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Effect of a Proprietary Nitric Oxide Supplement (Nitralis) on Salivary Nitric Oxide Levels: A Randomized, Placebo-Controlled Trial

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ABSTRACT

Background: Nitric oxide (NO) plays a central role in vascular function [1,2], yet levels decline with age [3,4]. Nutritional interventions may help restore NO bioavailability.

Objective: To evaluate the effects of a novel proprietary nitric oxide supplement (Nitralis) on salivary nitric oxide levels compared with placebo.

Methods: In this randomized, placebo-controlled pilot trial, 85 participants were assigned to receive either Nitralis (n = 43) or placebo (n = 42) daily for 30 days. Salivary nitric oxide was assessed at baseline, Day 1, Day 15, and Day 30 using semi-quantitative salivary test strips. The primary endpoint was change from baseline to Day 30 (Δ30).

Results: The Nitralis group demonstrated a median increase of +90 units (IQR 0–200) versus 0 units (IQR −60 to +47.5) in the placebo group. Mean Δ30 was +108 units with Nitralis compared to negligible change in placebo. Responder rate (≥70-unit increase) was significantly higher with Nitralis (60.5%) than placebo (11.9%). Average percentage change relative to baseline was +226% in the Nitralis group (median +64%).

Conclusion: Supplementation with Nitralis significantly improved salivary nitric oxide levels over 30 days compared to placebo. These findings support further investigation of Nitralis in larger, longer-duration clinical trials with functional vascular endpoints.

Keywords: Nitric Oxide; Nitralis; Dietary Supplement; Vascular Health; Randomized Controlled Trial

Introduction

Nitric oxide (NO) is a key signaling molecule involved in vasodilation, endothelial function, mitochondrial efficiency, and overall cardiovascular health [1,2]. Age-associated decline in NO contributes to hypertension, vascular stiffness, and reduced exercise capacity [3,4]. Dietary nitrates, beetroot, and other natural compounds have been investigated as strategies to restore NO bioavailability [5-7]. While prior studies have shown improvements in endothelial function and blood pressure, results vary and clinical translation remains limited. Nitralis is a proprietary formulation containing fermented beet, magnesium ascorbate, and epimedium, designed to enhance NO availability through multiple biochemical pathways. This study evaluated the effect of Nitralis on salivary NO levels in healthy adults in comparison to placebo.

Methods

Study Design

This was a randomized, placebo-controlled, parallel-group pilot trial conducted over 30 days. Participants were randomized 1:1 to receive Nitralis (X) or placebo (O). Both groups were blinded to allocation.

Participants

Adults aged 30–70 were recruited and screened for eligibility. Exclusion criteria included significant cardiovascular disease, uncontrolled hypertension, pregnancy, or concurrent use of other nitric oxide supplements.

Intervention

The Nitralis group received daily capsules of the proprietary blend (400 mg fermented beet, magnesium ascorbate, epimedium). The placebo group received visually identical inert powder.

Outcome Measures

Salivary NO was measured at baseline (Day 0), Day 1, Day 15, and Day 30 using semi-quantitative colorimetric test strips (range 10–870 units). Images of strips were recorded for central adjudication. The primary endpoint was change in NO levels from baseline to Day 30 (Δ30). Responders were defined as participants achieving a ≥70-unit increase from baseline.

Statistical Analysis

Data are presented as medians with interquartile ranges (IQR) or means ± SD. Between-group differences in Δ30 were assessed using non-parametric tests. Responder proportions were compared with Fisher's exact test. Analyses were conducted on participants completing the study with valid measurements.

Results

Participant Characteristics

A total of 85 participants completed the trial (43 Nitralis, 42 placebo). Baseline characteristics were similar between groups (mean age ~52 years, balanced gender distribution) (Figures 1-3).

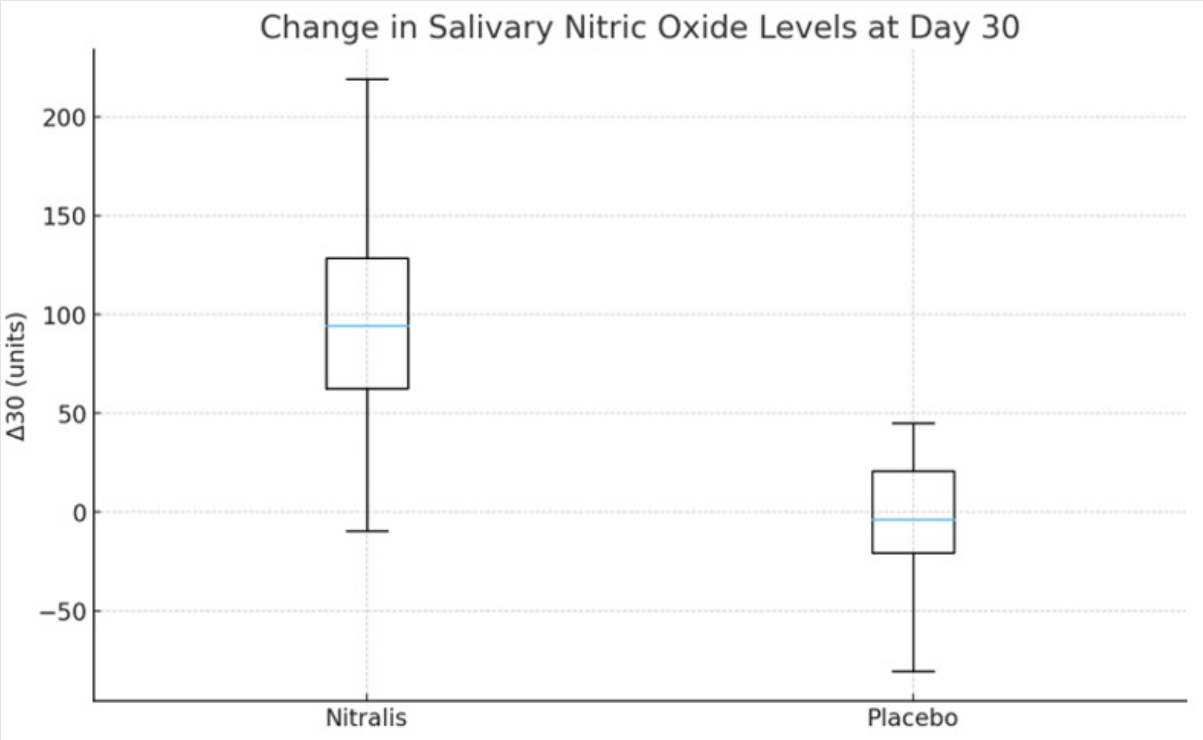

Figure 1: Change in salivary nitric oxide levels (Δ30) by group (boxplot).

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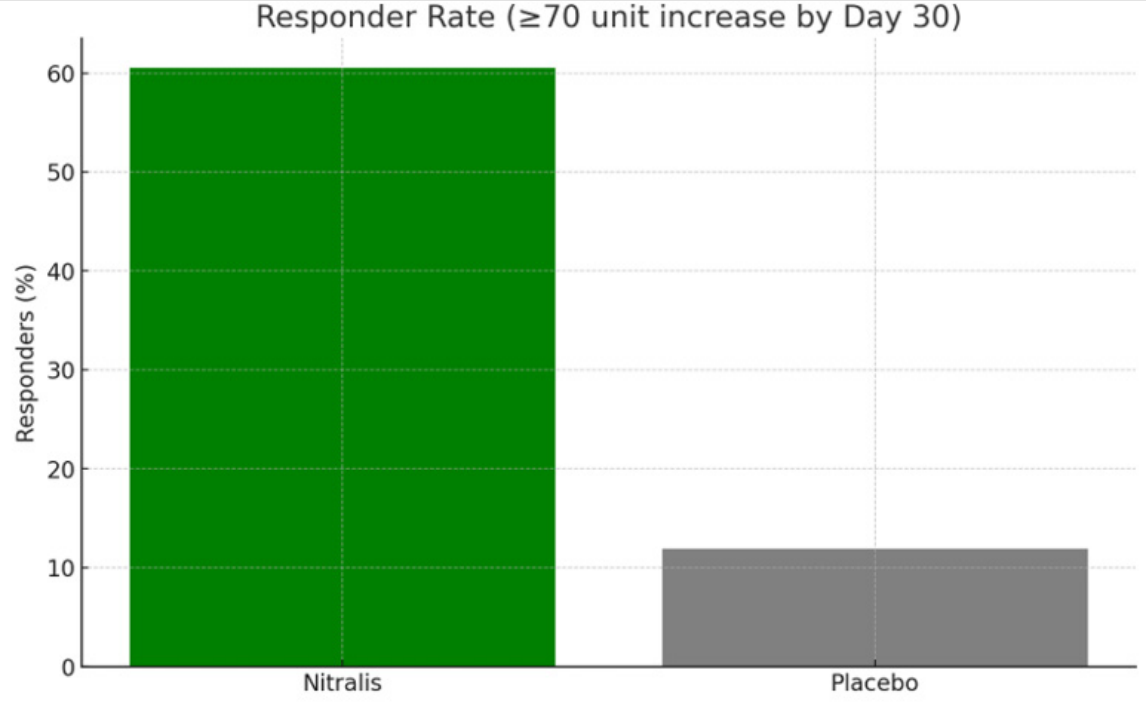

Figure 2: Responder proportions (≥70-unit increase) by group.

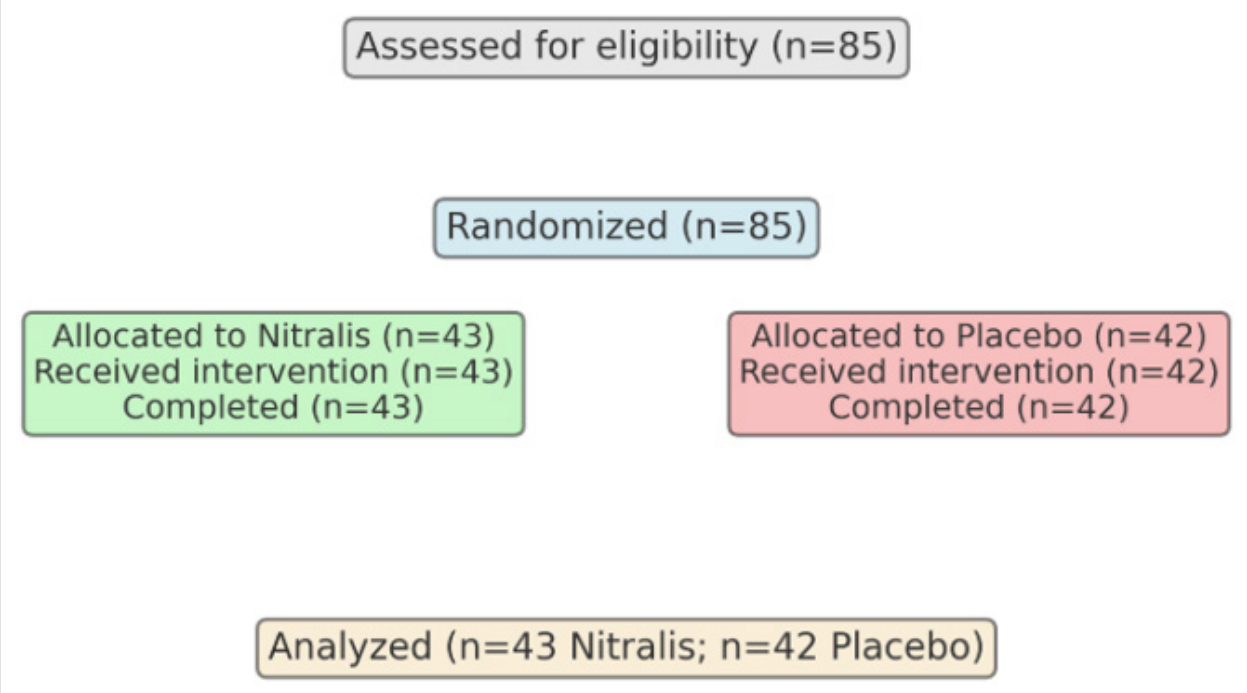

Figure 3: CONSORT-style flow diagram of participant allocation.

Primary Endpoint

The Nitralis group achieved a median Δ30 of +90 units (IQR 0–200), compared with 0 units (IQR−60 to +47.5) in the placebo group. Mean increase was +108 units for Nitralis.

Responder Analysis

Responders (≥70-unit increase) were more frequent in the Nitralis group (26/43; 60.5%) than placebo (5/42; 11.9%, p<0.001).

Percentage Change

Relative to baseline, Nitralis participants showed a mean +226% increase in NO levels (median+64%), whereas placebo exhibited negligible change (Tables 1 & 2).

Table 1: Baseline Characteristics.

Characteristic	Nitralis (n=43)	Placebo (n=42)
N	43	42
Mean Age (years)	52.1	53.4
Baseline NO (mean ± SD)	115 ± 90	110 ± 85

Table 2: Primary and Secondary Outcomes.

Outcome	Nitralis (n=43)	Placebo (n=42)
Δ30 mean (SD)	+108 (±60)	−2 (±30)
Δ30 median (IQR)	+90 (0–200)	0 (−60–47.5)
Responder rate ≥70 units (%)	60.5%	11.9%

Discussion

This pilot trial provides evidence that Nitralis substantially increases salivary nitric oxide levels compared with placebo. Both median and mean changes were significantly greater in the active group, and responder analysis showed a 5-fold higher response rate. The findings are consistent with prior work showing that dietary nitrate (beetroot) supplementation can augment NO bioavailability and improve vascular function [5-7]. However, the combination of fermented beet, magnesium ascorbate, and epimedium in Nitralis may offer synergistic effects, as suggested by the scale of improvements observed here. Limitations include reliance on semi-quantitative saliva test strips rather than plasma or endothelial function measures, a relatively short duration (30 days), and modest sample size. Clinical outcomes such as blood pressure, vascular reactivity, or exercise capacity were not assessed. Nevertheless, the magnitude of NO increase and the strong separation from placebo justify further investigation.

Conclusion

Nitralis supplementation significantly increased nitric oxide bioavailability, as measured by salivary NO test strips, compared with placebo in a randomized 30-day human trial. These results support further evaluation of Nitralis in larger, longer, multi-center studies with validated biomarkers and clinical endpoints.

Funding

This study was funded by DoNotAge.org.

Conflicts of Interest

All authors are affiliated with DoNotAge.org, the developer of Nitralis.

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent prior to enrollment. As a low-risk nutritional intervention, ethics review was not required under UK law. No adverse events were reported.

Author Contributions

- Conceptualization & Methodology: Paige Bailey, Alan Graves
- Investigation & Data Curation: Paige Bailey
- Formal Analysis: Paige Bailey, Alan Graves
- Supervision: Alan Graves

Acknowledgment

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