

# Solithromycin Reduces Inflammation In Mice Caused By Bleomycin-Induced Lung Injury

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**Introduction:** Solithromycin (SOLI) is a fourth generation oral and intravenous macrolide, the first fluoroketolide, which is in Phase III clinical development for the treatment of community-acquired bacterial pneumonia. SOLI has been reported to show strong effects on cytokine release and superior anti-inflammatory effects on cigarette smoke-induced airway inflammation in mice (Kobayashi, J. Pharmacol. Exp. Ther. 2013; 345:76-84).

**Aim:** To explore the effects of SOLI on the ability to prevent lung inflammation and fibrosis, it was tested in a bleomycin induced-lung inflammation and fibrosis model.

**Methods:** Lung inflammation was induced in female mice by a single intratracheal administration of bleomycin. Twenty mice were divided into two groups. From Day -2 to Day 6, one group was administered vehicle and the other was administered SOLI orally at a dose of 100 mg/kg. Animals were sacrificed on Day 7.

**Results:** The total numbers of cells in the bronchoalveolar lavage fluid (BALF), especially those of lymphocytes, neutrophils and eosinophils, were significantly decreased in the SOLI group compared to the vehicle group. BALF MMP-9 levels showed a decreasing trend in the SOLI group. Masson's Trichrome staining revealed focal fibrotic lesions in the interstitial region of the lung in the vehicle group and SOLI treated group with no significant differences between the groups.

BALF Analysis	Vehicle treated	SOLI treated
Lymphocytes	7.9 ± 3.9 X 10 <sup>4</sup>	3.9 ± 1.9 X 10 <sup>4</sup> **
Macrophages	22.6 ± 7.3 X 10 <sup>4</sup>	16.9 ± 9.6 X 10 <sup>4</sup>
Neutrophil	2.4 ± 1.3 X 10 <sup>4</sup>	0.7 ± 0.4 X 10 <sup>4</sup> ***
Eosinophil	0.8 ± 0.5 X 10 <sup>4</sup>	0.3 ± 0.2 X 10 <sup>4</sup> **
MMP-9	0.62 ± 0.25 ng/mL	0.37 ± 0.30 ng/mL
Values are means ± SD. **p <0.01, ***p <0.001		

**Conclusion:** SOLI treatment resulted in the reduction of inflammatory cells in the BALF. The mechanism of the decrease could be similar to that noted in previous studies in the smoking mouse model. A decrease in inflammatory cells could in the long term decrease lung fibrosis and longer term treatment studies are warranted. The results suggest that SOLI could be beneficial to prevent disease progression and development of pulmonary fibrosis in patients.