Chapter

Bionanomaterials: Advancements in Wound Healing and Tissue Regeneration

Priyanka Chhabra and Kajol Bhati

Abstract

Abnormal wound healing represents a major healthcare issue owing to upsurge number of trauma and morbid physiology which ultimately posed a healthcare burden on patient, society and health care organization. A wound healing is a complex process so effective management of chronic wounds is often hard. Recently in addition to many conventional wound treatment's advances in bionanomaterial are attaining much attention in wound care and skin tissue engineering. Bionanomaterials are biomolecule-based nanocomposite synthesized by plants, microbes and animals which possess high degree of biocompatibility, biodegradability, non-toxicity and bioactive assets. Bioactive assets like antimicrobial, immune modulatory, cell proliferation and angiogenesis of biomolecules forms fortunate microenvironment for the wound healing process. Nature has provided us with a significant set of biomolecules like chitosan, hyaluronic acid, collagen, cellulose, silk fucoidan etc. have been exploited to construct engineered bionanomaterials. These biopolymeric nanomaterials are currently researched comprehensively as they have higher surface to volume ratio and high chemical affinity showing a promising augmentation of deadly wounds. In this chapter we aimed to highlight the biological sources and bioengineering approaches adapted for biopolymers so they facilitate wound healing process.

Keywords: Biopolymers, Bionanomaterials, wound healing, nanocomposites, tissue engineering

1. Introduction

Wound healing process involves a series of intricate cellular events involving organized and regulated events such as hemostasis, inflammation, cell migration, proliferation, and remodeling [1]. Upon the onset of the inflammatory response, fibroblasts begin to proliferate and migrate into the wound area which involve the interaction and participation of different types of growth factors, cells and supporting cell-ECM interaction and ultimately reconstitute the wounded skin after injury [2]. Sometimes the normal wound healing process gets altered due to morbid physiology for example, in case of burns, accidents, diabetic foot ulcers, wound healing is delayed. This leads to the compromised mobility, amputation of limbs, even death, which cause the foremost social, and financial burden for decades [3]. Nowaday's nanotechnology and nanomedicine has created a new way to treat acute and chronic wound which ultimately encourage tissue regeneration and remolding. Indeed, many research studies and clinical trials data have already been published [4]. This chapter summarized the systematic evaluation of different types of bionanomaterials which promote wound healing process and introduce their future scope [5].

2. Physiology of normal wound healing

The normal wound healing cascade involves a complex series of cellular and biochemical events which begin with hemostasis and inflammation, proliferation, maturation, remodeling, and wound contraction. These phases are not exactly distinguishable from each other, because occasionally they overlap or proceed concurrently [6].

2.1 Hemostasis

It is the first stage of wound healing which start immediately after the injury and cause the stoppage of bleeding. In hemostasis various platelets factors are released by the degranulation thrombocytes cells like insulin-like growth factor (IGF-I), Platelet-derived growth factor (PDGF), Transforming growth factor beta (TGF-β) and Epidermal growth factor (EGF) followed by coagulation cascade. Coagulation cascade is the multifaceted chain reaction which begin at the site of injury in which the conversion of prothrombin to enzyme thrombin takes place. Thrombin converts the fibrinogen in to fibrin monomers at the site of the wound surface. Fibrinogen polymerizes the fibrin monomers to form a fibrin chain which are interlinked by coagulation factor XIII and form a stable fibrin network.

2.2 Inflammatory phase

After the hemostasis is achieved inflammation is initiated at the site of injury. Immediately after the rupturing of blood vessel mast cells releases various inflammatory factors like thromboxanes, histamins and prostaglandins which causes the vasoconstriction to prevent blood loss.

Initially, Polymorphonuclear neutrophils (PMNs) are arrived at the wounded area within an hour of injury. PMNs cells are the predominant cells for the first two days at the site of injury, which are attracted to the site by growth factors and fibronectins. Neutrophils release free radicals which phagocyte the debris and kill bacteria at the site of injury. This process is known as respiratory burst. Other leukocytes like helper T cells also present in the wounded area helps in the secretion of cytokine which divide T cells and increases inflammation, vasodilatation, vessel permeability and activity of macrophage. Macrophages are essential for the tissue regeneration and wound healing. Macrophages are stimulated by the low oxygen content to produce various factors which enhance the angiogenesis, stimulate the cells to re-epithelialise the wound, form granulation tissue, built a new ECM ultimately pushing the wound healing process into next phase. Macrophages become prominent by replacing the PAMs cells at the wound site. As inflammation decreases, few inflammatory factors are secreted and numbers of neutrophils and macrophages are decreased at the wound site create a clean wound bed which indicate that inflammatory phase is ending and enters in to the proliferative phase [7].

2.3 Migration and proliferation phase

After few days of injury migration and proliferation phase starts and last up to 21 days from the day of the wound takes place. This phase is characterized by angiogenesis, epithelisation and fibroplasias. In proliferation phase wound start to rebuilt with healthy granulation tissue. To form the granulation tissue sufficient supply of oxygen and nutrient is required by the blood vessels. A new network of blood vessels is replaced by the damaged one by the process of angiogenesis, formation of extra cellular matrix (ECM) and collagen takes place. With the formation of the granulation tissue damaged mesenchymal cells are converted into the fibroblast cells which act as a bridge for the movement of the cells around the affected area. In healthy wound these fibroblasts start to appear within three days of the injury and liberate liquids and collagen which help to strengthen the wound site. The wound continues to grow stronger in the proliferation phase with the reorganization of the fibroblast cells and help in the formation of new tissue and speed up the wound healing process [7].

2.4 Remodeling phase

Remodeling or maturation phase is the last phase of healing process which finalizes the wound healing process. Remodeling phase start approximately 21 days after the injury and can go up to 2 years with the change in the matrix composition over the time. During this phase, the collagen formation and organization takes place with the help of collagenases and matrix metalloproteinases. The tensile strength of the dermal tissue increases and nonfunctional fibroblasts are recouped by the functional ones. With the passage of the time cellular activity decreases and the blood vessels in the affected area reduced. Wound contraction takes place and type III collagen is remodeled in type I collagen which increase the tensile strength of the wound and wound is fully closed [8, 9].

3. Pathophysiology of chronic wounds

A chronic wound is defined as one in which the normal process of healing is disrupted at one or more points in the phases of hemostasis, inflammation, proliferation and remodeling and do not heal completely within 90 days after the onset of any injury [10]. Chronic wounds, unlike acute wounds, do not undergo the ordered molecular and cellular processes of physiological tissue repair previously discussed. However, the healing process of chronic wounds is thought to be stuck in inflammation [11]. Chronic wounds can also be considered to be an imbalance between tissue deposition stimulated by growth factors, and tissue destruction mediated by proteases. Hereby, the imbalance favors the destructive process [10]. Thus, the molecular and cellular processes are disrupted leading to significant differences in the microenvironment of the wound, both in terms of the constituents of the exudates and the cellular components of the wound area. In addition, oxidative damage by free radicals, condition specific factors of underlying diseases, and accumulated necrotic tissue as well contributes to the chronic state. The further healing of those wounds results in skin defects of excessive fibrous appearance, for instance keloids and scar contractures, or alternatively in insufficient tissue replacement, i.e., a non-healing wound [12].

4. Challenges in tissue regeneration

The role of ECM in wound healing has been traditionally thought of as a passive structural support for cells. It is now clear that cell-ECM interactions, in concert with growth factors, are necessary for rapid wound healing. Hence, the main challenge in wound therapeutics is to provide an ideal microenvironment for optimal cell migration and proliferation [13]. Many strategies have been adopted for accelerating tissue repair. Exogenous growth factors, ECM molecules, and short peptide sequences targeting specific integrin receptors have been shown to accelerate wound healing both *in vitro* and *in vivo*. However, native ECM molecules or growth factors lack structural properties, and are expensive to produce in large quantities [14]. On the other hand, polymeric materials offer excellent physical support, and enhance biological activity. To circumvent these disadvantages, polymeric materials have also been functionalized with bioactive peptide sequences, nanoparticles and growth factors in to bionanomaterial [4].

5. Biomaterials for wound healing

Recent years have witnessed extraordinary growth of research and applications in the field of nanoscience and nanotechnology. The field of nanoscience is one of the most dynamic research areas in modern material science and combination of physics, chemistry, biology, material science & medicine has materialized as nanotechnology. Nanoparticles and nanostructure are rapidly increasing for new application in the field of biomedicine and wound healing.

Nanomaterials are the materials which are having a maximum diameter of 100 nm and nanoproducts which lies in nanoscale are known as nanomaterial. Nanomaterial possesses large surface to volume ration due to which they offer wide-ranging application in the field of science and technology. There are variety of biomaterials which acquire excellent candidature for numerous biomedical applications. When these biomaterials are used in nanoforms like nanotubes, nanocomposite, nano pockets and nanoparticles they are known as bionanomaterial [15, 16].

The size of the bionanomaterial hold an important parameter in terms of biological application because of its similarity in size as compared to genetic material i.e., around 2.5 nm in width and to building block of cell i.e., protein which is around 1-20 nm. So, for biological application the size and surface properties of the bionanomaterial can be personalized as per the prerequisite.

The nature has provided us with a significant set of biomaterials like chitosan, cellulose, silk, hyaluronic acid, alginate, fucoidan, pectin, gelatin, keratin, carboxymethyl cellulose, Bovine serum albumin. These proteins and polysaccharides-based biomaterials possess a physiochemical property like biocompatibility, biodegradability and non-toxicity which makes them apposite for inclusion in living systems thereby accelerate or replace the function of bodily tissues, organs or damaged tissue & augment wound healing process. Polymeric biomaterials can be fabricated in to variety of nanostructures like nanotubes, nanoparticles, nano- capsules, nanopockets, nanocrystals, nanowhiskers which ultimately possess the potential to encourage self-healing mechanisms that can mimic tissue regeneration [17, 18]. The summery of all the biomaterials in provided in the **Table 1**.

5.1 Nano-biomaterials in wound healing

As we know wound healing is well orchestrated process involving a significant number of physiochemical events in different phases of healing process involving hemostasis, inflammation, proliferation and remolding. There are variety of factors which significantly influence the wound healing course and slow down their activities, completely disturb the wound healing process. It is difficult to visualize the necessity of altered tissue and ample the requirements for tissue regeneration. Nature has provided with us a significant set of biomaterials which possess fundamental properties like non-toxicity, biocompatibility, biodegradability and

Biomaterial	Monomer units and linkage	Biological Role in wound healing	Characteristics	Nano-biomaterial	Reference
Chitosan	*N*-acetyl glucosamine linked by β-1, 4 glycosidic linkages	It act as a hemostat during early blood clotting cascade It activates neutrophils infiltration & migration It also stimulates PMN leucocytes, macrophages & fibroblast for phagocytosis and cell proliferation. It provides non-protein matrix for 3D growth of tissue.	It is bio- degradable, biocompatible, antimicrobial, antifungal and non-toxic in nature	Chitosan can be engineered in to nanoparticles, nano- fibrils, nanotubes and nanorods	[18, 19]
Cellulose	β-d-Glucose linked by β-1,4-glycosidic linkage	It aids in the absorption of exudates resulting in the intake of cell debris (such as necrotic tissue and fibrinous coating) and the porous cellulose structure mimics ECM of skin thus helping in tissue regeneration	It is non-toxic, non-allergic and biocompatible, unique rheological properties, crystalline behaviors, sustainability and biodegradability	Nanocrystals, nanofibers, nano whiskers, nanorods, nanofibrils, and nanocellulose.	[20–22]
Silk fibroin	Disulphide bonds	Silk arouse cell migration and proliferation It trigger collagen formation & encourage epithelization by enhancing fibroblast and keratinocytes proliferation	It is bio- degradable, biocompatible, easily factionalized and its many physical properties can be modified non-immunogenic and bioresorbable material	Silk can transformed in to silk nanoparticles, nanofilms, nanocomposites	[23, 24]
Hyaluronic acid	β-d -glucuronic acid and *N*-acetyl-d-glucosamine linked by β-1,4 and β-1,3 glycosidic linkages	Hyaluronic acid attunes vital phases of wound healing like inflammation, cellular migration, and angiogenesis, It also stimulates TGFβ-1, b-FGF, PDGF, and EGF growth factors production and enhance keratinocytes proliferation in wound bed	Highly biocompatible, Biodegradable, Bacteriostatic, non-immunogenic and possess high water retention capacity	It can be architectures in to nanoparticles and nanotubes	[25]

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Biomaterial	Monomer units and linkage	Biological Role in wound healing	Characteristics	Nano-biomaterial	Reference
Alginate	β-d-Mannuronic acid and α-l-guluronic acid linked by α-1, 4 glycosidic linkages	Calcium alginates assist in hemostasis by releasing calcium ions at the wound site. Provide moist wound environment and confines pathogenic and bacterial access into the wound. It also augments proliferation and cell adhesion	Alginates and alginic acids are antibacterial, Biocompatible, Biodegradable moisture absorbent in nature	They can be transformed in to nanogels nanoparticles and nanofibers	[26]
Fucoidan	α-l-Fucose linked by α-1, 3 glycosidic linkages	It can bind and activate growth factors production at the wound site It also enhance the formation of neovascularization & collagen matrix and augment the wound healing process	Anti-inflammatory, antioxidant Anticoagulant, antiviral and immunomodulatory	It can be molded in to nanoflakes, nanospikes,nanofilms, nanoparticles	[27, 28]
Pectin	D-galacturonic acid linked by α-(1 → 4)-glycosidic bond...	pectin is hydrophilic in nature. It allows removal of wound exudates from wound bed. It also allows maintenance of acid environment which is impermeable to microbes.	Due to the presence of large number sof esters and galacturonic acid it possess anti-inflammatory properties It is also Antithrombogenic, biodegradable and biocompatible in nature	Nanocomposites, Nanofilms	[29, 30]
Gelatin	Sugar and amino acids	Gelatin stimulates signal transduction and cell adhesion in well-coordinated progression of wound healing process.	It is highly absorbent, biodegradable, Biocompatible, and non immunogenic in nature	Nanocomposites, nanofilms	[31]
Collagen	Amino acids linked by amide linkage	It fascinates fibroblast and boost collagen deposition. It inactivates matrix metalloproteinases (MMPs), also stimulates tissue growth, angiogenesis,autolytic debridement &reepithelization	Collagen is biodegradable, anti-inflammatory and non-toxic	Nanofibers, nanoparticles	[4, 32]

Table 1.
Biomaterials and their wound healing properties.

also mimic with the host extra cellular environment. Moreover, several of them are non-immunogenic and fulfill the demands of suitable wound healing dressing material. Biomaterials and their composites are comprehensively investigated by the researchers which can be tailored in nanostructure like nanoparticles, nanofilms, nanoflakes, nanocomposites, nano capsules, nanotubes, nanogels, nanofibrils, nanospikes and nanowhikers. These nanostructures encourage the potential to endorse self-healing mechanism that can mimic tissue regeneration. With the extended knowledge of nanotechnology and nanomedicine they represent a great prospect to improve currently available medical treatments and prognosis impaired wound healing [33].

5.1.1 Nanoparticles

As a functioning field of nano-research, the molecular designing of different self-assembling biocompatible nanoparticles has been created in recent years. Nanoparticle, exhibit unique physiochemical properties and maximized its use for biomedical and therapeutic application, including for wound healing. Using the nanoparticles, delayed wound healing and burn care has been enhanced. Polymeric nanoparticles are manufactured from biodegradable polymers or copolymers to remove, capture, encapsulate or bind the drug. They can be made up of natural ones, Synthetic and semi-synthetic polymers and their copolymers, such as alginate, chitosan, gelatin, poly (glycolic acid), albumin, poly-alkyl cyanoacrylate, PLGA, etc. They have the benefits of controlled and sustained discharge, enhanced bioavailability, elevate level of exemplification, and biocompatibility with tissues and cells. Chitosan nanoparticles have traditionally been among the most commonly researched groups of natural biopolymer products for biomaterials. Using either “bottom-up” or “top-down” methods or a mixture of both techniques, Chitosan nanoparticles can be synthesized. Chitosan can be used as a wound-healing agent due to its antimicrobial, haemostatic, film-forming, anti-inflammatory, and anticoagulant activities. Curcumin loaded chitosan nanoparticles accelerate the wound healing by regulating inflammation and neovascularisations. As chitosan is remarkable antimicrobial agent which modulate the production of reactive oxygen species, IL-6 secretion and augment proinflammatory activation and ultimately augment healing in chronic wound [34].

Hyaluronic acid (HA-NPs) nanoparticles also showed good stability and had a potential to be applied as blood contact material. Studies showed that HA-NPs showed excellent comprehensive biocompatibility, strongly promoting adhesion and proliferation of extra cellular while still exerting inhibitory effects on platelets, and macrophages [35].

Gelatin is a naturally produced collagen-derived polymer utilized specifically in the manufacture of biodegradable materials, and biocompatible fabrics for wound dressing. Fibrin is also a natural polymer which, in the presence of the enzyme thrombin, is made from fibrinogen polymerized into fibrin. Fibrin has distinctive properties, including inflammation reduction and enhanced immunological response and cell permeability, and has been broadly included in wound healing and tissue engineering [36]. Under acidic conditions, pectin has the ideal consistency also at higher temperatures, making it the perfect choice for use in the drug delivery system. In the presence of divalent cations, pectin has a peculiar gel forming capacity that makes it an excellent carrier for supplying bioactive agents. At low pH, pectin forms an accumulation of macromolecules, but the pectin aggregates appear to dissociate at neutral pH and form an extended network. Thiolated pectin-based nanoparticles have recently been explored and their potential for delivery of ocular drugs has been studied. The thiolated pectin nanoparticles have been prepared using magnesium chloride as an ionic crosslinker by ionotropic gelation and timolol maleate as the model drug. They indicated that the addition of cross-linker imparts a more pronounced effect on the nanoparticles' particle size, whereas the drug trap is influenced by polymer concentration. Mucoadhesive nanoparticles have been shown to extract the substance from the particles trapped in the cul-de-sac for a long period of time. Developed pectin nanoparticles through mechanical homogenization and showed enhanced drug dissolution [7].

Silk fibers are used by the textile industries and as suture material. Silk fibers are generated by the silkworm cocoons named *Bombyx mori*. Nowadays, silk is valuable in the biomedical sector because of its mechanical and biological properties like biodegradability, stiffness, biocompatibility, water vapor permeability, and anti-bacterial properties. Due to its different properties, silk can be used as a material for wound dressing. Hydrocolloid dressings loaded with silk fibroin nanoparticles showed enhanced effectiveness of medical dressing due to the hydrophobic nature of silk fibroin polymers, result in enhanced physical properties. It also maintains the environment of extra cellular matrix, furthermore cell viability is also increased in burn wound animals models [7].

5.1.2 Nanofilms

In current scenario of nanotechnology research, nanostructure of polymeric biomaterial has been attracted a great attention of researchers. Nanofilms are among them one type of nanomaterials which is widely used for wound healing applications. Nanofilms are the thin single or multilayer biomaterials structure which vary from few nanometers to several micrometers in thickness. They are flexible sheets and generally used in wound dressing. The nanofilms synthesized for wound healing applications are transparent in nature, also allow exchange of gases like oxygen and carbon dioxide and but impermeable to water, bacteria and other pathogens. The variety of biomaterials can easily be tailored in to nanofilms. Carboxymethylcellulose nano films own high absorption capacity of exude and also triggers the formation of new blood vessels and remove necrotic debris and devitalized tissues from a wound bed.

Chitosan and alginates based nanofilms augment the wound healing process in both excision and incision animal wound model studies and also facilitated cell viability, collagen deposition, tissue regeneration and remolding [37]. Nanofilms based on hyaluronic acid effectively accelerate wound healing process and cause less trauma while removing these nanofilms based wound dressing. Studies showed that low proportion of hyaluronic acid in chitosan-hyaluronic acid composite nanofilms will decrease the water vapor permeability and fibroblast adhesion which is beneficial to accelerate wound healing process. Collagen based nanofilms demonstrated in study enhance fibroblast migration which markedly improved wound healing process.

Fucoidan- is an emerging biomaterial from a family of sulfated polyfucose polysaccharides extracted from brown marine algae. Fucoidan comes under spot-light due to its significant properties like antioxidant, antivirus, anticoagulant and anti-inflammatory and non-toxicity. It was studied that fucoidan based nanofilms increase the potential wound healing in burns wounds by significantly induce wound contraction. It reacts with the basic fibroblast growth factor and transforming growth factor and mediate the wound healing process [38].

5.1.3 Nanofibers

Nanofibers display two main characteristics: a pore size and high surface/volume ratio which placed it under spot light in variety of biomedical application like drugs delivery and wound healing. High surface area and different fabrication process used for adjusting the composition of nanofibrils make it responsible to speed the wound healing process. It augments cell adhesion, proliferation and differentiation at the wound bed. The traditional method of processing these biomaterials is through the technique of electrospinning, which provides the possibility of operating with a high yield at a nano-scale. Low spinnability can be manage by adding synthetic polymers into the natural polymers. As we known natural polymers offers extensive variety of bioactive properties which makes then suitable for biomedical and wound healing applications. Many studies showed that nano porosity and large surface to volume ratio makes the nanofibers competent to smooth the wound healing process. Mesh like structure of nanofibers promote high absorption of wound exudate. It also promotes cell respiration and exchange of gases. Biopolymeric nanofibers boom the ability of fibrous mesh to react with biological components of wound healing process [39].

Gelatin is a natural polymer derived from collagen that is biocompatible and biodegradable. It enhanced the regeneration of tissue and helps in healing of wound. When used as a wound dressing material, gelatin nanofibers comply with all required specifications like haemostatic, low cytotoxicity, reduced antigenicity [40]. Their scarcity of antimicrobial properties, restricts the use of gelatin. The antimicrobial properties of gelatin have been enhanced by adding other substances into it like poly([2-(methacryloyloxy)ethyl] trimethylammonium chloride) (PMETAC) and showed good bacterial activity against *Staphylococcus aureus*, *Escherichia coli*, methicillin-resistant, and Acinetobacter baumannii. Further study on cell adhesion revealed that cells attached and proliferate on the nanofiber surface, resulted in the safe use of gelatin nanofibers as material for wound dressing [41].

Collagen type I nanofibers were also favored to enhance cell proliferation. 3D nanofibrous scaffolds as dressings of collagen accelerate the wound closure in 14 days [42].

Chitosan nanofibers are also emerging candidate in the area of biomaterials. Studies showed that many different types of drugs like chemotherapeutics agents, antibiotics and proteins can be successfully loaded in electrospun nanofibers. Chitosan nanofibers possess several bioactive properties and can be utilized for wound dressing, tissue engineering and drug delivery system [43].

Due the small pore size of chitosan nanofibers they reduce the bacterial infection at wound bed and also decrease dehydration during wound healing process [44].

As Ideal wound dressing should maintain the water loss at a range of 2000 and 2500 g^{-2} day^{-1} at the wound site indicates that the higher values dry the wound rapidly and cause hindrance in smooth wound healing progression. Studies showed that chitosan-based nanofibers has water vapor transmission rate of 1950 to 2050 g^{-2} day^{-1} makes it ideal candidate for wound healing dressing [45].

In addition to that nanofibers of hyaluronic acid [HA] also hold a potent position in the field of biomedical application due to their unique properties as an extracellular-matrix and accelerating wound healing. Hyaluronic acid nanofibers have very mechanical properties due to which they cannot be used alone as a wound healing dressing material. Thus, reinforcement agent is required to incorporate into nanofibers. Hyaluronic acid has carboxygroup, which is capable of forming hydrogen bond with the protonates amines. Chitosan possesses an amine group that helps in the formation of hydrogen bonds with hyaluronic acid. In turn, it increases the mechanical strength of hyaluronic acid nanofibers dressing [46].

5.1.4 Nanocomposites

Currently, due to the rapid development in the field of nanotechnology and nanomedicine formation of nanocomposites for biomedical and wound healing is more facile and development of biopolymer nanocomposites has bloomed due to its outstanding endorsements in structural, electrical, mechanical applications. They are enlightened materials to transport nanoparticles [47]. The distinct features of nanocomposite may reflect the mutual properties of their components; they can serve for different biomedical purpose. In wound dressing, nanocomposites aims to reinforce structural stability and increase antimicrobial activity [48].

Biopolymer nanocomposite loaded with nanoparticles of antimicrobial agent play a vital role in the tissue repair and regeneration. Due to high surface to volume ratio of nanoparticles, they significantly increase the efficacy of the wound dressing against different microorganisms by reducing the risk of developing bacterial resistance. Chitosan own functional amino group that can be further engineered for a wide range of applications. Studies showed that chitosan-based nanocomposites loaded with antimicrobial agent are attractive not only in food preservation but also in biomedical field. Antimicrobial nanoparticle loaded chitosan nanocomposites encourage controlled release of drug through the matrix at wound site which prevent the unwanted bacterial infection. Montmorillonite–chitosan–silver sulfadiazine nano composites were evaluated on skin lesions which showed increased efficacy of prepared nanocomposites and can be used as potent wound dressing material [49].

Silk nanocomposites also investigated for wound healing applications as silk own good permeability to oxygen and water vapors, also possess high thermal resistance, good tensile strength and antimicrobial properties [50].

Hyaluronic acid-based nanocomposite showed satisfied properties of an ideal wound dressing in terms of porosity, swelling, biocompatibility, biodegradation. They also showed haemostatic potential and antibacterial properties. Hyaluronic acid nanocomposite incorporated with silver nanoparticles own effective response against *S. aureus*, *E. coli*, *P. aeruginosa* and *K. pneumoniae* microbes. So they can be used as potential bio nanocomposite for wound dressing of chronic wound loaded with bacterial infections [51].

Guar gum loaded Carboxymethyl nanocomposites showed enhanced re- epithelial growth and very less inflammatory cells which confirm that they reduce microbial infections. Therefore, Guar gum loaded Carboxymethyl nanocomposites has the potential of effectively accelerate wound healing process and are a suitable candidate for wound dressing material [52].

6. Conclusions

The nanotechnology and nanomedicine-based therapies are an emerging trend in the field of biomedical and wound healing application. Plentiful researchers have designed and innovate nanoplatforms to enhance wound healing process which demonstrate promising results in the field of wound healing. Recently biopolymeric nano systems have attracted much attention which showed a great response and benefits in treating acute and chronic wounds. The potential of bionanomaterials for biomedical and wound healing application is enormous due to their bioactive physiological properties like biocompatibility, biodegradability, non-toxicity, non-immunogenic which synthetic polymers do not possess. These nanomaterials play a significant role in cell attachment, differentiation and proliferation as well as delivery of target protein, drugs, stem cells and growth factors. Various types of nanomaterial can be engineered using these biomaterials like nanoparticles, nanofilms, nanocomposites, nanofibers which enhance the administration of different drugs and reduce the cytotoxicity. Topical application of bionanomaterials not only improve controlled drug delivery but also favors cell fibroblast proliferation, and reduced tissue inflammation. Furthermore, the detailed insight of molecular mechanism in wound healing and the role of bionanomaterial in this process is needed attention to translate basic research into clinical application.

Conflict of interest

There are no conflicts of interest.

Author details

Priyanka Chhabra* and Kajol Bhati
Department of Forensic Science, School of Basic and Applied Sciences, Galgotias University, Greater Noida, Uttar Pradesh, India

*Address all correspondence to: pchhabra188@gmail.com

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