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Diosgenin improves vascular function by increasing aortic eNOS expression, normalize dyslipidemia and ACE activity in chronic renal failure rats

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Abstract In recent years, the role of endothelial dysfunction (ED) and excessive oxidative stress in the development of cardiovascular diseases has been highlighted. The aim of the present study is to evaluate the effect of diosgenin, an antioxidant on chronic renal failure (CRF) induced vascular dysfunction. CRF was induced by feeding the rats with a diet containing 0.75 % adenine and diosgenin was given orally (everyday at the dose of 40 mg/kg). Isometric force measurement was performed on isolated aortic rings in organ baths. Levels of reduced glutathione (GSH), nitric oxide metabolites, and endothelial nitric oxide synthase mRNA in rat aorta were examined. Further, plasma lipid profile, activity of enzymes of lipid metabolism, and aortic angiotensin converting enzyme (ACE) also studied. The overall results have proved that diosgenin attenuates CRF-induced impairment in acetylcholine induced endothelium-dependent and sodium nitroprusside induced endothelium-independent vascular relaxation. Moreover, it elevates the GSH and restores the eNOS mRNA expression level. CRF-induced dyslipidemia and ACE activity was also inhibited by diosgenin treatment. This study indicates that diosgenin have enough potential to protect vasculature against oxidative stress, dyslipidemia which in turn improves the vascular function in CRF milieu.

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Introduction

Cardiovascular complications are the leading cause of mortality, accounting for 50 % of all deaths among patients with end-stage renal failure in developed countries [1]. Patients with chronic renal failure (CRF) face a markedly increased risk of cardiovascular death. CRF is frequently complicated by hypertension and changes in both heart (left ventricular hypertrophy) and vasculature [endothelial dysfunction (ED) and accelerated atherosclerosis] [2]. Uremia is associated with increased vascular risk and premature death in both dialysis and nondialysis patients and may be up to 100-fold in certain patient groups [3].

Several mechanisms contribute to the impairment of endothelial function. Current concepts for the explanation of ED and accelerated atherosclerosis in uremia propose a reduced vascular bioavailability of nitric oxide (NO) [4]. Endothelial integrity is crucial for the maintenance of blood flow and anti-thrombotic capacity and vascular endothelium is highly sensitive to oxidative stress and this stress is the main cause of ED [5]. Oxidative stress plays an important role in the pathogenesis and development of cardiovascular diseases [6]. Thus, impaired NO output from endothelium is one of the causes of oxidative stress [7]. Experimental study have provided the support that uremic vascular calcification, even when not severe, significantly reduces arterial compliance and altered vascular smooth muscle and endothelial function in renal failure [8].

CRF results in profound lipid disorders, which stem largely from dysregulation of high-density lipoprotein