

Exploring the Role of Microbiome Dysregulation in PCOS: Pathophysiology, and Emerging Therapies Toward Targeted and Personalized Treatment

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AIM OR OBJECTIVE

We analyzed the role of gut microbiome dysregulation in PCOS and its impact on metabolic and hormonal dysfunction.

Particular attention was given to key mechanistic pathways, including intestinal permeability, inflammatory activation, and alterations in microbial metabolites. By examining outcomes across studies, we evaluated how effective microbiome-targeted therapies may influence insulin resistance, systemic inflammation, and overall disease progression.

INTRODUCTION

- Polycystic ovarian syndrome (PCOS) is a multifactorial endocrine disorder characterized by reproductive, metabolic, and psychological dysfunction. Key features include hyperandrogenism, insulin resistance, ovulatory dysfunction, menstrual irregularities, and infertility. Chronic low-grade inflammation plays a central role in disease progression and is often exacerbated by obesity.
- Emerging evidence highlights the gut microbiome as an important contributor to PCOS pathophysiology. Disruptions in normal gut microbial composition, or dysbiosis, are associated with increased intestinal permeability, systemic inflammation, and impaired metabolic regulation. These changes contribute to worsening insulin resistance and hormonal imbalance, reinforcing the complex interplay between metabolic and endocrine dysfunction in PCOS.
- Together, these findings suggest that the gut microbiome may serve as a key, modifiable factor in the development and progression of PCOS and represent a potential target for more effective and personalized treatment strategies.

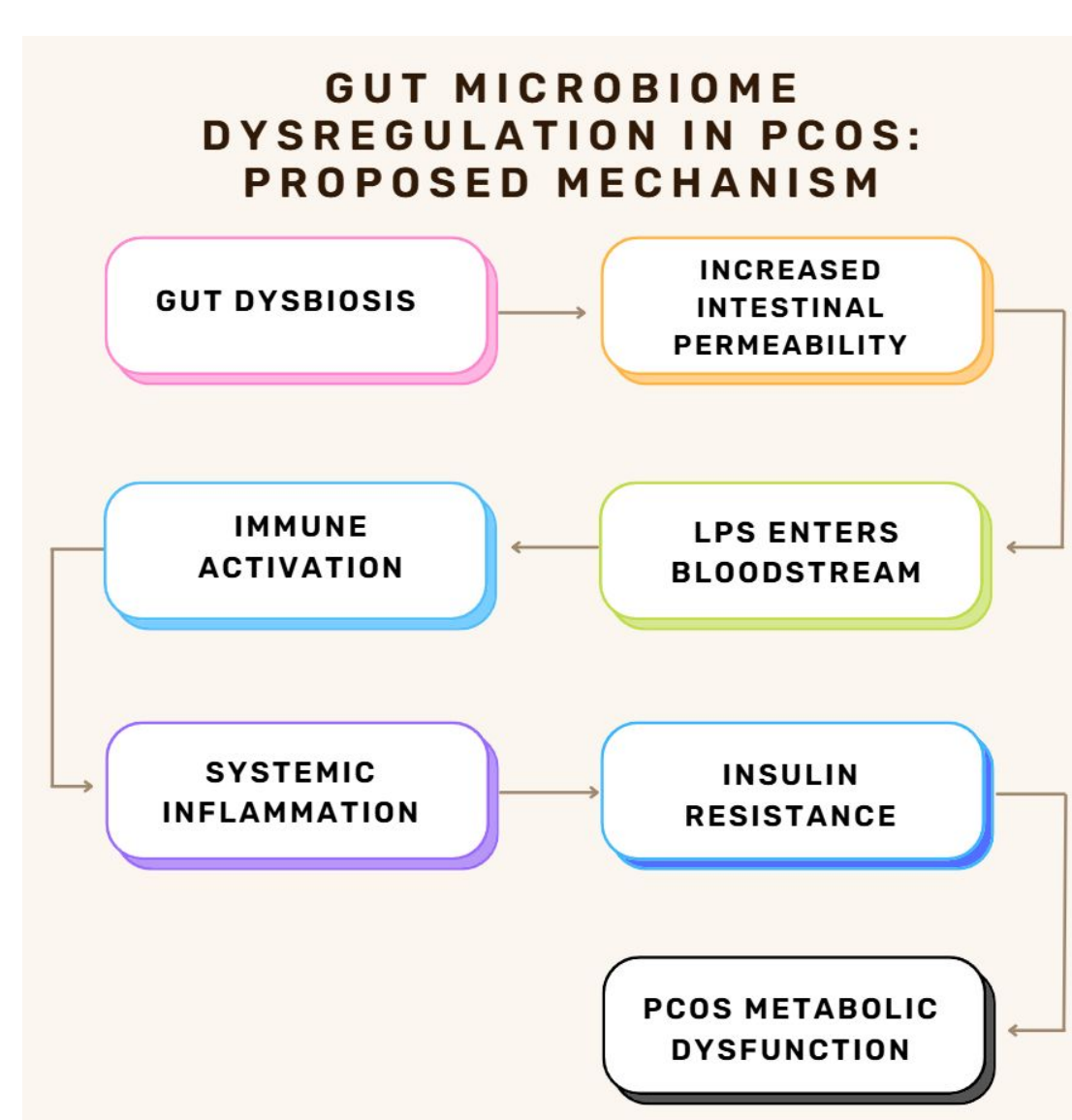


Figure 1. Proposed mechanism of gut dysbiosis in PCOS. Microbial imbalance increases intestinal permeability and LPS translocation, triggering inflammation, insulin resistance, and metabolic dysfunction (1,2)

METHOD

We conducted a narrative review to examine the role of gut microbiome dysregulation in PCOS pathophysiology and management. A structured approach was used to identify and synthesize relevant studies focusing on key mechanisms and therapeutic implications.

Inclusion Criteria:

- Studies evaluating the relationship between gut microbiome dysregulation and PCOS-related metabolic, hormonal, or inflammatory changes.
- Clinical and experimental studies addressing mechanisms or therapeutic interventions targeting the microbiome.

Exclusion Criteria:

- Studies not directly related to PCOS or lacking relevance to microbiome-associated mechanisms.
- Non-peer-reviewed sources, duplicate publications, or studies without clear outcomes.

Review Approach:

A structured narrative review methodology was applied to find studies with an emphasis on evaluating the potential impact of microbiome-targeted therapies on disease progression and management.

EFFECTS OF MICROBIOME TARGETED INTERVENTIONS	
PARAMETER	EFFECT
FASTING GLUCOSE	Decreased
INSULIN SENSITIVITY	Increased
Lipids	Decreased
SHBG	Increased

Figure 2. Effects of microbiome-targeted interventions, including probiotics and synbiotics, on metabolic and hormonal parameters in PCOS. These interventions are associated with decreased fasting glucose and lipid levels, improved insulin sensitivity, and modest increases in sex hormone-binding globulin (SHBG) (3).

RESULTS

- Current evidence demonstrates a strong association between gut microbiome dysregulation and PCOS pathophysiology, particularly in relation to insulin resistance, systemic inflammation, and hormonal imbalance (1,2).
- Studies show that dysbiosis increases intestinal permeability and inflammatory signaling, while reduced short-chain fatty acid-producing bacteria further worsen metabolic dysfunction (1,2).
- Microbiome-targeted interventions, including probiotics and synbiotics, have been shown to improve fasting glucose, insulin sensitivity, and lipid profiles, with modest improvements in hormonal markers such as SHBG (3).
- Emerging therapies such as GLP-1 receptor agonists and SGLT2 inhibitors demonstrate benefits in improving metabolic outcomes and modulating gut microbiota (4,5). Combination therapies (e.g., metformin with probiotics) show enhanced effects compared to monotherapy (6).
- Preclinical studies support additional therapeutic potential through fecal microbiota transplantation and microbial metabolites, while lifestyle interventions (diet and exercise) improve metabolic and inflammatory markers (7,8).

ANALYSIS

Findings demonstrate a clear relationship between gut microbiome dysregulation and the metabolic and hormonal abnormalities observed in PCOS. Increased intestinal permeability and altered microbial metabolite production are associated with systemic inflammation and insulin resistance, highlighting the link between gut health and endocrine function. Clinical studies show that microbiome-targeted interventions can improve metabolic parameters such as insulin sensitivity and lipid profiles, although responses vary across populations. Lifestyle modifications, including stress management, diet and exercise, help modulate metabolic and microbiome dysfunction to improve clinical outcomes. Overall, these findings demonstrate the complex, multifactorial nature of PCOS and support the microbiome as a clinically relevant and modifiable factor in disease progression and therapeutic response.

Conclusion

- Gut microbiome dysregulation plays a significant role in the pathophysiology of PCOS by contributing to inflammation, insulin resistance, and hormonal imbalance. Current treatment strategies primarily address symptoms rather than underlying causes.
- Targeting the gut microbiome represents a promising avenue for more effective and individualized management. However, further large-scale, longitudinal clinical studies are needed to better define causal relationships, optimize therapeutic approaches, and establish standardized, clinically applicable interventions.
- Future research should focus on integrating microbiome-targeted therapies with existing lifestyle and pharmacologic treatments to develop personalized, multi-modal strategies that improve both metabolic and reproductive outcomes in patients with PCOS.

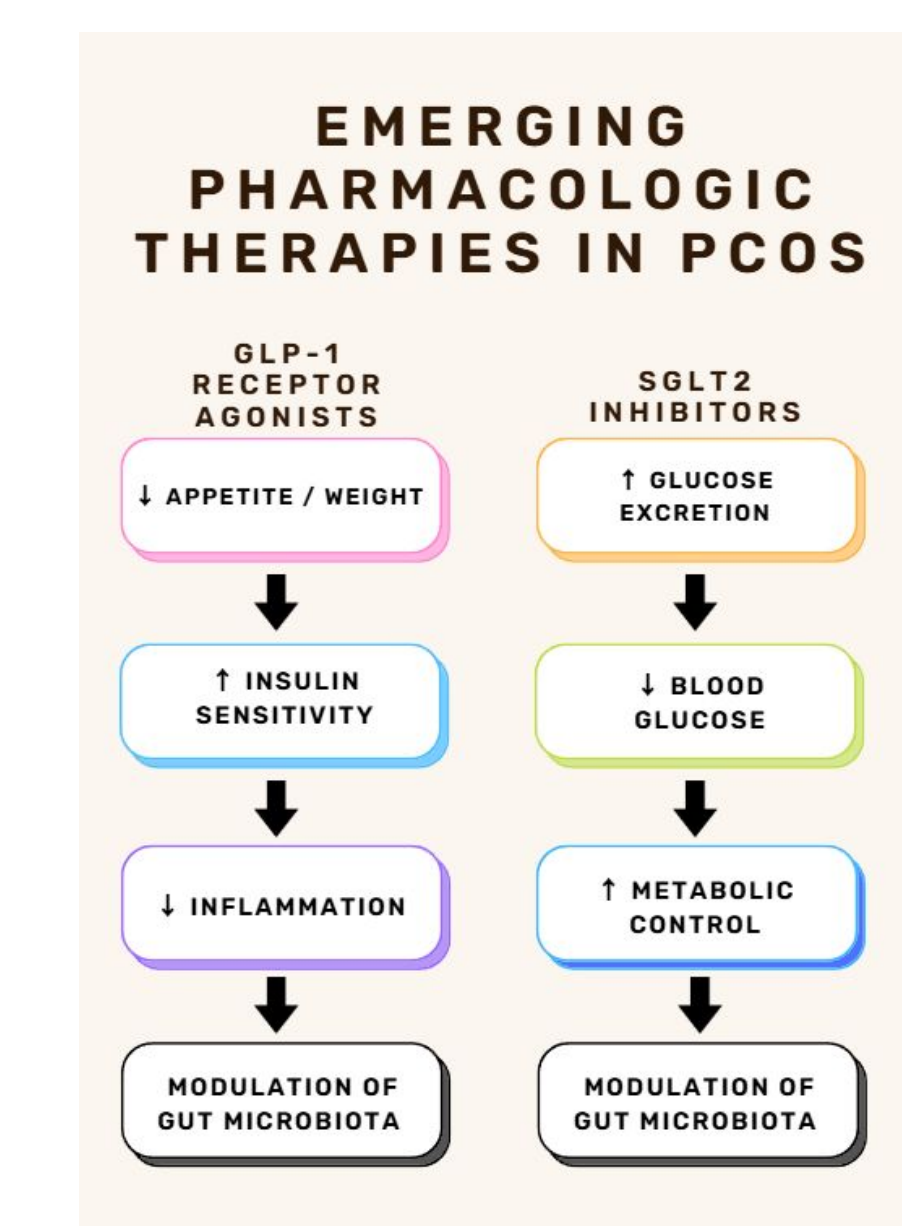


Figure 3. Emerging pharmacologic therapies in PCOS. GLP-1 receptor agonists and SGLT2 inhibitors improve metabolic outcomes through distinct mechanisms, including effects on appetite, glucose regulation, and inflammation, with downstream modulation of the gut microbiome (4,5).

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