

Protective effects of GHK-Cu in bleomycin-induced pulmonary fibrosis via anti-oxidative stress and anti-inflammation pathways.

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Abstract

Background

Idiopathic pulmonary fibrosis (IPF) is a serious lung problem with advancing and diffusive pulmonary fibrosis as the pathologic basis, and with oxidative stress and inflammation as the key pathogenesis. Glycyl-L-histidyl-L-lysine (GHK) is a tripeptide participating into wound healing and regeneration. GHK-Cu complexes improve GHK bioavailability. Thus, the current study aimed to explore the therapeutic role of GHK-Cu on bleomycin (BLM)-induced pulmonary fibrosis in a mouse model.

Methods

BLM (3 mg/kg) was administered via tracheal instillation (TI) to induce a pulmonary fibrosis model in C57BL/6j mice 21 days after the challenge of BLM. GHK-Cu was injected intraperitoneally (i.p.) at different dosage of 0.2, 2 and 20 $\mu\text{g/g/day}$ in 0.5 ml PBS on alternate day. The histological changes, inflammation response, the collagen deposition and epithelial-mesenchymal transition (EMT) was evaluated in the lung tissue. EMT was evaluated by α -SMA and fibronectin expression in the lung tissue. NF- κ B p65, Nrf2 and TGF β 1/Smad2/3 signalling pathways were detected by immunoblotting analysis.

Results

GHK-Cu complex inhibited BLM-induced inflammatory and fibrotic pathological changes, alleviated the inflammatory response in the BALF by reducing the levels of the inflammatory cytokines, TNF- α and IL-6 and the activity of MPO as well as reduced collagen deposition. In addition, the GHK-Cu treatment significantly reversed the MMP-9/TIMP-1 imbalance and partially prevented EMT via Nrf2, NF- κ B and TGF β 1 pathways, as well as Smad2/3 phosphorylation.

Conclusions

GHK-Cu presented a protective effect in BLM-induced inflammation and oxidative stress by inhibiting EMT progression and suppressing TGF β 1/Smad2/3 signalling in pulmonary fibrosis.