RCMOS - Multidisciplinary Scientific Journal of Knowledge.
ISSN: 2675-9128. São Paulo-SP.

Year V, v.1 2025. | submission: October 16, 2025 | accepted: October 18, 2025 | publication: October 20, 2025

Potential Application of Tirzepatide in the Management of Polycystic Ovary Syndrome: A Narrative Review

Potential Application of Tirzepatide in the Management of Polycystic Ovary Syndrome: A Narrative Review

Larissa Assumpção Gimenes de Souza[1], Allan Douglas Azevedo Brim[2], Augusto Cesar Carvalho da Silva Filho[3], Mayra da Silva Freireÿ, Renato Assumpção Gimenes de Souzaÿ, Mauricio Cupello Peixotoÿ

[1]Student at the University of Vassouras.
2 Student at the University of Vassouras.
3 Student at the University of Vassouras.
4 Student at the University of Vassouras.
5 Student at the University of Vassouras.
6 Professor at the University of Vassouras. Supervising professor.

Summary

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, characterized by hormonal dysfunction, insulin resistance, and an increased risk of obesity, type 2 diabetes, and cardiovascular disease. Tirzepatide, a dual GLP-1 and GIP receptor agonist, has demonstrated significant efficacy in glycemic control in patients with type 2 diabetes (FRIAS ET AL., 2021) and induces weight reductions of over 20% in obese patients (JASTREBOFF ET AL., 2022), suggesting its therapeutic potential also in women with PCOS. This work reviews the current knowledge on the use of tirzepatide in this context, addressing its mechanisms of action, expected metabolic effects, limitations, and evidence gaps. It is concluded that, although promising, tirzepatide lacks specific clinical studies in PCOS, and controlled longitudinal trials are necessary to confirm its efficacy and safety in this population (ANALA ET AL., 2023; CHÁVEZ, 2023).

Keywords: Polycystic Ovary Syndrome; Tirzepatide; GLP-1; GIP; obesity; insulin resistance.

Abstract

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, characterized by hormonal dysfunction, insulin resistance, and an increased risk of obesity, type 2 diabetes, and cardiovascular disease. Tirzepatide, a dual GLP-1 and GIP receptor agonist, has demonstrated significant efficacy in glycemic control in patients with type 2 diabetes (FRIAS ET AL., 2021) and induces weight reductions of over 20% in obese patients (JASTREBOFF ET AL., 2022), suggesting its therapeutic potential also in women with PCOS.

This paper reviews the current knowledge on the use of tirzepatide in this context, addressing its mechanisms of action, expected metabolic effects, limitations, and evidence gaps. It is concluded that, although promising, tirzepatide lacks specific clinical studies in PCOS, and controlled longitudinal trials are needed to confirm its efficacy and safety in this population (ANALA ET AL., 2023; CHÁVEZ, 2023).

Keywords: Polycystic Ovary Syndrome; Tirzepatide; GLP-1; GIP; obesity; insulin resistance.

RCMOS – Multidisciplinary Scientific Journal of Knowledge.
ISSN: 2675-9128. São Paulo-SP.

1. Introduction

Polycystic ovary syndrome (PCOS) affects a significant number of women of reproductive age, characterized by clinical manifestations such as hyperandrogenism, menstrual irregularities, and ovulatory dysfunction (ASHRAF ET AL., 2019). Furthermore, many patients present with metabolic comorbidities—such as obesity, dyslipidemia, and insulin resistance—
that increase the risk of cardiovascular and metabolic diseases (TEEDE ET AL., 2010).

Conventional treatments, such as lifestyle modifications and metformin use, have recognized benefits, but are not always sufficient for overall control of the syndrome (CENA ET AL., 2020). In this context, GLP-1 receptor agonists have been explored as therapeutic alternatives for women with PCOS, especially those with obesity and insulin resistance (CHAVDA ET AL., 2022).

Tirzepatide, a dual agonist of GLP-1 and GIP receptors, has shown promising results in patients with type 2 diabetes and obesity, with significant weight reduction and improved metabolic control (FRIAS ET AL., 2021; JASTREBOFF ET AL., 2022). These findings suggest a potential benefit also in women with PCOS, although specific clinical trials for this population are still needed (GRACIA ET AL., 2023).

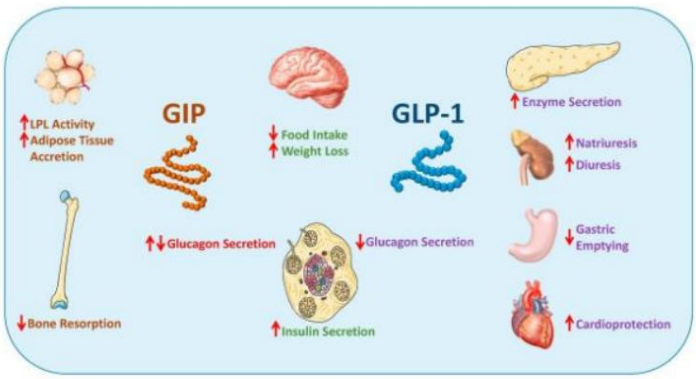


Figure GLP-1 and GIP mechanism of the 1 and GIP analogues

Source: Baggio LL, Drucker DJ. Glucagon-like peptide-1 receptor co-agonists for treating metabolic diseases. Mol Metab. 2021.

2. Methods

An exploratory narrative review was conducted in PubMed and Europe PMC databases, using the descriptors: *"tirzepatide," "polycystic ovary syndrome," "GLP-1, " "GIP agonist, " "obesity,"* and *"insulin resistance."* Original articles, narrative reviews, and systematic reviews published from 2021 to 2024 that addressed the physiological mechanisms, therapeutic applications, or potential metabolic effects of tirzepatide in populations with polycystic ovary syndrome, type 2 diabetes, or obesity were included.

Duplicate studies, non-peer-reviewed articles, publications without full text, isolated case reports, and materials lacking relevant clinical or experimental data were excluded. Article selection was conducted independently, prioritizing recent and scientifically relevant evidence.

3. Review and Discussion of Findings

Tirzepatide acts as a dual agonist of GLP-1 and GIP receptors, promoting synergy in glycemic control, weight reduction and improvement of insulin resistance (CHAVDA ET AL., 2022). High-impact clinical studies demonstrate that tirzepatide provides significant improvement in glycemic control in patients with type 2 diabetes (FRIAS ET AL., 2021) and induces weight reductions of over 20% in some cases of obesity (JASTREBOFF ET AL., 2022).

In women with Polycystic Ovary Syndrome (PCOS), theoretically, the improvement in insulin sensitivity promoted by incretin agonists may reduce androgen levels and favor the restoration of ovulation (CENA; CHIOVATO; NAPPI, 2020). Furthermore, recent reviews highlight that tirzepatide represents a promising therapeutic option for women with PCOS associated with obesity, although there are still no specific clinical trials confirming its efficacy and safety in this group (ANALA ET AL., 2023).

Metabolic benefits appear more evident in patients with PCOS and excess weight, including improved insulin resistance, reduced blood glucose, and improved lipid profiles in comparable metabolic settings (GRACIA ET AL., 2023). However, gastrointestinal adverse effects, such as nausea and abdominal discomfort, are consistently reported and should be monitored during treatment (CHÁVEZ, 2023).

Additionally, the potential of tirzepatide to reduce inflammatory markers and pro-inflammatory adipocytokines suggests beneficial effects on metabolic and cardiovascular function, which is particularly relevant for women with PCOS and obesity (FRIAS ET AL., 2021).

Important gaps remain in the literature, including the lack of long-term data, information on the reproductive impact, and the safety of tirzepatide use during pregnancy.
Therefore, dedicated clinical trials are needed to systematically evaluate the role of the drug in the metabolic and hormonal management of women with PCOS (JASTREBOFF ET AL., 2022).

3.1 Hyperandrogenism

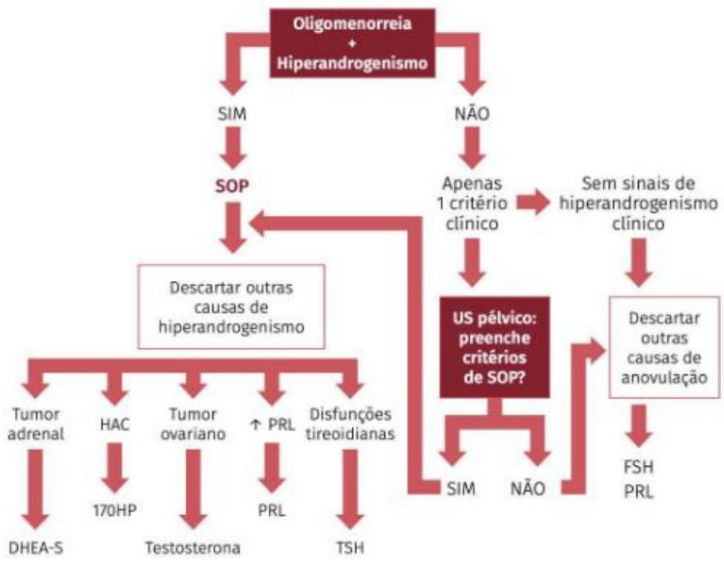
In Polycystic Ovary Syndrome (PCOS), there is an abnormal increase in androgen production by the ovaries, resulting in hyperandrogenism, both clinically and laboratory-wise. Androgens are sex hormones essential for the development of male sexual characteristics and the synthesis of steroids.

also playing relevant physiological roles in women (TEED; DEEKS; MORAN, 2010).

Hyperandrogenism manifests as elevated levels of total or free testosterone, increased ovarian secretion of androstenedione, and, in some cases, increased adrenal production of dehydroepiandrosterone sulfate (DHEAS), indicating both ovarian and adrenal contributions to androgen excess in some women with PCOS (ASHRAF et al., 2019). This excessive production is associated with dysregulation of steroidogenesis, primarily due to reduced activity of the aromatase enzyme in granulosa cells, which converts androgens into estrogens.

Furthermore, the predominance of luteinizing hormone (LH) over follicle-stimulating hormone (FSH) favors the continuous stimulation of theca cells, which begin to produce more androgens. The imbalance between LH and FSH compromises follicular maturation and intensifies the hyperandrogenism picture, worsening clinical manifestations (CENA; CHIOVATO; NAPPI, 2020).

Clinically, androgen excess manifests as acne, hirsutism, and androgenetic alopecia, and may also be associated with weight gain, menstrual irregularities, and the presence of acanthosis nigricans. These factors, combined with the aesthetic and reproductive impact of the syndrome, often contribute to the development of emotional symptoms such as anxiety, depression, and social isolation, which significantly affect patients' quality of life (HIMELEIN; THATCHER, 2006).



HAC: hiperplasia adrenal congênita; PRL: prolactina;
DHEA-S: deidroepiandrosterona sulfatada;
17OHP: 17-alfa-hidroxiprogesterona; TSH: hormônio estimulante da tireoide;
FSH: hormônio folículo-estimulante.

Figure 3: Polycystic Ovary Syndrome diagnostic flowchart.

Source: Polycystic Ovary Syndrome: concept, epidemiology and pathophysiology applied to clinical practice (ROSA E SILVA & DAMÁSIO, 2023).

3.2 Insulin resistance

Insulin resistance is a common finding in Polycystic Ovary Syndrome (PCOS), affecting a significant proportion of patients and playing a central role in the origin of the syndrome's metabolic and reproductive alterations. In many cases, the pancreas maintains normal insulin production, but peripheral tissues—especially muscle and adipose tissue—have a reduced response to its action, requiring higher concentrations of the hormone to maintain adequate blood glucose levels (TEEDE; DEEKS; MORAN, 2010).

This compensatory hyperinsulinemia stimulates ovarian androgen production and contributes to ovulatory dysfunction, in addition to favoring the accumulation of body fat, especially in the abdominal region (CHAVDA ET AL., 2022). Excess circulating insulin also influences steroidogenesis and reduces hepatic synthesis of sex hormone-binding globulin (SHBG), intensifying the hyperandrogenism characteristic of the syndrome.

Over time, insulin resistance can progress to glucose intolerance and type 2 diabetes, conditions observed more frequently in women with PCOS when compared to the general population (KNOCHENHAUER ET AL., 1998). In this context, dual GLP-1 and GIP agonists, such as tirzepatide, have shown potential to partially reverse insulin resistance by promoting increased peripheral glucose uptake and reduced compensatory insulin secretion (FRIAS ET AL., 2021).

Recent clinical studies also indicate that tirzepatide induces significant weight loss in obese individuals, which indirectly contributes to improved insulin sensitivity and reduced hyperandrogenism in women with PCOS (JASTREBOFF ET AL., 2022). These combined effects suggest that pharmacological intervention with tirzepatide may act in an integrated manner on the metabolic and reproductive disorders of PCOS, representing a promising approach, especially in patients with obesity-associated insulin resistance.

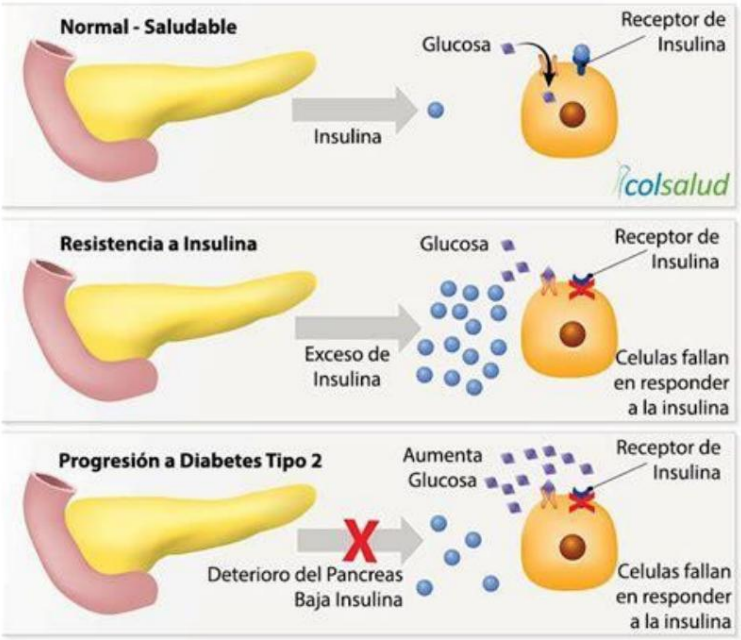


Figure 2: Resistance Insulin
Source: Colsalud – "Insulin Resistance | Learn how to change your metabolism"

3.3 Obesity

Obesity is a global public health problem and has a direct impact on Polycystic Ovary Syndrome (PCOS) (TEEDE ET AL., 2010). Women with PCOS often experience significant weight gain, which not only worsens insulin resistance but also interferes with reproductive function (ANALA ET AL., 2023). Obesity contributes to hyperinsulinemia, which can intensify ovarian androgen production, being a central factor in the hyperandrogenism observed in these patients (ASHRAF ET AL., 2019).

The increase in adipose tissue is also associated with greater aromatization of androgens into estrogens, increasing circulating levels of this hormone (TEEDE ET AL., 2010). This excess estrogen participates in a negative feedback loop on gonadotropin secretion, impairing ovulation and contributing to infertility in women with PCOS (HIMELEIN & THATCHER, 2006). Thus, obesity perpetuates a vicious cycle that amplifies both the metabolic and reproductive disorders of the syndrome (CENA ET AL., 2020).

Furthermore, the interaction between insulin resistance and hyperandrogenism can potentiate the effects of androgen excess. This is reflected in increased androgen receptor expression, worsening clinical manifestations such as hirsutism, acne, seborrhea, and androgenetic alopecia, significantly impacting patients' quality of life (TEEDE ET AL., 2010).

RCMOS – Multidisciplinary Scientific Journal of Knowledge.
ISSN: 2675-9128. São Paulo-SP.

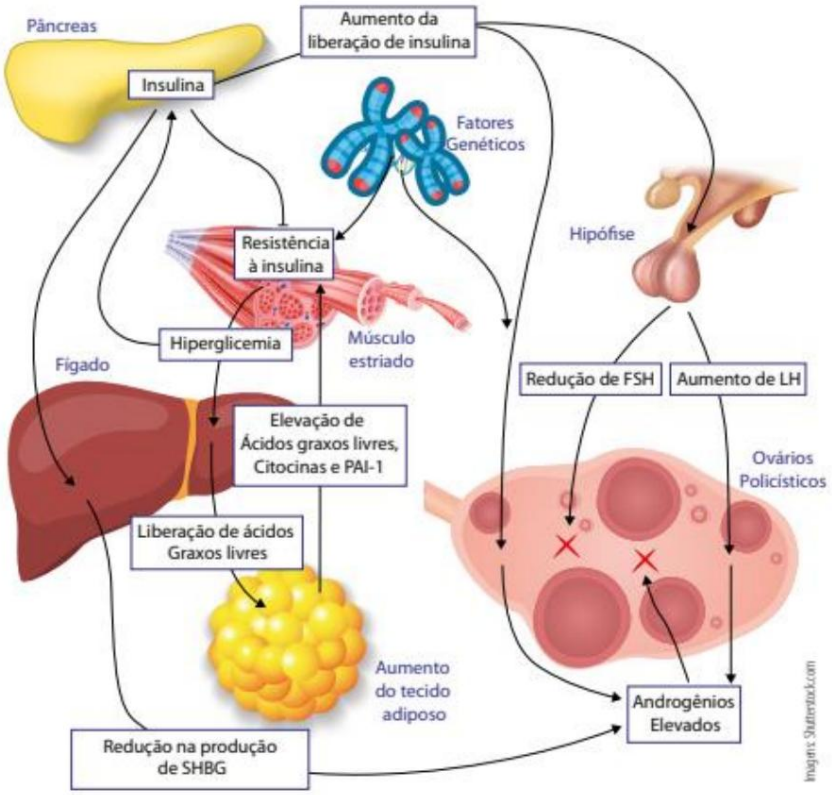


Figure 3: Pathophysiology from the Syndrome of the Ovaries Polycystic
Source: FEBRASGO, 2023

3.3 Therapeutic Approach to PCOS

The initial management of Polycystic Ovary Syndrome (PCOS) emphasizes lifestyle interventions and weight reduction as fundamental strategies (CENA ET AL., 2020). This involves adopting a balanced diet, regular physical activity, and behavioral changes that promote healthy habits (HIMELEIN & THATCHER, 2006). These measures aim to improve metabolic function, reduce insulin resistance, and contribute to hormonal regulation, constituting the basis for any further treatment (ANALA ET AL., 2023).

Pharmacological treatment of PCOS generally has two main goals: controlling infertility caused by anovulation and reducing symptoms related to androgen excess, such as hirsutism, acne, and menstrual irregularities (ASHRAF ET AL., 2019). Agents such as metformin, tirzepatide, tirliraglutide, and orlistat have been used as a complement to lifestyle interventions, particularly for patients with obesity or insulin resistance (CHAVDA ET AL., 2022). High-impact clinical studies demonstrate that tirzepatide promotes significant improvements in glycemic control in patients with type 2 diabetes and obesity (FRIAS ET AL., 2021) and induces weight reductions of over 20% in some cases (JASTREBOFF ET AL., 2022).

In recent years, there has been progress in the development of therapies targeting glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) receptors (CHÁVEZ, 2023). Tirzepatide, a dual agonist of these receptors, has the potential to improve obesity and insulin resistance by acting on specific signaling pathways and offering differentiated efficacy compared to selective GLP-1 agonists (GRACIA ET AL., 2023).

3.4 Lifestyle Modification

A loss of 5–10% of body weight is considered sufficient to promote significant clinical improvements in women with PCOS (BARBOSA ET AL., 2022). Dietary interventions should prioritize caloric reduction, favoring weight loss, improved insulin sensitivity, regularization of the menstrual cycle, and reduction of testosterone and circulating lipid levels (CENA ET AL., 2020). However, such isolated changes have not shown a consistent impact on biochemical hyperandrogenism, and the ideal dietary approach still requires further investigation (ASHRAF ET AL., 2019).

Regular physical exercise is recommended as an integral part of PCOS management (TEEDE ET AL., 2010). Moderate and continuous exercise contributes to the reduction of abdominal and liver fat and improves the cardiometabolic profile (ANALA ET AL., 2023). Strenuous activities should be avoided, as intense efforts can generate adverse cardiovascular effects and aggravate joint problems, especially in obese women (HIMELEIN & THATCHER, 2006).

Behavioral changes complement diet and exercise, aiding in adherence to and maintenance of weight loss goals (BARBOSA ET AL., 2022). Support strategies include setting realistic goals, creating adequate sleep routines, and accessing support groups (TEEDE ET AL., 2010). The frequent presence of depressive symptoms and anxiety among patients with PCOS can hinder the implementation and maintenance of these changes, resulting in relatively low adherence rates in structured lifestyle intervention programs (HIMELEIN & THATCHER, 2006).

RCMOS – Multidisciplinary Scientific Journal of Knowledge.
ISSN: 2675-9128. São Paulo-SP.

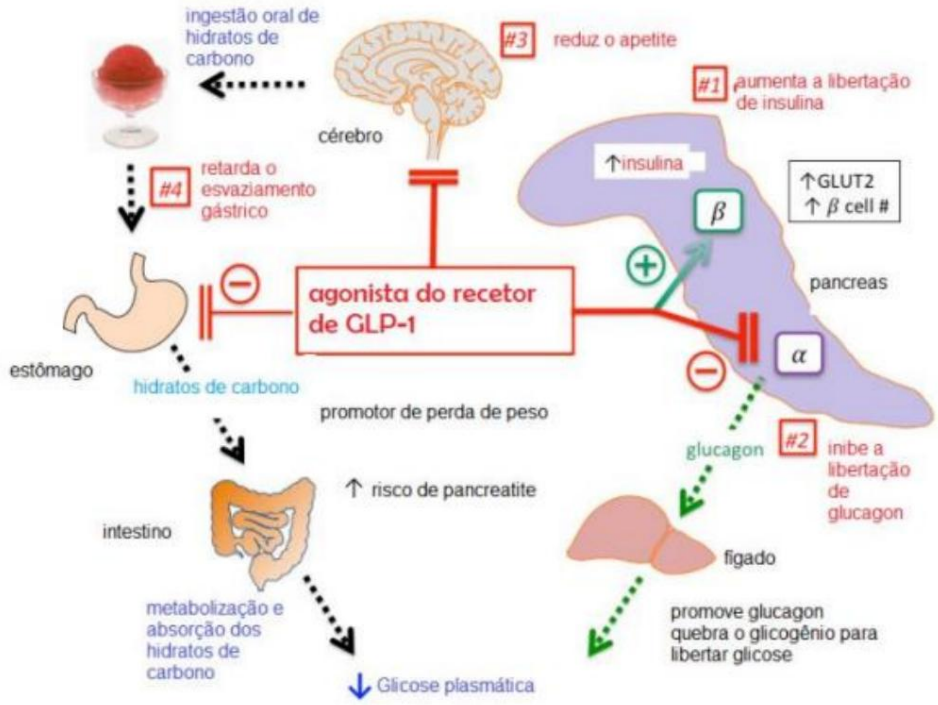


Figure 4: Effects of GLP-1 agonists in the treatment of obesity and insulin resistance.
Source: Baptista, 2022.

3.5 Pharmacotherapy of Tirzepatide for PCOS

Recently approved by the FDA, tirzepatide is indicated for the treatment of type 2 diabetes and combines the action of GLP-1 with the modulation of the gastric hormone glucose-dependent insulinotropic peptide (GIP) (CHAVDA ET AL., 2022). Although previous research suggested that GIP alone has a limited effect on insulin secretion in patients with type 2 diabetes, more recent studies demonstrate that the combination of GLP-1 and GIP promotes relevant synergistic effects (CHÁVEZ, 2023). The co-administration of GLP-1 and GIP agonists results in better glycemic control, as demonstrated by FRIAS ET AL. (2021), and body weight reduction compared to the use of each hormone alone, due to the more effective modulation of insulin secretion and energy metabolism (JASTREBOFF ET AL., 2022).

Tirzepatide is characterized as an unbalanced dual agonist of the GLP-1 and GIP receptors, presenting different affinities for each receptor (CHAVDA ET AL., 2022). Although its affinity for the GIP receptor is comparable to that of the endogenous hormone, its binding to the GLP-1 receptor is significantly lower. This difference in affinity is advantageous from a pharmacological perspective: it allows GLP-1R activation to be adjusted without causing intense gastrointestinal adverse effects, such as nausea and vomiting, while GIPR activation fully contributes to the desired metabolic effects without compromising tolerability (CHÁVEZ, 2023).

This balanced pharmacological profile, with a functional bias in favor of GIPR, enhances the efficacy of tirzepatide, improves treatment adherence and offers a promising therapeutic approach for women with PCOS who present obesity and insulin resistance (CENA ET AL., 2020).

Tirzepatide is administered subcutaneously and can be administered without regard to food intake (GRACIA ET AL., 2023). Treatment usually begins with the lowest available dose, which can be gradually adjusted to the maximum recommended dose, according to glycemic control and patient tolerability (FRIAS ET AL., 2021). The typical dosage ranges from 2.5 mg to 15 mg per week, allowing individualized management according to metabolic needs (CHAVDA ET AL., 2022).

In the context of PCOS, tirzepatide exerts multiple physiological effects that are particularly relevant. It stimulates insulin secretion in both phases while simultaneously inhibiting glucagon release, which contributes to reducing the often elevated blood glucose levels in patients with insulin resistance associated with PCOS (CHÁVEZ, 2023). Furthermore, it increases the sensitivity of peripheral tissues to insulin, facilitating glucose transport and aiding in overall metabolic control (BARBOSA ET AL., 2022).

Tirzepatide also promotes weight loss, a crucial effect for patients with PCOS, by reducing hepatic gluconeogenesis and delaying gastric emptying, decreasing food intake (JASTREBOFF ET AL., 2022). This weight loss is associated with improved hormonal profile, including decreased hyperandrogenism and regularization of the menstrual cycle, directly impacting the clinical symptoms of the syndrome, such as hirsutism, acne, and menstrual irregularities (ANALA ET AL., 2023).

Thus, tirzepatide combines glycemic control, weight loss promotion and hormonal modulation, offering a promising pharmacological approach for women with PCOS, especially those with obesity and insulin resistance, allowing more effective management of the metabolic and reproductive manifestations of the syndrome (CENA ET AL., 2020).

4. Conclusion

The use of tirzepatide represents a significant advance in the treatment of obesity and Polycystic Ovary Syndrome (PCOS), a complex and multifactorial condition. Clinical studies indicate that this dual GLP-1 and GIP receptor agonist not only improves glycemic control in individuals with type 2 diabetes and PCOS, but also promotes significant weight loss, with losses exceeding 20% of body weight in some cases (JASTREBOFF ET AL., 2022), in addition to contributing to the regulation of amenorrhea associated with PCOS. These findings suggest that tirzepatide may constitute an effective alternative treatment for PCOS, especially when combined with lifestyle interventions, including a balanced diet and regular exercise.

In addition to weight loss, additional metabolic and cardiovascular benefits are observed, such as improved lipid profile, decreased blood pressure and a potential protective effect on the

cardiovascular system (CHAVDA ET AL., 2022). The favorable pharmacokinetics of tirzepatide, with a half-life sufficient for weekly administration, contributes to treatment adherence, providing greater convenience for patients and strengthening its role in the comprehensive management of obesity and its comorbidities.

Therefore, tirzepatide represents a promising therapeutic alternative for the management of PCOS associated with obesity and insulin resistance. Although the available data are encouraging, they are still insufficient to make definitive clinical recommendations. Controlled clinical studies are needed to conclusively evaluate its efficacy, safety, and impact on reproductive parameters in women with PCOS (FRIAS ET AL., 2021; JASTREBOFF ET AL., 2022).

References

ANALA, AD; SAIFUDEEN, IJH; IBRAHIM, M.; NANDA, M.; NAAZ, N.; ATKIN, SL
The potential utility of tirzepatide for the management of polycystic ovary syndrome. *Journal of Clinical Medicine,* vol. 12, no. 14, p. 4575, 2023. DOI: 10.3390/jcm12144575. Accessed on: 24 Sep. 2025.

HIMELEIN, MJ; THATCHER, SS Polycystic ovary syndrome and mental health: a review. *Obstetrics and Gynecology Survey,* v. 61, p. 723–732, 2006. DOI: 10.1097/01.ogx.0000243772.33357.84. Accessed on: September 29, 2025.

TEEDE, H.; DEEKS, A.; MORAN, L. Polycystic ovary syndrome: a complex condition with psychological, reproductive, and metabolic manifestations that impacts health across the lifespan. *BMC Medicine,* v. 8, p. 41, 2010. DOI: 10.1186/1741-7015-8-41. Accessed: September 30, 2025.

ASHRAF, S.; NABI, M.; RASOOL, SUA; RASHID, F.; AMIN, S. Hyperandrogenism in polycystic ovary syndrome and the role of CYP gene variants: a review. *Egyptian Journal of Medical Human Genetics,* v. 20, p. 25, 2019. DOI: 10.1186/s43042-019-0031-4. Accessed on: October 1, 2025.

CENA, H.; CHIOVATO, L.; NAPPI, RE Obesity, Polycystic Ovary Syndrome and Infertility: A New Avenue for GLP-1 Receptor Agonists. *Journal of Clinical Endocrinology & Metabolism,* v. 105, p. e2695–e2709, 2020. DOI: 10.1210/clinem/dgaa285.
Accessed on: October 2, 2025.

KNOCHENHAUER, ES; KEY, T.J.; KAHSAR-MILLER, M.; WAGGONER, W.; Boots, L.
R.; AZZIZ, R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. *Journal of Clinical Endocrinology & Metabolism,* vol. 83, no. 9, p. 3078–3082, 1998. Accessed on: 2 Oct. 2025.

BARBOSA, MAS; REIS, FR DA S.; MARQUEZ, CO Pharmaceutical care in the treatment of obesity involving Glucagon-like Peptide 1 (GLP-1) analogues. *Research, Society and Development,* v. 11, n. 7, 2022. Accessed on: October 4, 2025.

CHAVDA, VP; et al. Tirzepatide, a new era of dual-targeted treatment for diabetes and obesity: a mini-review. *Molecules,* vol. 27, no. 13, 2022. Accessed on: 5 Oct. 2025.

CHÁVEZ, M. Tirzepatide: a revolutionary advance in the treatment of type 2 diabetes mellitus and obesity. *Eristas Magazine,* v. 4, no. 1, 2023. Accessed on: 6 Oct. 2025.

GRACIA, MFM; et al. Efficacy of tirzepatide in patients with type 2 diabetes mellitus and obesity: an innovative dual drug. *Ciencia Latina Multidisciplinary Scientific Journal,* v. 7, no. 1, p. 2370–2082, 2023. Accessed on: 7 Oct. 2025.

FRIAS, JP; DAVIES, MJ; ROSENSTOCK, J.; et al. Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. *New England Journal of Medicine,* vol. 385, p. 503–515, 2021. DOI: 10.1056/NEJMoa2107519. Accessed on: 12 Oct. 2025.

JASTREBOFF, AM; ARONNE, L.J.; AHMAD, NN; et al. Tirzepatide once weekly for the treatment of obesity. *New England Journal of Medicine,* vol. 387, p. 205–216, 2022. DOI: 10.1056/NEJMoa2206038. Accessed on: 12 Oct. 2025.