ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 6, 2025

Online - 2455-3891
Print - 0974-2441

Research Article

# HARNESSING THE POWER OF G-PROTEIN COUPLED RECEPTOR-120 IN REDEFINING INSULIN RESISTANCE AND INFLAMMATION MANAGEMENT IN POLYCYSTIC OVARY SYNDROME

**NEETI PATEL[1]*, IVVALA ANAND SHAKER[2], KANDARP PATEL[3]**

**[1]Department of Biochemistry, Parul Institute of Medical Sciences and Research, Parul University, Waghodiya, Gujarat, India. [2]Department of Biochemistry, Swaminarayan Institute of Medical Sciences and Research, Gandhinagar, Gujarat, India. [3]Department of Pharmacology, Kiran Medical College, Surat, Gujarat, India.**
***Corresponding author: Neeti Patel; E-mail: neetipatel44@gmail.com**

***Received: 02 April 2025, Revised and Accepted: 15 May 2025***

**ABSTRACT**

**Objectives:** This study aims to evaluate serum G-Protein Coupled Receptor 120 (GPR120) levels and its association with anti-inflammatory cytokine interleukin-10 (IL-10), homeostasis model assessment of insulin resistance (HOMA-IR), and female reproductive hormones in polycystic ovary syndrome (PCOS) subjects as it is disorder of affecting reproductive women with complex combination of symptoms, such as excess androgens, polycystic ovaries, ovulatory dysfunction, Insulin resistance and chronic low-grade inflammation.

**Methods:** In a cross-sectional study carried out at the tertiary care hospital of the South Gujarat district between March 2023 and December 2024. Using a convenience sampling technique, a total of 248 women (124 PCOS and 124 age-matched healthy controls) were assessed for markers, such as serum GPR120, IL-10, insulin, adiponectin, luteinizing hormone/follicle-stimulating hormone (LH: FSH), testosterone, and anthropometric parameters. Student's t-test (p-value) was applied for significance and Pearson's correlation (r-value) for finding the association between parameters as a part of statistical analysis.

**Results:** Elevated serum LH: FSH, testosterone, insulin, HOMA-IR, and significantly decreased levels of GPR120, IL-10, and adiponectin were reported in PCOS subjects as compared to the non-PCOS group. GPR120 showed a strong positive correlation with adiponectin (r=0.925), IL-10 (r=0.681) and a negative correlation with body mass index (r=−0.325), waist-to-hip ratio (r=−0.516), testosterone (r=−0.539), Insulin (r=−0.085), and HOMA-IR (r=−0.087) in women with PCOS disorder.

**Conclusion:** Lower levels of GPR120, and its strong correlation with HOMA-IR and inflammatory markers, suggest its key role in the pathophysiology of PCOS. GPR120 may serve as a novel therapeutic approach for alleviating metabolic and inflammatory disturbances in PCOS.

**Keywords:** G-protein coupled receptor-120, Interleukin-10, Inflammation, Insulin resistance, Polycystic ovary syndrome.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i6.54774. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

## INTRODUCTION

Polycystic ovary syndrome (PCOS), is an endocrine disorder with reproductive dysfunction affecting reproductive women with a worldwide prevalence of 8–15%. Hyperandrogenism, polycystic ovaries, and ovulatory dysfunction are the characteristic features of PCOS [1]. Apart from the compromised reproduction and hormonal imbalance PCOS is thought to be associated with metabolic disturbances, such as dyslipidemia, increased insulin resistance, and risk of type-2 diabetes mellitus [2].

G-protein coupled receptor-120 (GPR120) also designated as free fatty acid receptor-4, is a surface receptor that is activated by long-chain fatty acids, such as omega-3 fatty acids and is highly active in adipocytes [3]. Activation of GPR120 indicates strong anti-inflammatory effects and insulin sensitization by suppressing macrophage activation, reducing pro-inflammatory cytokine production, reducing inflammation, increasing insulin signaling in adipocytes, and ultimately restoring metabolic equilibrium [4]. Effects of GPR120 are widely investigated in obesity and type-2 diabetes mellitus [5], but its role in PCOS pathogenesis remains in the grey area. Chronic and low-grade inflammation has recently been recognized as a crucial element in the pathogenesis of PCOS in terms of both metabolic and reproductive disturbances [6]. Interleukin-10 (IL-10) is a pivotal anti-inflammatory cytokine involved in the inflammatory response associated with PCOS and IL-10 levels are found to be decreased in obese PCOS patients, indicating its key role in the pathogenesis and progression of disease [7].

It is hypothesized that GPR120 levels may be disrupted in PCOS women and identification of underlying mechanisms revolving around insulin resistance and inflammation through modulation of IL-10 is crucial for a better prognosis of disorder [8]. In this study, we investigated levels of serum GPR120 in women with PCOS and without PCOS and its correlation with insulin resistance and IL-10. It will provide novel insights into the role of GPR120 in the pathophysiology of PCOS and redefine the therapeutic landscape for insulin resistance and inflammation in PCOS, shedding light on a novel axis for intervention in this complex disorder.

## METHODS

This cross-sectional study was conducted on 248 adult women aged from 18 to 35 years to evaluate the association between serum GPR120, serum IL-10, serum adiponectin testosterone, luteinizing hormone/follicle-stimulating hormone (LH: FSH) ratio, and homeostasis model assessment of insulin resistance (HOMA-IR) at the tertiary care hospital of the South Gujarat district between March 2023 and December 2024, A convenience sampling technique was used for the selection of cases based on existing hospital records from previous years. Ethical Clearance was obtained from of Institutional Ethics Committee Biomedical and Health Research (EC/NEW/INST/2021/2173).

### Inclusion criteria

Patients with PCOS were selected as cases (PCOS group) based on Rotterdam diagnostic criteria [9], which require meeting at least two

out of three conditions: Ovulatory dysfunction (irregular or absent menstrual cycles), hyperandrogenism (clinical signs, such as hirsutism or elevated androgen levels), and polycystic ovaries (12 or more follicles per ovary or increased ovarian volume detected via ultrasound), and age-matched healthy individuals without any known metabolic, hormonal or psychiatric disorders were included in the control (non-PCOS group) group.

**Exclusion criteria**

Subjects who had previously used or were currently using medications such as oral contraceptive pills, ovulation induction agents, estrogenic or anti-androgenic drugs, antidiabetic drugs, such as metformin, glucocorticoids, anti-obesity drugs, or had a history of hormone therapy, insulin sensitizers, and Vitamin-D or calcium supplements within the past 6 months were excluded. In addition, diagnosed cases of chronic illnesses, such as cardiovascular disease, hyperprolactinemia, diabetes mellitus, thyroid disorders or psychiatric disorders, and recent history of pregnancy or lactation within the past 6 months were also excluded from the study.

**Clinical assessments**

After being informed about the purpose and procedure of the study, voluntary written informed consent and detailed medical history along with anthropometric data, including age, weight, height, waist and hip circumference were recorded. Fasting blood samples were collected after 10–12 h of overnight fasting, for biochemical analyses on the next day after menstruation ends. Blood samples were processed to obtain serum for the quantification of serum IL-10, serum adiponectin, serum GPR 120, serum insulin, serum LH, serum FSH, and serum testosterone levels using enzyme-linked immunosorbent assay (ELISA) kits.

**Statistical analysis**

Body mass index (BMI), Waist-to-hip ratio (WHR), LH: FSH ratio, and HOMA-IR were calculated. Continuous variables were denoted as mean with standard deviation (Mean±SD). Differences between study groups were assessed using a student's t-test, with a $p<0.05$ deemed statistically significant. Correlations between parameters were evaluated using Pearson's correlation coefficient as R-value. Interpretation was done according to r-values as 0.00–0.19 (very weak correlation), 0.20–0.39 (weak correlation), 0.40–0.59 (moderate correlation), 0.60–0.79 (strong correlation) and 0.80–1.00 (very strong correlation). Data were analyzed using IBM Statistical Packages for the Social Sciences 25.0 statistic software.

## RESULTS

This cross-sectional study included 248 adult females, comprising 124 patients diagnosed with PCOS based on Rotterdam criteria and age-matched 124 healthy controls.

Table 1 shows that PCOS subjects have significant differences in weight, BMI, waist and hip circumference, and WHR when compared to healthy non-PCOS controls. Age and height were not statistically significant between groups, which fulfilled the inclusion criterion.

Cohen's d-test was applied to measure the effect size between two groups to quantify how different the two means are in terms of SD units and waist circumference, WHR, BMI, hip circumference, and weight showed very large effect size based on the value of d 4.140, 3.354, 2.725, 1.834 and 1.293, respectively. Whereas age and height showed smaller effect sizes (0.0 and 0.09).

Table 2 depicts that, women with PCOS, have significant hormonal differences in comparison to healthy controls. Increased levels of LH, testosterone, an elevated LH: FSH ratio, higher serum insulin along with increased insulin resistance, decreased levels of serum FSH, adiponectin, GPR120, and IL-10 are seen with $p<0.01$ indicating statistically significant differences among the PCOS and non-PCOS.

Cohen's d-test showed a very large effect size for GPR120, adiponectin, testosterone, insulin, IL-10, HOMA-IR, FSH, LH: FSH, and LH in descending order with values of d 3.749, 3.718, 3.019, 2.683, 2.584, 2.381, 1.646, 1.520, and 1.458, respectively.

GPR120 correlation analysis in Table 3 reveals that the PCOS group showed statistically significant negative correlations with BMI, WHR, and serum testosterone suggesting metabolic disturbances, strong positive correlations with serum IL-10 and adiponectin indicating pivotal roles of inflammation and insulin sensitivity, and Serum insulin and HOMA-IR showed weak but significant negative correlations in PCOS subjects. In contrast, no significant associations among the measured parameters in the non-PCOS group.

## DISCUSSION

PCOS is a multifaceted complex endocrine disorder characterized by not only reproductive abnormalities but also metabolic disturbances, such

**Table 1: Age and anthropometric measures of the participants**

| Parameters | Non-PCOS (n=124) | PCOS (n=124) | p-value |
|---|---|---|---|
| Age (years) | 27.11±4.75 | 27.50±3.85 | 0.288 |
| Height (m) | 1.62±0.03 | 1.62±0.05 | 0.481 |
| Weight (kg) | 63.39±4.73 | 69.84±5.23 | <0.01** |
| BMI (kg/m$^2$) | 24.07±0.88 | 26.7±1.05 | <0.01** |
| Waist circumference (cm) | 68.88±2.98 | 89.23±6.28 | <0.01** |
| Hip circumference (cm) | 91.40±3.48 | 99.27±4.97 | <0.01** |
| Waist-hip ratio | 0.75±0.02 | 0.09±0.06 | <0.01** |

PCOS: Polycystic ovary syndrome, BMI: Body mass index. Values are presented as mean±SD with confidence intervals of 95%. *p<0.05, **p<0.01 indicate statistical significance

**Table 2: Comparison of laboratory parameters among the non-PCOS and PCOS groups**

| Parameters | Non-PCOS (n=124) | PCOS (n=124) | p-value |
|---|---|---|---|
| Serum LH (mIU/mL) | 9.08±3.41 | 15.63±5.36 | <0.01** |
| Serum FSH (mIU/mL) | 6.03±1.95 | 3.05±1.66 | <0.01** |
| Serum Testosterone (ng/mL) | 17.56±4.68 | 71.60±24.88 | <0.01** |
| Serum GPR 120 (ng/mL) | 25.35±5.06 | 8.64±3.76 | <0.01** |
| Serum IL-10 (pg/mL) | 19.98±3.57 | 10.21±3.98 | <0.01** |
| Serum adiponectin (µg/mL) | 12.20±2.45 | 4.39±1.68 | <0.01** |
| Serum insulin (µIU/mL) | 6.86±1.81 | 39.51±17.11 | <0.01** |
| LH: FSH ratio | 1.54±0.35 | 7.33±5.37 | <0.01** |
| HOMA-IR | 1.55±0.38 | 9.07±4.45 | <0.01** |

PCOS: Polycystic ovary syndrome, LH/FSH: Luteinizing hormone/Follicle-stimulating hormone, GPR120: G-protein coupled receptor 120, IL-10: Interleukin-10, HOMA-IR: Homeostasis model assessment of insulin resistance. Values are presented as mean±SD with confidence intervals of 95%. *p<0.05, **p<0.01 indicate statistical significance

**Table 3: Correlation of GPR120 with other parameters**

| Parameters | Non-PCOS | | PCOS | |
|---|---|---|---|---|
| | R† | p-value | R† | p-value |
| BMI | 0.026 | 0.776 | −0.325 | <0.01** |
| WHR | −0.042 | 0.640 | −0.516 | <0.01** |
| Serum testosterone | 0.016 | 0.862 | −0.539 | <0.01** |
| LH: FSH ratio | 0.008 | 0.932 | −0.067 | <0.01** |
| Serum IL-10 | 0.075 | 0.408 | 0.681 | <0.01** |
| Serum adiponectin | −0.058 | 0.522 | 0.925 | <0.01** |
| Serum insulin | 0.021 | 0.814 | −0.085 | <0.01** |
| HOMA-IR | 0.010 | 0.915 | −0.087 | <0.01** |

GPR120: G-protein coupled receptor 120, PCOS: Polycystic ovary syndrome, BMI: Body mass index, WHR: Waist-to-hip ratio, LH/FSH: Luteinizing hormone/Follicle-stimulating hormone, IL-10: Interleukin-10, HOMA-IR: Homeostasis model assessment of insulin resistance.†R-values represent correlation coefficients, where R>0 indicates a positive correlation and R<0 indicates a negative correlation; *p<0.05, **p<0.01 indicate statistical significance

as insulin resistance, chronic low-grade inflammation, and dyslipidemia, hence metformin is commonly prescribed in PCOS subjects due to its effectiveness in managing conditions that share similarities with type 2 diabetes mellitus [10]. The present study explored the role of GPR120 and found significantly decreased levels in PCOS subjects compared to age-matched non-PCOS controls. A noticeable decrease was also recorded for serum IL-10 and adiponectin, whereas increased levels of insulin, testosterone, and HOMA-IR were seen in PCOS patients. This indicated the hypothesis that impaired GPR120 signaling can play a pivotal role in the inflammatory and metabolic dysregulations in PCOS.

GPR120 being a lipid-sensitive receptor is activated by long-chain fatty acids specifically omega-3 polyunsaturated fatty acids, such as docosahexaenoic acid and Eicosapentaenoic acid [11] and has been used in the regulation of blood glucose, adipogenesis and inflammation. Liu *et al*. demonstrated that GPR120 activation inhibits macrophage-mediated inflammation and improves systemic insulin sensitivity in obese mice, identifying GPR120 as a potential therapeutic target in metabolic diseases in rats [12]. Ichimura *et al*., reported that GPR120-deficient mice exhibited obesity, glucose intolerance, and systemic inflammation due to impaired M2 macrophage polarization, and macrophage activation and adipose tissue inflammation are central to the pathogenesis of PCOS, reduced GPR120 signaling may exacerbate this immune-metabolic dysfunction [13]. Our study tried to extend these findings to PCOS women using human ELISA kits to make estimation easy and cost-effective compared to frequently used reverse transcriptase-polymerase chain reaction techniques. We reported that decreased GPR120 levels might be indicative of a compromised anti-inflammatory response, contributing to insulin resistance and hyperandrogenism. In a study related to PCOS. Liu *et al*. found that GPR120 agonists improved ovarian function and decreased insulin resistance was observed in the PCOS rat model [14]. Targeting GPR120 might be an effective method for the suppression of GPR120, regulation of ovarian function, and lowering of lipid accumulation in the liver as these all are mainly regulated by GPR120.

Chugh *et al*. and Shamsi *et al*. stated that the pathogenesis of PCOS is known to be associated with chronic low-grade inflammation; IL-10 has an anti-inflammatory and immune-suppressive effect. Studies showed that women with PCOS had considerably lowered serum levels of IL-10, especially in patients with obesity and insulin resistance [15,16]. The strong positive correlation between GPR120 and IL-10 observed in our PCOS group reinforces the anti-inflammatory role of GPR120. IL-10 is a critical cytokine that suppresses pro-inflammatory mediators, such as tumor necrosis factor-alpha and IL-6 [17]. Our data are in line with these reports, suggesting that diminished GPR120 levels may underlie the reduced IL-10 production, fostering a pro-inflammatory milieu that worsens insulin resistance and ovarian dysfunction.

Adiponectin, another adipokine with anti-inflammatory properties, depicted a very strong positive correlation with GPR120. By activating adenosine monophosphate-activated protein kinase (AMPK) and and peroxisome proliferator-activated receptor–alpha (PPAR-$\alpha$) pathways and suppressing gluconeogenesis adiponectin enhances insulin sensitivity [18]. As shown by Patil *et al*. [19] and Shorakae *et al*. [20] decreased adiponectin levels are consistently associated with dyslipidemia, obesity, and insulin resistance in PCOS. Lower levels of adiponectin can also be predictive of cardio-metabolic risk in PCOS subjects as per Groth [21]. Suryapani and Uniyal stated that decreased adiponectin levels, along with reduced adiponectin: Leptinratio, are significantly linked to insulin resistance and reproductive hormone disturbances in PCOS [22]. Our findings supported the hypothesis that in PCOS women, GPR120 may facilitate adiponectin secretion/signaling and its downregulation can impair the insulin sensitization mechanism.

The crucial role of GPR120 in metabolic homeostasis, particularly in PCOS patients, where it shows inverse correlations with Fasting insulin, HOMA-IR, androgens, and anthropometric parameters, such as BMI and WHR. GPR120's activation in adipose tissue enhances insulin receptor signaling and promotes glucose uptake, as demonstrated by Quesada-López *et al*. [23]. Our results also found reduced GPR120 levels that can impair these pathways by enhancing insulin resistance, which is an important part of hyperinsulinemia-induced hyperandrogenism in theca cells leading to major clinical manifestations of PCOS, such as ovulatory dysfunction and hirsutism.

The significant inverse correlation between GPR120 and serum Testosterone is found in PCOS subjects, which is still not widely explored yet, but it is hypothesized that metabolic inflammation contributes to hyperandrogenism. Yan *et al*. showed that lower GPR120 expression in granulosa cells of PCOS patients was associated with impaired PI3K/AKT signaling, which was playing a key role in follicular development and steroidogenesis [24].

A large number of vivisections have supported the therapeutic potential of GPR120 in PCOS. Wang *et al*. observed improvements in glucose tolerance, insulin sensitivity, ovarian morphology, and reduced levels of inflammatory cytokines when PCOS-induced rats were treated with a GPR120 agonist (TUG-891) [8]. These data parallel our pre-clinical findings and suggest that GPR120 activation might reverse some of the key pathological features of PCOS. Interestingly, dietary components such as omega-3 fatty acids are natural ligands for GPR120. Clinical trials done by Khani *et al*. [25] and, Mohammadi *et al*. [26] have shown that omega-3 supplementation in PCOS patients lead to improvement in insulin resistance, testosterone levels, and inflammatory markers. Oner and Muderris [27] and Nadjarzadeh *et al*. [28] in clinical trials suggested that omega-3 supplements can rectify insulin resistance, and female reproductive hormones, such as testosterone, LH/FSH ratio, BMI, and WHR in PCOS women. While these studies did not directly assess GPR120, their outcomes support the hypothesis that omega–3–mediated GPR120 activation could be a mechanism underlying the observed benefits [11]. Alpha-lipoic acid, is a powerful antioxidant, which has shown a promising role in PCOS management by appreciable hormonal benefits and improvements in metabolic issues, particularly done through the GPR120 pathway [29]. Thereby, GPR120 represents a unique intersection point for future therapeutic strategies. Targeted therapies focused on GPR120 activation, through supplementation of omega-3 fatty acid or synthetic agonists, can become a more comprehensive approach for the management of the disorder. These findings have paved the way for receptor-targeted interventions and precision medicine that can go beyond symptom control and address the underlying pathophysiology of PCOS.

Despite these promising findings, our study has limitations that as a cross-sectional analysis, it cannot establish causality. Furthermore, serum GPR120 levels may not fully represent receptor activity at the tissue level. Future research should involve longitudinal and interventional designs, assessing GPR120 expression and signaling in adipose, hepatic, and ovarian tissues, along with trials of GPR120 agonists or omega-3 fatty acid therapy in PCOS populations for validation.

## CONCLUSION

The role of GPR120 in the pathophysiology of PCOS has been accentuated as significantly lower levels of GPR120 along with its strong correlation with inflammatory and metabolic parameters such as IL-10, adiponectin, insulin resistance, and androgen levels are found in PCOS, which highlights it as a potential biomarker and important therapeutic target. Major two components of chronic inflammation and metabolic dysregulation are found to be linked through a single receptor pathway and enhancing GPR120 activity can offer a binary benefit by reducing systemic inflammation and restoring insulin sensitivity.

## AUTHORS' CONTRIBUTION

Neeti Patel: Conceptualization of the study, research design development, statistical analysis of the data, and drafting the manuscript. Ivvala Anand Shaker: Review, editing, and critical revision of the manuscript. Kandarp Patel: Data collection, laboratory sample testing, interpretation of data.

**CONFLICT OF INTEREST**

None.

**FUNDING**

Nil.

**REFERENCES**

1. Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, *et al*. Polycystic ovary syndrome: Etiology, current management, and future therapeutics. J Clin Med. 2023 Feb 11;12(4):1454. doi: 10.3390/jcm12041454, PMID 36835989, PMCID PMC9964744
2. Livadas S, Anagnostis P, Bosdou JK, Bantouna D, Paparodis R. Polycystic ovary syndrome and type 2 diabetes mellitus: A state-of-the-art review. World J Diabetes. 2022 Jan 15;13(1):5-26. doi: 10.4239/wjd.v13.i1.5, PMID 35070056, PMCID PMC8771268
3. Stuttgen GM, Sahoo D. FFAR4: A new player in cardiometabolic disease? Endocrinology. 2021 Aug 1;162(8):bqab111. doi: 10.1210/endocr/bqab111, PMID 34043793, PMCID PMC8218936
4. Paschoal VA, Walenta E, Talukdar S, Pessentheiner AR, Osborn O, Hah N, *et al*. Positive reinforcing mechanisms between GPR120 and PPARγ modulate insulin sensitivity. Cell Metab. 2020 Jun 2;31(6):1173-1188.e5. doi: 10.1016/j.cmet.2020.04.020, PMID 32413335, PMCID PMC7337476
5. Szukiewicz D. Potential therapeutic exploitation of G protein-coupled receptor 120 (GPR120/FFAR4) signaling in obesity-related metabolic disorders. Int J Mol Sci. 2025 Mar 11;26(6):2501. doi: 10.3390/ijms26062501, PMID 40141148, PMCID PMC11941992
6. Rudnicka E, Suchta K, Grymowicz M, Calik-Ksepka A, Smolarczyk K, Duszewska AM, *et al*. Chronic low grade inflammation in pathogenesis of PCOS. Int J Mol Sci. 2021 Apr 6;22(7):3789. doi: 10.3390/ijms22073789, PMID 33917519, PMCID PMC8038770
7. Vasyukova E, Zaikova E, Kalinina O, Gorelova I, Pyanova I, Bogatyreva E, *et al*. Inflammatory and anti-inflammatory parameters in PCOS patients depending on body mass index: A case-control study. Biomedicines. 2023 Oct 14;11(10):2791. doi: 10.3390/biomedicines11102791, PMID 37893164, PMCID PMC10604137
8. Wang J, Huang Z, Cao Z, Luo Y, Liu Y, Cao H, *et al*. Loureirin B reduces insulin resistance and chronic inflammation in a rat model of polycystic ovary syndrome by upregulating GPR120 and activating the LKB1/AMPK signaling pathway. Int J Mol Sci. 2024 Oct 17;25(20):11146. doi: 10.3390/ijms252011146, PMID 39456928, PMCID PMC11508921
9. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004 Jan;19(1):41-7. doi: 10.1093/humrep/deh098, PMID 14688154
10. Sudjaroen Y, Thongkao K, Thongmuang P. A physiochemical study on drug delivery of metformin HCl-loaded CS-PLGA nanoparticles. Int J Appl Pharm. 2023;15(1):66-71. doi: 10.22159/ijap.2023v15i1.45842
11. Oh DY, Talukdar S, Bae EJ, Imamura T, Morinaga H, Fan W, *et al*. GPR120 is an omega-3 fatty acid receptor mediating potent anti-inflammatory and insulin-sensitizing effects. Cell. 2010 Sep 3;142(5):687-98. doi: 10.1016/j.cell.2010.07.041, PMID 20813258, PMCID PMC2956412
12. Liu Y, Guo M, Li Y, Wang T, Ren Y, Wang R, *et al.* α-linolenic acid regulates macrophages via GPR120-NLRP3 inflammasome pathway to ameliorate diabetic rats. J Funct Foods. 2022 Dec 1;99:105348. doi: 10.1016/j.jff.2022.105348
13. Ichimura A, Hirasawa A, Poulain-Godefroy O, Bonnefond A, Hara T, Yengo L, *et al*. Dysfunction of lipid sensor GPR120 leads to obesity in both mouse and human. Nature. 2012 Feb 19;483(7389):350-4. doi: 10.1038/nature10798, PMID 22343897
14. Liu Y, Ding J, Tan X, Shen Y, Xu L, Li T, *et al*. GPR120 agonist ameliorated insulin resistance and improved ovarian function. Zygote. 2022 Jun;30(3):380-5. doi: 10.1017/S0967199421000873, PMID 34879886
15. Chugh RM, Park HS, El Andaloussi A, Elsharoud A, Esfandyari S, Ulin M, *et al*. Mesenchymal stem cell therapy ameliorates metabolic dysfunction and restores fertility in a PCOS mouse model through interleukin-10. Stem Cell Res Ther. 2021 Jul 7;12(1):388. doi: 10.1186/s13287-021-02472-w, PMID 34233746, PMCID PMC8261924
16. Shamsi M, Ghazavi A, Saeedifar AM, Mosayebi G, Pour SK, Ganji A. The immune system's role in PCOS. Mol Biol Rep. 2022 Nov;49(11):10689-702. doi: 10.1007/s11033-022-07695-5, PMID 35752698
17. Steen EH, Wang X, Balaji S, Butte MJ, Bollyky PL, Keswani SG. The role of the anti-inflammatory cytokine interleukin-10 in tissue fibrosis. Adv Wound Care (New Rochelle). 2020 Apr 1;9(4):184-98. doi: 10.1089/wound.2019.1032, PMID 32117582, PMCID PMC7047112
18. Li M, Chi X, Wang Y, Setrerrahmane S, Xie W, Xu H. Trends in insulin resistance: Insights into mechanisms and therapeutic strategy. Signal Transduct Target Ther. 2022;7(1):216. doi: 10.1038/s41392-022-01073-0, PMID 35794109
19. Patil S, Veerabhadra Goud GK, Shivashankar RN, Anusuya SK, Ganesh V. Association of adiponectin levels with polycystic ovary syndrome among Indian women. Bioinformation. 2022 Oct 31;18(10):864-9. doi: 10.6026/97320630018864, PMID 37654825, PMCID PMC10465762
20. Shorakae S, Abell SK, Hiam DS, Lambert EA, Eikelis N, Jona E, *et al.* High-molecular-weight adiponectin is inversely associated with sympathetic activity in polycystic ovary syndrome. Fertil Steril. 2018 Mar;109(3):532-9. doi: 10.1016/j.fertnstert.2017.11.020, PMID 29428305
21. Groth SW. Adiponectin and polycystic ovary syndrome. Biol Res Nurs. 2010 Jul;12(1):62-72. doi: 10.1177/1099800410371824, PMID 20498127, PMCID PMC3646519
22. Suryapani A, Uniyal SM. Correlation of leptin and adiponectin levels with metabolic and hormonal profiles in PCOS patients: A comparative study with normal controls. Int J Curr Pharm Res. 2024;16(6):62-5. doi: 10.22159/ijcpr.2024v16i6.6009
23. Quesada-López T, Cereijo R, Turatsinze JV, Planavila A, Cairó M, Gavaldà-Navarro A, *et al*. The lipid sensor GPR120 promotes brown fat activation and FGF21 release from adipocytes. Nat Commun. 2016 Nov 17;7:13479. doi: 10.1038/ncomms13479, PMID: 27853148, PMCID: PMC5118546
24. Yan H, Wang L, Zhang G, Li N, Zhao Y, Liu J, *et al*. Oxidative stress and energy metabolism abnormalities in polycystic ovary syndrome: From mechanisms to therapeutic strategies. Reprod Biol Endocrinol. 2024 Dec 26;22(1):159. doi: 10.1186/s12958-024-01337-0, PMID 39722030, PMCID PMC11670460
25. Khani B, Mardanian F, Fesharaki SJ. Omega-3 supplementation effects on polycystic ovary syndrome symptoms and metabolic syndrome. J Res Med Sci. 2017 May 30;22:64. doi: 10.4103/jrms.JRMS_644_16, PMID 28616051, PMCID PMC5461594
26. Mohammadi E, Rafraf M, Farzadi L, Asghari-Jafarabadi M, Sabour S. Effects of omega-3 fatty acids supplementation on serum adiponectin levels and some metabolic risk factors in women with polycystic ovary syndrome. Asia Pac J Clin Nutr. 2012;21(4):511-8. PMID 23017309
27. Oner G, Muderris II. Efficacy of omega-3 in the treatment of polycystic ovary syndrome. J Obstet Gynaecol. 2013;33(3):289-91. doi: 10.3109/01443615.2012.751365, PMID 23550861
28. Nadjarzadeh A, Dehghani-Firouzabadi R, Daneshbodi H, Lotfi MH, Vaziri N, Mozaffari-Khosravi H. Effect of Omega-3 supplementation on visfatin, adiponectin, and anthropometric indices in women with polycystic ovarian syndrome. J Reprod Infertil. 2015;16(4):212-20. PMID 27110520
29. Taha M. Therapeutic use of alpha - lipoic acid supplementation: A review on current use and future prospective. Int J Appl Pharm. 2024;16(6):21-7. doi: 10.22159/ijap.2024v16i6.51319