Trimsulin vs. Semaglutide vs. Tirzepatide for Weight Loss in Overweight Adults

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ABSTRACT

INTRODUCTION: Overweight and obesity are prevalent conditions linked to increased morbidity and mortality, requiring effective weight management interventions. Pharmacological agents such as glucagon-like peptide-1 receptor agonists (GLP-1RAs) like semaglutide and dual gastric inhibitory polypeptide (GIP) receptor agonists like tirzepatide have been shown to promote significant weight loss. However, these treatments are often associated with adverse effects, leading to poor compliance. Trimsulin, a nutraceutical weight-loss composition that stimulates endogenous GLP-1 and GIP release, represents a weight-loss solution with few potential side effects.

METHODS: A cohort of 503 overweight adults were monitored to compare weight change and adverse events associated with orally ingested Trimsulin versus injectable semaglutide and tirzepatide over 3 and 6 months. Data collected included weight, BMI, and adverse events, with primary endpoints focusing on percentage weight change and adverse event rates. Participants had an average baseline weight of 201.23 lbs and an average BMI of 27.5.

RESULTS: After three months, Trimsulin participants experienced more than double the average weight loss reported in published semaglutide data and substantially greater weight loss than outcomes reported for tirzepatide. After six months, Trimsulin participants demonstrated more than double the average weight loss reported in published semaglutide data and greater average weight loss than outcomes reported for tirzepatide.

Adverse event rates were substantially lower with Trimsulin. Only 4.8% of Trimsulin users reported any side effects, in stark contrast to the 89.7% of semaglutide users and 81.0% of tirzepatide users. Gastrointestinal disorders affected 2.9% of Trimsulin users, compared to 59.7% for semaglutide and 46.0% for tirzepatide. Additionally, nausea occurred in just 2.1% of Trimsulin users, compared to 44.2% in semaglutide and 35.5% in tirzepatide users. Trimsulin patients experienced no cases of vomiting, compared to 24.8% for semaglutide and 16.4% for tirzepatide. Serious side effects were reported in 3% of semaglutide patients and 5-7% of tirzepatide patients. No serious side effects were reported by Trimsulin users.

DISCUSSION: This study is the first to compare a non-pharmaceutical nutraceutical composition, which includes endogenous GLP-1 and GIP releasers, DPP-4 inhibitors, and thermogenesis activators, with pharmaceutical agents. Trimsulin participants demonstrated greater average weight loss within the observed cohort, alongside significantly fewer reported adverse effects. The combination of nutraceuticals and plant-based compounds in Trimsulin appears to activate multiple metabolic and hormonal pathways involved in weight management without overstimulating receptors, reducing the risk of gastrointestinal discomfort and other side effects.

CONCLUSIONS: The Trimsulin Weight Loss Program offers a promising weight loss alternative, achieving substantial weight loss with a low rate of reported side effects in the observed cohort. These findings suggest that Trimsulin may be a safer and more tolerable option for individuals seeking weight management solutions.

Introduction:

Overweight and obesity are highly prevalent conditions associated with increased morbidity and mortality. Pharmacological treatments, such as glucagon-like peptide-1 receptor agonists (GLP-1RAs) and dual gastric inhibitory polypeptide (GIP) receptor agonists, have gained popularity due to their beneficial effects on glucose regulation, eating behavior, and body weight, as demonstrated in randomized clinical trials.[1-5]

GLP-1RAs mimic the effects of the incretin hormone GLP-1, which is produced and secreted by intestinal enteroendocrine L-cells and specific neurons within the nucleus of the solitary tract in the brain. GIP is another incretin hormone secreted by intestinal enteroendocrine cells.

Endogenous releasers of GLP-1 or exogenously administered GLP-1RAs bind to and activate GLP-1 receptors. A notable feature of pharmaceutical GLP-1RAs is their resistance to degradation by dipeptidyl peptidase-4 (DPP-4), which prolongs their biological activity. Increasing evidence suggests that exogenous GLP-1RAs have little resemblance with endogenous

GLP-1 regarding how they act, although the clinical effects appear to be the same.[6] Endogenous GLP-1 releasers combined with the DPP-4 inhibitors elevated active endogenous GLP-1 in mice to levels approaching those of injectable exogenous pharmaceutical GLP-1 RAs.[7]

Endogenous GLP-1 and GIP releasers (e.g., secretagogues) comprise nutraceuticals, FDA-approved foods, food additives, and dietary supplements. Individual compounds include nutritional fibers, phytochemicals, botanical extracts, fatty acids, resistant starches, sweeteners, flavonoids, alkaloids, peptides, probiotics, and prebiotics.

Trimsulin is a nutraceutical program designed to stimulate the release of endogenous GLP-1 and GIP. It includes natural DPP-4 inhibitors to prevent degradation and enhance insulin sensitivity. Additionally, Trimsulin contains thermogenesis activators that promote the conversion of white adipocytes to brown adipocytes via uncoupling protein 1 (UCP-1), as well as activators of hormone-sensitive lipase to support fat metabolism.

Current pharmaceutical therapies, such as semaglutide and tirzepatide, have significantly reduced weight in patients. However, these treatments are associated with adverse effects in over 80% of patients.

Methods:
This study compared weight change and adverse event rates between orally ingested Trimsulin and injectable semaglutide and tirzepatide in 503 participants over a 3 and 6 month period in overweight adults. Data were normalized for comparison across treatments. This observational cohort analysis evaluated participants following the complete Trimsulin Weight Loss Program under real-world conditions and compared outcomes with publicly available clinical research data for semaglutide and tirzepatide.

Study Design:
The methodological framework for assessing the efficacy of Trimsulin in weight management was modeled after the protocols used in semaglutide GLP-1RA and tirzepatide GIP/GLP-1RA studies. Metrics collected included demographic data, racial background, height, waist circumference, baseline weight, BMI, monthly weight changes, and adverse event reporting. A total of 503 subjects were monitored.

Endpoints and Assessments

- **Primary Endpoints:**
    - The percentage change in body weight from baseline at week 12 and week 24 in overweight participants.
    - A comparison of the monthly weight loss percentage between Trimsulin, semaglutide, and tirzepatide, using weight loss data cited from the study by Rodriguez et al.[9]
    - A comparison of the rate of all adverse and gastrointestinal events between Trimsulin, semaglutide, and tirzepatide using reported adverse effects study data for semaglutide[8-11] and tirzepatide.[12-15]

Trimsulin Study Participants

- Initial weights of Trimsulin subjects ranged from 130 lbs to 360 lbs, with an average of 201.2 lbs.
- The duration of Trimsulin use ranged from 3 to 10 months, with an average of 5.4 months.
- Trimsulin subjects' BMI ranged from 20 to 50.1, with an average BMI of 27.5.

Semaglutide and Tirzepatide Weight Loss Research Data

- Weight loss study data for semaglutide and tirzepatide were collected from a large cohort of patients with overweight and obesity who initiated treatment between May 2022 and September 2023.
- This study cited a subset of Truveta weight loss data comparing semaglutide to tirzepatide from a collective of U.S. healthcare systems published in JAMA International in 2024.
- Data was normalized into a standard data model through syntactic and semantic normalization.

Semaglutide and Tirzepatide Adverse Effect Event Data:

- Adverse effect event data was based on a systematic review with meta-analysis of different databases (PubMed, Embase, CINAHL, Scopus, and Web of Science) for clinical trials reporting adverse events related to semaglutide and tirzepatide.
- Data was normalized into a standard data model through syntactic and semantic normalization

Results

Table 1: Comparative Weight Loss After 3 and 6 Months

Duration	Trimsulin	Semaglutide	Tirzepatide
3 Months	7.3%	3.6%	5.9%
6 Months	14.1%	5.8%	10.1%

After three months, Trimsulin participants experienced more than double the average weight loss reported in published semaglutide data and substantially greater weight loss than outcomes reported for tirzepatide. After six months, Trimsulin participants demonstrated more than double the average weight loss reported in published semaglutide data and greater average weight loss than outcomes reported for tirzepatide.

Adverse Effects of Trimsulin

Table 2 presents the adverse event rates among Trimsulin users.

Table 2:
Adverse Events for Trimsulin Users

Adverse Event	Percentage (%)
Any adverse effect	4.8%
Gastrointestinal disorder	2.9%
Nausea	2.1%
Loose stools	2.5%
Gastritis	1.0%
Insomnia	4.3%

Table 3:
Comparative Adverse Event Rates After 3 and 6 Months

Adverse Event	Trimsulin (%)	Semaglutide (%)[8-11]	Tirzepatide (%)[12-15]
Any adverse effect	4.8%	89.7%	81.0%
Gastrointestinal disorder	2.9%	59.7%	46.0%
Nausea	2.1%	44.2%	35.5%
Vomiting	0.0%	24.8%	16.4%
Diarrhea	2.5%	29.7%	21.1%
Headache	0.0%	22.7%	21.4%
Serious adverse effect	0.0%	3.0%	5-7%

Adverse event data for semaglutide and tirzepatide were derived from published clinical trials and meta-analyses, which typically capture adverse events more comprehensively than observational cohort reporting.

Serious adverse effects were reported in semaglutide and tirzepatide patients, including pancreatitis, gallbladder disease, bowel obstructions, kidney complications, psychiatric problems, and cardiovascular disorders. These adverse effects significantly impact tolerability and compliance, sometimes leading to discontinuation. Trimsulin subjects experienced fewer adverse events, with no reports of serious side effects compared to those taking semaglutide and tirzepatide.

Discussion

This study is the first to compare the effectiveness and safety of a non-pharmaceutical, nutraceutical composition comprised of endogenous GLP-1 and GIP releasers combined with natural DPP-4 inhibitors and thermogenesis activators against pharmaceutical GLP-1RAs and dual GIP/GLP-1RAs in humans. Differences in study design, participant populations, and reporting methods between the Trimsulin cohort and pharmaceutical clinical trials should be considered when interpreting comparative outcomes. The results suggest that participants following the Trimsulin Weight Loss Program achieved greater average weight loss compared with outcomes reported in published research on semaglutide and tirzepatide.

Pharmaceutical GLP-1RAs, such as semaglutide, and dual GIP/GLP-1RAs, like tirzepatide, act directly on peripheral GLP-1 receptors and central nervous system receptors, leading to significant gastrointestinal side effects. In contrast, endogenous GLP-1 and GIP releasers, like those in Trimsulin, trigger natural pathways to elevate GLP-1 and GIP levels, resulting in similar effects without causing the severe gastrointestinal discomfort frequently seen with pharmaceutical agents.

The significantly lower adverse effect profile of Trimsulin may be attributed to its indirect mechanism of action, which mimics natural hormone release rather than overstimulating receptors. Another factor to consider is daily oral administration versus weekly injections. This suggests Trimsulin's potential as a safer method for weight loss interventions, particularly for those who cannot tolerate the side effects of GLP-1RA medications.

The observed rapid weight loss associated with Trimsulin administration likely results from the synergistic activation of various molecular components across multiple cellular signaling pathways. According to research, these pathways are integral to regulating diabetes, appetite, glycemic control, lipid storage, and overall energy expenditure.[18]

Some of the key signaling pathways involved include:

- Insulin/Insulin Receptor Substrate (IRS) Pathway: This pathway plays a critical role in glucose metabolism, insulin sensitivity, and fat storage.

- Adipokine Signaling: Adipokines are hormones released from adipose tissue that influence inflammation and metabolism, which are crucial in weight management.

- Sirtuin1-AMPK Pathway: Known for regulating energy metabolism, this pathway promotes fat breakdown and improves metabolic health.

- AMPK & mTOR Pathways: These pathways are vital for energy balance and cellular growth, particularly under conditions of low energy availability.

- Inflammatory Pathways & PPARs: Modulation of inflammatory pathways can reduce chronic inflammation associated with obesity. PPARs (Peroxisome Proliferator-Activated Receptors) are nuclear receptors that regulate fat storage and glucose metabolism.

- PKG Signaling & Gut Hormones: These are important for maintaining energy balance and modulating gut hormones like GLP-1 and GIP.

- β_3-Adrenergic Signaling and Ob-R/JAK2 Complex: Both pathways are involved in fat breakdown and energy regulation in adipose tissues, playing a significant role in weight reduction.

Components of Trimsulin's nutraceutical formula, including phytochemicals, minerals, flavonoids, fibers, and sweeteners, have demonstrated the ability to modulate these pathways. For example, certain compounds in Trimsulin improve insulin sensitivity, reduce leptin resistance, and suppress ghrelin levels, all contributing to its effectiveness in weight reduction. The cumulative effect of these modulated pathways provides a comprehensive approach to weight management, suggesting that Trimsulin may represent an alternative approach to weight management compared with currently available pharmaceutical therapies.

Conclusion

Overweight adults following the Trimsulin Weight Loss Program experienced substantial weight loss and a low rate of reported adverse effects within the observed cohort. The weight loss results achieved with Trimsulin, and its minimal side effect profile underscores its potential as a safer approach to weight management. Trimsulin's natural mechanism, which stimulates endogenous GLP-1 and GIP release while inhibiting DPP-4, offers a strategy that aligns more closely with the body's natural metabolic processes.

Furthermore, Trimsulin's non-pharmaceutical nutraceutical composition eliminates the need for frequent injections, improving patient compliance and long-term adherence. This suggests that Trimsulin could be valuable in the management of overweight adults, especially for individuals who are intolerant of or unwilling to use pharmacological agents. Additional studies on more extensive and diverse populations are needed to validate these findings and explore broader applications.

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About the Author

Richard Clark Kaufman, Ph.D. is an innovative scientist, visionary thinker, and respected leader in the fields of healthcare and nanotechnology. As a researcher, inventor, and product formulator, Dr. Kaufman has consulted with leading healthcare companies worldwide and delivered countless lectures on advanced nanoparticle delivery systems, anti-aging, and wellness.

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