ORIGINAL ARTICLE

UDC: 616-001-08
DOI: https://doi.org/10.2298/VSP250912014X

Clinical treatment of wounds using nano platelet-rich plasma

Kliničko lečenje rana primenom nano plazme obogaćene trombocitima

[1]Yongjun Xu*, [1]Haifeng Zhu[†], Jian Feng[‡], Bin Shen[§]

Hangzhou Normal University, Affiliated Xiaoshan Hospital, *Department of Hand and Foot Surgery, [‡]Department of Orthopedics, [§]Department of Burn and Plastic Surgery, Hangzhou, Zhejiang, China; [†]Zhejiang University School of Medicine, Affiliated Shaw Hospital, Department of Orthopedics, Hangzhou, Zhejiang, China

[1]The two authors contributed equally to this study.

Abstract

Background/Aim. Chronic refractory wounds are hard-to-heal lesions that are susceptible to bacterial and other pathogenic infections, leading to additional tissue damage and a significant reduction in patients' quality of life. The aim of this study was to examine the efficacy of nano platelet-rich plasma (PRP) – nano-PRP compared with conventional PRP in the clinical treatment of wounds. **Methods.** The study included a total of 96 patients with chronic refractory wounds, including wounds caused by trauma and pressure ulcers, admitted between June 2021 and June 2023. According to the treatment applied, the patients were divided into two groups: the observation group (OG) (n = 47) with nano-PRP treatment and the control group (CG) (n = 49) with conventional PRP treatment. Group differences were analyzed using independent-samples *t*-tests for continuous variables and Chi-square tests for categorical variables. **Results.** The overall treatment efficacy in the OG was significantly higher than that in the CG ($p < 0.05$). After treatment, the visual analog scale score decreased in both groups compared with baseline, with the OG showing significantly lower scores than the CG ($p < 0.05$). The wound healing rate was also significantly higher in the OG ($p < 0.05$). Moreover, nano-PRP-treated patients exhibited improved outcomes for scar hyperplasia and a shorter wound healing time relative to the conventional PRP-treated group ($p < 0.05$). **Conclusion.** Compared with conventional PRP, nano-PRP demonstrates superior wound healing efficacy in patients with chronic refractory wounds, is associated with greater pain relief, and results in improved aesthetic outcomes. These findings suggest that nano-PRP may represent a more effective therapeutic option than conventional PRP for the clinical management of difficult-to-heal wounds.

Keywords:
platelet-rich plasma; quality of life; treatment outcome; wound healing; wounds and injuries.

Apstrakt

Uvod/Cilj. Hronične refraktorne rane su teško zarastajuće lezije koje su podložne infekcijama uzrokovanim bakterijama i drugim patogenima, što dovodi do dodatnog oštećenja tkiva i značajnog smanjenja kvaliteta života bolesnika. Cilj rada bio je da se ispita efikasnost nano plazme obogaćene trombocitima (*platelet-rich plasma* – PRP) – nano-PRP u poređenju sa konvencionalnom PRP u kliničkom lečenju rana. **Metode.** U studiju je bilo uključeno ukupno 96 bolesnika sa hroničnim refraktornim ranama, uključujući rane izazvane traumom i dekubitalne ulkuse, primljenih u periodu od juna 2021. do juna 2023. godine. U skladu sa primenjenim tretmanom, bolesnici su bili podeljeni u dve grupe: opservacionu grupu (OG) (n = 47) tretiranu nano-PRP i kontrolnu grupu (KG) (n = 49) tretiranu konvencionalnom PRP. Razlike između grupa analizirane su korišćenjem *t*-testa za nezavisne uzorke za kontinuirane varijable i Hi-kvadrat testa za kategorijske varijable. **Rezultati.** Ukupna efikasnost lečenja u OG bila je značajno veća nego u KG ($p < 0,05$). Nakon tretmana, vrednost skora na vizuelnoj analognoj skali se smanjila u obe grupe u poređenju sa početnim vrednostima, pri čemu je OG pokazala značajno niže rezultate od KG ($p < 0,05$). Brzina zarastanja rana je takođe bila značajno veća u OG ($p < 0,05$). Takođe, bolesnici tretirani nano-PRP pokazali su bolje ishode hiperplazije ožiljaka i kraće vreme zarastanja rane u odnosu na grupu tretiranu konvencionalnom PRP ($p < 0,05$). **Zaključak.** U poređenju sa konvencionalnom PRP, nano-PRP pokazuje bolju efikasnost u zarastanju rana kod bolesnika sa hroničnim refraktornim ranama, povezan je sa većim ublažavanjem bola i dovodi do boljih estetskih ishoda. Ovi nalazi ukazuju na to da nano-PRP može predstavljati efikasniju terapijsku opciju od konvencionalne PRP za kliničko lečenje teško zarastajućih rana.

Ključne reči:
plazma bogata trombocitima; kvalitet života; lečenje, ishod; rana, zarastanje; rane i povrede.

Correspondence to: Bin Shen, Hangzhou Normal University, Affiliated Xiaoshan Hospital, Department of Burn and Plastic Surgery, Hangzhou 310 200, Zhejiang Province, China. E-mail: shenbinaxhhnu@gpnu-edu.cn

Introduction

Chronic refractory wounds (CRWs) are persistent, hard-to-heal lesions that fail to progress through the expected sequential phases of healing [1]. Owing to their prolonged duration and impaired healing capacity, these wounds are highly susceptible to bacterial and other pathogenic infections, which can further exacerbate tissue damage and significantly compromise patients' quality of life. In severe cases, persistent local infection may progress to systemic involvement, posing serious health risks [1, 2]. As the wound area enlarges, adjacent tissues may undergo structural damage or functional impairment, leading to limitations in daily activities, reduced mobility, and diminished self-care abilities [3]. Additionally, prolonged treatment courses often impose psychological burdens on patients, contributing to anxiety, depression, and reduced self-esteem [4].

Platelet-rich plasma (PRP) has been widely applied in recent years to promote the healing of CRWs. However, conventional PRP therapy has several limitations, including difficulty in fully filling irregular wound defects and the inability to inject PRP gel into deeper or uneven tissue structures. Nano-clay, particularly synthetic laponite, is a nanoscale silicate material that has been extensively investigated for biomedical applications due to its favorable biocompatibility, low cytotoxicity, and ability to support cell adhesion and proliferation [5, 6]. Previous studies have demonstrated that laponite-based hydrogels exhibit good biocompatibility and have been safely used as carriers for bioactive molecules and growth factors in tissue regeneration. In addition, nano-clay offers adjustable wettability and permeability, making it a promising carrier material [7, 8].

The aim of this study was to examine the clinical therapeutic effects of nano-PRP in the management of CRWs, to provide a more effective treatment strategy, and to improve patient outcomes and quality of life.

Methods

General data

A total of 96 patients with CRWs secondary to trauma or pressure ulcers, admitted to our hospital between June 2021 and June 2023, were enrolled in this prospective controlled study. All enrolled patients were followed for 90 days after treatment. The study was approved by the Ethics Committee of the Affiliated Xiaoshan Hospital, Hangzhou Normal University, Zhejiang, China (No. HZNUXS-2021-089, from June 03, 2021). All participants were fully informed about the study procedures and voluntarily signed written informed consent forms prior to enrollment.

Inclusion and exclusion criteria

Inclusion criteria were as follows: patients diagnosed with CRWs, defined as wounds persisting for more than 4 weeks despite appropriate standard wound care, including regular debridement, infection control, and pressure offloading when indicated [9]; age ≥ 18 years; absence of known immune system diseases. Exclusion criteria included: presence of local or systemic infection; severe anemia; poor treatment compliance or refusal to cooperate; coexisting malignant tumors or other contraindications to the study intervention.

Group allocation

Patients were allocated to two groups based on the treatment they received. Because treatment selection depended on patient preference and clinical suitability, randomization was not applied in this study. Therefore, assignment to the conventional PRP, i.e., the control group (CG) (n = 49), or nano-PRP, i.e., the observation group (OG) (n = 47), was non-randomized. To reduce subjective bias, outcome assessors were blinded to the type of treatment administered. Patients and treating physicians were not blinded due to the nature of the interventions.

Examinations and treatments

All patients in both groups underwent routine pretreatment assessments, including complete blood count, electrocardiogram, and chest X-ray or chest computed tomography. Baseline wound images (frontal and lateral views) were collected before intervention.

The patients in the CG were treated with conventional PRP. A total of 10–40 mL of venous blood was collected into vacuum blood collection tubes, with the amount based on the patient's clinical condition. The collected blood was centrifuged at 1,500 revolutions *per* minute (rpm) for 10 min to remove erythrocytes, followed by a second centrifugation at 2,200 rpm for 15 min to obtain PRP. The PRP was transferred into a 4 × 4 cm square groove at the bottom of a disposable dressing change box (Yangzhou Songtian Medical Instrument Co., Ltd., China). One box was used *per* tube of collected blood. Thrombin (Kunming Baima Pharmaceutical Co., Ltd., China) dissolved in 3 mL of normal saline was added to PRP at a 1 : 1 ratio to produce PRP gel. After thorough debridement of the wound bed, the PRP gel was applied to cover and fill the wound fully. Vaseline gauzes and medical semipermeable membranes were used for coverage, followed by appropriate pressure bandaging. The wound was left undisturbed for 5–7 days and then managed with routine dressing changes. If adequate healing was not achieved, PRP treatment was repeated once.

The patients in the OG were treated with nano-PRP, defined in this study as a deferoxamine mesylate (DFO)-containing platelet-laponite gel. Venous blood collection and PRP preparation were performed as in the CG. For nano-clay preparation, montmorillonite nano-clay (Laponite XLG, BYK Additives, Germany; particle size ~30 nm) was used. Nano-clay powder was dispersed in distilled water to prepare a 2% w/v suspension and stirred for 30 min to obtain a homogeneous dispersion. PRP was mixed with the nano-clay suspension at a ratio of 4 : 1 v/v using a mechanical stirrer (800 rpm, 2 min), followed by ultrasonic homogenization for 30 s to ensure uniform mixing. A calcium chloride solution

at a final concentration of 20 mM was added dropwise to induce rapid gelation and form a bioactive nano-PRP hydrogel within approximately 2–3 min. Following repeat debridement, the nano-PRP hydrogel was injected into the wound using a double syringe through a three-way tube. The remaining portion was applied to cover and fill the wound surface. As in the CG, wounds were dressed with vaseline gauze and sealed with medical semipermeable membranes, followed by appropriate compression. The wound remained undisturbed for 5–7 days, after which routine dressing changes were performed. Nano-PRP treatment could be repeated once if the wound did not reach the expected healing stage.

Collection of clinical data

The following clinical data of patients were collected: baseline characteristics (age, sex, wound size, smoking history, alcohol consumption, presence of diabetes, wound type and condition body mass index) and, clinical and pathological parameters [overall treatment efficacy, Visual Analog Scale (VAS) score, wound aesthetics, incidence of complications, wound healing rate, degree of scar hyperplasia, and wound healing time]. All outcome data were collected during the 90-day follow-up period.

Evaluation of outcomes

Clinical efficacy was categorized as follows: basically healed (the wound was nearly completely closed with no infection or other complications); markedly effective (the wound showed substantial improvement but was not fully healed, and additional treatment or extended healing time might be required); effective (the wound exhibited partial improvement, but residual symptoms or defects remained, requiring further time or supplementary measures for complete healing); ineffective (minimal or no improvement was observed after treatment). The total effective rate was calculated as (total cases – ineffective cases)/total cases × 100%.

Pain intensity was assessed using the VAS score before treatment and 90 days after treatment, with lower scores indicating less pain.

Wound aesthetics were jointly evaluated by clinicians and patients using a 10-point scale: > 9 indicated very high satisfaction, 8–9 indicated satisfaction, and < 8 indicated dissatisfaction. The satisfaction rate was calculated as (total cases – dissatisfied cases)/total cases × 100%.

The complication rate was determined by calculating the incidence of postoperative complications, including wound infection, numbness, sepsis, and other adverse events.

The wound healing rate was calculated based on wound area measurements obtained on days 10, 30, and 90 after treatment.

Scar hyperplasia was assessed using the Vancouver Scar Scale, a validated clinician-rated tool that evaluates four key scar characteristics: vascularity (0–3), pigmentation (0–2), pliability (0–5), and height (0–3). Total scores range from 0 to 13, with higher scores indicating more severe scar hyperplasia and poorer scar quality [10].

Wound healing time was defined as the duration from initial debridement to complete wound closure within the 90-day follow-up period.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0. Measurement data were subjected to the normality test. The normally distributed measurement data were described using mean ± standard deviations, and compared between groups using an independent-samples *t*-test. Categorical variables were presented as numbers (percentages) and analyzed using the χ^2 test or Fisher's exact test when appropriate. A p-value < 0.05 was considered statistically significant.

Results

Baseline clinical data

The baseline demographic and clinical characteristics of the two groups were collected, including age, sex, body mass index, wound etiology, wound duration, wound size, and comorbidities. Both groups had similar baseline variables ($p > 0.05$), indicating good group comparability and homogeneity prior to treatment (Table 1).

Table 1

Baseline clinical data

Characteristics	Group		t/χ^2	p
	observation (n = 47)	control (n = 49)		
Age, year	58.42 ± 12.15	59.87 ± 11.69	0.623	0.535
Sex				
male	28 (59.57)	30 (61.22)	0.028	0.867
female	19 (40.43)	19 (38.78)		
BMI, kg/m^2	23.74 ± 3.18	24.06 ± 3.25	0.497	0.620
Wound etiology				
trauma	31 (65.96)	32 (65.31)	0.006	0.936
pressure ulcer	16 (34.04)	17 (34.69)		
Wound duration, months	3.82 ± 1.47	3.91 ± 1.52	0.301	0.764
Wound size, cm^2	18.46 ± 6.72	19.03 ± 7.15	0.423	0.673
Diabetes mellitus	12 (25.53)	13 (26.53)	0.011	0.916
Hypertension	15 (31.91)	14 (28.57)	0.138	0.711

BMI – body mass index; n – number.
All values are given as numbers (percentages) or mean ± standard deviations.

Clinical efficacy

At 90 days after treatment, the total effective rate of the OG was significantly higher than that in the CG ($p < 0.05$), indicating superior therapeutic outcomes with nano-PRP (Table 2).

Visual analog scale scores

Before treatment, there was no significant difference in the VAS scores between the two groups ($p > 0.05$). At 90 days after treatment, pain levels in both groups decreased compared with baseline, with the OG showing a significantly lower VAS score than the CG ($p < 0.001$) (Table 3).

Wound aesthetics

Following treatment, the OG demonstrated significantly better wound aesthetic outcomes compared with the CG ($p < 0.05$) (Table 4).

Complication rates

At 90 days after treatment, the OG exhibited a significantly lower incidence of complications compared with the CG ($p = 0.05$) (Table 5).

Wound healing rates

After treatment, the wound healing rate in the OG was significantly higher than that in the CG ($p < 0.001$) (Table 6).

Scar hyperplasia status

Following treatment, the OG showed significantly better outcomes for scar hyperplasia than the CG ($p < 0.001$) (Table 7).

Wound healing time

After treatment, the OG demonstrated a significantly shorter wound healing time than the CG (20.96 ± 5.37 vs.

Table 2

Clinical efficacy

Group	Basically healed	Markedly effective	Effective	Ineffective	Total effective rate
Observation (n = 47)	29 (61.70)	10 (21.28)	5 (10.64)	3 (6.38)	93.62%
Control (n = 49)	15 (30.61)	14 (28.57)	13 (26.53)	7 (14.29)	85.71%
χ^2					10.240
p					0.017

n – number.
All values are given as numbers (percentages).

Table 3

Visual analog scale scores

Group	Treatment	
	before	90 days after
Observation (n = 47)	5.87 ± 1.78	1.56 ± 0.94
Control (n = 49)	5.96 ± 2.03	2.78 ± 1.03
t	0.818	6.054
p	0.231	< 0.001

n – number.
All values are given as mean ± standard deviations.

Table 4

Wound aesthetics

Group	Very satisfied	Satisfied	Dissatisfied	Satisfaction rate	χ^2	*p*
Observation (n = 47)	26 (55.32)	19 (40.43)	2 (4.26)	45 (95.74)	6.76	0.034
Control (n = 49)	16 (32.65)	25 (51.02)	8 (16.33)	41 (83.67)		

n – number.
All values are given as numbers (percentages).

Table 5

Complication rates

Group	Wound infection	Numbness	Sepsis	Complication rate	**p*
Observation (n = 47)	0 (0)	2 (4.26)	0 (0)	2 (4.26)	<0.05
Control (n = 49)	4 (8.16)	5 (10.2)	0 (0)	9 (18.37)	

n – number.
All values are given as numbers (percentages).
***Note*: *Fisher's exact test.**

Table 6

Wound healing rates

Group	After treatment		
	10 days	30 days	90 days
Observation (n = 47)	58.26 ± 7.13	85.94 ± 5.46	95.58 ± 3.27
Control (n = 49)	51.45 ± 6.89	76.55 ± 7.16	87.84 ± 5.49
t	4.759	7.203	8.348
p	< 0.001	< 0.001	< 0.001

n – number.
All values are given as mean ± standard deviations.

Table 7

Scar hyperplasia status

Group	After treatment		
	10 days	30 days	90 days
Observation (n = 47)	8.78 ± 1.96	3.69 ± 1.34	2.13 ± 1.27
Control (n = 49)	10.21 ± 2.13	5.39 ± 1.86	3.24 ± 1.12
t	3.419	5.119	4.547
p	< 0.001	< 0.001	< 0.001

n – number.
All values are given as mean ± standard deviations.

29.89 ± 8.73 days, respectively), with a statistically significant difference ($t = 6.006$, $p < 0.05$).

Discussion

Common causes of wounds include trauma such as cuts, abrasions, and burns resulting from external forces. Some of the external forces include: surgery procedures, where incisions in the skin and underlying tissues create operative wounds; ulcers, which develop from tissue necrosis due to prolonged pressure, friction, or ischemia, as seen in pressure sores and leg ulcers; diabetic foot, where neuropathy and impaired circulation associated with diabetes predispose to foot ulceration; chronic inflammatory conditions, including eczema and other persistent inflammatory skin disorders [11–13].

CRWs often have more complex underlying mechanisms. These may include microcirculation disturbances, where inadequate local blood flow compromises oxygen and nutrient delivery, thereby impairing healing; chronic infection by bacteria, fungi, or other pathogens, leading to persistent inflammation that delays tissue repair; immunocompromise, which increases susceptibility to infection and slows regeneration; hyperglycemia, as seen in diabetes, which disrupts normal wound healing process; malnutrition, where insufficient intake of proteins, vitamins, and minerals hinders effective tissue repair [14–16].

Extracted from patients' own blood, PRP is widely used in the management of CRWs. Because it carries no risk of immunologic rejection or transmissible disease and allows for individualized therapy, PRP has gained considerable attention in clinical practice. Rich in platelets, growth factors, and other bioactive molecules, PRP provides an abundant source of mediators that promote angiogenesis, enhance collagen synthesis, and stimulate cellular proliferation, thereby accelerating wound repair and regeneration. However, PRP also has limitations and may not be suitable for all CRWs [17, 18]. Irregular wound cavities are often difficult to fill with PRP fully, and the gel form cannot be injected into deeper or structurally complex defects. Moreover, PRP releases growth factors rapidly, producing a strong but short-lived stimulatory effect on surrounding tissues [19, 20]. Although beneficial for promoting early healing, this rapid release may also lead to undesirable effects, such as excessive fibroblast proliferation and increased risk of hypertrophic scarring [21].

To address these shortcomings, this study employed, a bioactive hydrogel dressing composed of PRP and nano-clay, referred to as nano-PRP. Laponite nanosheets have been widely studied in regenerative medicine due to their ability to bind growth factors, form shear-thinning injectable hydrogels, and prolong growth-factor release [7, 22]. Previous studies have shown that laponite-based hydrogels create a pro-regenerative microenvironment, promote M2 macrophage polarization, enhance angiogenesis, and support sustained tissue repair [20, 23]. Furthermore, recent biomaterials research has demonstrated that nano-composite PRP hydrogels exhibit superior protein retention, improved mechanical stability, and enhanced biological activity compared with conventional PRP formulations [24, 25]. Despite these promising findings, only a limited number of clinical studies on nano-PRP have been published. Therefore, our results contribute additional clinical evidence to this emerging field.

The findings of this study demonstrated that the total effective rate in the OG was significantly higher than that in the CG. This improvement may be attributable to the hydrogel's capacity for controlled and sustained growth-factor release, enhanced wound-bed coverage, and superior bioavailability of incorporated agents such as DFO, which further promotes angiogenesis [20, 26]. After treatment, the VAS score in the OG was markedly reduced compared with baseline and significantly lower than that in the CG. In addition, patients in the OG exhibited better wound aesthetic outcomes, a

lower incidence of complications, a higher wound healing rate, more favorable scar hyperplasia status, and a shorter healing time. These results collectively indicate that nano-PRP not only alleviates pain but also inhibits excessive scarring and substantially enhances the overall healing process of chronic wounds. These findings align with a prior study reporting that nano-engineered hydrogels modulate inflammation and reduce fibroblast over-proliferation, thereby supporting more organized tissue repair [27].

Despite these promising findings, the use of nano-PRP is not without challenges. Although laponite-based hydrogels are generally regarded as biocompatible, potential risks include local immune reactions, variable degradation behavior, or altered inflammatory responses, particularly in infected or heavily exudative wounds [28]. Additionally, PRP composition varies across individuals, potentially affecting treatment consistency. The preparation of nano-PRP requires specific materials and controlled gelation conditions [29], which may limit its practicality in settings without adequate laboratory support. Further studies are required to standardize nano-PRP preparation, evaluate long-term safety, and determine optimal clinical indications.

Study limitations

The absence of a non-PRP CG limits our ability to assess the absolute treatment effect relative to standard care. The relatively small sample size and the single-center design may reduce statistical power and limit the generalizability of the findings. Subgroup analyses by wound type (e.g., traumatic wounds vs. pressure sores) could not be performed due to the small number of cases in each category, making it unclear whether the benefits of nano-PRP are consistent across different etiologies. The 90-day follow-up period may not fully capture long-term healing outcomes or scar progression. Despite these limitations, the study provides meaningful preliminary evidence supporting the comparative advantages of nano-PRP.

Conclusion

This non-randomized comparative study suggests that nano platelet-rich plasma is associated with improved clinical outcomes compared with conventional platelet-rich plasma in the treatment of chronic refractory wounds, including accelerated wound healing, greater pain reduction, and improved aesthetic outcomes. These findings should be interpreted in light of the non-randomized study design and indicate that nano platelet-rich plasma may represent a promising regenerative approach. Further large-scale, randomized controlled studies are warranted to confirm these preliminary observations.

Conflicts of interest

The authors declare no conflict of interest.

REFERENCES

1. *Frykberg RG, Banks J.* Challenges in the Treatment of Chronic Wounds. Adv Wound Care (New Rochelle) 2015; 4(9): 560–82. DOI: 10.1089/wound.2015.0635.
2. *Izadi M, Bozorgi M, Hosseine MS, Khalili N, Jonaidi-Jafari N.* Health-related quality of life in patients with chronic wounds before and after treatment with medical ozone. Medicine (Baltimore) 2018; 97(48): e12505. DOI: 10.1097/MD.0000000000001250.
3. *Wu J, Chen LH, Sun SY, Li Y, Ran XW.* Mesenchymal stem cell-derived exosomes: The dawn of diabetic wound healing. World J Diabetes 2022; 13(12): 1066–95. DOI: 10.4239/wjd.v13.i12.1066.
4. *Su YJ, Liang SH.* Long-term mental health outcomes of severe burn injury: A 5-year follow-up of the 2015 Formosa Fun Coast Water Park fire disaster. Gen Hosp Psychiatry 2022; 75: 10–6. DOI: 10.1016/j.genhosppsych.2022.01.007.
5. *Das SS, Neelam, Hussain K, Singh S, Hussain A, Faruk A,* et al. Laponite-based Nanomaterials for Biomedical Applications: A Review. Curr Pharm Des 2019; 25(4): 424–43. DOI: 10.2174/1381612825666190402165845.
6. *Katti KS, Jasuja H, Jaswandkar SV, Mohanty S, Katti DR.* Nanoclays in medicine: a new frontier of an ancient medical practice. Mater Adv 2022; 3(20): 7484–500. DOI: 10.1039/d2ma00528j.
7. *Stealey ST, Gaharwar AK, Zustiak SP.* Laponite-Based Nanocomposite Hydrogels for Drug Delivery Applications. Pharmaceuticals (Basel) 2023; 16(6): 821. DOI: 10.3390/ph16060821.
8. *Liu B, Li J, Lei X, Miao S, Zhang S, Cheng P,* et al. Cell-loaded injectable gelatin/alginate/LAPONITE® nanocomposite hydrogel promotes bone healing in a critical-size rat calvarial defect model. RSC Adv 2020; 10(43): 25652–61. DOI: 10.1039/d0ra03040f.
9. *Eriksson E, Liu PY, Schultz GS, Martins-Green MM, Tanaka R, Weir D,* et al. Chronic wounds: Treatment consensus. Wound Repair Regen 2022; 30(2): 156–71. DOI: 10.1111/wrr.12994. Erratum in: Wound Repair Regen 2022; 30(4): 536. DOI: 10.1111/wrr.13035.
10. *Hiremath SCS, Ahmed Z.* Comparison of Two Entry Methods and Their Cosmetic Outcomes in Creating Pneumoperitoneum: A Prospective Observational Study. Surg J (N Y) 2022; 8(3): e239–44. DOI: 10.1055/s-0042-1756182.
11. *Vu NB, Nguyen HT, Palumbo R, Pellicano R, Fagoonee S, Pham PV.* Stem cell-derived exosomes for wound healing: current status and promising directions. Minerva Med 2021; 112(3): 384–400. DOI: 10.23736/S0026-4806.20.07205-5.
12. *Bonkemeyer Millan S, Gan R, Townsend PE.* Venous Ulcers: Diagnosis and Treatment. Am Fam Physician 2019; 100(5): 298–305.
13. *Roshangar L, Soleimani Rad J, Kheirjou R, Reza Ranjkesh M, Ferdowsi Khosroshahi A.* Skin Burns: Review of Molecular Mechanisms and Therapeutic Approaches. Wounds 2019; 31(12): 308–15.
14. *Williams M.* Wound infections: an overview. Br J Community Nurs 2021; 26(Sup6): S22–5. DOI: 10.12968/bjcn.2021.26.Sup6.S22.
15. *Swaney MH, Kalan LR.* Living in Your Skin: Microbes, Molecules, and Mechanisms. Infect Immun 2021; 89(4): e00695–20. DOI: 10.1128/IAI.00695-20.
16. *Gupta S, Paliczak A, Delgado D.* Evidence-based indications of platelet-rich plasma therapy. Expert Rev Hematol 2021; 14(1): 97–108. DOI: 10.1080/17474086.2021.1860002.
17. *Fang J, Wang X, Jiang W, Zhu Y, Hu Y, Zhao Y,* et al. Platelet-Rich Plasma Therapy in the Treatment of Diseases Associated

with Orthopedic Injuries. Tissue Eng Part B Rev 2020; 26(6): 571–85. DOI: 10.1089/ten.TEB.2019.0292.

18. *Sharara FI, Lelea LL, Rahman S, Klebanoff JS, Moawad GN.* A narrative review of platelet-rich plasma (PRP) in reproductive medicine. J Assist Reprod Genet 2021; 38(5): 1003–12. DOI: 10.1007/s10815-021-02146-9.
19. *Carr BJ.* Platelet-Rich Plasma as an Orthobiologic: Clinically Relevant Considerations. Vet Clin North Am Small Anim Pract 2022; 52(4): 977–95. DOI: 10.1016/j.cvsm.2022.02.005.
20. *Zhang J, Luo Q, Hu Q, Zhang T, Shi J, Kong L,* et al. An injectable bioactive dressing based on platelet-rich plasma and nanoclay: Sustained release of deferoxamine to accelerate chronic wound healing. Acta Pharm Sin B 2023; 13(10): 4318–36. DOI: 10.1016/j.apsb.2022.11.006.
21. *Yu Z, Li Y, Fu R, Xue Y, Zhao D, Han D.* Platycodin D inhibits the proliferation and migration of hypertrophic scar-derived fibroblasts and promotes apoptosis through a caspase-dependent pathway. Arch Dermatol Res 2023; 315(5): 1257–67. DOI: 10.1007/s00403-022-02513-1.
22. *Kim YH, Yang X, Shi L, Lanham SA, Hilborn J, Oreffo ROC,* et al. Bisphosphonate nanoclay edge-site interactions facilitate hydrogel self-assembly and sustained growth factor localization. Nat Commun 2020; 11(1): 1365. DOI: 10.1038/s41467-020-15152-9.
23. *Zhou L, Zhang C, Shi T, Wu D, Chen H, Han J,* et al. Functionalized 3D-printed GelMA/Laponite hydrogel scaffold promotes BMSCs recruitment through osteoimmunomodulatory enhance osteogenic via AMPK/mTOR signaling pathway. Mater Today Bio 2024; 29: 101261. DOI: 10.1016/j.mtbio.2024.101261.
24. *Zhang Y, Wang ZL, Deng ZP, Wang ZL, Song F, Zhu LL.* An extracellular matrix-inspired self-healing composite hydrogel for enhanced platelet-rich plasma-mediated chronic diabetic wound treatment. Carbohydr Polym 2023; 315: 120973. DOI: 10.1016/j.carbpol.2023.120973.
25. *Huang S, Hong X, Zhao M, Liu N, Liu H, Zhao J,* et al. Nanocomposite hydrogels for biomedical applications. Bioeng Transl Med 2022; 7(3): e10315. DOI: 10.1002/btm2.10315.
26. *Fan F, Saha S, Hanjaya-Putra D.* Biomimetic Hydrogels to Promote Wound Healing. Front Bioeng Biotechnol 2021; 9: 718377. DOI: 10.3389/fbioe.2021.718377.
27. *Zhuang ZM, Wang Y, Xu FW, Guo K, Cao LL, Feng ZX,* et al. Programmed nanozyme hydrogel enabling spatiotemporal modulation of wound healing achieves skin regeneration after biofilm infection. J Nanobiotechnology 2025; 23(1): 694. DOI: 10.1186/s12951-025-03773-5.
28. *Karimi Hajishoreh N, Dadashpour M, Akbarzadeh A.* Preparation and in vitro evaluation of biological agents based on Zinc-laponite- curcumin incorporated in alginate hydrogel. J Biol Eng 2023; 17(1): 73. DOI: https://doi.org/10.1186/s13036-023-00391-3.
29. *Gonzalez-Pujana A, Igartua M, Hernandez RM, Santos-Vizcaino E.* Laponite nanoclays for the sustained delivery of therapeutic proteins. Eur J Pharm Sci 2024; 201: 106858. DOI: 10.1016/j.ejps.2024.106858.

Received on September 12, 2025
Revised on October 13, 2025
Revised on December 22, 2025
Accepted on January 28, 2026
Online First March 2026