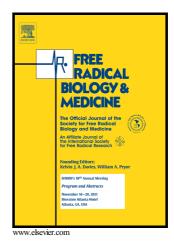
### Author's Accepted Manuscript

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 PII:
 S0891-5849(17)30642-1

 DOI:
 http://dx.doi.org/10.1016/j.freeradbiomed.2017.06.009

 Reference:
 FRB13363

To appear in: Free Radical Biology and Medicine

Received date: 7 April 2017 Revised date: 8 June 2017 Accepted date: 14 June 2017

Cite this article as: Bin Feng, Ran Meng, Bin Huang, Yan Bi, Shanmei Shen and Dalong Zhu, Silymarin protects against renal injury through normalization o lipid metabolism and mitochondrial biogenesis in high fat-fed mice, *Free Radica Biology and Medicine*, http://dx.doi.org/10.1016/j.freeradbiomed.2017.06.009

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#### **ACCEPTED MANUSCRIPT**

### Silymarin protects against renal injury through normalization of lipid metabolism and mitochondrial biogenesis in high fat-fed mice

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### Abstract

Obesity is associated with an increased risk of chronic kidney diseases and the conventional treatment with renin-angiotensin-aldosterone system (RAAS) inhibitors is not enough to prevent renal injury and prolong the progression of disease. Recently, silymarin has shown protective effects on renal tissue injury, but the underlying mechanisms remain elusive. The goal of this study was to investigate the potential capacity of silymarin to prevent renal injury during obesity induced by high fat diet (HFD) in mice. In vivo, male C57BL/6 mice received HFD (60% of total calories) for 12 weeks, randomized and treated orally with vehicle saline or silymarin (30 mg/kg body weight/d) for 4 weeks. In vitro, human proximal tubular epithelial cells (HK2) were exposed to 300  $\mu$ M palmitic acid (PA) for 36 hours followed by silymarin significantly ameliorated HFD induced glucose metabolic disorders, oxidative stress and pathological alterations in the kidney. Silymarin significantly mitigated renal lipid

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