Republic of Iraq
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POSSIBLE PROTECTIVE EFFECTS OF SAXAGLIPTIN ON BLEOMYCIN -INDUCED PULMONARY INJURY

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BACKGROUND & INTRODUCTION:

- Bleomycin is a glycopeptide antibiotic primarily used as a chemotherapeutic agent in the treatment of various malignancies.
- bleomycin is associated with a significant risk of pulmonary toxicity, which can manifest as interstitial pneumonitis and progress to pulmonary fibrosis—a Potentially life-threatening complication.

BACKGROUND & INTRODUCTION:

- Bleomycin induced lung injury is primarily due to its ability to generate ROS leading to oxidative stress and DNA strand breaks in pulmonary cells.
- The lungs are particularly vulnerable because they have relatively low levels of bleomycin hydrolase, the enzyme responsible for inactivating bleomycin.
- This enzymatic deficiency allows toxic concentrations to accumulate in lung tissue, triggering an inflammatory response, cytokine release, and ultimately, fibrotic remodeling of the alveolar architecture.

BACKGROUND & INTRODUCTION

- Saxagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor commonly used in the management of type 2 diabetes mellitus to improve glycemic control.
- Saxagliptin acting By inhibiting DPP-4. DPP4 plays an important role in the maturation and activation of T cells and immune responses, with independent catalytic activity .

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BACKGROUND & INTRODUCTION

- They inhibit the enzyme DPP-4, there for extending the physiological actions of the incretin (GLP-1) hormones.
- Note; GLP-1 (Glucagon-like Peptide-1) is one specific type of incretin hormone.
- Hence, DPP-4 inhibitors may valuably attenuate chronic inflammation and oxidative stress in different diseases. Among DPP-4 inhibitors, SAX has anti inflammatory , antioxidant and immunomodulatory properties.
- The GLP-1 receptor is a G protein-coupled receptor that widely distributed in the lungs ,pancreas ,kidneys, heart, gastrointestinal tract, and other organs.

BACKGROUND & INTRODUCTION

- Recent studies have shown that GLP-1 receptor agonists (GLP-1RAs) can regulate ECM anabolic homeostasis by inhibiting the mitogen-activated protein kinase (MAPK) signaling pathway, and the formation of BATF/JUN heterodimers ; furthermore, downregulation of transforming growth factor (TGF)-β1, a pro-fibrotic factor, inhibits activation of SMAD3 and extracellular signal-regulated kinase 1/2 (ERK1/2) signaling and enhances WNT/β-catenin signaling.

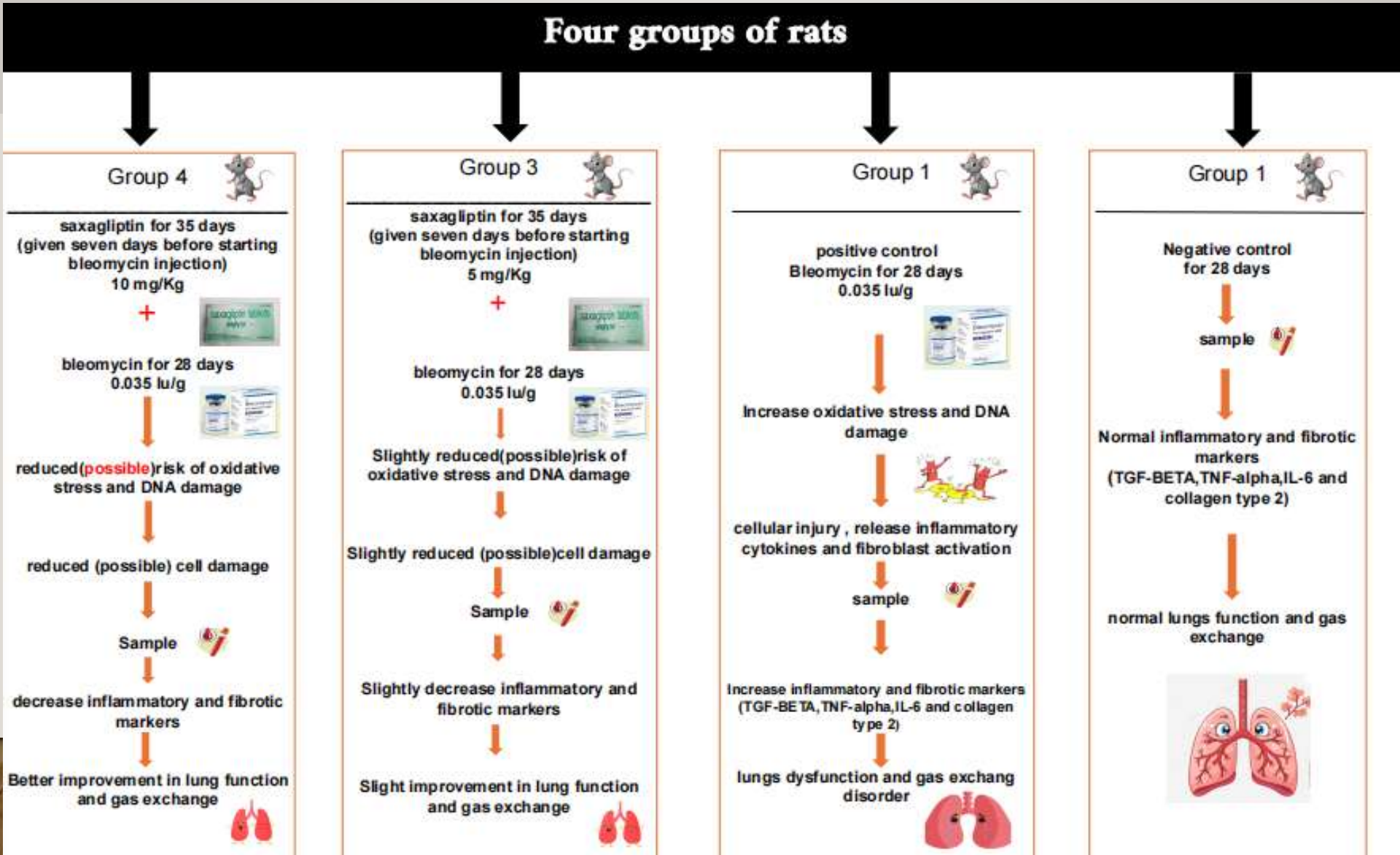
AIMS OF THE STUDY:

- Since have antioxidant and anti-inflammatory effects, Saxa may provide a therapeutic agent that can be valuable in the management of type 2 diabetic patient with Bleomycin – induced Pulmonary Injury.

METHODS

- Pulmonary fibrosis was induced experimentally with bleomycin (0.035 U/g, i.p.) given twice weekly for four weeks.
- saxagliptin (5 and 10 mg/kg/day, p.o) was given seven days prior to first injection of bleomycin and continued till 28 days after starting bleomycin injection.

ANIMALS AND EXPERIMENTAL



SUSPECTED RESULTS

- Saxa treatment decreased the apoptosis of lung celles
- Saxa treatment ameliorated inflammatory response in LPS-induced lung injury
- Saxa treatment attenuated histopathological changes of lung tissues in lung fibrosis
- Body weight: Moderate changes
- Oxidative stress markers and inflammatory cytokines Decreased.
- Decrease inflammatory cells in bronchoalveolar lavage
- Elevated endogenous antioxidants

THANK YOU ALL