## **ORIGINAL ARTICLE**



## The targets of $\beta$ -sitosterol as a novel therapeutic against cardio-renal complications in acute renal ischemia/reperfusion damage

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## Abstract

This research is the first to use  $\beta$ -sitosterol on myocardial and renal tissues in renal ischemia/reperfusion (IR) damage. Female Wistar rats were randomly divided into three groups: control (sham), renal IR (50 min ischemia – 3 h reperfusion), and renal IR + 150 mg/kg/p.o.  $\beta$ -sitosterol (the rats were treated with  $\beta$ -sitosterol orally once 1 h before the IR procedure).  $\beta$ -Sitosterol pretreatment caused an increase in superoxide dismutase and glutathione activities and a decrease in malondialdehyde levels in the kidney and heart. Moreover, it alleviated histopathological changes and downregulated the levels of tumor necrosis factoralpha and interleukin-6 and upregulated the levels of endothelial nitric oxide synthase. As conclusion, the potential of  $\beta$ -sitosterol for renal and cardiac necrosis and apoptosis appears to act by limiting inflammatory response and oxidative stress. Thus, the potential of this compound is noteworthy and may serve as a potential therapeutic in the treatment of acute organ damages due to renal IR.

Keywords Ischemia/reperfusion  $\cdot$  Kidney  $\cdot$  Heart  $\cdot \beta$ -Sitosterol  $\cdot$  Inflammation  $\cdot$  Oxidative stress

## Introduction

Renal ischemia/reperfusion (IR) injury is an important cause of acute kidney failure and also remote organ damages. Despite progress in the therapeutic approach in the recent years, it still has high prevalence and mortality rate. Ischemia commonly occurs due to occlusion in blood vessels generated hypoxia condition in the kidney (Zheng et al. 2019).

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Reperfusion following ischemia as an important cause of renal pathophysiology targets the restoration of arteriovenous kidney (Ono et al. 2019). All these episodes enhance the production of free radicals in kidney cells and thereby the injury cascade (Kim et al. 2019). Dysfunction induced by free radicals in the ischemic-reperfusive injury is well documented with regard to vital organs such as brain, kidney, heart, and liver. There is evidence that the antioxidant strategies may attenuate organ dysfunctions by reducing the production of ROS. However, no effective protective therapy is currently used for heart and kidney injuries associated with IR.

The numerous bioactive phytosterols are able to provide health benefits. Recently, one major interest for proposing as dietary supplement  $\beta$ -sitosterol is that it has antihypercholesterolemic impacts.  $\beta$ -Sitosterol is also recommended as neuroprotective, antimutagenic, antidiabetic, antifungal, antibacterial, and chemoprotective agent (Kuo et al. 2019). Considering the presence of  $\beta$ -sitosterol in different pharmacological applications, its effects have been especially associated with reduced oxidative stress in diseases such as cardiovascular disorders, aging, and cancer (Brinton et al. 2018; Jiang et al. 2019). On the other hand, the nanoribbons, which contain  $\beta$ -sitosterol, can be utilized as a promising antiinflammatory material in wound healing (Amina et al. 2017).