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The Effect of Pine Bark Extract Loaded Nanoparticles on Diabetic Wound Healing: Histological and Immunohistochemical Studies

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Abstract

THE problem of diabetic wounds has long been recognized as an unmet therapeutic challenge among medical society. In this study, we assess the wound healing potential of Pine Bark (PB) extract nanoparticles on diabetic wound healing through histopathological and immunohistochemical (IHC) studies. Eighteen Wister rats were divided into 3 groups (n = 6 each): control group (NC) (non-diabetic), diabetic control group (DC), and diabetic treated PB group (PN). Under general anesthesia, full-thickness wounds were conducted on the back of all the rats, and then the PB extract nanoparticles was applied topically to the wounds of the diabetic treated PB group. The percentage of wound areas was measured on days 0, 3, 6, 9, 12, 15, and 18 post-wounding. The wound granulation tissues were detected by histopathologic examination, and the CD31 micro vessels were investigated using immunohistochemistry. Our findings indicated that wounds treated with pine extract nanoparticles exhibited significantly accelerated closure rate compared to both the DC *($p < 0.01$)* and the NC group ($p < 0.05$).In addition, the process of re-epithelialization was significantly improved in the PN compared to the DC *($p < 0.0001$)* and the NC *($p < 0.05$)*. Angiogenesis was also increased in the PN wounds compared to the DC. These results suggest that Pine bark extract nanoparticles effectively promote both the rate and extent of diabetic wound healing. This study underscores the therapeutic potential of pine extract nanoparticles, as a natural product, as effective agents in enhancing wound healing in diabetic patients.

Keywords: Diabetic wounds, pine extract nanoparticle, chronic wound healing.

Introduction

Diabetic wounds represent one of the most serious long-term complications associated with diabetes mellitus. Recent research estimates that incidence of foot ulceration among individuals with diabetes ranges from 19% to 34%. This high prevalence highlights the considerable clinical and socioeconomic burden of diabetic wounds on both affected patients and healthcare systems[1]. These types of wounds exhibit a prolonged bleeding phase, impaired cellular proliferation, and sustained M1 macrophage polarization, which is hypothesized to Prolong inflammation and disrupt the physiological healing cascade [2]. Delayed diabetic wound healing frequently results in complications such as infection, limb amputation, and diminished quality of life[3,4]. Chronic wounds have emerged as a growing clinical concern, often described as a "silent epidemic" due to their increasing prevalence and associated complications [5].

The use of natural products as rich sources of bioactive chemicals for wound healing has become

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considerable. Among these products, pine bark extract from Pinus species has a special combination of bioactive compounds, including flavonoids, polymeric flavanols, tannic acid, and other phenolic acids including protocatechuic acid and caffeic acid [6,7]. Pine bark extract has shown to have potential pharmacological characteristics, such as pro-angiogenic effect, as reported by [8]. The pinus brutia extract enriched formulation exhibited improved performance such as increased vascularization and a reduction in the necrotic area. The antioxidant and anti-inflammatory actions of pine bark was proved by [9]. Furthermore, the antibacterial effect of pine bark help combating infection, which is a significant complication associated with diabetic wounds [10]. These properties suggest that pine extract may be a promising choice for diabetic wound treatment.

Current studies have demonstrated the efficacy of pine extract as potent antioxidant due to its content of proanthocyanidins component that can mitigate the effect of oxidation by combating free radicals [11]. By preventing oxidative stress on fibroblasts and keratinocytes, the collagen synthesis and re-epithelialization are promoted, consequently improving the structural integrity of newly formed tissue [12]. It has been demonstrated that pycnogenol, a standard extract from the pine bark, enhances endothelial function and improves blood flow by promoting vasodilation and elevating nitric oxide synthesis, which finally promotes blood vessel relaxation and better circulation [13]. Recent research has shown that the conversion of the crude form of plant extracts into nanoparticle form significantly improves their biological and physicochemical properties. An example is nanoformulated extract derived from Pluchea indica branch extract. This nanoformulation resulted in higher stability, improved antioxidant activity, and increased proliferation of keratinocytes and fibroblasts which are two important skin cells involved in wound healing [14]. Based on the previous results, it is expected that the nanoformulation of pine bark extract, a substance rich in proanthocyanidins and polyphenols, will provide comparable advantages. Pine bark extract has poor solubility and bioavailability in its raw state, these restrictions could be overcame by using nanoparticle form, which provides better dispersion and smaller particles that finally improve the stability, availability, absorption, extending the release, and targeting the wound site more precisely [15].

Current therapeutic approaches do not fully clarify the situation and solve the challenges of diabetic wound healing, so the development of novel therapeutic strategies needs to be investigated.

This study aims to investigate the impact of the Nano-formulations of pine bark extract on wound healing, as all previous studies investigated only the effect of the crude form of pine bark extract. Our aim is not to directly compare our findings with previous ones, but to explore whether this nano-form can improve the therapeutic potential of the pine bark by enhancing the solubility, and bioavailability. Based on previous studies, we hypothesize that by encouraging angiogenesis and cellular proliferation, pine extract loaded nanoparticles will improve diabetic wound healing. To evaluate this hypothesis, angiogenesis (CD31), wound healing rates, and histological changes will all be evaluated.

Material and Methods

The study was approved by the Institutional Animal Care and Use Committee (Approval number KFS-IACUC/264/2025) all animals were handeled according to their ethical guidelines.

Pine extract nanoparticle preparation

Pine bark extract (New Mstar Company, Changsha, Hunan, China) (0.5 g) was dissolved in deionized water and mixed with chitosan (1 mg /1 ml) with stirring for 30 min. under magnetic stirrer and the mixture cross-linked by Tripolyphosphate (0.5 mg / 1 ml). The final product was dialyzed against distilled water for 24h. After that, NPs were kept at refrigerator (4° C) to be used in solution form.

Pine bark extract loaded nanoparticles characterization

Zeta Potential Measurement

A Brookhaven Instruments Zeta Potential Analyzer (Software Version 5.59) was used to measure the surface charge (zeta potential) of the nanoparticles loaded with pine bark extract. Using water as the dispersant and a concentration of 0.30 mg/mL of nanoparticles, measurements were carried out at 20°C. The device used an applied electric field of 14.81 V/cm and a wavelength of 658.0 nm.

Particle Size Characterization

The hydrodynamic diameter and polydispersity index (PDI) of the pine bark extract nanoparticles were determined using a Brookhaven Instruments ZetaPALS Particle Sizing System (Software Version 5.23) for dynamic light scattering (DLS) analysis.

The measurements were performed at 25°C after the nanoparticle suspension had been appropriately diluted with deionized water.

Animals and study design

Eighteen Wistar male six-week-old rats weighing 200-250 gm were obtained from the Animal House Colony of Tanta Center, Egypt. Then prepared for the experiment. Prior to the beginning of the study, rats were kept in housing at 25 ± 1°C with a 12-hour light/dark cycle and fed ad libitum for three weeks. The rats were then divided into three equal groups, two of which will be used for diabetes induction.

Diabetes induction

For diabetes induction, the rats (n, 12) were fastened overnight (about 15 hours), were given a single intraperitoneal injection of freshly prepared streptozotocin (STZ, Glentham life science England) at a dose of 50 mg/kg after being dissolved in sterile citrate buffer (0.1 mol/L sodium citrate, pH 4.7). After four days, the blood glucose (BG) concentration (using a drop of tail capillary blood) was measured using a glucometer; all rats with fasting blood glucose (FBG) of 200 mg/dl or higher are considered diabetic, and the Type 2 Diabetes Mellitus rat model had been successfully established [16,17]

Diabetic Wound Model creation

Before wound creation, the animals were anesthetized by a combination of ketamine (70 mg/kg; Ketamine Hydrochloride®, ADWIA Pharmaceuticals, Cairo, Egypt) / xylazine (7 mg/kg) (Xylaject, ADWIA Pharmaceuticals Co. Cairo, Egypt) which was given through intraperitoneal injection in order to maintain immobilization and pain control throughout the process, then back hair shaved, and thorough alcohol disinfection of the back skin is done. The diabetic rats were used to create diabetic wound by excising 1.5 × 1.5 cm of full-thickness skin with sterile surgical Scalpel. Immediately upon creation, the wound area was measured using a ruler and photographed and dressed. In order to avoid cage-mates interfering with the incision site, each animal was housed singly [18]. Every two days, the area of the wound was measured, infection symptoms were checked. Finally the rats were then randomly grouped into three groups: Pine bark nanoparticle based group (PN = 6), the diabetic control group (DC = 6), and the normal control group (NC = 6) of non-diabetic rats that underwent the same type of surgery. Our study applied a dose of 100 µL of pine nanoparticle solution to completely cover the wound area[19,20].
The treatment was given every 48 h for 18 days. Tissue samples were collected for histopathological and immunological analysis on the 18th day to evaluate the granulation tissue, inflammation, neovascularization, and re-epithelialization.

Macroscopic assessment of the wound area

Macroscopically, wound healing was assessed by making periodic measurements of the wound area. A smartphone camera was used to capture high-resolution photographs of the wounds on days 0, 3, 6, 9, 12, 15 and 18 in a controlled lighting environment. For the purpose of calibration, a ruler was positioned next to the wound. ImageJ software (NIH, USA) was used to measure the areas of the wounds by using the freehand selection tool to trace the wound edges. Using the following equation, the percent of the wound area was determined:

Wound area (%) = ([area of actual wound] / [area of the initial wound]) × 100 [27]

Histological evaluation of wound healing

All rats were subjected to euthanasia, tissue samples were collected from the wound area with part of healthy skin on day 18 after wound creation and fixed in 10% neutral buffer formalin solution. The samples were dehydrated using ascending grades of ethanol. After clearing in xylene, samples embedded in paraffin blocks, serial thin sections (5 µm in thickness) obtained, mounted on slides and stained with H&E [28]. For capturing and evaluating the photographs of histological sections, bright-field microscope was used.

H&E-stained sections were used to evaluate re-epithelialization, neovascularization, and overall tissue morphology. To find statistically significant differences, the mean ± SD thicknesses of the epidermis and dermis were compared between the (PN), (DC), and (NC) groups.

Immunohistochemical assessment

Using CD31 immunohistochemical labeling, angiogenesis was assessed. Shortly, tissue sections were deparaffinized in a clearing agent and rehydrated using graded ethanol series. For 20 minutes, citrate buffer (pH 6.0) was used in a microwave to make antigen retrieval. In PBS, 3% hydrogen peroxide was used for 10 minutes to inhibit endogenous peroxidase activity. At room temperature, 5% normal goat serum was used for 30 minutes to inhibit non-specific binding sites. Sections were treated with a primary anti-CD31 rabbit monoclonal antibody (1:100 dilution in PBS) for a whole night at 4°C, then rinsed with phosphate buffer saline and incubated with a goat antirabbit secondary antibody coupled with horseradish peroxidase (HRP) for one hour at room temperature. The chromagen, diaminobenzidine tetrahydrochloride (DAB), was used to visualize positive reactions. Sections were dehydrated, cleaned, and covered with a coverslip after nuclei were counterstained with hematoxylin. By ImageJ software, four randomly selected digital photos were taken from each selected field at 400x magnification to quantify the positive immunohistochemical stained vessels. The number of CD31-positive microvessels in each high-power field was counted [29].

Statistics

Using the statistical software GraphPad Prism (version 10.4.1, GraphPad Software, San Diego, CA, USA), two-way analysis of variance with Tukey's multiple comparisons post hoc analysis was used to determine whether there were statistically significant differences between the treatment and control groups. For each experiment, the findings were presented as mean ± SD, and a value of $P < 0.05$ was determined as statistically significant.

Results

Pine bark extract loaded nanoparticles characterization

Zeta Potential Analysis

With an average zeta potential of -15.44 mV, the pine bark extract nanoparticles were found to have a moderately stable dispersion. The suspension's pH was 5.60 at the time of measurement. (Figure 1)displays the corresponding distribution of zeta potential.

Particle Size Characterization

The pine bark extract nanoparticles showed a median diameter of 470.4 nm and a mean d iameter of 573.6 nm, according to DLS analysis. A moderately uniform size distribution was indicated by the polydispersity index (The PDI), which was 0. 487.
(Figure 2) displays the particle size distribution profil e.

Macroscopic assessment of the wound area

The results showed that on day 6, the PN wounds showed faster wound closure than the DC *(p <0.0001)*, whereas there is no significant difference between PN and NC. On day 12, PN wounds showed significant reduction on wound area compared to DC *(p <0.05)*. While no significant difference observed between PN and NC. On day 18, the PN-treated group showed significant reduction in wound area compared to DC *(P < 0.05)* while no significant difference detected between PN and NC. Reduction in wound area between different groups is shown in (Figs. 3, 4) and Table 1.

Histological assessment

On day 18, the epidermal thickness of pine bark nanoparticles treated group (PN, 51.5 µm) was significantly thicker than the normal control (NC, 48.9 µm) *(p < 0.05)* and diabetic control (DC, 35.96 µm) *(p <0.0001)*. Also the dermal thickness of PN-treated group (619.8 µm) was significantly higher than the normal control (NC, 597.9 µm) ($p < 0.05$) and diabetic control (DC, 550.85 µm) *(p <0.0001)*. (Fig. 5, A and B).

Histological investigation of wound sections across the three groups revealed significant differences in the healing process. In the diabetic control group (DC), the epidermal layer showed thinning regions with some regions of tissue lost, and incomplete epidermal regeneration. Furthermore, the layers of epidermis showed ill-defined and ill differentiated appearance. Pale areas were also detected between the four epidermal layers (Figure 6, A and C). The dermis showed a highly inflamed papillary region with a marked infiltration of inflammatory cells. No skin accessories (hair follicle, sweat or sebaceous glands) were observed (Figure 6, D).

In comparison, the normal control group (NC) showed advanced features of wound healing and re-epithelization. The epidermal layer appeared intact with well-structured and well defined stratum spinosum, stratum granulosum, and stratum basale. Stratum corneum appeared to be deeply acidophilic without any retained nuclei. (Figure 6, C). The dermis displayed significant infiltration of spindle fibroblasts with some inflammatory cells. The collagen bundles of the reticular region of dermis were organized and some hair follicles started to develop at wound periphery. (Figure 6, B and D)

In PN group (PN), the epidermis was fully stratified, well identified layers and intact appearance. Fully formed uppermost stratum corneum was observed (Figure 6, C). The dermal layer formed of highly organized collagen bundles, with high number of fibroblasts with flattened nuclei, and newly formed hair follicles were also noticed. (Figure 6, B and D)

Immunohistochemical analysis

Immunohistochemical investigation of CD31 showed that the (NC) group had more pronounced CD+ brown stained microvessels. In addition, the density of the stain was greater compared to the (DC) and (PN). While the DC showed fewer CD+ vessels number with little brown color density. In (PN), the CD+ brown stained microvessels and density of staining were lower than (NC). (Fig. 7)

While the quantitative investigations that we mainly depend on in angiogenesis evaluation revealed that the number of CD+ microvessels in PN was significantly higher than in DC *(p < 0.05)*, however the (NC) showed higher number of CD+ microvessels than (PN) suggesting that the treatment had improved vascularization (Fig. 8).

Discussion

In the current study, we examined how pine bark nanoparticles affect the diabetic wound healing in a diabetic rat model, paying particular attention to histological features of skin wound healing, epidermal and dermal thickness, angiogenesis (CD31 expression), and macroscopic wound area reduction. Previous research demonstrated that the ability of pine bark extract to enhance the healing process is due to its anti-inflammatory and wound-healing properties as it is rich in proanthocyanidins (potent anti-inflammatory and antioxidants), it combats inflammation and oxidation. This consequently enhances the processes of healing (such as re-epithelialization and dermal remodeling) that finally accelerate the healing process [21,22,23]. In an agreement, our results show that pine bark extract greatly improves the cellular and structural mechanisms involved in wound healing.

Macroscopic wound area reduction

Although the healing rate didn't reach 100% in PN, DC, or NC throughout the study, the PN-treated group showed a faster decrease in wound area than both the normal and diabetic control groups. The wound area of PN was 5.25% compared to NC (5.4%) and DC (22%) on day 18, suggesting that PN wounds were contracting more quickly. Our finding matches [24] previous findings that has been shown that the proanthocyanidins-rich pine bark extract improves wound healing by acting as an anti-inflammatory and antioxidant. The results of the current study match with Karakaya et al.[25] who reported that wounds treated with pine bark extract embedded dressing showed faster wound reduction than the control group.

Histological assessment

The continuity, full stratification, fully differentiated epidermal cells, and greater epidermal thickness of PN group in this study indicated that keratinocyte proliferation and re-epithelialization were encouraged by pine bark nanoparticles, which is necessary to restore the barrier function of the skin. While the observations in DC group such as the epidermal eroded areas (incomplete healing), pale acidophilic separations between the epidermal cells that suggested to be edematous region, and retained stratum corneum nuclei all indicate inefficient healing process.

Similarly, the organized collagen bundles, high infiltration of spindle fibroblast, development of some hair follicles in the dermal layer, and increased dermal thickness in PN group than that of NC and DC groups, all these features indicate higher fibroblast activity, collagen synthesis and extracellular matrix deposition. In comparison the poor organization of collagen bundles and absence of all skin accessories from the dermal layer in DC group indicates delayed healing process [8]. reported that pine bark extract containing formulation significantly increased the tissue regeneration, dermal thickness and dermal organization which support our findings of pine bark potential effect on promoting the healing process.

Angiogenesis (expression of CD31)

The immunohistochemical labeling for CD31, an endothelial cell marker that is considered evidence of angiogenesis, showed a higher proportion of CD31-positive microvessels in the PN-treated group in comparison to the diabetic control group while NC group showed the highest CD31+ vessel number. This indicates that neovascularization is improved by pine bark extract nanoparticles, which consequently improves the blood flow to the healing tissue. Cetin et al. reported that The vascularization was improved by pine bark extract containing formulations which agree with the study results [8]

According to [26], pine bark extract-treated wounds in diabetic rat had greater collagen deposition and neovascularization than Cleanser/silver sulfadiazine-treated wounds. This confirmed that pine bark extract speeds up the process of diabetic wound healing.

Similar findings were noticed by [13], who discovered that Pycnogenol®, a standardized French maritime pine bark extract increases the production of nitric oxide (NO), a crucial signaling molecule that enhances endothelial cell proliferation and migration also promotes vasodilation and angiogenesis. These processes can enhance blood flow and promote angiogenesis, which is aligned with our findings that the PN-treated group had more CD31-positive microvessels.

In conclusion, the results revealed that pine bark nanoparticles positively enhance the process of wound healing. This was detected by the significant decrease in macroscopic wound area and improved histological parameters, such as enhanced re-epithelization and organized collagen bundles in the treated group compared to the diabetic control. In addition, the CD31 immunohistochemical labeling revealed enhanced blood vessel formation (angiogenesis) in PN compared to DC.

The long-term safety and potency of PB extract nanoparticles as well as the molecular mechanisms of the previous healing mechanisms require more investigation to be finally approved. Our study recommends the usage of plant-based treatments for promoting the process of diabetic wound healing.

Conclusion

Pine bark nanoparticles found to promote the healing process by enhancing the skin regeneration, and neovascularization. These findings support previous research demonstrating the pro-angiogenic and proliferative characteristics of pine bark's polyphenol component, underscoring the plant's effectiveness as a medicinal agent for the management of diabetic wounds. The macroscopic observations of the diabetic wounds demonstrated a significant improvement in wound contraction over time. The results of this study provide an encouraging new perspective on the therapeutic application of natural substances to enhance tissue regeneration.

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Declaration of Conflict of Interest

The authors declare that there is no conflict of interest.

TABLE 1. Impact of pine bark extract nanoparticles on wound healing. Wound area (%) over time.

Group	Zero d (%)	3 d (%)	6 d (%)	9 d (%)	12 d (%)	15 d (%)	18 d (%)
NC	100	63.2±2.6	46.8±6.5	21.8 ±8.5	15.2±7.1	11.3±7.4	5.4±3.5
DC	100	107.0±17	80±7.2	50.7±5.7	45.3±5.3	38.8±7.6	22±5.2
PN	100	71.1±1.5	38.025±5.4**	22.3±2	13.5±1.6*	9.1±1	5.25±1.2*

***** $p < 0.05$ vs DC group, ****** $p < 0.0001$ vs DC group

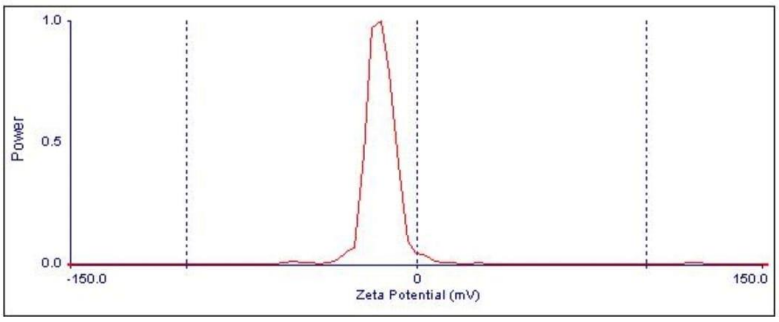

Fig. 1. Zeta potential distribution of pine bark extract loaded nanoparticles.

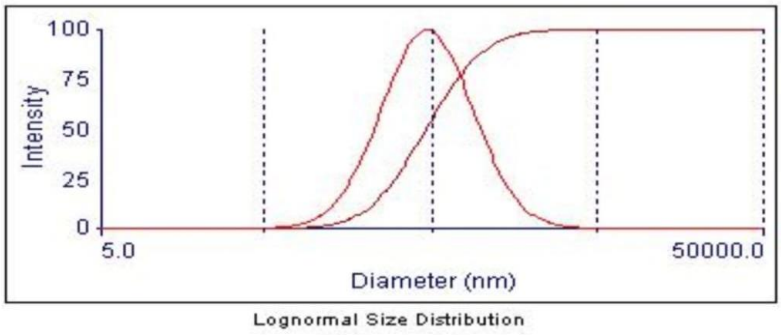

Fig. 2. Dynamic light scattering (DLS) analysis of pine bark extract nanoparticles.

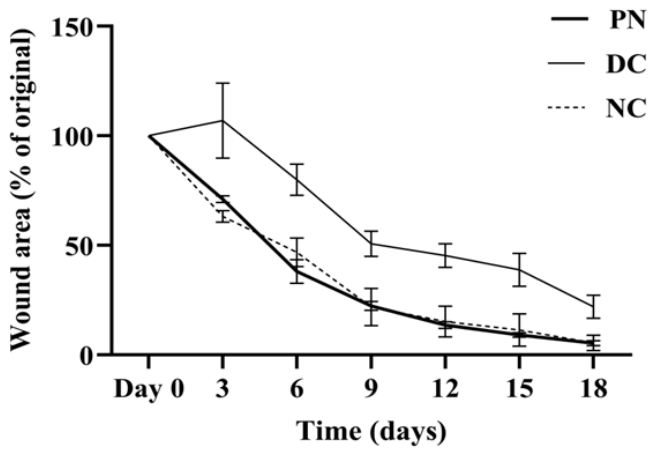

Fig. 3. Wound area rate. At day 0, 3, 6, 9, 12, 15, and 18. The DC group showed a significantly higher wound area rate than those of the PN-treated and NC groups.

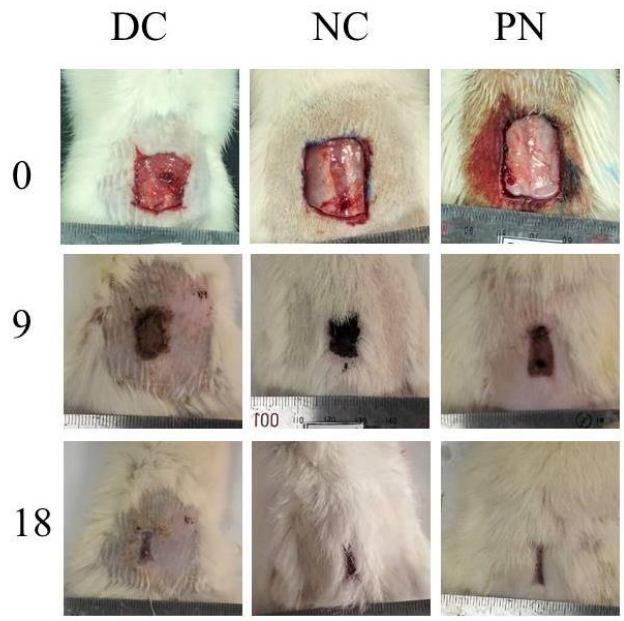

Fig. 4. Representative photographs of wound healing at day 0, 9, and 18 post-wound creation. DC = Diabetic Control group, NC = Normal Control group, PN = Pine Bark Extract-loaded Nanoparticle treated group.

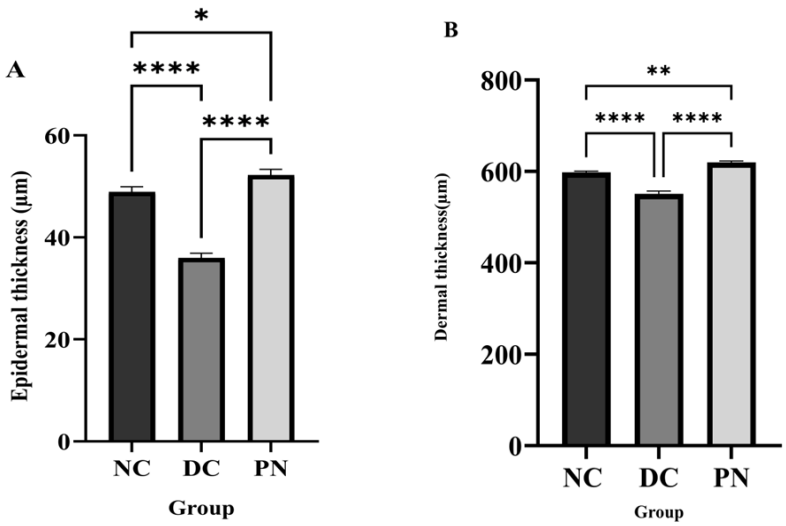

Fig. 5. A, Epidermal thickness (µm) of different wounds treated PN on day 18 after wound creation. The epidermal thickness was significantly greater in PN-treated group compared to the control groups (NC and DC). B, Dermal thickness (µm) of different wounds on day 18 after wound creation. The dermal thickness was significantly greater in the PN-treated group compared to the control groups (NC and DC).

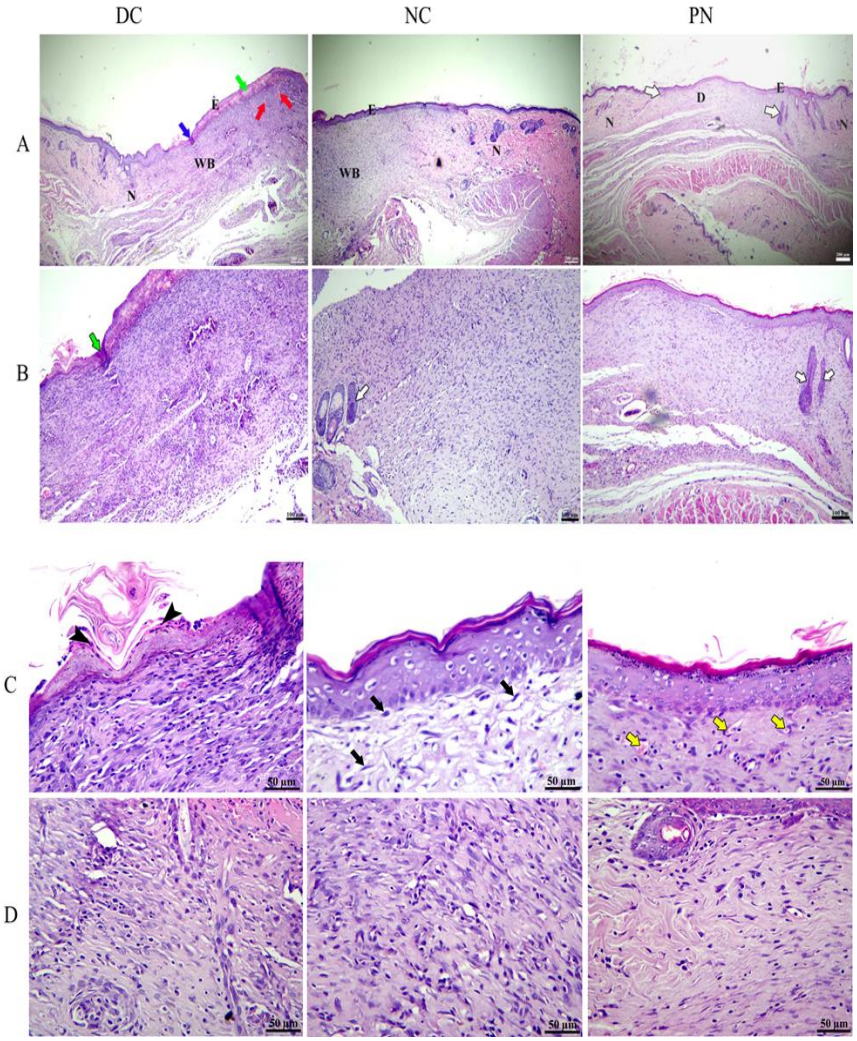

Fig. 6. Hematoxylin and eosin-stained tissue sections show the impact of applying pine extract nanoparticles on histopathological features of wound healing through various groups at day 18.

A, tissue sections show skin (4x); B, the dermal layer of skin (10x); C, the epidermal layer of skin (40x); D, the dermal layer of skin (40x) E, epidermis; D, dermis; N, normal skin; WB, wound bed; (white arrows) newly formed hair follicles, (black arrows) flattened shaped fibroblasts, (yellow arrows) newly formed blood vessels, (black arrow head) retained nuclei of keratinocyte (stratum corneum), (red arrows) areas of dermal separation, (blue arrows) incomplete epidermal proliferation; , (green arrows of A) pale areas, Scale bars: A, 200 µm; B, 100 C,D, 50 µm PN, pine extract nanoparticle-treated group; NC, normal control group; DC, diabetic control group.

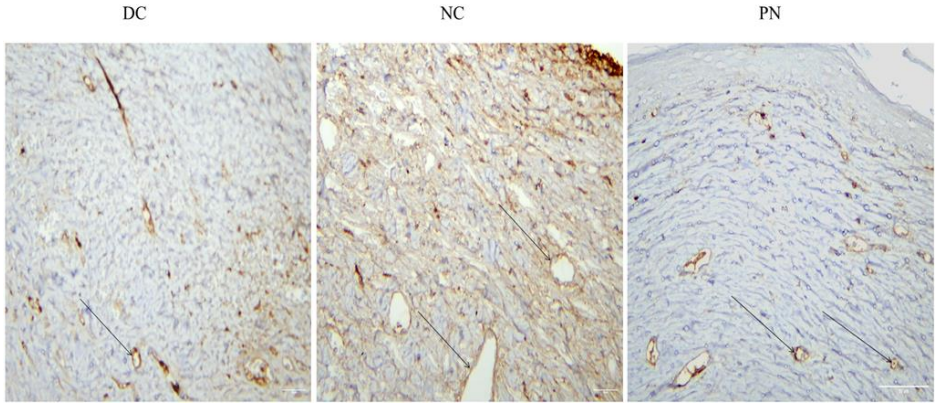

Fig. 7. Representative images of CD 31 positively stained microvessels in the dermal layer of DC, NC, and PN-treated groups at day 18. The brown-stained endothelial cells of newly formed blood vessels indicate better angiogenesis, scale bar: 50 µm (40x) (black arrows, CD 31 + stained microvessels).

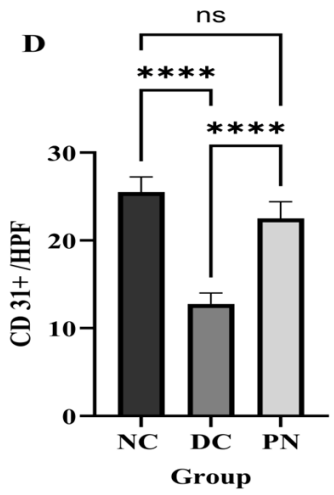

Fig. 8. (D) CD31 expression across groups. The (PN) group shows higher expression than the (DC), with no significant difference between the (PN) and (NC) groups.

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تأثير جسيمات مستخلص لحاء الصنوبر النانوية على التئام الجروح لدى مرضى السكري :دراسة نسيجية ومناعية كيميائية

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الملخص

تم التعرف منذ فترة طويلة على مشكلة الجروح الناتجة عن مرض السكري كأحد التحديات العلاجية غير المُلباة فيالمجال الطبي. في هذه الدراسة، قمنا بتقييم قدرة مستخلص لحاء الصنوبر (PB)النانوي على التئام الجروح الناتجة عن مرض السكري من خلال الدراسات النسيجية المرضية ودراسات الكيمياء المناعية النسيجية (IHC).تم تقسيم 18جرذًا من نوع ويستر إلى ثلاث مجموعات (n = 6) لكل مجموعة :(مجموعة ضابطة غير مصابة بالسكري (NC)، مجموعة ضابطة مصابة بالسكري (DC)، ومجموعة مصابة بالسكري ومعالجة بمستخلص لحاء الصنوبر (PN) .تحت تأثير التخدير العام، تم إنشاء جروح كاملة السماكة على ظهر جميع الجرذان، ثم تم اضافة مستخلص لحاء الصنوبر موضعيًا على جروح المجموعة المعالجة .تم قياس نسبة مساحة الجرح في الأيام 0، 3، 6، 9، 12، 15، و 18بعد الإصابة .تم تقييم أنسجة التحبب في الجرح من خلال الفحص النسيجي المرضي، كما تم تحليل الأوعية الدقيقة الإيجابية لمؤشر CD31باستخدام تقنية الكيمياء المناعية النسيجية .تشير نتائجنا إلى أن الجروح المعالجة بجزيئات مستخلص الصنوبر النانوية أظهرت معدل إغلاق أسرع بشكل ملحوظ مقارنة بكل من مجموعة ($p < 0.01$) DC ومجموعة ($p < 0.05$) NC بالإضافة إلى ذلك، تحسن بشكل كبير معدل إعادة التظهير في مجموعة PN مقارنةً بـ ($p < 0.0001$) DC و($p < 0.05$) NC.كما زاد التكوّن الوعائي في جروح PN مقارنةً بـ DC.تشير هذه النتائج إلى أن جزيئات لحاء الصنوبر النانوية تعزز بشكل فعال كلاً من سرعة ومدى التئام الجروح الناتجة عن مرض السكري .وتؤكد هذه الدراسة على الإمكانات العلاجية للمنتجات الطبيعية، مثل جزيئات مستخلص الصنوبر، كعوامل فعّالة في تعزيز التئام الجروح لدى مرضى السكري.

الكلمات الدالة: الجروح السكرية، جسيمات نانوية من مستخلص الصنوبر، التئام الجروح المزمنة.