Huperzine A and Methylprednisolone both elicit a significant reduction in histopathological score with mild congestion in alveolar capillaries and mild interstitial inflammatory cells infiltration as compared to figure (2).

Both Huperzine A and Methylprednisolone demonstrated a beneficial effect in reducing histopathological scores, suggesting a potential protective or therapeutic impact on lung tissue

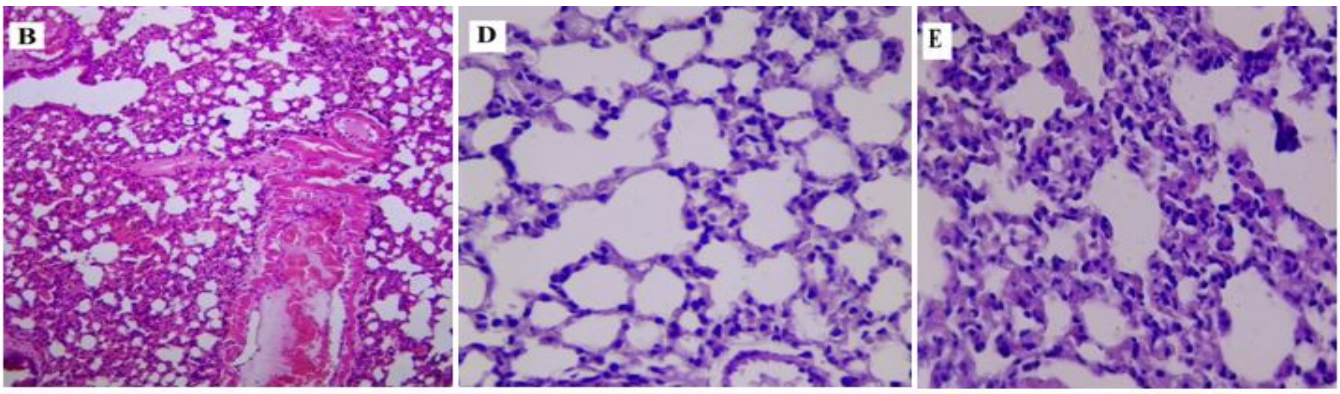

Figure 2: Lung histological section of LPS group (B) (x20), Huperzine A group (D) (x40), and Methylprednisolone group (E) (x40).

Discussion

-negative bacteria [23]; they maintain the bacterial cell structural integrity and act as a permeability barrier [24]
a potent stimulator of the innate immune system; typically, it's an exogenous agent that unleashes
immune cells [25, 26]
recognition will lead to a series of intracellular processes to activate NF-KB and MAPK kinase pathways that subsequently lead to an induction of many proinflammatory cytokines and chemokines.

Our results are similar to prior research that showed that -6, and TNF-1. [1 group [27, 28]. - treatment with 0.2 mg/kg Huperzine A significantly -6, and TNF-1 *et al*. and Cai *et al*. [29, 30] also found similar results to the present study. Huperzine A exhibited protective effects by inhibiting AChE activity, accumulating acetylcholine, and activating the cholinergic anti-inflammatory pathway [31, 32]. nAChRs expressed in neural and immune cells [33].

expression of anti-inflammatory cytokines [34], but it suppresses the production of proinflammatory cytokines [35, 36]. Huperzine A's cholinergic anti-inflammatory properties prevent the translocation of the NF- [37, 38] induce the activation of other inflammatory mediators, such as the synthesis of Nitric oxide (NO) and inflammatory process. Huperzine A suppresses the expression of inducible nitric oxide synthase (iNOS), COX-2, and their related inflammatory mediators NO W&X1 phosphorylation, which are key players in the MAPK pathway [39]. The common condition known as acute respiratory distress syndrome (ARDS) still has a high fatality rate in critical care medicine. Direct lung injury causes of ARDS include pneumonia and aspiration and extrapulmonary diseases that affect the lung secondarily (such as sepsis and pancreatitis) [40].

intraperitoneally, this causes an excessive formation of reactive oxygen species (ROS) and the release of inflammatory cytokines into the systemic circulation. That leads to indirect lung injury with interstitial edema [41, 42] have shown that the cholinergic anti-inflammatory pathway plays a role in suppressing the inflammatory response in acute lung damage. According to Mohseni-Moghaddam et al. [43], Acetylcholinesterase activity, oxidative stress, and inflammation are all inhibited by huperzine A. Nitrite and malondialdehyde (MDA) levels decreased while catalase and superoxide dismutase (SOD) activities enhanced.

The reduced oxidative stress could decrease caspase-1 - W Additionally, prevent ROS-mediated NF- activation [44, 45] proinflammatory cytokines, chemokines, and adhesion molecules like VCAM-1 and ICAM-1. These interactions enable leukocyte recruitment into inflamed tissues, endothelial cell apoptosis and promotes NO production, aids in vasodilatation, and raises endothelial permeability, which results in endothelial barrier damage . Yang et al. [46] found that huperzine A reduces oxidative stress, inflammatory cytokine production, and

caspase-3 activity to protect against Hepatic Ischemia-Reperfusion injury in mice. Ruan *et al*. mention that Huperzine A suppresses endothelial cell apoptosis and inhibits endothelial cell senescence by increasing endothelial cell proliferation.

CONCLUSION

Huperzine A demonstrates a protective effect against cytokine storm induced in Swiss Albino mice using LPS by suppressing serum levels of IL-1β, IL-6, and TNF-α and improving the lung histopathological changes.

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