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Boldine, a Plant Alkaloid, Attenuated LPS-induced Sepsis in Experimental Rats by Inhibiting the Oxidative and Inflammatory Pathway

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SUMMARY. **Boldine has been reported for its efficacy against lung injury by inhibiting elevated oxidative stress and inflammatory markers. Lipopolysaccharide (LPS) is a component of the cell wall of gram-negative bacteria that causes acute lung injury (ALI) in the lungs via upregulation of inflammatory cytokines. The objectivewas to determine the possible mechanism of boldine in LPS-induced ALI in experimental rats. Sprague-Dawley rats (180-200 g) was divided into various groups containing 16 rats in each group. Sepsis was induced by a single intraperitoneal dose of LPS (2 mg/kg), and boldine (25, 50, and 100 mg/kg) and vehicle (distilled water [DW]) was given orally for 28 days. Administration of LPS significantly ($p < 0.05$) increased differential and total cell counts in BALF (bronchoalveolar lavage fluid), which was effectively ($p < 0.05$) decreased by boldine (50 and 100 mg/kg) treatment. LPS-induced altered lung function tests were significantly restored ($p < 0.05$) by boldine. LPS-induced increased levels of myeloperoxidase (MPO) and oxidative stress levels in the lung and BALF were markedly ($p < 0.05$) decreased by boldine. LPS-induced down-regulated Nrf-2 and iNOs mRNA expressions and up-regulated TNF-α and IL-1β mRNA expressions were efficiently ($p < 0.05$) inhibited by boldine. Histopathological findings were consistent with biochemical findings. Administration of boldine exerted its anti-inflammatory efficacy via amelioration of elevated oxidative stress (SOD, GSH, MDA, Nrf-2), inflammatory mediator (nitric oxide and iNOs), and pro-inflammatory cytokines (TNF-α and IL-1β) in an experimental model of pneumonia.**

RESUMEN. Se ha informado que la boldina es eficaz contra la lesión pulmonar al inhibir el estrés oxidativo elevado y los marcadores inflamatorios. El lipopolisacárido (LPS) es un componente de la pared celular de las bacterias gramnegativas que causa lesión pulmonar aguda (ALI) en los pulmones a través de la regulación positiva de las citoquinas inflamatorias. El objetivo fue determinar el posible mecanismo de la boldina en la ALI inducida por LPS en ratas experimentales. Se dividieron ratas Sprague-Dawley (180-200 g) en varios grupos que contenían 16 ratas en cada grupo. La sepsis fue inducida por una sola dosis intraperitoneal de LPS (2 mg/kg) y boldina (25, 50 y 100 mg/kg) y vehículo (agua destilada [DW]) por vía oral durante 28 días. La administración de LPS aumentó significativamente ($p < 0,05$) el recuento diferencial y total de células en BALF (líquido de lavado broncoalveolar), que disminuyó de manera efectiva ($p < 0,05$) con el tratamiento con boldina (50 y 100 mg/kg). Las pruebas de función pulmonar alteradas inducidas por LPS se restauraron significativamente ($p < 0,05$) con boldina. Los niveles aumentados de mieloperoxidasa (MPO) inducidos por LPS y los niveles de estrés oxidativo en el pulmón y BALF se redujeron notablemente ($p < 0,05$) por la boldina. Las expresiones de ARNm de Nrf-2 e iNOs reguladas a la baja inducidas por LPS y las expresiones de ARNm de TNF-α e IL-1β reguladas al alza fueron inhibidas eficientemente ($p < 0.05$) por boldina. Los hallazgos histopatológicos fueron consistentes con los hallazgos bioquímicos. La administración de boldina ejerció su eficacia antiinflamatoria a través de la mejora del estrés oxidativo elevado (SOD, GSH, MDA, Nrf-2), mediador inflamatorio (óxido nítrico e iNO) y citoquinas proinflamatorias (TNF-α e IL-1β) en un modelo experimental de neumonía.

KEY WORDS: acute lung injury, boldine, lipopolysaccharide, Nrf-2, pneumonia.

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