



**PHARMACOLOGICAL ASSESSMENT OF TOPICAL
THERAPEUTIC FORMULATIONS FOR ACCELERATED WOUND
HEALING IN A DIABETIC RAT MODEL**

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ABSTRACT

Diabetes mellitus is a long-standing metabolic disease marked by persistently high blood glucose levels that interfere with the body's normal wound-healing mechanisms. In diabetic individuals, the healing process is often delayed due to extended inflammation, reduced collagen production, poor angiogenesis, and a higher risk of infection, which can ultimately lead to chronic ulcers and even amputations. Topical antimicrobial agents such as Mupirocin 2%, Silver sulfadiazine 1%, and Fusidic acid 2% are widely used to aid healing, but there is a lack of comparative experimental evidence evaluating their effectiveness in diabetic wound conditions. The present study was designed to assess and compare the wound-healing potential of these three antimicrobial formulations in a dexamethasone-induced diabetic rat model, with particular attention to fasting blood glucose levels, wound contraction,

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granulation tissue formation, and epithelialization time. Adult albino male rats were divided into control and diabetic groups, each consisting of 4–6 animals. Diabetes was induced by administering dexamethasone (10 mg/kg, SC) for 10 consecutive days. A 6 mm full-thickness excision wound was created, and the respective topical treatments were applied daily for 10 days. Key parameters were monitored, including fasting glucose levels on days 1, 3, 7, and 10; wound contraction on days 5 and 11; granulation tissue weight; and epithelialization period. By day 10, diabetic rats exhibited fasting glucose levels exceeding 200 mg/dl. On day 11, wound contraction was greatest with Mupirocin (99%), followed by Silver sulfadiazine (85%), Fusidic acid (74%), and control (57%). Wet granulation weight was highest in the Mupirocin group. Epithelialization occurred in 10.5 days with Mupirocin, 14 days with Silver sulfadiazine, 11.75 days with Fusidic acid, and 19.25 days in the control group. These findings indicate that Mupirocin 2% offers superior wound-healing effects compared to the other treatments, supporting its use in managing diabetic wounds.

Introduction

Diabetes mellitus is a long-term metabolic condition marked by elevated blood glucose levels due to insufficient insulin production, reduced insulin sensitivity, or a combination of both factors. Persistent hyperglycemia leads to a cascade of complications that interfere with normal physiological functions, particularly immune defense and tissue regeneration[1]. Among these complications, delayed wound healing is one of the most serious clinical concerns. Poor wound repair in diabetic individuals not only prolongs recovery but also increases the risk of infections, chronic ulcers, and amputations[2, 3]. Multiple biological mechanisms contribute to this impaired healing, including reduced growth factor release, compromised angiogenesis, neuropathic changes, diminished fibroblast activity, and weakened immune responses[2]. Collectively, these factors extend the inflammatory phase, reduce collagen synthesis, and delay epithelialization, making effective wound management in diabetic patients challenging[4]. Topical antimicrobial preparations are widely used to minimize infection and support healing in various wound types[5]. Mupirocin 2%, Silver sulfadiazine 1%, and Fusidic acid 2% are among the most frequently applied formulations due to their broad antibacterial coverage and ease of topical use. Mupirocin is especially valued for its effectiveness against *Staphylococcus aureus*, including resistant strains. Silver sulfadiazine remains a standard agent for burns because of its sustained silver ion release, while Fusidic acid is commonly used for superficial infections caused by Gram-positive bacteria. However, despite their popularity, there is limited experimental evidence comparing their relative wound-healing performance in diabetic conditions using standardized models. Earlier studies consistently report that diabetes delays all stages of wound healing, from inflammation through tissue remodeling[6]. Although many antimicrobial agents have been evaluated separately, few investigations have conducted direct comparisons of multiple agents within the same diabetic model. This gap limits evidence-based decisions for selecting the most effective treatment. The present study addresses this gap by comparing the

wound-healing efficacy of Mupirocin 2%, Silver sulfadiazine 1%, and Fusidic acid 2% in dexamethasone-induced diabetic rats. It focuses on key healing parameters, including blood glucose levels, wound contraction, granulation tissue development, and epithelialization time. The methodology, results, and discussion are presented systematically, followed by a conclusion summarizing the findings and their clinical implications for diabetic wound care.

Methodology

Experimental design

Animals were divided into different groups each comprising of 4-6 adult albino male rats. Control group received water for injection (2.5ml/kg SC for 10 days). Different groups were treated with Dexamethasone (10mg/kg SC for 10 days) to induce diabetes mellitus. Evaluation of hyperglycemia was routinely performed after every three days by obtaining a drop of blood from the tail vein, and measuring the fasting blood glucose level (mg/dl), with standard glucometer. Blood glucose was measured in animals after 12 hours fasting period at the same time of the day for minimizing variations.

All diabetic rats included in the experiment were anesthetized through intraperitoneal administration of ketamine and xylazine in a 10:1 ratio. Once adequate anesthesia was achieved, the hair on the dorsal surface was carefully removed using a depilatory cream, and the wound site was outlined. A circular full-thickness excision wound, approximately 6 mm in diameter, was then created on the marked area using a combination of toothed forceps, a surgical blade, and scissors with the aid of a punch perforator. Animals in the treatment groups received topical applications of Mupirocin 2%, Silver sulfadiazine 1%, or Fusidic acid 2% cream once daily. Each formulation was applied as a uniform thin layer over the wound surface for a period of ten consecutive days.

Weight of Wet and Dry Granulation:

The granulation tissue which was developed on the wound was removed and wet weight was noted on 11th day. The wet granulation tissue was dried in the oven at 60°C for 24 hours and weight was noted again.

Period of Epithelialization

It is measured as the number of days required for shedding of eschar, without leaving any residual raw wound.

Results & Discussion

Measurement of Fasting Blood Glucose Level

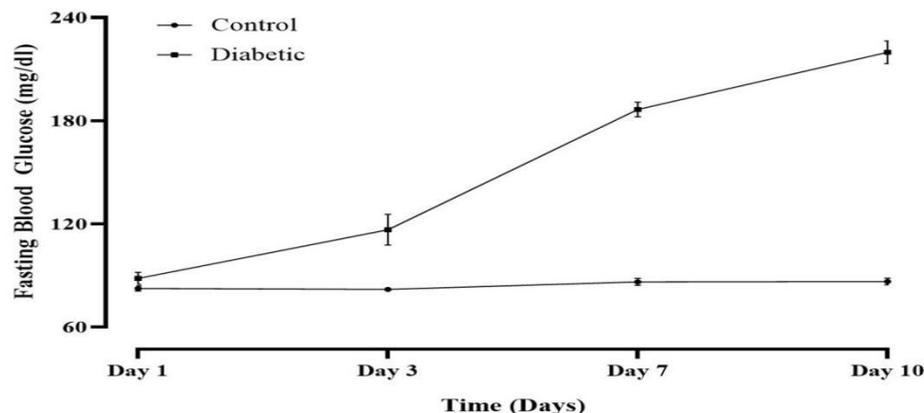


Figure 1: The graph showing the fasting blood glucose (mg/dl) levels of control group and diabetic group.

pronounced elevation in fasting blood glucose, whereas the control group maintained consistent values within the normal physiological range. Both groups began with nearly identical glucose concentrations on Day 1. By Day 3, the diabetic group showed a noticeable increase, which became more pronounced by Day 7. This upward trend persisted through Day 10, at which point their glucose levels exceeded 200 mg/dl. In contrast, no meaningful change was detected in the control group across the same time points.

Percentage wound contraction:

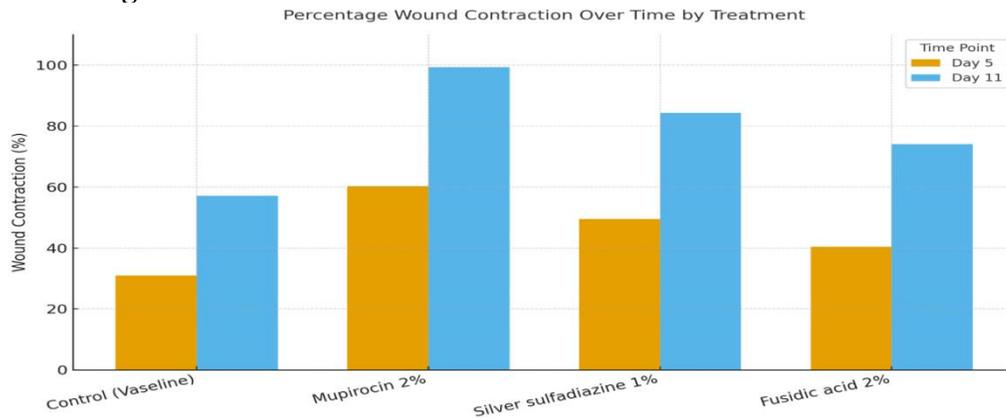
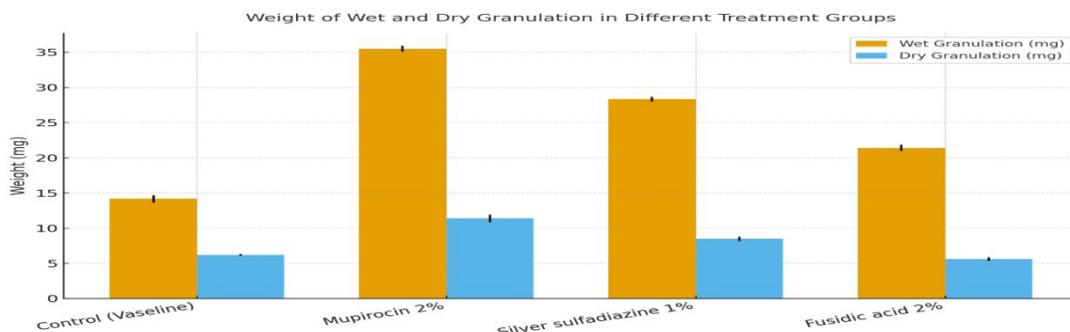


Figure 2: Percentage wound contraction on Day 5 and Day 11 showing the comparative healing efficacy of different antimicrobial creams in diabetic rats.

The bar graph presents the percentage of wound contraction measured on the 5th and 11th day in diabetic rats subjected to different topical treatments. A steady increase in wound contraction was observed in all groups over time, but the rate and extent of healing differed considerably. By the 5th day, animals treated with Mupirocin 2% showed a marked contraction of around 60%, which was higher than the other groups. Wounds treated with Silver sulfadiazine 1% and Fusidic acid 2% showed moderate contraction, whereas the control group exhibited the lowest percentage. By the 11th day, the Mupirocin 2% group demonstrated almost complete closure of the wound (approximately 99%), clearly indicating its superior healing effect. Silver sulfadiazine 1% also promoted considerable healing (about 85%), followed by Fusidic acid 2% (around 74%) and the control group (57%). These results emphasize the effectiveness of Mupirocin 2% in accelerating wound healing under diabetic conditions[7].

Weight of Wet and Dry Granulation:



The Figure 3 illustrates the comparison of wet and dry granulation tissue weights across various treatment groups in diabetic rats. Mupirocin 2% cream resulted in the greatest granulation mass in both wet and dry forms, reflecting its strong ability to stimulate tissue formation at the wound site. Silver sulfadiazine 1% cream also produced a noticeable increase in granulation tissue, followed by Fusidic acid 2%. In contrast, the control group treated with Vaseline showed the lowest values for both measurements. Overall, all treatment groups exhibited better granulation responses compared to control, with Mupirocin demonstrating the most pronounced wound-healing effect[8].

Period of epithelization:

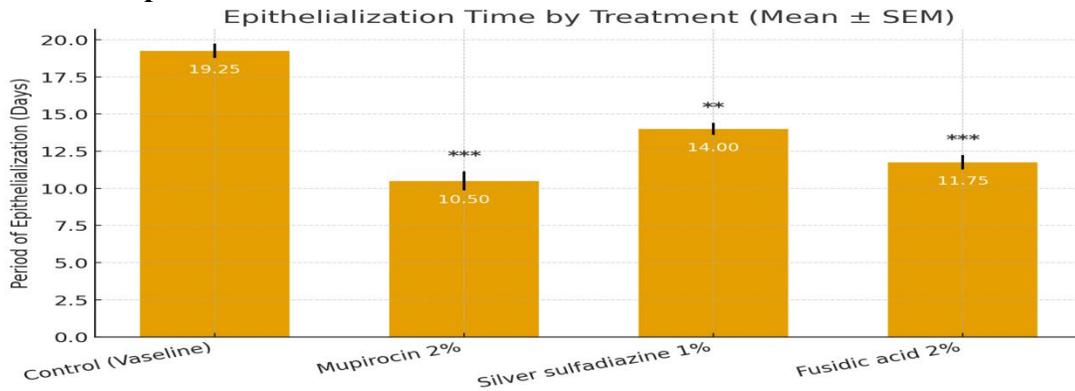


Figure 4: Mupirocin 2% and fusidic acid 2% significantly shortened the epithelialization period versus control, with Mupirocin showing the fastest closure.

The figure 4 illustrates the average epithelialization period observed in each treatment group. The control group had the slowest healing, requiring around 19.25 days for complete epithelialization. In contrast, wounds treated with Mupirocin 2% healed considerably faster, with an average epithelialization time of 10.5 days. Fusidic acid 2% also reduced the healing duration to 11.75 days, while treatment with Silver sulfadiazine 1% led to moderate improvement, with epithelialization achieved in approximately 14 days. The results clearly demonstrate that all topical antimicrobial treatments improved the rate of epithelialization compared to the control[9]. Mupirocin 2% showed the most marked reduction in healing time, indicating its strong wound-healing potential. Fusidic acid produced a similar beneficial effect, whereas Silver sulfadiazine promoted a moderate but statistically significant improvement.

Conclusion

Topical application of Mupirocin 2% significantly accelerated wound healing in diabetic rats, demonstrated by rapid contraction, enhanced granulation, and shortened epithelialization, outperforming Silver sulfadiazine 1% and Fusidic acid 2%. These findings support Mupirocin’s superior therapeutic potential in diabetic wound management.

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