Chapter 31

Hydrogel Based Nanoparticles for Enhanced Wound Healing

Awn Abbas[1], Sadia[2], Sameera Naseer[1], Dongbo Li[1], Chao Li[1], Nanxin Li[1], Yifan Zhang[1], Lian Chen[1], Shaungcai Qi[1] and Hualin Fu*

[1]College of Veterinary Medicine, Sichuan Agricultural University, Chengdu, China
[2]College of Animal Science and Technology, Sichuan Agricultural University, Chengdu, China
*Corresponding author: fuhl.sicau@163.com

ABSTRACT

Advanced wound healing techniques have shown considerable potential for hydrogel-based nanoparticles. Hydrogels, due to their substantial water content and ability to interact well with living organisms, are highly suitable for administering medicinal substances. Drug loading, mechanical strength, and stability are improved by nanoparticles in hydrogel matrices. These nanoparticles can be engineered to systematically release bioactive compounds, such as growth factors, antibacterial agents, and anti-inflammatory medications, in a regulated manner. This controlled release method can effectively target different stages of the wound healing process. Moreover, the adjustable properties of hydrogels enable accurate manipulation of the rate at which enclosed medicines are released. The integration of hydrogel matrices and nanoparticles fosters a milieu that enhances cellular proliferation, migration, and tissue regeneration. Incorporating stimuli-responsive features allows for the controlled release of drugs in response to certain physiological signals, enhancing the therapeutic efficacy. In summary, hydrogel-based nanoparticles provide an adaptable platform for creating advanced wound healing treatments that have enhanced effectiveness and accuracy.

KEYWORDS
Hydrogel, Nanoparticles, Wound healing

Received: 17-Jun-2024
Revised: 02-Jul-2024
Accepted: 11-Aug-2024

A Publication of Unique Scientific Publishers

Cite this Article as: Abbas A, Sadia, Naseer S, Li D, Li C, Li N, Zhang Y, Chen L, Qi S and Fu H, 2024. Hydrogel based nanoparticles for enhanced wound healing. In: Ahmed R, Khan A, Abbas RZ, Farooqi SH and Asrar R (eds), Complementary and Alternative Medicine: Nanotechnology-II. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 269-275. https://doi.org/10.47278/book.CAM/2024.479

INTRODUCTION

Hydrogel nanoparticles are vital in the fields of biomedical engineering and materials science, specifically in improving the process of wound healing. This novel method utilizes the distinct characteristics of hydrogels, which are composed of polymer networks that are highly hydrated and three-dimensional, and nanoparticles, which are minuscule particles with dimensions on the nanometer scale (Chakraborty et al., 2021). By amalgamating these two components, a potent synergy is produced, promoting effective and enhanced wound healing.

Wound healing is a key physiological process after tissue injury. This process involves a sequence of intricate biochemical events, such as hemostasis, inflammation, proliferation, and remodeling (Rodrigues et al., 2019). Historically, wound care techniques mostly involved simple bandages, stitches, and antibacterial substances. Nevertheless, these methods frequently demonstrate insufficiency in effectively handling intricate wounds such as diabetic ulcers, burns, and vast surgical sites. Fortunately, the advancement of hydrogel-based nanoparticles has arisen as an innovative answer. These nanoparticles are designed to overcome the limitations of traditional therapies by improving effectiveness, shortening recovery periods, and limiting the formation of scars.

Hydrogels are very suitable for wound healing applications due to their abundant water content, which closely mimics normal tissue (Ho et al., 2022). They provide a humid environment that promotes the movement and growth of cells, which is essential for the process of healing. Moreover, hydrogels can be precisely customized to fit the tissue at the wound site by adjusting their physical characteristics such as porosity and mechanical strength (Vedadghavami et al., 2017). This customization not only enhances the structural integrity of the wound but also allows for the regulated release of medicinal drugs. Integrating nanoparticles into hydrogels results in a distinct enhancement of functionality (Jiang et al., 2020). To improve the administration and effectiveness of medications, growth factors, and other bioactive compounds directly at the site of a wound, these particles can tightly interact with biological molecules due to their minute size (Rajendran et al., 2018). This allows the particles to improve the transport of these substances. This feature enables the use of precise therapy, where therapeutic substances are supplied in a regulated manner, minimizing general side effects and focusing treatment on the specific areas that require it the most. The utilization of nanocomposite hydrogels demonstrates the capacity to combine hydrogels with nanoparticles. These polymers serve as both carriers of drugs and reinforce the hydrogel matrix (Lavrador et al., 2021). By integrating silver nanoparticles, the hydrogel can obtain antibacterial characteristics, which are crucial for preventing infections in exposed wounds (Pangli et al., 2021). Moreover, bioactive nanoparticles can be utilized for the purpose of administering targeted growth factors, hence facilitating tissue regeneration and assisting in the process of healing. The synthesis of hydrogel-based nanoparticles is an intricate procedure that guarantees the durability, compatibility with organisms, and effectiveness of the result. Hydrogels are typically formed via different methods, including ionic cross-linking, covalent bonding, and freeze-thaw cycles (Hassan and Peppas, 2000). Nanoparticles can be included by either in situ polymerization or physical mixing (Li et al., 2017). It is imperative to carefully regulate these processes to create a composite that is not only safe for medical use but also efficient in delivering therapeutic outcomes. When it comes to the field of clinical applications, nanoparticles based on hydrogel have demonstrated promising results in the treatment of a variety of wounds. Regarding diabetic ulcers, which have poor healing, these composites can efficiently administer insulin or growth hormones to reinstate the normal healing process (Duarte et al., 2024). In burn instances, hydrogel-nanoparticle systems are utilized to provide cooling agents, pain-relieving drugs, and facilitate tissue regeneration (Mishra et al., 2017).

In addition to treating wounds, nanoparticles based on hydrogel have the potential to perform additional functions. These devices can be specifically engineered to incorporate sensors that observe various characteristics of the wound environment, such as the pH level and temperature (Dong and Guo, 2021). These sensors offer crucial data regarding the advancement of the healing process or the existence of an infection. The incorporation of diagnostic capabilities into a treatment matrix signifies a notable progress in personalized medicine for wound care. Nevertheless, despite the multitude of benefits and encouraging studies, there are obstacles and factors that must be dealt with as these materials go from the experimental stage to practical application in medical settings. Important considerations include the biocompatibility and biodegradability of materials used in the body, as they should not elicit negative immunological reactions or leave behind toxic substances after fulfilling their intended function. Furthermore, it is crucial to consider the potential to expand production and achieve cost efficiency to guarantee universal acceptance in clinical settings.

Section 1: Fundamentals of Wound Healing

Phases of Wound Healing

Wound healing is a complex and ever-changing process that takes place in multiple stages, including hemostasis, inflammation, proliferation, and remodeling (Rodrigues et al., 2019). Every stage is essential in the process of healing injured tissue and regaining its functionality. The procedure commences with hemostasis, which promptly takes place following the occurrence of skin injury. During this stage, the body's main objective is to stop the flow of blood. Blood arteries undergo vasoconstriction to decrease the volume of blood flowing through them, while platelets aggregate at the site of injury to form a clot (Hickman et al., 2018). This blood clot not only ceases additional blood loss but also serves as a temporary barrier against infection.

The inflammatory phase, which usually lasts for a few days, follows hemostasis. Pain, redness, and swelling at the location of the wound are the characteristics that define this phase. Neutrophils and macrophages, which are types of white blood cells, travel to the wound site to eliminate waste, bacteria, and injured tissue. These immune cells secrete many cytokines and growth factors that are crucial for the process of healing, thereby preparing for the subsequent phase (Matar et al., 2023).

The proliferation phase is the period during which the wound initiates the process of regenerating new tissue, typically commencing within a few days of the damage and enduring for several weeks. During this phase, important processes include angiogenesis, which is the development of new blood vessels, the generation of collagen and extracellular matrix by fibroblasts, and the growth of new epithelial tissue to cover the wound (Reinke and Sorg, 2012). The appearance of pink or red granulation tissue suggests a healthy healing process.

Ultimately, the remodeling phase can endure for a significant duration, ranging from several months to even years. During this phase, the recently developed tissue undergoes a gradual process of maturation and recovers its strength. Collagen fibers, which were originally deposited in a disorganized manner, undergo reorganization and cross-linking to enhance the skin's ability to withstand tension (Beldon, 2010). Consequently, the scar eventually becomes more even and less conspicuous, but it usually maintains a distinct texture and quality compared to the surrounding skin. These stages of wound healing collectively allow the efficient recovery of the skin from injury. Nevertheless, the efficacy and success of the treatment may differ based on factors such as the severity of the damage, the individual's overall health, and the quality of wound care provided.

Challenges in Wound Healing

Wound healing can be complicated by several circumstances, one of which is that of infection. Infections have the potential to extend the duration of the inflammatory phase and give rise to consequences, such as sepsis (Delano and Ward, 2016). Chronic diseases such as diabetes and vascular disorders can hinder the flow of blood, which is crucial for supplying the necessary oxygen and nutrients for tissue regeneration (Baltzis et al., 2014). Furthermore, inadequate nourishment can lead to insufficiencies in essential vitamins and proteins necessary for cellular regeneration, hence exacerbating the challenges of healing. Addressing wounds in elderly people is a notable difficulty due to their skin's diminished flexibility and cellular activity, which hampers the rate of healing. Inadequate wound care, including insufficient cleansing and dressing, might introduce or exacerbate issues. This underscores the significance of adequate medical supervision and patient instruction in the management of wounds.

Section 2: Overview of Hydrogels and Nanoparticles

Overview of Hydrogels

The ability of hydrogels, a versatile form of polymeric material, to retain considerable volumes of water within their three-dimensional networks is one of the most recognized characteristics of hydrogels. Consisting primarily of hydrophilic polymer chains, these gels can soak up water and retain a significant amount of fluid relative to their weight when dry, which makes them extremely absorbent (Guo et al., 2020). Hydrogels are created by either physically or chemically connecting molecules together, resulting in a structure that is stable and yet retains a soft and flexible nature, resembling natural tissue (Khandan et al., 2017). The distinctive amalgamation of these characteristics has resulted in a diverse array of uses in various domains, including biomedical engineering, drug delivery systems, tissue engineering, and agricultural goods. Moreover, their ability to interact harmoniously with living organisms and their ability to react to changes in their surroundings make them well-suited for developing highly sensitive and adaptable materials for a wide range of scientific and industrial applications.

Overview of Nanoparticles

The size of a nanoparticle is measured in nanometers, or billionths of a meter. Nanoparticles, which are usually between 1 and 100 nanometers in size, have distinct physical and chemical characteristics that significantly deviate from those of bigger materials (Tsuzuki, 2013). An example of a characteristic possessed by these entities is their heightened surface area to volume ratio, which amplifies their reactivity and strength. These characteristics make nanoparticles beneficial in health, electronics, and the environment (Singh et al., 2021). Nanoparticles are utilized in medicine for the purpose of delivering drugs to specific targets and for diagnostic imaging (Parveen et al., 2017). When it comes to environmental applications, nanoparticles help in the control of pollution and the purification of water (Pinto et al., 2020). In the field of electronics, they contribute to the creation of more efficient6 batteries and enhanced display technologies (Abdin et al., 2013). Scientific research is currently focused on manipulating and integrating nanoparticles into goods and processes. The aim is to utilize their potential while also addressing safety and environmental concerns.

Hydrogel nanoparticles, which are gaining popularity in biomedical fields like drug delivery, tissue engineering, and bio-sensing, exhibit distinct characteristics. Among these characteristics are a high-water content, biocompatibility, and environmental stimuli response capability. These nanoparticles can be synthesized using a range of materials, each possessing distinct benefits and difficulties. The main materials utilized comprise both organic and artificial polymers.

Section 3: Hydrogel based Nanoparticles in Wound Healing

Table 1: Composition and types of hydrogels forming polymers

Polymers	Types	Source	Properties	Applications	References
Natural Polymers	Alginate,	Extracted from brown seaweed	Highly biocompatible, gel-forming ability through ionic cross-linking with calcium ions.	Ideal for encapsulating proteins, cells, and drugs due to its mild gelation conditions.	(Tavakoli et al., 2023)
Natural Polymers	Chitosan	Derived from Chitin	Positively charged, biodegradable, and has antimicrobial properties	Its cationic nature allows it to form hydrogels through interactions with negatively charged molecules and polymers, useful in mucosal drug delivery.	(Tavakoli et al., 2023)
Synthetic Polymers	Polyethylene Glycol (PEG)		Non-toxic, non-immunogenic, and hydrophilic, which helps in evading the immune system	Often used as a hydrogel matrix or coating to enhance biocompatibility and reduce protein adsorption and cell adhesion.	(Xu et al., 2023)
Synthetic Polymers	Polylactic-co-glycolic Acid (PLGA):		It is biodegradable and the degradation rate can be adjusted by varying the ratio of PLA to PGA	Widely used in drug delivery systems due to its FDA-approved status and ability to degrade into lactic and glycolic acids, which are naturally metabolized by the body	(Xu et al., 2023)

a) Natural polymer, in general being more biocompatible than synthetic ones, can still change in composition and goods due to their natural origins (Bhatia and Bhatia, 2016).

b) Manipulation of Properties: Synthetic polymers provide greater precision in controlling the characteristics of nanoparticles, such as their degradation rates and mechanical strength. This control is essential for particular applications (Bhatia and Bhatia, 2016).

c) Immunogenicity and Toxicity: Synthetic polymers, particularly those that are not precisely engineered, may elicit an immunological reaction or exhibit hazardous effects. Conversely, natural polymers often have a reduced likelihood of causing an immune response (Bhatia and Bhatia, 2016).
d) Functionalization: Both types of polymers can be chemically modified to incorporate functional groups that can be used for targeting, imaging, or therapeutic applications.
The application and the features that are wanted are two of the most important factors to consider when choosing materials for nanoparticles based on hydrogel. Natural polymers are well-suited for applications that require sensitivity to biological systems, whereas synthetic polymers offer variety and durability for applications centered on engineering (Bhatia and Bhatia, 2016).

Mechanism of Action

Hydrogel nanoparticles have demonstrated significant potential around wound healing because of their distinct characteristics and mode of operation. The nanoparticles are predominantly composed of hydrophilic polymers that could absorb and hold substantial quantities of water, thereby generating an optimal moist environment for the healing of wounds (Stoica et al., 2020). The presence of moisture in this environment not only aids in maintaining cleanliness of the wound, but also facilitates the natural healing processes, such as the movement and growth of cells. The method by which hydrogel-based nanoparticles promote wound healing is complex and includes multiple factors. Firstly, they create a defensive barrier that covers the wound, protecting it from outside pollutants while yet allowing for the flow of gases, which is essential for cellular respiration and metabolism. Furthermore, these nanoparticles can be designed specifically to gradually release therapeutic medicines at the location of the wound (Choudhury et al., 2020). The controlled release mechanism can incorporate antibiotics to prevent infection, growth factors to facilitate tissue regeneration, or anti-inflammatory agents to diminish swelling and pain. Additionally, hydrogel-based nanoparticles possess the ability to react to environmental stimuli, such as variations in pH or temperature, thereby augmenting their efficacy (Lavrador et al., 2021). Inflamed wounds with decreased pH can cause nanoparticles to release more medication. This approach customizes the treatment to address the precise requirements of the wound, eliminating the need for any external interference. Finally, the physical characteristics of hydrogels enable them to conform to the wound surface, guaranteeing a uniform dispersion of the therapeutic substances. This adaptability also helps in absorbing wound exudate, which has a high concentration of proteolytic enzymes that might hinder the healing process. Hydrogel-based nanoparticles expedite and enhance the healing process by absorbing surplus fluids and inhibiting enzyme activity. Hydrogel-based nanoparticles greatly improve the healing process, making them a vital tool in advanced wound care management.

Section 4: Applications of Hydrogels Nanoparticles

Drug Delivery

Hydrogel nanoparticles offer an advanced method to wound management by enhancing the healing process by precise administration of medication. The nanoparticles are composed of polymeric networks that swell in water and enclose different medicinal substances, such as antibiotics, anti-inflammatory medicines, and analgesics. The hydrogel's structure is beneficial for wound healing because of its high concentration of water. It creates a damp environment which encourages tissue regeneration and minimizes scar formation. When administered to a wound, these nanoparticles slowly release their payload in reaction to stimuli at the wound site, such as changes in pH, fluctuations in temperature, or enzymes generated by bacteria during infections. The focused administration of this release optimizes the therapeutic impact of the medications while reducing overall contact and any adverse reactions (Divyashri et al., 2022). Hydrogel-based delivery of antibiotics efficiently targets and eliminates infection-causing bacteria at the location of the wound, hence facilitating the healing process. The local swelling and irritation that are caused by anti-inflammatory medications are reduced, which allows for stronger tissue repair. In addition, analgesic drugs can be targeted to the specific wounded location, offering both instant and long-lasting pain relief as the wound undergoes healing. This approach not only boosts the effectiveness of drug administration but also improves patient comfort and treatment results.

Growth Factor Delivery

Growth factors are vital for tissue regeneration. They facilitate the growth, specialization, and movement of cells, all of which are crucial for the restoration of injured tissues. These proteins function as signaling molecules that selectively attach to certain receptors on the surfaces of cells. This interaction triggers a series of biological reactions, ultimately resulting in the restoration and renewal of the tissue. The utilization of nanoparticles for the delivery of growth factors represents a notable breakthrough in the field of wound healing treatments. These nanoparticles can be manipulated to systematically release growth factors in a regulated manner. This guarantees the sustained presence of growth factors at the wound site for a longer duration. This targeted delivery system not only optimizes the utilization of growth factors but also mitigates their systemic exposure, thereby minimizing potential adverse effects (Gainza et al., 2015). Furthermore, nanoparticles can be engineered to safeguard growth ingredients against deterioration prior to reaching their intended destination. This enhances the overall therapeutic results. The use of nanoparticles facilitates the expedited distribution of growth factors, hence enhancing the process of wound healing. Consequently, it exhibits significant potential in the realm of regenerative medicine and tissue engineering.

Gene Therapy

Hydrogel-based nanoparticles show great potential in the field of gene therapy, specifically in improving wound healing processes by accurately managing gene expression. These nanoparticles are ideal for this purpose since they are biocompatible, have a high-water content, and can imitate the natural extracellular matrix. These conditions create an optimal environment for cellular contact and tissue integration. Hydrogel-based nanoparticles are designed to encapsulate different gene vectors, such as DNA, siRNA, or mRNA (Mo et al., 2021). Targeting genes that promote tissue regeneration, angiogenesis, and inflammation with these vectors is possible.

Section 5: Current Research and Case Studies

Recent Innovations

Hydrogel nanoparticles have made notable progress in wound healing because of their distinctive characteristics, which facilitate effective administration of drugs and regeneration of tissue. Recent investigations illustrate these materials' adaptability and efficacy. Aldakheel et al. (2023) formulated a hydrogel containing silver nanoparticles, which exhibited antibacterial characteristics and enhanced rates of wound closure. The study demonstrated that the hydrogel not only inhibited infection but also facilitated collagen deposition, a crucial process for tissue regeneration. (Liu et al., 2022) proposed a novel methodology employing temperature-responsive hydrogels. These hydrogels are designed to release therapeutic chemicals when exposed to the body's natural heat at the wound site, which helps improve the effectiveness of the healing process. The hydrogels demonstrated the ability to conform to the wound environment, retaining moisture and promoting expedited tissue regeneration. Furthermore, studies on hydrogels with dual functionality have demonstrated encouraging outcomes in diminishing inflammation and improving the healing process in persistent wounds. The hydrogels could provide growth factors and anti-inflammatory medicines at the same time. In summary, these improvements showcase the capacity of hydrogel-based nanoparticles to transform wound treatment. Their therapeutic options are focused, adaptable, and versatile.

Case Studies

Nanoparticles have been extensively studied for their ability to promote wound healing. They exhibit distinctive characteristics that enable the precise release of medications, safeguarding of active components, and focused administration. For example, silver nanoparticles have well-established antimicrobial properties that play a crucial role in preventing infections and facilitating the healing process. A study conducted by Paladini and Pollini in 2019 showed that dressings containing silver nanoparticles effectively decreased the presence of bacteria in chronic wounds. As a result, this resulted in accelerated wound healing and reduced healing durations in comparison to conventional dressings. Chitosan nanoparticles have been researched for their capacity to enhance blood clotting and support crucial cellular processes involved in wound healing. According to Yang et al.'s research from 2020, chitosan nanoparticles loaded with growth factors could boost the proliferation of fibroblasts and facilitate the deposition of collagen. Consequently, this results in accelerated healing of diabetic ulcers. Furthermore, the potential anti-inflammatory capabilities of gold nanoparticles have been investigated in the context of wound healing. (Leu et al., 2012) documented that the combination of gold nanoparticles with peptides promotes the polarization of macrophages towards a regenerative phenotype, which is essential for healing without scarring. This study also emphasized that these nanoparticles effectively decrease inflammation and promote tissue regeneration in acute wounds.

These case studies demonstrate the therapeutic efficacy of nanoparticles in the treatment of different types of wounds. They provide cutting-edge remedies by utilizing their antibacterial, anti-inflammatory, and regenerative characteristics. The safety profiles documented in these trials demonstrate little adverse responses, affirming that they are appropriate for usage in clinical settings. Every category of nanoparticle has demonstrated the ability to accelerate the healing process and enhance the quality of the recovered tissue. These factors indicate a positive outlook for the advancement of wound care management.

Section 6: Challenges and Future Perspectives

Biocompatibility and Toxicity

The introduction of nanoparticles into clinical applications poses substantial obstacles in terms of biocompatibility and potential toxicity, which might severely limit their practical utilization in the field of medicine. Nanoparticles, owing to their little size and substantial surface area in proportion to their volume, have the capacity to engage with biological systems in complicated manners that remain incompletely comprehended. These interactions can lead to unforeseen toxicological consequences, such as oxidative stress, inflammation, and even genotoxicity. Specifically, some metal oxide nanoparticles could generate reactive oxygen species, which can cause damage to biological structures, DNA, and proteins.

Additionally, because of their small size, nanoparticles can cross biological barriers including the placental and blood-brain barriers. The propensity of these substances to traverse barriers raises concerns over their potential systemic dissemination and accumulation in non-target tissues, hence emphasizing concerns about long-term toxicity. Another obstacle arises from the fluctuation in the physical and chemical characteristics of nanoparticles, encompassing dimensions, morphology, electrostatic charge, and surface covering. These characteristics can influence the biocompatibility of nanoparticles. Furthermore, a significant number of nanoparticles tend to clump or interact with serum proteins, resulting in modifications in their intended function and distribution within the body. Hence, it is imperative to conduct meticulous evaluations of the safety characteristics of nanoparticles via extensive preclinical investigations prior to considering them appropriate for clinical use. The requirement for customized toxicity assessment techniques adds extra complexity to the process of incorporating nanoparticles into clinical practice, highlighting the intricacies required in utilizing their promise in medicine.

Future Prospect

Hydrogel nanoparticles exhibit significant potential in the field of medicine, particularly in targeted drug administration, regenerative medicine, and biosensing. However, in order to maximize their potential, future research should prioritize enhancing the accuracy and regulation of drug release mechanisms. The advancement of stimuli-responsive hydrogels capable of reacting to specific biological signals has the potential to enhance the effectiveness of treatment while minimizing adverse reactions. Furthermore, it is imperative to improve the biocompatibility and biodegradability of hydrogel nanoparticles to guarantee their secure incorporation into the body. Another potential avenue is the incorporation of hydrogel nanoparticles into medical imaging systems, allowing for the live monitoring of drug administration and tissue regeneration procedures. Research should also investigate the scalability of the production process to enable the transfer from laboratory research to clinical and commercial applications. Understanding the interactions between hydrogel nanoparticles and the immune system has the potential to enable the development of nanoparticles that can either avoid being detected by the immune system or regulate immunological responses for therapeutic applications. The exploration of these research lines has the potential to greatly broaden the range of uses for hydrogel-based nanoparticles in the field of medicine, resulting in the development of more advanced therapies for various diseases.

Conclusion

Hydrogel-based nanoparticles hold significant potential in the field of enhanced wound healing technology. These nanocomposites combine hydrogels' biocompatibility, moisture retention, and mechanical support with nanoparticles' targeted drug delivery, antibacterial activity, and increased cellular interactions. Preclinical investigations have shown that advanced formulations have a considerable capacity to stimulate angiogenesis, regulate inflammatory responses, and improve cellular proliferation and migration. It has proven possible to produce significant improvements in wound closure rates, decreased infection risks, and quicker tissue regeneration with the incorporation of bioactive molecules into these matrices. Furthermore, the hydrogel-nanoparticle systems could be customized, enabling the creation of specific therapeutic strategies for various types and levels of wound severity. Future research should prioritize the optimization of these systems for clinical application, assuring scalability, and undertaking comprehensive in vivo investigations to evaluate their usefulness and safety. This novel strategy has the potential to revolutionize wound care and improve patient outcomes, and it has a great deal of promise in this department.

REFERENCES

Abdin, Z., Alim, M. A., Saidur, R., Islam, M. R., Rashmi, W., Mekhilef, S., and Wadi, A. (2013). Solar energy harvesting with the application of nanotechnology. *Renewable and Sustainable Energy Reviews*, *26*, 837-852.

Aldakheel, F. M., Mohsen, D., El Sayed, M. M., Alawam, K. A., Binshaya, A. S., and Alduraywish, S. A. (2023). Silver nanoparticles loaded on chitosan-g-PVA hydrogel for the wound-healing applications. *Molecules*, *28*(7), 3241.

Baltzis, D., Eleftheriadou, I., and Veves, A. (2014). Pathogenesis and treatment of impaired wound healing in diabetes mellitus: new insights. *Advances in Therapy*, *31*, 817-836.

Beldon, P. (2010). Basic science of wound healing. *Surgery (Oxford)*, *28*(9), 409-412.

Bhatia, S., and Bhatia, S. (2016). Natural polymers vs synthetic polymer. *Natural Polymer Drug Delivery Systems: Nanoparticles, Plants, and Algae*, 95-118.

Chakraborty, A., Roy, A., Ravi, S. P., and Paul, A. (2021). Exploiting the role of nanoparticles for use in hydrogel-based bioprinting applications: Concept, design, and recent advances. *Biomaterials Science*, *9*(19), 6337-6354.

Choudhury, H., Pandey, M., Lim, Y. Q., Low, C. Y., Lee, C. T., Marilyn, T. C. L., Loh, H. S., Lim, Y. P., Lee, C. F., and Bhattamishra, S. K. (2020). Silver nanoparticles: Advanced and promising technology in diabetic wound therapy. *Materials Science and Engineering: C*, *112*, 110925.

Delano, M. J., and Ward, P. A. (2016). The immune system's role in sepsis progression, resolution, and long-term outcome. *Immunological Reviews*, *274*(1), 330-353.

Divyashri, G., Badhe, R. V., Sadanandan, B., Vijayalakshmi, V., Kumari, M., Ashrit, P., Bijukumar, D., Mathew, M. T., Shetty, K., and Raghu, A. V. (2022). Applications of hydrogel-based delivery systems in wound care and treatment: an up-to-date review. *Polymers for Advanced Technologies*, *33*(7), 2025-2043.

Dong, R., and Guo, B. (2021). Smart wound dressings for wound healing. *Nano Today*, *41*, 101290.

Duarte, J., Mascarenhas-Melo, F., Pires, P. C., Veiga, F., and Paiva-Santos, A. C. (2024). Multifunctional hydrogels-based therapies for chronic diabetic wound healing. *European Polymer Journal*, 113026.

Gainza, G., Villullas, S., Pedraz, J. L., Hernandez, R. M., and Igartua, M. (2015). Advances in drug delivery systems (DDSs) to release growth factors for wound healing and skin regeneration. *Nanomedicine: Nanotechnology, Biology and Medicine*, *11*(6), 1551-1573.

Guo, Y., Bae, J., Fang, Z., Li, P., Zhao, F., and Yu, G. (2020). Hydrogels and hydrogel-derived materials for energy and water sustainability. *Chemical Reviews*, *120*(15), 7642-7707.

Hassan, C. M., and Peppas, N. A. (2000). Structure and applications of poly (vinyl alcohol) hydrogels produced by conventional crosslinking or by freezing/thawing methods. *Biopolymers· PVA Hydrogels, Anionic Polymerisation Nanocomposites*, 37-65.

Hickman, D. A., Pawlowski, C. L., Sekhon, U. D., Marks, J., and Gupta, A. S. (2018). Biomaterials and advanced technologies for hemostatic management of bleeding. *Advanced Materials*, *30*(4), 1700859.

Ho, T.-C., Chang, C.-C., Chan, H.-P., Chung, T.-W., Shu, C.-W., Chuang, K.-P., Duh, T.-H., Yang, M.-H., and Tyan, Y.-C. (2022). Hydrogels: Properties and applications in biomedicine. *Molecules*, *27*(9), 2902.

Jiang, Y., Krishnan, N., Heo, J., Fang, R. H., and Zhang, L. (2020). Nanoparticle–hydrogel superstructures for biomedical applications. *Journal of Controlled Release*, *324*, 505-521.

Khandan, A., Jazayeri, H., Fahmy, M. D., and Razavi, M. (2017). Hydrogels: Types, structure, properties, and applications. *Biomat Tiss Eng*, *4*(27), 143-169.

Lavrador, P., Esteves, M. R., Gaspar, V. M., and Mano, J. F. (2021). Stimuli-responsive nanocomposite hydrogels for biomedical applications. *Advanced Functional Materials*, *31*(8), 2005941.

Leu, J.-G., Chen, S.-A., Chen, H.-M., Wu, W.-M., Hung, C.-F., Yao, Y.-D., Tu, C.-S., and Liang, Y.-J. (2012). The effects of gold nanoparticles in wound healing with antioxidant epigallocatechin gallate and α-lipoic acid. *Nanomedicine: Nanotechnology, Biology and Medicine*, *8*(5), 767-775.

Li, X., Sotto, A., Li, J., and Van der Bruggen, B. (2017). Progress and perspectives for synthesis of sustainable antifouling composite membranes containing in situ generated nanoparticles. *Journal of Membrane Science*, *524*, 502-528.

Liu, H., Du, C., Liao, L., Zhang, H., Zhou, H., Zhou, W., Ren, T., Sun, Z., Lu, Y., and Nie, Z. (2022). Approaching intrinsic dynamics of MXenes hybrid hydrogel for 3D printed multimodal intelligent devices with ultrahigh superelasticity and temperature sensitivity. *Nature Communications*, *13*(1), 3420.

Matar, D. Y., Ng, B., Darwish, O., Wu, M., Orgill, D. P., and Panayi, A. C. (2023). Skin inflammation with a focus on wound healing. *Advances in Wound Care*, *12*(5), 269-287.

Mishra, B., Upadhyay, M., Reddy Adena, S., Vasant, B., and Muthu, M. (2017). Hydrogels: an introduction to a controlled drug delivery device, synthesis and application in drug delivery and tissue engineering. *Austin Journal Biomedicine Eng*, *4*(1), 1037-1049.

Mo, F., Jiang, K., Zhao, D., Wang, Y., Song, J., and Tan, W. (2021). DNA hydrogel-based gene editing and drug delivery systems. *Advanced Drug Delivery Reviews*, *168*, 79-98.

Paladini, F., and Pollini, M. (2019). Antimicrobial silver nanoparticles for wound healing application: progress and future trends. *Materials*, *12*(16), 2540.

Pangli, H., Vatanpour, S., Hortamani, S., Jalili, R., and Ghahary, A. (2021). Incorporation of silver nanoparticles in hydrogel matrices for controlling wound infection. *Journal of Burn Care and Research*, *42*(4), 785-793.

Parveen, S., Misra, R., and Sahoo, S. K. (2017). Nanoparticles: a boon to drug delivery, therapeutics, diagnostics and imaging. *Nanomedicine in Cancer*, 47-98.

Pinto, M., Ramalho, P., Moreira, N., Gonçalves, A., Nunes, O., Pereira, M., and Soares, O. (2020). Application of magnetic nanoparticles for water purification. *Environmental Advances*, *2*, 100010.

Rajendran, N. K., Kumar, S. S. D., Houreld, N. N., and Abrahamse, H. (2018). A review on nanoparticle based treatment for wound healing. *Journal of Drug Delivery Science and Technology*, *44*, 421-430.

Reinke, J., and Sorg, H. (2012). Wound repair and regeneration. *European Surgical Research*, *49*(1), 35-43.

Rodrigues, M., Kosaric, N., Bonham, C. A., and Gurtner, G. C. (2019). Wound healing: a cellular perspective. *Physiological Reviews*, *99*(1), 665-706.

Singh, V., Yadav, S. S., Chauhan, V., Shukla, S., and Vishnolia, K. K. (2021). Applications of nanoparticles in various fields. *Diagnostic Applications of Health Intelligence and Surveillance Systems*, 221-236.

Stoica, A. E., Chircov, C., and Grumezescu, A. M. (2020). Nanomaterials for wound dressings: an up-to-date overview. *Molecules*, *25*(11), 2699.

Tavakoli, M., Labbaf, S., Mirhaj, M., Salehi, S., Seifalian, A. M., and Firuzeh, M. (2023). Natural polymers in wound healing: From academic studies to commercial products. *Journal of Applied Polymer Science*, *140*(22), e53910.

Tsuzuki, T. (2013). Properties of Nanoparticulate Materials. *Nanotechnology Commercialization*, 1.

Vedadghavami, A., Minooei, F., Mohammadi, M. H., Khetani, S., Kolahchi, A. R., Mashayekhan, S., and Sanati-Nezhad, A. (2017). Manufacturing of hydrogel biomaterials with controlled mechanical properties for tissue engineering applications. *Acta Biomaterialia*, *62*, 42-63.

Xu, R., Fang, Y., Zhang, Z., Cao, Y., Yan, Y., Gan, L., Xu, J., and Zhou, G. (2023). Recent advances in biodegradable and biocompatible synthetic polymers used in skin wound healing. *Materials*, *16*(15), 5459.

Yang, S., Li, X., Liu, P., Zhang, M., Wang, C., and Zhang, B. (2020). Multifunctional chitosan/polycaprolactone nanofiber scaffolds with varied dual-drug release for wound-healing applications. *ACS Biomaterials Science and Engineering*, *6*(8), 4666-4676