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Case Report

Combined Treatment of Noninfected Diabetes-Related Foot Ulcerations with Preconditioned Autologous Platelet-Rich Plasma with the MCT System to Enhance Exosomes Release and Phototherapy: A Case Report

Alexandra Amesty*

Rosy Martín - Estética Integral (Aesthetic, Regenerative and Anti-Aging Medicine Department), La Salud, Los Llanos de Aridane, Santa Cruz de Tenerife, Canarias, Spain

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ABSTRACT

Diabetes-related foot ulceration is a common complication in patients with uncontrolled diabetes mellitus and is associated with high mortality. This case report describes an 83-year-old woman with more than 20 years of type Ib diabetes, hypertension, and five noninfected skin lesions on the lower limbs of a one-year evolution. The patient had failed previous treatments. Our treatment protocol consisted of a topical treatment using preconditioned autologous platelet-rich plasma with photothermal biomodulation using the MCT System, combined with phototherapy. The patient underwent three treatment sessions, one per week and a cleaning session four days after each treatment. The protocol applied was intended to increase the exosome released by platelets. After the three treatment sessions, the ulcers had a favorable evolution, reducing depth, size, and pain and allowing for their manipulation. The treatment had no technical difficulties or adverse effects. The patient regained mobility, which could improve her quality of life. Due to the results obtained, it can be concluded that the combined use of the topical application of preconditioned platelet-rich plasma with photothermal biomodulation using the MCT system and phototherapy could be an innovative regenerative option without immunogenic potential and low risk of complications for treating noninfected diabetes-related foot ulceration.

Introduction

Diabetes-related foot ulcerations (DRFUs) are serious and prevalent complications in patients with uncontrolled diabetes mellitus, with significant impairment of quality of life and a high mortality rate [1, 2]. The DRFUs' incidence is approximately 15% in patients with diabetes, with 14%-24% of patients requiring amputation due to bone infection or other ulcer-related complications [3, 4]. The refractory nature of DRFUs is reflected in their high recurrence rate, even after healing [5]. On average, a person who develops DRFU has a three-to-five-year lower survival rate than a person with diabetes, and survival is reduced by 40% within five years [6, 7]. Along with inflammation, alterations in the extracellular matrix (ECM) play a significant role in perpetuating the nonhealing DRFUs due to the increase of metalloproteinases' activity, which reduces collagen content and makes the ECM unable to support wound healing [8, 9].

Due to the difficulty of curing and the refractory nature of DRFUs, various adjuvant therapies have been studied to promote tissue regeneration [10]. In recent years, exosomes have emerged as a focus point due to their biological properties and potential for disease management and regenerative medicine applications [11]. Exosomes can be derived from various sources, including mesenchymal stem cells (MSCs) or platelet-rich plasma (PRP), and exhibit diverse functions in wound repair, independently or following stimulation. Nevertheless, they all reduce the inflammatory response and promote angiogenesis, epithelial growth, and scar formation [12]. Evidence has confirmed that exosomes promote diabetic wound healing by inducing angiogenesis, collagen fiber deposition, and inhibiting inflammation [13, 14]. The case

**Correspondence to: Alexandra Amesty, Rosy Martín - Estética Integral (Aesthetic, Regenerative and Anti-Aging Medicine Department). La Salud, 2. 38760 - Los Llanos de Aridane, Santa Cruz de Tenerife. Canarias. Spain; Tel: +34644776014; ORCID: 0009-0008-5806-314X; E-mail: alexamesty91@gmail.com*

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report described below provides an illustrative example of the potential therapeutic applications of autologous exosomes.

Case Presentation

The patient was an 83-year-old woman with more than 20 years of clinical record of type Ib diabetes and idiopathic hypertension. In the last year, the patient had several noninfected skin lesions of different sizes in both legs: three ulcers in the right lower limb and two in the left. The patient's daily medications included 30% soluble insulin aspart and 70% insulin aspart crystallized with protamine 100 U/mL (Novomix 30 FlexPen), sulodexide soft capsules 15 mg (Aterina), furosemide 40 mg (Seguril), pentoxifiline (Hemovas) 400 mg, ramipril 10 mg, telmisartan 80 mg, prednisone 30 mg, tizanidine 4 mg, tramadol hydrochloride/paracetamol 37.5 mg/325 mg (Pazital), lorazepam 1 mg, and ebastine 20 mg (Ebastel forte).

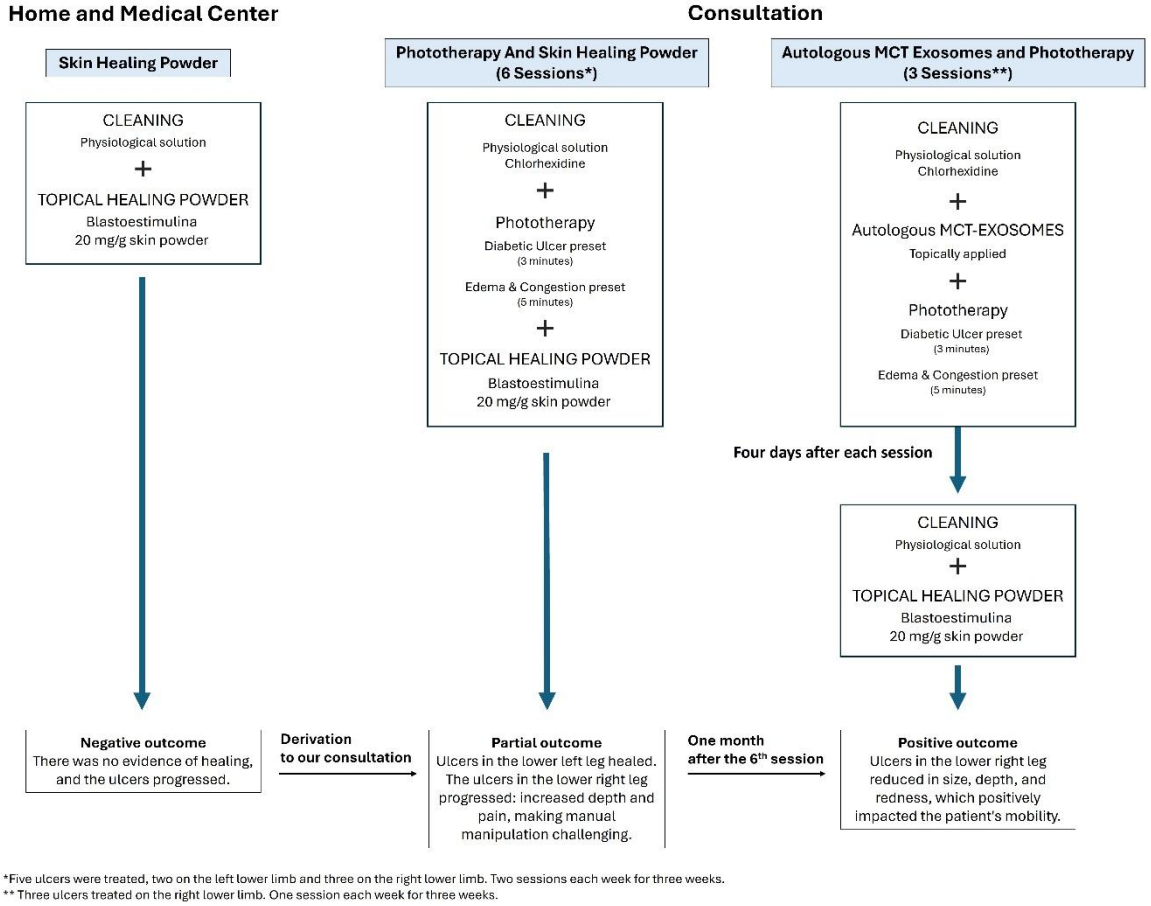
I Previous Treatments

The five ulcers were treated at home and later at a medical center. The treatment consisted of cleansing the area with 0.9% physiological solution to soften the gauze and facilitate its removal and topical application of a healing powder (Blastoestimulina 20 mg/g skin powder; Almirall, Spain) (Figure 1). However, not all ulcers treated had a positive evolution.

The patient was referred to our consultation by the medical center and was treated with six sessions of phototherapy with K-Laser Blue Derma (K-Laser Médica Ibérica S.L., Málaga, Spain) two per week for three weeks, followed by the topical application of blastoestimulina, the healing skin powder. The phototherapy was applied with the ENT handpiece, and the device was adjusted to the "Diabetic Ulcer" program (445 nm + 660 nm + 970 nm) for three minutes per lesion, followed by five minutes per lesion with the "Edema & Congestion" program (660 nm + 970 nm) (Figure 1). After the sixth session, the treatment was only effective on the two ulcers of the lower left limb. The other three ulcers increased in depth and pain, making manual manipulation challenging.

II Treatment with Autologous MCT Exosomes and Phototherapy

Due to the three ulcers on the lower right limb (two ulcers at two-thirds of the hamstring area measured 4 × 4 cm and 0.5 × 0.5 cm, and one in the lateral area measured 4 × 3 cm) did not respond to previous treatment, it was decided to modify the protocol including an innovative procedure with preconditioned autologous PRP. The treatment protocol included three weekly sessions combining topical preconditioned autologous PRP with phototherapy and three cleaning sessions four days after each treatment, with sterile gauze with chlorhexidine and a healing skin powder (Figure 1). The ulcer progressions were assessed at baseline and four days after each treatment session.



*Five ulcers were treated, two on the left lower limb and three on the right lower limb. Two sessions each week for three weeks.
** Three ulcers treated on the right lower limb. One session each week for three weeks.

Figure 1: Patient's treatment timeline and observed outcomes.

The preconditioning consisted of photothermal biomodulation (PTBM) of PRP using the MCT System (Meta Cell Technology, Sant Cugat, Spain). The MCT System is a novel device with specific presets that employ different energy, wavelength, temperature, and time combinations for priming platelets. In this protocol, the MCT Exosomes preset (10 minutes at 37ºC to 467 nm blue light and a fluence of 2 J/cm^2) was applied to promote the release of platelet-derived exosomes. From now on, the preconditioned autologous PRP will be called autologous MCT Exosomes.

A 15-to-20-milliliter peripheral blood sample was obtained from the patient using the RegenKit kit (RegenLab SA, Le Mont-sur-Lausanne, Switzerland) to obtain the MCT exosomes. The sample was double centrifuged at 1,500 rpm for five minutes and for nine minutes using a RegenLab PRP centrifuge (RegenLab SA, Le Mont-sur-Lausanne, Switzerland). After centrifugation, 7 to 9 mL of PRP was inserted into the MCT Kit (Meta Cell Technology, Sant Cugat, Spain), a disposable cassette classified as an MDR medical device class IIa. The cassette was placed into the MCT Unit (Meta Cell Technology, Sant Cugat, Spain), a photothermal biomodulation machine, and the exosomes preset was applied. Figure 2 graphically illustrates how autologous MCT exosomes were obtained. The autologous MCT exosomes were extracted from the cassette and topically applied by soaking a gauze, placing it on the wound, and simulating a dressing.

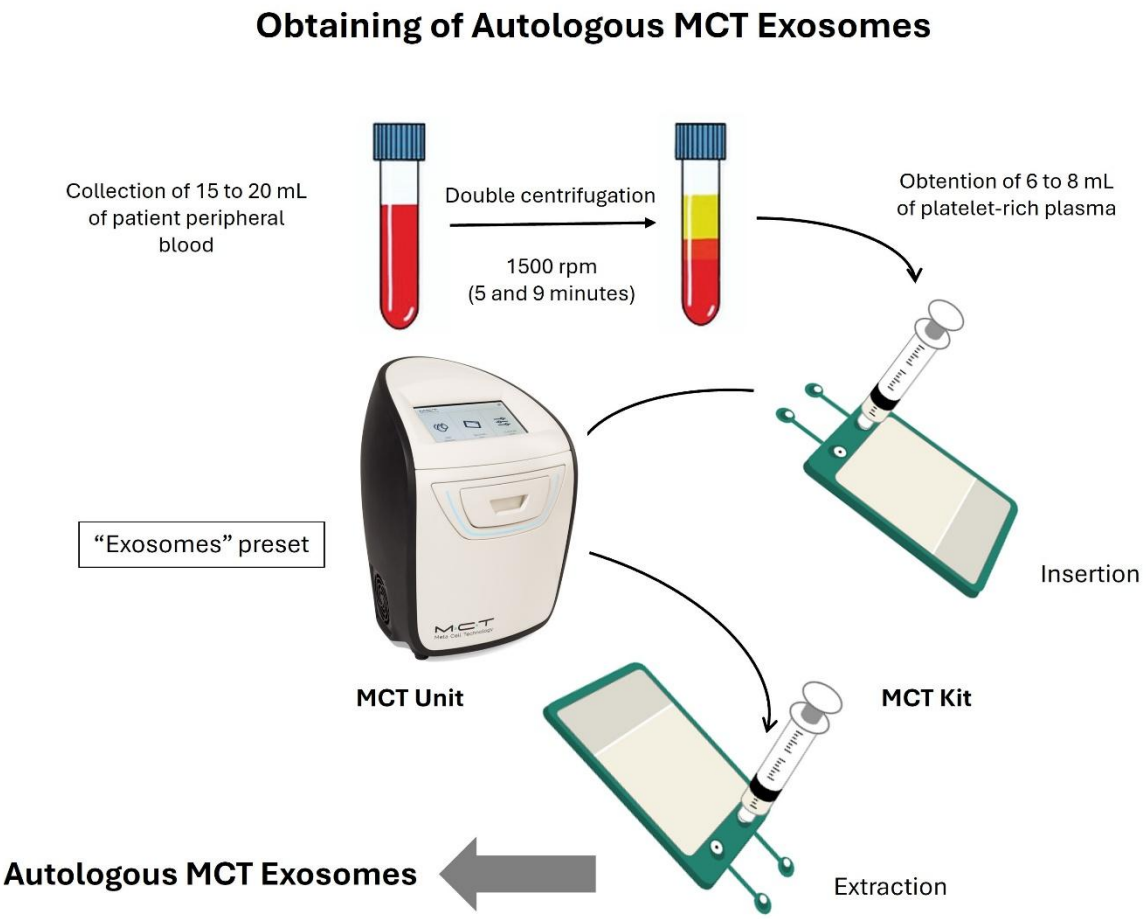
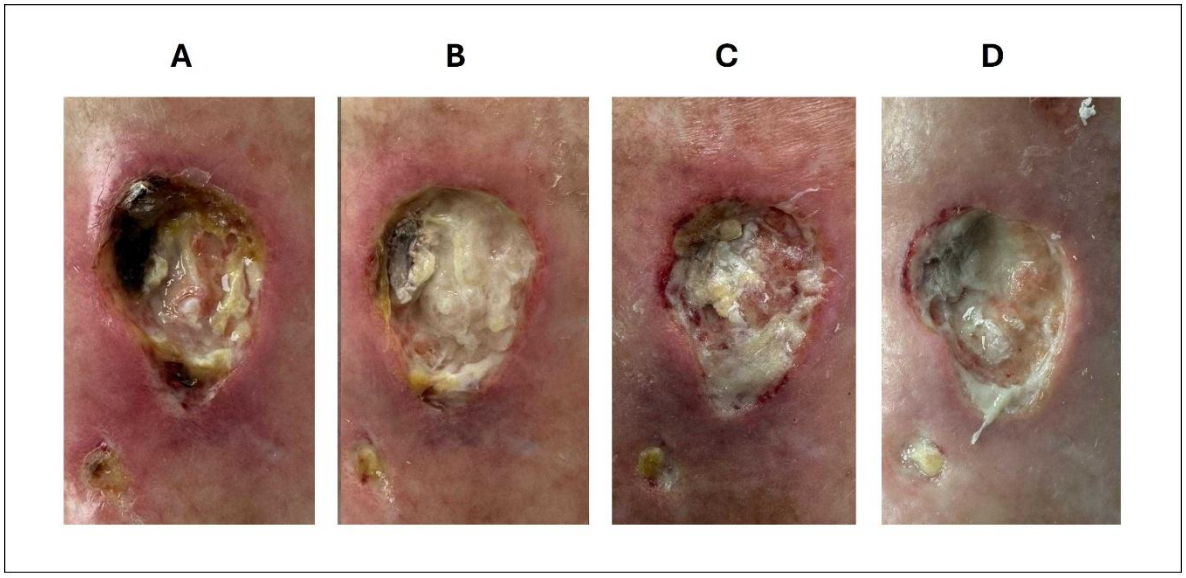


Figure 2: Scheme of the process for obtaining autologous MCT exosomes.

After applying for the MCT exosomes, phototherapy was performed. For this protocol, the same phototherapy device was used and was adjusted to the "Chronic Pain" (445 nm + 660 nm + 970 nm) and the "Edema & Congestion" (660 nm + 970 nm) programs. Each program was performed for three and five minutes per ulcer. After this procedure, a sterile gauze was applied, leaving the dressing as fixed as possible and closed with soft, elastic bandages without compromising circulation or drainage.

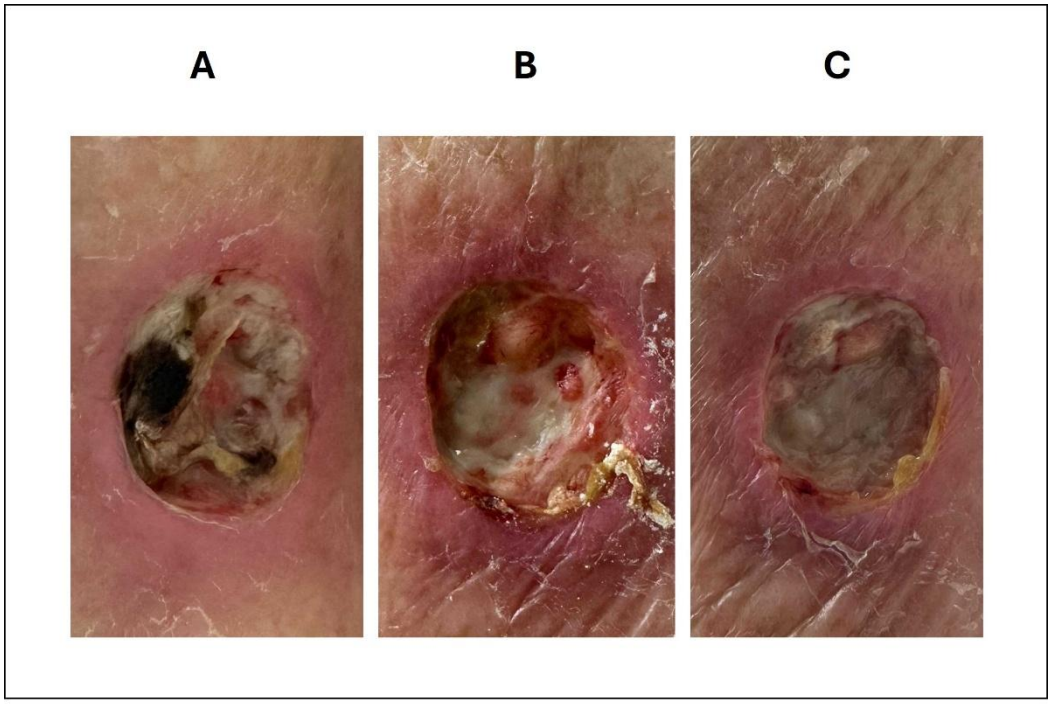
III Treatment Outcomes and Safety

After 21 days, the three ulcers showed a favorable evolution, reducing in depth, size, redness, and pain. This amelioration allowed the physician to manipulate the lesion during treatment without discomfort for the patient (Figures 1, 3 & 4). Furthermore, the treatment had no technical difficulties or adverse effects. The patient regained mobility, which could improve her quality of life.



A- Before the treatment.
B- Four days after the first treatment session.
C- Four days after the second treatment session.
D- Four days after the third treatment session.

Figure 3: The healing progression of the 4 × 4 cm and 0.5 × 0.5 cm ulcers, located at two-thirds of the hamstring area of the lower right limb, after each treatment session with autologous MCT exosomes and phototherapy.



A- Before the treatment.
B- Four days after the first treatment session.
C- Four days after the second treatment session.

Figure 4: The progression of the 4 × 3 cm ulcer, located in the lateral area of the lower right limb, after each treatment session with autologous MCT exosomes and phototherapy.

Discussion

In diabetes, the hyperglycemic environment and other changes lead to alterations in the ECM, such as decreased collagen deposition and increased production of matrix metalloproteinases (MMPs). Hyperglycemia inhibits cell proliferation and migration, inducing apoptosis through reactive oxygen species (ROS)-dependent activation of the c-Jun N-terminal kinase (JNK) and the p38 mitogen-activated protein kinase (MAPK) signaling pathways, which play key roles in cellular apoptosis in response to extracellular signals and stress [15]. These molecular changes, in turn, have a deleterious effect on cellular function, exacerbating the pathological state of the ECM and causing chronic wounds that can facilitate the entry of infectious agents that cause chronic infection and sepsis, which can lead to amputation and even death [16].

PBM enhances the release of platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), transforming growth factor ß (TGF-ß), vascular endothelial growth factor (VEGF), interleukins, hormones, and several hundred other proteins released by platelets [17-19]. PBM increases complexes I, II, III, IV, and succinate dehydrogenase activity in the electron transfer chain [20]. Furthermore, PBM increases adenosine triphosphate (ATP), AMPc, and nitric oxide (NO) levels, which can favor vasodilation, neurotransmission, and anti-inflammatory activity [21].

Our case ulcerations showed healing when autologous MCT exosomes applied topically were added to the phototherapy treatment protocol. This fact underscores the significance of autologous MCT exosomes in promoting successful ulcer progression. Exosomes released by PRP accelerate diabetic wound healing [15, 22]. Exosomes released by PRP stimulate fibroblast functions and protect diabetic wound healing by alleviating the process produced by the PDGF-BB/JAK2/STAT3/Bcl-2 signaling pathway [15]. In an animal study, exosomes derived from PRP promoted the re-epithelization of chronic cutaneous wounds in a diabetic rat model by activating Yes-associated protein (YAP) [23].

Case limitations include the impossibility of continuing with additional autologous MCT exosome treatment sessions due to the patient's hospitalization because of repeated hypoglycemic episodes related to diabetes. Furthermore, the quality of life was not assessed with validated surveys. However, as the patient's ailments eased, she began to engage in activities, experiencing a notable improvement in her mobility, which could have positively impacted her quality of life.

Conclusion

Treating noninfected diabetes-related foot ulcerations with preconditioned PRP with photothermal biomodulation using the MCT system combined with phototherapy could be an innovative regenerative option without immunogenic potential and low risk of complications to improve their progression, which is worth continuing to investigate.

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Conflicts of Interest

The author declared that Meta Cell Technology S.L. paid the article processing charges, but she did not receive any personal fee for conducting the study.

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Data Availability

The author declares that data supporting the findings of this case are available within the article.

References

1. Jalilian M, Ahmadi Sarbarzeh P, Oubari S (2020) Factors Related to Severity of Diabetic Foot Ulcer: A Systematic Review. *Diabetes Metab Syndr Obes* 13: 1835-1842. [Crossref]
2. Boulton AJM, Whitehouse RW, Feingold K, Ahmed SF, Anawalt B et al. (2020) The Diabetic Foot. [Crossref]
3. Yazdanpanah L, Shahbazian H, Nazari I, Arti HR, Ahmadi F et al. (2018) Incidence and Risk Factors of Diabetic Foot Ulcer: A Population-Based Diabetic Foot Cohort (ADFC Study)-Two-Year Follow-Up Study. *Int J Endocrinol* 2018: 1-9. [Crossref]
4. Oliver TI, Mutluoglu M (2023) Diabetic Foot Ulcer. [Crossref]
5. Wang X, Yuan CX, Xu B, Yu Z (2022) Diabetic foot ulcers: Classification, risk factors and management. *World J Diabetes* 13 (12): 1049-1065. [Crossref]
6. Chammas NK, Hill RLR, Edmonds ME (2016) Increased Mortality in Diabetic Foot Ulcer Patients: The Significance of Ulcer Type. *J Diabetes Res* 2016: 2879809. [Crossref]
7. Jupiter DC, Thorud JC, Buckley CJ, Shibuya N (2016) The impact of foot ulceration and amputation on mortality in diabetic patients. I: From ulceration to death, a systematic review. *Int Wound J* 13 (5): 892-903. [Crossref]
8. Huang Y, Kyriakides TR (2020) The role of extracellular matrix in the pathophysiology of diabetic wounds. *Matrix Biol Plus* 7: 100037. [Crossref]
9. Black E, Vibe-Petersen J, Jorgensen LN, Madsen SM, Agren SM et al. (2003) Decrease of Collagen Deposition in Wound Repair in Type 1 Diabetes Independent of Glycemic Control. *Arch Surg* 138 (1): 34-40. [Crossref]
10. Sledge I, Maislin D, Bernarducci D, Snyder R, Serena TE (2020) Use of a dual-layer amniotic membrane in the treatment of diabetic foot ulcers: an observational study. *J Wound Care* 29 (Sup9): S8-S12. [Crossref]
11. Omrani M, Beyrampour-Basmenj H, Jahanban-Esfahlan R, Jahanban-Esfahlan R, Talebi M et al. (2024) Global trend in exosome isolation and application: an update concept in management of diseases. *Mol Cell Biochem* 479 (3): 679-691. [Crossref]

12. Jing S, Li H, Xu H (2023) Mesenchymal Stem Cell Derived Exosomes Therapy in Diabetic Wound Repair. *Int J Nanomedicine* 18: 2707-2720. [Crossref]
13. Yu L, Qin J, Xing J, Dai Z, Zhang T et al. (2023) The mechanisms of exosomes in diabetic foot ulcers healing: a detailed review. *J Mol Med* 101 (10): 1209-1228. [Crossref]
14. Littig JPB, Moellmer R, Agrawal DK, Rai V (2023) Future applications of exosomes delivering resolvins and cytokines in facilitating diabetic foot ulcer healing. *World J Diabetes* 14 (1): 35-47. [Crossref]
15. Cao W, Meng X, Cao F, Wang J, Yang M (2023) Exosomes derived from platelet-rich plasma promote diabetic wound healing via the JAK2/STAT3 pathway. *iScience* 26 (11): 108236. [Crossref]
16. Singh N, Amstrong DG, Lipsky BA (2005) Preventing Foot Ulcers in Patients with Diabetes. *JAMA* 293 (2): 217. [Crossref]
17. Irmak G, Demirtaş TT, Gümüşderelioğlu M (2020) Sustained release of growth factors from photoactivated platelet rich plasma (PRP). *Eur J Pharm Biopharm* 148: 67-76. [Crossref]
18. Golebiewska EM, Poole AW (2013) Secrets of platelet exocytosis - what do we really know about platelet secretion mechanisms? *Br J Haematol* 165 (2): 204-216. [Crossref]
19. Zhu Y, Yuan M, Meng HY, Wang AY, Guo QY et al. (2013) Basic science and clinical application of platelet-rich plasma forcartilage defects and osteoarthritis: A review. *Osteoarthritis Cartilage* 21 (11): 1627-1637. [Crossref]
20. Hamblin MR (2018) Photodynamic Therapy and Photobiomodulation: Can All Diseases be Treated with Light? In: Guenther BD, Steel DG, eds. Encyclopedia of Modern Optics (Second Edition). Second Edition. Elsevier; 3: 100-135.
21. Yan B, Zhou J, Yan F, Gao M, Tang J et al. (2025) Unlocking the potential of photobiomodulation therapy for brain neurovascular coupling: The biological effects and medical applications. *J Cereb Blood Flow Metab* 7: 271678X241311695. [Crossref]
22. Zhang Y, Wang X, Chen J, Qian D, Gao P et al. (2022) Exosomes derived from platelet-rich plasma administration in site mediate cartilage protection in subtalar osteoarthritis. *J Nanobiotechnology* 20 (1): 56. [Crossref]
23. Guo SC, Tao SC, Yin WJ, Qi X, Yuan T et al. (2017) Exosomes derived from platelet-rich plasma promote the re-epithelization of chronic cutaneous wounds via activation of YAP in a diabetic rat model. *Theranostics* 7 (1): 81-96. [Crossref]