

New Drug Targets in Polycystic Ovary Syndrome (PCOS): A Pharmacological Review

¹Karishma R Tikariya, ² Ruchika A Gupta

¹ Assistant Professor ² Lecturer

¹ Angel College of Pharmacy, Hadapsar, Pune

² Manoharbai Patel Institute of Pharmacy, D.Pharm, Gondia

ABSTRACT

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine and metabolic disorders affecting women of reproductive age. It is characterized by hyperandrogenism, ovulatory dysfunction, menstrual irregularities, and polycystic ovarian morphology. In addition to reproductive complications, PCOS is strongly associated with insulin resistance, obesity, type 2 diabetes mellitus, dyslipidemia, and cardiovascular diseases. Conventional pharmacological therapies such as oral contraceptive pills, anti-androgens, and insulin sensitizers mainly provide symptomatic relief and are often associated with adverse effects. Recent advances in molecular biology and pathophysiology have identified several novel drug targets that address the underlying mechanisms of PCOS. This review focuses on emerging pharmacological targets including insulin signaling pathways, androgen biosynthesis, AMP-activated protein kinase, inflammatory mediators, gut microbiota modulation, incretin-based therapies, and novel hormonal targets. Understanding these new targets may provide improved therapeutic strategies with better efficacy and safety profiles.

KEYWORDS

Polycystic Ovary Syndrome, PCOS, New Drug Targets, Insulin Resistance, Hyperandrogenism, Pharmacology

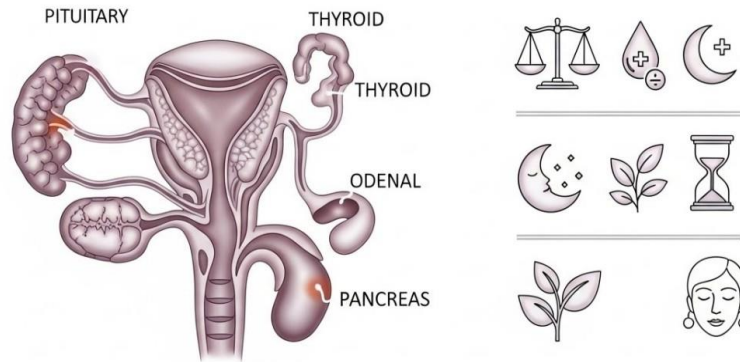
INTRODUCTION

PCOS is one of the most common endocrine disorders in women, yet it is frequently under-treated. Beyond reproductive health, PCOS affects metabolism, mental health, and cardiovascular risk, making comprehensive pharmaceutical care essential.

Polycystic Ovary Syndrome (PCOS) is a heterogeneous endocrine disorder affecting approximately 6–20% of women of reproductive age worldwide. The disorder is diagnosed based on the Rotterdam criteria, which include hyperandrogenism, oligo- or anovulation, and polycystic ovarian morphology on ultrasound. PCOS is a major cause of infertility and is associated with long-term metabolic and psychological complications.

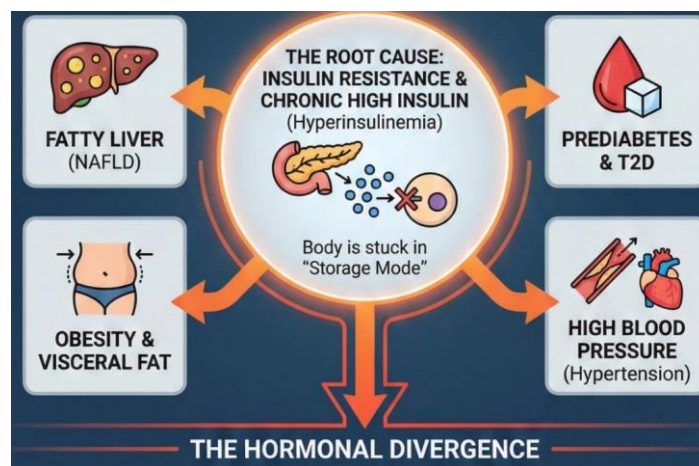
The etiology of PCOS is multifactorial, involving genetic, environmental, hormonal, and lifestyle factors. Insulin resistance and compensatory hyperinsulinemia play a central role in the pathogenesis of PCOS by enhancing androgen production and disrupting normal follicular development. Current pharmacological management includes lifestyle modification, oral contraceptives, metformin, and ovulation-inducing agents. However, these therapies do not address all pathophysiological aspects of PCOS and often fail to provide long-term benefits. Therefore, identification of novel drug targets has become an important area of research in PCOS management.

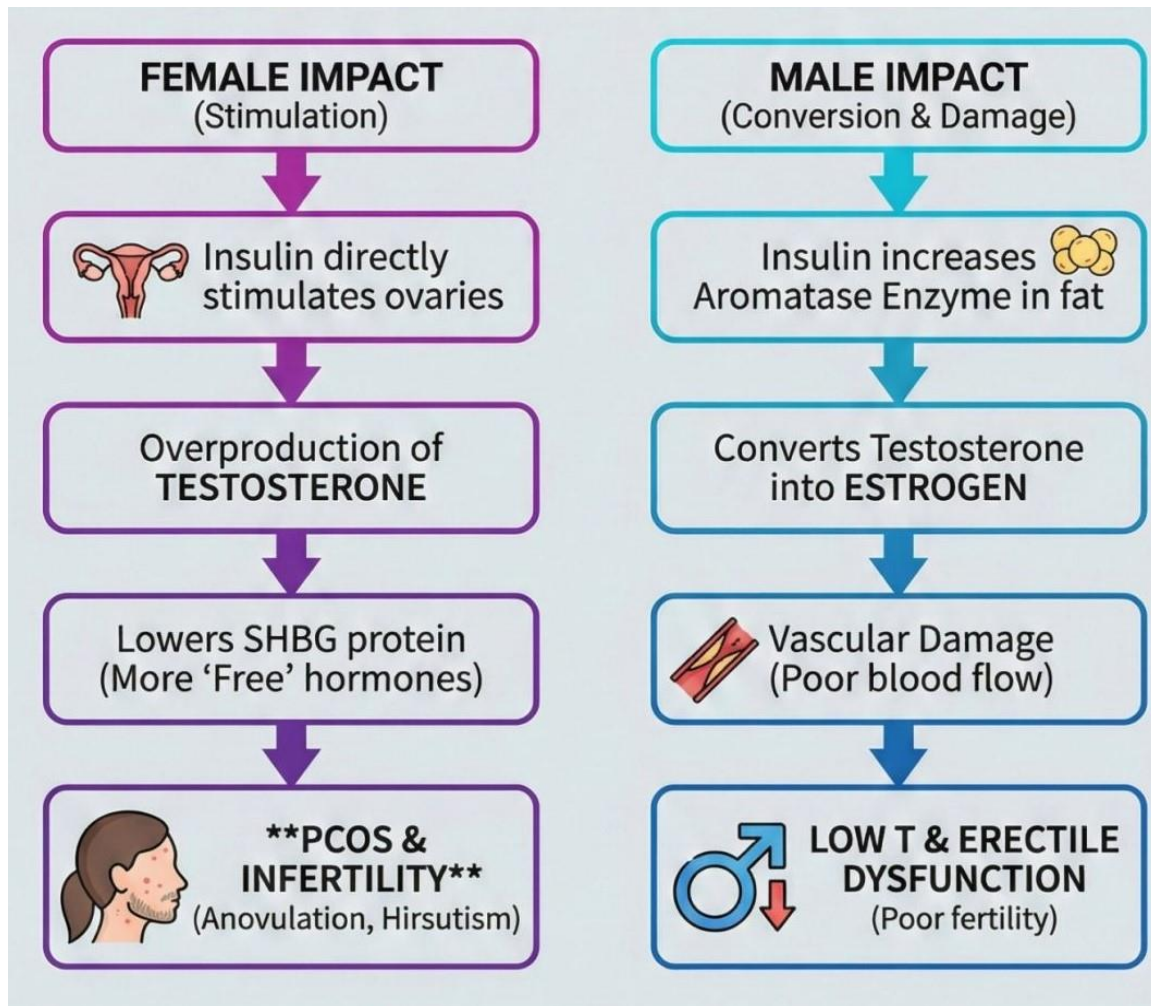
PCOS: MORE THAN A REPRODUCTIVE DISORDER



COMMON SYMPTOMS

- Irregular menstrual cycles: This is often one of the first signs of PCOS. Women may experience fewer than nine periods a year, more than 35 days between periods, frequent spotting, and/or abnormally heavy periods.
- Acne and hirsutism: Excess androgen levels High levels of male hormones may result in physical signs such as excess facial and body hair (hirsutism), severe acne and male-pattern baldness.
- Weight gain
- Anxiety and depression
- Polycystic ovaries: Enlarged ovaries containing Numerous small cysts can be detected via ultrasound.





PATHOPHYSIOLOGY OF PCOS

PCOS involves:

- Insulin resistance
- Hyperandrogenism
- Hormonal imbalance

It is not just a gynecological issue—it is a systemic metabolic disorder.

The pathophysiology of PCOS is complex and involves multiple interconnected mechanisms. Insulin resistance is present in both obese and lean PCOS patients, leading to hyperinsulinemia that stimulates ovarian theca cells to produce excess androgens. Elevated luteinizing hormone (LH) levels further contribute to androgen excess.

Chronic low-grade inflammation is another important factor in PCOS, characterized by increased levels of inflammatory cytokines such as TNF- α and IL-6. These inflammatory mediators worsen insulin resistance and ovarian dysfunction. Additionally, alterations in gut microbiota composition have been linked to metabolic and hormonal disturbances in PCOS. Understanding these mechanisms has led to the identification of several novel pharmacological targets.

LIFESTYLE CHANGE

A healthy lifestyle is a cornerstone of managing PCOS. Regular exercise, a nutritious diet, and weight management can help reduce symptoms and the risk of long-term health issues. In overweight patients, weight loss as little as 5% has been shown to improve symptoms of PCOS

NEW DRUG TARGETS IN PCOS

Insulin Signaling Pathway

Insulin resistance is a key therapeutic target in PCOS. In addition to metformin, newer insulin sensitizers such as myo-inositol and D-chiro-inositol have gained attention. These agents act as insulin second messengers and improve glucose uptake and ovulatory function. GLP-1 receptor agonists such as liraglutide and semaglutide have shown promising results in improving insulin sensitivity, promoting weight loss, and restoring menstrual regularity.

Androgen Biosynthesis Inhibitors

Hyperandrogenism is a hallmark of PCOS. Novel drugs targeting androgen biosynthesis include selective CYP17 inhibitors and newer anti-androgens with fewer side effects. These agents reduce ovarian androgen production and improve clinical features such as hirsutism and acne.

AMP-Activated Protein Kinase (AMPK) Activators

AMPK plays a crucial role in regulating cellular energy balance. Activation of AMPK improves insulin sensitivity, reduces hepatic gluconeogenesis, and enhances fatty acid oxidation. While metformin is a known AMPK activator, newer agents targeting this pathway are under investigation for improved metabolic control in PCOS.

Inflammatory Mediators

Targeting inflammation represents a novel therapeutic approach in PCOS. Drugs that inhibit pro-inflammatory cytokines such as TNF- α and IL-6 may improve insulin sensitivity and ovarian function. Anti-inflammatory agents and antioxidants are being explored as adjunct therapies.

Gut Microbiota Modulation

Alterations in gut microbiota have been implicated in PCOS pathogenesis. Probiotics, prebiotics, and synbiotics have shown beneficial effects on metabolic and hormonal parameters by restoring gut microbial balance. Modulation of the gut-ovary axis represents a promising therapeutic strategy.

Incretin-Based Therapies

Incretin-based therapies such as GLP-1 receptor agonists and dual GLP-1/GIP agonists are emerging as effective treatments for obese PCOS patients. These agents improve glycemic control, promote weight loss, and reduce androgen levels.

ADVANTAGES OF TARGET-BASED THERAPY

Target-based therapies focus on correcting underlying pathophysiological mechanisms rather than providing symptomatic relief. These approaches offer improved efficacy, reduced adverse effects, better fertility outcomes, and enhanced metabolic control.

FUTURE PERSPECTIVES

Future management of PCOS is expected to involve personalized medicine approaches based on genetic and metabolic profiling. Combination therapies targeting multiple pathways may offer superior outcomes. Further clinical trials are required to establish the long-term safety and efficacy of these novel agents.

CONCLUSION

The identification of new drug targets in PCOS has expanded therapeutic options beyond conventional treatments. Targeting insulin resistance, androgen excess, inflammation, and gut microbiota offers promising strategies for comprehensive management of PCOS. Continued research is essential to translate these advances into effective clinical therapies.

REFERENCES

1. Azziz R et al. Polycystic ovary syndrome. *Nat Rev Dis Primers*.
2. Diamanti-Kandarakis E et al. Insulin resistance in PCOS. *Endocr Rev*.
3. Teede HJ et al. Management of PCOS. *Hum Reprod*.
4. Unluhizarci K et al. Androgen excess disorders. *Endocrine*.
5. Escobar-Morreale HF. PCOS: Definition and diagnosis. *Lancet*.
6. Palomba S et al. Novel pharmacological approaches in PCOS. *Trends Endocrinol Metab*.
7. Moran LJ et al. Obesity and PCOS. *Hum Reprod Update*.
8. Genazzani AD et al. Inositols in PCOS. *Gynecol Endocrinol*.
9. Jensterle M et al. GLP-1 agonists in PCOS. *J Clin Endocrinol Metab*.
10. Tremellen K et al. Gut microbiota and PCOS. *Semin Reprod Med*.
11. Teede HJ et al., *Lancet Diabetes & Endocrinology*, 2018
12. Endocrine Society PCOS Guidelines, 2023