Journal of Basrah Researches (Sciences) **52**(1), 157 (2026)
DOI: https://doi.org/10.56714/bjrs.52.1.12

Histopathological Effects of *Pseudomonas aeruginosa* Exotoxin A on Diabetic Skin Wounds in Rats

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ARTICLE INFO

Received 25 December 2025
Revised 16 March 2026
Accepted 26 March 2026
Published 30 June 2026

Keywords:

Pseudomonas Aeruginosa, Exotoxin A, Diabetic Wounds, Wound Healing.

Citation: S. S. Al-Baydani et al. , J. Basrah Res. (Sci.) **52**(1), 157 (2026).
DOI:https://doi.org/10.56714/bjrs.52.1.12

ABSTRACT

Diabetes definitely affects the wound healing process by interfering with tissue remodeling and prolonging the inflammatory phase. This study aims to evaluate the histopathological effects of Exotoxin A (ETA), one of the main virulence factors of *Pseudomonas aeruginosa* bacteria, on the healing of skin wounds in diabetic rats. Techniques: Full-thickness skin wounds were created in rats with diabetes induced by alloxan. Rats were divided into three groups: a control group treated with phosphate-buffered saline (PBS) and two groups receiving Exotoxin A (ETA) at doses of 10 µg and 50 µg. Tissue samples were collected on days 4, 8, 12, and 16, and histological changes were evaluated using hematoxylin and eosin (H&E) staining. The diabetes control wounds showed prolonged inflammatory exudation, aberrant collagen organization, and a significant delay in epidermal reconstitution. Conversely, wounds treated with ETA showed poor regeneration and early cellular damage. Both doses (10 µg and 50 µg) demonstrated significant improvement in the later stages compared to the control, including thicker epidermis, more pronounced granulation tissue development, better collagen fiber organization, and nearly complete wound closure on days 12 and 16.Overall, Exotoxin A causes early damage to diabetic wounds but later promotes better tissue reconstruction. These results suggest that ETA may have a regulatory role in the healing of chronic wounds, necessitating further investigation to identify the precise mechanisms and evaluate the efficacy of therapy.

1. Introduction

Diabetic wounds represent one of the most serious complications of diabetes mellitus and are frequently associated with delayed healing [1] and increased susceptibility to bacterial infections, particularly those caused by *P. aeruginosa* [2] .

The Gram-negative opportunistic pathogen *Pseudomonas aeruginosa* can cause hospital-acquired infections as well as infections in the community, with potentially fatal or cosmetic consequences [3]. Skin and soft tissue infections, ulcerative keratitis, diabetic foot and wound infections [4], burn wound

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ISSN: 1817-2695 (Print); 2411-524X (Online)
Online at: https://jou.jobrs.edu.iq

infections, urinary tract infections, bacteremia, and pneumonia [5] are among the common and frequently debilitating illnesses it causes. Antimicrobial resistance and exotoxin generation are common in *P. aeruginosa*, which is responsible for 11–13.8% of all hospital-acquired infections [6]. This is a concerning scenario that necessitates quick action to create novel therapies and hospital *P. aeruginosa* infection prevention guidelines [7]. Exotoxin A (ETA), one of these toxins, penetrates the host's cells through the Alpha-2 macroglobulin receptor (α2MR), where it causes ribosylation of elongation factor-2, which ultimately results in cell death [8]. Due to its high toxicity, Exotoxin A (ETA) is considered one of the most important virulence factors produced by *P. aeruginosa*. The receptor α2-macroglobulin receptor (α2MR) is widely expressed in various human cell types, including resident cells of the sub-epidermal skin layers such as fibroblasts and certain leukocytes. It has been reported that up to 80% of clinical isolates of *P. aeruginosa* are capable of producing ETA [9]. The synergistic process by which ETA destroys the structural integrity of skin tissue and prevents reconstruction and repair was highlighted by further *in vitro* investigations employing ETA, which revealed that ETA inhibits protein synthesis and prevents cells from rebuilding the damaged tight junctions [10]. We hypothesized that these virulence factors might break down the extracellular matrix of subcutaneous tissue (ST) and eliminate fibroblasts that preserve the barrier of ST during *P.aeruginosa* infection after dermal damage, given the documented toxicity of ETA in other tissues [11]. Though only a few experimental approaches permit research involving the direct application of pure bacterial products onto ST, a large number of studies have contributed much to our understanding of *P.aeruginosa* infections [12].

In this study, incisions were made in the dorsal region using surgical scissors to separate ST in a dermal injury rate model, enabling the direct application of purified ETA to ST. The application of these VFs directly on ST has been studied to examine the impact on fibroblasts, inflammatory cells, and the structural integrity of tissue in a rat model of cutaneous injury. This novel approach offers substantial advantages over in vitro research [13].

2. Materials and Methods

2.1. Rats

All animal experiments were conducted in accordance with internationally accepted guidelines for the care and use of laboratory animals [14]. Rats weighing between 150 and 180 grams at ten to twelve weeks of age were acquired from Basrah University, Veterinary Medicine College. In the small animal holding facility, rats were kept in cages of four and exposed to a 12-hour light cycle while having unlimited access to food and water at the Basrah University, Science College, in the animal house.

2.2. Induction of Diabetes

Diabetes was induced in rats by intraperitoneal injection of alloxan at a dose of 200 mg/kg body weight. The alloxan was freshly prepared and dissolved in chilled physiological saline. Alloxan leads to the creation of an experimental model of type 1 diabetes due to its selective toxic effect on beta cells (β-cells) in the islets of Langerhans in the pancreas, resulting in decreased insulin secretion and hyperglycemia [15].

To prevent the initial phase of hypoglycemia after administering alloxan, the rats were provided with a 5% glucose solution for 24 hours. After 72 hours of injection, fasting blood glucose level was measured using a glucometer after 8–12 hours of fasting. The rats were considered diabetic when their fasting blood glucose level was ≥250 mg/dL, and they were included in the subsequent wound-healing experiments.

2.3. Animals and wounding

For the study outlined below, 48 male rats aged 12 weeks were acquired from the laboratory and diabetes was induced using alloxan. The rats were randomly divided into three experimental groups (Control, 10 µg ETA, and 50 µg ETA), with four rats allocated to each group at each time point (days 4, 8, 12, and 16), resulting in a total of 48 rats. In the Biology Department of the University of Basra, rats were kept in separate housing with unlimited access to water and rodent feed.
Ketamine (132 mg/kg body weight) and xylazine (20 mg/kg) were injected intraperitoneally to anesthetize the rats following commonly used rodent anesthesia protocols [16]. After shaving and removing the hair with a hair removal machine, the dorsal skin was cleansed with a povidone-iodine solution. A single circular full-thickness wound (approximately 15 mm in diameter) was then created on the dorsal skin of each rat using surgical scissors, and the wound diameter was standardized using a ruler [17].

2.4. Exotoxin A source

Lyophilized *P.aeruginosa* Exotoxin A (ETA) was purchased from Sigma-Aldrich (USA) (Cat. No. P0184-.5MG) and used in the experiments according to the manufacturer's instructions.

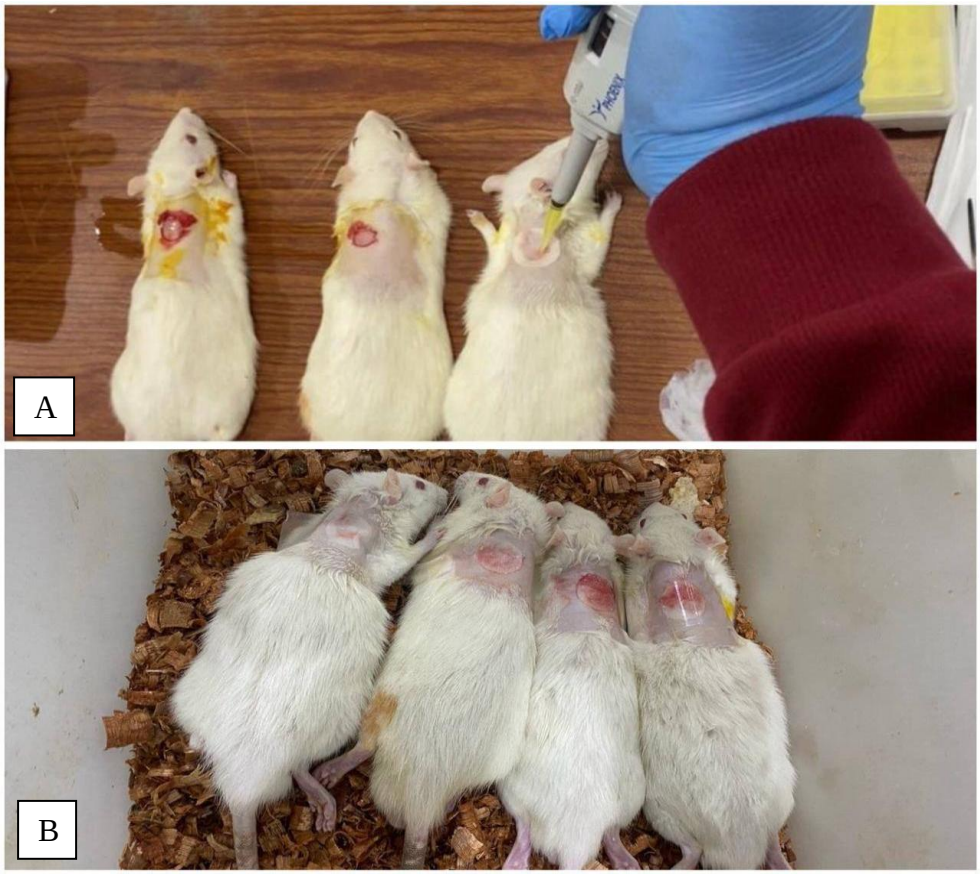

Fig. 1. Diabetic rats' local wound treatment techniques.

(A) Standardized, full-thickness dorsal wounds on three sedated rats are displayed. As part of the experimental methodology, a micro-pipe is used to apply local therapy.
(B) Following wound incision, diabetic rats are gathered in the animal pen. The rats are housed in a plastic container with bedding made of wood shavings, and it is easy to see how the circular lesions on their backs are healing under various treatment scenarios.

2.5. Treatment with Exotoxin A

Following wound induction, either 50 or 10 µg of ETA were put on filter paper Based on prior findings[18], which was subsequently placed directly on the wounds (or PBS for control rats). On

days 4, 8, 12, and 16, tissues were taken from the wounds for analysis without any additional help, doses of 10 and 50 µg were chosen because they were non-lethal but adequate to cause pathological alterations in tissue.

2.6. Histology

The histology laboratory at the University of Basrah ,College of Science, Department of Biology, removed tissues from the wound area and surrounding area, fixed them in 10% buffered formalin (pH 7.4), embedded them in paraffin wax, sectioned them, and stained them with either haematoxylin and eosin (H&E) .

2.7. Data analysis

The data were statistically analyzed using the Statistical Package for Social Sciences (SPSS). Results are presented as mean ± standard deviation (Mean ± SD). Two-way ANOVA was used to examine the effect of different treatments, concentrations, and time periods, as well as their interaction, on wound size (wm) and the studied variables. Where significant differences were found, post-hoc comparisons were performed using the least significant difference (LSD) test to determine differences between groups. A statistical significance level of $p \leq 0.01$ was adopted.

3. Results

3.1. Wound measurement (WM)

Wound measurements showed a time-dependent decrease in all experimental groups, with treated animals showing earlier wound shrinkage than the control group (Table1).

Table 1. Wound measurement at different time points.

Day	Treatment	Wound measurement (Mean ± SD)
Day 4	50 µg	9.875 ± 1.297
Day 4	10 µg	7.275 ± 0.665
Day 4	Control	6.650 ± 0.850
Day 8	50 µg	7.600 ± 2.843
Day 8	10 µg	9.775 ± 1.797
Day 8	Control	5.525 ± 1.417
Day 12	50 µg	3.625 ± 0.741
Day 12	10 µg	4.450 ± 2.213
Day 12	Control	3.850 ± 0.569
Day 16	50 µg	0.000 ± 0.000
Day 16	10 µg	0.000 ± 0.000
Day 16	Control	1.414 ± 1.414

With n = 4 animals per group, all results are presented as mean values with matching standard deviations. Two-way analysis of variance (ANOVA) and the least significant difference (LSD) post hoc test were used for statistical evaluation. Statistical significance was defined as a probability value of $p \leq 0.01$.
Mean ± SD.** $P \leq 0.01$ compared with control group.

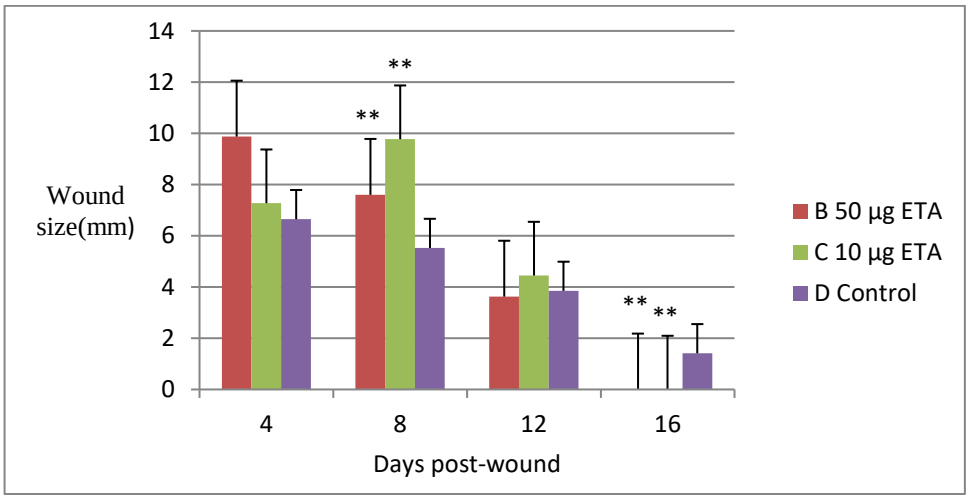

Fig.2 . Effect of *P. aeruginosa* Exotoxin A on wound size in diabetic rats at different time points. Data are presented as mean ± SD (n = 4). **P ≤ 0.01 compared with the control group.

3.2. Histopathological findings

Histological observations on wounded skin from diabetes group post (4th) days control of skin injury showed damage of surface layer & blood clots, vacuolated epidermis cells with mild keratin deposit at the margins (Figure 3A).

Moreover wounded skin from diabetic rats treated with (10 µg) post (4th) days showed infiltrations of inflammatory cells & granulation tissue formed contain fibrin in addition to scab that formed over wound surface (Figure 3B).

Microscopic exam on surgical wound from treated rats with (50 µg) post (4th) days of injury revealed mild bleeding & scab formation, new epidermis start to grow, some vacuolated cells at the base of epidermis and still granulation tissue observed beneath the scab layer(Figure 3C).

Results showed that diabetes impairs wound healing in all experimental rats, and the diabetics induced changes characterized by slower wound healing, less re-epithelization, partial closure of wounds, and altered tissue structures. This phase begins with a proliferative phase post 8 day control of skin wounds healing, and formation of granulation tissue by deposition of fibers, new blood vessels, and skin cell proliferation(Figure 4A)

Histological examination showed changes in the wounded skin at day(8th) of injury that treated with (10 µg), most changes showed well-developed epidermal layers and differentiation of epidermis layers, partial closure of wound margins, inflammatory cells proliferation and more regular collagen fibers formed the wounded matrix (Figure 4B).

Moreover surgical wounds from diabetic rats 8th days(50 µg) of skin healing revealed mild keratin deposits at surface layer (re-epithelization), still partial closure of the wound margins, several number of blood capillaries, and irregular deposits of collagen fibers with heavy infiltration of inflammatory cells, also scab formed at the epidermis surface(Figure 4C) .

Histological examination also showed that the histologic changes in a surgical wound from diabetic rats post 12th day control of healing and showed slower skin growth (re-epithelization), increased collagen deposits (remodeling), inflammation, still partial closure of wound margins, thick granulation tissue formed and obvious angiogenesis by the formation of capillaries and small blood vessels, also more adipocytes at deep layer(Figure 5A) .

Histological exam of wounded skin from diabetic wounds treated with (10 µg) post 12th days of injury showed skin with proliferative phase, differentiation of keratin layer (stratum corneum), still partial closure of wound margins, regular collagen deposition in dermis layer, differentiation of epidermis layers, increase thickness of epidermis, well developed dermal papillae, develop of hair follicles surrounded by epidermis sheath extend deep to invaginate the dermis layer and still mild inflammatory cells observed (Figure 5B).

Section from wounded skin post 12th days of injury related to diabetes rats treated with (50 µg) showed inflammatory infiltration skin, complete closure and well-developed of all skin layers, mild keratin deposit at surface layer, increase number of hair follicles, increase in small blood vessels and capillaries embedded in skin matrix (dermis) layer, regular distribution of collagen fibers and regeneration of superficial epidermis layer, the section mimic the architecture of normal skin (Figure 5C).

Moreover, histological changes observed in wounds from diabetic rats at 16th days control of healing revealed inflammation cell by infiltration and irregular collagen deposition. Semi-complete closure as thin epithelial layer formed at the wound surface, collagen ale post at the wound margins, and still granulation tissue obvious also Edema and irregular distribution of collagen fibers and adipose tissue at the deep layer of skin (Figure 6A).

Observations on transverse sections of wounded skin from diabetic rats treated with (10 µg) at day 16 showed changes at the remodeling phase and revealed complete closure of wound margins by the epithelial layer. Well- arrangement of collagen fibers, normal hair follicles and blood capillaries, mild inflammation, mild keratin deposition, and clear sebaceous glands accompanied the hair follicles (Figure 6B).

The study clarified histological changes on wounded skin from diabetic rats treated with (50 µg) at day 16 of healing and showed remodeling phase, complete normal re- epithelialization, normal epidermis layers, complete closure of wounds margins , mild keratin deposits, the dermis showed as loose connective tissue with collagen fibers, fabricates, and normal hair follicles with sebaceous glands. The skin appeared similar to normal structure of skin (Figure 6C).

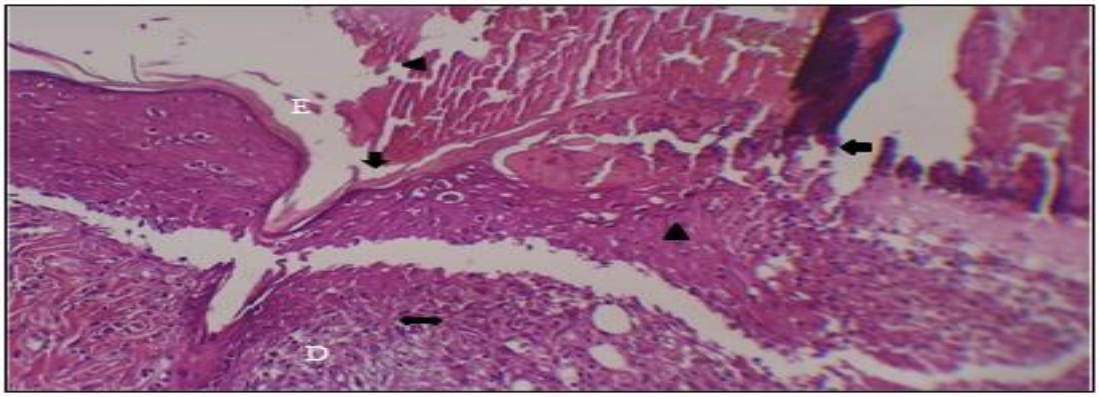

Figure 3A. Histopathological section of wounded diabetic rat skin on day 4 in the control group showing epidermis (E) and dermis (D). The section demonstrates disruption of the epidermis (⬅) with blood clot formation (◄), vacuolated cells (▲), mild keratin deposition (⬇), and granulation tissue formation (⬅). H&E stain, ×400.

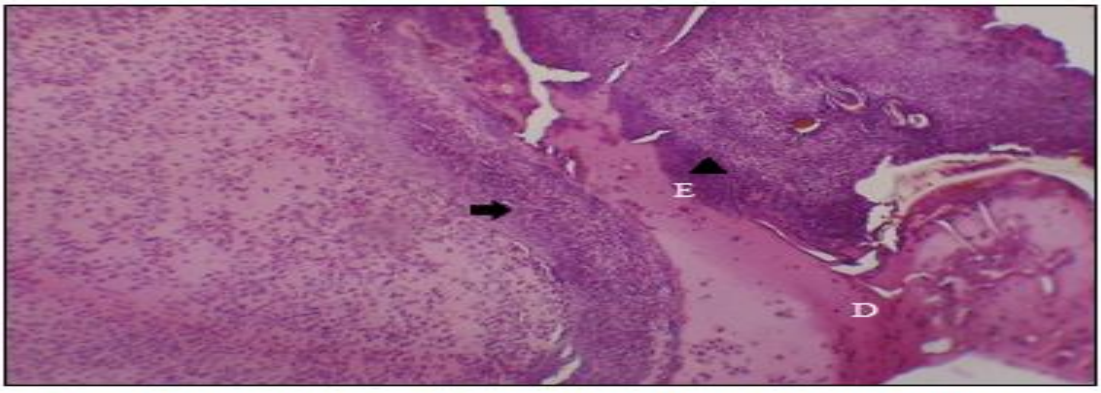

Figure 3B. Histopathological section of wounded diabetic rat skin on day 4 treated with 10 µg showing the epidermis (E) and dermis (D). The section shows thin epidermis (➡) and scab formation (▲). H&E stain, ×400.

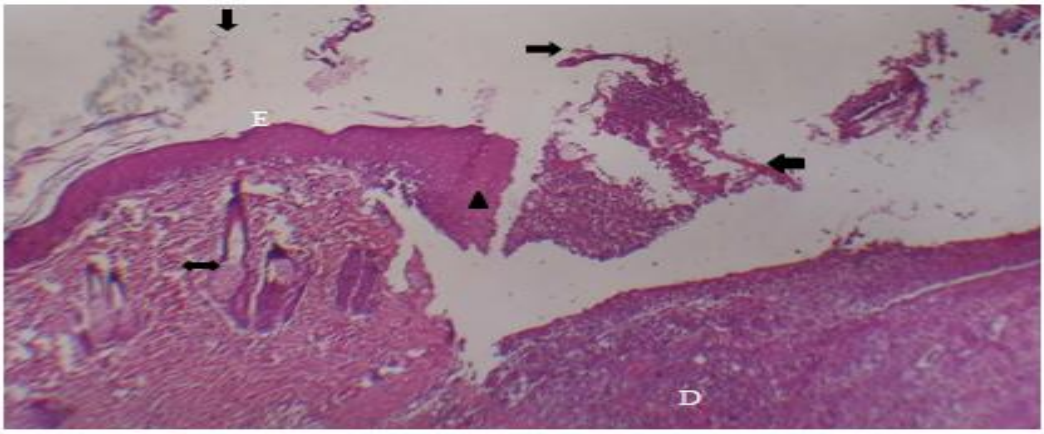

Figure 3C. Histopathological section of wounded diabetic rat skin on day 4 tre ated with 50 µg showing the epidermis (E) and dermis (D). The section demons trates scab formation (➡), partial closure of wound margins with newly formed epidermis (⬇), granulation tissue within the wound area (▲), hair follicles withi n the dermis (⬌), and fibrin deposition (⬅). H&E stain, ×40.

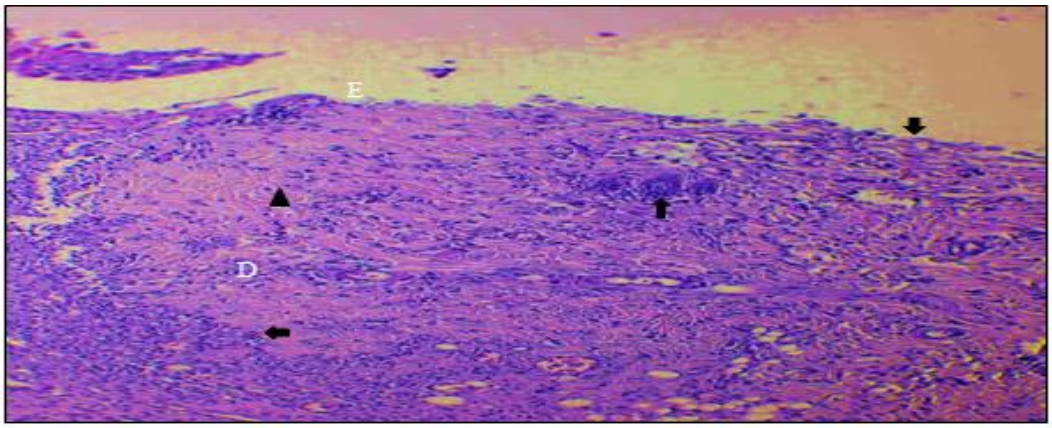

Figure 4A. Histopathological section of wounded diabetic rat skin on day 8control gro up showing the epidermis (E) and dermis (D). The section demonstrates the proliferat ive phase with partial closure of wound margins (⬇), inflammatory cell infiltration (⬅), thick granulation tissue (▲), and newly formed capillaries (⬆). H&E stain, ×100.

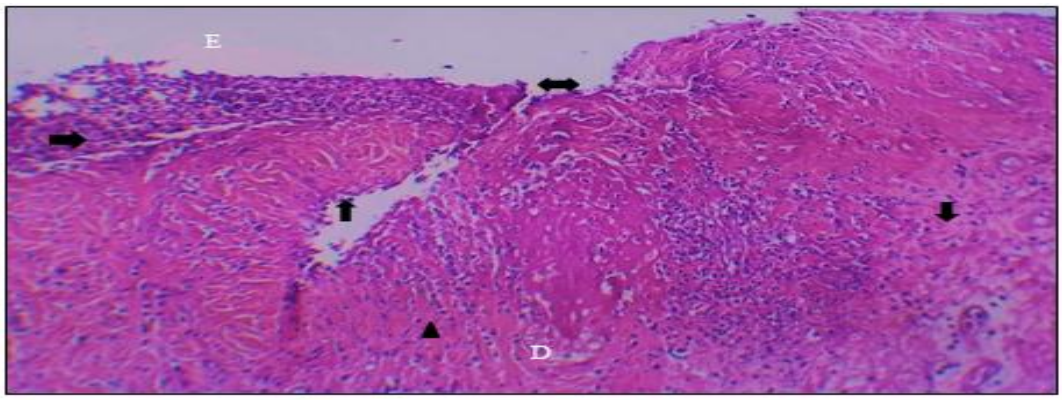

Figure 4B. Histopathological section of wounded diabetic rat skin on day 8 treated with 10 µg showing the epidermis (E) and dermis (D). The section demonstrates pa rtial closure of wound margins (⬌), regenerated epidermal layer (➡), mild inflame matory cell infiltration (⬆), formation of wound matrix (⬇), and regular collagen fib ers (▲). H&E stain, ×40.

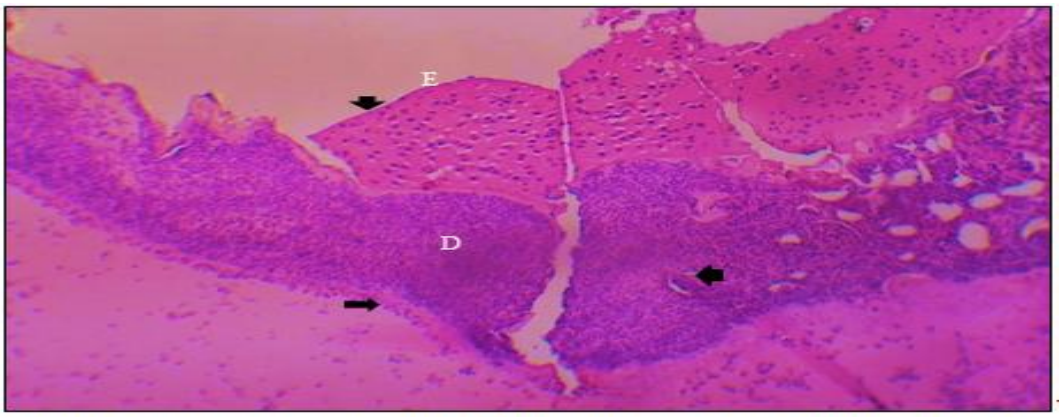

Figure 4C. Histopathological section of wounded diabetic rat skin on day 8 treated with 50 µg showing the epidermis (E) and dermis (D). The section demonstrates the early proliferative phase with partial closure of the wound area, marked infiltration of inflammatory cells (➧), irregular granulation tissue (⬅), and collagen fibers (➡) present in a disordered manner within the dermis, with incomplete remodeling of the epidermal surface. H&E stain, ×40.

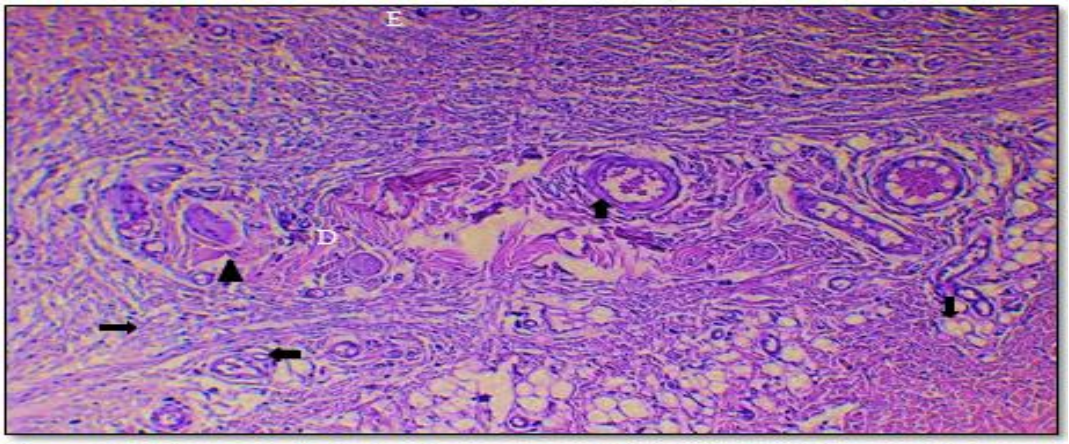

Figure 5A. Histopathological section of wounded diabetic rat skin on day 12 control group showing the epidermis (E) and dermis (D). The section demonstrates irregular deposition of collagen fibers (➡) in the deep dermis, angiogenesis (⬆), congested blood vessels (▲), capillaries (⬅), and adipose tissue (⬇) forming the hypodermis. H&E stain, ×40.

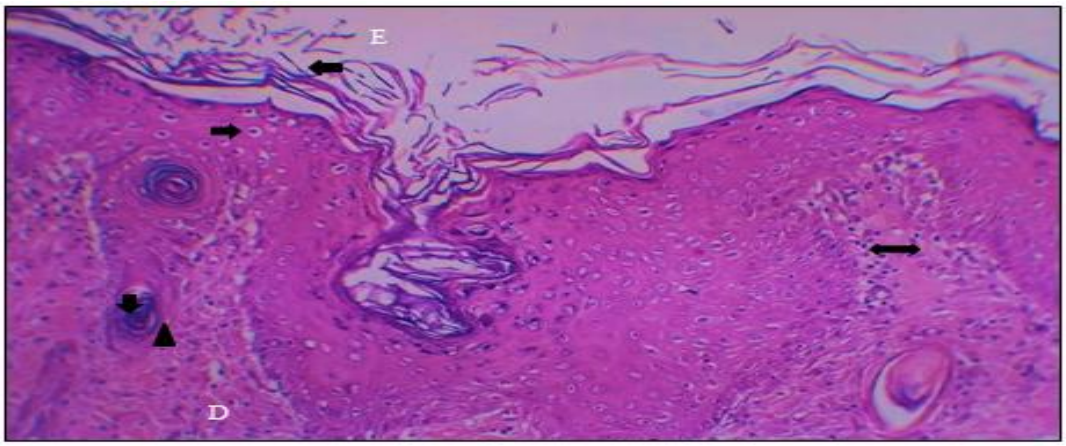

Figure 5B. Histopathological section of wounded diabetic rat skin on day 12 treated with 10 µg showing the epidermis (E) and dermis (D). The section demonstrates the proliferative phase with keratin deposition (⬅), well-developed epidermis (➡), developing hair follicles (▲), root sheath (⬇), and mild inflammatory response (⟷). H&E stain, ×40.

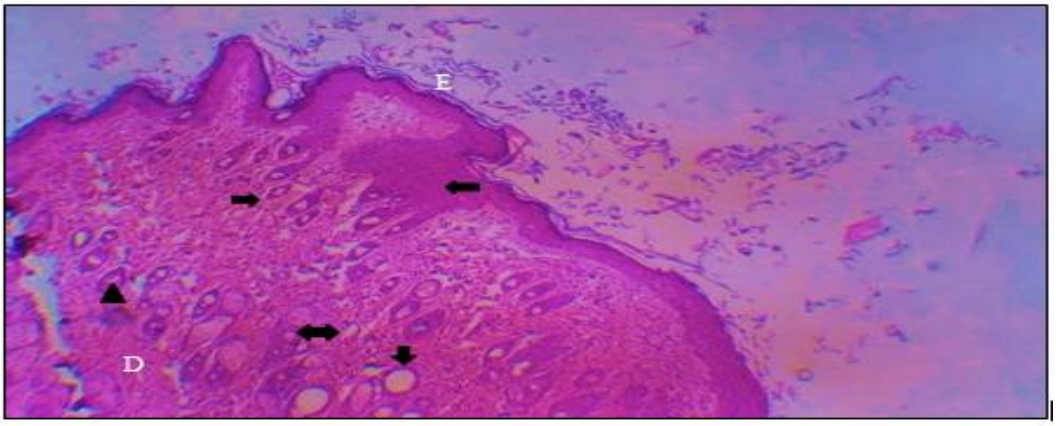

Figure 5C. Histopathological section of wounded diabetic rat skin on day 12 treated with 50 µg showing the epidermis (E) and dermis (D). The section demonstrates co mplete closure of the wound area with regeneration of the epidermis (⬅), increased hair follicles (▲), blood capillaries (⬇) within the dermis layer(⬌), and regularly a rranged collagen fibers (⬌). H&E stain, ×40.

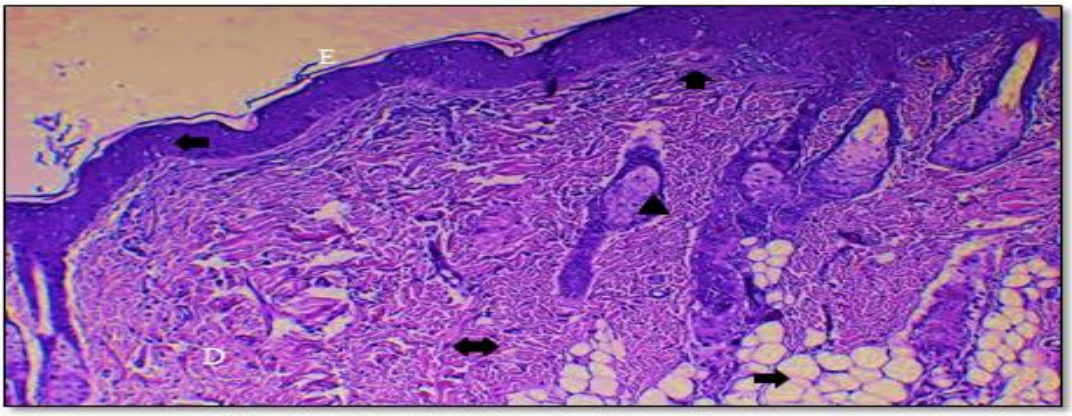

Figure 6A. Histopathological section of wounded diabetic rat skin on day 16 control group showing the epidermis (E) and dermis (D). The section demonstrates weak (se mi-complete) wound closure with a thin epidermal layer (⬅), irregular collagen dep osition (⬌), mild inflammatory cells (⬆), sebaceous glands (▲), and normal hyp odermis (adipose) layer (➡). H&E stain, ×40

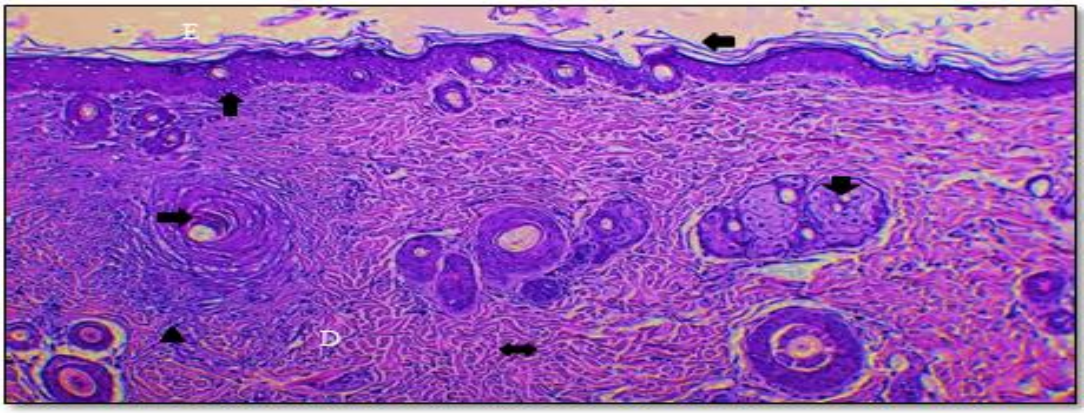

Figure 6B. Histopathological section of wounded diabetic rat skin on day 16 treated with 10 µg showing the epidermis (E) and dermis (D). The section demonstrates co mplete wound closure with a thin epidermis (⬆), keratin deposition (⬅), thick colla gen deposition (⬌), mild inflammatory cells (▲), increased hair follicles (➡),and sebaceous glands (⬇). H&E stain, ×40.

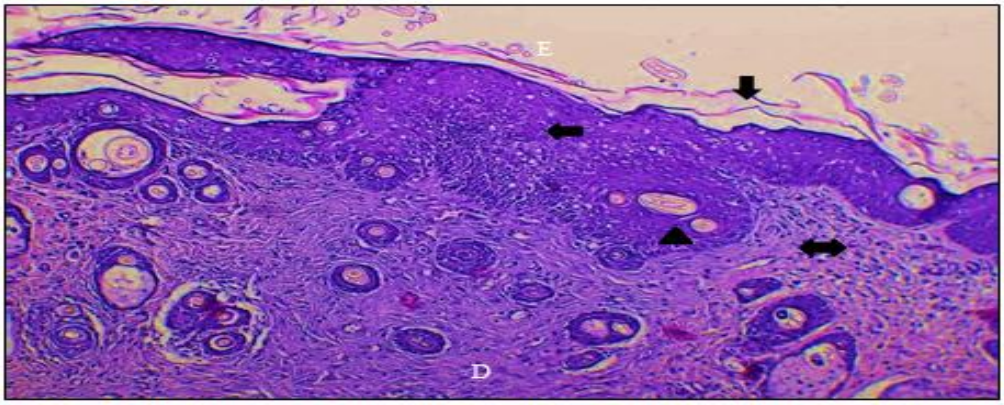

Figure 6C. Histopathological section of wounded diabetic rat skin on day 16 treated with 50 µg showing the epidermis (E) and dermis (D). The section demonstrates regular mature dermal tissue (⬌) and epithelialization module (⬅), mild keratin deposit (⬇), and mature hair follicles (▲). H&E stain, ×40.

4. Discussion

Control wounds in diabetic rats in this investigation exhibited a substantial delay in epidermal remodeling, with persistent infiltration of inflammatory cells and abnormal collagen fiber synthesis. These findings are in line with new research that indicates diabetic wounds stay in the inflammatory phase for a longer amount of time, showing decreased cell proliferation and poor collagen fiber modulation, which eventually results in slower and insufficient wound healing [19].

Among the virulence factors of *P. aeruginosa*, Exotoxin A is considered one of the most potent toxins that may influence wound healing processes [20]. According to recent research, these bacterial substances cause dysregulation of collagen fibers, extend the inflammatory phase, and reduce keratinocyte and fibroblast activity. The prolonged inflammatory infiltration and structural alterations seen in the study's control wounds are consistent with these pathways, indicating that bacterial virulence may worsen the delayed wound healing process in diabetic tissue [21].

One of *P. aeruginosa* most powerful virulence agents is Exotoxin A (ETA). By preventing intracellular protein synthesis through ADP-ribosylation of elongation factor EF-2 [22], it directly influences wound healing pathways. The emergence of vacuolated cells and poor early tissue remodeling in ETA-treated wounds in this study can be explained by this mechanism, which lowers keratinocyte and fibroblast viability [23]. In diabetic tissues, these biological effects inhibit wound healing by postponing the change from the inflammatory phase to the proliferative and remodeling stages.

The wounds treated with the 10 µg and 50 µg doses in this investigation demonstrated a progressive improvement in the structural organization of the tissue over the following days, especially on days 12 and 16, despite the early inhibitory effects of Exotoxin A. In comparison to the diabetic control wounds, better collagen fiber synthesis, thicker epidermis, and the emergence of more mature granulation tissue were noted [24]. These findings suggest that the wounds gradually progressed toward the remodeling phase, which is in line with new research that suggests partial inflammation regulation may help restore tissue balance and enhance skin regeneration in chronic wounds, including diabetic ulcers [25].

A potential mechanism can be proposed based on the current results, where Exotoxin A in the early stages causes cellular damage and inflammatory stress in diabetic wounds by inhibiting intracellular protein synthesis. This early toxic effect may contribute to delayed re-epithelialization and increased infiltration of inflammatory cells. As the healing process progresses, partial regulation of the inflammatory response and activation of fibroblasts and keratinocytes may allow for collagen deposition and tissue remodeling during the later stages of wound healing [11].

Despite these results, some limitations should be taken into consideration. This study was conducted using an experimental model on rats, which may not fully reflect the complex pathological environment of diabetic wounds in humans. Although the study provided important histological observations on the effect of Exotoxin A in the wound healing process, further studies are required to

explore additional molecular pathways that may contribute to elucidating the mechanisms associated with diabetic wound repair [26].

Understanding the impact of bacterial virulence factors, such as Exotoxin A, on the wound healing process in diabetic patients may provide important insights for developing effective therapeutic strategies. Targeting bacterial toxins and regulating inflammatory responses may represent a potential approach to improving chronic wound healing outcomes, including diabetic foot ulcers [1].

5. Conclusion

According to the study findings, diabetic rats wounds heal more slowly and stay inflamed for longer. The Exotoxin A-treated wounds seemed weaker at first and had more obvious tissue damage, but as the days passed, they started to become better than the control group. Granulation tissue developed more clearly, collagen fibers were more organized, and the incision eventually got closer to closure. These findings suggest that the Exotoxin A has two effects: it first negatively alters the tissue remodeling process, but it later aids in its improvement. Thus, more research is required to fully comprehend the exact mechanisms and the possibility of using this impact to treat chronic wounds.

References

[1] Q. Wang, Y. Zhang, H. Liu, L. Chen, and X. Li, "Mechanisms of microbial infection and wound healing in diabetic foot ulcers," *Int. J. Mol. Sci.*, vol. 26, no. 19, p. 9677, 2025, DOI: 10.3390/ijms26199677.

[2] M. Garousi, J. Sadeghi, R. Ranjbar, and M. Dehghani, "Epidemiology of *Pseudomonas aeruginosa* in diabetic foot infections: A systematic review and meta-analysis," *Microorganisms*, vol. 11, no. 4, p. 1034, 2023, DOI: 10.3390/microorganisms11041034.

[3] M. G. Wilson and S. Pandey, "*Pseudomonas aeruginosa*," in *StatPearls*, Treasure Island, FL, USA: StatPearls Publishing, 2023.

[4] C. Polk, M. M. Sampson, D. Roshdy, and L. E. Davidson, "Skin and soft tissue infections in patients with diabetes mellitus," *Infect. Dis. Clin. North Am.*, vol. 35, no. 1, pp. 183–197, 2021, DOI: 10.1016/j.idc.2020.10.007.

[5] D. Church, S. Elsayed, O. Reid, B. Winston, and R. Lindsay, "Burn wound infections," *Clin. Microbiol. Rev.*, vol. 19, no. 2, pp. 403–434, 2006, DOI: 10.1128/CMR.19.2.403-434.2006.

[6] S. J. Wood, T. M. Kuzel, and S. H. Shafikhani, "*Pseudomonas aeruginosa*: infections, animal modeling, and therapeutics," *Cells*, vol. 12, no. 1, p. 199, 2023, DOI: 10.3390/cells12010199.

[7] M. K. Abban, E. A. Ayerakwa, L. Mosi, and A. Isawumi, "The burden of hospital-acquired infections and antimicrobial resistance," *Heliyon*, vol. 9, no. 10, p. e20561, 2023, DOI: 10.1016/j.heliyon.2023.e20561.

[8] M. Michalska and P. Wolf, "*Pseudomonas exotoxin A*: optimized by evolution for effective killing," *Front. Microbiol.*, vol. 6, p. 963, 2015, DOI: 10.3389/fmicb.2015.00963.

[9] M. Pollack, N. S. Taylor, and R. L. T. Callahan, "Exotoxin production by clinical isolates of *Pseudomonas aeruginosa*," *Infect. Immun.*, vol. 15, no. 3, pp. 776–780, 1977, DOI: 10.1128/iai.15.3.776-780.1977.

[10] M. L. Vasil, "*Pseudomonas aeruginosa*: virulence and pathogenesis," in *Vaccines for Biodefense and Emerging and Neglected Diseases*, A. D. T. Barrett and L. R. Stanberry, Eds. Academic Press, 2015, pp. 413–432.

[11] I. Yamberla *et al.*, "*Pseudomonas aeruginosa* pathogenicity and its interaction with other microorganisms during the skin wound healing process," *Int. J. Mol. Sci.*, vol. 26, no. 19, p. 9677, 2025, DOI: 10.3390/ijms26199677.

[12] B. M. Wagener *et al.*, "The role of *Pseudomonas aeruginosa* virulence factors in cytoskeletal dysregulation and lung barrier dysfunction," *Toxins*, vol. 13, no. 11, p. 776, 2021, DOI: 10.3390/toxins13110776.

[13] M. N. Sarian *et al.*, "A review with updated perspectives on in vitro and in vivo wound healing models," *Turk. J. Biol.*, vol. 47, no. 4, pp. 236–246, 2023, DOI: 10.55730/1300-0152.2659.

[14] National Research Council, *Guide for the Care and Use of Laboratory Animals*, 8th ed. Washington, DC, USA: National Academies Press, 2011.

[15] J. M. Kim, "Induction of diabetes mellitus using alloxan in Sprague Dawley rats," *Cureus*, vol. 16, no. 6, p. e63359, 2024, DOI: 10.7759/cureus.63359.
[16] B. Mentese, H. Arslan, and S. Demir, "Effects of ketamine-xylazine and urethane anesthesia on physiological parameters in rats," *Neurosciences (Riyadh)*, vol. 28, no. 4, pp. 240–247, 2023, DOI: 10.17712/nsj.2023.4.20230065.
[17] M. B. Rowland *et al.*, "Assessing wound closure in mice using skin-punch biopsy," *STAR Protoc.*, vol. 4, no. 1, p. 101989, 2023, DOI: 10.1016/j.xpro.2022.101989.
[18] R. N. Morgan *et al.*, "New insights on *Pseudomonas aeruginosa* exotoxin A-based immunotoxins in targeted cancer therapeutic delivery," *Ther. Deliv.*, vol. 14, no. 1, pp. 31–60, 2023, DOI: 10.4155/tde-2022-0055.
[19] M. Fernandez-Guarino *et al.*, "Aberrances of the wound healing process: A review," *Cosmetics*, vol. 11, no. 6, p. 209, 2024, DOI: 10.3390/cosmetics11060209.
[20] P. S. Yadav, M. Singh, R. Vinayagam, and P. Shukla, "Therapies and delivery systems for diabetic wound care," *Front. Pharmacol.*, vol. 16, p. 1628252, 2025, DOI: 10.3389/fphar.2025.1628252.
[21] M. F. Moradali, S. Ghods, and B. H. A. Rehm, "*Pseudomonas aeruginosa* lifestyle: A paradigm for adaptation, survival, and persistence," *Front. Cell. Infect. Microbiol.*, vol. 7, p. 39, 2017, DOI: 10.3389/fcimb.2017.00039.
[22] A. Gholami *et al.*, "Structural insights into *Pseudomonas aeruginosa* exotoxin A," *J. Chem. Inf. Model.*, vol. 63, no. 4, pp. 917–929, 2023, DOI: 10.1021/acs.jcim.3c00064.
[23] S. P. Yates, R. Jørgensen, G. R. Andersen, and A. R. Merrill, "Stealth and mimicry by deadly bacterial toxins," *Trends Biochem. Sci.*, vol. 31, no. 2, pp. 123–133, 2006, DOI: 10.1016/j.tibs.2005.12.008.
[24] H. Li *et al.*, "Qualitative assessment of collagen remodeling and granulation tissue maturation in diabetic wounds," *Sci. Rep.*, vol. 13, p. 33372, 2023, DOI: 10.1038/s41598-023-33372-z.
[25] M. Rodrigues, N. Kosaric, C. A. Bonham, and G. C. Gurtner, "Wound healing: A cellular perspective," *Physiol. Rev.*, vol. 99, no. 1, pp. 665–706, 2019, DOI: 10.1152/physrev.00067.2017.
[26] M. Ghanbari *et al.*, "The rat as an animal model in chronic wound research," *Int. J. Mol. Sci.*, vol. 25, p. 3837, 2024, DOI: 10.3390/ijms25073837.

Journal of Basrah Researches (Sciences) **52**(1), 157 (2026)
DOI: https://doi.org/10.56714/bjrs.52.1.12

التأثيرات النسيجية المرضية للسموم الخارجية A aeruginosa Pseudomonas على جروح الجلد لدى مرضى السكري لدى الفئران

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معلومات البحث

الاستلام 25 كانون أول 2025
المراجعة 16 اذار 2026
القبول 26 اذار 2026
النشر 30 حزيران 2026

الكلمات المفتاحية

الزائفة الزنجارية، الإكسوتوكسين A، جروح السكري، شفاء الجروح.

الملخص

يؤثر مرض السكري بشكل واضح في عملية التئام الجروح من خلال إعاقة إعادة تشكيل الأنسجة وإطالة المرحلة الالتهابية. تهدف هذه الدراسة إلى تقييم التأثيرات النسيجية المرضية للسم الخارجي A (Exotoxin A, ETA)، والذي يُعد أحد عوامل الضراوة الرئيسية لبكتيريا*Pseudomonas aeruginosa* ، على التئام جروح الجلد في الجرذان المصابة بالسكري.

الطريقة: تم إحداث جروح جلدية كاملة السماكة في جرذان تم تحفيز الإصابة بالسكري فيها باستخدام مادة الألوكسان. قُسِّمت الجرذان إلى ثلاث مجموعات: مجموعة سيطرة عولجت بمحلول الفوسفات المنظم(PBS) ، ومجموعتان عولجتا بالسم الخارجي A بجرعتين قدرهما 10 ميكروغرام و50 ميكروغرام. جُمعت العينات النسيجية في الأيام 4 و8 و12 و16، وتم تقييم التغيرات النسيجية باستخدام صبغة الهيماتوكسيلين والإيوزين.(H&E)

أظهرت جروح مجموعة السيطرة المصابة بالسكري استمرار الارتشاح الالتهابي، وتنظيماً غير طبيعي لألياف الكولاجين، وتأخراً واضحاً في إعادة تكوين البشرة. في المقابل، أظهرت الجروح المعالجة بالسم الخارجي A ضعفاً في التجدد في المراحل المبكرة مع حدوث تلف خلوي مبكر. ومع ذلك، أظهرت كلتا الجرعتين (10 و50 ميكروغرام) تحسناً ملحوظاً في المراحل المتأخرة مقارنةً بمجموعة السيطرة، حيث لوحظت زيادة في سماكة البشرة، وتطور أوضح للنسيج الحبيبي، وتنظيم أفضل لألياف الكولاجين، مع اقتراب الجروح من الانغلاق الكامل في اليومين 12 و16.

بشكل عام، يُظهر السم الخارجي A تأثيراً مزدوجاً، إذ يسبب ضرراً مبكراً في الجروح السكرية، لكنه يعزز لاحقاً إعادة بناء الأنسجة. وتشير هذه النتائج إلى أن لهذا السم دوراً تنظيمياً محتملاً في عملية التئام الجروح المزمنة، الأمر الذي يتطلب المزيد من الدراسات لتحديد الآليات الدقيقة وتقييم إمكانية الاستفادة منه علاجياً.

Citation: S. S. Al-Baydani et al. , J. Basrah Res. (Sci.) **52**(1), 157 (2026).
DOI:https://doi.org/10.56714/bjrs.52.1.12

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ISSN: 1817-2695 (Print); 2411-524X (Online)
Online at: https://jou.jobrs.edu.iq