Contents list available at Science Letters

Science Letters

journal homepage: http://www.scienceletters.org/

Applications of Nanomaterial in Medicine and Wound Healing

Anoop Sharma, Lokesh Verma, Vishal Sharma, Charu Rajpal*

Department of Biotechnology, Faculty of Engineering and Technology, Manav Rachna International Institute of Research and Studies, Faridabad, Haryana, India

ARTICLE INFO

Article History
Received 10 January 2020
Revised 1 May 2020
Accepted 9 May 2020
Available Online 10 May 2020

Keywords:
Colloidal agents,
hemostasis,
keratinocytes,
Fibrin,
scaffolds,
chitosan,
nanofibers,
cytotoxicity,
biocompatibility.

ABSTRACT

Nanomaterial can be defined as the "material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale", with nanoscale defined as the "length range approximately from 1 nm to 100 nm". Over a period of time a number of innovative therapies have been emerged in the field of wound healing. Nanostructured systems have been used to improve wound healing at different stages. The drug itself may be formulated at a nanoscale such that it can function as its own "carrier" or nanomaterials may be used as drug delivery vehicles. If we observe the latest advancements on innovative nano-based organic and inorganic materials we find that these novel drug delivery systems possess high stability, large surface area and tunable compositions and have demonstrated their wound-healing properties using in vitro and in vivo models. The nanotechnology-based platforms are an exciting emerging field with many applications on wound healing in the last decade. Numerous investigators have designed several inorganic and metal nanoparticles including magnetic, silica silver, nano graphene oxide scaffolds, copper and gold terbium oxide, cerium and titanium dioxide, etc. and demonstrated their wound healing properties. Hence nanomaterials play a vital role in tackling with the wound healing process tremendously.

1. Introduction

Nanomaterial can be defined as the "material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale", with nanoscale defined as the "length range approximately from 1 nm to 100 nm". This includes both nano-objects, which are discrete pieces of material, and nanostructured materials, which have internal or surface structure on the nanoscale; a nanomaterial may be a member of both these categories (Baran-2018; Sari and Piyal 2019).

Current products, devices and techniques are failed to respond to the need of efficient recovery while preserving skin function. Due to this reason wound healing has been an intense area of research. Ideal healing system should be able to swift the wound closure, reduce infection, stimulate healing mechanisms, mimic the extracellular matrix feature, moisture the wound, and lessen scar formation. A new chapter was opened by Nanotechnology through the application of nanomaterials in wound healing treatment offering solutions for the quickening of wound healing, as well as presenting unique properties as bactericidal agents (Kathawala *et al.*, 2019; Singh and Seed 2017) .

Contemporary treatments denote the classic approach to wound management. Colloidal agents, antiseptics and antibacterials are used by this approach in order to prevent infections. Recently, several kinds of approaches have been explored for the production of organic nanoparticles or synthesis of inorganic nanoparticles. In the last case, Physical and chemical methods like laser ablation, pyrolysis, lithography, chemical vapor deposition, sol–gel techniques and electro-deposition, were included by the synthesis in the last case which are very expensive and hazardous. In an effort to develop a low-cost, eco-friendly and energy-efficient approach, researchers have exploited the potential of much greener methods using microbial systems and plant systems (Kabashin *et al.*, 2019; Manawi *et al.*, 2018). Other impact will be gained by Innovative nano-based therapies if

*Corresponding Author: Charu Rajpal
E-mail Address: rajpalcharu5@gmail.com
DOI: 10.46890/SL.2020.v01i03.005

we use simple preparation methods. In the wound healing research, formulation development is based on three main steps: the assessment of in vitro biological compatibility, the in vitro evaluation of anti-microbial activity and the in vivo effectiveness confirmation. Keratinocytes and fibroblasts isolated from mice or humans are popular in vitro models to test formulation skin compatibility. Anti-bacterial effect is an important property to assess in wound-healing solutions. Mouse and rat models, chiefly incisional models are readily available and cost effective systems for pre-clinical evaluation of wound treatment. By means of scientific experiments, synergic effects have been achieved through the link of different therapeutic nano-based approaches expanding the range of opportunities for nanomaterials (Shanmugapriya and Kang 2019; Arafa *et al.,* 2018).

Wounds have an immense financial burden on health-care systems worldwide. Chronic wounds not only contribute major costs to health-care systems but also have devastating consequences for patients. It has been noticed that the number of recent publications regarding the potential application of nanomaterials in wound healing has increased; however, there is some concern on toxicity acceptability and efficacy when compared to conventional treatment options. This review emphasizes the importance of these nanomaterial-based approaches in wound management, encouraging scientists to expand the studies on this type of materials based on multidisciplinary collaboration among experts in materials science and engineering, biotechnology, and medicine for their faster clinical application (Jakovljevic *et al.,* 2018; Matlin,*et al.,* 2018).

As we know, wound healing is a complex four-staged process which involves hemostasis, inflammation, proliferation and remodeling. It is critical to visualize the requirements of damaged tissue and fulfill the probability for regeneration. The rational of each material strongly depends on the phase but also the duration of the therapeutic effect, dose, deepness and mechanism of action. The different nano-based approaches investigated for wound healing application. A variety of natural and synthetic materials and their combinations have been engineered for individual pathways in wound healing. Herein, natural polymers have been applied to a myriad of wound healing strategies due to their prominent biological functions. Collagen is considered as an ideal healing support with outstanding and quite strong mechanical properties as it can provide a moist and protect environment to the tissues. Fibrin is another example; it captures platelets to form a primary clot and reduce bleeding. Silk fibroin is also used due to its mechanical robustness. Keratin is another example of nanomaterial broadly used in wound healing (Nguyen *et al.,* 1933; Zhou *et al.,* 2018).

Usages of nanomaterials create massive potential to promote self-healing mechanisms that can mimic regeneration. However, the heterogeneous nature of the wounded tissues requires a better understanding of the underlying mechanisms and cellular cascades to personalize those nanomaterials for different wound healing applications. Metal nanoparticles such as silver, gold and zinc possess outstanding properties such as stimulation of wound healing and antibacterial activity, making them good candidates for integration in wound dressings. Silver nanoparticles can modify anti-inflammatory cytokine release and promote rapid wound closure without increasing scarring. They can also stimulate epidermal re-epithelization through the creation of keratinocytes. It also noticed that this last effect is dose-dependent. If we look at the gold nanoparticles, they have ability to promote healing and inhibit microbial colonization. Zinc oxide nanoparticles also represent a reliable antibacterial agent, by inducing bacterial cell membrane perforations and when they are incorporated in hydrogel-based wound dressings, the overall contact time is generally increased, promoting keratinocyte migration, thus improving re-epithelialization. In addition, polymeric nanoparticles (e.g., chitosan, alginate, cellulose, hyaluronic acid) as wound dressings or as delivery vectors show good antibacterial and re-epithelialization properties. Chiefly, alginate has a high-water absorptivity and therefore alginate can easily create a moist wound environment and limits wound exudation. Due to its hygroscopicity, hyaluronic acid regulates cell adhesion and attachment during wound healing. It is described that hyaluronan oligosaccharides stimulated endothelial cell proliferation, motility and angiogenesis, through enhanced expression of vascular endothelial growth factor. In addition, cellulose accelerates wound closure through multiple growth factors such as epidermal growth factor and basic fibroblast growth factor that are released locally. Schematic representation of the nanomaterials employed in wound healing in each type of healing phase (Hemostasis, Inflammation, Proliferation, and Remodeling). The rational for using each material strongly depends on the phase but also the duration of the therapeutic effect, dose, deepness and mechanism of action. NPs, nanoparticles

Finally, another option for wound healing could be the production of scaffolds that mimic the properties of extracellular matrix. Here, polymeric nanofibers can improve adherence and development of fibroblasts in wounds (Ahn *et al.,* 2019; Joseph *et al.,* 2019; Dash *et al.,* 2018).

Micelles have a hydrophobic inner core surrounded by hydrophilic shell in aqueous solution, making them an ideal deliver candidate for both hydrophilic and hydrophobic agents. Polymeric micelles present good colloidal stability, greater cargo capacity, biocompatibility, non-toxicity, and controlled drug release.

Another example was based on the encapsulation of silver sulfadiazine in chitosan oleate micelles. In this case, this association proved not only to increase drug concentrations, surface to volume ratio and dispersion but also to protect human cells against the drug's cytotoxic effects without affecting its antimicrobial properties.

Recently, an in vitro study in diabetic rats evaluated the anti-diabetic and wound healing effects of Cur-loaded mixed polymeric micelles based on chitosan, alginate, maltodextrin, Pluronic F127, Pluronic P123, and Tween 80. It was concluded that the developed formulations with highest amounts of Cur (higher than 48.74 ppm) could accelerate the wound healing response showing visible improvement in wound closure on the 14th day and reducing the elevated blood glucose level and lipid profile, clearly demonstrating its potential as diabetes-controlling and wound healing agent (Vigani *et al.,* 2019; Alberti *et al.,* 2017).

2. Conclusion

The nanotechnology-based platforms is an exciting emerging field with many applications on wound healing in the last decade considering the remarkable impact and number of publications regarding this context. Numerous investigators have designed several inorganic and metal nanoparticles (including magnetic, silica silver, nano graphene oxide scaffolds, copper and gold terbium oxide, cerium and titanium dioxide, etc.) and demonstrated their wound healing properties. Recently, organic nanomaterials mainly, lipid and polymeric based systems have also shown great benefits on treating different wounds and achieving tissue repair as they play significant roles in tissue adhesion and differentiation as well as in delivery and targeting of drugs, proteins, growth factors, stem cells, and so on. Wound healing is a complex process and also it is quite expensive in terms of its methods of treatment and the medicine used for it. Nanoparticles have really played a tremendous role to make the wound healing process easy and effective. Researchers have done many experiments in order to make the wound healing process fast and result oriented.

References

[1] Baran, A. (2018). Legal aspects of patenting nanotechnological inventions. *Ius Novum*, *12*(3), 100-116.

[2] Sarı, G., & Piyal, B. (2019). Nanomaterials and Their Effects on Health. *Istanbul Medical Journal= Istanbul Tip Dergisi*, *20*(6), 497.

[3] Kathawala, M. H., Ng, W. L., Liu, D., Naing, M. W., Yeong, W. Y., Spiller, K. L., ... & Ng, K. W. (2019). Healing of chronic wounds: an update of recent developments and future possibilities. *Tissue Engineering Part B: Reviews*, *25*(5), 429-444.

[4] Singh, V. K., & Seed, T. M. (2017). A review of radiation countermeasures focusing on injury-specific medicinals and regulatory approval status: part I. Radiation sub-syndromes, animal models and FDA-approved countermeasures. *International journal of radiation biology*, *93*(9), 851-869.

[5] Kabashin, A. V., Singh, A., Swihart, M. T., Zavestovskaya, I. N., & Prasad, P. N. (2019). Laser-processed nanosilicon: a multifunctional nanomaterial for energy and healthcare. *ACS nano*, *13*(9), 9841-9867.

[6] Manawi, Y. M., Samara, A., Al-Ansari, T., & Atieh, M. A. (2018). A review of carbon nanomaterials' synthesis via the chemical vapor deposition (CVD) method. *Materials*, *11*(5), 822.

[7] Shanmugapriya, K., & Kang, H. W. (2019). Engineering pharmaceutical nanocarriers for photodynamic therapy on wound healing. *Materials Science and Engineering: C*, *105*, 110110.

[8] Arafa, M. G., El-Kased, R. F., & Elmazar, M. M. (2018). Thermoresponsive gels containing gold nanoparticles as smart antibacterial and wound healing agents. *Scientific reports*, *8*(1), 1-16.

[9] Jakovljevic, M., Jurisevic, M., & Mouselli, S. (2018). Antibiotic resistance in Syria: a local problem turns into a global threat. *Frontiers in public health*, *6*, 212.

[10] Matlin, S. A., Depoux, A., Schütte, S., Flahault, A., & Saso, L. (2018). Migrants' and refugees' health: towards an agenda of solutions. *Public Health Reviews*, *39*(1), 1-55.

[11] Nguyen, T. P., Nguyen, Q. V., Nguyen, V. H., Le, T. H., Huynh, V. Q. N., Vo, D. V. N., ... & Le, Q. V. (2019). Silk fibroin-based biomaterials for biomedical applications: a review. *Polymers*, *11*(12), 1933.

[12] Zhou, Z., Zhang, S., Cao, Y., Marelli, B., Xia, X., & Tao, T. H. (2018). Engineering the future of silk materials through advanced manufacturing. *Advanced Materials*, *30*(33), 1706983.

[13] Ahn, S., Ardoña, H. A. M., Campbell, P. H., Gonzalez, G. M., & Parker, K. K. (2019). Alfalfa nanofibers for dermal wound healing. *ACS applied materials & interfaces*, *11*(37), 33535-33547.

[14] Joseph, B., Augustine, R., Kalarikkal, N., Thomas, S., Seantier, B., & Grohens, Y. (2019). Recent advances in electrospun polycaprolactone based scaffolds for wound healing and skin bioengineering applications. *Materials Today Communications*, *19*, 319-335.

[15] Dash, B. C., Xu, Z., Lin, L., Koo, A., Ndon, S., Berthiaume, F. & Hsia, H. (2018). Stem cells and engineered scaffolds for regenerative wound healing. *Bioengineering*, *5*(1), 23.

[16] Vigani, B., Rossi, S., Sandri, G., Bonferoni, M. C., Caramella, C. M., & Ferrari, F. (2019). Hyaluronic acid and chitosan-based nanosystems: A new dressing generation for wound care. *Expert opinion on drug delivery*, *16*(7), 715-740.

[17] Alberti, Thais, Daniela S Coelho, Ana Voytena, Heloisa Pitz, Manuel de Pra, Leticia Mazzarino, Shirley Kuhnen, Rosa M Ribeiro-do-Valle, Marcelo Maraschin, and Beatriz Veleirinho. "Nanotechnology: a promising tool towards wound healing." *Current pharmaceutical design* 23, no. 24 (2017): 3515-3528.