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Efficacy Of Papain-Urea Ointment And Superoxide Solution In Diabetic Foot Ulcer

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Abstract

Background:

Diabetic foot ulcers (DFUs) remain a serious complication of diabetes mellitus, frequently resulting in infection, prolonged hospitalization, and even amputation. Prompt and effective wound debridement plays a pivotal role in facilitating healing. This study aimed to compare the clinical efficacy of superoxidized solution and papain–urea ointment in managing Wagner Grade I and II DFUs.

Materials and Methods:

A prospective, randomized, comparative study was conducted on 68 patients diagnosed with DFUs. Participants were randomly allocated into two equal groups: Group A underwent daily dressings with superoxidized solution, while Group B received papain–urea ointment dressings. All patients were followed for four weeks. Outcome measures—ulcer size, slough percentage, granulation tissue percentage, and time to complete healing—were recorded weekly. Data analysis was performed using SPSS v25, with $p < 0.05$ considered statistically significant.

Results:

Baseline demographic and clinical variables, including age, gender, BMI, HbA1c levels, socioeconomic status, ulcer size, formation of granulation tissue and healing time were comparable between the two groups. By the end of week four, Group A demonstrated significantly superior results, with smaller residual ulcer size (1.1 ± 0.5 cm² vs. 4.5 ± 1.1 cm²), reduced slough (5% vs. 17%), and higher granulation tissue coverage (95% vs. 78%) compared to Group B ($p < 0.01$ for all). The mean healing time was notably shorter in Group A (28 ± 5 days) than in Group B (35 ± 7 days, $p < 0.001$).

Conclusion:

Superoxidized solution demonstrated greater effectiveness than papain–urea ointment in promoting DFU healing, offering faster granulation, better wound cleansing, and antimicrobial benefits, making it a safe and reliable option for Wagner Grade I and II ulcers.

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I. Introduction

Diabetes mellitus has emerged as a major global health challenge, with its prevalence rising sharply, particularly in developing nations. India ranks second worldwide in the number of individuals living with diabetes, and the associated complications are increasing in parallel. Among these, diabetic foot ulcers (DFUs) represent one of the most debilitating and costly consequences, with a lifetime risk estimated between 15% and 25% for people with diabetes. If inadequately managed, DFUs can progress to severe infection, gangrene, and, in many cases, necessitate limb amputation.[1] Beyond the medical consequences, these outcomes impose profound psychological distress and significant financial burdens on patients and their families.

Effective DFU management requires a comprehensive approach, with wound debridement being a cornerstone of therapy. Debridement facilitates healing by removing devitalized tissue, reducing bacterial load, and preparing the wound bed for regeneration. While surgical debridement is generally considered the gold standard, it is not always feasible—particularly in patients with poor surgical fitness, in resource-limited settings, or where trained personnel are scarce.[2] In such cases, chemical and enzymatic debridement agents serve as valuable alternatives.

Superoxidized solutions have gained attention for their potent antimicrobial activity, anti-inflammatory effects, and capacity to enhance oxygenation of the wound bed. In contrast, papain–urea ointment, a well-established enzymatic agent, acts by breaking down necrotic tissue while promoting granulation and epithelialization. Despite their widespread use, there is a paucity of head-to-head comparative data evaluating these two agents for DFU management.[3-4] This study aims to address this gap by assessing the comparative effectiveness of superoxidized solution and papain–urea ointment in Wagner Grade I and II DFUs, thereby guiding clinicians toward evidence-based, cost-effective wound care strategies.

II. Materials And Methods

This prospective, randomized, comparative study was conducted over an 18-month period, from July 2024 to December 2025, in the Department of General Surgery at Geetanjali Medical College and Hospital, Udaipur. Ethical clearance was obtained from the Institutional Ethics Committee prior to initiation, and written informed consent was secured from all participants.

A total of 68 adult patients (≥18 years) with type 2 diabetes mellitus presenting with Wagner Grade I or II diabetic foot ulcers were enrolled. Patients were randomly assigned into two equal groups (n = 34 each) using a simple randomization technique. Group A received daily wound dressings with a commercially available superoxidized solution, whereas Group B received daily dressings with papain–urea ointment. All dressings were applied under sterile conditions once daily.

Inclusion criteria comprised adults with confirmed type 2 diabetes and Wagner Grade I or II ulcers. Exclusion criteria included Wagner Grade III or higher ulcers, evidence of osteomyelitis (clinical or radiological), immunosuppressive conditions, active malignancy, bleeding disorders, and ongoing long-term corticosteroid or chemotherapy treatment. Before initiating the dressing protocol, all patients underwent wound debridement to remove necrotic tissue. The parameters assessed included ulcer size (measured using transparent graph paper tracing), percentage of slough covering the wound bed, proportion of granulation tissue, and clinical signs of infection such as edema and discharge. Assessments were performed on days 0, 7, 14, 21, and 28. The primary outcome measure was time to complete healing, defined as full epithelialization without discharge. Data analysis was carried out using SPSS software (version 25.0), and statistical significance was set at $p < 0.05$.

III. Discussion

Diabetic foot ulcers (DFUs) remain one of the most complex and resource-intensive complications of diabetes mellitus, particularly in patients with moderate-to-severe wounds where healing is often impaired by microvascular disease, infection, and suboptimal glycaemic control.[5] The challenge is especially pronounced in India, where the prevalence of diabetes continues to rise and healthcare access is uneven across socioeconomic groups. Against this backdrop, our study offers meaningful comparative evidence on the clinical effectiveness of two commonly used topical debriding agents—superoxidized solution and papain–urea ointment—in the management of Wagner Grade I and II DFUs.

The results indicate a clear advantage of superoxidized solution in accelerating wound healing. Its dual mechanism—broad-spectrum antimicrobial activity combined with oxidative stimulation of the wound bed—facilitates rapid slough removal and promotes early granulation tissue formation. These findings are consistent with previous reports, such as those by Sarabahi et al., who demonstrated that superoxidized solution enhances epithelialization and reduces microbial load without harming healthy tissue, and Kumar et al., who observed shorter times to graft readiness compared to conventional dressings. Importantly, no adverse reactions were observed in our study, reinforcing its reputation as a non-cytotoxic, well-tolerated dressing agent.[6-8]

Practical advantages further strengthen its clinical utility: superoxidized solution is easy to apply, non-irritating, leaves no residue, and can be used safely in outpatient or home-based care settings—an important consideration in rural areas where daily hospital visits may be impractical. In comparison, papain–urea ointment remains a well-established enzymatic debrider, effectively breaking down necrotic tissue through proteolytic action.[9-10] However, its lack of inherent antimicrobial activity necessitates reliance on systemic antibiotic coverage to control infection. Papain–urea improves wound bed preparation, it does not significantly accelerate granulation or epithelialization compared to oxidative or honey-based dressings.[11-13] Moreover, its use can be associated with increased exudation and occasional discomfort, particularly during the initial days of application—a trend echoed in our anecdotal observations of stinging sensations reported by some patients in the papain–urea group. One of the more significant implications of our findings lies in their potential to influence wound care policy and practice. Faster healing with superoxidized solution could shorten hospital stays, reduce dressing costs, lower the risk of major amputations, and ultimately decrease both direct and indirect healthcare costs. In a country where DFUs represent a substantial economic burden, such benefits could translate into considerable system-wide savings.[14-15] Nonetheless, certain limitations warrant consideration. Our sample size, while adequate to detect moderate differences, may not reveal less common complications or outcomes in specific subgroups such as smokers, patients with advanced peripheral arterial disease, or those with nutritional

deficiencies.[16] The follow-up duration of four weeks was appropriate for Wagner Grade I ulcers but may be insufficient to fully capture long-term outcomes in more complex wounds. Furthermore, although objective markers such as ulcer size, slough percentage, and granulation coverage were measured, incorporating histopathological or microbiological assessments could provide deeper insight into the biological mechanisms underlying the observed clinical effects. Despite these constraints, our findings add to the growing body of evidence supporting oxidative wound care strategies in DFU management. Future studies could investigate combination treatment protocols—such as initial enzymatic debridement followed by oxidative maintenance—or tailor dressing selection based on ulcer etiology, vascular status, and microbial profile.

IV. Conclusion

Both superoxidized solution and papain–urea ointment demonstrated clinical benefits in the management of diabetic foot ulcers; however, superoxidized solution consistently showed superior outcomes for Wagner Grade II ulcers. Its advantages included faster healing times, greater reduction in ulcer size, and better patient comfort, without any observed systemic side effects. These findings support its recommendation as a first-line topical dressing for infected diabetic foot ulcers, offering a safe, effective, and patient-friendly option for wound care.

V. Limitations And Suggestions

The patients required any treatment/therapy that could jeopardize the evaluation of the test product, such as surgical debridement or skin grafting. A preliminary experience shows that, while the initial outcomes of using Superoxide solution to control infected diabetic wounds are positive, further multicenter clinical trials are needed before this antiseptic can be recommended for widespread usage.

Table

Table 1: Baseline demographic and clinical characteristics of study participants

Parameter	Group A (Superoxidized)	Group B (Papain-Urea)	p-value
Number of patients (n)	34	34	—
Age (years)	56.2 ± 9.8	55.1 ± 10.4	0.64
Gender (Male:Female)	1.6: 1	1.27: 1	0.61
BMI (kg/m²)	25.3 ± 2.1	25.1 ± 2.2	0.68
Socioeconomic status			0.84
• Upper	2 (5.8%)	1 (2.9%)	—
• Middle	21 (61.7%)	22 (64.7%)	—
• Lower	11 (32.3%)	11 (32.3%)	—
HbA1c (%)	7.8 ± 0.6	7.7 ± 0.7	0.53
Random Blood Sugar (mg/dL)	198.3 ± 26.5	201.7 ± 24.9	0.58
Wagner Classification			0.79
• Grade I	22 (64.7%)	21 (61.7%)	—
• Grade II	12 (35.3%)	13 (38.3%)	—

Table 2: Weekly progression of healing parameters in Group A and Group B with p-values

Day	Ulcer Size (cm²)			Slough (%)			Granulation Tissue (%)		
	Group A	Group B	*p*-value		Group A	Group B	*p*-value		Group A
0	9.6 ± 1.2	9.7 ± 1.3	0.71	0	9.6 ± 1.2	9.7 ± 1.3	0.71	0	9.6 ± 1.2
7	6.2 ± 1.0	7.1 ± 1.1	0.02	7	6.2 ± 1.0	7.1 ± 1.1	0.02	7	6.2 ± 1.0
14	3.8 ± 0.9	5.8 ± 1.0	<0.01	14	3.8 ± 0.9	5.8 ± 1.0	<0.01	14	3.8 ± 0.9
21	2.1 ± 0.7	4.9 ± 0.8	<0.01	21	2.1 ± 0.7	4.9 ± 0.8	<0.01	21	2.1 ± 0.7
28	1.1 ± 0.5	4.5 ± 1.1	<0.01	28	1.1 ± 0.5	4.5 ± 1.1	<0.01	28	1.1 ± 0.5

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Figures

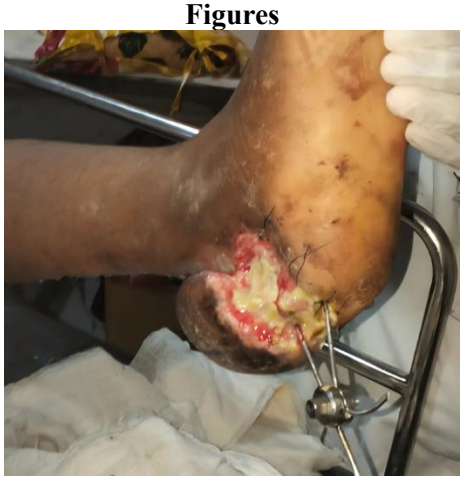

Figure 1. Dressing done using Papin-urea ointment.

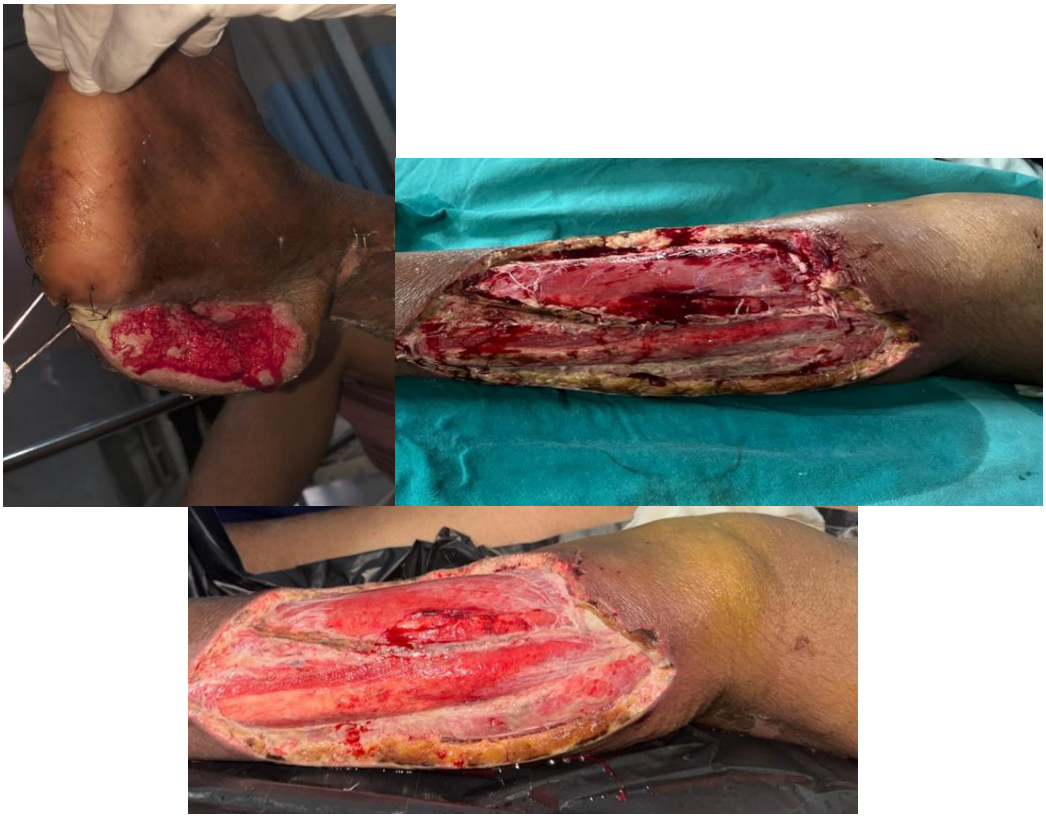

Figure 2. Dressing done using Superoxide solution.