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Ageing is associated with increased endothelial sodium-glucose cotransporter 1 expression at arterial sites at risk promoting enhanced anthocyanin accumulation and improved vascular oxidative stress

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Introduction: Ageing is characterized by endothelial dysfunction and vascular oxidative stress affecting initially arterial sites at risk. Anthocyanin-rich products are potent stimulators of the endothelial formation of nitric oxide. Sodium-glucose co-transporter 1 (SGLT1) expression has been shown to be increased by oxidative stress and mediate anthocyanin uptake in endothelial cells.

Purpose: The study determined whether ageing is associated with an upregulation of SGLT1 in arteriosusceptible (aortic arch) and resistant (aorta) sites, and evaluated the vascular SGLT1-mediated anthocyanin uptake. In addition, the impact of a 2-week ingestion of an anthocyanin-rich blackcurrant concentrate (ARBC) by old rats on vascular anthocyanin uptake and oxidative stress, and systolic blood pressure (SBP) was assessed.

Methods: Male Wistar rats (22-month old) were either untreated or treated with ARBC (60 and 120 mg/kg/day) in the drinking water for 2 weeks. SGLT1 expression was assessed by immunofluorescence, anthocyanin accumulation by Neu A reagent using a purified extract (BCE) prepared from ARBC, oxidative stress by dihydroethidium using confocal microscopy, and SBP by tail-cuff sphygmonanometry.

Results: SGLT1 immunofluorescence was observed predominantly in the endothelium and was higher in the aortic arch than the aorta in old rats whereas only low levels were observed in young rats (12-week old). Exposure of vascular sections to BCE resulted in anthocyanin uptake exclusively in the endothelium, which was higher in the aortic arch than the aorta, and more pronounced in old than young rats. Anthocyanin uptake induced by BCE in the aorta was markedly reduced by LX4211 (a SGLT1/2 inhibitor) both in old and young rats. A high level of oxidative stress was observed throughout the aortic wall of old compared to young rats, which was inhibited by LX4211. Ingestion of ARBC by old rats resulted in a dose-dependent accumulation of anthocyanins throughout the aorta wall and the aortic arch. The tissue accumulation of anthocyanins was associated with a reduced level of oxidative stress. Ageing was associated with increased SBP by about 8 mmHg, which was reduced by ARBC 60 and 120 mg/kg/day treatment by about 5 and 7 mmHg, respectively.

Conclusion: The present findings indicate that ageing is associated with an upregulation of SGLT1 predominantly in the endothelium and that this effect is more pronounced at the aortic arch than the aorta. The increased endothelial expression level of SGLT1 promoted a greater accumulation of anthocyanins sensitive to LX4211. In addition, a 2-week ingestion of ARBC by old rats resulted in the accumulation of anthocyanins throughout the arterial wall of the aortic arch and aorta, and resulted in a reduced level of oxidative stress and systolic blood pressure. Thus, SGLT1 may be an attractive target to restore vascular protection at arterial sites at risk by promoting endothelial and vascular uptake of anthocyanins.