Dark chocolate to treat peripheral artery diseases?

Thomas Kahan

Karolinska Institutet, Department of Clinical Sciences
Danderyd Hospital, Division of Cardiovascular Medicine,
Department of Cardiology, Danderyd University Hospital
Corporation
Stockholm, Sweden

Endothelial dysfunction, impaired generation of nitric oxide, oxidative stress, reduced glucose oxidation and accumulation of toxic metabolites are likely to contribute importantly to the reduced blood flow to peripheral skeletal muscle characteristic of intermittent claudication and other forms of peripheral arterial diseases¹. Nitric oxide is a vasodilatory molecule rapidly degraded by reactive oxygen species. Cocoa is rich on polyphenols and causes arterial vasodilatation by reducing oxidative stress and thus increasing the generation of nitric oxide. Dark chocolate is rich in cocoa and dark chocolate has been shown to induce arterial vasodilatation, which has been suggested to be mediated by an enhanced availability of nitric oxide².

Loffredo and co-workers set out to examine the acute effects of chocolate ingestion on endothelial function, assessed by forearm post-ischemic flow mediated vasodilatation, and on walking performance in patients with intermittent claudication. They randomized 20 patients with stable peripheral artery disease to single blind treatment with 40g of dark chocolate (containing at least 85% cocoa) or milk chocolate, and measured maximum walking distance and time by treadmill (3.5 km/h and 12% inclination), flow mediated vasodilatation, and various markers of oxidative stress before and 2 h after the ingestion of chocolate in a crossover design, with one week in between the two examinations³. Mean age was 69 years, one third were women, most patients were hypertensive and former smokers, and one third had diabetes. Primary outcomes were walking distance and flow mediated vasodilatation.

Dark chocolate increased maximum walking distance and time (from 111±64 to 122±61 m, and from 124±61 to 142±62 s, respectively; both $P < 0.001$) while no change was observed by milk chocolate (from 116±72 to 109±65 m, and from 124±60 to 125±64 s respectively; both $P \leq 0.01$ vs dark chocolate). Similarly, dark chocolate improved flow mediated vasodilatation (indicating improved endothelial function) more than milk chocolate ($P < 0.01$). Compared to milk chocolate, dark chocolate increased circulating polyphenols and reduced biomarkers of oxidative stress more (all $P < 0.001$). Furthermore, in a multivariable analysis the magnitude of change in oxidative stress after chocolate was independently related to the increase in walking distance ($P < 0.05$).

This study shows that dark chocolate can acutely (within 2 h) improve endothelial function and walking performance in patients with intermittent claudication. Milk chocolate had no such effects,

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suggesting that this beneficial effect may be a result of an enhanced availability of nitric oxide due to down-regulation of NOX2 mediated oxidative stress by polyphenols in dark chocolate. There are some limitations with this study. The study population was small and there was no placebo control. The authors only investigated acute effects following one single dose of chocolate. However, the results are supported by findings in fatty liver steatosis, where oxidative stress plays a pivotal role in inducing endothelial dysfunction and disease progression⁴. In those patients, the same authors reported that dark chocolate given for 14 days improved forearm flow mediated vasodilatation, increased circulating polyphenols and reduced biomarkers of oxidative stress more than milk chocolate. Whether long-term administration of dark chocolate may have beneficial effects on walking performance and symptoms in patients with peripheral arterial disease require further study.

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Thomas Kahan
thomas.kahan@sll.se

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