Chronic Nitrate Supplementation on Biochemical and Hemodynamic Parameters of Individuals Presenting Risk Factors for Cardiovascular Diseases

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Red beetroot has a high nutrition value and is considered a source of bioactive compounds, such as NO3-, antioxidant substances and phenolic compounds. Beneficial effects of dietary NO3- ingestion on the cardiovascular system include stimulating vasodilation by relaxing vascular smooth muscles, regulating blood flow and reducing blood pressure (BP) in both normal and hypertensive individulas, and improving physical performance during endurance exercises were consistently demonstrated. These effects can be explained by beet NO3- content, which stimulates the synthesis of nitric oxide (NO). Dietary NO3- is reduced to nitrite (NO2-) in the oral cavity by the enzyme NO3- reductase in the acidic gastric environment, NO2- is non-enzymatically decomposed to NO and other nitrogen oxides, which promote the aforementioned beneficial health-effects. Beetroot dietary interventions can be performed in the form several formulations, such as drinking beetroot juice or eating beetroot chips or powder to provide a convenient and alternative source of beetroot instead of the consumption of the entire vegetable *in natura* while still reaching effective NO3- concentrations. The challenge to design a beet product enriched in NO3-, attractive and easy to administer has been overcome by a novel formulation associating beet juice and beet powder into a food product displaying high acceptability. Cereal bars have gained great popularity as healthy and nutritious food, and are formulated by the compaction of dehydrated fruits, vegetables and cereals, and can be enriched in nutrients, but in a small serving portion. Furthermore, cereal bars are easy to carry, can be stored at room temperature, and are well-tolerated.

OBJECTIVES

The aim of the present study was to design a new functional beetroot cereal bar and evaluate its suitability as a dietary intervention for NO3- supplementation. The in vitro accessibility of NO3-/ NO2-, phenolic compounds, total antioxidant potential at gastrointestinal digestion were simulated. The beet cereal bar (60g) was offered to five women displaying at least three risk factors for developing CVD, recruited in a 3-week randomized controlled crossover trial followed by biochemical and hemodynamic parameter assessments, such as NO synthesis, endothelial function, arterial stiffness and blood pressure.

MATERIALS

The beetroot-cereal bars were prepared by joining the ingredients of two phases, namely the binder (beetroot juice, brown sugar, corn glucose and citric acid) and dry (rolled oats, whole oats, rice flakes, beetroot powder) phases. NO3-/NO2- and phenolic contents were evaluated by HPLC. Soluble phenolics were extracted by ethanol and H2O-DD (80:20, v/v) and conjugate phenolics by alkaline and acid hydrolysis. Antioxidant capability was evaluated by TAP, FRAP, TEAC and ORAC assays and gastrointestinal digestion was simulated in vitro. Plasmatic NO2- and NO3-, biomarkers for NO availability, were determined by HPLC and, BP and HR were recorded using an automated Omron HEM-705CP sphygmomanometer. Endothelial function was evaluated using a laser speckle contrast imaging at 785 nm in a PeriCam PSI System. Arterial stiffness was evaluated by aplanation tonometry using SphygmoCor system and by the oscillometric method using the Arteriograph system. Pulse wave velocities (PWV) were evaluated using the Complior SP apparatus.

RESULTS

NO3- and NO2- beetroot-cereal bar contents were 9.57±0.13 and 0.26±0.13 mmol • 60 g-1 fresh weight bases (fwb), respectively. Decreases in NO3- content after oral (6 %) and gastric (15 %) digestion were observed, and a discrete increase in NO2- was noted after gastric and intestinal digestions. The total phenolic compounds in the beetroot-cereal bar comprised 146.88±5.16 mg • 60 g-1 fwb. Nine beetroot-cereal bar phenolic compounds were identified and quantified (60 g): 3,4-dihydroxybenzoic (9.97±0.21 mg), caffeic (5.94±1.08 mg), 5-caffeoylquinic (5.69±0.99 mg), ferulic (3.23±0.01 mg), gallic (60.50±0.19 mg), p-coumaric (39.68±0.11 mg), rosmarinic (4.25±0.76 mg), syringic (4.48±1.14 mg) and vanillic acids (13.14±0.67 mg). The release of total phenolic compounds from beetroot cereal bar after the gastric and intestinal digestions comprised 62% and 68%, accompanied by an increase in antioxidant activities. The TAP, FRAP and ORAC assays indicated decreases of 4%, 12% and 30%, respectively, after the intestinal digestion when compared to the gastric digestion. The NO availability test indicated increased plasmatic NO3- and NO2- concentrations after 3 weeks supplementation with beetroot-cereal bar (Post: 505.24±7.14 and 3.75±0.06 µmol • L-1), when compared to the baseline (Pre: 28.56±5.20 and 0.47±0.09 µmol • L-1) or placebo interventions (Pre: 25.11±2.30 and 0.52±0.06 µmol • L-1). Systolic BP and diastolic BP decreased after supplementation when compared to the baseline (Pre: 164.8±24.25 and 91.75±6.23 mm Hg; Post: 150.3±20.68 and 83.25±5.18 mm Hg). No changes in HR were observed after supplementation, although improvements in vascular parameters were noted. AIx, aoAIx and PWV were reduced by 15%, 10% and 13% when compared to the baseline and 18%, 12% and 11.5% when compared to the placebo intervention, respectively. Furthermore, cSBP, cDBP, aoSBP and aoPP were reduced after supplementation by 12%, 12.5%, 9% and 22% when compared to the baseline and 11%, 10%, 8% and 22.5% when compared to the placebo intervention, respectively. After the 3-week intervention, arterial age was reduced by 6 years when compared to the baseline and 5.5 years compared to placebo. No differences in the assessed vascular parameters were observed after the placebo intervention. Furthermore, endothelial function was improved as demonstrated by increased cutaneous microvascular conductance and perfusion, by 20% and 30% when compared to the baseline, and 17% and 50%, compared to the placebo intervention.

CONCLUSION

Beetroot-cereal bars can be considered a supportive dietary intervention to reduce the intermediate endpoint for CV events by aiding in the maintenance of healthy endothelial function through arterial stiffness and BP reduction. The chronic dietary intervention described herein was successful due to the attractiveness, convenience and high acceptance of the designed beetroot-cereal bar, guaranteeing long-term supplementation adherence and promoting the bioconversion of NO3- to NO, improving arterial stiffness and endothelial function in patients presenting risk factors for the development of CVD.

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