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Nanotechnology in Wound Healing- A Review

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Abstract

Wound healing is a natural and well-structured process, where several factors inhibited in the sequence of healing process. Nanotechnology has emerged as a major platform to treat acute and chronic wounds. Numerous nanotechnology based drug delivery systems have been proposed demonstrating with multiple functions and unique properties associated with mechanism of wound healing. This mini review focus on the current trends and applications of nanotechnology to promote wound healing process.

Keywords: Nanoparticles; Nanotechnology; Wound healing; Nanofibers; Antioxidants

Introduction

Wound may occur on multiple occasions in a person's lifetimes. In worldwide around one billion people are likely to suffer acute and/or chronic wounds. Wound healing is a normal but a complex biological process which mainly involves four different phases (hemostasis, inflammation, proliferation, maturation [1]. Hemostatic events occur immediately after injury. The inflammatory phase begins immediately after injury and may continue for up to 6 days [2]. The proliferation phase is characterized by the beginning of angiogenesis and the formation of the extra cellular matrix (ECM). The maturation phase usually begins 3 weeks after injury and can take up to 2 years to complete [3].

Nanotechnology, a rapidly growing and challenging research field worldwide. Nanomaterials have gained access into daily life, including healthcare and biomedical applications. Numerous products emerging from the application of nanotechnology to the science of wound healing is currently under investigation. Nanomaterials have attracted considerable attention in research due to their interesting physical and chemical properties [4]. The study of biomaterials on wound healing has gained special attention because of their unique chemical, physical, and biological properties. In this chapter, we review the various types of nanoparticles that promotes wound healing process (Figure 1).

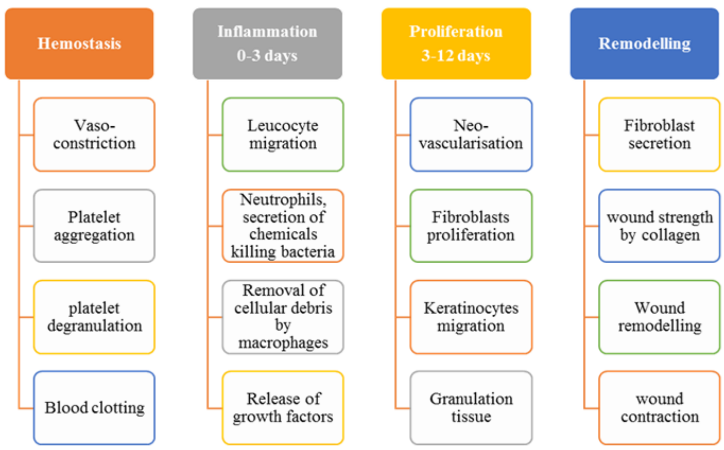

Figure 1: Phases and events of wound healing process

Silver nanoparticles (AgNPs)

Silver has been commonly used as an anti-bacterial agent for the treatment of burns, open wounds, and several chronic infected wounds [5]. The role of AgNPs and their anti-microbial activity was also indirectly observed in numerous studies [6-11]. The topical administration of AgNPs shows efficient anti-microbial activity compared to test formulations by interacting with sulfur and phosphorus containing proteins present in bacteria membranes. AgNPs are more efficient even at a very low concentration. AgNPs have shown antimicrobial activity against strains of *B. subtilis, E. coli*, and *S. aureus* and other skin pathogens [12,13].

Gold nanoparticles (AuNPs)

AuNPs are promising biologically active materials and cancer diagnostic agents Leu et al. [14]. Showed that combining AuNPs with antioxidants rich compounds (epigallocatechin gallate and α-lipoic acid) significantly accelerated wound healing in mice [15]. The results indicated that the topical application of the product accelerated normal and diabetic wound healing because of the triggering properties of anti-oxidant agents and AuNPs [16] (Figure 2).

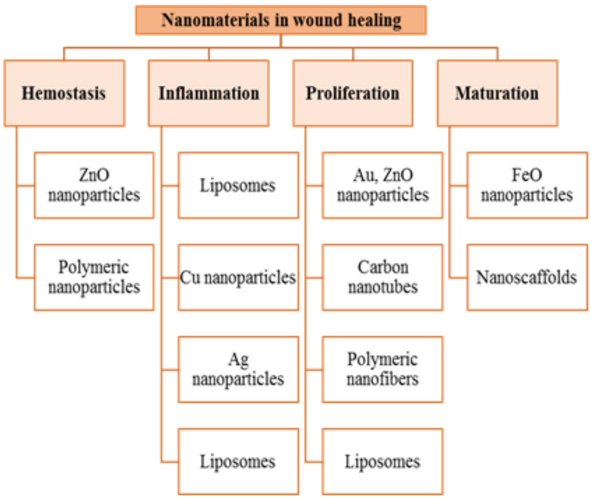

Figure 2: Nanomaterials in different stages of wound healing

Copper (Cu), titanium Dioxide (TiO_2) and zinc Oxide (ZnO) nanoparticles

CuNPs are effective against *E. coli* and *S. aureus*, among other skin pathogens found in diabetic foot-ulcer and burn wound infections [17-19]. TiO_2 and ZnO nanoparticles are widely used in the cosmetic and pharmaceutical industry as UV protectors and also as a wound healing material [20]. The formulation of TiO_2 nanoparticles containing *Origanum vulgare* was evaluated using the excision wound model revealed significant wound healing activity [21].

Tissue engineered nanofibers and nanoparticles

The engineered tissue regeneration technique involves the construction of a biocompatible scaffold combined with bioactive molecules, regenerates/ repairs damaged skin tissues. Electro spun nanofibers enables good permeability for oxygen and water because of its large surface area and porosity which protects the wound from bacterial infection. This feature shows electrospun nanofibers can be a suitable nanomaterial for wound dressing, especially for diabetic ulcers and burns. This technique can provide both degradable and non-degradable nanofibers for two-dimensional Nano fibrous sheets.

Both sorts of biomaterials (Chitosan, Collagen, and Poly lactic acid) have been tested animals showing an increased rate of wound contraction and epithelialization [22], and also reported to have good anti-bacterial activity [23]. Numerous strategies of nanofibrous constructs with a 3D profile have been developed to improve cell infiltration, showed promising results [24]. A cost-effective composite proposed by Chong et al. consisting of a nanofibrous scaffold directly electrospun onto a polyurethane dressing for dermal wound healing [25]. This tissue engineering in vivo approach offers a technology to promote wound healing.

Tissue engineered nanoparticles can be found as polymer and carbon-matrix nano composites with montmorillonite clays, carbon nanotubes and graphene and sunscreens [26]. Carbon nanotubes mainly used to develop nanocarriers, nano sensors and smart material for tissue engineering purposes that promotes wound healing process [27].

Antioxidant and Antibiotics based Nanoparticles

NO (Nitric oxide), a powerful free radical and also a wound healing agent in which its activity is observed during the inflammatory and proliferative phase of wound healing. The antibacterial activities of the NO designed nanoparticles enhance the wound healing process [28-30]. Antimicrobial

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peptides formulated with gold Nano dots inhibit the growth of multi drug-resistant bacteria pathogen and also promotes wound healing in animal model [31]. Although there has been considerable development in the areas of synthetic drug chemistry, antibiotics still occupy an important place in drug development therapy [32]. Antibiotics based nanoparticles are used to treat the diabetic foot ulcer [33]. The drug delivery of curcumin using various nanomaterial-based vehicles has been investigated in wound healing given its anti-biotic, anti-viral and antioxidant properties [34,35].

Conclusion

Today, nanotechnology is overcoming the barrier of commonly used therapies for treating acute and chronic wounds such as burns and diabetic foot ulcers. The therapeutic use of nanotechnology based drugs in the near future should be widely spread because of its biodegradable and non-toxic properties. Nanoparticles-based drug delivery systems have high therapeutic potentials of biological as well as synthetic molecules. However the promising outcome brought by new nanotechnology based drugs, the real therapeutic effects of nanomaterials have to be analyzed, evaluated and examined carefully before it involves in clinical practice.

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