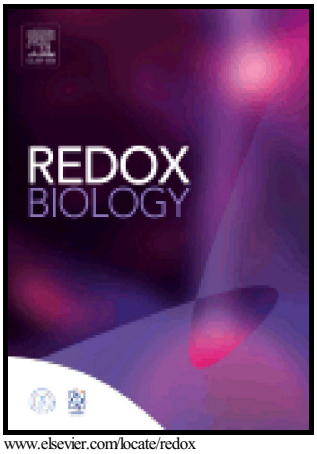

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The novel organic mononitrate NDHP attenuates hypertension and endothelial dysfunction in hypertensive rats

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ABSTRACT

RATIONALE

Development and progression of cardiovascular diseases, including hypertension, are often associated with impaired nitric oxide synthase (NOS) function and nitric oxide (NO) deficiency. Current treatment strategies to restore NO bioavailability with organic nitrates are hampered by undesirable side effects and development of tolerance. In this study, we evaluated NO release capability and cardiovascular effects of newly synthesized organic nitrate NDHP.

METHODS

A combination of *in vitro* and *in vivo* approaches was utilized to assess acute effects of NDHP on NO release, vascular reactivity and blood pressure. The therapeutic value of chronic NDHP treatment was assessed in an experimental model of angiotensin II-induced hypertension in combination with NOS inhibition.

RESULTS

NDHP mediates NO formation in both cell-free system and small resistance arteries, a process which is catalyzed by xanthine oxidoreductase. NDHP-induced vasorelaxation is endothelium independent and mediated by NO release and modulation of potassium channels. Reduction of blood pressure following acute infusion of NDHP was more pronounced in hypertensive rats (two-kidney-one-clip model) than in

[1] Equal contribution.