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TARGETING MULTIPLE PATHWAYS WITH ONE MOLECULE: THE THERAPEUTIC VERSATILITY OF TIRZEPATIDE

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ABSTRACT

Tirzepatide is a novel dual agonist of glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors that offers promising therapeutic potential beyond glycemic control. Originally developed for the treatment of type 2 diabetes mellitus, tirzepatide has demonstrated a wide array of pleiotropic effects in clinical studies. These include significant reductions in body weight, improvements in lipid profiles, decreased blood pressure, and attenuation of hepatic steatosis. Emerging data also support its cardioprotective and nephroprotective roles, as well as efficacy in patients with heart failure with preserved ejection fraction (HFpEF). Furthermore, tirzepatide is currently under investigation for the treatment of obstructive sleep apnea and shows early promise in neuroprotection. This review summarizes the current evidence on the diverse biological actions of tirzepatide and discusses their potential clinical implications in the context of metabolic syndrome and associated comorbidities.

Materials and methods: A review of the literature available in the PubMed database was performed, using the key words: "tirzepatide", "obesity treatment", "GIP", "GLP-1", "glucose-dependent insulinotropic polypeptide", "glucagon-like peptide-1".

Conclusion: The clinical benefits of tirzepatide extend well beyond glucose lowering, encompassing a broad spectrum of metabolic, cardiovascular and renal effects. These pleiotropic actions position tirzepatide as a valuable pharmacological agent in the multifactorial management of type 2 diabetes, obesity and related conditions. Continued investigation into its mechanisms of action and therapeutic scope may further redefine its role in the treatment of complex metabolic disorders. Given the growing body of evidence, tirzepatide represents a paradigm shift toward integrated care for patients with metabolic syndrome and its systemic manifestations.

KEYWORDS

Tirzepatide, Obesity Treatment, GIP, GLP-1, Glucose-Dependent Insulinotropic Polypeptide, Glucagon-Like Peptide-1

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1. Introduction

Type 2 diabetes and obesity constitute significant health challenges in today's world. They lead to heightened morbidity and death from cardiovascular, renal, and other metabolic conditions. Effective management of these disorders necessitates not only glycemic control but also addressing other components of metabolic syndrome. In recent years, incretin medicines, especially GLP-1 receptor agonists, have garnered significant interest for their benefits that surpass simple blood glucose reduction.

Tirzepatide is a new chemical distinguished by its dual mechanism of action, functioning as an agonist for both GLP-1 and GIP receptors. This combination enables synergistic effects in the regulation of glycemia, satiety, body weight, and lipid metabolism [1]. The clinical trials from the SURPASS and SURMOUNT programs have demonstrated its remarkable efficacy in lowering HbA1c and body weight, surpassing the benefits of traditional GLP-1 agonists. Increasing data suggests the pleiotropic effects of tirzepatide, which may be crucial in the prevention and management of cardiovascular, renal, and metabolic problems, including nonalcoholic fatty liver disease (NAFLD) [2]. The results of the latest clinical trials indicate the therapeutic benefits of tirzepatide in patients with heart failure and preserved ejection fraction. Tirzepatide is presently employed in the pharmacological treatment of obstructive sleep apnea. Additionally, new research has underscored the possible neuroprotective properties of tirzepatide. *Table 1* summarizes the effects of tirzepatide on various organs and systems.

Table 1. Tirzepatide's effects on various organs and systems

Area of action	Effects	
Endocrine system	↑insulin secretion ↓glucagon	↑glycemic control ↓body weight
Stomach	↓gastric emptying ↓gastric acid secretion	
Central nervous system	↑saziety ↓apetite ↓food intake	
Adipose tissue	↑lipolysis ↑lipid buffering capacity	
Cardiovascular system	↑glycemic control, ↓body weight ↓blood pressure ↓Total Cholesterol, ↓Tg, ↓LDL-C, ↑HDL-C	↓cardiovascular risk
Liver	↓Liver fat	
Kidney	↓albuminuria Impede the advancement of chronic kidney disease	

This article aims to evaluate the existing data on the pleiotropic effects of tirzepatide and to examine its possible role in a modern, comprehensive approach to treatment patients with type 2 diabetes, obesity, and other components of metabolic syndrome.

2. Molecular structure and mechanism of action of tirzepatide

Tirzepatide is an innovative compound authorized for the treatment of type 2 diabetes and, more recently, for the control of obesity. This is the first dual agonist for glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) receptors. The drug's mechanism entails the creation of two incretin hormones that regulate insulin secretion and appetite control [3].

GLP-1 and GIP are gastrointestinal hormones released from the digestive tract shortly after the ingestion of food, subsequent to the absorption of glucose, protein, and fat. They signify a physiological connection between intake and the release of insulin from the pancreatic islets. GLP-1 is mostly secreted by L cells situated in the ileum and colon. It binds to a specific GLP-1 receptor located in various organs, including pancreatic beta cells, pancreatic ducts, gastric mucosa, kidneys, lungs, heart, skin, immune cells, and the hypothalamus. Its principal role is to enhance insulin secretion in reaction to glucose concentrations. It has been shown to slow gastric emptying, inhibit inappropriate glucagon secretion after meals, enhance satiety, and encourage a reduction in food intake. GIP is a hormone synthesized by K cells located in the duodenum and jejunum. It binds to a specific GIP receptor located in several organs, including pancreatic beta cells, pancreatic alpha cells, subcutaneous and visceral adipose tissue, bone, and heart. Its function is to enhance insulin secretion. GIP exerts unique effects on glucagon production relative to GLP-1; in nondiabetic individuals, GIP enhances glucagon activity, however its insulinotropic effect is reduced in individuals with T2D, potentially due to downregulation and/or desensitization of GIP receptors. GIP improves energy storage and insulin sensitivity in adipose tissue while mitigating nausea. Animal studies suggest that the hormone may reduce hunger [4]. During the postprandial phase, GIP is co-secreted with GLP-1, and they may interact additively, hence enhancing glucose-induced insulin secretion [5]. This discovery has heightened interest in the development of single-molecule agonists for GLP-1 and GIP receptors, including tirzepatide.

Tirzepatide is a synthetic peptide consisting of 39 amino acids. Due to acylation technology, it possesses a half-life of 5 days, allowing for weekly administration [6]. It exhibits a variable affinity for the GIP and GLP-1 receptors. It has demonstrated a high affinity for the GIP receptor, equivalent to or exceeding that of natural GIP; conversely, it has approximately five times lower affinity for the GLP-1 receptor than natural GLP-1 or synthetic analogues (e.g., semaglutide). Notwithstanding its reduced affinity for GLP-1 receptor, tirzepatide exhibits comparable or even superior biological effects, attributable to "biased agonism" (the preferential activation of specific signaling pathways, such as cAMP production, while minimizing β-arrestin recruitment), potentially resulting in enhanced tolerance and efficacy, including a diminished risk of receptor desensitization. Tirzepatide is characterized as an unbalanced dual agonist, favoring the GIP receptor and exhibiting biased activity at the GLP-1 receptor [7].

Pharmacological suppression of the GIP receptor has shown effectiveness in limiting weight gain in animal models of obesity. Furthermore, the inhibition of the GIP receptor in conjunction with the activation of the GLP-1 receptor has exhibited synergistic benefits in reducing body weight in animal models of obesity. According to these findings, maridebartcafraglutide, a monoclonal antibody that acts as a GIP receptor antagonist and is conjugated to two modified GLP-1 peptides activating the GLP-1 receptor, is currently in the early stages of clinical development as a potential treatment for obesity management [8].

3. Effects of tirzepatide on glycemic regulation and weight reduction

Tirzepatide has shown significant effectiveness in lowering glycated hemoglobin (HbA_1c) levels and body weight in clinical trials. Tirzepatide is believed to enhance glycemic control by reducing fasting and postprandial glucose levels in individuals with type 2 diabetes through various mechanisms, including the enhancement of beta-cell function and insulin sensitivity, a reduction in glucagon levels, and the postponement of gastric emptying (although this postponement diminishes over time) [9].

The SURPASS clinical trial series [10] aimed to establish the therapeutic efficacy, tolerability, and safety of tirzepatide for treating obesity and type 2 diabetes patients. Participants received subcutaneous tirzepatide at doses of 5, 10, and 15 mg weekly, either as monotherapy or in conjunction with other glucose-lowering medications, accompanied by lifestyle modifications. The impact of tirzepatide was evaluated against placebo, basal insulins (glargine and degludec), and GLP-1 receptor agonists (dulaglutide 0.75 mg and semaglutide 1 mg). The primary endpoint was the assessment of the alteration in HbA1c from baseline. Tirzepatide effectively lowered HbA1c in a dose-dependent manner compared to other rivals and placebo, regardless of age [11], duration of T2D [12] or baseline HbA1c. During treatment durations of up to 104 weeks, HbA1c reductions of 1.9–2.6% were attained across the spectrum of type 2 diabetes [13].

In the SURPASS program, tirzepatide exhibited more weight reduction than all other evaluated drugs across all tirzepatide cohorts [14]. Tirzepatide 15 mg resulted in a weight reduction of 11.7–12.9 kg after 52 weeks in SURPASS-3, -4, and -6, and between 9.5 and 12.4 kg at 40 weeks in SURPASS-1, -2, and -5 [15]. The shown success of tirzepatide in the SURPASS program warranted the initiation of the SURMOUNT program, which assessed the effectiveness and safety of tirzepatide for chronic weight loss in overweight and obese individuals [16].

The SURMOUNT-1 research is a 72-week clinical experiment involving obese individuals without type 2 diabetes [17]. Patients were randomly allocated to four groups: placebo, tirzepatide 5 mg, tirzepatide 10 mg, or tirzepatide 15 mg. The tirzepatide cohort experienced a weight reduction ranging from 16% to 22.5%, in contrast to a mere 2.4% in the placebo group (moderate intensity lifestyle only) [16]. The SURMOUNT-2 research [18] encompassed diabetic patients administered either 10 mg or 15 mg of tirzepatide or a placebo. In this 72-week study, the tirzepatide cohort exhibited clinically significant weight loss, with a safety profile akin to that of GLP-1 receptor agonist treatments. In the SURMOUNT-3 [19] research, participants first underwent a structured intensive lifestyle modification for 12 weeks, followed by administration of either a placebo or tirzepatide at the highest tolerated dose for 72 weeks. The administration of tirzepatide following the initial lifestyle intervention led to enhanced weight loss. SURMOUNT-4 [20] is a study that investigates weight maintenance in patients who are obese or overweight. The study comprises two phases: an initial lead-in phase where all participants are administered TZP, followed by a treatment phase in which individuals, post-randomization, will either persist with tirzepatide medication or transition to a placebo. Participants administered tirzepatide sustained a minimum of 80% of the weight reduction during the lead-in phase, in contrast to 16.6% of those receiving a placebo. In individuals with obesity or overweight, discontinuation of tirzepatide resulted in significant weight return, but ongoing treatment preserved and enhanced initial weight loss.

Moreover, nearly all prediabetic patients in the SURMOUNT-1 trial administered tirzepatide attained normoglycemia (HbA1c <5.7%), in contrast to merely 62% of participants in the control group [16]. In the follow-up, 13.3% of overweight or obese prediabetics in the placebo cohort progressed to type 2 diabetes, whereas merely 1.3% in the tirzepatide cohort did so, indicating a 93% reduction in the risk of acquiring type 2 diabetes with tirzepatide [21]. In the SURMOUNT-2 research [18] HbA1c levels enhanced by 2.1–2.2% with tirzepatide, with 84–87% of patients attaining HbA1c $\leq$ 6.5%, in contrast to merely 16% with placebo. The impact of tirzepatide on glycemic control in individuals with type 2 diabetes was thoroughly evaluated in the SURPASS program, as previously mentioned. Tirzepatide shown greater efficiency compared to placebo and other frequently utilized hypoglycemic agents.

4. Effects of tirzepatide on cardiovascular risk

The SURMOUNT trials demonstrated improvements in other cardiovascular risk factors beyond diabetes and obesity, including glycemic metrics, blood pressure, and cholesterol levels.

Subjects in the clinical trial who received tirzepatide had significant reductions in blood pressure. The SURPASS studies exhibited a drop in systolic blood pressure between 2.8 and 12.6 mmHg and a decrease in diastolic blood pressure from 1 to 5.5 mmHg, respectively [22]. In the SURMOUNT studies, systolic blood pressure decreased by 5.9–10.5 mmHg in patients receiving tirzepatide, whereas the reduction with placebo was 0.9–2.4 mmHg. Diastolic blood pressure demonstrated an improvement, decreasing by 2.1–6.2 mmHg with tirzepatide, compared to a drop of 0.3–1.7 mmHg with placebo. Nonetheless, heart rate increased with tirzepatide by 2.1–5.4 beats per minute relative to placebo [23].

Tirzepatide also improved the lipid profile. The effects are partially due to the weight loss and improved insulin sensitivity caused by the drug. In December 2024, the findings of a meta-analysis conducted by Mahar et al. [24] regarding the alteration of the lipid profile in individuals administered tirzepatide during clinical trials were released. *Table 2* summarizes the key findings of this study.

The beneficial effect on lipid profiles in persons with diabetes, obesity, and metabolic syndrome leads to a reduced risk of atherosclerotic cardiovascular and cerebrovascular outcomes [25]. Tirzepatide's capacity to induce a dose-dependent decrease in ApoC-3 and Apo-B, markers linked to heightened cardiovascular event risk, is highlighted [26]. Current research indicates that tirzepatide can enhance the amounts of circulating adipokines and biomarkers, including adiponectin and proinsulin, which are linked to inflammation, insulin resistance, and dyslipidemia [27]. Research suggests that tirzepatide may increase HDL-C levels more markedly than insulin or GLP-1 agonists. This discovery is noteworthy because to previous difficulties in developing drugs that effectively elevate HDL-C levels.

Table 2. Efficacy data regarding alterations in lipid profiles during clinical trials involving patients administered tirzepatide. According to [24]

	Dose of tirzepatide			
	5 mg	10 mg	15 mg	
	compared to controls			
TC	-4,77%	-5,39%	-6,55%	No statistically significant difference was seen between the placebo, insulin, and GLP-1 agonist subgroups across all three doses of tirzepatide. Across doses, no significant differences were seen between tirzepatide and the GLP-1 agonist subgroup. Moderate to high heterogeneity was seen across the 5 mg , 10 mg and 15 mg doses.
LDL-C	-5,6%	-5,84%	-7,83%	The test for subgroup differences was insignificant across tirzepatide doses. No significant difference between tirzepatide and the control was seen in the GLP-1 agonist subgroup regardless of the tirzepatide dose. Moderate to high heterogeneity was seen across the 5 mg, 10 mg and 15 mg doses.
TG	-13,18%	-17,59%	-22,08%	The test for subgroup differences was significant in the 15 mg dose analysis, where a greater advantage with tirzepatide was seen versus GLP-1 agonists or placebo, as opposed to insulin. Moderate to high heterogeneity was seen across the 5 mg, 10 mg and 15 mg doses.
HDL-C	+3,78%	+5,75%	+6,94%	The test for subgroup differences was insignificant across all three doses of tirzepatide. Tirzepatide was significantly superior to the controls in all three subgroups across all three doses. Moderate to high heterogeneity was seen across the 5 mg, 10 mg, and 15 mg doses.

Furthermore, a post hoc study of the SURMOUNT-1 trial evaluated the alteration in the 10-year projected risk of atherosclerotic cardiovascular disease (ASCVD) in patients administered tirzepatide vs those receiving a placebo, particularly in people devoid of a prior ASCVD history. At baseline, the median ASCVD risk score was low (1.5–1.6%). However, the relative change in ASCVD risk from baseline to week 72 showed a more significant reduction with tirzepatide (-16.4% to -23.5%) compared to placebo, which exhibited an increase of +12.7% [28]. The SURPASS-CVOT clinical trial [29] is currently underway, featuring a randomized, controlled phase 3 design aimed at assessing the safety and efficacy of tirzepatide in comparison to dulaglutide among patients with type 2 diabetes who are at heightened cardiovascular risk. The study seeks to provide definitive evidence regarding the safety and efficacy of tirzepatide concerning cardiovascular risk in individuals with type 2 diabetes, projected completion date of June 2025. This evidence will play a crucial role in shaping clinical decisions surrounding the application of tirzepatide.

The upcoming clinical trial focused on assessing the impact of tirzepatide on cardiovascular risk is the SURMOUNT-MMO study [2]. This research is a randomized, placebo-controlled phase 3 experiment aimed at enrolling over 15,000 obese (non-diabetic) participants with elevated cardiovascular risk. The investigation will evaluate the effects of tirzepatide against placebo on reducing morbidity and mortality, with the primary outcome defined as a composite of all-cause mortality, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or heart failure events. The anticipated completion date is October 2027.

5. Tirzepatide for the treatment of heart failure with preserved ejection fraction

The findings of the SUMMIT trial [30] about tirzepatide for the treatment of heart failure with preserved ejection fraction (HFpEF) in obese individuals (with or without type 2 diabetes) were released in November 2024, revealing significant therapeutic benefits. The trial comprised 731 patients aged 40 and older, all diagnosed with chronic heart failure (New York Heart Association class II–IV), with a left ventricular ejection fraction of 50% or greater, and a body mass index of 30 kg/m² or higher. Participants were assigned to either tirzepatide or placebo through a randomized process. Patients underwent therapy for 52 weeks, followed by an extensive follow-up period of up to 120 weeks. Tirzepatide lowered the risk of the composite endpoint (cardiovascular mortality or exacerbation of heart failure) by 38% relative to placebo. The secondary significant endpoint of the study demonstrated a notable enhancement in the Kansas City Cardiomyopathy Questionnaire (KCCQ-CSS) score, with an average increase of 6.9 points in the tirzepatide group relative to the placebo group, indicating an amelioration of clinical symptoms and an improvement in patients' quality of life. Tirzepatide led to significant reductions in body weight, with patients achieving an average loss of 15.7% compared to 2.2% with the placebo. An additional consequence noted was an improvement in physical capacity, as individuals receiving tirzepatide could walk approximately 18 meters further within a six-minute period compared to those provided a placebo. A 38.8% reduction in C-reactive protein levels was also noted. Eli Lilly has submitted regulatory applications for tirzepatide to the US FDA and the European Medicines Agency (EMA) to target HFpEF and obesity.

6. Tirzepatide in the treatment of liver diseases associated with metabolic dysfunction

Tirzepatide exhibits promise in the treatment of liver disorders, specifically Metabolic Dysfunction-Associated Steatohepatitis (MASH), previously known as NASH. In clinical trials, patients receiving tirzepatide exhibited reductions in liver fat content (LFC), likely associated with the overall decrease in body weight and improved glucose metabolism. The SURPASS-3 clinical research [31] exemplifies this type of investigation, evaluating the effects of tirzepatide on persons with obesity and type 2 diabetes, and demonstrating a more pronounced reduction in liver fat levels relative to insulin degludec. After a 52-week duration, tirzepatide exhibited a decrease in LFC between 30% and 47% relative to baseline, whereas insulin degludec attained an 11% drop.

The SYNERGY-NASH study [32], a randomized, double-blind, placebo-controlled phase 2 trial, evaluated the efficacy of tirzepatide in treating patients with biopsy-confirmed MASH and stage F2 or F3 liver fibrosis. The proportion of patients attaining remission of MASH without any deterioration in liver fibrosis on liver histology was found to be greater in the tirzepatide group compared to the placebo group over a 52-week period (44–62% of participants receiving tirzepatide versus 10% receiving placebo). A larger percentage of patients in the tirzepatide cohort demonstrated an improvement of at least one grade of fibrosis without any worsening of MASH compared to those in the placebo group (51–55% vs. 30%).

A study conducted by Hartman et al. in 2020 [33] indicated a positive impact of tirzepatide on liver parameters, including ALT, AST, keratin-18 (K-18), and procollagen III (Pro-C3) levels, as well as an increase in adiponectin levels, a hormone known for its anti-inflammatory and protective properties on the liver. In studies involving persons with type 2 diabetes, higher dosages of tirzepatide (10 mg and 15 mg) shown significant reductions in these indicators compared to placebo and dulaglutide.

7. The effect of tirzepatide on renal function

Clinical studies suggest that tirzepatide may have the ability to decrease albuminuria and impede the advancement of chronic kidney disease (CKD). In a post hoc analysis of the SURPASS-1–5 studies [34], tirzepatide administered at doses of 5, 10, and 15 mg demonstrated mean reductions in the albumin-to-creatinine ratio (UACR) of 19.3%, 22%, and 26.3%, respectively, when compared to placebo and other agents. The observed effect was notably stronger in individuals exhibiting a baseline UACR of 30 mg/g or higher.

A crucial consideration in the application of tirzepatide is the safety profile of the medication during extended follow-up periods. The findings indicated that the occurrence of significant renal events, including acute kidney injury (AKI), was minimal and similar to that of other antidiabetic medications, with no impact on GFR noted [35].

The dual agonist activity at GLP-1 and GIP receptors may influence renal function by enhancing glycemic control and promoting weight reduction, perhaps leading to reduced intrarenal pressure and albumin filtration. This also results in a reduction in inflammation, consequently improving renal tubular function.

Tirzepatide is being studied for its ability to impede the advancement of chronic renal disease in overweight or obese patients. The ongoing investigation of tirzepatide in individuals with overweight or obesity and chronic kidney disease (CKD), irrespective of type 2 diabetes status (TREASURE-CKD) [36], seeks to assess the mechanistic effects of tirzepatide on renal function and will enhance our understanding of the potential mechanisms underlying UACR reduction. If the findings are favorable, tirzepatide could provide a new therapeutic option for CKD, similar to current drugs such as SGLT2 inhibitors or GLP-1 agonists. The study's findings are expected to be released in 2025.

8. Tirzepatide in the treatment of Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is characterized by the repeated collapse of the pharyngeal airway during sleep, causing episodes of apnea and hypopnea, which lead to hypoxemia, hypercapnia, and frequent arousals. It is associated with serious cardiovascular conditions, including hypertension and stroke [37].

Studies indicate that over 70% of persons diagnosed with obstructive sleep apnea (OSA) are categorized as obese. A 10% rise in body weight leads to a six-fold elevation in the likelihood of developing obstructive sleep apnea (OSA). Weight reduction in patients with obstructive sleep apnea can significantly diminish the severity of the disease's symptoms [38]. Moderate to severe OSA is identified when the apnea-hypopnea index (AHI) exceeds 15 per hour. The most effective approach for managing this form of severe OSA is the implementation of positive airway pressure (PAP) therapy. Tirzepatide does not directly address OSA, yet it may have an indirect positive impact on its progression by facilitating weight loss, decreasing the length of apnea episodes, and enhancing oxygen saturation levels.

The SURMOUNT-OSA phase 3 trials evaluated the effects of tirzepatide in maximum tolerated dose (MTD – 10mg or 15 mg) compared to placebo on parameters related to obstructive sleep apnea, involving two groups of participants with obesity (without type 2 diabetes) and moderate to severe obstructive sleep apnea. SURMOUNT-OSA 1 involved participants who were not undergoing PAP therapy, whereas SURMOUNT-OSA 2 was carried out with individuals who were utilizing PAP therapy. In study 1, tirzepatide MTD demonstrated a reduction in the AHI by 27.4 events/hour, whereas the placebo group showed a reduction of only 4.8 events/hour [37]. In study 2, tirzepatide MTD demonstrated a reduction in the AHI by 30.4 events/hour, in contrast to the placebo, which showed a reduction of 6 events/hour [37]. In summary, the findings from these two studies indicate that tirzepatide MTD resulted in a reduction of the AHI by 50.7% to 58.7% from baseline, as well as improvements in patient-reported sleep outcomes relative to placebo.

Positive research findings indicating that tirzepatide markedly decreases apnea episodes and enhances sleep quality and metabolic function in overweight or obese individuals prompted the U.S. Food and Drug Administration (FDA) to authorize tirzepatide as a pharmacological intervention for obstructive sleep apnea (OSA) in obese adults in December 2024.

9. Neuroprotective properties of tirzepatide in experimental studies

A growing body of research suggests that tirzepatide may have neuroprotective effects. A study utilizing a mouse model of Alzheimer's disease shown that tirzepatide reduced amyloid plaque levels in the cerebral cortex, lowered neuronal mortality, and improved glucose metabolism in the brain. This effect was associated with the activation of GLP-1 receptors and increased mitochondrial activity in astrocytes. In a separate study [39] involving mice on a high-fat diet, tirzepatide enhanced cognitive performance by activating the SIRT3 protein and suppressing the NLRP3 inflammatory pathway. This impact correlated with decreased oxidative

stress and inflammation in the brain. Research [40] indicates that tirzepatide markedly improves spatial learning and memory deficits, reduces Aβ buildup, averts structural damage, promotes synaptic protein production, and augments dendritic spine formation in diabetic rats. A recent study published in 2025 [41] utilizing a rat model of Parkinson's disease demonstrated that tirzepatide enhances motor capabilities, diminishes inflammatory cytokines (TNF-α, IL-6), elevates dopamine levels in the striatum, and mitigates oxidative stress and α-synuclein aggregation.

Tirzepatide's capacity to influence neuronal growth, glucose metabolism, inflammation, and epigenetic processes renders it a prospective candidate for the treatment of neurodegenerative illnesses, especially those linked to diabetes. Continued work is crucial to thoroughly clarify its mechanisms and therapeutic potential in clinical applications.

10. Summary

Type 2 diabetes and obesity are significant health concerns that lead to heightened morbidity and death from cardiovascular, renal and metabolic consequences. Effective treatment necessitates glycemic regulation and influences additional components of metabolic syndrome, including body weight, blood pressure, lipid profile, and hepatic function. Incretin medicines, especially GLP-1 receptor agonists, have garnered interest for their prospective advantages beyond mere blood glucose lowering.

Tirzepatide, an innovative chemical, operates through a dual mechanism, acting as an agonist for both GLP-1 and GIP receptors. Its effects extend beyond simple glucose regulation, encompassing other beneficial metabolic, cardiovascular, hepatic, and renal protective attributes. Tirzepatide has shown exceptional effectiveness in reducing HbA1c levels and body weight, surpassing the outcomes of traditional GLP-1 agonists. The SURPASS clinical trial series sought to determine the therapeutic efficacy, tolerability, and safety of this chemical in treating patients with obesity and type 2 diabetes. The SURMOUNT program assessed the effectiveness and safety of tirzepatide for sustained weight reduction in overweight and obese people. The SURMOUNT trials have demonstrated that this medication can enhance cardiovascular risk factors beyond diabetes and obesity, including blood pressure and cholesterol levels. The results of the latest clinical trials indicate the therapeutic benefits of tirzepatide in patients with heart failure with preserved ejection fraction. Tirzepatide has demonstrated efficacy in addressing liver illnesses linked to metabolic dysfunction, including Metabolic Dysfunction-Associated Steatohepatitis (MASH). Furthermore, clinical investigations indicate that this innovative medicine may reduce albuminuria and hinder the advancement of chronic renal disease. Tirzepatide has demonstrated encouraging outcomes in reducing apnea episodes and improving sleep quality and metabolic efficiency in overweight or obese patients. The FDA sanctioned tirzepatide for the treatment of OSA in obese persons in December 2024. Tirzepatide may exhibit neuroprotective qualities, as evidenced by studies related to Alzheimer's disease and Parkinson's disease. Experimental investigations utilizing animal models have demonstrated a reduction in amyloid plaque levels, a decrease in neuronal mortality, and an enhancement of glucose metabolism in the brain.

Tirzepatide exhibits substantial effectiveness in weight loss, improvement of lipid profiles, decrease of blood pressure, and alleviation of fatty liver, positioning it as a potentially transformative therapy for metabolic syndrome. The results of the clinical research to date confirm the efficacy and safety of this medication in a varied population of persons with overweight, obesity, and/or type 2 diabetes. Concurrent research is underway to assess the long-term effects of tirzepatide on cardiovascular risk, the progression of chronic kidney disease, and possible neuroprotective benefits.

Disclosure

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Methodology – Kinga Dyndał, Marcelina Broda
Software – Olga Żuczek, Katarzyna Urbańska
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