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## Associations between source-specific nitrate intakes and inflammation and cardiovascular risk factors

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There is growing interest in the role that dietary nitrate plays in cardiovascular health, with plant-sourced and animal-sourced nitrate showing potentially positive or negative effects. Inflammation is a key factor in the development and progression of atherosclerosis, a major contributor to cardiovascular disease (CVD). A recent review highlighted the potential of nitrate to modulate inflammatory processes.<sup>(1)</sup> However, research investigating the association between dietary nitrate intake from different sources (plant-sourced nitrate, nitrate-additive-permitted meat, and meat with naturally-occurring nitrate) and inflammation in humans is limited. This study aimed to investigate associations between source-dependent nitrate intake and inflammatory markers—namely lipoprotein-associated phospholipase A2 (Lp-PLA2) and high sensitivity C-reactive protein, (hs-CRP)—as well as traditional CVD risk factors. Among 100 non-smoking adults (mean age 49 ± 13 years, 31% male), cross-sectional associations between nitrate intakes from plant and animal sources (estimated from food frequency questionnaire data in combination with comprehensive food databases specifying food nitrate content)<sup>(2,3)</sup> and 1) Lp-PLA2 and hs-CRP measured in fasting plasma samples, and 2) blood lipid levels, blood pressure and waist circumference, were examined. Linear and logistic regression models were adjusted for sociodemographic, lifestyle and dietary confounders. Participants were classified as high-risk (either diagnosis of type 2 diabetes or two or more other CVD risk factors), or low-risk (normal health metrics and an absence of chronic disease). After adjusting for demographic and lifestyle confounders, a 1 standard deviation (SD) (95.73 mg/day) increment in plant-sourced nitrate intake was associated with a 0.191 SD lower LDL cholesterol ( $\beta = -0.191$ , 95% CI [-0.376, -0.004],  $p = 0.045$ ; equivalent to -0.21 mmol/L), but not with any of the other outcomes. In contrast, intakes of naturally occurring animal-sourced nitrate were not associated with any of the outcomes. A 1 SD (0.32 mg/day) increment in nitrate intake from additive-permitted meat-sources was associated with a 0.192 SD higher waist circumference ( $\beta = 0.192$ , [0.005, 0.380],  $p = 0.042$ ; equivalent to +1.29 cm) and a 0.208 SD lower HDL cholesterol ( $\beta = -0.208$ , [-0.362, -0.054],  $p = 0.009$ ; equivalent to -0.10 mmol/L), but not with LDL cholesterol, triglycerides, blood pressure, Lp-PLA2, or CRP. No clear differences between CVD risk groups were observed. In conclusion, while no associations were found between naturally occurring animal-sourced nitrate and inflammatory markers or any CVD risk factors, nitrate from additive-permitted meat-sources were negatively associated with waist circumference and HDL cholesterol, whereas plant-sourced nitrate showed favourable associations with LDL cholesterol.

### References

1. Raubenheimer K, Bondonno C, Blekkenhorst L *et al.* (2019) *Nutr Rev* 77(8), 584–599.
2. Zhong L, Blekkenhorst LC, Bondonno NP *et al.* (2022) *Food Chem* 394, 133411.
3. Zhong L, Blekkenhorst LC, Bondonno NP *et al.* (2022) *Mol Nutr Food Res* 66, e2100272.