



# Acute Effect of a Proprietary Blend Containing L-Arginine and Antioxidants on GLP-1 Release

Katie Harnen BS<sup>1\*</sup>, Shannon Matthews<sup>2</sup>, Olivia Landis<sup>1</sup>, Ashlyn Dooley<sup>2</sup>, Anne George<sup>2</sup>, Isabella Jose<sup>2</sup>, Matthew Loritz<sup>1</sup>, Jenna Chrabolowski, Sarah-McKinley Barnard PhD<sup>2</sup>, Ryan Porter PhD<sup>2#</sup>, and Elisa Marroquin PhD<sup>1#</sup>



<sup>1</sup>Department of Nutritional Sciences, Texas Christian University, Fort Worth, TX

<sup>2</sup>Department of Kinesiology, Texas Christian University, Fort Worth, TX

\*presenting author, #corresponding authors

## Abstract

**Background:** Glucagon-like peptide 1 (GLP-1) is a key gut hormone regulating glucose homeostasis and satiety. This triple-blind, crossover, placebo-controlled randomized study investigated the effect of an L-Arginine-based supplement on active GLP-1 secretion, appetite, and food intake.

**Methods:** Sixteen participants (N=16) completed three conditions: a placebo and two doses of the supplement (Low-Dose, 5g; High-Dose, 10g). Supplements were consumed at time 0, and an *ad libitum* meal was consumed at 60 minutes. Serum samples were collected at eight time points over 120 minutes to assess circulating active GLP-1 levels.

**Results:** Supplementation with L-Arginine significantly augmented circulating GLP-1 levels compared to the control condition. Both doses triggered an immediate, transient rise in GLP-1, followed by a robust and significantly enhanced post-meal response relative to placebo. Analysis of the Area Under the Curve (AUC) confirmed this finding: total GLP-1 exposure was 607% greater in the High-Dose group (~340n pg/ml/min,  $p < 0.0001$ ) and 544% greater in the Low-Dose group (~130 pg/ml/min,  $p = 0.0076$ ) compared to placebo (~50 pg/ml/min). No significant differences in GLP-1 concentrations were observed between the two supplement doses. Secondary analyses found no differences in subsequent food intake or subjective hunger ratings between conditions, a result likely limited by the study's power for these secondary variables ( $\eta^2 \sim 0.023$ ).

**Conclusions:** L-Arginine is a potent secretagogue for GLP-1. These findings demonstrate that supplementation significantly increases the body's overall exposure to this crucial gut hormone, suggesting a potential role for L-Arginine in supporting metabolic health.

## Background

Glucagon-like peptide 1 (GLP-1) is a hormone that regulates glucose homeostasis and promotes satiety. L-Arginine has previously shown to elevate both GLP-1 levels, which correlated with improved glucose tolerance and reduced energy intake.<sup>1</sup> The 10g dosage used in this study is based on previous research confirming the safety of daily L-Arginine consumption.<sup>2</sup>

The supplement includes co-ingredients designed for synergistic enhancement of GLP-1 activity: 1) Resveratrol, to enhance GLP-1's activity by inhibiting DPP-IV, the enzyme that degrades the GLP-1<sup>3</sup>; 2) Tart Cherry to inhibit arginase activity, thereby increasing L-Arginine's availability for GLP-1 production<sup>4,5</sup>; 3) Vitamin C to reduce oxidative stress and increase the hormone's independent antioxidant capacity.<sup>6</sup>

Therefore, this study aims to quantify in a population with overweight or obesity, the acute effect of this multi-component formulation on GLP-1 secretion, appetite and meal intake.

## Objectives

To assess the impact of an L-Arginine-based supplement on post-prandial GLP-1 release, satiety, and meal intake.

## Methods

### Study Design:

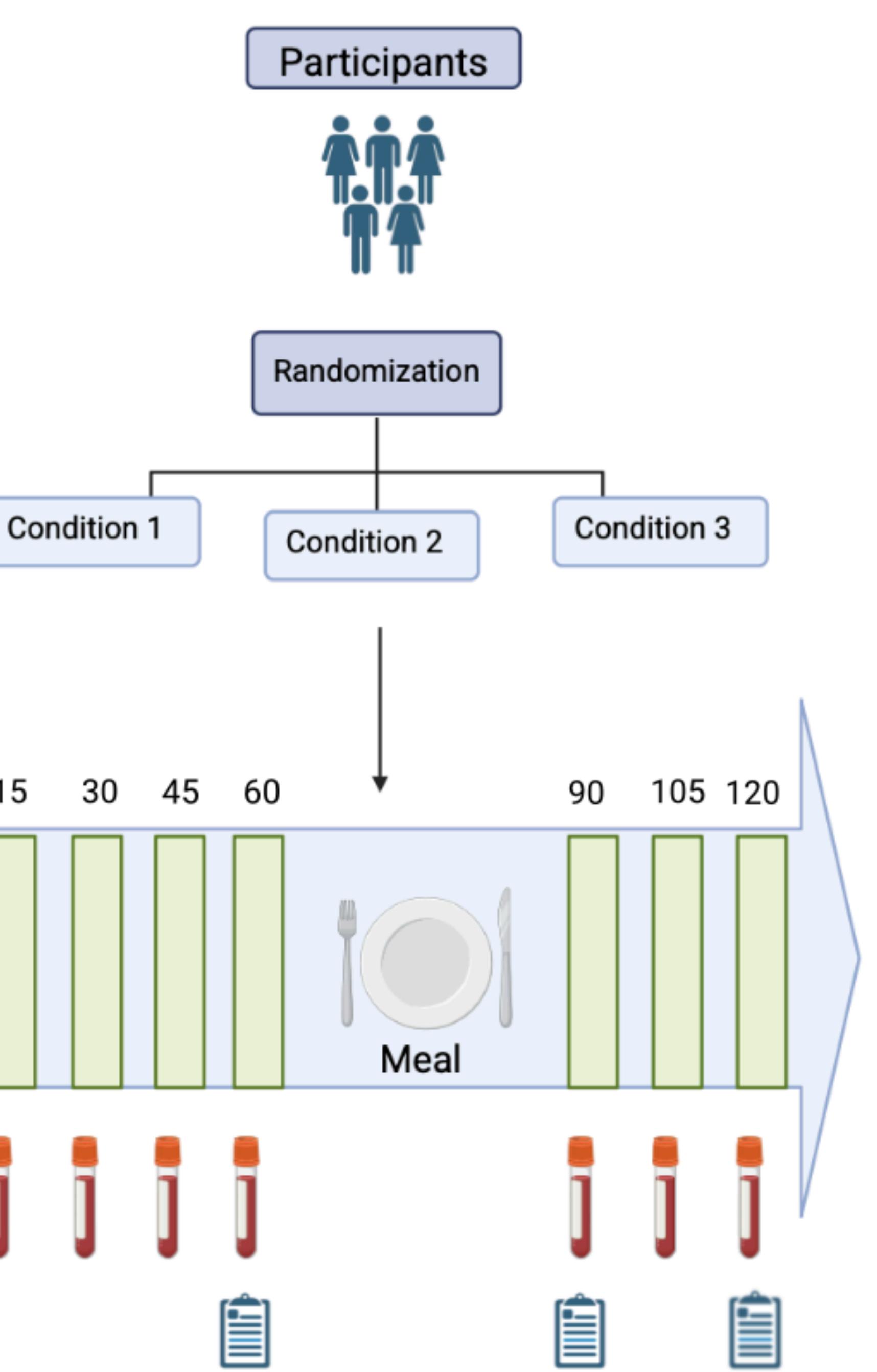
Randomized crossover trial

**Participants:** 16 participants aged 18-60 years old with a BMI between 25 and 40 kg/m<sup>2</sup>, willing to stick to their current diet and physical activity regime.

**Intervention:** Participants underwent the three conditions (placebo, low dose supplement, or high dose supplement) in a random order separated by a washing period of 1 week. The supplement was provided after baseline sampling and an *ad libitum* meal was provided at 60 min.

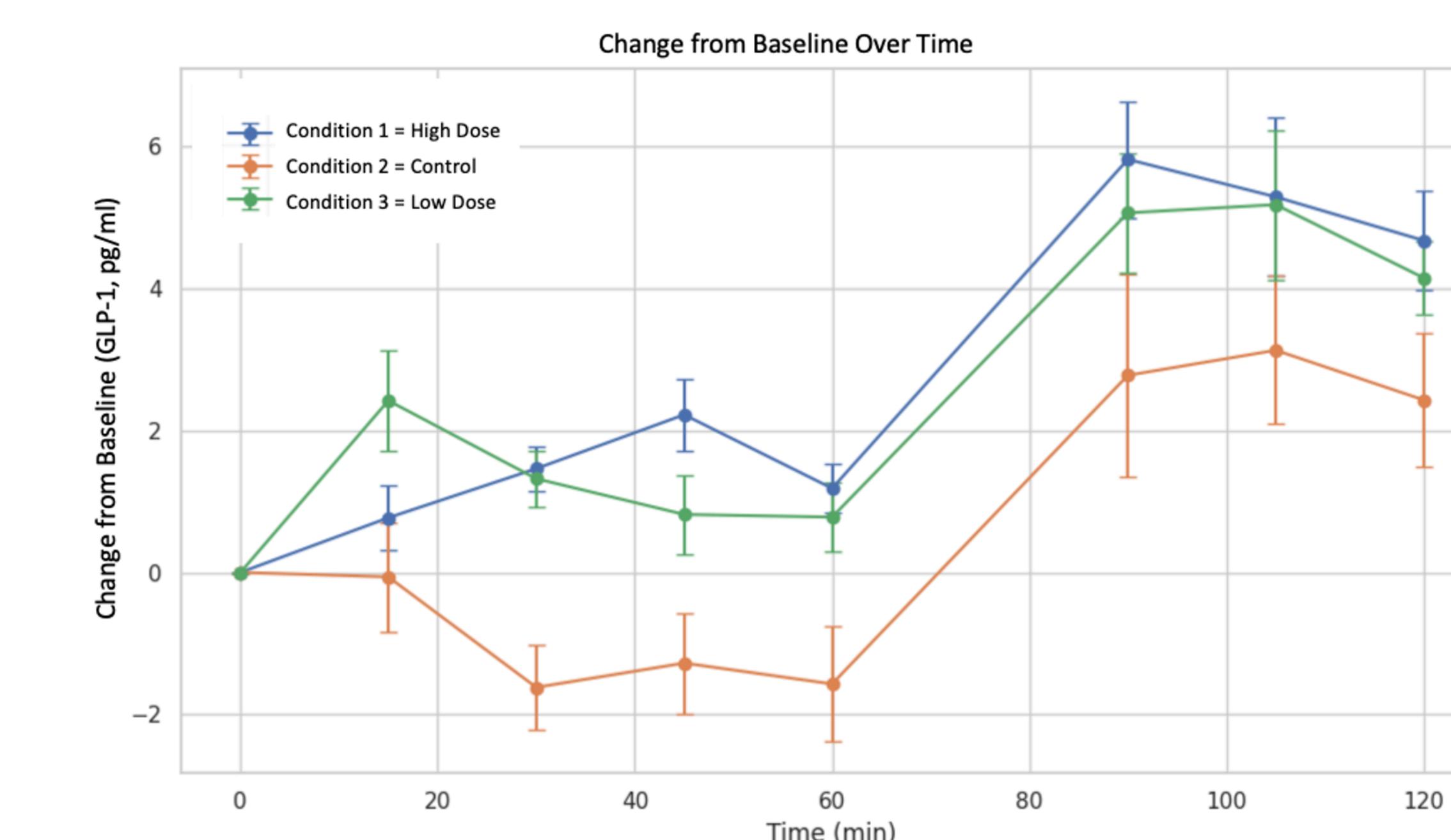
### Measured Outcomes:

- GLP-1 was measured at 8 time points (baseline, 15, 30, 45, 60, 90, 105, and 120 minutes after the supplement ingestion).
- Satiety rating was measured at baseline, 60, 90, and 120 min.
- Meal weight was measured before and after meal ingestion.

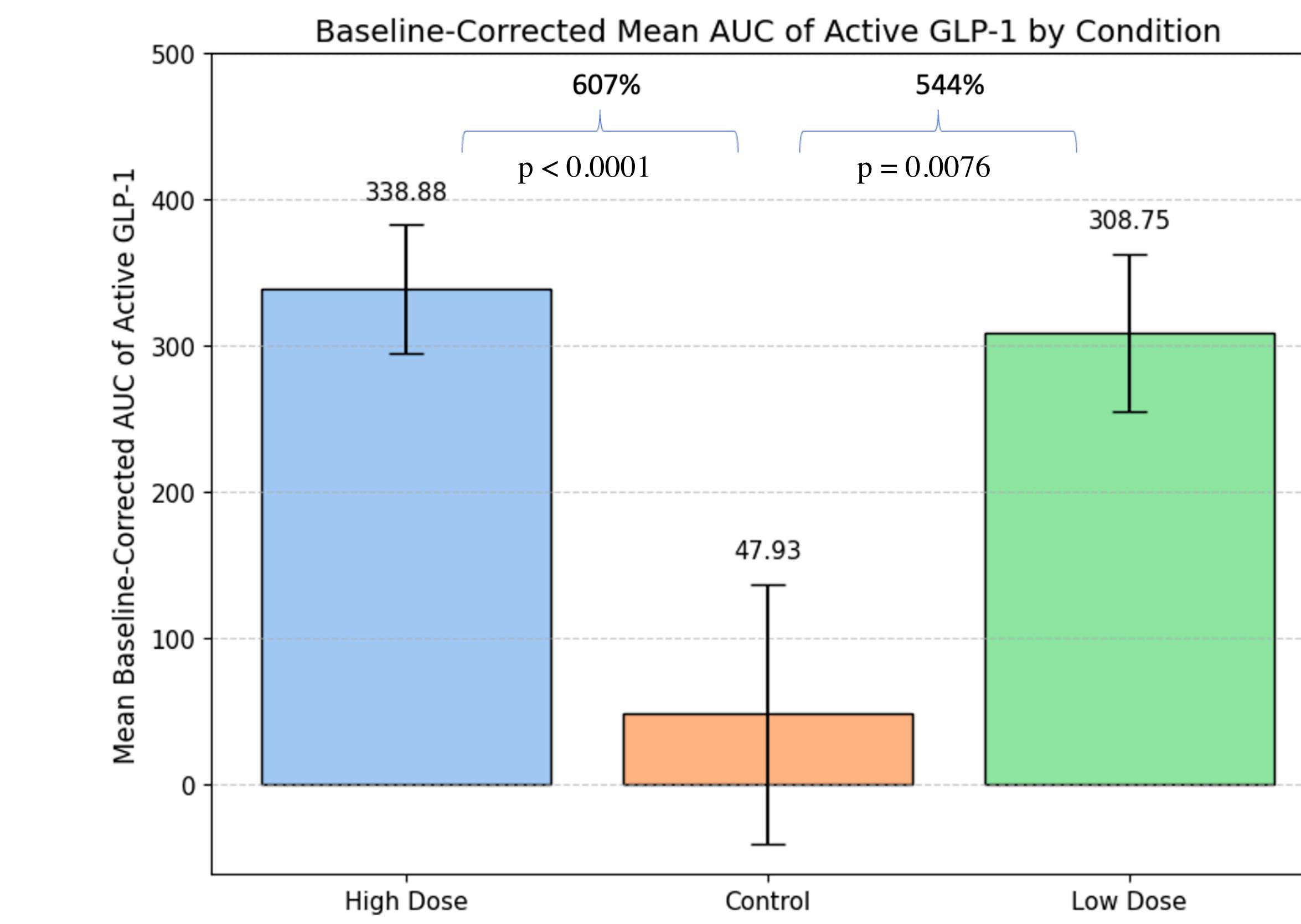


**Figure 1. Conceptual Framework.** This figure illustrates the structure of the randomized, controlled crossover trial. Participants blindly received 3 treatments: a high-dose supplement, a low-dose supplement, and a placebo in a randomized sequence. A washout period of 1 week was enforced between treatments. The primary endpoints (active GLP-1 secretion, meal intake, and satiety) were measured following the administration of each intervention.

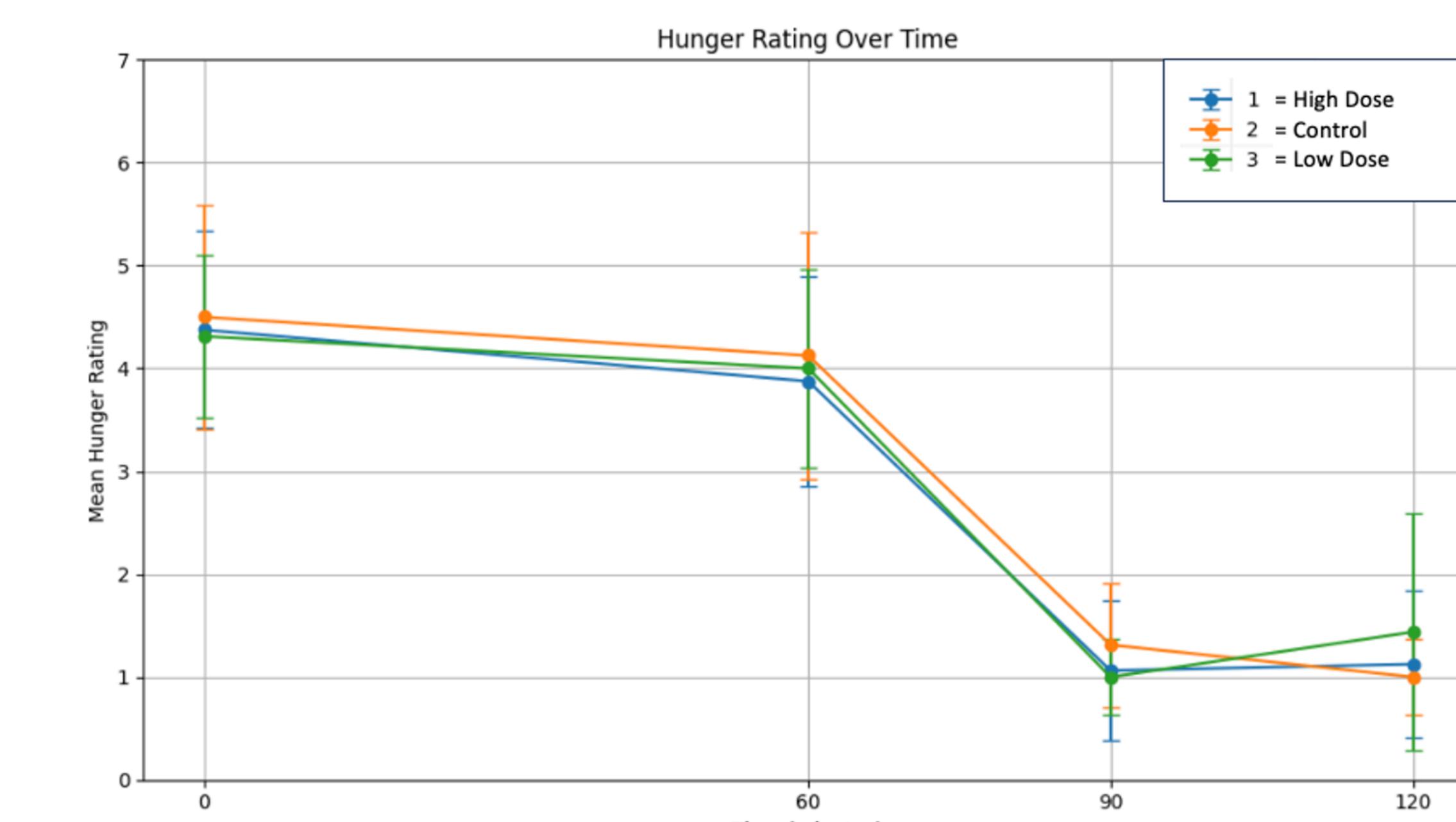
## Results



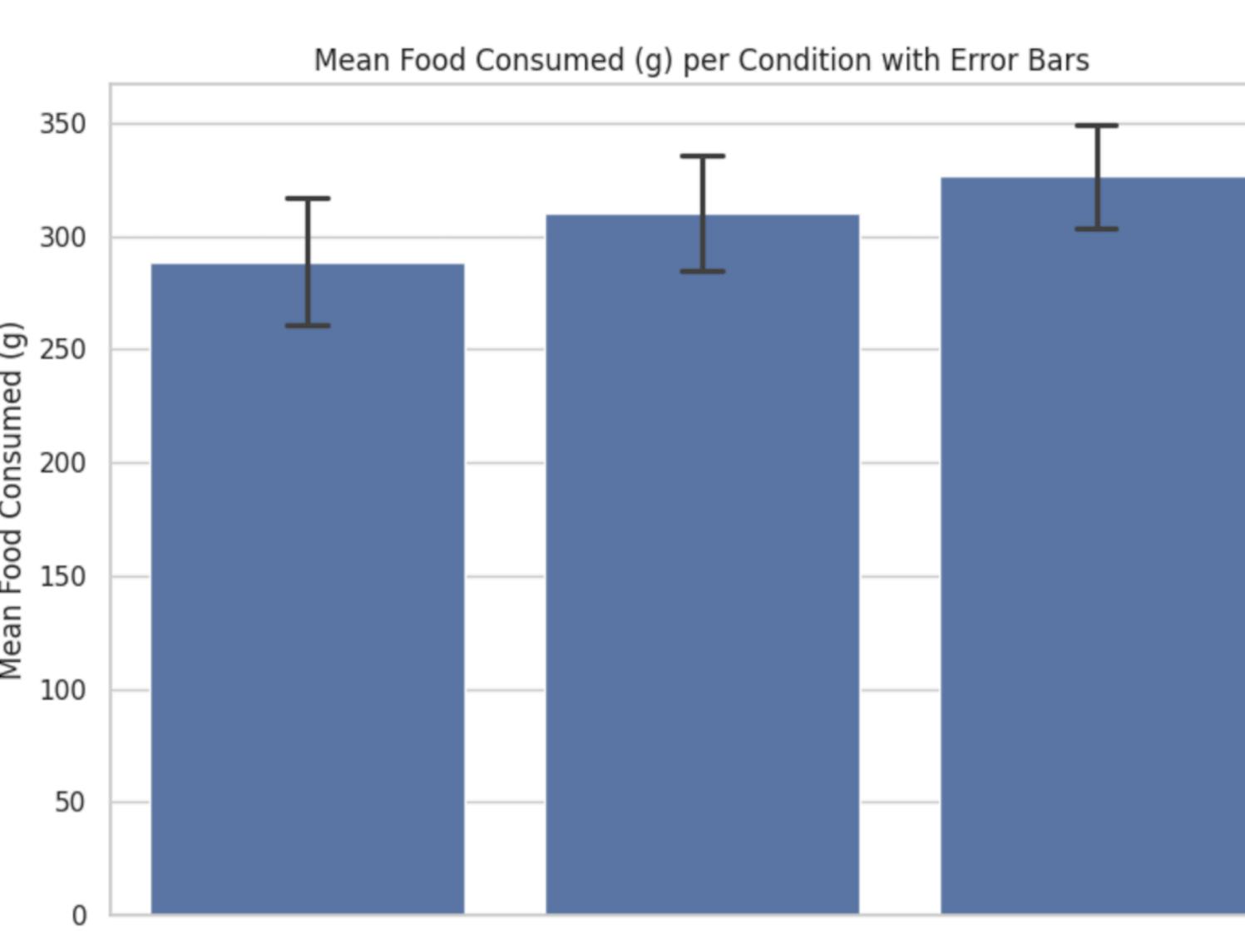
**Figure 2. Change from Baseline in Active GLP-1 (pg/mL).** The baseline-adjusted analysis demonstrates that both low and high doses of the L-Arginine-based supplement resulted in significantly increased GLP-1 levels compared to the control condition.



**Figure 3. Baseline-Adjusted Area Under the Curve (AUC) for Active GLP-1 (pg·min/ml).** The AUC demonstrates a 607% greater GLP-1 AUC in the high-dose group relative to control ( $p < 0.0001$ ) and a 544% greater AUC in the low-dose group relative to control ( $p = 0.0076$ ).



**Figure 4. Change in Hunger Ratings over Time.** Hunger ratings decreased following meal consumption with no significant differences between the three conditions ( $p > 0.05$ ).



**Figure 5. Mean Food Consumed (g) Across Conditions.** Mean food intake during the test meal showed no statistical differences among the three conditions ( $p = 0.102$ ).

## Conclusions

This study confirms that both low and high doses of the L-Arginine-based supplement significantly augment the body's overall exposure to active GLP-1 (up to 607% greater AUC), validating L-Arginine as a robust GLP-1 secretagogue. Although the high circulating GLP-1 did not translate into immediate, measurable differences in food intake or subjective hunger, the success in boosting this crucial gut hormone suggests its strong potential for use in dietary strategies aimed at improving glucose control. Future trials must be powered specifically to detect the expected small-to-moderate effects on appetite regulation and should also seek to study the effect of this supplement on glucose metabolism.

## References

1. Clemmensen C, Smajilovic S, Smith EP, Woods SC, Bräuner-Osborne H, Seeley RJ, D'Alessio DA, Ryan KK. Oral L-arginine stimulates GLP-1 secretion to improve glucose tolerance in male mice. *Endocrinology*. 2013 Nov;154(11):3978-83. doi: 10.1210/en.2013-1529. Epub 2013 Aug 19. PMID: 23959939; PMCID: PMC3800753.
2. Ryan T, Hurt J, O'Elbert, Darrell R, Schroeder, Ivana T, Croghan, Brent A, Bauer, Stephen A, McClave, John M, Miles & Craig J, McClain (2014) L-Arginine for the Treatment of Centrally Obese Subjects: A Pilot Study. *Journal of Dietary Supplements*, 11:1, 40-52, DOI: 10.3109/193902113.859216
3. Huang PK, Lin SR, Chang CH, Tsai MJ, Lee DN, Weng CF. Natural phenolic compounds potentially hypoglycemia via inhibition of Dipeptidyl peptidase IV. *Sci Rep*. 2019 Oct 30;9(1):15585. doi: 10.1038/s41598-019-52088-7. PMID: 31666589; PMCID: PMC6821704.
4. Bordage S, Pham TN, Zedet A, Guggiari Metti AS, Nappey M, Demougeot C, Girard-Therrien C. Investigation of Mammal Arginase Inhibitory Properties of Natural Ubiquitous Polyphenols by Using an Optimized Colorimetric Microplate Assay. *Planta Med*. 2017 May;83(7):647-653. doi: 10.1055/s-0042-118711. Epub 2016 Oct 24. PMID: 27776374.
5. Kim DW, Jung DH, Sung J, Min IS, Lee SJ. Tart Cherry Extract Containing Chlorogenic Acid, Quercetin, and Kaempferol Inhibits the Mitochondrial Apoptotic Cell Death Elicited by Airborne PM<sub>10</sub> in Human Epidermal Keratinocytes. *Antioxidants (Basel)*. 2021 Mar 13;10(3):445. doi: 10.3390/antiox10030443. PMID: 33805724; PMCID: PMC8001120.
6. Cericello A, Novials A, Ortega E, Canivell S, Pujadas G, La Sala L, Bucciarelli L, Rondinelli M, Genovese S. Vitamin C further improves the protective effect of GLP-1 on the ischaemia-reperfusion-like effect induced by hyperglycemia post-hypoglycemia in type 1 diabetes. *Cardiovasc Diabetol*. 2013 Jun 27;12:97. doi: 10.1186/1475-2840-12-97. PMID: 23806096; PMCID: PMC3699412.