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Effect of betalain (betanin) supplementation on endothelial dysfunction and vascular tone in human umbilical vascular endothelial cells

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Cardiovascular disease (CVD) has become the leading cause of death in many western-industrialised countries and recent animal studies revealed that supplementation of betalain-rich foods may improve key vascular parameters[1,2]. Betalains are bioactive alkaloidal colour pigments that naturally occur in plants like beetroot and dragon fruit[3]. Using cell culture models, we aimed to determine the direct cause-and-effect and cardioprotective properties of beetroot-derived betanin (also known as one of the most common food dyes E162).

In this study, we employed two different experimental models namely: preventative and therapeutic models. The former is based on previous work[4] while the latter is a model we developed as a more physiologically possible alternative. In the preventative model, primary HUVECs were pre-treated with betanin (0·5–20 μM) before challenged with TNF-α (200 U/mL) to induce endothelial dysfunction followed by a second betanin treatment of the same concentration. In contrast, the therapeutic model does not utilise a pre-treatment phase. In brief, HUVECs were first subjected to TNF-α (200 U/mL) prior to a shorter treatment duration of betanin (0·5–20 μM). All experiments were done in quadruplicate and relative gene expression of vascular inflammatory biomarkers (ICAM-1, VCAM-1, and ET-1) were evaluated using real-time reverse-transcriptase quantitative Polymerase Chain Reaction (RT-qPCR).

We observed similar results in both models (Fig. 1a–c & Fig. 1d–f). Upon stimulation with TNF-α, all inflammatory genes were significantly upregulated. Treatment with betanin completely ameliorated this change but we observe no dose-dependent reaction.

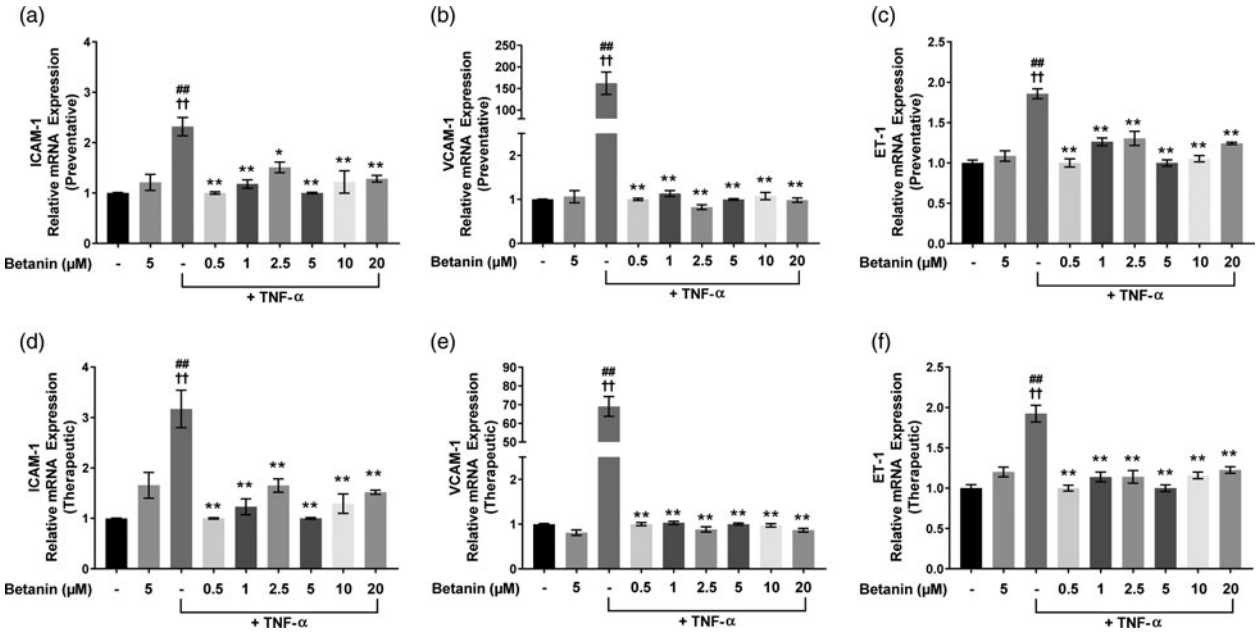

Fig. 1. Preventative model: Relative mRNA expression of (a) ICAM-1, (b) VCAM-1 and (c) ET-1. Therapeutic model: Relative mRNA expression of (d) ICAM-1, (e) VCAM-1 and (f) ET-1. Relative expression is calculated using formula $2^{-(\Delta\Delta Ct)}$ with control = 1. Data represented as means and SEM of 6 independent experiments (n = 4). $^{\#\#}p < 0{\cdot}0001$, vs. control; $^{\dagger\dagger}p < 0{\cdot}0001$, vs. betanin control (5 μM); $^{*}p < 0{\cdot}05$, $^{**}p < 0{\cdot}0001$, vs. TNF-α control (ANOVA, followed by Tukey's test)

Betanin's ability to downregulate ICAM-1 and VCAM-1 confirms its potential as a strong anti-atherogenic agent. Furthermore, it may also promote vasodilatation by suppressing ET-1 expression, consequently lowering blood pressure. Taken together, betanin may offer novel therapeutic options in the treatment and prevention of atherosclerosis and hypertension.

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