



# Effect of Exercise and Nutrition on GLP-1

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## Introduction

Glucagon-like peptide-1 is a hormone synthesized in the gastrointestinal tract that exhibits potential as a therapeutic intervention for individuals with type 2 diabetes and obesity. Its primary functions include regulating glucose levels and maintaining energy balance through stimulating insulin secretion while inhibiting glucagon release (Klotsman et al., 2021). Additionally, GLP-1 acts to decrease appetite and promote satiety, thereby aiding in weight loss efforts. Researchers are currently exploring the impact of exercise and dietary factors on GLP-1 production and efficacy due to its promising metabolic advantages (Beiroa et al., 2014)(Potts et al., 2015).

Numerous studies have explored the influence of physical activity and diet on GLP-1 levels and their potential implications for metabolic well-being (Mráziková et al., 2023). Physical exercise has demonstrated acute augmentation in GLP-1 release, while regular exercise has evidenced increased expression of GLP-1 receptors and enhanced glucose absorption (Hamasaki, 2018). Conversely, dietary factors including macronutrient composition, meal dimensions, and fiber content also exert an impact on GLP-1 secretion as well as its functionality. For instance, high-protein diets have been found to heighten the release of GLP-1; conversely, though, high-fat diets are associated with impaired elucidation of this hormone (Hibi et al., 2019)(Fujiwara et al., 2019).

The impact of exercise and nutrition on GLP-1 secretion and activity is a topic of increasing interest. However, there is still uncertainty about the most effective strategies for triggering GLP-1 and its potential role in fat loss and improving insulin sensitivity. This review aims to provide an updated summary of the evidence regarding the influence of exercise and nutrition on GLP-1 secretion and activity, as well as their potential implications for metabolic health. Drawing from various peer-reviewed studies in endocrinology, nutrition, and exercise physiology, we aim to synthesize this literature to offer insights into possible therapeutic interventions for metabolic diseases.

## Overview of GLP-1

Glucagon-like peptide-1 is an incretin hormone that is primarily produced in the intestine, specifically by L-cells located in the distal ileum and colon. The secretion of GLP-1 is stimulated by the ingestion of food, with a particular response to carbohydrates and fats (Klotsman et al., 2021). This hormone plays a role in regulating multiple organs and tissues throughout the body, including the pancreas, liver, brain, and adipose tissue (Watanabe et al., 2016).

Glucagon-like peptide 1 is present in two active forms, with GLP-1 7–36 being the primary form found circulating in human subjects (Flint et al., n.d)(Hirai et al., 2017). After being released from L-cells, GLP-1 undergoes rapid degradation by the dipeptidyl peptidase-4 enzyme, resulting in a short half-life of only a few minutes (Schwartz, 2010). Its role is vital for maintaining metabolic balance as it stimulates post-meal insulin secretion and inhibits glucagon secretion. Furthermore, GLP-1 slows down gastric emptying, induces feelings of satiety, and decreases appetite (Flint et al., n.d)(Godinho et al., 2015). Furthermore, research indicates that GLP-1 plays a vital role in promoting beta-cell function and growth, as well as providing protection against cell death (Park et al., 2021). It also enhances insulin sensitivity in peripheral tissues like muscle and adipose tissue, leading to improved glucose regulation (Capucho et al., 2022).

The physiological functions of GLP-1 include glucose-dependent insulin secretion, suppression of glucagon secretion, gastric emptying delay, and promotion of satiety. Additionally, GLP-1 impacts fat metabolism and improves insulin sensitivity (Ślupski et al., 2018). These factors highlight the importance of GLP-1 in addressing obesity and type 2 diabetes prevention and management.

The involvement of GLP-1 in regulating feelings of fullness, reducing hunger sensation, and enhancing the body's response to insulin underscores its potential significance for combating obesity and type 2 diabetes (Goldspink et al., 2020). Thus, GLP-1 is currently being explored as a promising target for therapeutic approaches aimed at managing these prevalent health conditions involving glucose metabolism-related impairments and lipid imbalances within the body (Goldspink et al., 2020)(Jiang et al., 2018).

## GLP-1 and its role in fat loss and insulin sensitivity

GLP-1 has been extensively studied for its role in weight management and diabetes prevention. It plays a crucial role in improving insulin sensitivity and promoting fat loss (Potts et al., 2015). GLP-1 interacts with receptors present in multiple tissues such as the pancreas, brain, and peripheral organs. Notably, it enhances glucose-stimulated insulin secretion while inhibiting glucagon secretion and reducing gastric emptying rates (Xu et al., 2022).

The diverse mechanisms that contribute to the effects of GLP-1 on fat loss and insulin sensitivity are quite remarkable. Firstly, GLP-1 stimulates energy expenditure by increasing thermogenesis and activating brown adipose tissue (Lee et al., 2018). Secondly, it promotes satiety through appetite reduction and improved meal satisfaction, which leads to decreased food intake and subsequent weight loss (Ren et al., 2019). Lastly, GLP-1 enhances glucose uptake in skeletal muscle and improves insulin sensitivity in adipose tissue and liver (Liu et al., 2022).

Studies conducted on animals have confirmed the impacts of GLP-1 agonists on weight, glucose regulation, and insulin sensitivity (Bhateja et al., 2020). Specifically, administering GLP-1 agonists has been shown to result in substantial weight loss by reducing food consumption and increasing energy expenditure (Secher et al., 2014). Furthermore, clinical investigations involving humans have provided evidence for the efficacy of GLP-1 receptor agonists and analogs in combating obesity and improving glucose metabolism among individuals with type 2 diabetes. (Rajan et al., 2015)

The use of GLP-1 modulation to address obesity and diabetes has shown promising potential. The approval of GLP-1 agonists and analogs for the treatment of type 2 diabetes, along with ongoing research on their effectiveness in treating obesity, underscores the clinical significance of this approach (Lopaschuk et al., 2019). Exploring dietary and exercise interventions that enhance GLP-1 secretion and activity also holds promise for preventing and managing metabolic diseases. Recognizing the multifaceted effects of GLP-1 on fat reduction and insulin sensitivity establishes it as a valuable target in addressing these prevalent health concerns.

## Nutritional Implication on GLP-1

The impact of nutrition on regulating the secretion of GLP-1 is widely recognized, with implications for metabolic well-being that go beyond just dietary content and also encompass meal timing and order.

The diverse impact of macronutrients such as carbohydrates, proteins, and fats on the secretion of GLP-1 has been observed (Vannan et al., 2018). Notably, dietary fats and proteins have been identified as significant factors that stimulate the release of GLP-1. The consumption of dietary fats prolongs gastric emptying and intestinal transit time, thereby sustaining GLP-1 responses (Wang et al., 2015). On the other hand, proteins, particularly whey proteins, exert a strong influence on activating GLP-1 (Nong & Hsu, 2021). In contrast to this pattern, carbohydrates—especially those with high glycemic indexes—prompt rapid but short-lived increases in GLP-1 levels (Jang et al., 2017).

The interaction between nutrition and GLP-1 also extends to the timing and order of nutrient consumption. Recent research highlights that gut L-cells, responsible for secreting GLP-1, are more responsive to nutrients during morning hours. Therefore, consuming larger meals earlier in the day may optimize levels of GLP-1 (Hibi et al., 2019).

Additionally, meal sequence, combined with nutritional composition, further influences the release of GLP-1. Studies have shown that consuming protein and fat before carbohydrates results in increased secretion of GLP-1. The concept referred to as the "second-meal phenomenon" effect demonstrates a significant link between increased consumption of dietary fiber and amplified secretion of GLP-1 (Hartman-Petrycka et al., 2022)(Gentilcore et al., 2006).

Different nutrients and dietary choices can also influence the secretion of GLP-1. Increased consumption of fiber-rich foods, whole grains, and low-glycemic-index foods have been found to promote the release of GLP-1, which in turn enhances feelings of fullness and aids in weight control (Lin et al., 2020). These findings suggest that nutrition plays a significant role in regulating GLP-1 levels and presents promising avenues for interventions aimed at improving metabolic health outcomes and preventing disease.

## Impact of Exercise on GLP-1

The influence of exercise on GLP-1 concentrations has been extensively studied in the scientific community. Researchers have examined different aspects of exercise, such as type, duration, demographic factors, and timing, to better understand their impact on GLP-1 concentrations.

### *Type of Exercise*

Various forms of physical activity have differing effects on the secretion of GLP-1. Endurance and high-intensity interval training, which involve prolonged and intense exercise, have been shown to result in higher post-exercise levels of GLP-1 (Hamasaki, 2018). A study demonstrated that individuals who engaged in high-intensity workouts exhibited more substantial elevations in GLP-1 compared to those who partook in moderate exercise regimens (Dorling et al., 2018).

### *Duration of Exercise*

The duration of exercise also seems to play a role in the impact on GLP-1 concentrations. Research suggests that longer durations of exercise result in greater increases in GLP-1 levels (Ebina et al., 2020). For example, a study comparing short-duration, high-intensity exercise with longer-duration, moderate-intensity exercise found that the longer-duration exercise led to significantly higher GLP-1 concentrations (Hamasaki, 2018). This indicates that sustained physical activity may have a more pronounced effect on GLP-1 secretion.

### *Population Factors*

The effect of exercise on GLP-1 concentrations may vary among different populations, highlighting the importance of considering population factors. Research indicates that while GLP-1 levels increased following exercise in overweight individuals, there was no significant change observed in individuals of normal weight (Ueda et al., 2013). These findings indicate the potential for variation in the regulation and release of GLP-1 based on individual body compositions.

In addition, the response of GLP-1 to exercise may also be influenced by age and sex. Certain studies have observed that older adults exhibit lower increases in GLP-1 levels following exercise compared to younger individuals (Tsai et al., 2018).

Furthermore, there may be differences in the response of GLP-1 to exercise between males and females. For example, a study conducted by Ueda et al. examined the effect of exercise on GLP-1 levels in both men and women and found that women had a greater increase in GLP-1 levels compared to men following exercise (Ueda et al., 2013)(Dorling et al., 2018).

### *Timing of Exercise*

The timing of exercise is an important factor to consider when investigating the impact on GLP-1 secretion. Recent evidence suggests that the timing of exercise may influence the release of GLP-1 and its subsequent effects on food consumption and energy intake (Chae et al., 2015).

One study found that exercising in a fasted state, such as in the morning before breakfast, resulted in higher GLP-1 levels compared to exercising after a meal (Takahashi et al., 2018)(Ueda et al., 2013). The time-dependent rise in GLP-1 levels may have implications for managing weight and controlling appetite. Exercising while fasting could potentially lead to greater reductions in food consumption and improved metabolic health. However, further research is necessary to fully comprehend the connection between the timing of exercise and GLP-1 secretion.

## Synergistic Role of Nutrition and Exercise

The complex interaction between diet and exercise in regulating GLP-1 levels highlights a multifaceted relationship influenced by various factors. The combined effects of these two important components provide valuable insights into the intricate mechanisms involved in GLP-1 regulation within the human body.

Exploring the effects of dietary factors, it is apparent that different nutrients have varying effects on the secretion of GLP-1. Research has shown that certain nutrients can stimulate the release of GLP-1 from intestinal L-cells (Inabu et al., 2021)(Adam & Westerterp-Plantenga, 2004). Additionally, it has been found that the timing and order in which meals are consumed also play a crucial role in regulating GLP-1 levels (Haldar et al., 2019). Notably, a recent study highlighted that lipids have the strongest impact on stimulating GLP-1 secretion, followed by carbohydrates and amino acids (Pizarroso et al., 2021). This emphasizes how altering the macronutrient composition of meals can significantly influence GLP-1 levels.

The influence of exercise on the secretion of GLP-1 is apparent, as multiple studies have demonstrated that short-term exercise sessions lead to a notable increase in GLP-1 levels. Various forms of physical activity, such as aerobic workouts and resistance training, possess the ability to stimulate the production and release of GLP-1. This potential enhancement may contribute to improved insulin sensitivity and more efficient regulation of glucose metabolism.

Recent research suggests that the combination of diet modification and exercise has a synergistic effect on GLP-1 secretion. For example, when aerobic exercise is combined with calorie restriction in obese adults, it results in increased GLP-1 concentrations (Dorling et al., 2018)(Ueda et al., 2013)(Son et al., 2017). This emphasizes the potential advantages of combining dietary and exercise interventions to effectively enhance GLP-1 levels, surpassing the impact of either intervention alone. Another study examines the effects of incorporating moderate-intensity exercise with high-protein meal consumption on GLP-1 secretion. The findings demonstrate a significant increase in GLP-1 secretion among participants who simultaneously engage in both interventions, exceeding the effect observed in groups following only one approach (Muntis et al., 2023)(Janus et al., 2019). This empirical evidence validates the efficacy of strategically integrating nutrition and exercise to optimize regulation of GLP-1 production.

In a distinct investigation, the researchers examined the effects of combined weight loss through diet and physical activity on GLP-1 secretion. The results revealed that participants who followed both interventions experienced an increase in GLP-1 secretion (Adam & Westerterp-Plantenga, 2004)(Hibi et al., 2019). This underscores the potential benefits of interdisciplinary approaches for achieving improved metabolic outcomes and modulating GLP-1 levels.

Another study underscores the relationship between meal timing and physical activity in influencing the secretion of GLP-1 hormone. Notably, individuals who engaged in exercise prior to breakfast demonstrated a heightened GLP-1 response compared to those who exercised after meals (Ueda et al., 2013)(Takahashi et al., 2018). This finding emphasizes the importance of timing both meals and exercise for optimal regulation of GLP-1.

These findings underscore the significance of a holistic approach that combines nutrition and exercise in impacting GLP-1 secretion. Each study contributes valuable insights into the various strategies and synergistic effects that influence GLP-1 regulation. However, due to the complexity of these interactions, further research is needed to uncover the optimal combinations that can maximize health outcomes through modulation of GLP-1 levels.

## Evidence from Clinical Trials

Several clinical trials provide a profound understanding of the correlation among diet, exercise, and GLP-1. Research on obese adults has shown that weight loss, facilitated by energy deficits, raises GLP-1 concentrations, thereby affirming a link between diet, exercise, and GLP-1 levels (Adam & Westerterp-Plantenga, 2004). Significant increases in GLP-1 plasma levels have also been observed following moderate to high-intensity exercise in a study by Ueda et al (Ueda et al., 2013). Such findings suggest that exercise has a direct impact on GLP-1 secretion. In another study, the effects of a 12-week exercise intervention on GLP-1 secretion in overweight individuals were examined. The results demonstrated a significant increase in GLP-1 secretion following the exercise intervention, indicating that regular physical activity can positively influence GLP-1 levels and potentially improve metabolic outcomes (Ueda et al., 2013)(Ueda et al., 2013)(Janus et al., 2019).

Notably, a study investigating the combined approach of exercise and dietary interventions in overweight and obese individuals recorded a rise in GLP-1 concentrations post-intervention. This research further validates the potentiated effect of a multi-pronged nutritional and exercise methodology on GLP-1 levels (Hamasaki, 2018)(Ueda et al., 2013)(Janus et al., 2019).

Despite these substantial findings, it's important to acknowledge that our understanding of the mechanisms underlying these correlations is not complete. Many of the trials have been on populations with specific characteristics, such as being obese or overweight, and for this reason, the extension of these findings to other populations may be limited.

Therefore, future research should aim toward exploring the influence of various dietary and exercise-induced modulations on GLP-1 in different population groups, right from pediatric to elderly populations.

Additionally, the standardization of exercises and diets used in these trials is inconsistent, making comparison and synthesis of results difficult. Future trials must leverage rigorous and standardized methodologies to ensure that the findings are reliable, valid, and comparable across different experiments. Lastly, more long-term trials are necessary to understand and highlight the lasting impacts of nutrition and exercise on GLP-1 secretion and its subsequent metabolic effects.

## Summary and Future Directions

This review emphasizes the significance of GLP-1 in promoting fat loss and improving insulin sensitivity. The intricate interplay between nutrition and exercise in modulating GLP-1 secretion emerges as a crucial aspect for advancing our understanding of metabolic health. A comprehensive exploration of these connections lays the groundwork for future research endeavors.

From a nutritional standpoint, specific nutrients have been found to impact the release of GLP-1. Various factors such as macronutrient composition, meal timing, and overall dietary patterns have demonstrated their ability to influence GLP-1 production. Furthermore, engaging in exercise at moderate to vigorous intensities has also been observed to directly stimulate an increase in GLP-1 secretion. When these interventions are effectively combined, they work synergistically to significantly elevate levels of GLP-1.

These findings offer valuable insights for healthcare professionals, affirming the effectiveness of lifestyle modifications in utilizing GLP-1 to address metabolic disorders like obesity and type 2 diabetes. This enhanced understanding equips clinicians with evidence-based strategies to optimize patient care.

In order to advance our knowledge in this field, it is crucial to investigate the potential areas of research that show promise. To obtain a thorough understanding, it is necessary to explore how different exercise modalities, types of exercises, and levels of intensity interact with various dietary patterns in regulating GLP-1 production. An all-encompassing approach would involve including individuals from diverse age groups, ethnic backgrounds, and metabolic health statuses within study populations. It is crucial to conduct well-controlled clinical trials implementing standardized dietary and exercise interventions to facilitate comparative effectiveness research. Furthermore, it is imperative to investigate the long-term effects of nutritional and exercise interventions on GLP-1 regulation and their impact on metabolic outcomes.

In summary, the intricate interplay between diet, physical activity, and GLP-1 presents significant opportunities for practical and clinical applications. Additional research on the underlying mechanisms and broader implications of these associations is warranted. By deepening our understanding of how GLP-1 engages with nutrition and exercise, we can develop more impactful therapeutic strategies that capitalize on the multifaceted potential of GLP-1 to enhance metabolic well-being.



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