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RESEARCH ARTICLE

The Effect of Polyvinylpyrrolidone Hydrogel with Silver Nanoparticles on Wound Healing in Rats

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ABSTRACT

Polyvinylpyrrolidone (PVP) hydrogel and silver nanoparticle-loaded PVP hydrogel (PVP–AgNPs) have been investigated as potential wound dressing materials. In this study, their wound-healing effects were compared with those of a conventional non-adherent dressing in a rat full-thickness excisional wound model. Fifteen male Wistar rats were assigned to three groups: control dressing, PVP hydrogel, and PVP–AgNP hydrogel. Wound area was measured on postoperative days 2, 4, 6, 8, 10, 12, and 14, and histological evaluation was performed on day 14. The PVP–AgNP hydrogel showed *in vitro* antibacterial activity against the tested bacterial strains, whereas PVP hydrogel alone had no detectable antibacterial effect. By day 14, complete wound closure and re-epithelialization were observed in all groups. No statistically significant differences were found among groups in wound area, granulation of tissue thickness, or neovascularization. However, the PVP–AgNP group showed a non-significant numerical trend toward higher neovascularization compared with the PVP hydrogel and conventional dressing groups. Overall, both PVP and PVP–AgNP hydrogels were biocompatible and supported wound closure and day-14 histological repair comparable to conventional dressing. Although PVP–AgNP hydrogel did not demonstrate significant superiority, its antibacterial activity and favorable histological trend suggest that it may serve as an alternative wound dressing when antimicrobial properties are needed. Further studies with larger sample sizes, longer follow-up periods, and infected-wound models are required to confirm its therapeutic value.

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INTRODUCTION

Full-thickness skin wounds involve the complete loss of both epidermis and dermis and remain important models for studying tissue repair because they are associated with extensive tissue injury, delayed healing, and increased risk of secondary infection (Werner *et al.,* 2007). In surgical pathology, full-thickness excisional skin wounds were commonly used to study the secondary intention healing that related to subsequent inflammation, granulation tissue formation, neovascularization, re-epithelialization, and extracellular matrix remodeling (Singer and Clark, 1999; Holloway *et al*., 2020). Complex interactions among keratinocytes, fibroblasts, endothelial cells, inflammatory cells, cytokines, chemokines, and growth factors coordinate the chronological phases of cutaneous wound healing, driving cellular migration, angiogenesis, and extracellular matrix remodeling (Cha and Falanga, 2007).

Wound repair processes are a series of concurrent inflammatory, proliferative, and remodeling phases (Beanes *et al*., 2003). The inflammatory phase is characterized by vascular damage, fibrin deposition, and infiltration of neutrophils and macrophages to clear the damaged tissue and initiate tissue repair signaling (Clark, 1996). The proliferative phase involves fibroblast proliferation, provisional extracellular matrix deposition, angiogenesis, and re-epithelialization that restores the full extent of the wound and maintains cellular activity within the wound bed (Gambino *et al*., 2002; Werner *et al*., 2007). During the remodeling phase, collagen fibers mature and reorganize, leading to increased tensile

strength; however, adnexal structures such as hair follicles are generally not regenerated in full-thickness defects (Singer and Clark, 1999). Therefore, histopathological evaluation provides information that cannot be derived from gross wound closure alone, especially in relation to the organization of granulation tissue and vascular response.

Synthetic wound dressings such as polyvinylpyrrolidone (PVP) hydrogels have gained interest due to their potential for maintaining a moist wound environment and possibly acting as a temporary matrix for epithelial migration and extracellular matrix deposition (Field and Kerstein, 1994; Hasan *et al*., 2023). The integration of silver nanoparticles (AgNPs) into hydrogel matrices has also been studied as a conventional approach to improve antimicrobial activity against pathogenic bacteria associated with wounds (Nair and Laurencin, 2007; Jangid *et al*., 2024). Several mechanisms have been shown to play a role in the inhibition of bacterial growth by AgNPs, including membrane disruption, interaction with microbial proteins and DNA, and induction of oxidative stress (Jangid *et al*., 2024). Previous research on PVP hydrogels containing silver nanoparticles has shown their material viability and biological compatibility, indicating potential as wound dressings (Khampieng *et al*., 2014).

Recent studies have raised the use of hydrogel systems containing AgNPs for wound repair. Alginate/gelatin hydrogels with silver nanoparticles and biogenic silver nanoparticle hydrogels were shown to demonstrate antibacterial activity and beneficial effects for wound healing in experimental models (Diniz *et al*., 2020; Scandorieiro *et al.,* 2023). Systematic reviews and experimental studies have also indicated the potential of silver nanoparticle-loaded hydrogels and multifunctional nanocomposite dressings for their antimicrobial activity, cytocompatibility, angiogenesis, and tissue regeneration (Dong *et al*., 2022; Amiri *et al*., 2023; Aldakheel *et al*., 2023; Ahmad *et al*., 2024; Kaya *et al*., 2025). Furthermore, bioactive compound and nanoparticle-based delivery platforms have been considered for controlling inflammation, oxidative stress, fibroblast activity, and scar formation (Mercy *et al*., 2025). However, the biological performance of these materials can differ with the type of nanoparticle, concentration, released profile, hydrogel composition, wound model, and outcome evaluation.

Although AgNPs have been implicated in biological processes involving wound healing, such as inflammation and neovascularization (Lansdown *et al*., 1997; Tian *et al*., 2007), these consequences should be interpreted cautiously unless confirmed by molecular, immunohistochemical, or functional data. This is particularly relevant for rat excisional wound models, in which wound contraction is a significant component of wound closure, in contrast to human and many clinical wounds, where re-epithelialization is more prominent (Ghanbari *et al.*, 2024). The quality of tissue repair may therefore not be sufficiently described by the average gross closure rate, and histological evaluation is still necessary to evaluate the fibrovascular granulation of tissue and the vascular response.

The present study compared PVP hydrogel and PVP hydrogel containing silver nanoparticles with a conventional non-adherent dressing in a rat full-thickness excisional wound model. Gross wound closure was monitored over 14 days, and day-14 histopathological features, including re-epithelialization, granulation of tissue thickness, and neovascularization, were assessed. Because molecular pathways, oxidative stress markers, collagen remodeling, and angiogenic signaling were not directly examined, interpretation was restricted to the observed gross and histomorphometry findings. The objective was to determine whether PVP and PVP–AgNP hydrogels produced wound-healing outcomes comparable to those of conventional dressings and whether PVP–AgNPs showed histological trends that would justify further investigation as an alternative antimicrobial wound dressing.

MATERIALS AND METHODS

Study design: This randomized, controlled experimental pathology study was designed to evaluate the gross and histopathological effects of polyvinylpyrrolidone (PVP) hydrogel and silver nanoparticle-loaded PVP hydrogel (PVP–AgNPs) in a rat full-thickness excisional wound model. A conventional non-adherent dressing was included as the standard dressing control. Rats were randomly assigned to treatment groups, and both gross wound measurement and histopathological evaluation were performed by blinded observers to minimize bias. Each rat received one standardized wound and was regarded as the experimental unit for analysis.

Test materials and hydrogel preparation: PVP hydrogel and PVP–AgNP hydrogel sheets were provided by the Department of Petrochemical Engineering, Chulalongkorn University, Thailand. The hydrogels were prepared using a radiation-induced simultaneous cross-linking and reduction technique, following the method previously described for silver nanoparticle-embedded PVP hydrogel dressings (Khampieng *et al*., 2014). Briefly, an aqueous solution containing high molecular weight PVP was mixed with polyethylene glycol as a plasticizer and isopropyl alcohol as a radical scavenger. For the PVP–AgNP formulation, silver nitrate was added to a final nominal silver concentration of 5mM. Solutions were rolled, vacuum-packed in sealed bags, and irradiated with gamma irradiation from a cobalt-60 source at an absorption rate of 25kGy. This process resulted in simultaneous polymer cross-linking, reduction of silver ions to metallic silver nanoparticles, and sterilization of hydrogel sheets. The control group was treated with conventional non-adherent wound dressing (Melolin®), representing routine wound management and the benchmark for the PVP and PVP–AgNP hydrogel dressings.

Characterization of materials and *in vitro* biocompatibility data: The physicochemical and biological properties of the PVP–AgNP hydrogel structure were previously reported from characterizations of the same material platform (Khampieng *et al*., 2014). These included nanoparticle morphology and distribution in the

hydrogel matrix, swelling behavior, moisture-retention capacity, and cytocompatibility. The previous study showed successful integration of AgNPs in a cross-linked PVP network and indicated that the hydrogel system was suitable to maintain a moist wound environment. These data were used as background information to interpret the biological findings, as not all material characterization assays were repeated in the present *in vivo* study.

***In vitro* antibacterial screening:** The antibacterial activity was determined by using a modified agar diffusion assay adapted for hydrogel dressing materials, based on the common principles used for antimicrobial wound dressings (Boonkaew *et al*., 2014; Khampieng *et al*., 2014). The tested bacterial species included representative wound- and skin-associated organisms: Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, methicillin-resistant Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pyogenes. Bacterial suspensions were adjusted to a 0.5 McFarland standard, corresponding to approximately 1.5×10^8 CFU/mL, and were spread uniformly onto agar plates.

Uniform discs of PVP hydrogel and PVP–AgNP hydrogel were placed on the inoculated agar surface. PVP hydrogel was used as the hydrogel negative control, whereas PVP–AgNP hydrogel was evaluated as the antimicrobial test material. Plates were incubated aerobically at 37°C for 18–24h. Antibacterial activity was recorded qualitatively according to the presence or absence of inhibition zones around the hydrogel discs. PVP hydrogel alone produced no inhibition zone, while PVP–AgNP hydrogel showed inhibition against all tested bacterial species.

***In vitro* cytocompatibility information:** Cytocompatibility data for the gamma-irradiated hydrogel materials were taken from previous testing using mouse fibroblast L929 cells in the same PVP–AgNP hydrogel platform (Khampieng *et al.,* 2014). Briefly, sterile hydrogel samples were incubated in culture medium to prepare hydrogel extracts, and L929 fibroblasts were then exposed to these extracts. Cell viability and morphology were evaluated to determine potential cytotoxicity. The previously reported findings indicated acceptable fibroblast compatibility, supporting the subsequent use of these hydrogels for *in vivo* wound application.

Animals and group allocation: Fifteen male Wistar rats, 10 weeks of age, were used. The animals were randomly divided into three groups, with five rats in each group: conventional dressing control, PVP hydrogel, and PVP–AgNP hydrogel. Rats were maintained under standard laboratory conditions with free access to food and water. All procedures were conducted in accordance with institutional guidelines for animal care and use and were approved by the relevant institutional ethics committee. The protocol and approval number for animal use was 0831016.

Anesthesia and perioperative procedures: Before wound creation, rats received tramadol at 25mg/kg subcutaneously for analgesic premedication and were anesthetized with ketamine hydrochloride at 60mg/kg intramuscularly. Anesthesia was maintained with isoflurane in oxygen delivered through a face mask. The dorsal skin was clipped and aseptically prepared before surgery. Body temperature was supported by a heating pad throughout the anesthetic period.

Full-thickness wound creation: A sterile circular template with a diameter of 1cm was placed on the mid-dorsal skin. A standardized full-thickness excisional wound was then created by complete removal of the epidermis and dermis. The wound extended through the full thickness of the skin and included removal of epidermal and dermal structures, including adnexal structures and dermal collagen. Each rat received a single wound to avoid within-animal treatment interactions.

Wound treatment and postoperative management: Immediately after wound creation, each wound was treated according to group allocation. Control wounds were covered with conventional non-adherent dressing. Wounds in the PVP group received PVP hydrogel, while those in the PVP–AgNP group received 5mM PVP–AgNP hydrogel. All wounds were covered with a secondary non-adherent dressing and secured with an occlusive fixation dressing. Dressings were changed every 2 days. At each dressing change, the wound bed was gently rinsed with lactated Ringer's solution before application of the assigned dressing material.

Gross wound assessment: Gross wound healing was monitored by serial digital photography on postoperative days 2, 4, 6, 8, 10, 12, and 14. Images were obtained under standardized conditions with a dimensional reference scale for calibration. The wound area was measured using calibrated image-analysis software by an investigator blinded to treatment group. The wound margin was defined as the visible boundary between the wound bed and surrounding intact skin. Wound area was expressed as the mean wound surface area for each group at each time point.

Histopathology: On postoperative day 14, wound tissues were collected for histopathological examination. Tissue samples, approximately 1.5×2.0cm in size, were excised to include the wound bed and adjacent normal skin. Samples were fixed in 10% neutral-buffered formalin, routinely processed, embedded in paraffin, sectioned at 4–5µm, and stained with hematoxylin and eosin.

Histological evaluation was performed by a veterinary pathologist blinded to treatment group. Re-epithelialization was assessed based on the continuity, thickness, and maturation of the newly formed epidermis covering the wound surface. Fibrovascular granulation tissue was defined as newly formed repair tissue consisting of proliferating fibroblasts, provisional extracellular matrix, and newly formed capillaries within the wound bed.

Histopathologic evaluation: Granulation of tissue thickness was measured in the central wound region. For each rat, three non-overlapping high-power fields at ×200 magnification were selected systematically. Thickness

was measured from the wound surface or regenerated epithelial surface to the underlying muscle layer using calibrated digital image-analysis software. The mean value from each animal was used for statistical analysis.

Neovascularization was evaluated within the granulation tissue on hematoxylin and eosin-stained sections. Newly formed vessels were identified as small, thin-walled capillary profiles lined by endothelial cells, often containing erythrocytes. Five non-overlapping high-power fields at ×400 magnification were examined per section, and capillary profiles were counted. The mean neovascularization count for each animal was used for group comparison.

Reproducibility and bias reduction: Randomization was used for group distribution. Gross wound measurements and histopathological assessment were performed under blind conditions. Predefined field-selection criteria were applied for histopathologic analysis to reduce sampling bias. Each animal, rather than each microscopic field, was considered an experimental unit.

Statistical analysis: Data were expressed as mean±standard deviation. Wound area, granulation of tissue thickness, and neovascularization counts were compared among groups. One-way analysis of variance was used for normally distributed data, while the Kruskal–Wallis test was applied to confirm non-parametric comparisons when appropriate. Statistical significance was set at $P<0.05$. Because the sample size was small, and histological assessment was performed at a single terminal time point, non-significant numerical differences were interpreted cautiously as trends rather than confirmed biological effects.

RESULTS

Gross wound healing: Gross wound appearance was monitored on postoperative days 2, 4, 6, 8, 10, 12, and 14. During the early postoperative period, wounds in all groups showed moist wound surfaces with variable amounts of serosanguineous exudate. Wounds treated with PVP hydrogel and PVP–AgNP hydrogel appeared to maintain greater surface moisture than those treated with the conventional non-adherent dressing. Mild peri-wound erythema and swelling were observed in some wounds, particularly in the control group.

Between days 6 and 8, all groups showed progressive wound contraction, drying of wound margins, and scab formation. Wound size continued to decrease throughout the observation period. By day 10, wounds in the PVP and PVP–AgNP groups appeared drier and showed no obvious exudate. By day 12, exudate was no longer observed in any group. Complete macroscopic wound closure was evident in all groups by day 14, with broadly comparable scar appearance among the conventional dressing control, PVP hydrogel, and PVP–AgNP hydrogel groups (Fig. 1).

Quantitative analysis of wound areas revealed a gradual decrease in average wound area throughout the period in all groups. In the initial postoperative days, the wound areas of PVP and PVP–AgNP groups were smaller than the control group of conventional dressing quantitatively. but no significant statistical differences were found at any of the evaluated times points ($P>0.05$) (Fig. 2). These results indicate that both hydrogel dressings achieved gross wound closure comparable to that of conventional non-adherent dressing.

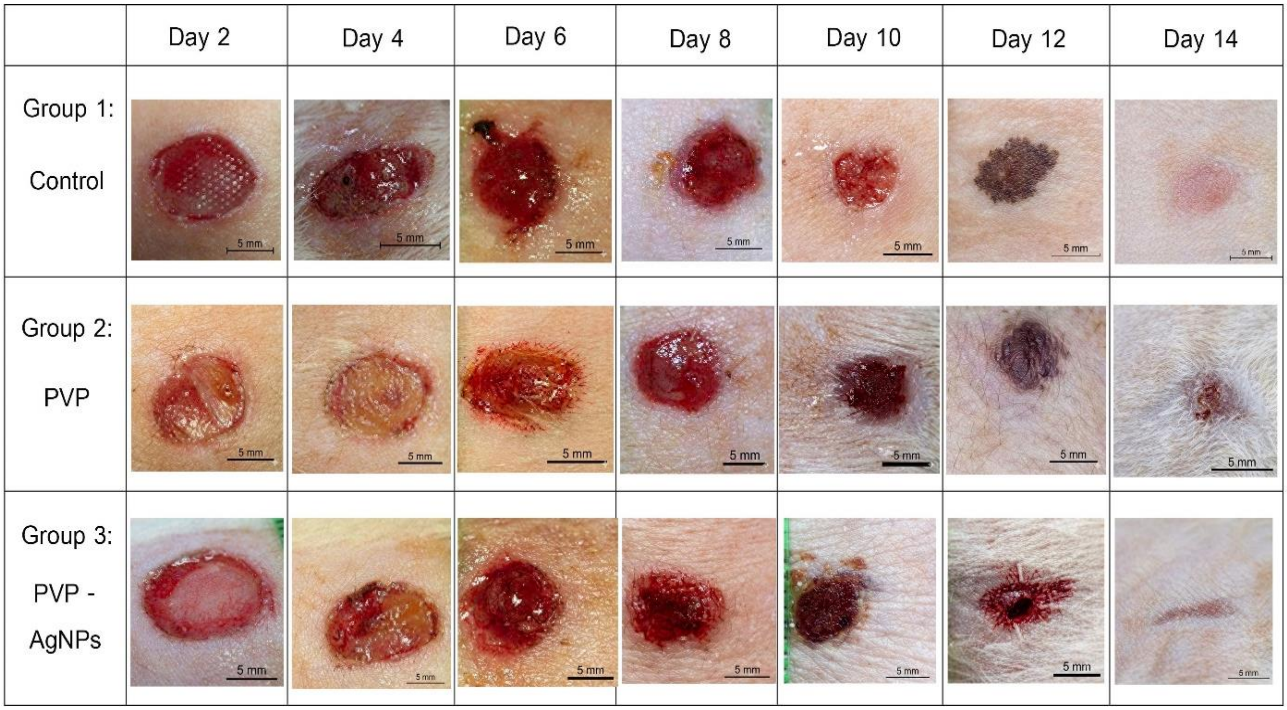

Fig. 1: Representative macroscopic images of full-thickness excisional wound healing in rats treated with a conventional non-adherent dressing control, PVP hydrogel, or PVP–AgNP hydrogel. Sequential images were taken on postoperative days 2, 4, 6, 8, 10, 12, and 14. In the early phase, wounds showed moist wound beds with variable serosanguineous exudate. This was followed by progressive wound contraction, drying of the wound margins, scab formation, and re-epithelialization. By day 14, complete macroscopic wound closure was observed in all groups, with comparable scar formation. Scale bars=5mm.

Histopathological evaluations: Histopathological examination on day 14 showed complete re-epithelialization in all groups. The wound surface was covered by newly formed epidermis composed of approximately 7–8 cell layers with a superficial keratin layer. Beneath the re-epithelialized surface, fibrovascular granulation tissue was present in all groups and consisted of proliferating fibroblasts, collagenous extracellular matrix, and newly formed capillary profiles (Fig. 3).

Granulation of tissue thickness was measured in the central wound region. The mean thickness was 1033.69±17.91µm in the conventional dressing control group, 1198.39±19.51µm in the PVP hydrogel group, and 1135.22±11.59µm in the PVP–AgNP hydrogel group. Although the hydrogel-treated groups showed numerically greater granulation of tissue thickness than the control group, with the highest mean value observed in the PVP group, these differences were not statistically significant (P>0.05) (Fig. 4).

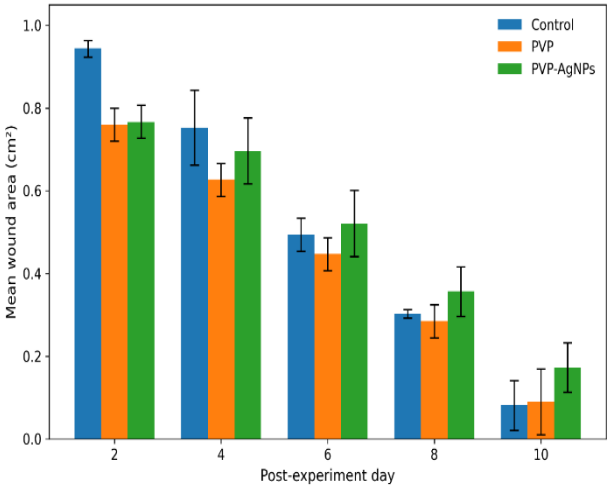

Fig. 2: Mean wound area of full-thickness excisional wounds in rats treated with a conventional non-adherent dressing control, PVP hydrogel, or PVP–AgNP hydrogel on postoperative days 2–10. Data are presented as mean±SD (n=5 per group).

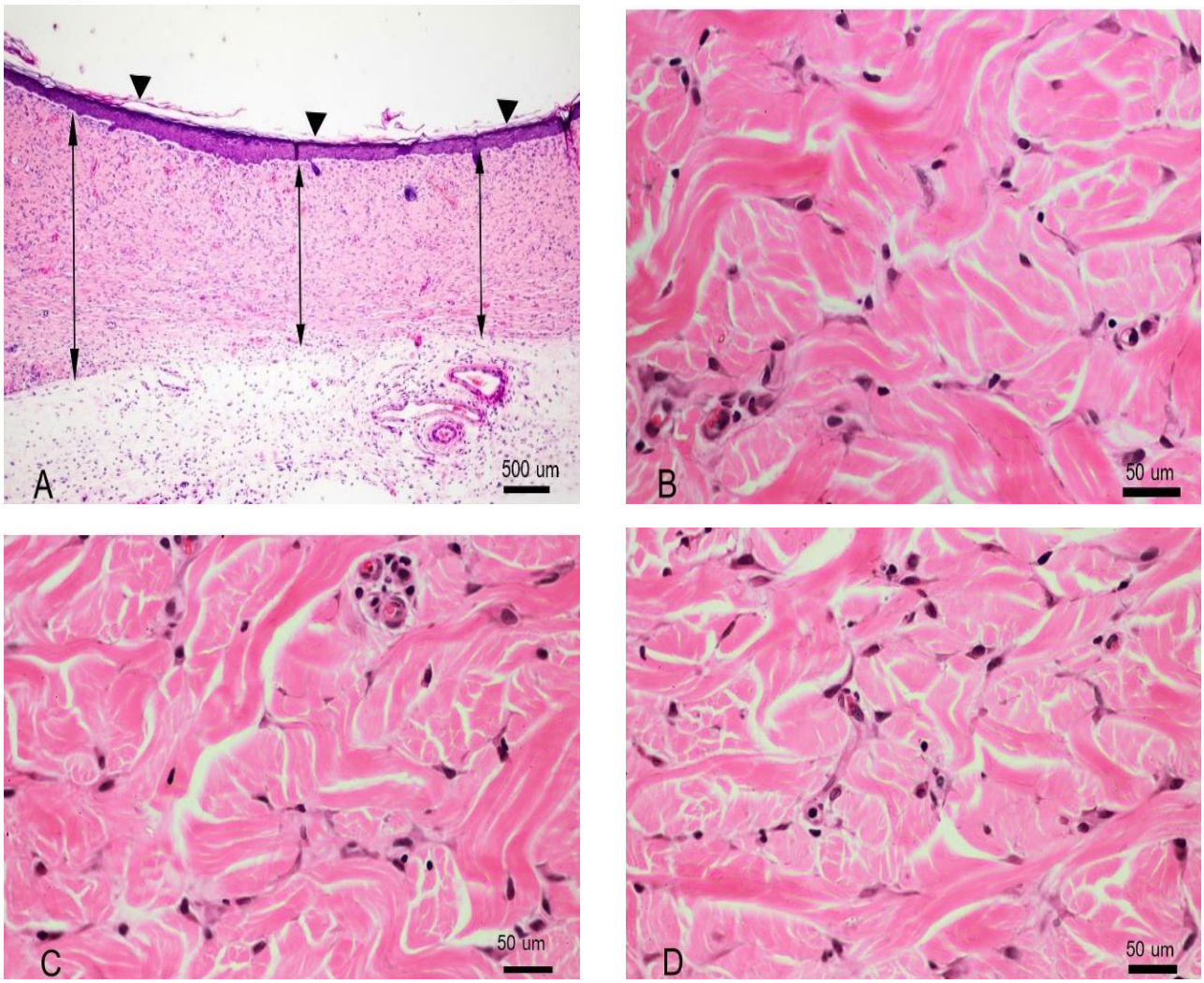

Fig. 3: Histopathological features of wound healing on day 14 post-wounding. (A) Representative section showing fibrovascular granulation tissue beneath the re-epithelialized wound surface. Arrowheads indicate the regenerated epidermis, and double-headed arrows indicate granulation of tissue thickness measured from the wound surface to the underlying muscle layer. H&E stain; ×200. Scale bar=500 µm. (B) High-power photomicrograph of the control group showing collagen fiber deposition and fibroblasts within the extracellular matrix of the granulation tissue. H&E stain; ×400. Scale bar=50 µm. (C) High-power photomicrograph of the PVP hydrogel-treated group showing prominent collagen deposition and fibroblast proliferation within the granulation tissue. H&E stain; ×400. Scale bar=50 µm. (D) High-power photomicrograph of the PVP–AgNP hydrogel-treated group showing collagen fibers and fibroblasts within remodeling granulation tissue. H&E stain; ×400. Scale bar=50 µm.

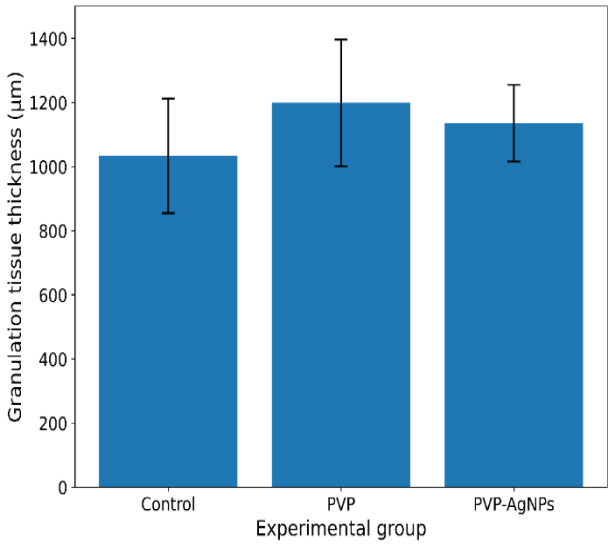

Fig. 4: Granulation of tissue thickness in full-thickness excisional wounds of rats treated with a conventional non-adherent dressing control, PVP hydrogel, or PVP–AgNP hydrogel on day 14 post-wounding. Data are presented as mean±SD (n=5 per group).

Neovascularization was observed within the granulation of tissue in all groups. It was characterized by small, thin-walled capillary profiles lined by endothelial cells and frequently containing erythrocytes (Fig. 5). The mean neovascularization score was 12.70±0.31 in the conventional dressing control group, 13.39±0.64 in the PVP hydrogel group, and 14.37±0.34 in the PVP–AgNP hydrogel group. The PVP–AgNP group showed the highest numerical mean value, followed by the PVP hydrogel and control groups. However, the differences among groups were not statistically significant (P>0.05) (Fig. 6). Therefore, the higher neovascularization value observed in the PVP–AgNP group should be interpreted as a non-significant numerical trend rather than confirmed evidence of enhanced angiogenesis.

Overall, PVP hydrogel and PVP–AgNP hydrogel supported complete macroscopic wound closure and day-14 histological repair comparable to the conventional non-adherent dressing. No significant differences were identified among groups in wound area, granulation of tissue thickness, or neovascularization.

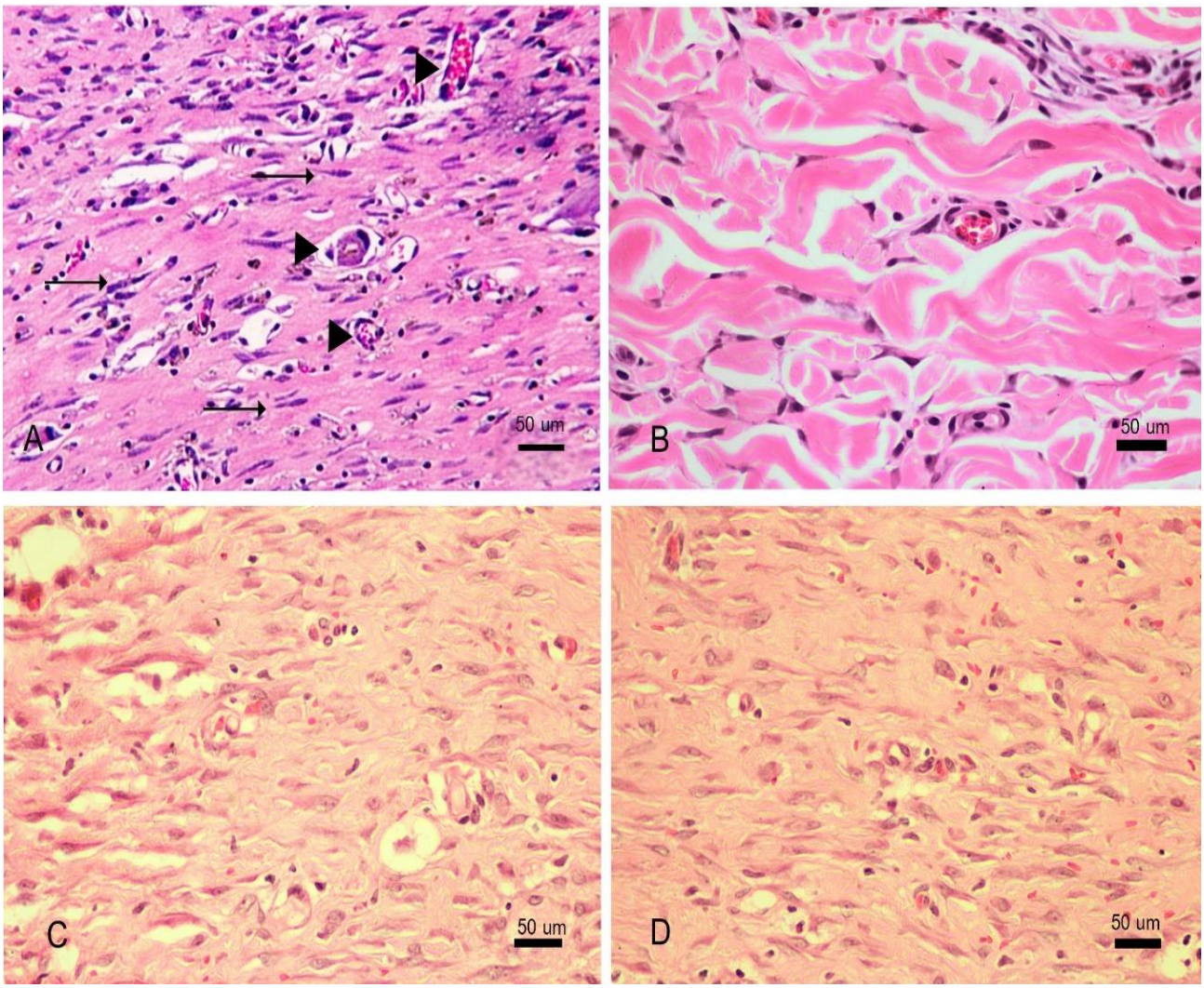

Fig. 5: Representative high-power photomicrographs showing neovascularization within granulation tissue on day 14 post-wounding. (A) Fibrovascular granulation tissue showing newly formed capillaries containing erythrocytes (arrowheads) and proliferating fibroblasts (arrows). (B–D) Representative granulation tissue from the conventional dressing control (B), PVP hydrogel (C), and PVP–AgNP hydrogel (D) groups, showing newly formed capillary profiles, spindle-shaped fibroblasts, and collagenous extracellular matrix within the healing wound bed. H&E stain; ×300. Scale bar=50 µm.

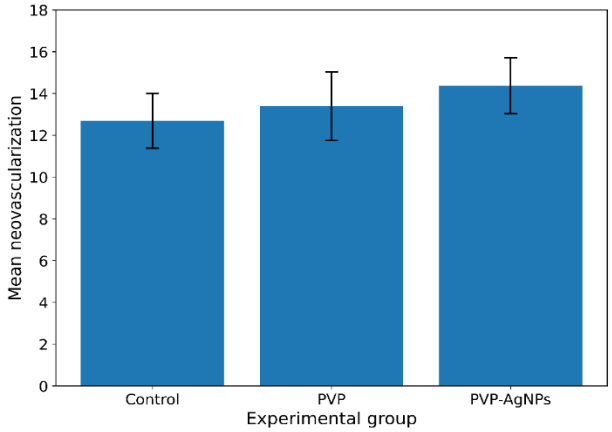

Fig. 6: Mean neovascularization score in full-thickness excisional wounds of rats treated with a conventional non-adherent dressing control, PVP hydrogel, or PVP–AgNP hydrogel on day 14 post-wounding. Data are presented as mean±SD (n=5 per group).

DISCUSSION

This study evaluated PVP hydrogel and silver nanoparticle-loaded PVP hydrogel (PVP–AgNPs) in a rat full-thickness excisional wound model, using a conventional non-adherent dressing as the standard control. Both hydrogel dressings supported complete macroscopic wound closure and day-14 histological repair that were comparable to those observed in the control group. No statistically significant differences were found among groups in wound area, granulation of tissue thickness, or neovascularization. Accordingly, the present findings should be interpreted cautiously and should not be taken as evidence that either hydrogel dressing was statistically superior to conventional dressings. Even so, PVP–AgNP hydrogel showed clear *in vitro* antibacterial activity and a non-significant numerical trend toward higher neovascularization than PVP hydrogel alone and the conventional control, suggesting that this formulation may warrant further evaluation as an alternative wound dressing, especially where antimicrobial activity is desirable.

Gross wound healing progressed consistently in all groups during the observation period. In the initial postoperative period, wounds treated with PVP hydrogel and PVP–AgNP hydrogel appeared to preserve more surface moisture than wounds treated with conventional dressing. This observation is consistent with the general idea that a moist wound environment can minimize tissue dehydration and improve epithelial migration throughout the healing process (Field and Kerstein, 1994; Hasan *et al*., 2023). However, no statistically significant differences in wound areas were noted in these initial macroscopic differences. Average wound size decreased gradually in all groups, and complete wound closure was observed by day 14. The results showed that PVP and PVP–AgNP hydrogels did not interfere with wound closure and resulted in gross healing outcomes comparable to the conventional non-adherent dressing. Since wound closure in rats is predominantly dependent on contraction and not re-epithelialization alone, the gross wound area may be less susceptible to detecting insignificant treatment-related differences in quality of tissue repair (Ghanbari *et al*., 2024).

Histopathological examination showed complete re-epithelialization in all groups on day 14. Fibrovascular granulation tissue was observed under the regenerated epidermis. The mean granulation of tissue thickness was highest in the PVP hydrogel group followed by PVP-AgNP and conventional control groups. Although this trend was not statistically significant, the quantitatively greater granulation of tissue thickness in the PVP group may be correlated to physical properties of the hydrogel matrix such as moisture retention and temporary support of fibroblast proliferation and extracellular matrix deposition. Similar functions of hydrogels in wound management have been reported previously, especially in relation to the maintenance of a hydrated wound bed and facilitating cellular migration during the repair process (Field and Kerstein, 1994; Werner *et al*., 2007; Hasan *et al*., 2023).

Neovascularization was present in all groups of granulation tissue. The highest mean neovascularization score was seen in the PVP-AgNP group, followed by the PVP hydrogel and conventional control groups. Since this difference was not statistically significant, it should be reported as a numerical trend but not as confirmed as an increase in angiogenesis. Previous studies have suggested that silver nanoparticles may impact wound repair via antimicrobial activity and possible regulation of inflammatory and vascular responses (Lansdown *et al*., 1997; Tian *et al*., 2007). Therefore, the higher neovascularization value in the PVP–AgNP group cannot be interpreted as direct evidence of AgNP-induced angiogenesis. However, endothelial immunohisto-chemistry, angiogenic markers, inflammatory cytokines, oxidative stress assays, and molecular pathway analysis were not included in the present study. In particular, the use of specific markers such as CD31, von Willebrand factor, or VEGF will be useful to study the reliability of histological study.

An important supporting finding is the antibacterial activity of PVP–AgNP hydrogel. *In vitro* screening demonstrated inhibition zones against all tested bacterial species, whereas PVP hydrogel alone showed no antibacterial effect. This finding is consistent with prior reports showing the antimicrobial efficacy of silver nanoparticles and silver-containing hydrogel dressings against wound pathogens (Boonkaew *et al*., 2014; Khampieng *et al*., 2014; Jangid *et al*., 2024). In the present non-infected wound model, however, antibacterial activity did not result in a statistically significant improvement in gross wound area or histomorphometric parameters. The potential advantage of PVP–AgNP hydrogel may therefore become more apparent in contaminated or infected wounds, where antimicrobial activity could help reduce microbial burden and limit infection-associated delay in repair. This possibility remains to be tested in future infected-wound models.

The comparative results also show that PVP–AgNP hydrogel produced wound-healing outcomes close to those of the conventional non-adherent dressing. This finding is relevant because the conventional dressing represented routine wound management and served as the standard comparator. Although PVP–AgNP hydrogel was not statistically superior to the control dressing, it supported complete closure, re-epithelialization, and

granulation tissue formation without apparent adverse effects. When considered together with its antibacterial activity, these findings suggest that PVP–AgNP hydrogel may have potential as an alternative dressing for veterinary wound care. Nevertheless, this interpretation should remain preliminary because of the limited sample size, short observation period, absence of infected-wound conditions, and lack of long-term remodeling assessment.

Several limitations should be considered. First, the number of animals was small, with only five rats per group, which may have limited the ability to detect biologically meaningful differences. Second, histological assessment was performed only on day 14, preventing evaluation of early inflammation, sequential granulation tissue development, collagen deposition, and late scar remodeling. Third, neovascularization was assessed on hematoxylin and eosin-stained sections without confirmation by endothelial immunohistochemical markers. Fourth, collagen maturation and organization were not evaluated using special stains such as Masson's trichrome or picrosirius red. Finally, because the model was non-infected, the antimicrobial benefit of PVP–AgNP hydrogel could not be fully assessed under clinically challenging wound conditions.

Conclusions: In conclusion, PVP hydrogel and PVP–AgNP hydrogel were biocompatible in this rat full-thickness excisional wound model and produced complete wound closure with day-14 histological repair comparable to that achieved with a conventional non-adherent dressing. PVP–AgNP hydrogel showed *in vitro* antibacterial activity and a non-significant numerical trend toward higher neovascularization than PVP hydrogel alone. These findings suggest that PVP–AgNP hydrogel may be a useful alternative wound dressing with added antimicrobial potential. Further studies using larger sample sizes, longer observation periods, infected-wound models, and specific markers of angiogenesis, inflammation, and collagen remodeling are needed to confirm its therapeutic benefit.

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Conflict Of Interest: The authors declare that they have no competing interests or conflicts of interest related to this study.

Data Availability: The data supporting the findings of this study are available from the corresponding author upon reasonable request. All relevant data generated or analyzed during the study are included in the manuscript and its figures.

Ethics Statement: All animal procedures were reviewed and approved by the Chulalongkorn University Animal Care and Use Committee. The study was conducted in accordance with institutional regulations and ethical principles for the care and use of laboratory animals. The animal use protocol and approval number was 0831016.

Authors Contribution: Pasakorn Brikshavana: Conceptualization, Methodology, Investigation, Formal analysis, Theerawat Tharasanit: Conceptualization, Methodology, Formal analysis. Theerayuth Kaewamatawong: Conceptualization, Methodology, Histopathological evaluation, Formal analysis, Writing–original draft, Writing–review and editing. All authors reviewed and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Generative AI Statement: Generative artificial intelligence tools were used only to assist with language editing, grammar improvement, organization of manuscript sections, and refinement of wording during manuscript revision. The authors critically reviewed, edited, and verified all AI-assisted text. No generative AI tool was used to generate original experimental data, perform statistical analysis, create or manipulate research results, or replace the authors' scientific interpretation.

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