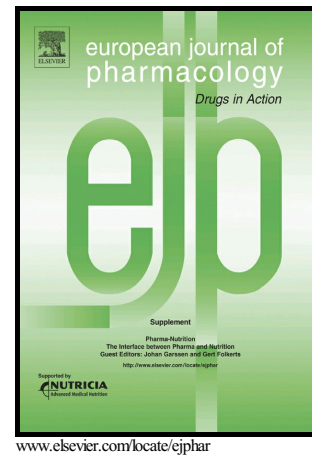


Author's Accepted Manuscript

Role of Oleanolic acid in maintaining BBB integrity by targeting p38MAPK/VEGF/Src signaling pathway in rat model of subarachnoid hemorrhage

Yu-wei Han, Xiu-juan Liu, Ying Zhao, Xiao-ming Li



PII: S0014-2999(18)30551-X
DOI: <https://doi.org/10.1016/j.ejphar.2018.09.018>
Reference: EJP71987

To appear in: *European Journal of Pharmacology*

Received date: 4 April 2018
Revised date: 10 September 2018
Accepted date: 18 September 2018

Cite this article as: Yu-wei Han, Xiu-juan Liu, Ying Zhao and Xiao-ming Li, Role of Oleanolic acid in maintaining BBB integrity by targeting p38MAPK/VEGF/Src signaling pathway in rat model of subarachnoid hemorrhage, *European Journal of Pharmacology*, <https://doi.org/10.1016/j.ejphar.2018.09.018>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Role of Oleanolic acid in maintaining BBB integrity by targeting p38MAPK/VEGF/Src signaling pathway in rat model of subarachnoid hemorrhage

Yu-wei Han^a, Xiu-juan Liu^a, Ying Zhao^b, Xiao-ming Li^{a*}

^a Institute of Neurology, General Hospital of Shenyang Military Command, Shenyang, Liaoning, 110016, China

^b Physical Examination Center, Shenyang Red Cross Hospital, Shenyang, Liaoning, 110013, China

*Authors to whom correspondence should be addressed.

Correspondence: Dr. Xiaoming Li, Dr. Institute of Neurology, General Hospital of Shenyang Military Command, 83# Wenhua Road, Shenhe District, Shenyang, Liaoning, 110016, China. Tel. /fax: +86-24-2885-1284; E-mail: lxm5668sw@yahoo.com

Abstract

Vasogenic brain edema after subarachnoid hemorrhage (SAH) is an independent risk factor for death and poor prognosis. Disruption of the blood-brain barrier (BBB) is the main cause of vasogenic brain edema induced by SAH. Oleanolic acid (OA) is a natural pentacyclic triterpenoid with various biological functions. Previous studies have shown that prophylactic administration of OA could prevent the BBB disruption in autoimmune encephalomyelitis mice. In this context, we speculate that OA may play a neuroprotective role by protecting the integrity of the BBB and reducing vasogenic cerebral edema after SAH. To validate this hypothesis, a SAH model was established on Sprague Dawley rats using a standard intravascular puncture model. The effects of OA on various physiological indexes were observed, including SAH grades, mortality, neurological function score, brain edema and BBB permeability. Related proteins of the brain endothelial cell junction complex were also detected, including tight junctions (TJs) and adherent junctions (AJs). Results showed that OA significantly reduced the permeability of BBB and relieved brain edema by increasing protein expression of TJs and AJs, and decreased the SAH grades by increasing the protein expression of heme oxygenase-1 (HO-1) in SAH rats. Additionally, we found OA could inhibit up-regulation of VEGF and the phosphorylation of p38 mitogen-activated protein kinase (MAPK), and suppress p38MAPK/VEGF/Src signaling pathway which involved in BBB disruption following SAH. From the experimental results, we speculate that OA effectively alleviated SAH-induced vasogenic edema by targeting p38 MAPK/VEGF/Src axis.

Download English Version:

<https://daneshyari.com/en/article/11025727>

Download Persian Version:

<https://daneshyari.com/article/11025727>

[Daneshyari.com](https://daneshyari.com)