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Original Article

Herniarin Alleviates Lipopolysaccharide-Induced Acute Lung Injury in Mice via Regulating Oxidative Stress, Inflammation and Apoptosis Mechanisms

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ABSTRACT

Background: Acute Lung Injury (ALI) is a severe, serious condition characterized by the development of pulmonary edema, hypoxemia and respiratory distress. **Objectives:** The current work was intended to disclosing the beneficial activities of the herniarin against LPS-induced ALI in murine model. **Materials and Methods:** The mice were exposed to LPS for 3 days via the intra-tracheal route to trigger the ALI response. Oral administration of herniarin was given for 3 days to the mice subsequent to the LPS challenge. The mice underwent scarification under anaesthesia, subsequently lungs were excised and weighed accurately. The commercially procured assay kits were utilized to estimate the biochemical factors related to the apoptosis, inflammation and oxidative stress. The histopathological analysis was conducted on the lung tissues of the experimental mice. **Results:** In the present study, the treatment with the herniarin successfully reduced pulmonary edema, total protein and LDH activity in the mice with ALI. The MDA level was decreased, while the antioxidants GSH and SOD concentrations were elevated by the herniarin treatment. The herniarin treatment significantly decreased the inflammatory factor levels and inflammatory cell counts in the ALI mice. In addition, the herniarin treatment effectively decreased the Bax and caspase-3 expressions, whereas the Bcl-2 expression was increased in the ALI mice. Furthermore, the outcomes of histological investigation confirmed the therapeutic efficacy of herniarin against ALI. **Conclusion:** The present study revealed that herniarin successfully inhibited LPS-induced ALI in mice via inhibiting lung edema, inflammation, oxidative stress, apoptosis and lung damage. Hence, it can be concluded that herniarin has the potential for the management of ALI.

Keywords: Apoptosis, Herniarin, Inflammation, Lung edema, Malondialdehyde, Pulmonary.

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INTRODUCTION

Acute Lung Injury (ALI) is a severe and life-threatening condition characterized by the rapid onset of respiratory distress due to the damage to the alveoli, severe lack of oxygen, an unregulated inflammatory reaction and accumulation of inflammatory cells and cytokines, which may advance to Acute Respiratory Distress Syndrome (ARDS). The global prevalence of ALI has been a growing concern, with significant implications for public health and healthcare systems worldwide.[1] The global prevalence of ALI is significant, with studies estimating that it affects millions of individuals annually across the world. Infection in lower respiratory tracts, which can result in ALI, are a pivotal cause of morbidity and mortality globally, contributing to a significant burden on healthcare systems.[2] The underlying pathophysiology of ALI is complex and multifactorial, involving an inflammatory responses that lead to injury to the alveolar-capillary layer. The injury to this membrane leads to augmented permeability, resulting in the protein-rich fluid accumulation in the alveolar spaces, which deregulates gas exchange and causes respiratory distress.[3] Factors that participate in the progression of ALI include direct pulmonary damage, such as from pneumonia, as well as indirect lung damage, which may occur in the context of sepsis, trauma, or other systemic conditions.[4]

The pathophysiology of ALI involves the activation of various inflammatory signaling, including the discharge of

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proinflammatory factors, the stimulation of neutrophils and other immune cells and the disruption of the normal regulation of the coagulation system.[5] These processes can be triggered by the discharge of injury-related molecular patterns, which are endogenous signals released by injured or stressed cells. The resulting inflammatory response can result in further injury to the alveolar-capillary membrane, ultimately compromising the capability of lungs to efficiently exchange O_2 and CO_2.[6] Understanding the pathophysiology of ALI is essential to develop potential prevention and treatment methods. Improved global epidemiology and the allocation of resources, such as vaccines, antiviral medications and critical care support, can help mitigate the burden of ALI.[7]

One well-established model for studying this condition is the lipopolysaccharide-induced ALI model in rodents. Lipopolysaccharide, a ingredient of the outer membrane of Gram-negative bacteria, is an effective inducer of the immune reactions and can trigger an intense inflammatory cascade when administered systemically.[8] The inflammatory response triggered by lipopolysaccharide in this model can result in the disruption of the alveolar-capillary barrier, the protein-rich fluid production in the alveolar space and the recruitment of inflammatory cells like neutrophils, all of which are hallmarks of ALI. This model has been widely used to investigate the pathophysiology of ALI, as well as to evaluate potential therapeutic intervention.[9] Several works have revealed the role of various molecular pathways in the development of lipopolysaccharide-exposed ALI, including the activation of the inflammatory pathways.[10,11] The lipopolysaccharide-induced ALI model in mice has been instrumental in advancing our understanding of the pathophysiology of this disease and has facilitated the progression of new therapeutic methods.[12]

Herniarin or 7-methoxycoumarin is a simple coumarin compound, extensively found in numerous herbal plant families, including Caryophyllaceae, Labiatae, Moraceae, Rutaceae and Compositae. Moreover, it has been reported to possess several pharmacological properties like antimicrobial,[13] antigenotoxic,[14] anticancer,[15] anxiolytic and antidepressive,[16] and antioxidant and neuroprotective properties.[17] Apart from these biological properties, the beneficial effects of herniarin against airway inflammatory conditions, particularly ALI was not scientifically assessed yet. Consequently, the current work was aimed at disclosing the salutary effects of the herniarin against LPS-induced ALI in mice model.

MATERIALS AND METHODS

Chemicals

The major chemicals employed in this work, including herniarin, LPS and other reagents were acquired from Sigma-Aldrich, USA. The diagnostic kits for the estimation of biochemical markers were commercially procured from Abcam, Elabscience and CusaBio, USA, respectively.

Experimental mice

The present study utilized 3-4 weeks aged healthy C57BL/6 mice (20-25 g), which is procured from institutional animal facility. The mice were accommodated in hygienic polypropylene enclosures with unrestricted availability of the rodent pelleted food and pure drinking water. The mice were caged in a controlled laboratory circumstances featuring a temperature of 24°C, air humidity ranging from 60% to 70% and 12 hr periods of light and darkness. Prior to initiating the experiments, each mouse was acclimated for one week to the laboratory environmental conditions. Institutional animal ethics committee has approved all the protocols conducted on the experimental animals.

Experimental groupings

A one week acclimated mice were distributed uniformly into four groups. Group I mice was normal control. Mice from group II was received an intra-tracheal administration of 5 mg/kg of LPS for 3 days was to induce the ALI. The mice from group III and IV was received the treatments of 10 and 20 mg/kg, respectively, prior to the exposure of LPS for a duration of 3 days. Following the conclusion of the treatments, the mice were sacrificed under anesthesia and their pulmonary tissues were removed. Following collection, the tissues were precisely weighed to note their Wet weight (W). Afterwards, the lungs underwent dehydration in an oven set at 80°C, followed by accurate weighing to note the Dry weight (D).

Preparation of Bronchoalveolar Lavage Fluid (BALF)

The BALF was gathered by administering saline aliquots (30 mL) into the central lobe of experimental mice. The collected BALF was centrifuged at 4000 rpm for 10 min. The cells-free supernatant was further separated and employed to biochemical estimations. The inflammatory cells present in the BALF pellets was measured by differential cell counting technique. The total protein content and the LDH and MPO enzyme activities was determined in the BALF samples using the commercial diagnostic kits (Elabscience, USA).

Analysis of oxidative stress-related biomarker levels

The lungs from control and treated mice were collected and subsequently homogenized using saline solution. The homogenized lung tissues were then centrifuged at 4000 rpm for 15 min and the resultant supernatant suspension was utilized to measure the oxidative stress-related marker levels. The Malondialdehyde (MDA), Glutathione (GSH) and Superoxide Dismutase (SOD) concentrations was assessed using the assay kits. Each assay was performed with three replicates using the manufacturer's recommended protocols (RayBiotech, USA).

Pro-inflammatory cytokine levels

The pro-inflammatory cytokines, like IL-6 and TNF-α, in the BALF of the experimental mice were assessed using commercial diagnostic kits. Each assay was performed with three replicates using the manufacturer's recommended protocols (R&D Systems, USA).

Apoptotic marker levels

The Bax, Bcl-2 and caspase-3 expressions in the BALF of the experimental mice were examined using the appropriate commercial diagnostic kits. Each assay was performed with three replicates using the manufacturer's recommended protocols (LSBio, USA).

Histopathological analysis

The histopathological analysis was conducted on the lung tissues dissected from the experimental mice. The collected lung tissues underwent treatment with a 10% neutral formalin solution and then paraffinized using paraffin wax. The paraffinized tissues were then cut into sections of 5 µm in thickness and subsequently stained with eosin and hematoxylin. The dyed tissues were then investigated using optical microscope at a magnification of 40×in order to detect any histological alterations.

Statistical analysis

The data taken from assays were scrutinized statistically by one-way ANOVA and Tukey's post hoc assay using SPSS software. The final results are given as a mean±SD of three replicate assays with $p<0.05$ as significant.

RESULTS

Effect of herniarin on the lung weight ratio, total protein, LDH and MPO levels in the BALF of the experimental mice

The changes in the levels of lung wet/dry weight ratio, LDH, MPO and total protein levels in the BALF of control and experimental mice were assessed and the findings are presented in Figure 1. The present results indicated that the mice with LPS-induced ALI demonstrated increased lung weight, MPO, LDH and total protein in the BALF. Remarkably, the treatment of herniarin at 10 and 20 mg/kg concentrations successfully reduced the lung weight, MPO, LDH and total protein in the BALF of the mice with ALI (Figure 1).

Effect of herniarin on the inflammatory cells in the BALF of the experimental mice

Figure 2 illustrates the inflammatory cell count levels, such as eosinophils, neutrophils, total cells, macrophages and lymphocytes in the BALF samples of the experimental mice. The findings are clearly showed a drastic increase in the in the eosinophils, neutrophils, total cells, macrophages and lymphocytes in the BALF of the ALI mice. Nevertheless, the treatment of herniarin at dosages of 10 and 20 mg/kg resulted in a considerable diminution in the eosinophils, neutrophils, total cells, lymphocytes and macrophage cell counts in the ALI mice (Figure 2).

Effect of herniarin on the oxidative stress-related biomarker levels in the BALF of the experimental mice

The impact of herniarin on the oxidative stress-related marker levels in the BALF samples of the experimental mice were assessed and the outcomes are revealed in Figure 3. The mice with ALI mice demonstrated the substantial increase in MDA level and showed drastic decrease in SOD and GSH levels in their BALF. Fascinatingly, the herniarin treatment at 10 and 20 mg/kg concentrations demonstrated reduction in MDA concentration and successful elevation in the antioxidant levels in the BALF of the mice with ALI (Figure 3). These findings evidenced the antioxidant properties of the herniarin.

Effect of herniarin on the pro-inflammatory cytokine levels in the BALF of the experimental mice

Analysis of IL-6 and TNF-α concentration in the BALF sample of mice were conducted and findings are shown in Figure 4. A remarkable elevation in the IL-6 and TNF-α concentrations was observed in the BALF of mice with ALI. Notably, herniarin treatment at a concentrations of 10 and 20 mg/kg, respectively considerably diminished the IL-6 and TNF-α concentrations in the ALI mice. The aforementioned results demonstrated the anti-inflammatory capacity of herniarin (Figure 4).

Effect of herniarin on the apoptotic protein expression levels in the BALF of the experimental mice

Figure 5 depicting the findings of an analysis on the expressions of apoptotic proteins, like Bcl-2, Bax and caspase-3 in the BALF of the experimental mice. The mice with ALI revealed a notable up-regulation in the Bax and caspase-3 expressions, while their BALF showed a reduction in the Bcl-2 expression. However, the herniarin at 10 and 20 mg/kg of concentrations showed notable decrease in the Bax and caspase-3 expressions and elevated the Bcl-2 expression. These findings shown that the herniarin treatment reduced the occurrence of apoptosis in airway cells of the ALI mice (Figure 5).

Effect of herniarin on the histopathological analysis of lung tissues of the experimental mice

Figure 6 presents the results of the histopathological analysis conducted on the lungs of the experimental mice. Elevated levels of inflammatory cell infiltrations, alveolar epithelial damage, pulmonary edema and alveolar cell death were seen in the lungs of the ALI mice. In contrast, the 10 and 20 mg/kg of herniarin revealed a remarkable diminution in histopathological changes,

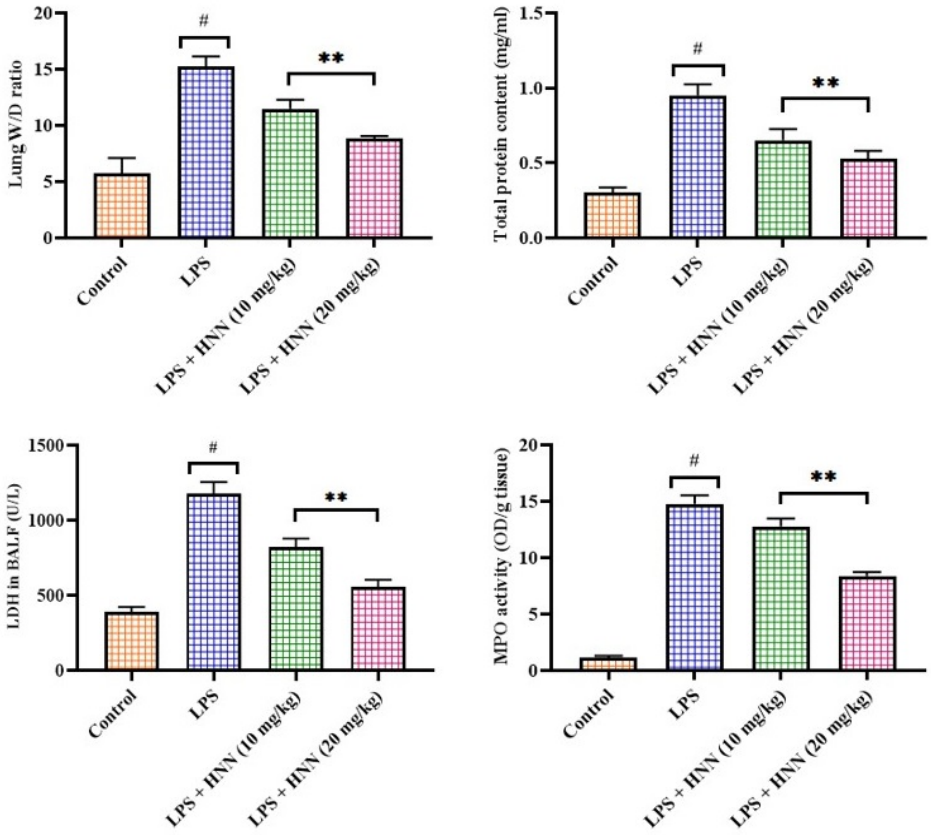

Figure 1: Effect of herniarin on the lung weight ratio, total protein, LDH and MPO levels in the BALF of the experimental mice. The data obtained from the assays were scrutinized statistically by one-way ANOVA and Tukey's *post hoc* assay using the GraphPad Prism software. The final results are given as a mean±SD of three replicate assays. Note: '#' denotes that values are significant at $p<0.01$ when compared with control; '**' denotes that values are significant at $p<0.05$ when compared with LPS-induced ALI group.

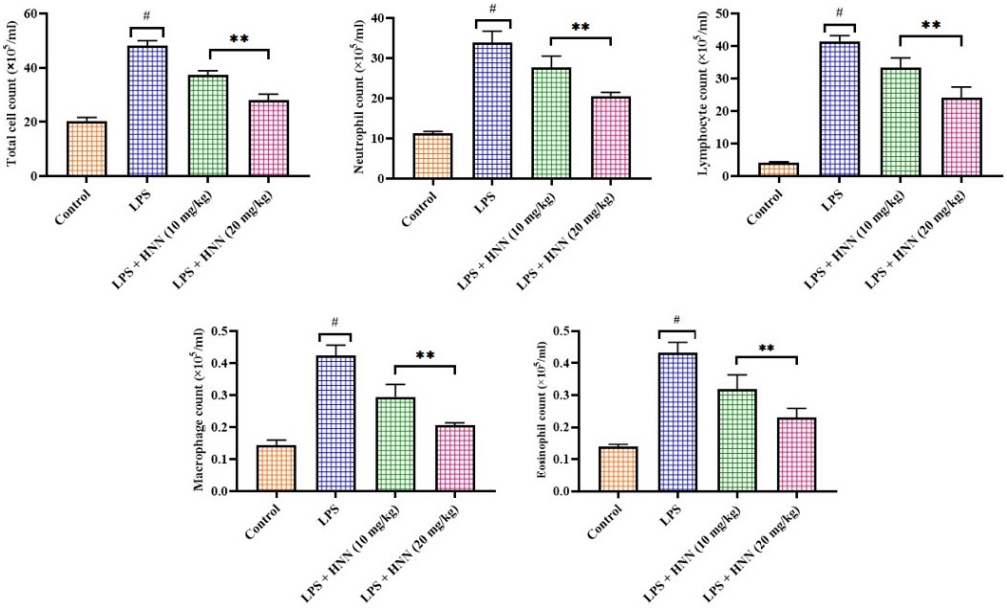

Figure 2: Effect of herniarin on the inflammatory cell counts in the BALF of the experimental mice. The data obtained from the assays were scrutinized statistically by one-way ANOVA and Tukey's *post hoc* assay using the GraphPad Prism software. The final results are given as a mean±SD of three replicate assays. Note: '#' denotes that values are significant at $p<0.01$ when compared with control; '**' denotes that values are significant at $p<0.05$ when compared with LPS-induced ALI group.

including decreased inflammatory cell infiltrations, damage to the alveolar epithelium and death of alveolar cells. These results demonstrate that the herniarin treatment remarkably diminished the histological damage caused by LPS in the lung tissues (Figure 6).

DISCUSSION

ALI is a severe, life-threatening condition characterized by the development of lung edema, hypoxemia and respiratory distress, often leading to ARDS. ALI and its more serious condition, ARDS, are devastating conditions with high mortality rates. The pathogenesis of these disorders involves a complex interplay of various molecular and cellular processes, which are not yet fully understood. One key aspect of the pathogenesis is the role of damage-associated molecular patterns, which are endogenous danger signals released by the body in response to injury.[18] The pathogenesis of LPS-induced ALI is a complex and multifaceted process involving the stimulation of the immune response, the disruption of the endothelial barrier and the induction of oxidative stress and apoptosis. Understanding these underlying mechanisms is essential to develop potential therapies to improve the prognosis of patients with ALI.[19] The assessment of lung wet and dry weight ratio and total protein was crucial in evaluating the severity and progression of ALI. Previous works was highlighted that LPS-challenged ALI is connected with elevated vascular permeability and protein extravasation into the alveolar space.[20] The increased wet-to-dry weight ratio indicates the presence of lung edema, which is a sign of ALI. Additionally, the elevated total protein level reflects the elevated vascular permeability and protein leakage into the alveolar space, which can further exacerbate lung injury and impair gas exchange.[21] Our present results demonstrate that the lung wet-to-dry ratio and total protein was remarkably higher in the mice with ALI.

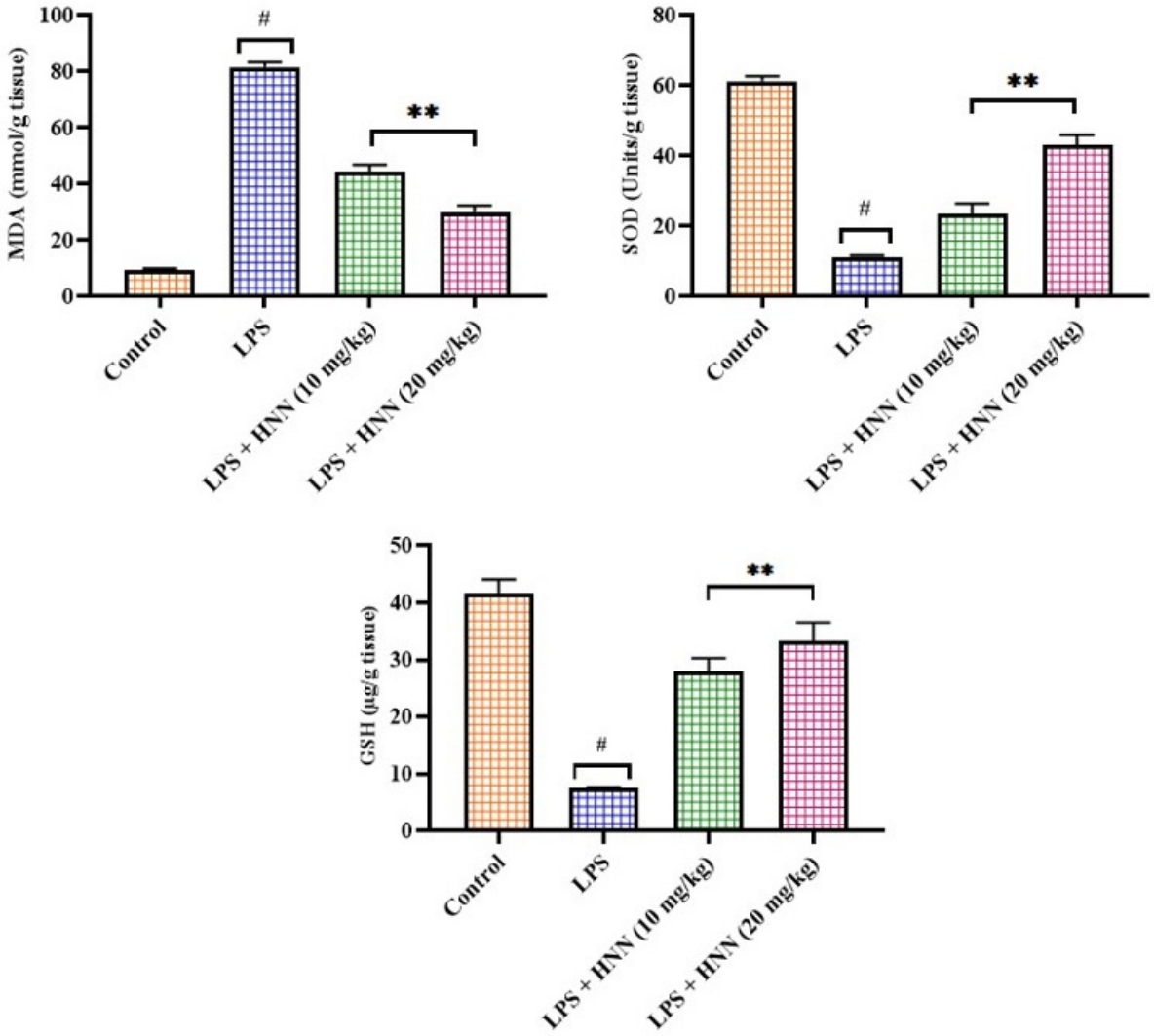

Figure 3: Effect of herniarin on the oxidative stress-related biomarker levels in the BALF of the experimental mice. The data obtained from the assays were scrutinized statistically by one-way ANOVA and Tukey's *post hoc* assay using the GraphPad Prism software. The final results are given as a mean±SD of three replicate assays. Note: '#' denotes that values are significant at $p<0.01$ when compared with control; '**' denotes that values are significant at $p<0.05$ when compared with LPS-induced ALI group.

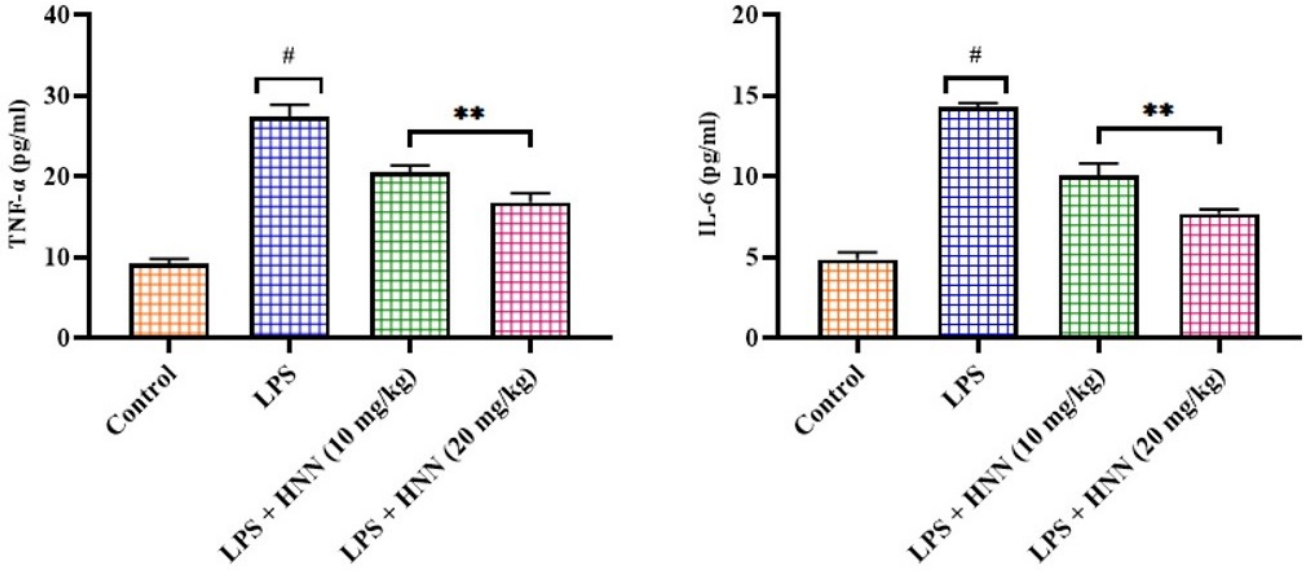

Figure 4: Effect of herniarin on the pro-inflammatory cytokine levels in the BALF of the experimental mice. The data obtained from the assays were scrutinized statistically by one-way ANOVA and Tukey's *post hoc* assay using the GraphPad Prism software. The final results are given as a mean±SD of three replicate assays. Note: '#' denotes that values are significant at $p<0.01$ when compared with control; '**' denotes that values are significant at $p<0.05$ when compared with LPS-induced ALI group.

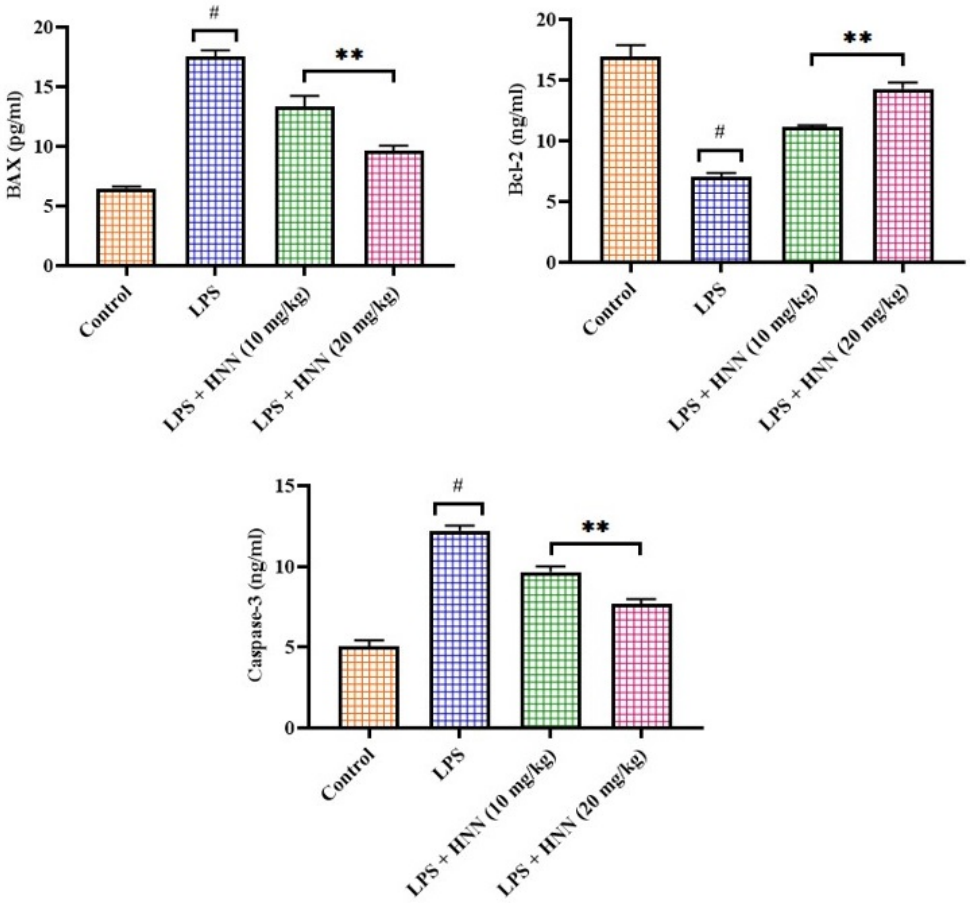

Figure 5: Effect of herniarin on the apoptotic protein expression levels in the BALF of the experimental mice. The data obtained from the assays were scrutinized statistically by one-way ANOVA and Tukey's *post hoc* assay using the GraphPad Prism software. The final results are given as a mean±SD of three replicate assays. Note: '#' denotes that values are significant at $p<0.01$ when compared with control; '**' denotes that values are significant at $p<0.05$ when compared with LPS-induced ALI group.

Interestingly, the herniarin treatment effectively reduced the total protein and lung wet/dry weight ratio in the ALI mice. These findings suggest that the analysis of lung mass and total protein concentrations are valuable biomarkers for assessing the severity of ALI.

Two key enzymes that have been participated in the progression of ALI are LDH and MPO. LDH is an enzyme found in almost all body tissues and its levels can be elevated in various conditions, including liver disease, anemia, heart attacks and infections. In the context of ALI, elevated levels of LDH are often associated with increased tissue damage and cell death. Lactic acidosis is a common complication of ALI and can contribute to the overall severity of the condition.[22] MPO, on the other hand, is an enzyme primarily produced by neutrophils, a type of WBCs. During the inflammatory reaction associated with ALI, MPO can catalyze the ROS accumulation, which can lead to further tissue damage and perpetuate the inflammatory cascade.[23] The role of antioxidant defenses in mitigating the effects of oxidative stress induced by MPO activity has been an area of ongoing research. The interplay between LDH and MPO in the pathogenesis of ALI is complex. Elevated levels of LDH can indicate tissue damage, while increased MPO activity can enhance the ROS accumulation and perpetuate the inflammatory response. Understanding the precise mechanisms by which these enzymes participate in the progression of ALI is crucial for the effective therapies.[24] The present findings showed the increased MPO and LDH concentrations in the ALI mice. However, the herniarin treatment effectively reduced the MPO and LDH enzymes in the BALF of ALI mice.

Macrophages, as the first responders of the immune system, are pivotal in coordinating the inflammatory reactions. They release a cascade of pro-inflammatory factors, like IL-1 and TNF-α, which orchestrate the recruitment of other immune cells. Macrophages also have the capacity to phagocytize pathogens, cellular debris and other harmful materials, thereby mitigating the tissue injury.[25] Eosinophils, though typically associated with allergic and parasitic diseases, have been observed in augmented numbers in the lungs of ALI patients. These granulocytes release a variety of cytotoxic factors, like eosinophil cationic protein, which can contribute to lung epithelial cell injury and the propagation of the inflammatory response.[26] Neutrophils, the most abundant type of leukocytes, are essential in the initial phase of ALI. They are rapidly recruited to the site of inflammation, where they release a barrage of ROS, proteolytic enzymes and neutrophil extracellular traps to combat invading pathogens. However, uncontrolled neutrophil activity can also result in collateral damage to the delicate alveolar-capillary barrier, further exacerbating the lung destruction.[27] Lymphocytes, particularly T cells, play a more imperative role in ALI. While they contribute to the adaptive immune response and facilitate the clearance of pathogens, they can also perpetuate the inflammatory cascade through the cytokine accumulation and the activation of other immune cells.[28] The present findings exhibited increased inflammatory cell counts, including eosinophils, neutrophils, total cells, macrophages and lymphocytes in the BALF of the ALI mice. Interestingly, the herniarin treatment successfully reduced these inflammatory cells in the mice with ALI, which proves its anti-inflammatory properties.

The pathophysiology of ALI is complex and involves various mechanisms, including oxidative stress, which plays an essential role in the onset of disease stress. Oxidative stress, a condition of disproportion between ROS accumulation and the body's antioxidant mechanisms, has been extensively studied in the context of ALI.[29] MDA, a byproduct of lipid peroxidation is a pivotal marker of oxidative stress. Increased MDA concentrations was observed in patients with ALI and it has been connected with the extend of the disease. MDA can cause further injury to cellular components thereby aggravating the injury.[30] Another imperative marker of oxidative stress is SOD, an essential antioxidant enzyme that facilitate the conversion of superoxide radicals into O_2 and H_2O_2. In ALI, the SOD activity may be changed, either increased as a compensatory mechanism or decreased due to the overwhelming oxidative stress. The imbalance in SOD activity can participate in the accumulation of ROS and the progression of lung damage.[31] GSH, a critical antioxidant molecule, also plays an imperative role in the onset of ALI. Reduced GSH concentrations was noted in the ALI patients, indicating a depletion of the body's antioxidant reserves. This depletion can result in further oxidative injury to cellular structures and impaired lung function.[32] The interplay between these oxidative stress factors is crucial in understanding the pathophysiology of ALI. Increased MDA levels and reduced SOD and GSH levels all contribute to the overwhelming oxidative stress that characterizes ALI.[33] The current findings demonstrate the drastic elevation in MDA and diminution in SOD and GSH concentrations in the pulmonary tissues of the mice with ALI. However, the treatment with herniarin successfully reduced the MDA level and improved the antioxidant concentrations in the pulmonary tissues of the ALI mice, which evidences its antioxidant activities.

The dysregulation of the immune system and inflammatory mechanisms playing an imperative role in the progression of ALI. Specifically, the excessive accumulation and release of pro-inflammatory factors was participated in the progression of this condition.[34] IL-6 is a major cytokine that plays an imperative role in the immune response and the inflammatory process. In the context of ALI, IL-6 is considered a relevant indicator in detecting the severe course of the condition and a potential target for therapies. The "cytokine storm" resulting from a sudden and acute elevation in circulating IL-6 concentrations, as well as other pro-inflammatory factors like TNF-α, can lead to a various events that result in tissue damage, impaired gas exchange and respiratory failure.[35] Similarly, TNF-α is another pivotal cytokine

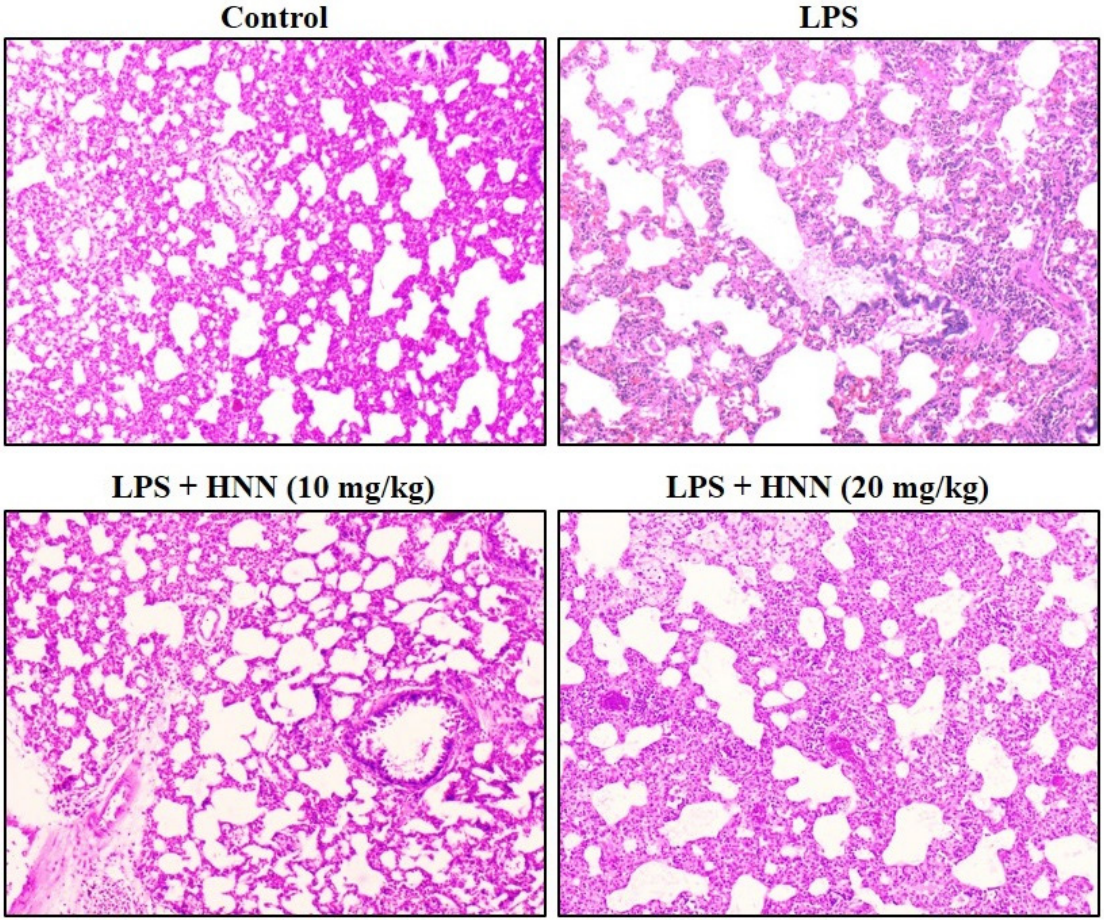

Figure 6: Effect of herniarin on the histopathological analysis of lung tissues of the experimental mice. Control: Normal control group; LPS: LPS-induced ALI group; LP+HNN (10 mg/kg): LPS-induced ALI+10 mg/kg of Herniarin (HNN)-treated group; LPS+HNN (20 mg/kg): LPS-induced ALI+20 mg/kg of Herniarin (HNN)-treated group.

involved in the onset of ALI. TNF-α, along with IL-1β, can cause excessive activation and recruitment of immune cells leading to further damage to the alveolar epithelial cells and the vascular endothelium.[36] The resulting damage to the lung tissue can result in the progression of ARDS.[37] The role of inflammation and the dysregulation of cytokine signaling, particularly IL-6 and TNF-α, in the pathophysiology of ALI is well-established.[38] In this work, the mice with ALI demonstrated a drastic elevation in the IL-6 and TNF-α concentrations; however, the herniarin treatment was successfully diminished the IL-6 and TNF-α concentrations in the ALI mice. These findings witnessed the anti-inflammatory properties of the herniarin.

Apoptosis, driven by the intrinsic and extrinsic signaling pathways, plays an imperative role in the onset of ALI.[39,40] The intrinsic apoptotic signaling is primarily controlled by the mitochondria and is mediated by Bcl-2 protein family, including pro-apoptotic (e.g., Bax) and anti-apoptotic (e.g., Bcl-2) members.[41] The Bax enhances the discharge of cytochrome c from the mitochondria, resulting in the caspase-3 activation, a key effector caspase that drives the execution phase of apoptosis. Conversely, the Bcl-2 protein inhibits this process, thereby enhancing cell growth.[42,43] In the context of ALI, the equilibrium between Bcl-2 and Bax expression is imperative in determining the fate of lung cells. Elevated Bax expression and diminished Bcl-2 expression was noted in animal models and human studies of ALI, highlighting an imperative role of apoptosis in the progression of this condition. Additionally, the activation of caspase-3 has been implicated as a hallmark of apoptosis in ALI, contributing to the destruction of lung tissue and impaired respiratory function.[44] Understanding the intricate interplay between apoptosis, Bcl-2, Bax and caspase-3 in the context of ALI is crucial to develop targeted therapies. By modulating these key players in the apoptotic pathway, researchers and clinicians may be able to mitigate the devastating consequences of ALI and improve patient outcomes.[45] Similarly, the present findings demonstrated an elevated Bax and caspase-3 expressions while diminished Bcl-2 expression was noted in the mice with ALI. Interestingly, the treatment with the herniarin effectively decreased the Bax and caspase-3 expressions and reduced the Bcl-2 expression in the ALI mice. These findings evidenced that the herniarin can show antiapoptotic properties on the lung and airway cells thereby protect these from ALI.

CONCLUSION

The present study revealed that herniarin successfully inhibited LPS-induced ALI in mice. The findings revealed that the treatment of herniarin significantly decreased lung edema, inflammation, oxidative stress, apoptosis and pulmonary damage in the ALI mice. Hence, it can be concluded that herniarin has the potential for the management of ALI. Moreover, we highly advise conducting additional molecular-level investigations in the future to completely understand the specific therapeutic mechanisms of herniarin in treating the ALI condition.

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ETHICAL STATEMENT

This study was approved by the Ethics Committee of The Third People's Hospital of Chengdu, (2024-S-230).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ALI: Acute lung injury; **LPS:** Lipopolysaccharide; **MDA:** Malondialdehyde; **SOD:** Superoxide dismutase; **GSH:** Glutathione; **ARDS:** Acute respiratory distress syndrome; **BALF:** Bronchoalveolar lavage fluid.

SUMMARY

Acute Lung Injury (ALI) is a severe, serious condition characterized by the development of pulmonary edema, hypoxemia and respiratory distress. Consequently, the current work was aimed at disclosing the salutary effects of the herniarin against LPS-induced ALI in mice model. The mice were exposed to LPS for 3 days via the intra-tracheal route to trigger the ALI response. Oral administration of herniarin was given for 3 days to the mice subsequent to the LPS challenge. The findings revealed that the treatment of herniarin significantly decreased lung edema, inflammation, oxidative stress, apoptosis and pulmonary damage in the ALI mice. Hence, it can be concluded that herniarin has the potential for the management of ALI.

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