Immunological and Safety Profile of CCL3 Therapy in Diabetic Wound: A Pre-Clinical Study

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***Abstract*:**

Diabetic foot ulcers are a complication of diabetes, accounting for 60–75.5% of lower-extremity amputations and adding $9–12 billion annually to U.S. healthcare costs. Impaired neutrophil recruitment during injury compromises early infection control, rendering diabetic wounds vulnerable to infection and delayed healing. CCL3 (MIP-1α) is a chemokine that recruits immune cells and enhances innate immune defense. We previously demonstrated that topical CCL3 restores neutrophil function, reduces bacterial burden by ~99%, and accelerates wound healing in diabetic mice. However, its systemic safety profile under diabetic conditions remains unclear.

We conducted a 14-day toxicity study in diabetic (db/db) and normoglycemic (db/+) mice. Animals were randomized into four groups: db/+ + PBS, db/db + PBS, db/db + CCL3 (1 µg), and db/db + CCL3 (10 µg). Full-thickness dorsal wounds were created and treated with a single topical dose. Animals were monitored, and hematological, biochemical, and histopathological analyses were performed on day 14.

CCL3 treatment caused no mortality or adverse clinical effects. Hematological and biochemical parameters remained within normal ranges, and no additional organ injury was observed. Diabetic control mice exhibited hepatic and renal pathology, which was not exacerbated by CCL3. These findings demonstrate that topical CCL3 is well tolerated and supports further translational evaluation.

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