JPPIPA 12(1) (2026)

Jurnal Penelitian Pendidikan IPA

http://jppipa.unram.ac.id/index.php/jppipa/index

Red Ginger as a Potential SDG-3 Herbal Therapy: Molecular and Flow Cytometry Evaluation of CD4, CD8, and CD62L Lymphocyte Modulation in PCOS-Induced Rattus norvegicus

Siti Mudrikatin[1*], Hany Puspita Aryani[2], Risha Setyowati[1]

[1] Undergraduate Midwifery Study Program, Husada College of Health Sciences Jombang, Surabaya, Indonesia.
[2] Undergraduate Nursing Study Program, Husada College of Health Sciences Jombang, Surabaya, Indonesia.

Received: November 01, 2025
Revised: December 23, 2025
Accepted: January 25, 2026
Published: January 31, 2026

Corresponding Author:
Siti Mudrikatin
mudrisiti@gmail.com

DOI: 10.29303/jppipa.v12i1.13687

Abstract: Polycystic Ovary Syndrome (PCOS) is a highly prevalent endocrine disorder associated with hyperandrogenism, inflammation, and immune system dysfunction. Elevated levels of testosterone are known to affect lymphocyte profiles and contribute to the inflammatory processes in PCOS. The aim of this study was to evaluate the impact of red ginger extract (Zingiber officinale var. rubrum) on lymphocyte subpopulations in a testosterone-induced PCOS rat model. This experimental study involved 30 female Rattus norvegicus divided randomly into five groups: a normal control, a PCOS control (testosterone-induced without treatment), and three PCOS treatment groups receiving different doses of red ginger extract. PCOS induction was done using testosterone propionate. Following the treatment period, lymphocyte subpopulation analysis was performed using flow cytometry based on the $CD4^+$, $CD8^+$, and $CD62L^+$ surface markers. The results indicated significant differences in the expression of $CD4^+$, $CD8^+$, and $CD62L^+$ among all red ginger treatment groups compared to the PCOS control group ($p < 0.05$), suggesting an immunomodulatory effect of red ginger. In conclusion, the administration of red ginger extract was able to modulate the lymphocyte subpopulation profile in the PCOS model, potentially contributing to controlling immune responses associated with hyperandrogenism.

Keywords: Red ginger; Results flow cytometry of lymphocyte cells; Testosterone Propionate

Introduction

Women with Polycystic Ovarian Syndrome (PCOS) experiencing insulin resistance often present with hyperinsulinemia, which can compromise the response to ovulation induction. The high LH levels characteristic of insulin-resistant individuals contribute to reduced oocyte quality. Conventional induction agents do not effectively lower the elevated insulin, luteinizing hormone, or androgen levels (Lizneva et al., 2016; Mareta et al., 2018). Treating hyperinsulinemia in PCOS patients will improve folliculogenesis, leading to ovulation and high pregnancy rates (Baptiste et al., 2010; Wang et al., 2020). PCOS is increasingly recognized as a low-grade chronic inflammatory condition associated with disrupted immune response, primarily involving changes in adaptive T cell subsets rather than absolute changes in the total number of CD4 or CD8 cells. Previous investigations have uncovered that the inflammatory pathway in PCOS is closely related to metabolic disorders, including insulin resistance, which contributes to ovarian dysfunction and a decline in oocyte quality (Tang et al., 2015).

PCOS is a heterogeneous endocrine disorder characterized by ovulation dysfunction, hyperandrogenism, and polycystic ovary morphology, affecting approximately 5–21% of women of reproductive age. This syndrome is often accompanied by insulin resistance and obesity, both of which exacerbate metabolic and inflammatory disorders

How to Cite:
Mudrikatin, S., Aryani, H. P., & Setyowati, R. Red Ginger as a Potential SDG-3 Herbal Therapy: Molecular and Flow Cytometry Evaluation of CD4, CD8, and CD62L Lymphocyte Modulation in PCOS-Induced Rattus norvegicus. *Jurnal Penelitian Pendidikan IPA*, *12*(1), 375-386. https://doi.org/10.29303/jppipa.v12i1.13687

(Cholili & Wiyasa, 2022; Zuo et al., 2016). Using testosterone propionate administration can be an effective method for creating animal models that exhibit a physiopathology similar to that seen in women with Polycystic Ovary Syndrome (PCOS) (Sam, 2019; Taylor et al., 2019).

The relationship between PCOS and inflammation has been extensively studied, particularly in Indonesia, confirming that this condition is consistently associated with insulin resistance, obesity, and metabolic disorders that trigger low-grade chronic inflammation. The correlation between PCOS and inflammation has been widely reported, including evidence of disruptions in the regulation of the adaptive immune system. Franciska et al. (2025) demonstrated an imbalance between pro-inflammatory Th17 cells and anti-inflammatory regulatory T cells (Treg) in PCOS patients with insulin resistance, emphasizing the immune mechanisms involved in the disease's pathogenesis. This discovery aligns with reports confirming that insulin resistance and obesity trigger systemic inflammatory responses that exacerbate PCOS symptoms (Wahyuni et al., 2015). On the other hand, red ginger (*Zingiber officinale var. rubrum*) has been extensively explored in Indonesia as an anti-inflammatory and immunomodulatory agent. Its bioactive components, such as gingerol and shogaol, have been proven capable of suppressing pro-inflammatory mediators including IL-6, TNF-α, and IL-1β, while simultaneously increasing antioxidant capacity (Marlina et al., 2023). These findings strengthen the relevance of red ginger to be tested for its effects on lymphocyte markers and metabolic inflammatory conditions such as PCOS (Handayani et al., 2022; Leslie & Gunawan, 2023; Luhurningtyas et al., 2021). Nutritional intervention and anti-inflammatory diets in PCOS patients have been reported to reduce inflammatory markers, thus supporting the idea that modulation of metabolic-inflammatory pathways is a potential strategy in PCOS management (Setiawan et al., 2018).

Red ginger, also known as *Zingiber officinale var. rubrum*, is often utilized for its aromatic and pungent flavor as a rhizome (Iksan et al., 2023). Red ginger (*Zingiber officinale var. Rubrum*) has been widely utilized in various applications, ranging from food processing to traditional medicine (Asyik et al., 2025; Winarni et al., 2023). The red ginger (Zingiber officinale var. rubrum) Has been thoroughly examined in Indonesia for its anti-inflammatory and immunomodulatory properties. Its main bioactive compounds, gingerol and shogaol, have been shown to suppress major proinflammatory mediators such as IL-6, TNF-α, and IL-1β, while enhancing antioxidant defenses through modulation of the oxidative stress pathway (Carmona & Pereira, 2013; Marlina et al., 2023; Tosi et al., 2017). These characteristics prove that red ginger may have beneficial effects on metabolic-inflammatory conditions, including PCOS.

Although the red ginger plant's active ingredients possess anti-inflammatory and antioxidant properties, additional clinical studies are required to identify the correct dosage, efficacy, and potential adverse reactions of red ginger for treating PCOS (Velaga et al., 2017). Shogaol and gingerol are bioactive phenolic compounds with anti-inflammatory and antioxidant properties. These compounds regulate the immune response by controlling inflammatory signaling pathways and reducing excessive cytokine production, rather than by increasing overall CD4 or CD8 T cell populations (Pertiwi et al., 2022; Supu et al., 2018). These compounds inhibit the expression of pro-inflammatory mediators involved in chronic inflammation processes (Diapati et al., 2020; Rachman, 2019; Riduan, 2015).

In the research conducted by Puspita et al. (2024), the approach used still focused on reducing insulin and IL-6 levels through a high-protein diet intervention in the PCOS insulin resistance model, so that the adaptive immune aspect has not been part of the analysis. Meanwhile, Fahrumnisa (2019) highlights the potential of Curcuma longa in improving PCOS conditions, but has not evaluated changes in lymphocyte subsets that play a role in the inflammatory pathogenesis of PCOS. Research on red ginger conducted by Dwiloka et al. (2023), Mantiri et al. (2013), Marsenia et al. (2025), Siregar et al. (2022), Verawati et al. (2023) only emphasizes biological effects such as hypocholesterolemic, antibacterial, in silico-based immunomodulatory, increased mineral content, or analgesic activity, without linking red ginger to immune response regulation in PCOS. Based on these limitations, this study offers novelty in the form of the first analysis that evaluates the effect of red ginger administration on CD4–CD8–CD62L–G1 (R1) lymphocyte subsets using flow cytometry in the context of PCOS prevention in Rattus norvegicus. This approach provides a new scientific contribution by opening an understanding regarding the role of adaptive immune modulation by red ginger on PCOS development, which has never been reported in the nine previous studies.

According to a review of previous research, to date there have been no studies specifically investigating the role of red ginger (Zingiber officinale var. rubrum) in modulating the adaptive immune response in Polycystic Ovary Syndrome (PCOS), particularly through the analysis of the CD4–CD8–CD62L–G1 (R1) lymphocyte subset using flow cytometry. Previous works have predominantly focused on general metabolic and inflammatory parameters, such as insulin levels, proinflammatory cytokines, or hormonal profiles, without directly assessing the involvement of the

adaptive immune system in PCOS pathogenesis. Hence, this study presents scientific novelty by integrating a cellular immunology approach to evaluate the preventive effect of red ginger ethanol extract on PCOS development, which has not been reported in prior investigations.

This investigation is essential given that PCOS is increasingly understood as a chronic metabolic-inflammatory disorder that involves not only hormonal imbalances but also accompanying adaptive immune system dysfunction. Conventional PCOS therapy typically focuses on ovulation induction or improving insulin resistance, yet it does not optimally target the underlying immunological inflammatory mechanisms that contribute to decreased oocyte quality and impaired ovarian function. A natural substance-based approach, such as using red ginger with its anti-inflammatory and immunomodulatory properties, has the potential to serve as a safer and more sustainable preventive strategy. Thus, the results of this study are expected to provide a scientific contribution to understanding the role of adaptive immune modulation in PCOS and to open opportunities for developing preventive herbal-based therapies.

Based on this background, the author wants to analyze the administration of ethanol extract of red ginger (*Zingiber officinale var. rubrum*) through the results of flow cytometry of lymphocyte cells through CD4-CD8-CD62L-G1=R1 in preventing the occurrence of Polycystic Ovary Syndrome (PCOS) in *Rattus norvegicus* rats.

Method

This research took place in April 2025 at the Laboratory of the Faculty of Veterinary Medicine, Airlangga University, Surabaya. The ethics approval certificate was obtained from the Faculty of Veterinary Medicine, Airlangga University on April 28, 2025, bearing the number 2.KEH.59.04.2025. This study employed only a post-test design within the framework of a Completely Randomized Design (CRD), in which 30 rats were randomly divided into five groups.

Thirty Rattus norvegicus rats (100-200 g) were acclimated for two months. Despite the standard acclimation period usually being shorter, an intentionally extended duration was applied to stabilize hormonal and metabolic profiles before androgen induction, particularly as endocrine parameters are the main outcomes of current investigation.

Experimental animals were divided into five groups (I-V). Group I (negative control) received standard food and water without any additional treatment. No vehicle was administered to avoid the emergence of unnecessary variables, as both testosterone propionate and extract were given in a stable form without additional solvents. Group II (positive control) received testosterone propionate at a dose of 100 mg/kg body weight, subcutaneously, once a day for 21 days, and was terminated on the 22nd day.

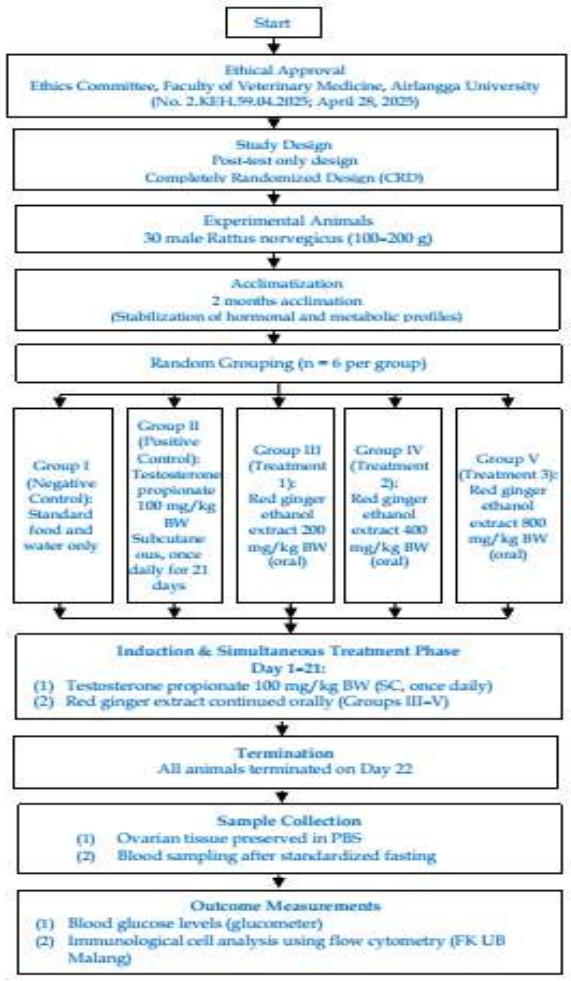

Figure 1. Research flowchart

Group III (treatment 1) received 200 mg/kg BW of red ginger ethanol extract for 3 days, followed by co-administration of testosterone propionate (100 mg/kg BW) and the same extract dose for 21 days, and was terminated on day 22. Group IV (treatment 2) underwent the same protocol using 400 mg/kg BW of the extract, and Group V (treatment 3) used 800 mg/kg BW (Chaudhari & Nampoothiri, 2017; Ebeye et al., 2025; Gulan et al., 2019). Ovarian tissues were preserved in PBS. Flow cytometry was conducted at FK UB Malang, and glucose concentrations were assessed via glucometer. Each treatment group received the extract for three days as a pre-treatment phase to allow the active compounds (gingerol and shogaol) to reach stable physiological levels before testosterone induction. This pre-treatment approach is commonly used in prevention models to assess protective effects.

Afterwards, the extract was administered simultaneously with testosterone propionate (100 mg/kg BW, subcutaneously, once daily) for an additional 21 days. The simultaneous administration was intentionally used as a preventive protocol to evaluate the protective effect of red ginger on the characteristics of PCOS induced by testosterone. All animals were terminated on day 22.

The ovarian tissue samples were preserved in PBS for this study, which concentrates on cell-based immunological evaluation using flow cytometry rather than histopathological analysis. Flow cytometry analysis was performed at FK UB Malang. Blood glucose levels were measured with a glucometer after a standardized fasting period as an initial metabolic indicator.

Result and Discussion

Table 1 implies a trend where the treatment group (P1-P3) showed an increase in the number of CD4 cells compared to the positive group (K2). This increase is more pronounced at higher doses, as seen from the higher accumulation of CD4 values in P2 and P3.

The study findings revealed that the flow cytometry results on the lymphocyte cells of Rattus norvegicus rats varied. There were K1 (healthy group), K2 (sick group), P1 (EJM treatment 200 mg/kg/BW), P2 (EJM treatment 400 mg/kg/BW), P3 (EJM treatment 800 mg/kg/BW), which were treatment groups given red ginger (Zingiber officinale var. rubrum).

Table 1. Flow Cytometry Results on Cluster of Differentiation 4 (CD4)

Cluster Of Differentiation 4 (CD-4)					
	K1 (Negative)	K2 (Positive)	P1	P2	P3
Replicate	% gated	% gated	% gated	% gated	% gated
1	2.37	5.18	1.31	10.32	7.45
2	3.04	5.71	1.90	6.66	1.14
3	0.34	0.86	2.43	2.69	95.55
4	0.53	0.78	5.20	5.18	20.54
5	1.33	1.17	3.31	94.6	10.32
6	1.26	1.17	58.19	2.63	74.76
Mean	1.47	2.49	12.05	20.34	34.96

Table 2. Flow Cytometry Results of Cluster of Differentiation 4 (CD4) Lymphocyte Cells in the Healthy Group (K1), Sick Group (K2), Treatment Group Given 200 mg/kg/BB Red Ginger Extract (P1), Treatment Group Given 400 mg/kg/BB Red Ginger Extract (P2), Treatment Group Given 800 mg/kg/BB Red Ginger Extract (P3)

Cluster of Differentiation 4 (CD4)		
Group	Mean ± SD	ρ
K1 (negative)	13.90 ± 29.80	
K2 (positive)	1.13 ± 0.71	
P1	34.60 ± 39.70	<0.001*
P2	47.70 ± 37.90	
P3	74.80 ± 34.50	

(*): significant α=0.05

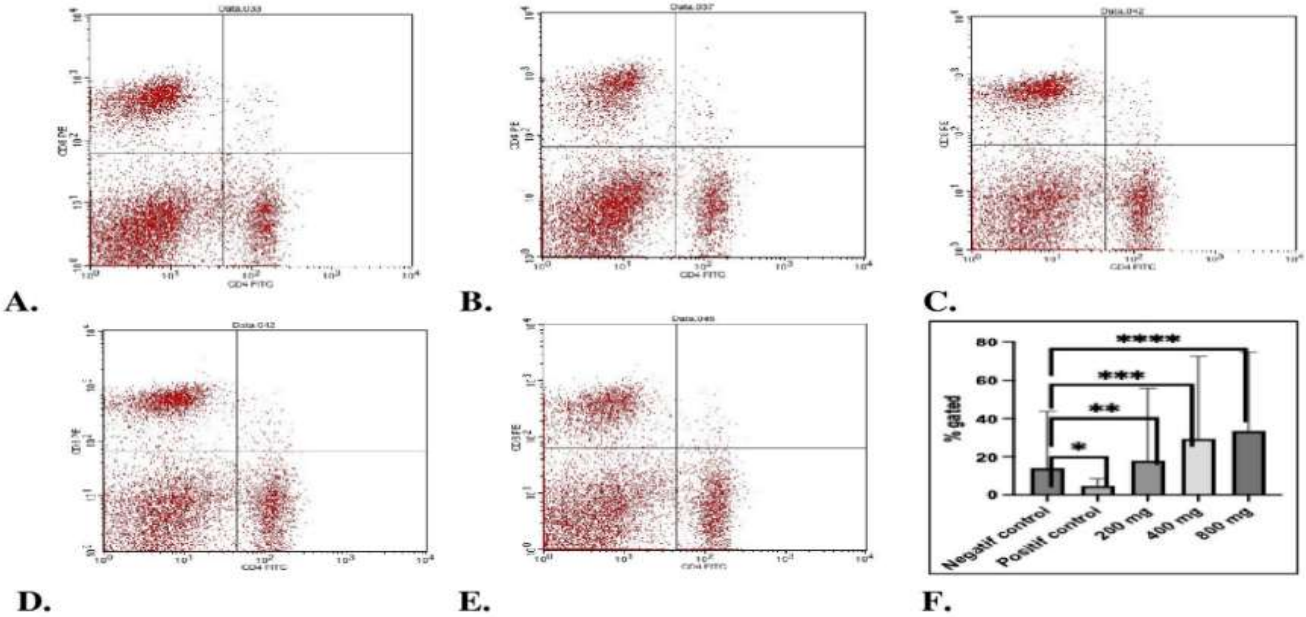

Figure 2. The results of flow cytometry *Cluster of Differentiation* 4 (CD4) in lymphocyte cells show that: **A.** healthy group mean±SD 13.90 ± 29.80. **B.** Sick group mean±SD 1.13 ± 0.71. **C.** P200 group mean±SD 34.60 ± 39.70. **D.** P400 group mean±SD 47.70 ± 37.90. **E.** P800 group mean±SD 74.80 ± 34.50. **F.** The results of one-way anova statistics show significant results

Table 2 shows the Cluster of Differentiation 4 (CD4) lymphocyte cells, showing that Group I, the healthy group, is significantly different from Group II, the sick group, with a p value of 0.001. Group I, the healthy

group, is also very significantly different from Group III, the treatment group given 800 mg/kg/BW red ginger ethanol extract, with a p value of 0.001.

The results of flow cytometry Cluster of Differentiation 4 (CD4) in lymphocyte cells showed that the treatment group was significantly different from the positive group. Treatment group 3 (P3) with the administration of 800 mg/kg/BW red ginger ethanol extract was better than Treatment group 1 (P1) with the administration of 200 mg/kg/BW red ginger ethanol extract and Treatment group 2 (P2) with the administration of 400 mg/kg/BW red ginger ethanol extract.

Table 3. Flow Cytometry Results on Cluster of Differentition 8 (CD8)

Cluster Of Differentiation 8 (CD-8)					
	K1 (Negative)	K2 (Positive)	P1	P2	P3
Replicate	% gated	% gated	% gated	% gated	% gated
1	0.12	0.91	0.40	0.39	3.24
2	6.73	1.17	0.70	0.21	0.90
3	0.22	0.19	0.28	1.05	97.73
4	0.51	0.81	0.39	0.75	95.42
5	1.45	5.05	0.86	98.17	1.70
6	0.75	17.96	60	6.80	95.57
Mean	1.63	4.34	10.43	17.89	49.09

Table 3 presents the fluctuation of CD8 lymphocyte percentage between replications in all groups, with the negative group (K1) showing consistently low values, while the positive group (K2) indicates a slight increase within the low to moderate range. The treatment groups (P1-P3) exhibit a greater increase in CD8 expression, including some extreme values, such as 60.00% in P1 and 97.73% and 95.57% in P3, which are common biological variations in flow cytometry analysis due to differences in gating, cell distribution, and individual responses to testosterone induction and red ginger extract administration.

Table 4. Flow Cytometry Results of Cluster of Differentiation 8 (CD8) Lymphocyte Cells in the Healthy Group (K1), the Sick Group (K2), the Treatment Group Given 200 mg/kg/BW Red Ginger Extract (P1), the Treatment Group Given 400 mg/kg/BW Red Ginger Extract (P2), the Treatment Group Given 800 mg/kg/BW Red Ginger Extract (P3)

Cluster of Differentiation 8 (CD8)		
Group	Mean ± SD	ρ
K1 (negative)	10.30 ± 21.00	
K2 (positive)	4.34 ± 6.89	
P1	21.10 ± 35.90	<0.001*
P2	50.10 ± 38.70	
P3	74.60 ± 23.80	

(*): significant α=0.05

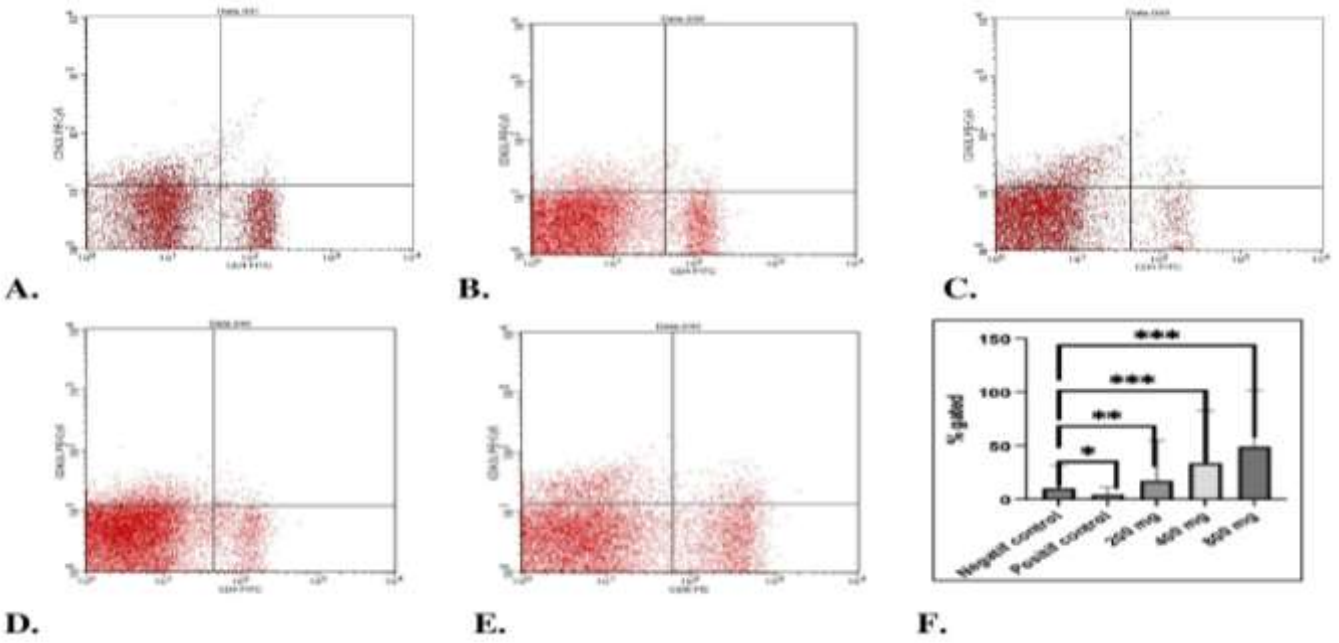

Figure 3. The results of flow cytometry *Cluster of Differentiation 8* (CD8) in lymphocyte cells showed in the groups: A. Healthy group mean±SD; 13.90±29.80. B. Sick group mean±SD; 1.13±0.71. C. P200 group mean±SD; 34.60±39.70. D. P400 group mean±SD; 47.70±37.90. E. P800 group mean±SD; 74.80±34.50. F. The results of one-way anova statistics showed significant results

Table 4 shows that Cluster of Differentiation 8 (CD8) lymphocyte cells in Group I, the healthy group, are significantly different from Group II, the sick group, with a p value of 0.001. Group I, the healthy group, is very significantly different from Group III, the treatment group given 800 mg/kg/BW red ginger ethanol extract, with a p value of 0.001.

The flow cytometry analysis of Cluster of Differentiation 8 (CD8) in lymphocyte cells indicated that the treatment groups differed significantly from the positive control group. Treatment group 3 (P3), which received 800 mg/kg BW of red ginger ethanol extract, demonstrated superior results compared to Treatment group 1 (P1) receiving 200 mg/kg BW and Treatment group 2 (P2) receiving 400 mg/kg BW.

Table 5. Flow cytometry Results on L-Selectin (CD26L)

	L-Selectin (CD26L)				
	K1 (Negative)	K2 (Positive)	P1	P2	P3
Replicate	% gated	% gated	% gated	% gated	% gated
1	2. 37	5.18	1.31	10.32	7.45
2	3.04	5.71	1.90	6.66	1.14
3	0.34	0.86	2.43	2.69	95.55
4	0.53	0.78	5.20	5.18	20.54
5	1.33	1.17	3.31	94.60	10.32
6	1.26	1.17	58.19	2.63	74.76
Mean	1.47	2.49	12.05	20.34	34.96

Table 5 illustrates the fluctuation of CD62L expression in six replications in each group, with the negative (K1) and positive (K2) groups showing relatively low and stable values. In the treatment groups (P1-P3), an increase in CD62L expression is observed with some extreme values, such as 58.19% in P1 and 94.60% and 95.55% in P2 and P3. These extreme values represent common biological variation in flow cytometry, attributable to differences in gating strategy, inherent cellular response, and the experimental effects of either testosterone propionate induction or red ginger extract administration.

Table 6. Flow Cytometry Results of L-Selectin (CD26L) in Lymphocyte Cells of the Healthy Group (K1), the Sick Group (K2), the Treatment Group Given 200 mg/kg/BW Red Ginger Extract (P1), the Treatment Group Given 400 mg/kg/BW Red Ginger Extract (P2), the Treatment Group Given 800 mg/kg/BW Red Ginger Extract (P3)

	L-Selectin (CD26L)	
Group	Mean ± SD	ρ
K1 (negative)	13.90 ± 29.80	
K2 (positive)	1.13 ± 0.71	
P1	34.60 ± 39.70	<0.001*
P2	47.70 ± 37.90	
P3	74.80 ± 34.50	

(*): significant α=0.05

Table 6 shows that L-Selectin (CD62L) lymphocyte cells in Group I, which is the healthy group, are significantly different from Group II, which is the sick group, with a p value of 0.001. Group I, the healthy group, is very significantly different compared to Group III, the treatment group given 800 mg/kg/BW of red ginger ethanol extract.

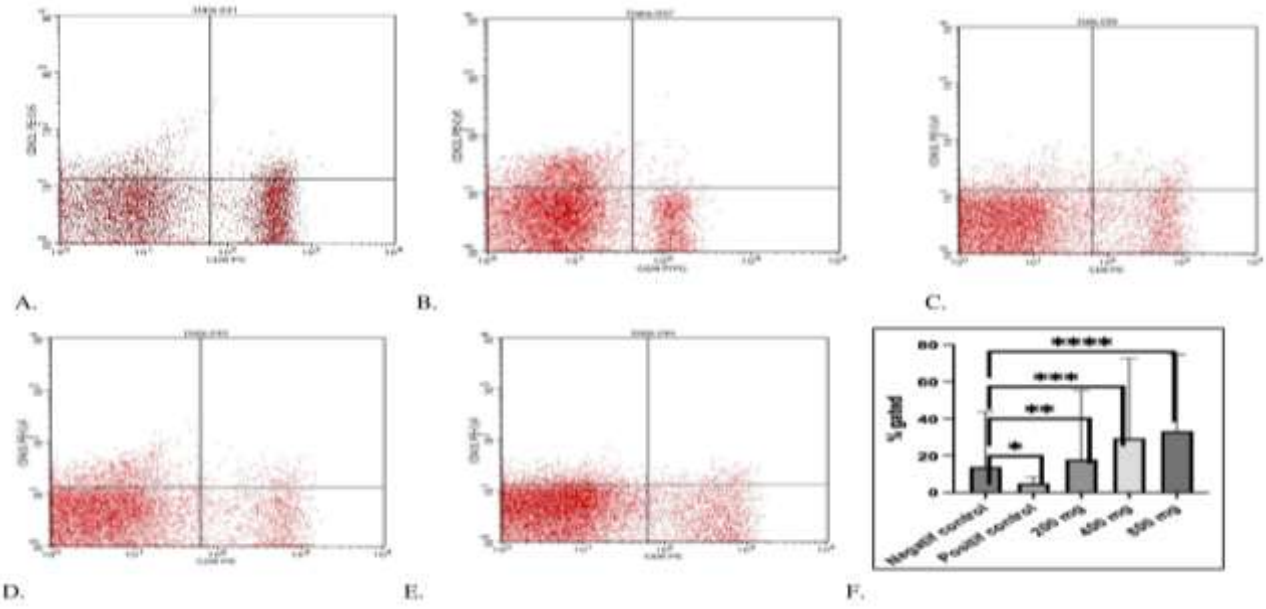

Figure 4. Flow cytometry results of L-Selectin (CD26L) in lymphocyte cells show: A. healthy group mean±SD; 10.30±21.00. B. Sick group mean±SD; 4.34±6.89. C. P200 group mean±SD; 21.10±35.90. D. P400 group mean±SD; 50.10±38.70. E. P800 group mean±SD; 74.60±23.80. F. The statistical results of one-way anova show significant results

Discussion

Herbal ingredients can be defined as medicines containing active ingredients derived from traditional plants commonly used in the treatment of diseases by local communities. Most herbal plants that function as health supplements (Rasyid et al., 2024) contain essential oils and secondary metabolites (Yanis et al., 2024). Herbal medicinal products are a mixture of organic chemical compounds obtained (Wahyuni et al., 2023) from the processing of some or all parts of traditional plants (Sam, 2019). The use of herbal products, or what in Indonesia is known as nutritional support and general body health, requires intervention in the form of therapy (Taylor et al., 2019). Phytochemicals are also a major focus of the government in efforts to overcome drug imports. Medicinal plants are rich in bioactive compounds like flavonoids, alkaloids, saponins, steroids, and terpenoids. These compounds possess diverse biological properties such as antimicrobial, antioxidant, and immunomodulatory effects (Rasmi et al., 2023; Wulandari & Yuniarti, 2023). The advantage of herbal ingredients compared to modern medicines is that herbal ingredients are believed to have fewer side effects than modern medicines (Nurhayati & Medistriani, 2024; Sari et al., 2025), in addition to herbal ingredients containing various active substances that work synergistically to produce various benefits in one extract (Carmona & Pereira, 2013).

Based on previous research, there has been no in vivo research data on the use of ethanol extract of red ginger (Zingiber officinale var rubrum) to prevent Polycystic Ovary Syndrome (PCOS) in Rattus norvegicus mice. The ethanol extract of red ginger contains active substances that have antioxidants and anti-inflammatory properties. The research chose to utilize the red ginger variety (Zingiber officinale var rubrum) due to previous in vitro studies indicating its superior anti-inflammatory properties when compared to other ginger varieties (Pertiwi et al., 2022; Supu et al., 2018). The preference for red ginger (Zingiber officinale var. rubrum) reflects findings from High Performance Liquid Chromatography (HPLC) analyses showing elevated concentrations of 6-gingerol and 6-shogaol relative to those measured in elephant ginger and emprit ginger (Riduan, 2015).

Examination of the active ingredients in the red ginger ethanol extract, performed at the Pharmacology Laboratory of Brawijaya University Malang, confirmed the presence of anti-inflammatory compounds such as 6-shogaol and 6-gingerol. These components inhibit the activation of protein kinase B (Akt) and nuclear factor kappa B (NF-κB), leading to enhanced anti-inflammatory cytokine production and reduced pro-inflammatory cytokine levels. In vitro experiments showed that red ginger ethanol extract exhibited immunomodulatory, anti-inflammatory, and antioxidant effects, which can be seen from changes in the expression of three gene categories, namely immune system signaling, anti-inflammatory cytokines, and antioxidants (Lushchak & Gospodaryov, 2012).

The research design utilized the induction of testosterone propionate for 21 days to establish a PCOS model, however, based on the results, the induction did not fully produce a consistent portrayal of PCOS across all groups. The inconsistencies in this model raise issues of internal validity as the treatment effects become difficult to separate from the instability of the disease model itself. Hence, conclusions regarding the potential protective effects of red ginger on PCOS should be interpreted cautiously as the treatment effectiveness was tested on a model that was not fully developed optimally.

The administration of red ginger doses (200-800 mg/kgBW) has been proven to improve immune parameters such as CD4, CD8, and L-selectin. Yet, the improvement in these parameters does not result in complete recovery of ovarian structure in all PCOS-induced groups. This suggests that although red ginger has immunomodulatory and anti-inflammatory effects, the dose, duration of administration, or level of ovarian damage due to androgen induction is not sufficient to demonstrate a conclusively protective effect on the ovaries. Thus, the interpretation of ginger's effectiveness should take into consideration therapeutic limitations in the context of induction duration and disease progression.

The preparation process of red ginger ethanol extract and examination of bioactive content of 6-gingerol and 6-shogaol has been carried out; yet some methodological steps such as the final concentration of the extract, the standardization method of active compound levels, and quality control have not been detailed extensively. The lack of this information could potentially decrease the reproducibility of the research because other researchers may not be able to repeat the procedure with the same consistency of extract levels. Likewise, variations in immune responses may also be influenced by uncertainties in material standardization.

Data analysis indicates changes in immunological markers, however, the relationship between the increase in these markers and the degree of improvement in PCOS has not been deeply or quantitatively analyzed. The lack of further analysis, such as correlation between hormone levels, ovarian morphology, and immunological markers, limits the strength of mechanistic interpretation. Although ginger's immunomodulatory effects are well documented, analytical evidence supporting its comprehensive protective role remains limited.

The administration of red ginger ethanol extract in groups P1-P3 pointed to an increase in CD4, CD8, and L-selectin levels compared to the sick group. This increase may be linked to the bioactive mechanisms of ginger, particularly 6-gingerol and 6-shogaol, which are known to inhibit NF-κB activation, thereby reducing proinflammatory cytokine production and suppressing systemic inflammation. This decrease in inflammation allows the adaptive immune system to function more optimally, as reflected in the increased lymphocyte proliferation observed in the CD4 and CD8 data. Further, ginger is also reported to modulate L-selectin expression, an important adhesion molecule for lymphocyte homing and trafficking, so the elevated L-selectin levels in groups P1-P3 reflect an improvement in the immune cell migration ability to target tissues. As such, the pharmacological mechanisms of ginger align with the findings of increased CD4, CD8, and L-selectin in this study.

The results of a systematic review and meta-analysis conducted on research on red ginger using the Randomized Controlled Trials (RCT) method, showed that oral consumption of red ginger was able to reduce inflammatory markers in blood serum, including TNF-α (Morvaridzadeh et al., 2021).

This research in vitro study, ginger extract was proven to be able to increase insulin release in pancreatic β cells of rats (Chakraborty et al., 2012). A glucose tolerance test confirmed that the ethanol extract of red ginger also increased plasma insulin levels, thereby lowering blood glucose levels (Rani et al., 2011). One of the most important components of red ginger in reducing blood glucose levels is gingerol, which shows a protective effect on pancreatic β-cells in DM rats and restores plasma insulin levels (Li et al., 2012; Nazir et al., 2014). On the other hand, it can lower blood glucose levels by increasing serum insulin levels and also reducing serum glucose and fructosamine concentrations. Bahri et al. (2023) state that Zingiber Officinale (ginger extract), can be used as an alternative antibiotic to replace synthetic antibiotics. This is supported by research results of Farlikhatun et al. (2025) which recommend red ginger as therapy, because its effectiveness has been proven in the wound healing process. The combination of antidiabetic drugs can enhance antioxidant defenses and reduce oxidative damage in the kidneys and pancreas of diabetic rat models (Gaytán et al., 2002; Hu et al., 2011).

Red ginger is known as an herbal plant containing chemical compounds that can be beneficial in treating various diseases, such as those with anti-inflammatory and antioxidant properties. These effects are due to the bioactive components contained in red ginger, such as 6-gingerols and 6-shogaol. In this study, flow cytometry results on lymphocytes given red ginger showed intact lymphocytes, while the positive control group developed polycystic ovary syndrome (PCOS). This indicates that red ginger administration protects ovarian cells.

Based on previous research, administration of testosterone propionate for 21 days by interperitoneal injection macroscopically gives a picture of polycystic ovary syndrome (PCOS) while red ginger can actually act as an anti-inflammatory. In groups III, IV, V with testosterone propionate administration, treatment was not given for more than 21 days because it can cause damage to the ovaries so that it cannot be cured. The results of flow cytometry of lymphocyte cells in this study showed polycystic ovary syndrome (PCOS) in all treatment groups given red ginger (groups III, IV, and V) and a picture of polycystic ovary syndrome (PCOS) in the treatment group without red ginger (group I). In addition to being caused by insufficient testosterone administration, insufficient red ginger dosage, and the duration of red ginger dosage also play a role.

Although there was an increase in immune markers (CD4, CD8, and L-selectin) in the treatment group, this improvement has not completely suppressed the pathologic process of PCOS. The increase in CD4/CD8 in groups P1-P3 indicates immune activation and recovery of adaptive immune response due to the anti-inflammatory effects of ginger. Nevertheless, this response is not strong enough to balance hyperandrogenism and chronic inflammation, which are the basis of PCOS pathophysiology. This can be seen from the continued presence of PCOS features in all groups receiving testosterone propionate, including those given ginger. Hence, these findings suggest that although ginger has a positive immunomodulatory effect, the duration of administration, dosage, and level of ovarian damage due to androgen induction may not allow for full recovery of ovarian structure.

Overall, the data suggests that red ginger is capable of enhancing immune cell activity by improving the parameters of CD4, CD8, and L-selectin. Yet, this immune enhancement does not automatically eliminate the PCOS condition, thus further research with higher doses, longer durations, or combination with other therapies is needed to optimize the protective effects of red ginger on reproductive pathology.

Conclusion

The administration of red ginger (Zingiber officinale var. rubrum) extract highlights a potential protective effect in a testosterone-induced polycystic ovary syndrome (PCOS) model in Rattus norvegicus. The most optimal response was observed at a dose of 800 mg/kg body weight, which exhibited a better immunological profile compared to doses of 200 mg/kg

BW and 400 mg/kg BW. The ethanol extract of red ginger increased the expression of $CD4^+$–$CD8^+$–$CD62L^+$ lymphocyte subpopulations during the G1 phase, indicating immunomodulatory activity. These findings suggest that red ginger may contribute to the regulation of immune responses associated with PCOS and holds potential as a complementary herbal agent in PCOS management, thus warranting further investigation. In essence, these results highlight the potential of red ginger as a supportive herbal agent in PCOS management, although further studies are required to elucidate its molecular mechanisms and clinical relevance.

Acknowledgments
The authors thank the technical staff of the Faculty of Veterinary Medicine, Airlangga University, Surabaya, and the flow cytometry facility at Brawijaya University, Malang, for their expert support. We also thank our colleagues for their insightful discussions.

Author Contributions
Conceptualization, S.M. and H.P.A.; methodology, S.M. and H.P.A.; formal analysis, S.M. and R.S.; investigation, S.M., H.P.A. and R.S.; resources, S.M.; data curation, S.M.; writing—original draft preparation, S.M.; writing—review and editing, H.P.A. and R.S.; visualization, S.M.; supervision, H.P.A. and R.S.; project administration, S.M. All authors have read and agreed to the published version of the manuscript.

Funding
No external funding was received for this work.

Conflict of Interest
The authors have no conflicts of interest to declare.

References

Asyik, N., Herdiansyah, D., & Sadimantara, M. S. (2025). Study on The Addition of Red Ginger (Zingiber officinaleVar. Rubrum) and Black Rice (Oryza sativaL. Indica) to The Organoleptic Evaluation and Physical-Chemical Properties of Robusta Coffee (Coffeacanephora) from Southeast Sulawesi. *Jurnal Penelitian Pendidikan IPA*, *11*(7), 280–287. https://doi.org/10.29303/jppipa.v11i7.10946

Bahri, S., Umami, R., Ferniawan, F., Qadafi, M., & Partiwi, S. (2023). Comparison of The Effectiveness Antibacterial Test of Natural Ingredients and Antibiotic in Salmonella typhi Isolated from Hospital Waste and Household Waste. *Jurnal Penelitian Pendidikan IPA*, *9*(4), 2068–2074. https://doi.org/10.29303/jppipa.v9i4.3783

Baptiste, C. G., Battista, M.-C., Trottier, A., & Baillargeon, J.-P. (2010). Insulin and hyperandrogenism in women with polycystic ovary syndrome. *The Journal of Steroid Biochemistry and Molecular Biology*, *122*(1–3), 42–52. https://doi.org/10.1016/j.jsbmb.2009.12.010

Carmona, F., & Pereira, A. M. S. (2013). Herbal medicines: old and new concepts, truths and misunderstandings. *Revista Brasileira de Farmacognosia*, *23*(2), 379–385. https://doi.org/10.1590/S0102-695X2013005000018

Chakraborty, D., Mukherjee, A., Sikdar, S., Paul, A., Ghosh, S., & Khuda-Bukhsh, A. R. (2012). [6]-Gingerol isolated from ginger attenuates sodium arsenite induced oxidative stress and plays a corrective role in improving insulin signaling in mice. *Toxicology Letters*, *210*(1), 34–43. https://doi.org/10.1016/j.toxlet.2012.01.002

Chaudhari, N. K., & Nampoothiri, L. P. (2017). Neurotransmitter alteration in a testosterone propionate-induced polycystic ovarian syndrome rat model. *Hormone Molecular Biology and Clinical Investigation*, *29*(2), 71–77. https://doi.org/10.1515/hmbci-2016-0035

Cholili, M. N., & Wiyasa, A. (2022). Recurrent Pregnancy Loss. *Pharmacology, Medical Reports, Orthopedic, And Illness Details (COMORBID)*, *1*(1), 1–14. https://doi.org/10.55047/comorbid.v1i1.33

Diapati, A. M., Herbani, M., & Wahyuningsih, D. (2020). Pengaruh Kombinasi Dekokta Zingiber officinale var rubrum dan Imperata cylindrica Terhadap Kadar TNF-α Serum Tikus Osteoartritis. *Jurnal Bio Komplementer Medicine*, *7*(1), 1–7. Retrieved from https://jim.unisma.ac.id/index.php/jbm/article/view/6633/5380

Dwiloka, B., & Putri, S. A. W. (2023). Pengaruh Marinasi Jahe Merah (Zingiber Officinale Rosc.) Terhadap Perubahan Kadar Mineral Esensial Pada Daging Sapi Kering. *Jurnal Pangan Dan Gizi*, *13*(2), 45–55. https://doi.org/10.26714/jpg.13.2.2023.45-55

Ebeye, M. O., Nwogueze, B. C., Naiho, O. A., & Igweh, J. C. (2025). Dietary supplementation of Red and White Ginger (Zingiber officinale) Rhizomes and Gingerol improves male reproductive capacities. *Phytomedicine Plus*, *5*(2), 100758. https://doi.org/10.1016/j.phyplu.2025.100758

Fahrumnisa, A. R. (2019). Ekstrak Kunyit (Curcuma longa) sebagai Tatalaksana Sindrom Polikistik Ovarium. *Jurnal Ilmiah Kesehatan Sandi Husada*, *8*(2), 115–120. https://doi.org/10.35816/jiskh.v10i2.125

Farlikhatun, L., Husna, A., Restuti, B. P., Munarti, I., Putri, K. A., Mutiah, R., & Sundari, S. (2025). Exploring the Role of Complementary Herbal Therapies (Red Ginger, Aloe Vera, Tangerang Turmeric, Cinnamon, Binahong Leaves, Green Betel Leaves) in Science Education: A Case Study on the Healing Process of Second-Degree Perineal

Wounds in Postpartum Mother. *Jurnal Penelitian Pendidikan IPA*, *11*(7), 1235–1242. https://doi.org/10.29303/jppipa.v11i7.10621

Franciska, S., Hestiantro, A., & Kartika, T. (2025). Ketidakseimbangan Th17 dan Treg Pada Pasien PCOS Dengan Resistensi Insulin: Tinjauan Literatur Terhadap Potensi Suntikan Terapi. *Jurnal Kedokteran Universitas Palangka Raya*, *13*(1), 1–13. https://doi.org/10.37304/jkupr.v13i1.17456

Gaytán, F., Tarradas, E., Morales, C., Bellido, C., & Sánchez-Criado, J. E. (2002). Morphological evidence for uncontrolled proteolytic activity during the ovulatory process in indomethacin-treated rats. *Reproduction*, *123*(5), 639–649. https://doi.org/10.1530/rep.0.1230639

Gulan, T., Yeernuer, T., Sui, S., & Mayinuer, N. (2019). A rat model of maternal polycystic ovary syndrome shows that exposure to androgens in utero results in dysbiosis of the intestinal microbiota and metabolic disorders of the newborn rat. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, *25*, 9377. https://doi.org/10.12659/MSM.918600

Handayani, P. A., Kolong, Y., Ayunda, F. D., Debora, O., & Putri, M. K. (2022). Penggunaan Jahe Merah (Zingiber Officinale) Sebagai Imunomodulator Dimasa Pandemi. *Jurnal Ilmu Kesehatan (JIKA)*, *1*(2), 40–46. https://doi.org/10.36307/b1j2gn68

Hu, J., Guo, Z., Glasius, M., Kristensen, K., Xiao, L., & Xu, X. (2011). Pressurized liquid extraction of ginger (Zingiber officinale Roscoe) with bioethanol: An efficient and sustainable approach. *Journal of Chromatography A*, *1218*(34), 5765–5773. https://doi.org/10.1016/j.chroma.2011.06.088

Iksan, M., Yusuf, F. M., & Al Zarliani, W. O. (2023). Antipyretic Drug Candidates Through Reverse Docking Techniques Used In Science Learning. *Jurnal Penelitian Pendidikan IPA*, *9*(8), 6398–6405. https://doi.org/10.29303/jppipa.v9i8.4863

Leslie, A. G. J., & Gunawan, S. (2023). Ekstrak Jahe Merah (Zingiber officinale Var. Rubrum): uji fitokimia, analisa sidik jari, kapasitas total antioksidan, dan penentuan kadar fenolik. *Jurnal Kesehatan Tambusai*, *4*(2), 2007–2016. https://doi.org/10.31004/jkt.v4i2.15922

Li, Y., Tran, V. H., Duke, C. C., & Roufogalis, B. D. (2012). Preventive and protective properties of Zingiber officinale (ginger) in diabetes mellitus, diabetic complications, and associated lipid and other metabolic disorders: a brief review. *Evidence-Based Complementary and Alternative Medicine*, *2012*(1), 516870. https://doi.org/10.1155/2012/516870

Lizneva, D., Suturina, L., Walker, W., Brakta, S., Gavrilova-Jordan, L., & Azziz, R. (2016). Criteria, prevalence, and phenotypes of polycystic ovary syndrome. *Fertility and Sterility*, *106*(1), 6–15. https://doi.org/10.1016/j.fertnstert.2016.05.003

Luhurningtyas, F. P., Susilo, J., Yuswantina, R., Widhihastuti, E., & Ardiyansah, F. W. (2021). Aktivitas imunomodulator dan kandungan fenol ekstrak terpurifikasi rimpang jahe merah (Zingiber officinale Rosc. Var. Rubrum). *Indonesian Journal of Pharmacy and Natural Product*, *4*(1), 51–59. https://doi.org/10.35473/ijpnp.v4i1.974

Lushchak, V., & Gospodaryov, D. V. (2012). *Oxidative stress and diseases*. BoD–Books on Demand.

Mantiri, N. C., Awaloei, H., & Posangi, J. (2013). Perbandingan efek analgesik perasan rimpang jahe merah (Zingiber officinale Var. rubrum thelaide) dengan aspirin dosis terapi pada mencit (Mus musculus). *EBiomedik*, *1*(1), 518–523. https://doi.org/10.35790/ebm.v1i1.4593

Mareta, R., Amran, R., & Larasati, V. (2018). Hubungan polycystic ovary syndrome (PCOS) dengan infertilitas di praktik swasta dokter obstetri ginekologi Palembang. *Majalah Kedokteran Sriwijaya*, *50*(2), 85–91. https://doi.org/10.36706/mks.v50i2.8552

Marlina, U., Maulitanti, S. D., Annisa, Y., & Masitha, D. (2023). Pengaruh Penerapan Diet Anti Inflamasi Pada Perubahan Manifestasi Klinis Dan Penanda Inflamasi Wanita Dengan Polycystic Ovary Syndrome (PCOS). *Jurnal Pendidikan Indonesia*, *4*(5), 475–488. https://doi.org/10.59141/japendi.v4i05.1821

Marsenia, E., Putranto, R. A., & Binartha, C. T. O. (2025). Potensi seduhan jahe merah (Zingiber officinale Rubrum) terhadap bakteri Porphyromonas gingivalis. *MKGK (Majalah Kedokteran Gigi Klinik)(Clinical Dental Journal) UGM*, *11*(1), 19–24. https://doi.org/10.36418/syntax-literate.v10i5.58019

Morvaridzadeh, M., Sadeghi, E., Agah, S., Fazelian, S., Rahimlou, M., Kern, F. G., Heshmati, S., Omidi, A., Persad, E., & Heshmati, J. (2021). Effect of ginger (Zingiber officinale) supplementation on oxidative stress parameters: A systematic review and meta-analysis. *Journal of Food Biochemistry*, *45*(2), e13612. https://doi.org/10.1111/jfbc.13612

Nazir, L., Samad, F., Haroon, W., Kidwai, S. S., Siddiqi, S., & Zehravi, M. (2014). Comparison of glycaemic response to honey and glucose in type 2 diabetes. *J. Pak. Med. Assoc*, *64*(1), 69–71. Retrieved from https://www.researchgate.net/profile/Faiza-Samad/publication/260642298_Comparison_of_glycaemic_response_to_honey_and_glucose_in_type_2_diabetes/links/55b85e0208ae092e96588845/Comparison-of-glycaemic-response-to-honey-and-glucose-in-type-2-diabetes.pdf

Nurhayati, U., & Medistriani, D. (2024). Enhancing

Spermatozoa Quality and Spermatogenic Cell in Hyperglycemic Mice (Mus musculus L.) with Sambung Nyawa (Gynura procumbens) and Mahagany (Swietenia mahagoni jacq) extracts, Alone and in Combination. *Jurnal Penelitian Pendidikan IPA*, *10*(6), 3118–3131. https://doi.org/10.29303/jppipa.v10i6.7180

Pertiwi, F. D., Rezaldi, F., & Puspitasari, R. (2022). Uji aktivitas dan formulasi sediaan liquid body wash dari ekstrak etanol bunga telang (Clitoria ternatea L) sebagai antibakteri Staphylococcus epidermidis. *Jurnal Ilmiah Kedokteran Dan Kesehatan*, *1*(1), 53–66. https://doi.org/10.55606/klinik.v1i1.257

Puspita, H. A., Agrisidan, Z., & Sari, W. A. (2024). Decreased Insulin and Interleukin-6 Levels in Rattus Norvegicus Model of Polycystic Ovary Syndrome-Insulin Resistance Treated with a High Protein Diet. *Jurnal Ners Dan Kebidanan (Journal of Ners and Midwifery)*, *11*(2), 209–215. https://doi.org/10.26699/jnk.v11i2.ART.p209-215

Rachman, D. F. (2019). Efek Kombinasi Dekokta Rimpang Zingiber Officinale Var Rubrum dan Rimpang Imperata Cylindrica Terhadap Kadar Superoxide Dismutase (SOD) Serum dan Malondialdehyde (MDA) Serum Tikus Osteoartritis. *Jurnal Bio Komplementer Medicine*, *6*(3), 1–10. Retrieved from https://jim.unisma.ac.id/index.php/jbm/article/view/4826

Rani, M. P., Padmakumari, K. P., Sankarikutty, B., Lijo Cherian, O., Nisha, V. M., & Raghu, K. G. (2011). Inhibitory potential of ginger extracts against enzymes linked to type 2 diabetes, inflammation and induced oxidative stress. *International Journal of Food Sciences and Nutrition*, *62*(2), 106–110. https://doi.org/10.3109/09637486.2010.515565

Rasmi, D. A. C., Zulkifli, L., & Ahadia, N. (2023). Antimicrobial activity test of bitter melon (Momordica charantia L.) plant extract against Staphylococcus epidermidis, Escherichia coli bacteria and Candida albicans. *Jurnal Penelitian Pendidikan IPA*, *9*(2), 454–458. https://doi.org/10.29303/jppipa.v9i2.3699

Rasyid, A., Glacio, R., Meiwinka, M., & Fernando, L. (2024). Managing the Merchandise Planning Process in SME. *Journal Of Sustainable Community Service*, *5*(1), 31–36. https://doi.org/10.55047/jscs.v5i1.877

Riduan, R. J. (2015). Pengaruh pemberian ekstrak jahe merah terhadap gambaran histopatologi pankreas yang diinduksi aloksan. *Jurnal Majority*, *4*(8), 11–16. Retrieved from https://juke.kedokteran.unila.ac.id/index.php/majority/article/view/1466

Sam, S. (2019). Importance and effectiveness of herbal medicines. *Journal of Pharmacognosy and Phytochemistry*, *8*(2), 354–357. Retrieved from https://www.phytojournal.com/archives/view-pdf/9074/8-4-205

Sari, W. D. P., Suriani, C., & Nasution, A. (2025). Ethnobotanical Study of Medicinal Plants in Traditional Medicine of The Karo Tribe Based on Local Wisdom. *Jurnal Penelitian Pendidikan IPA*, *11*(9), 34–39. https://doi.org/10.29303/jppipa.v11i9.12291

Setiawan, I., Lindawati, N. Y., & Amalia, B. (2018). Formulasi dan uji antiinflamasi sediaan hidrogel ekstrak jahe merah (Zingiber officinale). *Media Farmasi Indonesia*, *13*(1), 1330–1334. Retrieved from https://mfi.stifar.ac.id/MFI/article/view/45/32

Siregar, P. N. B., Pedha, K. I. T., Resmanto, K. F. W., Chandra, N., Maharani, V. N., & Riswanto, F. D. O. (2022). Kandungan Kimia Jahe Merah (Zingiber officinale var. Rubrum) dan Pembuktian In Silico sebagai Inhibitor SARS-CoV-2. *Jurnal Pharmascience*, *9*(2), 185–200. https://doi.org/10.20527/jps.v9i2.13149

Supu, R. D., Diantini, A., & Levita, J. (2018). Red ginger (Zingiber officinale var. rubrum): Its chemical constituents, pharmacological activities and safety. *Fitofarmaka Jurnal Ilmiah Farmasi*, *8*(1), 25–31. https://doi.org/10.33751/jf.v8i1.1168

Tang, Q., Li, X., Song, P., & Xu, L. (2015). Optimal cut-off values for the homeostasis model assessment of insulin resistance (HOMA-IR) and pre-diabetes screening: Developments in research and prospects for the future. *Drug Discoveries & Therapeutics*, *9*(6), 380–385. https://doi.org/10.5582/ddt.2015.01207

Taylor, H. S., Pal, L., & Seli, E. (2019). *Speroff's clinical gynecologic endocrinology and infertility (9th ed.)*. Wolters Kluwer.

Tosi, F., Bonora, E., & Moghetti, P. (2017). Insulin resistance in a large cohort of women with polycystic ovary syndrome: a comparison between euglycaemic-hyperinsulinaemic clamp and surrogate indexes. *Human Reproduction*, *32*(12), 2515–2521. https://doi.org/10.1093/humrep/dex308

Velaga, V., Suryadevara, N., Chee, L. L., & Ismail, N. E. (2017). Phytochemical analysis and immuno-modulatory effect of Moringa oleifera flowers. *Int J Pharm Pharm Sci*, *9*(6), 24–28. https://doi.org/10.22159/ijpps.2017v9i6.16285

Verawati, N., Aida, N., & Yani, A. (2023). Pengaruh Perbandingan Jenis Jahe dan Konsentrasi Jahe pada Karakteristik Kimia, Mikrobiologi Minuman Herbal Tradisional Minaserua. *G-Tech: Jurnal Teknologi Terapan*, *7*(4), 1732–1739.

https://doi.org/10.33379/gtech.v7i4.3387

Wahyuni, M., Decroli, E., & Lasmini, P. S. (2015). Hubungan Resistensi Insulin dengan Gambaran Klinis Sindrom Ovarium Polikistik. *Jurnal Kesehatan Andalas*, *4*(3), 908–916. https://doi.org/10.25077/jka.v4i3.385

Wahyuni, S., Wati, R., & Hidayatullah, M. (2023). Analysis of Differences in the Effectiveness of Giving Red Beet Juice (Beta vulgaris L) and Cucumber Juice (Cucumis sativus) on Reducing Blood Pressure in Hypertensive Patients. *Pharmacology, Medical Reports, Orthopedic, And Illness Details*, *2*(4), 192–200. https://doi.org/10.55047/comorbid.v2i4.1104

Wang, M.-X., Yin, Q., & Xu, X. (2020). A rat model of polycystic ovary syndrome with insulin resistance induced by letrozole combined with high fat diet. *Medical Science Monitor: International Medical Journal of Experimental and Clinical Research*, *26*, e922136-1. https://doi.org/10.12659/MSM.922136

Winarni, E., Nasution, A. N., & Nasution, S. W. (2023). Antifungal Activity of Red Ginger (Zingiber officinale var. Rubrum) and Garlic (Allium sativum) against HIV Patients-Isolated Candida albicans. *Jurnal Penelitian Pendidikan IPA*, *9*(10), 9038–9044. https://doi.org/10.29303/jppipa.v9i10.4981

Wulandari, P., & Yuniarti, E. (2023). Bioactivity potential and chemical compounds of Cinnamomum: literature review. *Jurnal Penelitian Pendidikan IPA*, *9*(5), 1–7. https://doi.org/10.29303/jppipa.v9i5.3284

Yanis, M. A., Amirsyah, M., & Harsono, A. D. (2024). Healing Potential of Chromolaena odorata Extract: Modulation of Neutrophil, Macrophage, and Lymphocyte Response in Infected Wounds of Mus musculus. *Jurnal Penelitian Pendidikan IPA*, *10*(12), 10670–10676. https://doi.org/10.29303/jppipa.v10i12.9423

Zuo, T., Zhu, M., & Xu, W. (2016). Roles of oxidative stress in polycystic ovary syndrome and cancers. *Oxidative Medicine and Cellular Longevity*, *2016*(1), 8589318. https://doi.org/10.1155/2016/8589318