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Protective effect of *R. glutinosa* oligosaccharides against high L-carnitine diet-induced endothelial dysfunction and hepatic injury in mice

Wenfeng Li, Ruijun Zhang, Jianjun Guo, Hongjun Shao*, Xingbin Yang*

College of Food Engineering and Nutritional Science, Shaanxi Normal University, Xi'an 710062, China

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ABSTRACT

Current research for the first time demonstrated that endothelial dysfunction and hepatic injury in mice were induced by ingestion of 3% L-carnitine water for consecutive 10 weeks. Interestingly, oral administration of dietary raffinose family oligosaccharides (RFOs) at 400 and 800 mg/kg bw significantly reduced the impact of L-carnitine on the serum total cholesterol, triglycerides, high- and low-density lipoproteins, alanine aminotransferase, aspartate amino-transferase, NO, endothelin-1 and C-reactive protein. Furthermore, L-carnitine-induced elevation of hepatic lipid contents and malonaldehyde formation, and the inhibition of SOD and GSH-P*x* activities in mice were markedly ameliorated by oral administration of RFOs. Moreover, histopathology of H&E and Oil Red O staining of the liver also confirmed the protective effect of RFOs against hepatic steatosis and oxidative injury induced by high L-carnitine diet in mice. These findings for the first time suggest that RFOs may alleviate endothelial dysfunction and liver injury from ingestion of high L-carnitine diet.

1. Introduction

Cardiovascular disease (CVD) is the threatening disease to human health in the world, and it can be induced by unreasonable dietary structure [1]. In the past few decades, saturated fats and cholesterol in meat were cognized as risk factors of CVD [2]. However, recent researches surprisingly reported that dietary L-carnitine had a particularly close connection to the build-up of endothelial dysfunction [3,4], which was considered as the earliest stage of CVD [5]. L-Carnitine is an abundant nutrient in red meat and contains a trimethylamine structure, which is metabolized by gut microbiota to produce trimethylamine-*N*-oxide (TMAO), directly leading to the occurring of CVD [3]. In addition, high level ingestion of L-carnitine can also cause metabolic disorders of serum cholesterol, sterol and some of lipids [6,7], and reduce synthesis of nitric oxide (NO), which is associated with endothelial dysfunction [3,8]. These studies have explicitly indicated that TMAO indeed mediated the endothelial damage of high L-carnitine intake, and thus, L-carnitine has been applied to establish animal model of endothelial dysfunction as reliable scheme [3,4]. Accordingly, a novel dietary strategy to intervene vascular damage of high L-carnitine ingestion is necessary.

α-Galactosides, called as galacto-oligosaccharides or raffinose family oligosaccharides (RFOs), are widely distributed in the plant kingdom [9,10]. RFOs are considered as one of the major bioactive components in *Rehmannia glutinosa* Libosch., which are responsible for many bioactivities of *R. glutinosa* Libosch., such as hepatoprotective, hypoglycemic, immunomodulatory, and prebiotic effects [11]. In our previous study, the RFOs isolated from *R. glutinosa* Libosch. were shown to exhibit various protective effects against CCl_4-induced acute oxidative hepatotoxicity, lipid peroxidation, and the damage of enzymatic antioxidant defense system in mice [12]. In this regard, RFOs from Chinese *R. glutinosa* might be an alternative dietary supplement for preventing cardiovascular disease and hepatic damage, inducing high L-carnitine diet-caused injury in animals. Therefore, the purpose of the present study was to determine the protective effects of RFOs against high L-carnitine-induced vascular endothelial dysfunction and liver oxidative stress injury in mice.

* Corresponding author. Fax: +86 29 85310517.
E-mail addresses: shaohj@snnu.edu.cn (H. Shao), xbyang@snnu.edu.cn (X. Yang).

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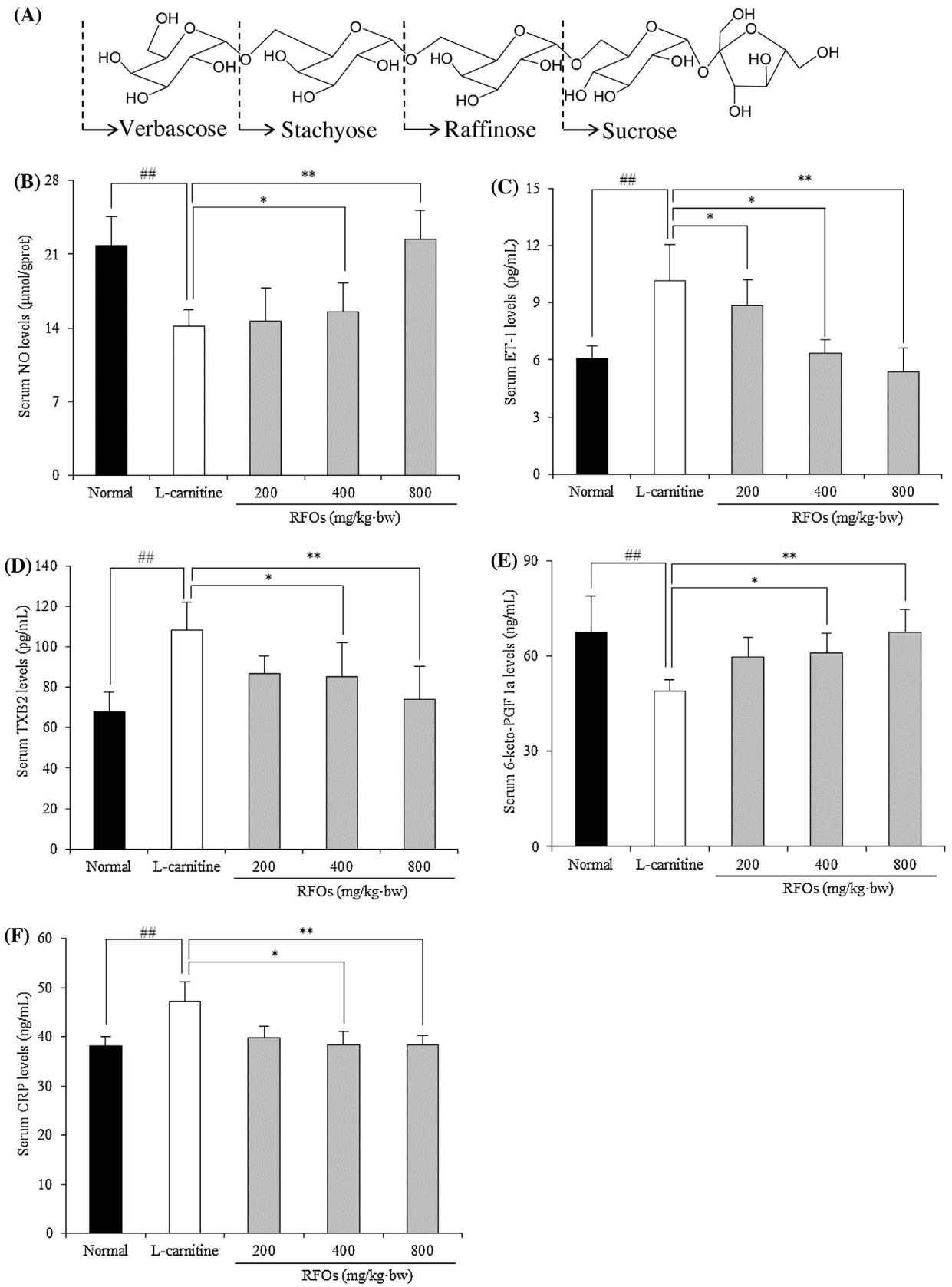

Fig. 1. Structure of compositional oligosaccharides of RFOs (A) and their effects on serum NO (B), ET-1 (C), TXB_2 (D), 6-keto-PGF1a (E) and CRP (F) levels in 3% L-carnitine water-fed mice for consecutive 10 weeks. Values are expressed as means ± SD of 10 mice in each group. $^{\#\#}p < 0.01$, vs the normal group. $^{*}p < 0.05$ and $^{**}p < 0.01$, compared to the L-carnitine-fed mice.