Biomedicine & Pharmacotherapy 103 (2018) 248–252

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha

Paeoniflorin attenuates depressive behaviors in systemic lupus erythematosus mice

Song Wang, Xiaoyu Zhao, Zhengwei Qiao, Xuedong Jia, Yuedong Qi*

Department of Pharmacy, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, 450052, China

ARTICLE INFO

Keywords:
Paeoniflorin
Systemic lupus erythematosus
Depressive behaviors

ABSTRACT

The present study was to evaluate the effects of paeoniflorin (PA) on systemic lupus erythematosus induced depressive behaviors. 10 wild type mice and 20 MRL/lpr mice were applied for the research. The animals were randomly assigned to wild type, MRL/lpr group and MRL/lpr + PA group. PA restored depressive-like behaviors, such as sucrose consumption, immobile time in the tail suspension tests (TST) and forced swimming tests (FST). PA significantly decreased the levels of interleukin-6 (IL-6), IL-1β, tumor necrosis factor-α (TNF-α) in serum and hippocampus of MRL/lpr mice. Western blot results demonstrated PA inhibited the levels of HMGB1/TLR4/NF-κB pathway. The findings showed that PA was beneficial for the prevention of systemic lupus erythematosus induced depressive behaviors, which possibly by suppressing HMGB1/TLR4/NF-κB pathway.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disorder that mainly affects multiple organ systems [1]. The onset of SLE occurs in childhood or adolescence and accounts for around 15% of affected individuals [2]. In children, SLE is associated with significant morbidity consequent to the disease [3,4]. It has been demonstrated SLE could bring many complications to children such as few words, depression, suicide [5,6]. So SLE induced depressive behaviors has attracted our attention.

The cellular stressors and inflammation caused by the many stimulates promote the release of danger-associated molecular pattern (DAMP) molecules such as high mobility group box 1 protein (HMGB1) [7]. HMGB1 signaling is considered to be implicated in the immune cascade and production of pro-inflammatory molecules. HMGB1 are associated with nuclear transcription factor-κB (NF-κB) [8,9]. However, the relationship between HMGB1 and NF-κB related immune/inflammatory progression involved in systemic SLE induced depressive behaviors has not been well elucidated. Therefore, in the present study, we investigated the potential involvement of PA in an experimental SLE induced depressive behaviors model and tested the possible protective effect of PA on SLE induced depressive behaviors.

2. Methods and materials

2.1. Regeants

PA was purchased from Sigma-Aldrich (Saint Louis, MO, USA). TNF-α, IL-1β, IL-6 enzyme-linked immunosorbent assay (ELISA) kits were produced by Nanjing KeyGEN Biotech. CO., LTD. (Nanjing, China). All the antibodies were provided by Cell Signaling Technology (Danvers, USA).

2.2. Animals

10 wild type mice and 20 MRL/MpJ-Faslpr/2 J (MRL/lpr) mice (male, 8 weeks, 18–22 g) were purchased from the Nanjing University Animal Center (Nanjing, China) and maintained under specific pathogen-free conditions in GLP laboratory in accordance with institutional guidelines. The animals were kept in a conventional animal facility with a 12 h light/12 h dark cycle circumstance at a constant temperature of 22–24 °C. The mice had free access to standard water and food pellets *ad libitum*.

2.3. Experiment protocol

The 20 MRL/lpr mice were randomly divided into two groups : MRL/lpr group and MRL/lpr + PA (20 m g/kg) group. The animals were intravenously injected with 20 mg/kg PA. Simultaneously, the wild type group and MRL/lpr were intravenously

* Corresponding author.
E-mail address: qiyuedong2014@163.com (Y. Qi).

https://doi.org/10.1016/j.biopha.2018.03.149
Received 13 January 2018; Received in revised form 21 March 2018; Accepted 26 March 2018
0753-3322/ © 2018 Elsevier Masson SAS. All rights reserved.

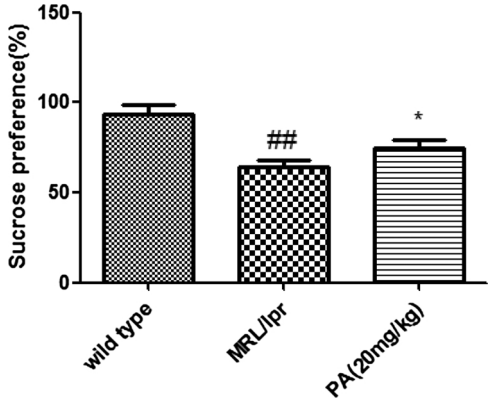

Fig. 1. Effect of PA on Sucrose consumption (n = 10). The data are expressed as mean values ± SDs. $^{\#\#}p < 0.01$ compared with wild type group. $^{**}p < 0.001$ compared with MRL/lpr group.

injected with an equal volume of vehicle. Behavior tests were performed 6 h after the last drug administration. Then the mice were anesthetized with chloral hydrate and sacrificed. Blood samples were obtained from orbit and allowed to clot for 20 min in laboratory temperature and then centrifuged at 3000 rpm/min for 10 min to obtain serum.

2.4. Sucrose preference test (SPT)

The SPT is used to assess anhedonia by the change in sucrose consumption, a symptom of depression-like behaviors. This test was performed as described previously [12].

2.5. Tail suspension test (TST) and forced swimming test (FST)

For TST, rats were acoustically and visually isolated in a quiet environment. Rats were individually suspended by placing adhesive tape on their tails (about 50 cm above the floor). Each mouse was suspended for a period of 6 min. The time of immobility was recorded at the last 4 min. The animals selected for the hippocampus research is statistically significant in the behavior tests. For FST rats were individually subjected to a glass cylinder (20 cm in height, and 14 cm in diameter) filled with water up to a height of 10 cm (25 ± 2 °C). The immobility time was recorded as the time when rats floated in the water, and only made small movements necessary to keep their heads above water. The total duration of immobility was measured at the last 4 min of the 6-min testing period.

2.6. Cytokine assay

The levels of inflammatory cytokines including TNF-α, IL-1β, IL-6 in serum and hippocampus were detected using ELISA kits obtained from KeyGEN (Nanjing, China) according to the instructions. Afterward, the absorbance of each well was read at 450 nm with a microplate spectrophotometer. Finally, the contents were calculated according to the standard curves.

2.7. Western blot

The hippocampus tissues were minced, homogenized, washed by PBS and incubated with ice-cold RIPA lysis buffer. Dissolved proteins were collected and centrifugated at 12,000 rpm for 5 min at 4 °C to remove the debris. Based on the concentration determined by BCA assay, equal amounts of protein extracts were loaded on electrophoresis on 8–12% sodium dodecyl sulfate polyacrylamide gel and transferred to polyvinylidene difluoride membranes. Target sheets were blocked with 5% skim milk for 2 h at the room temperature and incubated overnight at 4 °C using specific antibodies. After washing with TBST for three times, the bands were incubated for 1 h at room temperature with the corresponding secondary antibodies. Enhanced chemiluminescence detection (ECL) reagents and a gel imaging system (Tanon Science & Technology Co., Ltd., China) were applied to visualize the protein bands. Three representative figures of each group were shown.

2.8. Immunohistochemistry staining

Briefly, the hippocampus tissues were fixed with 4% paraformaldehyde (PFA), embedded in paraffin and sectioned. The paraffin sections were dewaxed in xylene and dehydrated ethanol, microwaved in sodium citrate buffer and washed with PBS. Endogenous peroxidase activity was blocked by 3% hydrogen peroxide for 20 min. Each sample were blocked with 5% goat serum for 20 min and then treated with primary antibodies HMGB1 (1:1000) at 4 °C overnight. Next day, after washed three times with PBS, each sample were treated with goat anti-rabbit IgG secondary antibody for 20 min and then incubation ahorseradish enzyme tag chain enzyme avidin working fluid for 20 min, washed three times with PBS. Then, samples were stained with 3-3′diaminobenzidine (DAB) and then stained with hematoxylin. After dehydrating and drying, the sections were mounted with neutral gum and observed under a microscope.

2.9. Statistical analysis

The data are expressed as mean values ± SDs. Differences between groups were analyzed by one-way analysis of variance(ANOVA) with

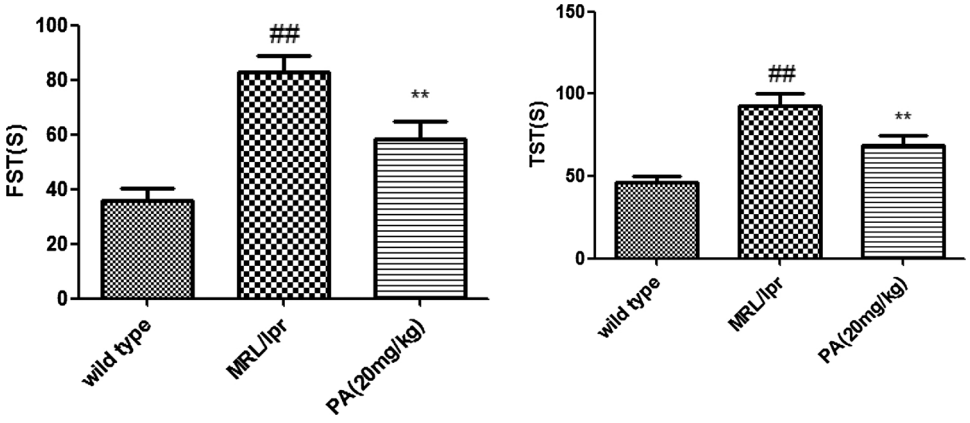

Fig. 2. The effects of PA on TST and FST (n = 10).
The data are expressed as mean values ± SDs. $^{\#\#}p < 0.01$ compared with wild type group. $^{**}p < 0.001$ compared with MRL/lpr group.

Download English Version:

https://daneshyari.com/en/article/8525234

Download Persian Version:

https://daneshyari.com/article/8525234

Daneshyari.com