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## Dietary protein does not alleviate postprandial endothelial dysfunction in healthy elderly people with cardiometabolic risk factors – a randomized controlled crossover trial

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Dietary protein have been reported to reduce postprandial vascular endothelial dysfunction, an early marker of atherosclerosis<sup>(1)</sup>, but this could depend on amino acids content, such as e.g. arginine. Here we aimed to assess the effect of an optimized plant protein blend with high contents of leucine, arginine and cysteine on postprandial endothelial dysfunction as compared to milk protein and no protein addition.

In a randomized, double-blind, 3-period crossover (2-wk washout), controlled trial, we compared the postprandial vascular effects of a plant protein-based meal (PP) [1145 kcal; protein 15%E (43g); SFA 46% (58g); sucrose 16% (44g)] with a milk protein meal (MP) [1118 kcal; protein 15% (41g); SFA 46% (58g); sucrose 16% (44g)] and with a meal without protein (WP) [974 kcal; protein 3% (6g); SFA 53% (57g); sucrose 18% (44g)]. The trial was conducted in 29 healthy adults >65y presenting at least 2 risk factors among: dyslipidemia [plasma triglycerides > 150 mg/dL or HDL cholesterol under <50 mg/dL (female) or <40 mg/dL (male)]; elevated waist circumference [>88 cm (female) or >94 cm (male)]; hyperglycemia [100 <fasting glucose< 1.26 mg/dL]; hypertension [SBP > 130mmHg or DBP > 85 mmHg]. Postprandial vascular function was evaluated at fasting, 3 hours and 5 hours postprandially as brachial flowmediated dilation (FMD), hand microvascular reactivity (by Flowmetry Laser Doppler, FLD) and finger reactive hyperhemia index (RHI, using Peripheral Arterial Tonometry). Data were analyzed using mixed linear models with repeated measurements on volunteers for meal interventions and time of sampling (SAS). This trial was registered at clinicaltrials.gov as NCT04923555.

At the macrovascular level, as compared to fasting values, FMD decreased (P < 0.05) 3 hours [-0.15 percentage points (pp); 95% CI: -0.92 to 0.62pp] and 5 hours (-0.85 [-1.52; -0.17]) following meals. At the peripheral level, RHI also decreased with time (P < 0.01). At the microvascular level, only time to half after hyperemia (TH2) tended to vary postprandially (P = 0.0595) indicating a deleterious effect of HFHS meals on return time to homeostasis (fasting: 48.02 sec [40.24; 57.31]; 3 hours: 55.32 sec [46.99; 65.14]; 5 hours: 45.51 sec [38.64; 53.59]).

Overall, we found no effect of meal composition (PP, MP or WP) on postprandial changes in FMD (P = 0.7379), RHI score (P = 0.7379) 0.1177), AI 75 BPM (P = 0.7324), peak flow (P = 0.8126), AO/AH ratio (P = 0.3419) or TH2 (P = 0.5320).

In healthy adults over 65 years presenting cardiometabolic risk, adding dietary protein to a high saturated fat high sucrose challenge meal does not mitigate endothelial dysfunction, whatever the source of protein. This could be attributed to a weaker vascular response to the challenge in elderly volunteers resulting from metabolic inflexibility<sup>(2)</sup>, slower gastric emptying or lower fat absorption and antihypertensive drugs secondary effects<sup>(3)</sup>. This study suggests that literature findings in younger adults may not be transferable to the elderly.

## References

- 1. Charakida M, Masi S, Lüscher TF et al. (2010) Eur Heart J 31, 2854-61.
- Fewkes JJ, Kellow NJ, Cowan SF et al. (2022) J Clin Nutr 116, 699–729. Soenen S, Rayner CK, Horowitz M et al. (2015) Clin Geriatr 31, 339–53.