Xanthine Oxidase Inhibition by Febuxostat Attenuates Experimental Atherosclerosis in Mice

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Supplementary Figure S1

Febuxostat Inhibits Endothelial Dysfunction in ApoE^{-/-} Mice

Increased levels of ROS can react with nitric oxide to generate metabolites that result in endothelial dysfunction[1]. We therefore examined whether the inhibition of ROS generation by febuxostat had an effect on endothelial dysfunction in ApoE^{-/-} mice. ACh-responsiveness of aorta from ApoE^{-/-} mice was significantly reduced compared to that from WT mice, indicating endothelial dysfunction in aorta of ApoE^{-/-} mice. Treatment with febuxostat for 12 weeks significantly improved ACh-responsiveness in ApoE^{-/-} mice. On the other hand, SNP-induced relaxation and PE-induced contraction were not affected by febuxostat treatment. Altogether, these data suggest that the increased XOR and subsequent oxidative stress in endothelial cells, cause endothelial dysfunction.

Supplementary Figure S1. Febuxostat inhibits endothelial dysfunction in ApoE^{-/-} mice.

a, Endothelial cell-dependent relaxation to ACh in PE-precontracted aortic rings from vehicle-treated WT (n=8), vehicle-treated ApoE^{-/-} (n=9), and febuxostat-treated ApoE^{-/-} mice (n=8). Data are pooled from two independent experiments in which similar results were obtained, and shown as mean±SEM. [#]$P<0.05$, [##]$P<0.01$ versus vehicle-treated WT,

*$P<0.05$, **$P<0.01$ versus vehicle-treated ApoE$^{-/-}$ mice. **b,** Endothelial cell-independent relaxation to SNP in PE-precontracted aortic rings from vehicle-treated WT (n=8), vehicle-treated ApoE$^{-/-}$ (n=9), and febuxostat-treated ApoE$^{-/-}$ mice (n=8). Data are pooled from two independent experiments in which similar results were obtained, and shown as mean±SEM. **c,** Contraction to PE in aortic rings from vehicle-treated WT (n=8), vehicle-treated ApoE$^{-/-}$ (n=9), and febuxostat-treated ApoE$^{-/-}$ mice (n=8). Data are pooled from two independent experiments in which similar results were obtained, and shown as mean±SEM.

1.   Mudau, M., Genis, A., Lochner, A. & Strijdom, H. Endothelial dysfunction: the early predictor of atherosclerosis. *Cardiovasc J Afr* **23**, 222-31 (2012).

a

WT/Vehicle
ApoE$^{-/-}$/Vehicle
ApoE$^{-/-}$/Febuxostat

Relaxation (%)

Log[ACh(M)]

b

Relaxation (%)

Log[SNP(M)]

c

Contraction
(% to 60 mM KCl)

Log[PE(M)]