INSIGHTS-JOURNAL OF
HEALTH AND REHABILITATION

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

BIOCHEMICAL AND PHARMACOLOGICAL ANALYSIS OF DIABETIC WOUND HEALING EFFICACY OF QUERCETIN POWDER VERSUS QUERCETIN NANOPARTICLES

Original Research

Muhammad Zeeshan Basheer[1], Muhammad Tariq[1], Rafia Rafi[2], Mubashir Ali Khalique[3], Tooba Rameen[4], Khadija Karim[5], Zain Arsalan[5], Hassaan Ahmed[6], Abdul Aziz[7], Hafiz Muhammad Usman Abid[5,8]*

[1]Faculty of Pharmaceutical sciences, Times institute, Multan, Pakistan.
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, The Islamia University of Bahawalpur, Pakistan.
[3]Faculty of veterinary and animal sciences, University of Poonch Rawalakot, Pakistan.
[4]Shah Abdul Latif University, Khairpur, Pakistan.
[5]Department of Pharmaceutics, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan.
[6]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan.
[7]University of Poonch, Rawalakot, Kashmir, Pakistan.
[8]Health Services Academy, Islamabad, Pakistan.
Corresponding Author: Hafiz Muhammad Usman Abid, Department of Pharmaceutics, Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan, Health Services Academy, Islamabad, Pakistan, usman.abid@hsa.edu.pk

Acknowledgement: The authors sincerely acknowledge the institutional support provided for conducting this research.

Conflict of Interest: None

Grant Support & Financial Support: None

ABSTRACT

Background: Diabetes mellitus is a chronic metabolic disorder often associated with impaired wound healing due to persistent inflammation, oxidative stress, and inadequate tissue regeneration. Chronic diabetic wounds, particularly foot ulcers, pose a serious clinical challenge and may lead to infection, prolonged hospitalization, or limb amputation. While quercetin—a natural flavonoid—offers antioxidant and anti-inflammatory benefits, its clinical potential is limited by poor solubility and low bioavailability. Nanoparticle-based drug delivery systems offer a promising solution to overcome these limitations.

Objective: This study aimed to enhance the therapeutic efficacy of quercetin by formulating quercetin nanoparticles (QNPs) and evaluating their wound healing potential in a diabetic rat model.

Methods: Quercetin nanoparticles were prepared using the solvent evaporation technique. Characterization was performed using Fourier Transform Infrared Spectroscopy (FTIR), Zeta potential analysis, and Dynamic Light Scattering (DLS), which confirmed an average particle size of 29 nm and a zeta potential of −30 mV. Diabetes was induced in albino Wistar rats via subcutaneous administration of dexamethasone (10 mg/kg). Animals were assigned to four groups: control, standard treatment, quercetin powder, and QNPs. Full-thickness dorsal wounds (2 cm^2) were created and treated topically on days 2, 5, 8, and 11. Healing parameters including epithelialization period, wound contraction, and granulation tissue weight were recorded.

Results: The QNP-treated group showed significantly improved outcomes with a mean epithelialization period of 11 ± 0.65 days, wet granulation tissue weight of 35 ± 0.25 mg, dry weight of 12.48 ± 0.30 mg, and wound contraction exceeding 88% by day 11, outperforming all other groups.

Conclusion: Quercetin nanoparticles demonstrated superior wound healing efficacy in diabetic rats compared to quercetin powder and conventional treatment. These findings support the potential application of QNPs in diabetic wound management, warranting further optimization and clinical investigation.

Keywords: Diabetes Mellitus, Drug Delivery Systems, Nanoparticles, Quercetin, Rats, Wound Healing, Zeta Potential.

INTRODUCTION

Diabetes mellitus is a chronic and multifaceted metabolic disorder characterized by persistent hyperglycemia, arising from insufficient insulin production, insulin resistance, or both (1). It presents a significant global health burden due to its rising prevalence and association with serious complications such as neuropathy, nephropathy, retinopathy, cardiovascular diseases, and delayed wound healing (2). While Type 1 diabetes mellitus (T1DM) is predominantly autoimmune in etiology, Type 2 diabetes mellitus (T2DM) is more often associated with lifestyle factors like obesity and physical inactivity, compounded by genetic predisposition (3). The complexity of diabetes lies in its systemic impact, disturbing not only glucose homeostasis but also vascular integrity and immune competence, ultimately predisposing individuals to chronic wounds, especially diabetic foot ulcers (4). These wounds are notoriously difficult to treat, primarily due to a convergence of pathological factors including peripheral neuropathy, poor blood circulation, and impaired immune function. Such conditions inhibit the physiological wound-healing cascade, leading to persistent inflammation, oxidative stress, and microbial colonization (5). Although conventional wound care approaches—such as debridement, application of dressings, antimicrobial therapy, and pressure offloading—are widely used, they often fall short in addressing the underlying molecular and cellular disruptions. Furthermore, the efficacy of these treatments is frequently compromised by issues such as poor patient compliance and the growing threat of antimicrobial resistance (6).

In recent years, attention has shifted toward natural compounds with therapeutic potential, among which quercetin has emerged as a promising candidate due to its strong antioxidant, anti-inflammatory, and antimicrobial properties (7). Despite these benefits, quercetin's clinical utility remains limited because of its poor solubility in water, rapid metabolism, and low systemic bioavailability. Nanotechnology offers a viable solution to these pharmacokinetic challenges. Specifically, the development of quercetin-loaded nanoparticles (QNPs) has shown promise in enhancing solubility, stability, and site-specific delivery. By encapsulating quercetin in biodegradable nanocarriers, sustained drug release and increased local bioavailability can be achieved, potentially leading to more effective wound healing outcomes in diabetic patients (8). However, there is a noticeable gap in comparative research evaluating the therapeutic efficacy of QNPs versus traditional quercetin powder, particularly in vivo. Addressing this research gap, the present study was designed to synthesize and characterize QNPs and to assess their wound-healing potential relative to quercetin powder in a diabetic rat model. The objective of this investigation is to generate preclinical evidence that supports the use of nanoparticle-based delivery systems in enhancing the therapeutic benefits of natural compounds for chronic diabetic wounds, ultimately contributing to the development of more effective and patient-friendly treatment strategies.

METHODS

This experimental study was conducted to evaluate and compare the wound healing efficacy of quercetin powder and quercetin-loaded nanoparticles in a diabetic rat model. Male Albino Wistar rats, weighing between 150–200 g, were used for the in vivo analysis. All animals were kept under controlled environmental conditions with a 12-hour light-dark cycle and had free access to food and water. Diabetes was induced using subcutaneous administration of dexamethasone (10 mg/kg/day) for 10 consecutive days. Rats were included in the study if, on day 21 post-induction, their fasting blood glucose level exceeded 250 mg/dL (9,10). Animals with glucose levels below this threshold or those exhibiting signs of severe distress or systemic illness were excluded. Ethical approval was obtained from the Institutional Animal Care and Use Committee (IACUC), and all experimental protocols adhered strictly to ethical guidelines. Informed consent was not applicable as this was an animal-based study.

Preparation of Quercetin nanoparticles by solvent evaporation: Quercetin nanoparticles were prepared using the solvent evaporation method. In this technique, dimethyl sulfoxide (DMSO) served as the organic phase to dissolve quercetin. Simultaneously, an aqueous phase was prepared using deionized water containing polyvinyl alcohol (PVA) as a stabilizer. The organic phase containing quercetin was added dropwise to the aqueous phase under continuous magnetic stirring, and this emulsion was stirred overnight. To reduce the particle size and enhance stability, the emulsion was subjected to high-speed homogenization. After the formation of the nanoemulsion, solvent evaporation was achieved through controlled heating. Nanoparticles were then collected by centrifugation and washed multiple

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

times with deionized water to remove residual solvent. The final product was vacuum-dried to obtain quercetin nanoparticle powder suitable for further analysis (8).

IN-VITRO ACTIVITIES:

FTIR: Fourier-transform infrared spectroscopy (FTIR) was employed to identify functional groups and confirm the successful incorporation of quercetin into the nanoparticle formulation. Spectra were recorded at room temperature over a frequency range of 4000–400 cm^{-1}, with each sample undergoing 32 scans to optimize the signal-to-noise ratio. Background correction was performed before each measurement to minimize atmospheric interference. The spectra obtained from quercetin nanoparticles were compared with spectra of pure quercetin and excipients to detect any shifts in absorption bands, which would indicate interactions and successful encapsulation.

Zeta potential and zeta sizer: Zeta potential and particle size analysis were carried out using a Zetasizer instrument. Nanoparticle suspensions were diluted in deionized water prior to measurement to ensure proper dispersion. The electrophoretic mobility of the particles was used to calculate the zeta potential, indicating colloidal stability. Dynamic light scattering (DLS) was used to determine particle size distribution by monitoring the scattering of light in a cuvette. All measurements were conducted in triplicates at room temperature, and average values were recorded for analysis.

IN-VIVO ACTIVITIES

Healing of diabetic wound: The wound healing activity was evaluated in diabetic rats by creating standardized excisional wounds on the dorsum. A total of four groups (n = 6 per group) were assigned as follows: (1) Control (diabetic untreated), (2) Standard treatment, (3) Quercetin powder-treated, and (4) Quercetin nanoparticle-treated. Rats were anesthetized using a suitable anesthetic, and their dorsal fur was shaved and sterilized. Using a sterile biopsy punch, a circular full-thickness wound of 2 cm^2 was created on each rat's back. The respective treatments were topically applied on days 2, 5, 8, and 11. The study evaluated wound healing through physical parameters including wound contraction percentage, epithelialization time, and granulation tissue weight.

Wet and Dry Granulation Weight: On day 11, granulation tissue from the wound site was surgically excised and immediately weighed to obtain the wet granulation tissue weight. The samples were then dried in a hot air oven at 60ºC for 24 hours to record the dry weight. These weights were used to assess tissue formation and the extent of healing under each treatment condition.

Period of Epithelialization: The period of epithelialization was determined by the number of days taken for the eschar (dead tissue) to completely detach from the wound site without leaving any raw or unhealed tissue. This parameter was used as an indicator of complete wound closure and surface tissue regeneration.

Percent Wound Contraction: Wound contraction was calculated using the formula: **Wound contraction (%) = (Healed area / Total wound area) × 100.** Wound dimensions were measured at designated time points using a Vernier caliper to ensure accuracy in tracking the healing process. All quantitative data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using GraphPad Prism software. One-way analysis of variance (ANOVA) was employed to assess differences among groups, followed by appropriate post-hoc tests. A p-value < 0.05 was considered statistically significant.

RESULTS

FTIR: Fourier-transform infrared spectroscopy analysis confirmed the presence of functional groups in both quercetin powder and its nanoparticle form. In quercetin powder, a broad absorption peak was observed at 3415 cm^{-1}, indicative of O–H stretching, while the peaks at 1654 cm^{-1} and 1600 cm^{-1} corresponded to C=O and C=C stretching, respectively. Additional peaks at 1243 cm^{-1} and 1082 cm^{-1} confirmed C–O stretching, supporting the presence of hydroxyl groups. In comparison, quercetin nanoparticles exhibited slightly shifted peaks with reduced intensity. The O–H stretching peak appeared at 3420 cm^{-1}, the C=O peak shifted to 1650 cm^{-1}, and C–O stretching peaks moved to 1244 cm^{-1} and 1084 cm^{-1}. These spectral shifts suggested changes in hydrogen bonding and molecular interactions due to nanoparticle formation and stabilization.

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

Zeta potential and zeta sizer: Quercetin nanoparticles exhibited a zeta potential of -30 mV, indicating moderate stability in suspension. The mean particle size was found to be 71.29 nm, with a polydispersity index (PDI) of 0.0, signifying a monodisperse particle population. Size distribution analysis by intensity revealed a dominant peak at 11.7 nm, suggesting a homogeneous dispersion of primarily smaller-sized particles within the formulation.

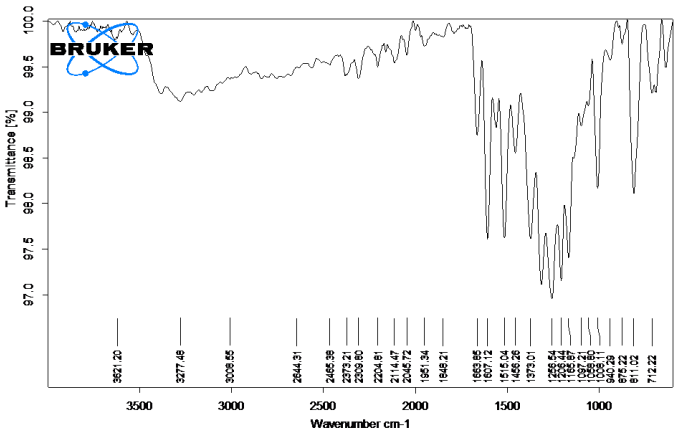
Wet and Dry Granulation Weight: The group treated with quercetin nanoparticles demonstrated a markedly higher wet granulation tissue weight of 35 ± 0.25 mg and dry weight of 12.48 ± 0.30 mg, outperforming the control, standard treatment, and quercetin powder groups. This result indicated that quercetin nanoparticles enhanced tissue formation and overall wound granulation.

Period of Epithelialization: Quercetin nanoparticles significantly reduced the epithelialization period to 11 ± 0.65 days, compared to 14 ± 0.48 days in the control group. Both standard treatment and quercetin powder also showed improved healing durations of 12 ± 0.41 and 12 ± 0.65 days, respectively. These results suggested a faster wound closure rate with nanoparticle treatment.

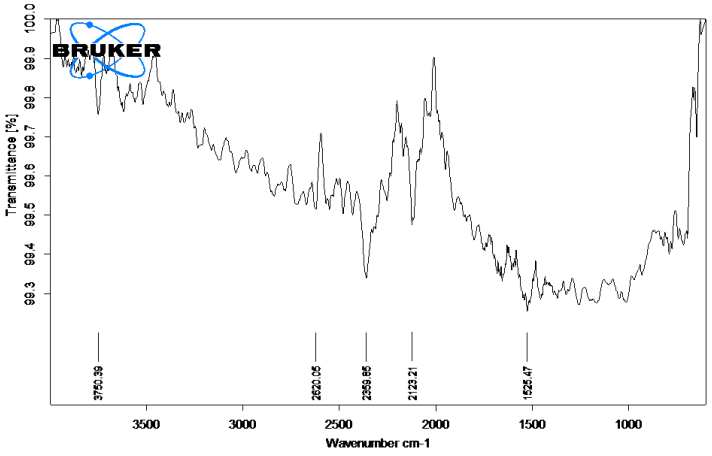
Percentage of Wound Contraction: Initial observations showed no significant differences on day 1 across all groups. By day 4, the wound contraction rate in the quercetin nanoparticles and standard treatment groups significantly increased ($P < 0.001$). On day 7, quercetin nanoparticles achieved a contraction rate of approximately 70%, compared to 65% in the standard group and 25% in control. By day 11, the contraction reached 88% in the quercetin nanoparticle group, maintaining statistical significance with $P = 0.001$. These findings confirmed enhanced healing efficacy of the nanoparticle formulation over other treatments.

Table 1: Period of epithelization in diabetic wounds

Group	Epithelialization period (Days)
Control	14± 0.48
standard treatment	12± 0.41*
Quercetin powder	12 ± 0.65 *
Quercetin nanoparticles	11 ± 0.65 *



Quercetin powder



Quercetin nanoparticles

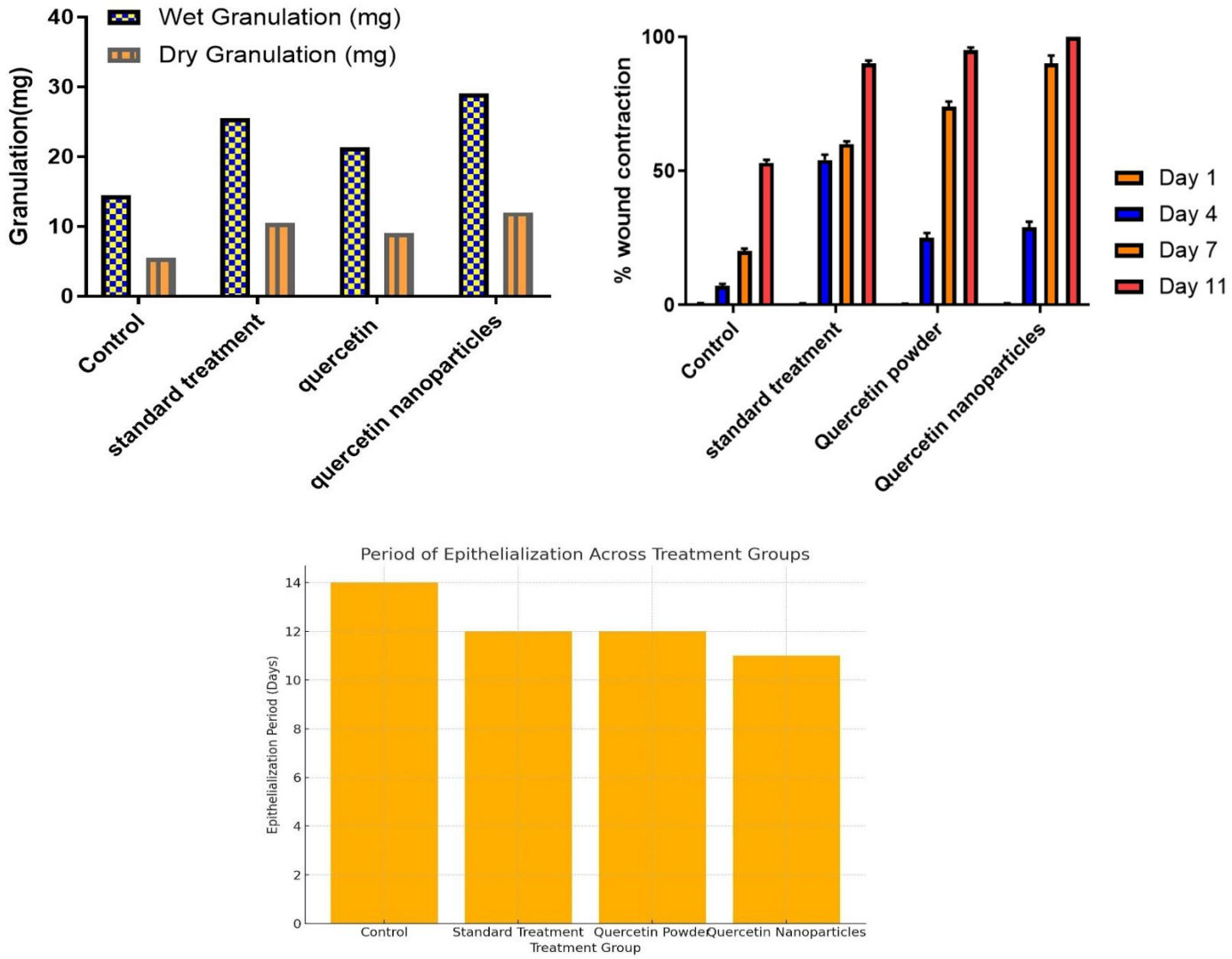


Figure 1 Period of Epithelialization Across Treatment Groups

DISCUSSION

The findings of this study demonstrated that the formulation of quercetin into nanoparticles significantly influenced its physicochemical properties and therapeutic performance in a diabetic wound model. FTIR analysis confirmed the retention of the major functional groups associated with quercetin's flavonoid structure, including O–H, C=O, C=C, and C–O stretches, with characteristic peaks shifting slightly in the nanoparticle formulation. These spectral shifts indicated modified hydrogen bonding and interactions with stabilizers used during nanoparticle synthesis, supporting successful encapsulation and stabilization of the bioactive compound (11,12). The altered peak intensities and positions were consistent with nanoparticle formation and implied changes in molecular interaction that are critical for improving solubility and bioavailability of poorly water-soluble compounds like quercetin (13). The nanoparticle characterization revealed a mean particle size of approximately 70 nm with a peak intensity at 11 nm, reflecting a population dominated by small-sized particles. While this particle size is favorable for cellular uptake and controlled drug release, the zeta potential of approximately -30 mV indicated only moderate colloidal stability. The relatively low conductivity and polydispersity index (PDI) of 0.345 suggested some degree of particle uniformity, though not ideal for prolonged suspension stability. This limitation, along with the slightly negative charge, raises concerns about potential aggregation over time, especially in physiological environments where ionic strength and protein

INSIGHTS-JHR
INSIGHTS-JOURNAL OF HEALTH AND REHABILITATION

interactions can destabilize suspensions (14,15). Nevertheless, the nanoparticle system retained a therapeutic particle size range favorable for transdermal and topical delivery applications.

In vivo experiments provided compelling evidence for the therapeutic potential of quercetin nanoparticles in enhancing wound healing outcomes. The group treated with nanoparticles exhibited significantly greater granulation tissue formation, as reflected by higher wet and dry tissue weights. Additionally, the period of epithelialization was notably shorter at 11 ± 0.65 days compared to the control group, which required up to 14 days. This accelerated epithelialization underscores the biological efficacy of the nanoparticle system in promoting tissue regeneration, likely due to increased local bioavailability and sustained release of quercetin at the wound site (16,17). Wound contraction rates further supported the effectiveness of nanoparticle-based treatment. Although no initial difference was noted on day 1, highly significant improvements were observed from day 4 onward, with P values < 0.001 maintained throughout the healing period. The consistent enhancement in wound closure suggests that quercetin nanoparticles may exert effects through multiple mechanisms, including modulation of inflammation, stimulation of fibroblast proliferation, and improved collagen deposition. These findings are consistent with earlier studies that emphasized the role of flavonoid-based nanoparticles in modulating oxidative stress and inflammatory responses in wound environments (18,19).

A major strength of this study lies in the comprehensive evaluation of both physicochemical properties and biological efficacy of quercetin nanoparticles, using well-established in vitro and in vivo models. The use of dexamethasone-induced diabetes in rats provides a relevant model to mimic delayed wound healing in diabetic conditions, thereby enhancing the translational relevance of the findings. Moreover, the inclusion of control, standard treatment, and quercetin powder groups allowed for clear comparative analysis, highlighting the superiority of the nanoparticle formulation. However, the study was not without limitations. The absence of histopathological examination of wound tissues restricted the ability to directly observe cellular architecture and collagen remodeling. Similarly, oxidative stress markers, pro-inflammatory cytokines, and angiogenic factors were not quantified, leaving mechanistic pathways of healing only inferential. Additionally, the moderate zeta potential and high polydispersity in some samples pointed to formulation issues that may affect long-term stability and scalability of the nanoparticle system. These challenges underscore the need for optimization of formulation parameters and rigorous stability testing under simulated physiological conditions.

Future studies should incorporate mechanistic evaluations through immunohistochemistry, molecular assays, and extended toxicity profiling. Inclusion of pharmacokinetic analysis to determine systemic absorption and local drug concentrations at wound sites would also offer valuable insights. Moreover, evaluating the nanoparticle system under chronic wound conditions with microbial burden would expand its applicability to more clinically relevant scenarios (20). Overall, the results supported the hypothesis that nanoparticle-based delivery enhances the therapeutic potential of quercetin in diabetic wound healing. By improving bioavailability and sustaining local drug release, quercetin nanoparticles represent a promising strategy in wound care, particularly for patients with metabolic complications.

CONCLUSION

This study concluded that quercetin nanoparticles exhibit superior wound healing potential compared to conventional quercetin powder in a diabetic rat model. By enhancing quercetin's solubility, stability, and bioavailability, the nanoparticle formulation significantly improved key healing parameters, including wound contraction, epithelialization, and granulation tissue development. These findings highlight the promising role of quercetin nanoparticles as a therapeutic strategy for managing chronic diabetic wounds. The results support further exploration of this formulation in clinical settings, with future research needed to optimize its design and assess long-term safety and efficacy in human applications.

AUTHOR CONTRIBUTION

Author	Contribution
Muhammad Zeeshan Basheer	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Tariq	Substantial Contribution to study design, acquisition and interpretation of Data

Author	Contribution
	Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Rafia Rafi	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Mubashir Ali khalique	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Tooba Rameen	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Khadija Karim	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Zain Arsalan	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Hassaan Ahmed	Writing - Review & Editing, Assistance with Data Curation
Abdul Aziz	Writing - Review & Editing, Assistance with Data Curation
Hafiz Muhammad Usman Abid*	Writing - Review & Editing, Assistance with Data Curation

REFERENCES

1. Sajawal, H.M., et al., Evaluating the Healing Properties of Quercetin-Enhanced Nanoparticle Ointments in Diabetic Rats. Journal of Health and Rehabilitation Research, 2024. 4(3): p. 1-7.
2. Mahmood, H.M.U.A.M.H.M.N.B.A.M.A.D.e.S.K., Global Prevalence and Mortality of Type-2 Diabetes from 1990 to 2019, with Future Projections to 2023 and 2050: a Systematic Review. Global Drug Design & Development Review, 2024. IX(March-2024): p. 1-10.
3. Abid, H., et al., Navigating the Vascular Frontier: Exploring Quercetin-Based Drug Delivery Strategies in Cardiovascular Therapy. Journal of Population Therapeutics and Clinical Pharmacology, 2024. 31(1): p. 1702-19.
4. Zahra, S., et al., Comparative Efficacy of Aloe Vera Gel Versus Normal Saline in Accelerating Episiotomy Wound Healing: A Randomized Controlled Trial. Journal of Health and Rehabilitation Research, 2024. 4(2): p. 949-956.
5. Usman Abid, H.M., et al., Exploring the Potent Combination of Quercetin–Boronic Acid, Epalrestat, and Urea Containing Nanoethosomal Keratolytic Gel for the Treatment of Diabetic Neuropathic Pain: In Vitro and In Vivo Studies. Molecular Pharmaceutics, 2023. 20(7): p. 3623-3631.
6. Abid, H.M.U., et al., Wound-healing and antibacterial activity of the quercetin–4-formyl phenyl boronic acid complex against bacterial pathogens of diabetic foot ulcer. ACS omega, 2022. 7(28): p. 24415-24422.
7. Azeem, M., et al., An insight into anticancer, antioxidant, antimicrobial, antidiabetic and anti-inflammatory effects of quercetin: A review. Polymer Bulletin, 2023. 80(1): p. 241-262.
8. Sahdev, A.K., et al., Chitosan-Folic Acid-Coated Quercetin-Loaded PLGA Nanoparticles for Hepatic Carcinoma Treatment. Polymers, 2025. 17(7): p. 955.
9. Gopakumari Satheesh Chandran, L., et al., Engineering of Brewery Waste-Derived Graphene Quantum Dots with Zno Nanoparticles for Treating Multi-Drug Resistant Bacterial Infections.
10. Pasieczna-Patkowska, S., M. Cichy, and J. Flieger, Application of Fourier Transform Infrared (FTIR) Spectroscopy in Characterization of Green Synthesized Nanoparticles. Molecules, 2025. 30(3): p. 684.

11. Parveen, S., et al., Design, synthesis and spectroscopic characterizations of medicinal hydrazide derivatives and metal complexes of malonic ester. Current Bioactive Compounds, 2023. 19(4): p. 31-46.
12. Mourshed, M., H.Q. Nguyen, and B. Shabani, Using electrical conductivity to determine particle sedimentation status of carbon-based slurry electrodes in electrochemical energy storage systems. Materials Science for Energy Technologies, 2023. 6: p. 290-300.
13. Nalini, T., et al., Fabrication and evaluation of nanoencapsulated quercetin for wound healing application. Polymer Bulletin, 2023. 80(1): p. 515-540.
14. Huzum, R., et al., Modulating Polyphenol Activity with Metal Ions: Insights into Dermatological Applications. 2025.
15. Panthi, V.K., et al., The significance of quercetin-loaded advanced nanoformulations for the management of diabetic wounds. Nanomedicine, 2023. 18(4): p. 391-411.
16. Jintao X, Nanqian Z, Yuping Y, Yun J, Yue Q, Yanhua L, et al. Puerarin-loaded ultrasound microbubble contrast agent used as sonodynamic therapy for diabetic cardiomyopathy rats. Colloids Surf B Biointerfaces. 2020;190:110887.
17. Wang A, Ruan X, Wang X, Ren Y, Shen C, Zhang K, et al. A one-stop integrated natural antimicrobial microneedles with anti-inflammatory, pro-angiogenic and long-term moisturizing properties to accelerate diabetic wound healing. Eur J Pharm Biopharm. 2024;203:114448.
18. Wei Z, Robertson M, Qian J, Qiang Z, Ren J. In Situ Self-Assembled Naringin/ZIF-8 Nanoparticle-Embedded Bacterial Cellulose Sponges for Infected Diabetic Wound Healing. ACS Appl Mater Interfaces. 2025;17(4):6103-15.
19. Wafaey AA, El-Hawary SS, El Raey MA, Abdelrahman SS, Ali AM, Montaser AS, et al. Gliricidia sepium (Jacq.) Kunth. ex. Walp. leaves-derived biogenic nanohydrogel accelerates diabetic wound healing in rats over 21 days. Burns. 2025;51(2):107368.
20. Vendidandala NR, Yin TP, Nelli G, Pasupuleti VR, Nyamathulla S, Mokhtar SI. Gallocatechin-silver nanoparticle impregnated cotton gauze patches enhance wound healing in diabetic rats by suppressing oxidative stress and inflammation via modulating the Nrf2/HO-1 and TLR4/NF-κB pathways. Life Sci. 2021;286:120019.