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Assessment of antidiabetic potential of natural hydrogels derived from *Plantago ovata* seed husk for enhanced diabetic wound healing

Muhammad Zubair, Javaria Mehmood, Eisha Javed and Tayyaba Shaheen*
Department of Bioinformatics and Biotechnology, Government College University Faisalabad, Pakistan

Abstract: Diabetes is a challenging health condition, posing a considerable financial burden. Diabetic wounds represent a significant and growing health concern worldwide, as they often fail to heal properly and pose severe consequences for diabetic patients. Hydrogels have emerged as a potential treatment for diabetic ulcers, showing promise in modern wound care. This research explores the potential of Psyllium husk (Isabagol) in the formation of a hydrogel to treat diabetic ulcers. Psyllium mucilage hydrogel was prepared, and its efficacy was assessed using various assays. The Alpha-glucosidase inhibition assay assessed its anti-diabetic activity, with extracts prepared at concentrations of 25mg/mL, 50mg/mL and 25mg/mL in PBS solvents. Additionally, the DPPH assay was used to predict the hydrogel's radical scavenging property. Results indicated that Psyllium mucilage extract demonstrated significant medicinal properties, inhibiting alpha glucosidase and scavenging free radicals produced by DPPH in a concentration-dependent manner. The highest inhibition activity was observed at 125mg/mL, with 92.75% for antidiabetic activity and 50.1% for DPPH radical scavenging. Moreover, an *In vivo* experiment on a mice model confirmed the hydrogel's significant wound healing activity. In conclusion, Psyllium mucilage hydrogel exhibits promising antidiabetic and anti-oxidative properties, making it a potential candidate for the treatment of diabetic wounds.

Keywords: Antioxidants; Alpha-glucoside; Diabetes; DPPH; Grafting; Hypoxia; Psyllium husk

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INTRODUCTION

Since 2000 there is a 70% increase in diabetes mellitus (DM), which is among the top ten causes of most deaths representing a devastating health condition (Shafras *et al*., 2024). DM is a chronic endocrine condition characterized by high blood glucose levels resulting from inadequate insulin production or impaired insulin activity (Chaudhury *et al*., 2017). It is classified into two types: Type 1 diabetes, also known as Insulin Dependent Diabetes Mellitus (IDDM) and Type 2 diabetes, which is associated with metabolic disorders and an increased risk of cardiovascular disease (Krause and De Vito, 2023). Type 1 diabetes is caused by genetic factors and requires insulin treatment, while Type 2 diabetes is influenced by lifestyle and genetic background (Ozougwu *et al*., 2013). Diabetes affects over 9% of adults worldwide aged 18 and above, with the fastest global growth among health diseases (Cho *et al*., 2018).

Wounds, arising from injuries to living tissue, encompass a range of conditions where the skin's integrity is compromised (Krishtul *et al*., 2020). The delay in wound healing presents substantial medical and financial challenges in healthcare. Proper wound categorization, distinguishing between acute and chronic wounds, is critical for optimizing treatment efficacy (Vopat *et al*., 2017). A thorough assessment of the wound's type, cause and extent of tissue damage facilitates the implementation of personalized treatments, leading to improved healing outcomes (Langemo & Brown, 2006). A thorough approach to wound care management is necessary to address this critical issue.

Diabetes is associated with delayed wound healing (Liu *et al*., 2022). People with diabetes have a 15 to 25% chance of acquiring chronic sores, like foot and venous ulcers, which fall under the category of chronic, non-healing wounds, leading to skin damage and delaying wound recovery (Sen *et al*., 2009). Diabetic foot ulceration is a prevalent and disabling complication of diabetes, often leading to limb amputation and high mortality rates (Rubio *et al*., 2022). Around 15 to 20% of the 16 million people with diabetes in the United States would be hospitalized for foot issues (Pierce-Williams *et al*., 2020). Recent multicenter research indicates that approximately 63% of diabetic foot ulcers are associated with peripheral sensory neuropathy, trauma and deformity (Fard *et al*., 2007).

Wound healing is a complex physiological response to tissue damage involving various cell types and mediators (Christian *et al*., 2007). It occurs through either primary healing (rapid closure) or secondary healing (delayed closure) (Elce, 2016). Effective wound management requires a comprehensive understanding of these factors to optimize patient care (Eming *et al*., 2014).

Dressings are crucial in managing diabetic foot ulcers, but an optimal and adaptable choice remains elusive (Fard *et al*., 2007). An ideal wound dressing should maintain

**Corresponding author:* e-mail: tayyabashaheen@gcuf.edu.pk

moisture, prevent infections, manage, exudate and promote tissue regeneration (Yu *et al.*, 2022).

Hydrogel dressings have emerged as promising alternatives to traditional wound contact dressings in the treatment of diabetic foot ulcers and other skin problems (Ramirez-Acuña *et al.*, 2019). Their hydrophilic structure allows for the retention of substantial amounts of water without sacrificing flexibility, making them effective in moist wound environments. The remarkable flexibility and biocompatibility of hydrogels have led to their implementation in wound dressing applications, offering the potential for adhesion, antioxidant properties, mechanical strength and antibacterial effects (Fang *et al.*, 2019). Notably, plant-based hydrogels derived from polysaccharides have shown great potential in various biomedical applications, including tissue engineering, diagnostics and wound healing (Mohammadinejad *et al.*, 2019). Their ability to form three-dimensional networks capable of holding large quantities of water or biological fluids while maintaining stability makes them highly desirable for advanced medical uses. As research continues, hydrogel dressings, especially those derived from plant-based sources, may further revolutionize wound care and biomedical therapies (Sun *et al.*, 2022).

Plantago ovata, also known as ispaghula, produces psyllium mucilage, a natural polysaccharide used as a laxative in traditional Chinese medicine (Kumar *et al.*, 2017). The mucilage primarily consists of arabinoxylan (arabinose 22.6%, xylose 74.6%). Psyllium husk, a non-toxic biomaterial, has shown potential as a glucose-lowering agent in diabetes patients and healthy individuals, with immediate blood glucose reduction even after a single dose (Kumar *et al.*, 2022). Psyllium has a long history of medicinal use and the *Plantago* genus comprises around 200 species with psyllium-like properties. The main polysaccharide found in the plant is psyllium polysaccharide complex heteroxylans composed of arabinose and xylose monosaccharides (Kumar *et al.*, 2017). While psyllium is increasingly used in wound treatment through hydrogel films and fibers, its full therapeutic efficacy remains to be established, as it requires chemical synthesis through free radical polymerization (Ponrasu *et al.*, 2018).

Naturally occurring dietary antioxidants found in plants such as vitamins A, C and E, flavonoids, carotenoids, polyamines, alpha-lipoic acid, plant polyphenols and glutathione all provide significant protection against diabetes by combating the oxidative stress caused by elevated glucose levels in diabetic patients (Shafras *et al.*, 2024). Alpha- glucosidase inhibition assay and DPPH radical scavenging assay both have been found effective methods to check antidiabetic potential of a proposed treatment source against diabetes (Bhatia *et al.*, 2019; Shafras *et al.*, 2024).

This research aims to investigate the potential of Psyllium husk-based hydrogel for treating diabetic ulcers. The study also evaluates the anti-diabetic and anti-oxidative activity of the natural polymer-based hydrogel. The findings may contribute to the development of innovative treatments for diabetic ulcer management.

MATERIALS AND METHODS

Hydrogel preparation

The psyllium husk sample was obtained from the Faisalabad local market. Hydrogel was created from psyllium husk mucilage (PHM) by dissolving psyllium husk powder in water (1:100 w/v) and stirring at 80°C for 1-2 hours (Pooresmaeil & Namazi, 2020). After cooling to 4°C, the sample was filtered to obtain PHM for later use.

PHM was grafted using Fenton reagent. Mucilage (100g) was mixed with Tween 20 and water (5:1), agitated with nitrogen (20 mins) and allowed to react with 3% H_2O_2 and FAS (6:4 v/w, 20 mins) (Ahmed, 2015). After separation and rinsing, saponification occurred in 0.7M NaOH (1/9 w/v) at 95°C for an hour. The resulting poly AN-grafted polysaccharide hydrogel shows potential for several applications. The final hydrogel was brown in color (Fig. S1).

In vitro experiment

Anti-diabetic activity

The anti-diabetic potential of psyllium husk polysaccharide was assessed by alpha-glucosidase inhibition assay. PHM (12.5µL) was mixed with alpha-glucosidase (40µL, 0.5U/ml) in phosphate buffer (140µL) and incubated at 37°C for 5 mins. P-nitrophenyl-α-D glucopyranoside (5mM) was added and incubated with the enzyme for 30 mins at 37°C. Enzyme activity was measured at 405nm using a microplate reader (Kim *et al.*, 2005). Acarbose (10mM) was used as positive control. The percentage of inhibition was then estimated using a formula:

$$\text{Percentage inhibition} = \frac{Ac - As}{Ac} X\ 100$$

Where, Ac is absorbance of control and As is absorbance of sample.

Antioxidant activity

The PHM's radical scavenging capacity was determined using the DPPH test. A 10µL extract was used to scavenge DPPH (190µL, 0.3mM). Gallic acid (0.3mM) served as the positive control. Absorbance was measured at 490 nm after a 30-minute incubation at 37°C (Dauthal & Mukhopadhyay, 2013). The psyllium mucilage's capacity to scavenge radicals was calculated using the percentage inhibition formula.

$$\text{Percentage inhibition} = \frac{Ac - As}{Ac} X\ 100$$

In vivo animal trials

In a preclinical diabetes study, albino mice were sourced from Government College University Faisalabad, Pakistan. Fourteen male mice were housed individually under controlled conditions with a 12-hour light-dark cycle with specific temperature and humidity settings (Furman, 2015). Streptozotocin (STZ) was used to induce diabetes in mice. Blood glucose levels of the STZ-treated mice were monitored using a one-touch basic blood glucose monitoring device. Following the STZ injections, all mice were subjected to a six-hour daily fasting period for nine consecutive days (Furman, 2015). After the induction of diabetes, two full-thickness lesions measuring 6mm were created on the dorsal skin of each mouse as shown in fig. (S2). Mice were divided into two groups each including 7 mice, (1) control and (2) Experimental; hydrogel was applied topically to the wounds of experimental while control group was not treated with hydrogel. Ethical considerations were followed throughout the study to ensure the welfare of the animals.

Wound margin size (in mm) was measured daily using Vernier calipers before treatment application. The measure of wound edge contraction was determined by calculating the reduction in the initial wound diameter. To calculate the proportion of the wound that was healed, the following equation was used:

$$\% woundinghe\ aling = \frac{woundareaa\ today - woundareaa\ fter\ 2days}{woundareaa\ today} \times 100$$

Wound healing was observed in both groups from day 1 to day 18 fig (3).

Statistical analysis

A t-test was performed to find the significance of differences between the treated and untreated groups.

RESULTS

Antidiabetic activity

The PHM dilutions (25 mg/mL, 50 mg/mL and 125 mg/mL) exhibited inhibitory activity on α-glucosidase. GlucoBay (Acarbose) served as the positive control and PBS as the negative control in the experiment. At 125 mg/mL concentration, the percentage inhibition was the highest (92.75%), indicating strong anti-diabetic potential, even higher than the positive control (88%). Comparatively, lower inhibitory activities were observed in 50 mg/mL and 25 mg/mL concentrations showing 40.8% and 25.6% respectively. The percentage inhibition caused by psyllium mucilage against diabetes mellitus using the α-glucosidase assay is shown in fig. (1a).

Antioxidant activity

Psyllium husk mucilage extract was dissolved in three different concentrations (125 mg/mL, 50 mg/mL and 25 mg/mL) to assess its antioxidant potential. Gallic acid (0.3 mM) served as a positive control and DPPH (0.3 mM) provided free radicals. Antioxidant activity was concentration-dependent, with the concentration (125 mg/mL) exhibiting the highest activity of 50.1%. Dilution to 50 mg/mL reduced activity to 47.2% and further dilution to 25 mg/mL decreased it to 27.12%. Optical density was measured at 490 nm. The percentage inhibition caused by psyllium mucilage against ROS using the DPPH assay is shown in fig. (1b).

In vivo trials

Administration of multiple dosages of Streptozotocin (STZ) to mice resulted in severe hyperglycemia within one week. The mice became diabetic during the 2nd week and remained so until the 5th week of their lives. One mouse in the experimental group died at the end of the study.

We compared the wound healing activity of a hydrogel-treated group and a non-treated group. The hydrogel-treated group exhibited rapid improvement, with wound healing percentages of 14.65% on day 2, 47.67% on day 9, 80% on day 13 and 98% on day 15, as shown in fig (2). In contrast, the non-treated group showed slower progress, with healing percentages of 10.35% on day 2, 35.67% on day 9, 50% on day 13 and 75.67% on day 15. The non-treated group's wound was not completely healed even by day 18 when it reached 80% as shown in fig. (3). These findings emphasize the significant and beneficial impact of hydrogel treatment on wound healing. The wound closure rate in mice of experimental group and control group on different days is shown in fig. 3. In this experiment hydrogel treated group showed maximum wound healing activity as compared to control group. There was a significant ($p < 0.0001$) difference in wound healing activity of control group as in hydrogel treated group, all animals were healed completely at day 15 but in control group they were healed at day 18 (Fig. 3).

DISCUSSION

Among dietary sources of fiber available presently, Psyllium is the most beneficial dietary source. Furthermore, a gel-forming mucilage is derived from its seed husk (Gholami *et al.*, 2024). In this study, the anti-diabetic potential of mucilage extracted from *Plantago ovat*a (psyllium husk) using *In vitro* testing was assessed. Dissolving Psyllium mucilage extracts in PBS significantly inhibited α-glucosidase enzyme activity, with a concentration of 125 mg/mL showing 92.75% inhibition as compared to other concentrations (50 mg/mL, 25 mg/mL). This finding suggests substantial antidiabetic activity, potentially achieved by delaying carbohydrate digestion and lowering blood glucose levels.

The α-glucosidase enzyme plays a key role in converting starch to glucose for absorption in the small intestine, leading to elevated blood glucose levels (Bhatia *et al.*,

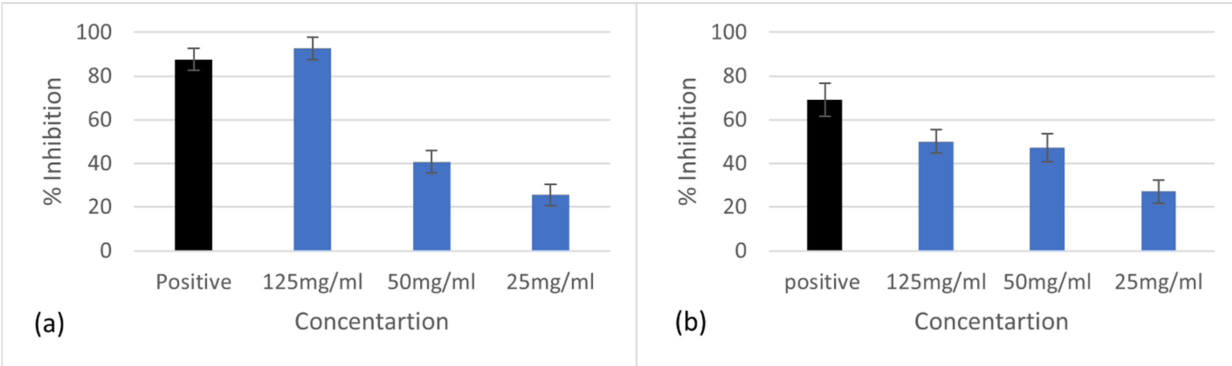

Fig. 1: Inhibitory activities of α-glucosidase assay (a) and antioxidant activity against free radicals (b) of *Plantago ovata* mucilage at different concentrations.

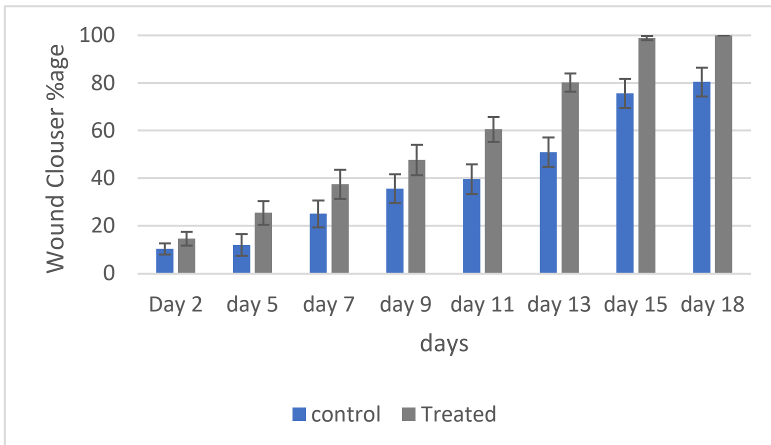

Fig. 2: Comparison of rate of wound healing between control and hydrogel treated mice groups.

2019). Previously, antidiabetic potential of some common plants using α-glucosidase inhibition assay was assessed by Bhatia *et al.* (2019), demonstrating it as a promising tool in diabetes research.

The role of Psyllium husk in management of diabetes has been studied previously. In a study it showed a significant reduction in hemoglobin A1C (HbA1c), in comparison with the placebo group, while insulin levels remained unaffected (Ziai *et al.*, 2005). Kamalpour *et al.* (2018) observed that, even for a limited time of supplementing a moderate carbohydrate diet with psyllium, can significantly reduce fasting plasma insulin in diabetic patients (Kamalpour *et al.*, 2018). Psyllium shows a similar effect to intestinal α-glucosidase inhibitors by delaying absorption, which consequently decreases carbohydrates digestion and absorption, leading to increased levels of the glucoregulatory factor glucagon-like peptide 1 (GLP-1). It was also observed that psyllium could significantly decrease FBS, HbA1c and HOMA IR levels, but not insulin levels, as compared to placebo (Ziai *et al.*, 2005: Gholami *et al.*, 2024). Antioxidant activity of Psyllium husk mucilage extract was assessed using DPPH assay at three different concentrations (125 mg/mL, 50 mg/mL and 25 mg/mL). The highest antioxidant activity (50.1%) was observed with concentration 125 mg/mL as compared to control (Gallic acid) which showed 69% inhibition. In a previous study Waleed *et al.* (2022) reported a higher antioxidant potential of Psyllium Husk (Waleed *et al.*, 2022). A substantial connection between dietary antioxidant consumption and safety against DM has been demonstrated in epidemiological studies (Shafras *et al.*, 2024). Antioxidant therapy has shown enhanced protection of beta-cells against oxidative stress-induced apoptosis preserving their function and in consequence reducing diabetes related complications (Kanwugu *et al.*, 2022). It has been observed that elevated glucose levels have an underlying link with the development of reactive oxygen species. A disparity in antioxidant defense system and free radicals of RNS, ROS and RSS lead to oxidative stress, which can consequently result in aetiology and pathogenesis of multiple diseases, including diabetes (Shafras *et al.*, 2024). Oxidative stress can also lead to development of chronic non-healing wounds (Schäfer & Werner, 2008).

In normal wound healing, strict regulation of ROS production and detoxification is essential for optimal healing processes (Yang *et al.*, 2024).

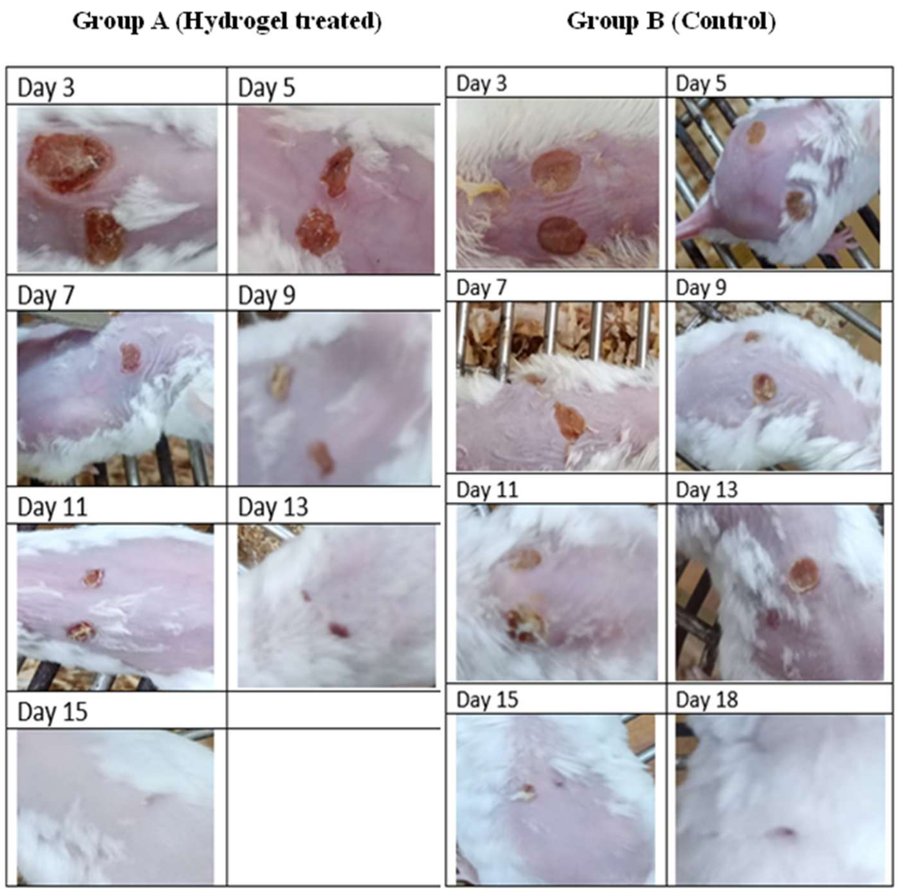

Fig. 3: Time-lapse images showing wound healing progression in diabetic mice treated with psyllium-based hydrogel (left panel) versus untreated control group (right panel). Visual observations from Day 3 to Day 15 (treated) and Day 3 to Day 18 (control) demonstrate faster wound closure and reduced scab formation in the hydrogel-treated group.

In this study a natural polysaccharide-based hydrogel was formed for diabetic wound healing in an animal model. In vivo evaluation involved creating 6mm wounds in albino mice and treating them daily for 18 days. The hydrogel-treated group showed significantly higher wound healing activity, with complete healing observed in 15 days. In contrast, the control group exhibited slower and incomplete healing even after 18 days. The natural polysaccharide hydrogel, derived from psyllium husk, holds promise as a safe and effective topical treatment for wound healing.

Hyperglycemia can significantly hinders the wound healing process, leading to delays and elevated infection risks (Burgess *et al.*, 2021). Tissue repair and regeneration following injury involve sequential molecular and cellular events including exudative phase, proliferative phase and extracellular matrix remodeling phase. This process is completed with contribution of soluble agents, blood cells and parenchymal cells (Prabhu, 2023). Some factors including inadequate oxygenation, smoking, sex hormones, infection, advanced age, stress, diabetes, alcoholism, obesity, certain pharmaceuticals and dietary patterns may cause delayed wound healing (Patel *et al.*, 2019).

Diabetic patients experience a substantially delayed wound healing rate compared to healthy individuals, attributed to various factors such as elevated blood glucose levels, infection colonization, reactive oxygen species and prolonged inflammation. Globally 6.3 % diabetic patients suffer from diabetic foot ulcer (DFU). This high occurrence of DFU is a common reason for hospitalization which may associate with mortality and morbidity (Wang *et al.*, 2022).

Maintaining a moist environment around the wound aids the wound healing process (Fan *et al.,* 2014). The application of hydrocolloid occlusive dressings serves as an effective accessory in promoting wound healing by creating a moist environment while also preventing infection (Field & Kerstein, 1994). Hydrogels provide a crucial moist environment and effective fluid absorption, both of which are essential elements in facilitating the wound healing process (Zhang *et al.*, 2022).

Results of the study reveal the antidiabetic and anti-oxidative potential of the hydrogel derived from Psyllium husk. These findings suggest that the gel can be potentially very effective in diabetic wound healing. Previous studies revealed that hydrogels stand out among wet dressings which enhance wound healing by promoting cell division and migration along with collagen synthesis. Hydrogels are biodegradable and more biocompatible due to similarity with natural extra cellular matrix environment and can be stimulus responsive (Li *et al.*, 2024).

The anti-oxidative potential of the hydrogel reported in the study is very promising because self-antioxidant hydrogels do not release antioxidants explosively and are stable and complete. Furthermore, self-antioxidant hydrogels get clinical success by avoiding the regulatory hurdles of biological products (Li *et al.*, 2024).

CONCLUSION

The current research focused on exploring the potential of plant-based medicine as a cost-effective and readily available solution. Specifically, the study aimed to develop a hydrogel from psyllium mucilage and investigate its efficacy in treating diabetes and promoting wound healing in both *In vitro* and *In vivo* settings. *In vitro* evaluations assessed the plant extract's antidiabetic and antioxidant properties. At a dose level of 125mg/ml, the extract demonstrated maximum antidiabetic activity by inhibiting the alpha-glucosidase enzyme up to 72.45%. The extract also exhibited significant antioxidant potential, displaying a radical scavenging activity of 50.1% in the DPPH assay at a dose level of 1mg/ml. For *In vivo* assessments, a psyllium-based hydrogel was topically applied to wounds in diabetic mice, resulting in accelerated healing compared to the control group. By meeting these design requirements, a viable and affordable psyllium mucilage hydrogel delivery system has been developed, offering a natural and effective approach for wound treatment, with potential applicability in clinical settings.

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Authors' contributions
JM conducted mouse model, JM and EJ performed experiments in lab and prepared first draft of the manuscript. MZ and TS planned the experiments, supervised the study, applied stat to results and wrote final version of manuscript.

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Data availability statement
Data will be available on request to authors.

Ethical approval
The study was conducted in Government College University Faisalabad, Pakistan, in January 2022. Ethical approval for the study was obtained from the Ethics Review Committee (Letter No. GCUF/ERC/2022/156).

Conflict of interest
The authors declare that they have no Conflict of interest.

Supplementary data
https://www.pjps.pk/uploads/2025/10/SUP1760945801.pdf

REFERENCES

Ahmed EM (2015). Hydrogel: Preparation, characterization and applications: A review. *J. Adv. Res.*, **6**(2): 105-121.

Bhatia A, Singh B, Arora R and Arora S (2019). In vitro evaluation of the α-glucosidase inhibitory potential of methanolic extracts of traditionally used antidiabetic plants. *BMC Complement. Altern. Med.*, **19**: 1-9.

Burgess JL, Wyant WA, Abdo Abujamra B, Kirsner RS and Jozic I (2021). Diabetic wound-healing science. *Med.*, **57**(10): 1072.

Chaudhury A, Duvoor C, Reddy Dendi VS, Kraleti S, Chada A, Ravilla R, Marco A, Shekhawat NS, Montales MT and Kuriakose K (2017). Clinical review of antidiabetic drugs: implications for type 2 diabetes mellitus management. *Front. Endocrinol.*, **8**: 6.

Cho NH, Shaw J, Karuranga S, Huang Y, da Rocha Fernandes J, Ohlrogge A and Malanda B (2018). IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res. Clin. Pract.*, **138**: 271-281.

Christian LM, Graham JE, Padgett DA, Glaser R and Kiecolt-Glaser JK (2007). Stress and wound healing. *NIM*, **13**(5-6): 337-346.

Dauthal P and Mukhopadhyay M (2013). *In-vitro* free radical scavenging activity of biosynthesized gold and silver nanoparticles using *Prunus armeniaca* (apricot) fruit extract. *J. Nanopart. Res.*, **15**: 1-11.

Elce YA (2016). Approaches to wound closure. *EWM.*, 157-172.

Eming SA, Martin P and Tomic-Canic M (2014). Wound repair and regeneration: mechanisms, signaling and translation. *Sci. Transl. Med.*, **6**(265): 265-266.

Fan Z, Liu B, Wang J, Zhang S, Lin Q, Gong P, Ma L and Yang S (2014). A novel wound dressing based on Ag/graphene polymer hydrogel: effectively kill bacteria and accelerate wound healing. *Adv. Funct. Mater.*, **24**(25): 3933-3943.

Fang H, Wang J, Li L, Xu L, Wu Y, Wang Y, Fei X, Tian J and Li Y (2019). A novel high-strength poly (ionic liquid)/PVA hydrogel dressing for antibacterial applications. *Chem. Eng. J.*, **365**: 153-164.

Fard AS, Esmaelzadeh M and Larijani B (2007). Assessment and treatment of diabetic foot ulcer. *Int. J. Clin. Pract.*, **61**(11): 1931-1938.

Field CK and Kerstein MD (1994). Overview of wound healing in a moist environment. *Am. J. Surg.*, **167**(1): S2-S6.

Furman BL (2015). Streptozotocin-induced diabetic models in mice and rats. *Curr. Protoc. Pharmaco.*, **70**(1): 41-45.

Gholami Z, Clark CC and Paknahad Z (2024). The effect of psyllium on fasting blood sugar, HbA1c, HOMA IR and insulin control: A GRADE-assessed systematic review and meta-analysis of randomized controlled trials. *BMC Endocr. Disord.*, **24**(1): 82.

Kamalpour M, Ghalandari H and Nasrollahzadeh J (2018). Short-term supplementation of a moderate carbohydrate diet with psyllium reduces fasting plasma insulin and tumor necrosis factor-α in patients with type 2 diabetes mellitus. *J. Diet. Suppl.*, **15**(4): 507-515.

Kanwugu ON, Glukhareva TV, Danilova IG and Kovaleva EG (2022). Natural antioxidants in diabetes treatment and management: Prospects of astaxanthin. *Crit. Rev. Food Sci. Nutr.*, **62**(18): 5005-5028.

Kim YM, Jeong YK, Wang MH, Lee WY and Rhee HI (2005). Inhibitory effect of pine extract on α-glucosidase activity and postprandial hyperglycemia. *Nutrients*, **21**(6): 756-761.

Krause M and De Vito G (2023). Type 1 and type 2 Diabetes Mellitus: Commonalities, differences and the importance of exercise and nutrition. *Nutrients*. **15**(19): 4279.

Krishtul S, Baruch L and Machluf M (2020). Processed tissue–derived extracellular matrices: tailored platforms empowering diverse therapeutic applications. *Adv. Funct. Mater.*, **30**(18): 1900386.

Kumar D, Gautam A, Rohatgi S and Kundu PP (2022). Synthesis of vildagliptin loaded acrylamide-g-psyllium/alginate-based core-shell nanoparticles for diabetes treatment. *Int. J. Biol. Macromol.,* **218:** 82-93.

Kumar D, Pandey J, Kumar P and Raj V (2017). Psyllium mucilage and its use in pharmaceutical field: an overview. *Curr. Synth. Sys. Biol.*, **5**(134): 2332-0737.1000134.

Langemo DK and Brown G (2006). Skin fails too: acute, chronic and end-stage skin failure. *Adv. Skin Wound Care*, **19**(4): 206-212.

Li Y, Leng Y, Liu Y, Zhong J, Li J, Zhang S, Li Z, Yang K, Kong X and Lao W (2024). Advanced multifunctional hydrogels for diabetic foot ulcer healing: Active substances and biological functions. *J. Diabetes*, **16**(4): e13537.

Liu Y, Liu Y, He W, Mu X, Wu X, Deng J and Nie X (2022). Fibroblasts: Immunomodulatory factors in refractory diabetic wound healing. *Front. Immunol.*, **13**: 918223.

Mohammadinejad R, Maleki H, Larraneta E, Fajardo AR, Nik AB, Shavandi A, Sheikhi A, Ghorbanpour M, Farokhi M and Govindh P (2019). Status and future scope of plant-based green hydrogels in biomedical engineering. *Appl. Mater. Today*, **16**: 213-246.

Ozougwu J, Obimba K, Belonwu C and Unakalamba C (2013). The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *J. Physiol. Pathophysiol.*, **4**(4): 46-57.

Patel S, Srivastava S, Singh MR and Singh D (2019). Mechanistic insight into diabetic wounds: Pathogenesis, molecular targets and treatment strategies to pace wound healing. *Biomed. Pharmacother.,* **112**: 108615.

Pierce-Williams RA, Burd J, Felder L, Khoury R, Bernstein PS, Avila K, Penfield CA, Roman AS, DeBolt CA and Stone JL (2020). Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: A United States cohort study. *Am. J. Obstet. Gynecol. MFM.*, **2**(3): 100134.

Ponrasu T, Veerasubramanian PK, Kannan R, Gopika S, Suguna L & Muthuvijayan V (2018). Morin incorporated polysaccharide-protein (psyllium-keratin) hydrogel scaffolds accelerate diabetic wound healing in Wistar rats. *RSC Adv.*, **8**(5): 2305-2314.

Pooresmaeil M and Namazi H (2020). Application of polysaccharide-based hydrogels for water treatments. In: Yu Chen editor. Hydrogels based on natural polymers, 1st ed., Elsevier., pp.411-455.

Prabhu S (2023). Healing: Tissue regeneration and repair. In: Textbook of general pathology for dental students, *Springer*., 49-56.

Ramirez-Acuña JM, Cardenas-Cadena SA, Marquez-Salas PA, Garza-Veloz I, Perez-Favila A, Cid-Baez MA, Flores-Morales V and Martinez-Fierro ML (2019). Diabetic foot ulcers: Current advances in antimicrobial therapies and emerging treatments. *Antibiotics*, **8**(4): 193.

Rubio JA, Jiménez S and Lázaro-Martínez JL (2020). Mortality in patients with diabetic foot ulcers: Causes, risk factors and their association with evolution and severity of ulcer. *J. Clin. Med*. **9**(9): 3009.

Schäfer M and Werner S (2008). Oxidative stress in normal and impaired wound repair. *Pharmacol. Res.*, **58**(2): 165-171.

Sen CK, Gordillo GM, Roy S, Kirsner R, Lambert L, Hunt TK, Gottrup F, Gurtner GC and Longaker MT (2009). Human skin wounds: A major and snowballing threat to public health and the economy. *Wound Repair Regen.*, **17**(6): 763-771.

Shafras M, Sabaragamuwa R and Suwair M (2024). Role of dietary antioxidants in diabetes: An overview. *Food Chem. Adv.*, **4**: 100666.

Sun Y, Li D, Yu Y and Zheng Y (2022). Insights into the role of natural polysaccharide-based hydrogel wound dressings in biomedical applications. *Gels*, **8**(10): 646.

Vopat ML, Vopat BG, Lubberts B and DiGiovanni CW (2017). Current trends in the diagnosis and management of syndesmotic injury. *Curr. Rev. Musculoskelet. Med.*, **10**: 94-103.

Waleed M, Saeed F, Afzaal M, Niaz B, Raza MA, Hussain M, Tufail T, Rasheed A, Ateeq H and Al Jbawi E (2022). Structural and nutritional properties of psyllium husk arabinoxylans with special reference to their antioxidant potential. *Int. J. Food Prop.*, **25**(1): 2505-2513.

Wang X, Yuan CX, Xu B and Yu Z (2022). Diabetic foot ulcers: Classification, risk factors and management. *WJD*, **13**(12): 1049.

Yang Y, Zhong S, Meng F and Cui X (2024). Multi-functional hydrogels to promote diabetic wound Healing: A review. *Chem. Eng. J.*, 154855.

Yu R, Zhang H and Guo B (2022). Conductive biomaterials as bioactive wound dressing for wound healing and skin tissue engineering. *Nanomicro Lett.*, **14**: 1-46.

Ziai SA, Larijani B, Akhoondzadeh S, Fakhrzadeh H, Dastpak A, Bandarian F, Rezai A, Badi HN and Emami T (2005). Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients. *J. Ethnopharmacol.*, **102**(2): 202-207.

Zhang S, Ge G, Qin Y, Li W, Dong J, Mei J, Ma R, Zhang X, Bai J, Zhu C, Zhang W and Geng D (2022). Recent advances in responsive hydrogels for diabetic wound healing. *Mater. Today Bio.*, **1**(8):100508.