World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 4
Page: 1061-1068

ADVANCED HYDROGEL DRESSINGS FOR IMPROVED WOUND HEALING: AN IN-DEPTH REVIEW

Zohra Fatima*, Jyoti Singh and Dr. Sanjay Kumar Kushwaha

Bhavdiya Institute of Pharmaceutical Sciences and Research, Ayodhya, Uttar Pradesh, India.

Article Received: 4 August 2025 | | ***Article Revised: 25 August 2025*** | | ***Article Accepted: 15 September 2025***

***Corresponding Author: Zohra Fatima**
Bhavdiya Institute of Pharmaceutical Sciences and Research, Ayodhya, Uttar Pradesh, India.
DOI: https://doi.org/10.5281/zenodo.17132255

How to cite this Article: Zohra Fatima, Jyoti Singh and Dr. Sanjay Kumar Kushwaha (2025) ADVANCED HYDROGEL DRESSINGS FOR IMPROVED WOUND HEALING: AN IN-DEPTH REVIEW. World Journal of Pharmaceutical Science and Research, 4(4), 1061-1068. https://doi.org/10.5281/zenodo.17132255

ABSTRACT

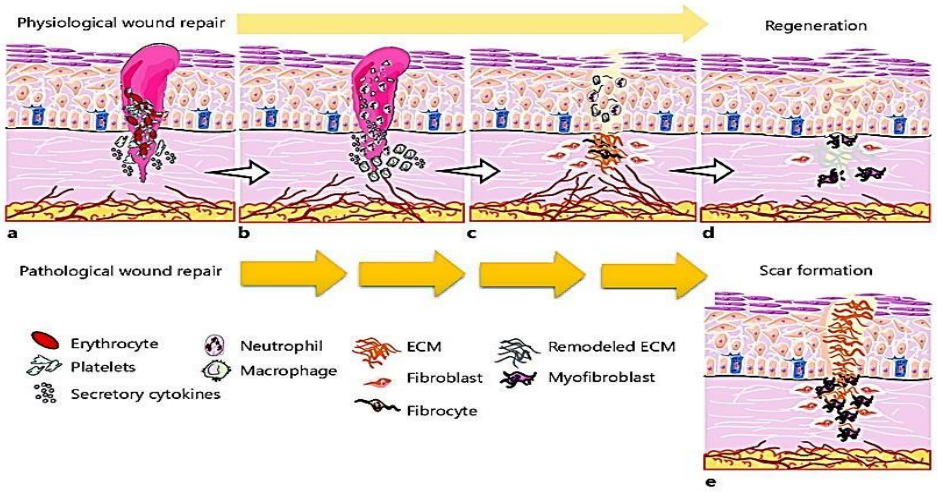
The management of skin wounds, especially chronic wounds that fail to heal effectively, remains a significant challenge in modern healthcare. Traditional wound dressings offer limited therapeutic benefits, primarily serving as passive barriers. This limitation has spurred the evolution of wound care towards advanced, active dressings designed to create an optimal healing microenvironment and participate directly in the regenerative process. Among these, hydrogels have emerged as a superior platform due to their unique physicochemical properties, including high water content, structural similarity to the native extracellular matrix (ECM), and their capacity to be loaded with therapeutic agents. This review provides a comprehensive overview of the wound healing cascade, detailing the fundamental biology of its four phases: hemostasis, inflammation, proliferation, and remodelling. It explores the pathophysiology of impaired healing and the subsequent evolution of wound dressings from passive coverings to active therapeutic systems. The primary focus is on hydrogels, detailing the roles of both natural and synthetic polymers, with a special emphasis on chitosan for its inherent biocompatibility, biodegradability, and bioactivity. Furthermore, the review discusses the rationale and strategies for creating multifunctional dressings by incorporating bioactive agents like antimicrobials, anti-inflammatories, and antioxidants to target key pathological barriers simultaneously. The development of "smart" systems, such as injectable, self-healing, and stimuli-responsive hydrogels, is also examined as a frontier in the field. Ultimately, this review synthesizes current knowledge to highlight that multifunctional hydrogels represent a highly promising and dynamic area of research poised to revolutionize advanced wound care.

KEYWORDS: Chronic wounds, hydrogel dressings, wound healing, chitosan, bioactive agents, stimuli-responsive hydrogels, multifunctional biomaterials, tissue regeneration.

1. INTRODUCTION

1.1. The Imperative of Wound Healing

The skin is the human body's largest organ, forming a complex, multi-layered barrier that separates our internal biology from the external world. Its primary role is to provide protection from environmental threats such as mechanical trauma, pathogens, and harmful radiation (Yuan et al., 2023). When this barrier is breached by injury, the body initiates a highly orchestrated biological cascade known as wound healing. This process is not merely about closing a physical gap but is a dynamic sequence of cellular and molecular events aimed at restoring the skin's structural and functional integrity. The success of this process is fundamental to survival, as failure can lead to chronic pain, persistent infection, and significant morbidity (Yuan et al., 2023).

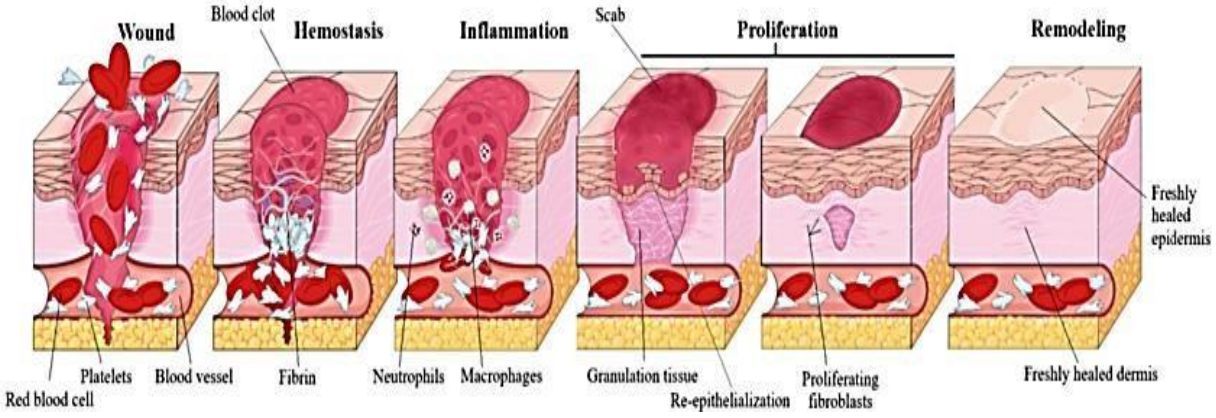


1.2. The Biological Cascade of Healing

Normal wound healing is traditionally segmented into four distinct yet overlapping phases: hemostasis, inflammation, proliferation, and remodelling.

- **Hemostasis:** This is the immediate response to vascular injury, designed to halt bleeding. Damaged blood vessels constrict, and exposed collagen triggers platelet aggregation at the injury site. These platelets release chemical signals that initiate the coagulation cascade, culminating in the formation of a fibrin mesh. This mesh traps blood cells to form a stable clot, which provides hemostasis and serves as a provisional scaffold for subsequent cellular infiltration (Zhang et al., 2024).
- **Inflammation:** Once bleeding is controlled, the inflammatory phase begins. Neutrophils are recruited to cleanse the wound of bacteria and debris through phagocytosis (Xu et al., 2023). Subsequently, macrophages arrive to continue the cleanup process and, critically, release growth factors and cytokines that signal the transition to the next phase. While inflammation is essential, a prolonged or dysregulated inflammatory response is a hallmark of chronic wounds and can lead to further tissue damage (An et al., 2024).
- **Proliferation:** This is the rebuilding phase, focused on filling the wound defect with new tissue. It involves several concurrent processes: fibroblasts migrate into the wound to synthesize a new extracellular matrix (ECM) and form granulation tissue; angiogenesis, the formation of new blood vessels, occurs to supply the new tissue with oxygen and nutrients (Dawood et al., 2024); and finally, epithelial cells migrate across the wound bed in a process called re-epithelialization to restore the skin's outer layer.
- **Remodelling (Maturation):** The final and longest phase involves the maturation of the newly formed tissue into a

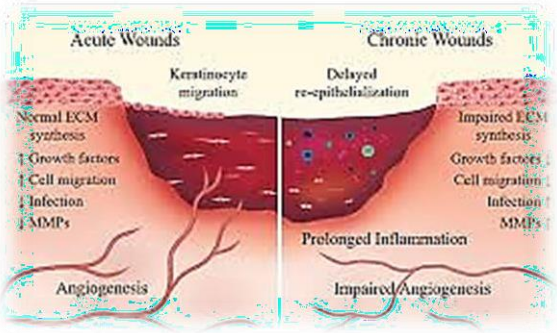
scar. The initially deposited Type III collagen is gradually replaced by the stronger, more organized Type I collagen, increasing the tensile strength of the healed tissue. However, this scar tissue rarely achieves the full strength of uninjured skin.



2. The Challenge of Impaired Healing and the Evolution of Wound Care

2.1. From Acute to Chronic Wounds

While the healing cascade is robust, it can be easily disrupted by local factors like infection or systemic conditions such as diabetes mellitus and vascular disorders. When the process is derailed, often becoming "stuck" in the inflammatory phase, an acute wound can progress into a chronic, non-healing state. Chronic wounds, including diabetic foot ulcers and venous leg ulcers, are characterized by a hostile microenvironment with persistent inflammation, high levels of destructive enzymes, elevated oxidative stress, and often, the presence of bacterial biofilms (Li et al., 2021). These biofilms are organized communities of bacteria encased in a self-produced matrix, making them notoriously resistant to antibiotics and the host immune system, thereby perpetuating the inflammatory state (Sun et al., 2023).

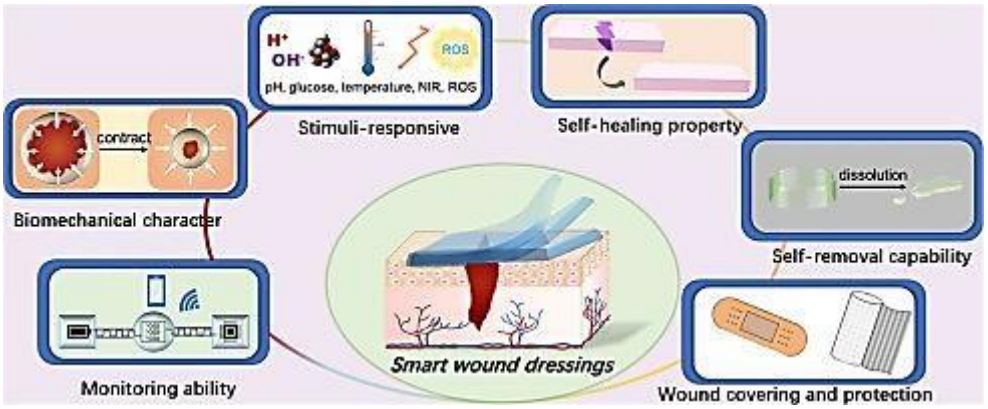


2.2. The Shift from Passive to Active Dressings

The approach to wound management has evolved dramatically in response to a deeper understanding of healing biology. For centuries, traditional dressings like cotton gauze were used as passive coverings to absorb exudate and protect the wound. However, these dressings create a dry environment that impedes cell migration and often adhere to the wound bed, causing trauma upon removal (Yuan et al., 2023).

The discovery in the 1960s that wounds heal faster in a moist environment revolutionized wound care. This principle of "moist wound healing" led to the development of modern advanced dressings, including films, foams, alginates, and

hydrogels. These dressings maintain a hydrated environment that supports cellular processes, helps control exudate, and does not adhere to the wound, making them far superior to traditional options (Zhang et al., 2024).



3. Hydrogels as a Superior Platform for Wound Dressings

3.1. Defining Hydrogels

Among modern dressings, hydrogels have gained particular attention as a superior platform for advanced wound care. Hydrogels are three-dimensional networks of hydrophilic polymer chains that can absorb and retain large volumes of water or biological fluids while maintaining their structural integrity (Andrade del Olmo, Pérez-Álvarez, et al., 2022). This unique structure gives them a soft, pliable consistency that closely resembles the native extracellular matrix (ECM) of soft tissues.

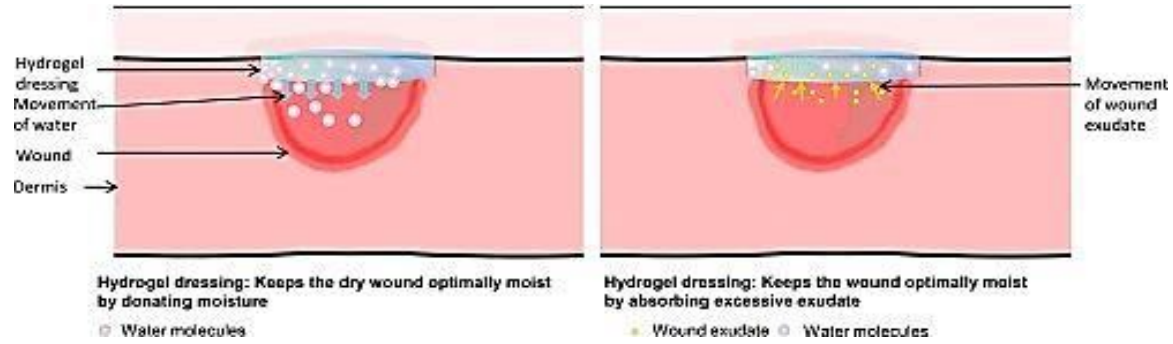
3.2. Advantages in the Wound Microenvironment

The inherent properties of hydrogels make them exceptionally well-suited for wound healing:

- **Optimal Moisture Balance:** Hydrogels can either donate moisture to dry wounds or absorb excess fluid from highly exuding ones, creating a balanced microenvironment that is universally recognized as optimal for healing (Nazemoroaia et al., 2024).
- **ECM Mimicry and Biocompatibility:** Their high-water content and soft consistency create a cell-friendly environment that supports cell adhesion, migration, and proliferation (Xie et al., 2018).
- **Soothing and Non-Adherent:** The hydrated surface provides a cooling, pain-relieving effect and prevents the dressing from sticking to the delicate wound bed, allowing for painless removal.
- **Platform for Controlled Drug Delivery:** The porous network of a hydrogel can serve as a reservoir for therapeutic agents, which can be released in a sustained and controlled manner directly at the wound site, maximizing local efficacy (Andrade Del Olmo, Alonso, et al., 2022).

4. Engineering Multifunctional Hydrogels

The true potential of hydrogels is realized when they are engineered to be multifunctional, transforming them from a simple hydrating layer into an active therapeutic system. This is typically achieved by selecting a bioactive polymer as the scaffold and incorporating additional therapeutic agents.



4.1. The Role of the Polymeric Scaffold: A Focus on Chitosan

The choice of polymer is critical in determining a hydrogel's performance. Natural polymers are often preferred for their biocompatibility and bioactivity. Chitosan, a polysaccharide derived from chitin, is a standout candidate for wound healing applications due to its unique combination of properties (Bai et al., 2023; Aderibigbe, 2023).

- **Biocompatibility and Biodegradability:** Chitosan is non-toxic and is safely broken down and absorbed by the body (Kandaswamy et al., 2024).
- **Inherent Antibacterial Activity:** In the slightly acidic wound environment, chitosan becomes positively charged and can disrupt the negatively charged membranes of bacteria and fungi, providing broad-spectrum antimicrobial protection (Sun et al., 2023; Peng et al., 2024).
- **Effective Hemostatic Properties:** Its positive charge also attracts negatively charged red blood cells and platelets, promoting rapid blood clot formation (Zhou et al., 2022).
- **Acceleration of Tissue Regeneration:** Chitosan is not merely a passive scaffold; it actively stimulates the proliferation and migration of key healing cells, including fibroblasts and keratinocytes, and enhances the production of crucial ECM components (Dawood et al., 2024; Mushtaq et al., 2023).

4.2. Enhancing Functionality through Bioactive Agents

To address the multifaceted challenges of chronic wounds, hydrogels can be loaded with bioactive molecules that target specific pathological barriers.

- **Targeting Inflammation:** Chronic inflammation is a major impediment to healing. Incorporating natural anti-inflammatory compounds, such as rutin or flavonoids from *Passiflora edulis*, into a chitosan hydrogel can modulate the inflammatory response and promote a transition to the proliferative phase (An et al., 2024; Soares et al., 2019).
- **Targeting Oxidative Stress:** The wound environment is characterized by high levels of reactive oxygen species (ROS) that cause cellular damage. Loading hydrogels with powerful antioxidants, such as the enzyme superoxide dismutase (SOD) or α-lipoic acid, can protect newly forming cells and foster a more robust healing response (Zhang et al., 2018; Li et al., 2021).
- **Dual-Action Agents: Punicic Acid:** Punicic acid, an omega-5 fatty acid from pomegranate seed oil, is an excellent example of a natural bioactive agent with dual functionality. It has been shown to be a potent anti-

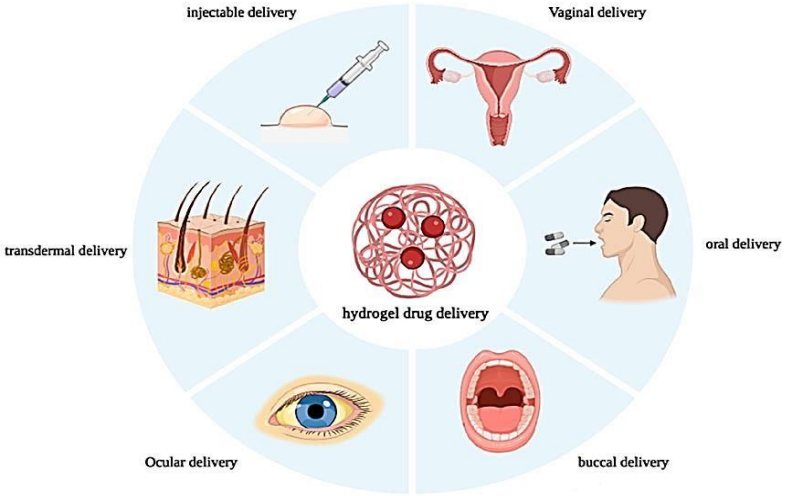
inflammatory agent by inhibiting key enzymes in inflammatory pathways (Ju et al., 2022). Simultaneously, its chemical structure makes it a strong antioxidant capable of scavenging harmful free radicals, thereby protecting cells from oxidative damage (Yang et al., 2024; Liu et al., 2021). The combination of chitosan and punicic acid creates a synergistic system where the scaffold provides structural and pro-migratory support while the released drug provides a targeted biochemical intervention.

5. Advanced and "Smart" Hydrogel Systems

The field is rapidly moving beyond simple matrix hydrogels toward more sophisticated and responsive systems designed to meet complex clinical needs.

Injectable and Self-Healing Hydrogels: Traditional pre-formed hydrogel sheets may not conform well to deep or irregular wounds. Injectable hydrogels, which are liquid at application and form a gel *in situ*, can perfectly fill such cavities, ensuring complete wound contact (Mushtaq et al., 2023; Ding et al., 2024). Furthermore, self-healing hydrogels, often based on dynamic chemical bonds, have the remarkable ability to repair themselves after mechanical damage, ensuring the dressing maintains its structural integrity and protective barrier function, even on mobile parts of the body (Zhou et al., 2022; Zhang et al., 2024).

- **Stimuli-Responsive Systems:** "Smart" hydrogels can sense changes in the wound microenvironment and respond accordingly. For instance, pH-responsive hydrogels can be engineered to release an antibacterial agent preferentially in the alkaline environment of an infected wound, providing on-demand therapy (Sun et al., 2023).
- **Composite and Hybrid Systems:** Combining chitosan with other biopolymers can create composite hydrogels with superior properties. Chitosan-alginate complexes offer improved mechanical strength and are suitable for highly exuding wounds (Nazemoroaia et al., 2024). Blending chitosan with hyaluronic acid, a major component of the skin's ECM, creates a highly biomimetic hydrogel that actively promotes cell migration and proliferation in infected wounds (Bai et al., 2023). Similarly, incorporating sericin (a silk protein) can add antioxidant and cell-proliferating properties (Kanoujia et al., 2018; Chu et al., 2023).



6. Conclusion and Future Perspectives

The development of advanced wound dressings has fundamentally shifted the paradigm of wound care from passive coverage to active therapeutic intervention. Hydrogels have unequivocally emerged as a premier platform for this new

generation of dressings, owing to their intrinsic properties that create an optimal, moist healing environment. The use of bioactive polymers like chitosan provides a foundational advantage, as the scaffold itself participates in the healing process by promoting hemostasis, inhibiting microbial growth, and stimulating cellular regeneration.

The true innovation, however, lies in the creation of multifunctional systems. By incorporating therapeutic agents that can simultaneously target the key barriers of chronic wounds— inflammation, oxidative stress, and infection—these hydrogels can offer a holistic and synergistic treatment. The future of the field is bright, with ongoing research into "smart," responsive hydrogels that can be injected, self-heal, and deliver drugs on demand.

Despite the immense promise shown in laboratory settings, the path from the bench to the bedside remains challenging. Overcoming hurdles related to scalable manufacturing, cost- effectiveness, sterilization, and rigorous regulatory approval will be critical for the clinical translation of these advanced technologies. Nonetheless, multifunctional hydrogels represent a dynamic and powerful frontier in medicine, with the potential to significantly improve healing outcomes and enhance the quality of life for patients suffering from difficult-to-heal wounds.

7. REFERENCES

1. Aderibigbe, B. A., Recent advances in the development of chitosan-based hydrogels for wound healing. *Pharmaceutics*, 2023; *15*(4): 1239.
2. An, R., Shi, C., Tang, Y., Cui, Z., Li, Y., Chen, Z., Xiao, M., & Xu, L., Chitosan/rutin multifunctional hydrogel with tunable adhesion, anti-inflammatory and antibacterial properties for skin wound healing. *Carbohydrate Polymers*, 2024; *343*: 122492.
3. Andrade Del Olmo, J., Alonso, J., Sáez-Martínez, V., Benito-Cid, S., Moreno-Benítez, I., Bengoa-Larrauri, M., Pérez-González, R., Vilas-Vilela, J., & Pérez-Álvarez, L., Self-healing, antibacterial and anti-inflammatory chitosan-PEG hydrogels for ulcerated skin wound healing and drug delivery. *Biomaterials Advances*, 2022; *139*: 212992.
4. Andrade del Olmo, J., Pérez-Álvarez, L., Martínez, V., Benito Cid, S., Ruiz-Rubio, L., Pérez González, R., Vilas-Vilela, J., & Alonso, J. Wound healing and antibacterial chitosan-genipin hydrogels with controlled drug delivery for synergistic anti-inflammatory activity. *International Journal of Biological Macromolecules*.
5. Bai, Q., Gao, Q., Hu, F., Zheng, C., Chen, W., Sun, N., Liu, J., Zhang, Y., Wu, X., & Lu, T., Chitosan and hyaluronic-based hydrogels could promote the infected wound healing. *International Journal of Biological Macromolecules*, 2023; *123271*.
6. Chu, W., Wang, P., Ma, Z., Peng, L., Guo, C., Fu, Y., & Ding, L., Lupeol-loaded chitosan-Ag+ nanoparticle/sericin hydrogel accelerates wound healing and effectively inhibits bacterial infection. *International Journal of Biological Macromolecules*, 2023; *125310*.
7. Dawood, H. Z., Ara, C., Asmatullah, Jabeen, S., Islam, A., & Ghauri, Z. H. Chitosan/fibroin biopolymer-based hydrogels for potential angiogenesis in developing chicks and accelerated wound healing in mice. *Biopolymers, e* 2024; *23633*.
8. Ding, P., Ding, X., Liu, X., Lu, Y., Zhao, Y., Chu, Y., Fan, L., & Nie, L. Injectable, self-healing, antibacterial hydrogel dressing based on oxidized dextran and sialic acid substituted chitosan with incorporation of tannic acid. *European Polymer Journal*, 2024; *113297*.
9. Ju, J.-H., Kim, J., Choi, Y., Jin, S., Kim, S., Son, D., & Shin, M., Punicalagin- loaded alginate/chitosan-gallol

hydrogels for efficient wound repair and hemostasis. *Polymers*, 2022; *14*.

10. Kandaswamy, K., Panda, S. P., Shaik, M. R., Hussain, S. A., Deepak, P., Thiyagarajulu, N., Jain, D., Antonyraj, A., Subramanian, R., Guru, A., & Arockiaraj, J. Formulation of Asiatic acid-loaded polymeric chitosan-based hydrogel for effective MRSA infection control and enhanced wound healing in zebrafish models. *International Journal of Biological Macromolecules*, 2024; *137425*.
11. Kanoujia, J., Parashar, P., Singh, M., Tripathi, R., & Saraf, S. Genipin initiated crosslinked sericin/chitosan hydrogels: Accelerated wound healing in an animal model. *Pharmaceutical Nanotechnology*, 2018; *10*: 37–57.
12. Li, Q., Liu, K., Jiang, T., Ren, S., Kang, Y., Li, W., Yao, H., Yang, X., Dai, H., & Chen, Z., Injectable and self-healing chitosan-based hydrogel with MOF-loaded α- lipoic acid promotes diabetic wound healing. *Materials Science & Engineering C*, 2021;*131*: 112519.
13. Liu, M., Su, Z., Wang, Y., Zhang, M., & Long, Y., Punicic acid, a conjugated linolenic acid, promotes wound healing in diabetic rats. *Journal of Agricultural and Food Chemistry*, 2021; *69*(1): 162–169.
14. Liu, S., Jiang, N., Chi, Y., Peng, Q., Dai, G., Qian, L., Xu, K., Zhong, W., & Yue, W., Injectable and Self-Healing Hydrogel Based on Chitosan-Tannic Acid and Oxidized Hyaluronic Acid for Wound Healing. *ACS Biomaterials Science & Engineering*, 2022,
15. Mushtaq, F., Ashfaq, M., Anwar, F., Ayesha, B., Latif, H. S., Khalil, S., Sarwar, H. S., Khan, M. I., Sohail, M., & Maqsood, I., Injectable Chitosan-Methoxy Polyethylene Glycol Hybrid Hydrogel Untangling the Wound Healing Behavior: In Vitro and In Vivo Evaluation. *ACS Omega*, 2023; *9*: 2145–2160.
16. Nazemoroaia, M., Bagheri, F., Mirahmadi-Zare, S. Z., Eslami-Kaliji, F., & Derakhshan, A., Asymmetric natural wound dressing based on porous chitosan-algin, 2024