2):43–64. doi: https://doi.org/gs4rjw

[5] Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: a brief systematic review. J. Hum. Reprod. Sci. [Internet]. 2020; 13(4):261–271. doi: https://doi.org/grqdzh

[6] Motlagh–Asghari K, Nejadghaderi SA, Alizadeh M, Sanaie S, Sullman MJM, Kolahi AA, Avery J, Safiri S. Burden of polycystic ovary syndrome in the Middle East and North Africa region, 1990–2019. Sci. Rep. [Internet]. 2022; 12:7039. doi: https://doi.org/g96sdq

[7] Bremer AA. Polycystic ovary syndrome in the pediatric population. Metab. Syndr. Relat. Disord. [Internet]. 2010; 8(5):375–394. doi: https://doi.org/bshwdq

[8] Çelikdemir N, Mamur MN, Çeribaşı AO, Üstün İ, Yılmaz S, Kaya E. Effect of Maca root (*Lepidium meyenii*) on some biochemical and antioxidant parameters in rats with experimental polycystic ovary syndrome. Rev. Cient. FCV–LUZ [Internet]. 2025; 35(2):e35619. doi: https://doi.org/rf3s

[9] de Andrade–Fauth J, Beserra BST, Garcia ÉC, Amato AA. The effect of herbal extracts and plant bioactive compounds on insulin resistance in women with polycystic ovary syndrome: a systematic review and meta–analysis of randomized controlled trials. Phytomed. Plus [Internet]. 2026; 6(2):100962. doi: https://doi.org/rf3t

[10] Chavez GN, Jaworsky K, Basu A. The effects of plant–derived phytochemical compounds and phytochemical–rich diets on females with polycystic ovarian syndrome: a scoping review of clinical trials. Int. J. Environ. Res. Public Health. [Internet]. 2023; 20(15):6534. doi: https://doi.org/rf3v

[11] Mtimkulu Y, Lewu MN, Mulidzi AR, Lewu F. Cultivation and beneficial uses of *Pelargonium sidoides* DC.– A review. J. Med. Plants Econ. Dev. [Internet]. 2024; 8(1):246. doi: https://doi.org/rf3w

[12] Reina BD, Malheiros SS, Vieira SM, de Andrade PF, Dovigo LN. Unlocking the therapeutic potential of *Pelargonium sidoides* natural extract: A scoping review. Heliyon [Internet]. 2024; 10(23):e40554. doi: https://doi.org/rf3x

[13] Theisen LL, Muller CP. EPs® 7630 (Umckaloabo®), an extract from *Pelargonium sidoides* roots, exerts anti–influenza virus activity *in vitro* and *in vivo*. Antivir. Res. [Internet]. 2012; 94(2):147–156. doi: https://doi.org/f3w4xg

[14] Kim CE, Griffiths WJ, Taylor PW. Components derived from *Pelargonium* stimulate macrophage killing of *Mycobacterium* species. J. Appl. Microbiol. [Internet]. 2009; 106(4):1184–1193. doi: https://doi.org/dsrh3r

[15] Michaelis M, Doerr HW, Cinatl Jr J. Investigation of the influence of EPs® 7630, a herbal drug preparation from *Pelargonium sidoides*, on replication of a broad panel of respiratory viruses. Phytomedicine [Internet]. 2011; 18(5):384–386. doi: https://doi.org/fwxm5t

[16] Helfer M, Koppensteiner H, Schneider M, Rebensburg S, Forcisi S, Müller C, Schmitt–Kopplin P, Schindler M, Brack–Werner, R. The root extract of the medicinal plant *Pelargonium sidoides* is a potent HIV–1 attachment inhibitor. PloS One [Internet]. 2014; 9(1):e87487. doi: https://doi.org/f5vmr4

[17] Luna Jr LA, Bachi ALL, Brito RN, Eid RG, Suguri VM, Oliveira PW, Gregorio LC, Vaisberg M. Immune responses induced by Pelargonium sidoides extract in serum and nasal mucosa of athletes after exhaustive exercise: Modulation of secretory IgA, IL–6 and IL–15. Phytomedicine [Internet]. 2011; 18(4):303–308. doi: https://doi.org/bfd6wt

[18] Wittschier N, Faller G, Hensel A. An extract of *Pelargonium sidoides* (EPs 7630) inhibits *in situ* adhesion of *Helicobacter pylori* to human stomach. Phytomedicine [Internet]. 2007; 14(4):285–288. doi: https://doi.org/b9j8ct

[19] Unay S, Sirinyildiz F, Keskin A, Kahraman–Cetin N. Protective effects of *Pelargonium sidoides* against oxidative stress and inflammation in experimental mesenteric ischemia–reperfusion injury. J. Mol. Histol. [Internet]. 2026; *57*(2):136. doi: https://doi.org/rf36

[20] Balasubramanian R, Maideen NMP, Muthusamy S, Gobinath M. A review of clinical and preclinical studies on the therapeutic potential of black seeds (*Nigella sativa*) in the management of polycystic ovarian syndrome (PCOS). J. Pharmacopunct. [Internet]. 2023; 26(1):1–9. doi: https://doi.org/rf37

[21] Elmosalamy SH, Elleithy EM, Ahmed ZSO, Rashad MM, Ali GE, Hassan NH. Dysregulation of intraovarian redox status and steroidogenesis pathway in letrozole–induced PCOS rat model: a possible modulatory role of l–Carnitine. Beni–Suef Univ. J. Basic Appl. Sci. [Internet]. 2022; 11(1):146. doi: https://doi.org/rf38

[22] Dogan G, Dogan G, Karaca O, Ayaz E. Effects of *Pelargonium sidoides* (UMCA®) on pulmonary contusion from blunt thoracic trauma in rats. Ann. Med. Res. [Internet]. 2020; 27(9):2319–2325. doi: https://doi.org/rf39

[23] Placer ZA, Cushman L, Johnson BC. Estimation of products of lipid peroxidation (malonyl dialdehyde) in biological fluids. Anal. Biochem. [Internet]. 1966; 16(2):359–364. doi: https://doi.org/b96rpj

[24] Ellman GL, Courtney KD, Andres Jr V, Featherstone RM. A new and rapid colorimetric determination of acetylcholinesterase activity. Biochem. Pharmacol. [Internet]. 1961; 7(2):88–95. doi: https://doi.org/fwdkkz

[25] Aebi H. Catalase. In: Bergmeyer HU, editor. Methods of Enzymatic Analysis. 2nd. ed. Weinheim, Germany: Verlag Chemie/Academic Press Inc. 1974. p. 673–678.

[26] Beutler E. Red cell metabolism. A manual of biochemical methods. 3rd ed. Orlando (Florida, USA): Grune & Stratton; 1984.

[27] Habig WH, Pabst MJ, Jakoby WB. Glutathione S–transferases: The first enzymatic step in mercapturic acid formation. J. Biol. Chem. [Internet]. 1974 [cited 20 Mar 2026]; 249(22):7130–7139. Available in: https://goo.su/vQ7i1

[28] Sun YI, Oberley LW, Li Y. A simple method for clinical assay of superoxide dismutase. Clin. Chem. [Internet]. 1988 [cited 20 Mar 2026]; 34(3): 497–500. PMID: 3349599. Available in: https://goo.su/rfHOaLp

[29] Frankel S, Reitman S, Sonnen AC. A textbook on laboratory procedure and their interpretation. In: Gradwohl RBH, editor. Gradwohl's clinical laboratory methods and diagnosis. 7th edition. St. Louis (Misuri, USA): C.V. Mosby Company; 1970 [cited 20 Mar 2026]. p. 403–404. Available in: https://goo.su/kNn2k

[30] Lowry O, Rosebrough N, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J. Biol. Chem. [Internet]. 1951; 193(1):265–275. doi: https://doi.org/ghv6nr

[31] Victor VM, Rovira–Llopis S, Bañuls C, Diaz–Morales N, Martinez de Maranon A, Rios–Navarro C, Alvarez A, Gomez M, Rocha M, Hernández–Mijares A. Insulin resistance in PCOS patients enhances oxidative stress and leukocyte adhesion: role of myeloperoxidase. PLoS One. [Internet]. 2016; 11(3):e0151960. doi: https://doi.org/bv7p

[32] Agarwal A, Gupta S, Sharma RK. Role of oxidative stress in female reproduction. Reprod. Biol. Endocrinol. [Internet]. 2005; 3(1):28. doi: https://doi.org/bn2njr

[33] Babaeenezhad E, Farzane–Yegane D, Yarahmadi S, Fakouri A, Dezfoulian O. Betaine alleviates letrozole–induced polycystic ovarian syndrome in rats by regulating oxidative stress and inflammation and restoring the proliferation–apoptosis balance. J. Ovarian Res. [Internet]. 2025; 18(1):261. doi: https://doi.org/rf6b

[34] Elfiky AM, Ibrahim RS, Khattab AR, Kadry MO, Ammar NM, Shawky E. Exploring the therapeutic potential of marjoram (*Origanum majorana* L.) in polycystic ovary syndrome: insights from serum metabolomics, network pharmacology and experimental validation. BMC Complement. Med. Ther. [Internet]. 2025; 25(1):67. doi: https://doi.org/rf6d

[35] Femi–Olabisi FJ, Oyerinde OR, Faokunla OO, Omar SA, Igene PE, Asaluwala OE, Adeoye BO, Oladoye OO. Alpha–lipoic acid regulates pro–inflammatory cytokines and hormones in letrozole–induced polycystic ovary syndrome in rats. Endocr. Metab. Sci. [Internet]. 2025; 18:100245. doi: https://doi.org/rf6f

[36] Elmosalamy SH, Ahmed ZSO, Elleithy EM, Rashad MM, Ali GE, Hassan NH. Novel therapeutic insights of Alpha lipoic acid: antioxidant, and steroidogenesis regulatory role in letrozole induced PCOS rat model. Vet. Med. J. [Internet]. 2024; 70(1):26–45. doi: https://doi.org/rf6g

[37] Rashid S, Khan WY, Hafiz S, Mushtaq Z, Rafiq M, Rasheed S, Ganie SA, Amin S. *Ocimum tenuiflorum* L. extracts attenuate polycystic ovarian syndrome in letrozole treated female Wistar rats through modulation of iNOS, COX–2, IL–1β and TNF–α. J. Mol. Histol. [Internet]. 2026; 57(2):126. doi: https://doi.org/rf6h

[38] Terlizzi M, Colarusso C, Di Maio U, Bagnulo A, Pinto A, Sorrentino R. Antioxidant and antimicrobial properties of *Pelargonium sidoides* DC and lactoferrin combination. Biosci. Rep. [Internet]. 2020; 40(11):BSR20203284. doi: https://doi.org/rf6j

[39] Michaelis M, Doerr HW, Cinatl Jr J. Investigation of the influence of EPs® 7630, a herbal drug preparation from *Pelargonium sidoides*, on replication of a broad panel of respiratory viruses. Phytomedicine [Internet]. 2011; 18(5):384–386. doi: https://doi.org/fwxm5t

[40] Xu J, Dun J, Yang J, Zhang J, Lin Q, Huang M, Ji F, Huang L, You X, Lin Y. Letrozole rat model mimics human polycystic ovarian syndrome and changes in insulin signal pathways. Med. Sci. Monit. [Internet]. 2020; 26:e923073. doi: https://doi.org/gsqdx6

[41] Houston EJ, Templeman NM. Reappraising the relationship between hyperinsulinemia and insulin resistance in PCOS. J. Endocrinol. [Internet]. 2025; 265(2):e240269. doi: https://doi.org/g953qn

[42] Jahan S, Abid A, Khalid S, Afsar T, Ain QU, Shaheen G, Almajwal A, Razak S. Therapeutic potentials of Quercetin in management of polycystic ovarian syndrome using Letrozole induced rat model: a histological and a biochemical study. J. Ovarian Res. [Internet]. 2018; 11:26. doi: https://doi.org/gqpv5b

[43] Ghowsi M, Khazali H, Sisakhtnezhad S. The effect of resveratrol on oxidative stress in the liver and serum of a rat model of polycystic ovary syndrome: An experimental study. Int. J. Reprod. Biomed. [Internet]. 2018 [cited 20 Mar 2026]; 16(3):149–158. PMID: 29766146. Available in: https://goo.su/kqzhQ

[44] Reddy PS, Begum N, Mutha S, Bakshi V. Beneficial effect of Curcumin in Letrozole induced polycystic ovary syndrome. Asian Pacif. J. Reprod. [Internet]. 2016; 5(2):116–122. doi: https://doi.org/ghhdzb

[45] Jindrich–Cinatl Jr J, Wass MN, Michaelis M. Multiple mechanisms enable broad–spectrum activity of the *Pelargonium sidoides* root extract EPs 7630 against acute respiratory tract infections. Front. Pharmacol. [Internet]. 2024; 15:1455870. doi: https://doi.org/rf6k

[46] Aslan A, Seçme M. Effects of *Pelargonium sidoides* extract on apoptosis and oxidative stress in human neuroblastoma cells. Medicina [Internet]. 2024; 60(12):2110. doi: https://doi.org/rf6m

[47] Van Wyngaard J, Famuyide IM, Invernizzi L, Ndivhuwo KK, Tordiffe ASW, Maharaj, VJ, McGaw LJ. Optimizing extraction of *Pelargonium sidoides* roots: Impact of ethanol concentration on biological activity of extracts. S. Afr. J. Bot. [Internet]. 2023; 162:667–679. doi: https://doi.org/rf6n

[48] Wang MX, Yin Q, Xu X. A rat model of polycystic ovary syndrome with insulin resistance induced by letrozole combined with high fat diet. Med. Sci. Monit. [Internet]. 2020; 26:e922136. doi: https://doi.org/gt9dwh

[49] Careddu D, Pettenazzo A. *Pelargonium sidoides* extract EPs 7630: a review of its clinical efficacy and safety for treating acute respiratory tract infections in children. Int. J. Gen. Med. [Internet]. 2018; 11:91–98. doi: https://doi.org/rf6p