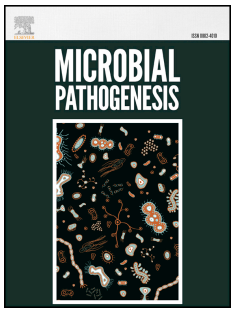
Accepted Manuscript



Esculin prevents Lipopolysaccharide/D-Galactosamine-induced acute liver injury in mice

Aiyun Liu, Yongbin Shen, Yaju Du, Jing Chen, Fenghua Pei, Weiran Fu, Jiutao Qiao

PII: S0882-4010(18)30909-4

DOI: 10.1016/j.micpath.2018.10.003

Reference: YMPAT 3197

To appear in: *Microbial Pathogenesis*

Received Date: 18 May 2018

Revised Date: 30 September 2018

Accepted Date: 1 October 2018

Please cite this article as: Liu A, Shen Y, Du Y, Chen J, Pei F, Fu W, Qiao J, Esculin prevents Lipopolysaccharide/D-Galactosamine-induced acute liver injury in mice, *Microbial Pathogenesis* (2018), doi: https://doi.org/10.1016/j.micpath.2018.10.003.

Esculin prevents Lipopolysaccharide/D-Galactosamine-induced acute liver injury in mice

Aiyun Liu[1], Yongbin Shen[2], Yaju Du[1], Jing Chen[1], Fenghua Pei[1], Weiran Fu[1], Jiutao Qiao[3*]

1. Department of Gastroenterology, the Second affiliated hospital of Harbin Medical University, Harbin, China.
2. Department of Vascular Surgery, the Second affiliated hospital of Harbin Medical University, Harbin, China.
3. Department of Orthopedist, the Second affiliated hospital of Harbin Medical University, Harbin, China.

*Correspondence to: Jiutao Qiao**,** Department of Orthopedist, the Second affiliated hospital of Harbin Medical University, Harbin, China. E-mail: drqiao1983@163.com

Abstract

Liver injury is an important cause of serious liver disease and is characterized by inflammatory and oxidative responses. Esculin, a coumarinic derivative found in *Aesculus hippocastanum L.*, has been shown to exhibit anti-inflammatory and anti-oxidative effects. Here, we investigated the effects and molecular mechanism of esculin on Lipopolysaccharide/D-Galactosamine (LPS/D-Gal)-induced acute liver injury. A mouse model for acute liver injury was induced by intraperitoneal injection with D-Gal and LPS, and was assessed by histology, and serum transaminase analyses. The results showed that esculin significantly reduced the pathological symptoms of acute liver injury, as well as serum AST and ALT levels. LPS/D-Gal-induced liver myeloperoxidase (MPO) activity and malondialdehyde (MDA) content were also suppressed by esculin. Furthermore, LPS/D-Gal-induced liver tumor necrosis factor-α (TNF-α) and interleukin-1β (IL-1β) production were attenuated by esculin. Our data demonstrate that esculin can inhibit nuclear factor kappa B (NF-κB) activation as well as increase nuclear factor E2-related factor 2 (Nrf2) and heme oxygenase-1 (HO-1) expression. In conclusion, this paper demonstrates that esculin protects liver injury induced by LPS/D-Gal via inhibiting inflammatory and oxidative responses.

Keywords: esculin; LPS; liver injury; Nrf2

1. Introduction

The liver is the largest substantive organ in the abdominal cavity and, bears a profound physiological function. Liver injury is a clinical syndrome that is seriously detrimental to liver health and is mainly caused by immune damage, drug-induced injury and alcohol-induced injury [1, 2]. The mechanisms of liver injury are complex, and previous studies have shown that inflammatory and oxidative responses play critical roles in the development of liver injury [3, 4]. The LPS/D-Gal-induced liver injury mouse model is widely accepted as a model to investigate mechanisms and drugs for liver injury [5, 6]. Currently, there is no effective way to prevent or treat liver damage. Thus, there is an urgent need to develop new treatments.

Esculin, a coumarinic derivative isolated from Aesculus hippocastanum L., has been shown to exhibit anti-inflammatory effects. In vitro, esculin was found to suppress inflammatory cytokine production through the inhibition of the mitogen-activated protein kinase (MAPK) pathway in mouse peritoneal macrophages [7]. Esculin also inhibited LPS-induced NO production in macrophages [8]. In vivo, esculin has been reported to protect against LPS-induced lung injury in mice [9]. Furthermore, esculin was found to attenuate cognitive impairment in experimental