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Advancements in wound dressings: The role of chitin/chitosan-based biocomposites

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ABSTRACT

This review explores recent advancements in chitin and chitosan-based biocomposites for wound dressing applications, emphasizing their unique physicochemical properties such as biocompatibility, biodegradability, and antimicrobial activity that underpin their therapeutic efficacy. It discusses their pivotal role in wound healing and evaluates innovative dressing technologies, including antimicrobial, smart, and stimuli-responsive systems. Additionally, the review covers their clinical applications across various wound types, including acute, chronic, and surgical wounds, while emphasizing emerging trends and future directions for integrating these biocomposites into next-generation wound management strategies. The insights provided aim to underscore the potential of chitin/chitosan-based materials in advancing wound care practices.

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1. Introduction

Wound healing is a critical procedure in restoring the integrity and functionality of damaged tissue, yet it remains a significant challenge, particularly in cases of chronic or problematic wounds [1-3]. Over the years, advancements in wound care have focused on developing innovative dressing materials that not only protect the wound but also actively enhance the healing process [4-8]. Among these, biocomposites based on chitin and chitosan have emerged as promising candidates due to their remarkable biological properties, such as biocompatibility, biodegradability, antimicrobial activity, and capability to accelerate tissue regeneration [9].

Chitin, a natural polysaccharide derived from crustacean shells, and its derivative chitosan have demonstrated exceptional potential in wound management applications [10]. These biopolymers possess intrinsic antibacterial and hemostatic properties, making them ideal for addressing microbial infections and promoting coagulation at wound sites [11]. Furthermore, their ability to modulate inflammation and stimulate granulation tissue formation has positioned them as versatile components in advanced wound dressings [9, 12, 13].

Recent research has focused on enhancing the functionality of chitosan-based materials by incorporating bioactive compounds, nanoparticles [14], and other chemical modifications. These advancements have led to the development of multifunctional wound dressings capable of addressing diverse clinical needs, such as irregularly shaped wounds, chronic ulcers, and burns [15]. Researchers are exploring the unique characteristics of chitin and chitosan to transform wound care with materials that speed up healing and minimize complications from infections and inflammation [16].

This review provides a detailed analysis of recent advancements in chitin/chitosan-based biocomposites used for wound dressings, focusing on their key physicochemical attributes such as biocompatibility, biodegradability, and antimicrobial properties, which enhance their therapeutic potential. It examines their versatile functions in facilitating wound healing, including incorporation into novel dressing platforms like antimicrobial, intelligent, and stimuli-responsive systems. Furthermore, the review highlights emerging clinical applications for various wounds, from acute and chronic cases to surgical repairs, while also discussing future prospects for developing advanced wound management strategies utilizing chitin and chitosan biocomposites.

2. Properties of chitin and chitosan

This section will discuss the key properties of chitin and chitosan, focusing on three main aspects: chemical structure and composition, biocompatibility and biodegradability, and antimicrobial properties.

First, the chemical structure and composition of these polysaccharides will be explored, highlighting the molecular arrangements and functional groups that impart unique characteristics. Next, their biocompatibility and biodegradability will be examined, emphasizing the suitability of chitin and chitosan for several biomedical applications. Finally, the antimicrobial properties of chitin and chitosan will be investigated, assessing their efficacy against a range of pathogens and their potential use in preventing infections. Each of these topics is considered crucial for understanding the applications and benefits of chitin and chitosan in different fields.

Chitosan has unique biological properties such as non-toxicity, biocompatibility [17], biodegradability [18], mucoadhesion [19], antimicrobial activity [20], antioxidant activity [21], hypocholesterolemic [22], and hemostatic effects [23]. Moreover, it also exhibits permeation enhancement effects [24]. These properties have led to its increased use in distinct applications such as controlled release coatings [25], antibacterial/anti-biofouling coatings [26, 27], nanofiltration [28, 29], microcapsules [30], hydrogel-based drug delivery systems [7, 31], gene delivery [32], and tissue engineering scaffolds [33-36].

Fig. 1 illustrates various properties of chitosan. Table 1. summarizes the effect of degree of *N*-acetylation (DA) and molecular weight (M_w) on the physicochemical and biological characteristics of chitin/chitosan [37].

Fig. 1. Various characteristics of chitosan.

2.1. Chemical structure and composition

Chitin, chemically known as poly (β-(1-4)-N-acetyl-D-glucosamine), ranks as the second most prevalent biopolymer in nature and serves as the precursor for chitosan synthesis [33]. It usually originates in crustacean exoskeletons, insect cuticle, and fungal cell walls [38, 39]. Chitosan is a derivative of chitin, consisting of a linear chain of repeating units, specifically, 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose. It is produced by partially removing acetyl groups from chitin through alkaline deacetylation, typically requiring at least 50% deacetylation [1, 40]. Thanks to its amino and hydroxyl functionalities, chitosan can participate in chemical modifications such as etherification, esterification, and reductive amination, forming stable covalent bonds [1].

Its physicochemical attributes like solubility, molecular weight, and chain structure are influenced by factors such as the pattern of acetyl group distribution (whether random or blockwise), the degree of acetylation, and overall polymer size [33, 41]. It is also readily broken down by chemical hydrolysis and specific human enzymes, such as lysozyme [9, 42].

Chitosan is a weak polybase that exhibits pH-sensitive behavior due to its high amino group content. It dissolves in low pH conditions but becomes insoluble at higher pH levels (above pH 6.0). The swelling mechanism of chitosan is governed by the protonation of its amine groups in acidic environments. Moreover, chitosan dissolves readily in dilute organic acids and can bind to negatively charged entities, enabling its fabrication into diverse formats like particles, films, fibers, and sponges [43].

With the growing demand for sustainable alternatives to conventional materials, chitosan has attracted considerable interest from researchers [38]. Fig. 2 displays the structure of chitin and chitosan.

Table 1
Effect of degree of *N*-acetylation (DA) and molecular weight (M_W) on the physicochemical and biological characteristics of chitin/chitosan [37].

Property	Property	Notes
Physicochemical Properties	Solubility	As DA increases (more deacetylation), solubility decreases.
	Crystallinity	Higher DA leads to increased crystallinity.
	Viscosity	Increased DA tends to decrease viscosity.
	Biodegradability	Higher DA increases biodegradability; Higher M_w decreases biodegradability;
	Biocompatibility	Increased DA can reduce biocompatibility.
Biological Properties	Antimicrobial	Higher DA reduces antimicrobial activity.
	Anticholestatic	Higher M_w reduces anticholestatic activity.
	Antioxidant	Higher DA and M_w reduce antioxidant activity.
	Haemostatic	Higher DA reduces haemostatic effect.
	Mucoadhesion	Higher M_w enhances mucoadhesion. Higher DA reduces mucoadhesion.

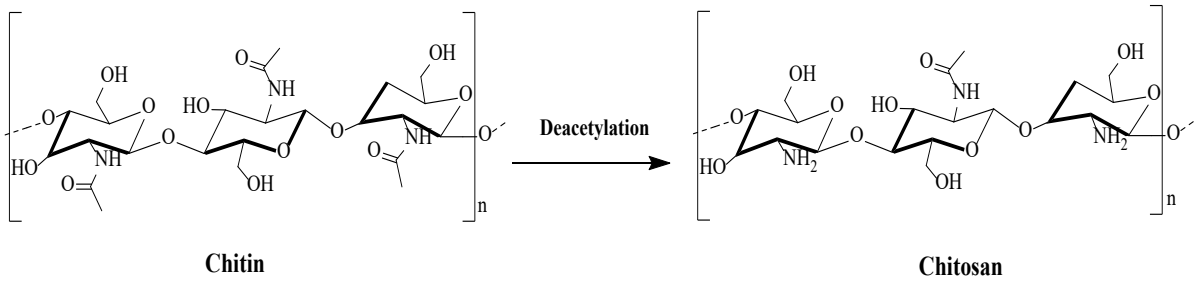

Fig. 2. The structural configurations of chitin and chitosan.

2.2. Biocompatibility and biodegradability

Chitin and chitosan possess excellent biocompatibility and biodegradability, making them highly suitable for biomedical applications [44, 45]. Chitosan, in particular, plays a substantial role in wound healing, tissue engineering, and drug delivery, as it interacts safely with biological tissues without causing harmful effects [44]. It is enzymatically degraded in vivo by lysozyme, guaranteeing safe breakdown within the body. Additionally, their biodegradability contributes to eco-friendly solutions, supporting sustainable practices in agriculture and food packaging [46].

2.3. Antimicrobial properties

The antimicrobial capabilities of chitosan have attracted considerable interest, especially for use in wound dressings. Its activity largely stems from its positive charge, as the amino groups in chitosan interact electrostatically with negatively charged microbial membranes, destabilizing their structure and causing cellular contents to leak [47, 48]. This antimicrobial action is effective against various microorganisms, including both gram-positive and gram-negative bacteria, fungi, and certain viruses [49].

Its capacity to inhibit microbial growth is only seen in acidic environments, where the chitosan is soluble and has a net positive charge. This feature limits the application of chitosan in various water-based bioactivity assessments. Consequently, the derivatization of chitosan focuses on enhancing its solubility in aqueous solutions while simultaneously boosting its antimicrobial properties. For instance, quaternizing the 2-amino group or adding cationic groups and quaternary ammonium groups has enhanced both the solubility and antimicrobial effectiveness of chitosan. In contrast, incorporating hydrophobic groups like N-acetyl (with a degree of substitution of up to 0.5) enhances solubility for low molecular weight chitosan without significantly increasing its antimicrobial activity [41].

The arrangement of N-acetyl groups in chitosan can influence its antimicrobial properties. Chitosan with a lower degree of acetylation (DA) or an increased number of free amino groups has been shown to improve its effectiveness against different fungal strains and both Gram-positive and Gram-negative bacteria, particularly *Staphylococcus aureus* (*S. aureus)* and *Escherichia coli* (*E. coli*) [41].

A study incorporated two natural extracts, Allium sativum (garlic extract) and Cleome droserifolia, into nanofibers composed of honey, PVA, and chitosan (HPCS) to develop antimicrobial wound dressings. The resulting mats designated HPCS-AE, HPCS-CE, and HPCS-AE/CE demonstrated that HPCS-AE and HPCS-AE/CE effectively suppressed S. aureus growth, surpassing the performance of the commercial Aquacel®Ag dressing, which mainly reduced bacterial proliferation. The enhanced activity was mainly attributed to the garlic extract. The combined HPCS-AE/CE mat showed some activity against methicillin-resistant S. aureus (MRSA), though it was not statistically significant relative to controls and less effective than Aquacel®Ag. None of the nanofibers inhibited *E. coli* or multidrug-resistant *Pseudomonas aeruginosa*, whereas the comparison dressing completely inhibited *E. coli* and was more potent against *MDR P. aeruginosa* [50].

Another study developed antimicrobial chitosan/bacterial nanocellulose structures for potential wound dressing applications, and the results showed that the addition of chitosan to bacterial nanocellulose structures provided good antibacterial activities. These mats reduced *E. coli* bacterial density by more than 99 % [51].

3. Role of chitin/chitosan in wound healing

Chitin and chitosan are widely utilized in biomedical applications, particularly in wound dressings, due to their biocompatibility, biodegradability, and antimicrobial activity. Chitin and chitosan promote hemostatic immunity, accelerate collagen synthesis, and enhance fibroblast attachment and angiogenesis, aiding early wound healing. Chitosan, with its polycationic nature, improves fibroblast proliferation and overall tissue organization. Their ability to be complexed or cross-linked with other materials optimizes adhesion, antibacterial properties, and exudate absorption, leading to faster healing and improved skin regeneration. Additionally, chitosan-based hydrogels and scaffolds mimic the extracellular matrix, facilitating cell growth and moisture retention, making them valuable for regenerative

medicine and wound care [9, 43, 52-54]. Blended nanofibrous scaffolds made from chitosan and gelatin have been explored for skin tissue engineering due to chitosan's antimicrobial properties and gelatin's cell adhesion qualities. Other combinations of chitosan with materials like collagen, PVA, PHBV, and PCL have also shown good cytocompatibility and antibacterial activity, promoting wound healing. Additionally, PHB combined with organic-soluble chitosan has been found to effectively enhance cell attachment and proliferation [52]. Having pH-sensitive properties has made chitosan and its derivatives valuable as delivery matrices in pharmaceutical applications. Under acidic conditions, chitosan becomes positively charged, which promotes stronger interactions with negatively charged biomolecules such as proteins, anionic polysaccharides, and nucleic acids present in skin tissue. Furthermore, chitosan-based materials are known for their film-forming abilities, mild gelation, strong adhesion to wound tissue, and ability to enhance blood coagulation, all of which contribute to accelerated wound healing [43]. Fig. 3 illustrates different biomedical applications of chitosan.

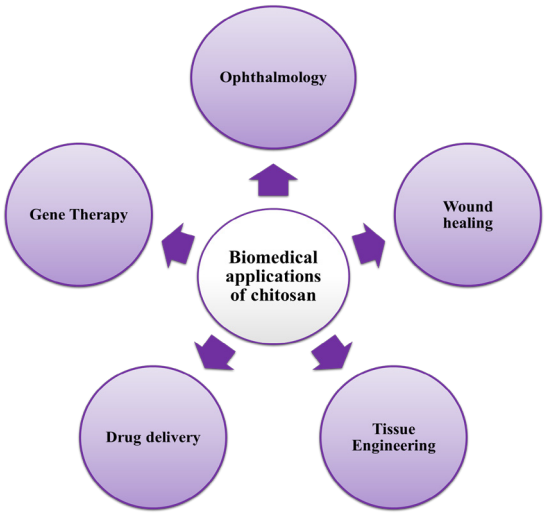

Fig. 3. Innovative uses of chitosan in healthcare.

4. Advancements in wound dressing technologies

Innovative wound care technologies must be developed to address the increasing strain that chronic wounds place on national healthcare budgets and the severe effects these wounds have on patients' quality of life [55].

The design and production of wound dressings are crucial components of the global medical and pharmaceutical wound care market. To facilitate wound healing, wound dressings have been developing considerably with the introduction of advanced biomaterials that possess enhanced therapeutic properties. Traditional dressings, including gauze and bandages made from natural and/or synthetic materials, have primarily been used to manage wounds by protecting dermal and epidermal tissues, maintaining moisture balance, and preventing contamination [56]. These conventional wound dressings primarily function as passive and protective barriers, providing essential coverage to injured areas and not actively contributing to the healing process. However, these dressings often lack the advanced functionalities necessary for effective management of complex wounds. Modern dressings are essential systems that integrate the physical and biochemical characteristics of natural and synthetic polymers with active compounds that promote wound healing. Currently, the production of wound dressings emphasizes advanced standards aimed at establishing ideal healing conditions supporting rapid tissue repair, skin regeneration, effective oxygen transfer, and minimizing microbial contamination [56].

4.1. Cutting-edge antimicrobial dressings

Modern wound dressings apply biocomposite materials, including natural polymers such as chitin and chitosan, which have demonstrated notable antimicrobial and regenerative properties. Incorporating cutting-edge methodologies, such as bioactive additives, antimicrobial, and smart dressing technologies, enhances the versatility and efficacy of these modern dressings, enabling them to not only protect but also actively promote and accelerate the healing process.

A diverse range of biocompatible materials, including cellulose, chitosan, alginate, silk, gelatin, polyurethane, PVA, poly(lactide-co-glycolide), and polycaprolactone, can be utilized in various forms such as nanofibers, woven fabrics, filaments, films, foams, hydrocolloids, hydrogels, hydrofibers, powders, sponges, and composites for the fabrication of wound dressings [57, 58]. While various techniques like self-assembly, phase separation, and template synthesis have been used to create nanofibers for wound dressings, electrospinning remains one of the most effective and practical methods. This adaptable technique enables the production of nanoscale fibrous mats with a controlled pore structure and a high surface-to-volume ratio [56, 59-61]. To speed up the wound healing process, many studies have concentrated on creating polymer-based scaffolds infused with different biochemical factors to improve cellular behavior [62]. Electrospinning presents a highly promising approach in wound care, enabling easy embedding of bioactive agents and producing nanofibrous mats that mimic the architecture of the native extracellular matrix [63], thereby promoting cell attachment and growth [64, 65]. Creating chitosan-based nanofiber scaffolds is difficult because of its poor solubility in many organic solvents and its ionic nature in solution. To overcome this, chitosan is often blended physically with other polymers like polyvinyl alcohol (PVA) and gelatin to improve its processability [52].

Hydrogels, on the other hand, are excellent wound dressings because they can rapidly absorb exudate and help sustain a moist environment. For instance, Chen et al. developed an antibacterial nanocomposite hydrogel composed of PVA, chitosan, and iron–copper–zinc oxide using a freeze–thaw method. This hydrogel featured a porous matrix, high swelling efficiency, strong water retention, good biocompatibility, and notable antibacterial properties [66].

To prevent bacterial infections on wounds and dressings, various approaches have been utilized. However, the reliance on traditional antibiotics like penicillin and methicillin has diminished due to the rise of antibiotic-resistant bacteria. Consequently, alternative antimicrobial materials such as silver ions or nanoparticles [67], quaternary ammonium compounds, and antimicrobial polymers have been investigated for wound care. Among these, chitosan stands out as a particularly promising option [57, 58]. Moreover, the use of nanoparticles such as zinc oxide in chitosan-based dressings has significantly enhanced antimicrobial efficacy and accelerated tissue regeneration, making them highly effective for managing infected or chronic wounds [68-70]. The potential cytotoxic effects of nanoparticles have been extensively studied in vitro, with evidence indicating their toxicity across various cell types. For instance, Wang et al. [71] investigated the impact of TiO_2, ZnO, and Ag nanoparticles on human aortic smooth muscle cells (SMCs), finding that ZnO nanoparticles exhibited greater cytotoxicity compared to TiO_2 and Ag at equivalent concentrations. This increased toxicity was likely linked to the generation of reactive oxygen species, the release of zinc ions, and endoplasmic reticulum stress within the cells.

Similarly, Song et al. [72] assessed the effects of ZnO and Ag nanoparticles on Caco-2 human epithelial colorectal adenocarcinoma cells, demonstrating that both types of nanoparticles, within a concentration range of 0–200 μg/mL, significantly decreased cell activity. Notably, ZnO nanoparticles showed higher cytotoxicity than Ag nanoparticles at the same doses. Dong and colleagues [73] created a wound dressing using chitosan-dialdehyde cellulose nanocrystals integrated with silver nanoparticles (CS-DCNC-AgNPs). Their findings showed that the silver nanoparticles formed in situ markedly improved antimicrobial effectiveness against gram-positive and gram-negative bacteria, as well as fungi. Cytotoxicity assessments on NIH3T3 cells indicated that this complex was biocompatible and safe for use. In a recent study, nanofiber mats composed of chitosan, PVA, and 40 nm zinc oxide nanoparticles (ZnO) were created using the electrospinning technique. The results indicated that the chitosan/PVA/ZnO nanofibrous membranes exhibited enhanced antibacterial activity against *E. coli*, *P. aeruginosa*, *B. subtilis*, and *S. aureus*. Additionally, these membranes demonstrated improved antioxidant properties and accelerated wound healing in vivo compared to the chitosan/PVA nanofibers, making them a promising option for promoting the healing of diabetic wounds [74].

4.2. Smart and responsive dressings

As the burden of chronic wounds grows due to economic and social factors, wound management approaches must adapt accordingly. This effort has led to the development of non-invasive diagnostic systems capable of tracking important biomarkers like wound fluid pH, heralding a new era of smart wound dressings [75]. Smart dressings incorporate sensors that can monitor and respond to the changes occurring in the wound, releasing therapeutic agents as needed. Emerging "smart" dressings incorporate stimuli-responsive properties, such as pH-sensitive drug release, temperature-triggered antimicrobial activity, and so on [69]. These sensors provide real-time data about wound conditions to healthcare providers, enabling timely interventions.

Recently, advanced telemetric sensors have been developed to monitor various wound parameters, including pH, temperature, moisture, oxygen, and pressure. These sensors can be placed directly on wounds, transmitting data to a portable display via a cable. While effective, they require direct contact with the wound to collect fluid. In contrast, other sensor types can produce visible, colorimetric signals on the wound pad without the need for electronic components, activating upon contact with bacterial virulence factors. These simple, responsive dressings are typically made from biocompatible hydrogels like agarose or chitosan and are designed as standard moisture-retentive dressings [76].

Advanced dressings are engineered to deliver therapeutic agents, such as antibiotics or growth factors, in a controlled way to promote healing [69]. Advanced chitosan-based dressings are engineered to respond dynamically to environmental changes such as pH or temperature. This feature enables the controlled and targeted release of therapeutic agents, ensuring that wounds receive necessary treatments precisely when needed. Moreover, smart chitosan-based biocomposites are particularly promising, allowing real-time wound monitoring and targeted therapy.

Kassal et al. [55] developed a wearable and wireless uric acid biosensor that incorporates screen-printed Prussian blue modified carbon electrodes into a commercial bandage, with the enzyme uricase immobilized on the working electrode. The bandage was connected to a potentiostat with wireless capabilities correlating with uric acid concentration. Data was wirelessly transferred via RFID to a computer or NFC to a smartphone. To minimize leaching of the sensor components into the sample medium, a biocompatible chitosan layer was added.

5. Clinical applications of chitin/chitosan-based biocomposites

The increasing frequency of untreatable and chronic wounds highlights the urgent need for improved wound healing materials and techniques [77]. Moreover, Trauma and surgical wounds have significant challenges in modern medicine, necessitating innovative solutions to enhance healing and minimize bleeding complications. Chitosan is an ideal material for medical devices and dressings in wound management due to its ability to induce hemostasis and its high biocompatibility with biological tissues [78]. Monteiro and colleagues [58] created a versatile electrospun chitosan nanofiber scaffold capable of incorporating liposomes that release gentamicin. Antimicrobial testing through disk diffusion and broth dilution methods revealed the susceptibility of *S. aureus*, *E. coli*, and *P. aeruginosa* to the antibiotic released. The gentamicin-loaded liposomes were evenly distributed within the nanofiber matrix, releasing the drug steadily over 16 hours and maintaining effective concentrations up to 24 hours. In vitro assessments confirmed that the released gentamicin exerted bactericidal effects against the tested pathogens.

Alawadi et al. [77] developed a novel nanocomposite gel made from chitosan (CS), aloe vera (AV), and zinc oxide NPs (ZnO NPs) for its wound healing properties. Various formulations of CS/AV gel were prepared with different ratios and loaded with ZnO NPs. These formulations underwent in vitro antimicrobial testing, and the most effective ones were used in an animal study over 21 days. The results indicated significant wound area reduction in the CS/AV/ZnO NPs group compared to the negative control. Histopathological analysis showed enhanced collagen deposition (76.6 ± 3.3 for CS/AV/ZnO NPs vs. 46.2 ± 3.7 for control) and epitheliogenesis (3 ± 0.9 vs. 0.8 ± 0.8 for control). The CS/AV gel loaded with ZnO NPs proved effective for wound healing, suggesting it as a promising formulation, with further studies needed to validate these findings. Macroscopic images of wound healing for various groups over a 21-day period are displayed in Fig. 4.

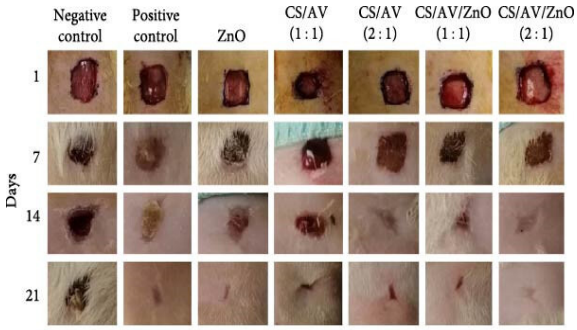

Fig. 4. Macroscopic images of wound healing progress in treated animals over 21 days across various subjected groups i.e., ZnO, CS/AV (1:1), CS/AV (2:1), CS/AV/ZnO (1:1) and CS/AV/ZnO (2:1) [77].

Li et al. [79] created biodegradable, non-toxic hydrogels from N, O-carboxymethyl chitosan (N, O-CS) and oxidized dextran (ODA) as self-healing, injectable anti-adhesion barriers to prevent postoperative peritoneal adhesions. These hydrogels showed significantly less bleeding (30 ± 5.1 mg for liver and 23 ± 4.8 mg for ear) compared to commercial (125 ± 18.9 mg and 105 ± 4.8 mg) and control hydrogels (318 ± 15.9 mg and 302 ± 14.8 mg), and had shorter hemostatic times (38 ± 5.9 s for liver and 40 ± 7.8 s for ear). The hydrogels also exhibited excellent

hemocompatibility and significant antibacterial activity, making them suitable for wound repair and preventing postoperative adhesions. As shown in the Fig. 5, the amount of bleeding and hemostatic time were measured for the control group, commercial hydrogels, and N, O-CS/ODA hydrogels, with mean values calculated from six replicates for each material (*p < 0.05 compared to the control group).

5.1. Acute wounds

Wound healing is a complex biological process essential for tissue regeneration, characterized by four interdependent phases: hemostasis, inflammation, proliferation, and remodeling. Acute wounds arise suddenly and typically heal rapidly, including injuries like abrasions, lacerations, mild burns, and minor surgeries. The primary goal of healing is to restore tissue that resembles intact skin; however, some differences may persist, and improper healing can lead to chronic or non-healing wounds. Although acute wound healing generally poses low risks, ensuring aesthetic outcomes remains a challenge [80]. Mushtaq et al. [81] developed an innovative and cost-effective injectable chitosan–methoxy polyethylene glycol (chitosan–mPEG) hybrid hydrogel with adjustable physicochemical and mechanical properties for wound healing. The results revealed its appropriate stiffness, swelling ability, excellent cytocompatibility, antibacterial properties, and in vitro biodegradability. In vivo studies on rat models demonstrated that the chitosan–mPEG hydrogel achieved hemostasis quickly and accelerated wound closure compared to controls, significantly enhancing acute wound healing. Overall, it led to earlier wound closure, considerable tensile strength, and increased hydroxyproline levels in healed tissue, effectively addressing oxidative stress. Fig. 6 (A and B) shows improved wound closure and healing in rats treated with chitosan-mPEG hydrogel. It includes images of wounds for each group: untreated (Group I), 5% CMC (Group II), Flaminal Hydro (Group III), and two chitosan-mPEG formulations (Groups IV and V).

Aldakheel et al. [82] developed chitosan-grafted PVA, including Ag nanoparticles (AgNPs), exhibiting excellent antibacterial activity against *E. coli* and *S. aureus* using the agar diffusion method. Wound healing was evaluated using dispersion hydrogel on dorsal wounds in Dawley rats, and the results indicated that the open wounds were successfully treated with these composites. As shown in Fig. 7, the non-treated control group for S1 wounds healed more than the others, but differences among the S1, S1Ag0.3, and S1Ag0.8 groups were not significant due to relative measurements.

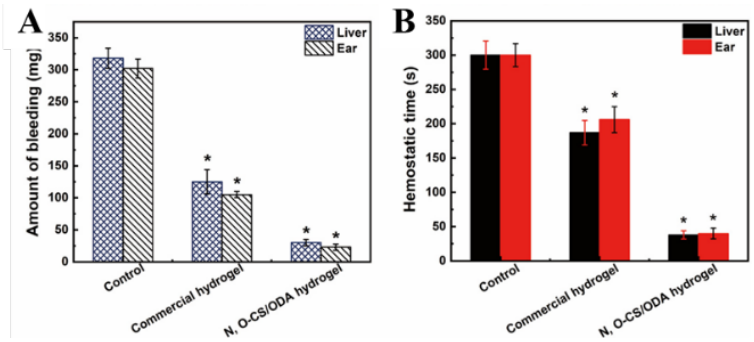

Fig. 5. (A) Bleeding volume measured and (B) time required to achieve hemostasis in the control group, commercial hydrogel samples, and N, O-CS/ODA hydrogel samples (Data are represented as mean ± standard deviation, n= 6) (*p < 0.05 compared to the control group) [79].

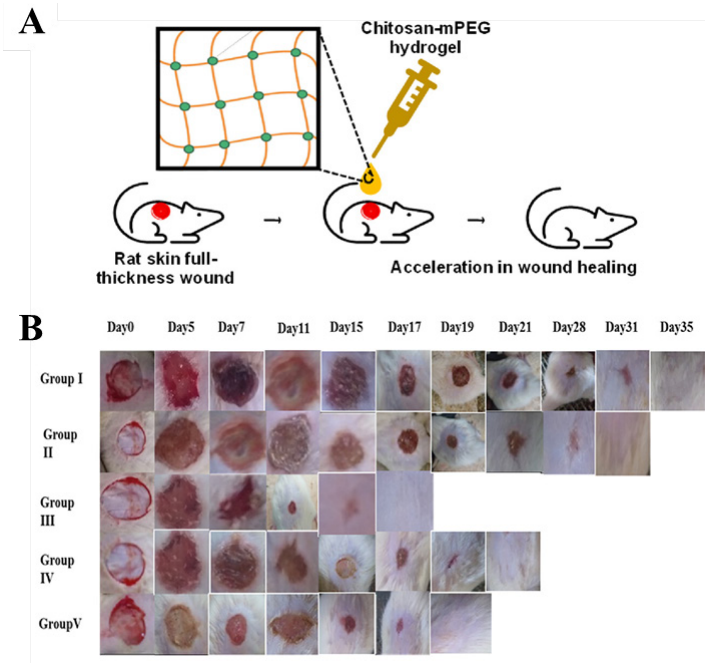

Fig. 6. (A) Schematic illustration showing the enhancement in wound closure and full healing following site application of injectable chitosan-mPEG hydrogel on rat full-thickness skin wounds. (B) Photographic images illustrating wounds across different groups: Group I (no treatment), Group II (treated with 5% CMC), Group III (treated with Flaminal Hydro), Group IV (F4 chitosan-mPEG hydrogel), and Group V (F5 chitosan-mPEG hydrogel) [81].

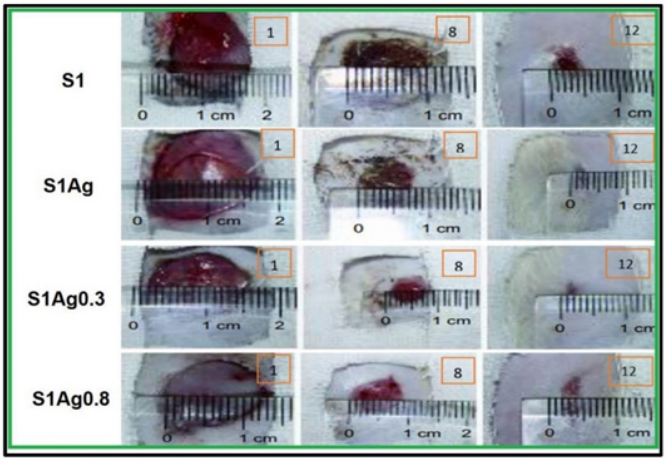

Fig. 7. Rate of wound size decrease observed at days 1, 8, and 12 post-grafting with the four tested samples [82].

By day 7, all wounds (23% to 30% size reduction) formed scabs, obscuring accurate size measurements. On day 8, partial closure was observed in all groups, ranging from 60% to 75%.

Mice were euthanized on day 12, revealing 98% to 99% healing after scab removal. Mice treated with S1Ag hydrogel showed greater wound size reduction compared to S1, with S1Ag0.3 and S1Ag0.8 being the most effective hydrogels.

A study investigated the properties of electrospun PVA/Chitosan and PVA/Chitosan/Tetracycline hydrochloride (THC) mats for wound dressing. The mats feature cross-linked, three-dimensional nanofibers with uniform drug incorporation, showing no significant changes in morphological or thermal properties. The THC release profile exhibits a burst effect within the first 2 hours, ensuring effective antibacterial activity against *E. coli*, *S. epidermidis*, and *S. aureus*. In vitro tests demonstrated good cytocompatibility, suggesting these drug-loaded nanofibrous scaffolds are suitable for promoting wound healing [83].

In one study, electrospun PVA/Chitosan/Starch nanofibrous mats were developed for wound dressing applications. Results indicated high cell viability rates of 72%-95% after 24 hours (compared to 100% for the control), reaching 68%-98% after 48 hours with L929 fibroblast cells. The mats exhibited an antibacterial efficiency of 60%-84% against Gram-positive *S. aureus* and 47%-72% against Gram-negative *E. coli*, with greater effectiveness observed against *S. aureus* due to differences in cell wall structure. A higher chitosan content in the mats enhanced antibacterial activity, attributed to interactions between chitosan's protonated amino groups and the negatively charged bacterial cell membranes [84].

In another study, a membrane was created using electrospinning, consisting of deacetylated and arginine-modified chitosan. The produced membrane exhibited a highly hydrophilic and porous three-dimensional nanofibrous structure, resembling that of the native extracellular matrix in humans. Additionally, this nanofiber-based biomaterial demonstrated bactericidal properties against two bacterial strains. In vitro results showed that human fibroblasts were able to adhere to and proliferate on the membranes, confirming their biocompatibility. When applied in vivo to full-thickness wounds, this electrospun membrane enhanced tissue regeneration and accelerated wound closure compared to non-modified membranes [85].

Furthermore, Azuma et al. [86] demonstrated that chitin nanofibrils enhanced clinical outcomes, reduced colonic inflammation, and protected against tissue damage in mice with dextran sulfate sodium (DSS)-induced acute ulcerative colitis (UC). It was also shown that these nanofibrils mitigated mucosal inflammation by decreasing MPO-positive cells such as leukocytes and lowering serum IL-6 levels. In contrast, chitin powder did not produce similar effects in our DSS-induced acute UC model. Additionally, in another study, Azuma et al. [87] evaluated the anti-inflammatory and anti-fibrotic properties of α-chitin nanofibrils in a DSS-induced UC mouse model. The treatment reduced nuclear factor-κB-positive staining in colon tissue (7.2 ± 0.5%/fields versus 10.7 ± 0.9%/fields in controls; $p < 0.05$) and decreased serum monocyte chemotactic protein-1 levels (24.1 ± 7.8 pg/ml vs. 53.5 ± 3.1 pg/ml; $p < 0.05$). Moreover, α-chitin nanofibrils lessened the extent of collagen deposition observed with Masson's trichrome staining (6.8 ± 0.6%/fields compared to 10.1 ± 0.7%/fields in controls; $p < 0.05$). Conversely, α-chitin powder suspension did not exhibit these effects in the UC model. These findings indicate that α-chitin nanofibrils exert anti-inflammatory effects by inhibiting NF-κB activation and demonstrate anti-fibrotic benefits in DSS-induced UC. Furthermore, Ito et al. [88] examined the impact of chitin nanofibrils (NF) and nanocrystals (NC) on skin tissue using a three-dimensional skin culture model and Franz diffusion cells. Application of NF and NC improved the structure of the epithelial granular layer and increased granular density. Additionally, their use resulted in reduced TGF-β production compared to controls, suggesting that NF and NC may have protective effects on the skin. Consequently, exploring their potential inclusion in skin-protective formulations is warranted.

5.2. Chronic wounds

Unlike acute wounds, chronic wounds fail to heal properly or achieve full recovery within three months, often categorized as infected wounds, diabetic ulcers, severe burns, venous/arterial ulcers, and pressure ulcers. These wounds are characterized by persistent infections, excessive inflammation, biofilm formation, and inadequate responses from skin cells, which collectively impede the healing process [80].

Most tympanic perforations heal spontaneously within 7 to 10 days due to natural processes like epithelial migration and fibroblastic activity. However, chronic tympanic perforations, which do not heal within 3 months, require intervention. Although surgical options are effective (>90%), they can be costly and carry anesthesia risks. Chitosan has emerged as a promising biomaterial due to its biocompatibility, mechanical properties, and antibacterial effects, making it effective in enhancing tympanic membrane healing. Researchers have developed 3D chitosan porous scaffolds that enhance cell migration and tissue restoration in perforated tympanic membranes. Additionally, chitosan scaffolds loaded with epithelial growth factor (EGF) have been

shown to improve cell viability and increase the wound-healing rate in vitro. While these chitosan-based approaches may not match surgical effectiveness, they offer a non-invasive alternative for less severe cases and could potentially complement surgical interventions for improved outcomes [89].

As previously stated, stimuli-responsive hydrogels can adjust to changes in the wound environment, making them particularly beneficial for chronic wounds. Additionally, hydrogels and foams help maintain optimal moisture levels while effectively absorbing exudates.

5.3. Surgical applications

Chitosan exhibits remarkable versatility in surgical medicine, playing a key role in applications such as surgical coatings that inhibit bacterial growth and enhance the efficacy of antimicrobial drugs through nanofiber technology. It is essential in the development of FDA-approved surgical adhesives, including laser-activated films, and is utilized in small-diameter vascular grafts and carotid grafts that effectively maintain arterial pressure. Additionally, chitosan is employed to create hydroxyapatite-chitosan patches for effective mastoid cavity obliteration. Its innovative radiopaque derivatives also improve gastrointestinal imaging in diagnostic procedures. Overall, the diverse surgical applications of chitosan highlight its significant potential to advance medical technologies [89].

Currently, a variety of chitosan-based hemostatic dressings are commercially available, including the InnoSeal hemostatic pad [90], Clo-Sur^{Plus} Radial^{TM} pad [91], Trauma Gauze, ChitoGauze, Celox Gauze, HemCon, and ChitoFlex [92]. These products vary in their mechanisms of action—such as fluid absorption, red blood cell cross-linking, and mucoadhesive barrier formation as well as in their formats (e.g., granular gauze, flexible bandages), which affects their effectiveness for different wound types [78, 89, 93].

Surgical interventions require minimizing blood loss to reduce complications and healthcare costs. The HemCon patch has been shown to effectively reduce waiting times and hospital stays after elective procedures, achieving hemostasis in 76.6% of cases within two minutes compared to 10-12 minutes with conventional gauze. Its flexibility allows for better site conformity and control, while also reducing localized pain and providing antibacterial properties. In comparison, Celox, evaluated alongside Algan (AHA) in animal studies, demonstrated rapid hemostatic effects, achieving bleeding control within two minutes. Both agents highlight the importance of effective hemostasis in surgical settings. Chitosan dressings like Axiostat are also notable, achieving hemostasis in about 8.9 minutes with a 91.7% success rate in femoral artery access procedures and minimal complications, making them valuable in surgeries for coagulopathic patients [78].

Winebrake et al. [94] evaluated the effectiveness of chitosan-based dressings compared to bioresorbable polyurethane packing and no packing following balloon-assisted, middle meatal endoscopic dacryocystorhinostomy in patients with acquired nasolacrimal duct obstruction. A retrospective analysis was conducted on adult patients from 2015 to 2018, excluding those with previous nasal or lacrimal surgeries. Patients were categorized into three groups based on postoperative packing: no packing, bioresorbable packing, and chitosan-based dressing. Outcomes were assessed based on subjective reports and anatomical findings at least three months post-surgery, alongside recommendations for surgical revision. Among the 43 cases (36 patients), significant variations in outcomes were found among the groups ($P = 0.0495$), particularly between the no-packing and chitosan dressing groups ($P = 0.033$). Chitosan-based dressings showed a trend toward reduced revision surgery recommendations ($P = 0.203$, $P = 0.113$). Zheng et al. [95] investigated the effectiveness of carboxymethyl chitosan anti-adhesion solution in preventing postoperative adhesions in Wistar rats. Forty adult male rats were categorized into three groups: normal saline (group A), hyaluronic acid gels (group B), and carboxymethyl chitosan solution (group C). Treatments were applied during surgery, and after 2 to 3 weeks, the degree of adhesions and histological effects were assessed. Results showed that groups B and C had significantly fewer adhesions, with group C exhibiting lower levels of TGF-β1 and hydroxyproline compared to group A ($P < 0.05$). Histopathological analysis revealed fewer inflammatory cells and fibroblasts in group C. Overall, carboxymethyl chitosan was effective in preventing postoperative adhesions, indicating its potential as a promising drug delivery system for anti-adhesion.

Madrazo-Jiménez et al. [96] evaluated a chitosan hydrogel containing allantoin, dexpanthenol, and chlorhexidine. The results indicated that while the gel with 0.2% chlorhexidine, allantoin, and dexpanthenol did not enhance postoperative comfort for patients, it did improve wound healing.

Huang et al. [97] developed an innovative Chitosan-PVA composite hydrogel that showed remarkable tissue adhesion and anti-swelling characteristics. This hydrogel exhibited strong biocompatibility and biodegradability, along with a notable decrease in inflammation around the cells. In a rabbit model with cecum and abdominal wall injuries, the hydrogel successfully prevented intraperitoneal adhesions, indicating its potential efficacy in preventing postoperative abdominal wall adhesion.

6. Limitations and future perspectives

Although chitin and chitosan are considered promising biomass resources with wide potential applications, their use remains limited by several factors. The variability in biological activities due to structural modifications, high production costs, and reliance on crustacean sources pose significant challenges [98]. Harsh chemical extraction methods can affect quality and pose environmental concerns, while eco-friendly alternatives are still under development [98-100]. Additionally, inconsistent safety and toxicity data, especially regarding human applications, highlight the need for more standardized and comprehensive toxicity assessments [101]. Chitosan's versatility is offset by limitations such as poor solubility in neutral and basic conditions and weak antibacterial activity due to its limited positive charge. Its effectiveness depends on factors like degree of deacetylation, molecular weight, source, and environment [102, 103]. Despite these issues, most studies show chitosan nanoparticles have low toxicity and are safer than free chitosan, especially for oral and topical applications [103, 104]. However, human toxicity data are limited, and testing methods vary. Future research should focus on standardizing safety assessments and optimizing formulations for clinical use [101]. Additionally, efforts should be dedicated to developing sustainable extraction from non-animal sources and enhancing the structural stability and bioactivity of chitin and chitosan.

7. Conclusion

Chitin and chitosan-based biocomposites represent a significant leap in wound management, combining natural healing properties with advanced material science. Their versatility makes them suitable for acute, chronic, and surgical applications, positioning them as promising next-generation wound dressings. Future research should focus on scalability and clinical validation to maximize their therapeutic potential. These biopolymers exhibit excellent biocompatibility, biodegradability, and antimicrobial properties. They significantly enhance wound healing by

stimulating fibroblast proliferation, promoting collagen deposition, and reducing inflammation, leading to faster closure rates. Chitin/chitosan materials also retain moisture, lower infection risks, and accelerate tissue repair, outperforming traditional dressings. Innovative combinations with other biopolymers or synthetic materials result in dressings with improved mechanical strength and functionality. These advancements include enhanced healing properties, antimicrobial action, and the ability to support tissue regeneration. Incorporating nanoparticles further enhances their effects. Moreover, these biocomposites are eco-friendly, addressing environmental concerns, and include recent developments of stimuli-responsive materials that adapt to changes in the wound environment, such as pH and temperature. Collectively, these innovations underscore the transformative potential of chitin/chitosan-based biocomposites in the future of wound care technologies. Future research should focus on scaling production, clinical validation, and optimizing formulations to fully realize their therapeutic potential in diverse wound care applications.

Author contributions

Majid Salehi: Conceptualization and Writing – Original Draft Preparation, Writing – Review & Editing; **Marjan Mirhaj:** Writing – Original Draft Preparation and Writing – Review & Editing, **Nadia Banitorfi Hoveizavi:** Investigation, Writing – Original Draft Preparation and Writing – Review & Editing**; Mohamadreza Tavakoli:** Writing – Original Draft Preparation, Writing – Review & Editing. **Naimeh Mahheidari:** Writing – Original Draft Preparation, Writing – Review & Editing.

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Data availability

No data is available.

REFERENCES

[1] D.S.R. Rajkumar, K. Keerthika, V. Vijayaragavan, Chitosan-based biomaterial in wound healing: a review, Cureus 16(2) (2024).
[2] O.A. Peña, P. Martin, Cellular and molecular mechanisms of skin wound healing, Nature Reviews Molecular Cell Biology 25(8) (2024) 599-616.
[3] R. Dong, B. Guo, Smart wound dressings for wound healing, Nano Today 41 (2021) 101290.
[4] J. Nandhini, E. Karthikeyan, S. Rajeshkumar, Nanomaterials for wound healing: Current status and futuristic frontier, Biomedical Technology 6 (2024) 26-45.
[5] B.R. Freedman, C. Hwang, S. Talbot, B. Hibler, S. Matoori, D.J. Mooney, Breakthrough treatments for accelerated wound healing, Science Advances 9(20) (2023) eade7007.
[6] A. Gupta, Z.A. Bozcheloei, A. Ghofrani, S.K. Nejad, P. Chakraborty, R.S. Ambekar, E. Barati, Electroactive composite for wound dressing, Journal of Composites and Compounds 4(10) (2022) 13-23.
[7] A.N. Tahneh, B. Dashtipour, A. Ghofrani, S.K. Nejad, Crosslinked natural hydrogels for drug delivery systems, Journal of Composites and Compounds 4(11) (2022) 109-123.
[8] F.E. Ismaeel, H.R. Kareem, M.F. Abbas, M.H. Al-Musawi, M.M. Kamil, M. Shahriari-Khalaji, F. Sharifianjazi, K. Tavamaishvili, M. Tavakoli, F. Azamian, Fabrication and characterization of an asymmetric bilayer wound dressing for healing acceleration of full thickness wounds, International Journal of Pharmaceutics (2025) 125638.
[9] R. Singh, K. Shitiz, A. Singh, Chitin and chitosan: biopolymers for wound management, International Wound Journal 14(6) (2017) 1276-1289.
[10] M. Jones, M. Kujundzic, S. John, A. Bismarck, Crab vs. Mushroom: A Review of Crustacean and Fungal Chitin in Wound Treatment, Marine Drugs 18(1) (2020) 64.
[11] K. Piekarska, M. Sikora, M. Owczarek, J. Jóźwik-Pruska, M. Wiśniewska-Wrona, Chitin and chitosan as polymers of the future—obtaining, modification, life cycle assessment and main directions of application, Polymers 15(4) (2023) 793.
[12] P. Feng, Y. Luo, C. Ke, H. Qiu, W. Wang, Y. Zhu, R. Hou, L. Xu, S. Wu, Chitosan-based functional materials for skin wound repair: Mechanisms and applications, Frontiers in Bioengineering and Biotechnology 9 (2021) 650598.
[13] D. Jiang, K. Scharffetter-Kochanek, Mesenchymal Stem Cells Adaptively Respond to Environmental Cues Thereby Improving Granulation Tissue Formation and Wound Healing, Frontiers in Cell and Developmental Biology Volume 8 - 2020 (2020).
[14] G. Hojnik Podrepšek, Ž. Knez, M. Leitgeb, Development of chitosan functionalized magnetic nanoparticles with bioactive compounds, Nanomaterials 10(10) (2020) 1913.
[15] J. Xu, L. Chang, Y. Xiong, Q. Peng, Chitosan-Based Hydrogels as Antibacterial/Antioxidant/Anti-Inflammation Multifunctional Dressings for Chronic Wound Healing, Advanced Healthcare Materials 13(30) (2024) 2401490.
[16] M. Yang, H. Wang, K. Li, Z. Chen, D. Seamirumi, A new soft tissue constructed with chitosan for wound dressings-incorporating nanoparticles for medical and nursing therapeutic efficacy, Regenerative Therapy 24 (2023) 103-111.
[17] A.A. Essawy, A. El-Nggar, Biocompatible chitosan in unique applications for tissue engineering, Materials for Biomedical Engineering, Elsevier2019, pp. 279-308.
[18] C.P. Jiménez-Gómez, J.A. Cecilia, Chitosan: a natural biopolymer with a wide and varied range of applications, Molecules 25(17) (2020) 3981.
[19] T.M. M. Ways, W.M. Lau, V.V. Khutoryanskiy, Chitosan and its derivatives for application in mucoadhesive drug delivery systems, Polymers 10(3) (2018) 267.
[20] K.S. Dhlamini, C.T. Selepe, B. Ramalapa, L. Tshweu, S.S. Ray, Reimagining Chitosan-Based Antimicrobial Biomaterials to Mitigate Antibiotic Resistance and Alleviate Antibiotic Overuse: A Review, Macromolecular Materials and Engineering 309(9) (2024) 2400018.
[21] S. Chen, X. Wei, Z. Sui, M. Guo, J. Geng, J. Xiao, D. Huang, Preparation of antioxidant and antibacterial chitosan film from Periplaneta americana, Insects 12(1) (2021) 53.
[22] M. Moon, H. Lee, Y. Kim, Hypocholesterolemic Effects of Chitosan in Rats Fed with High Cholesterol Diet, Wiley Online Library, 2006.
[23] D.H. Keast, A. Janmohammad, The Hemostatic and Wound Healing Effect of Chitosan Following Debridement of Chronic Ulcers, Wounds: a Compendium of Clinical Research and Practice 33(10) (2021) 263-270.
[24] S. Sahudin, N. Sahrum Ayumi, N. Kaharudin, Enhancement of skin permeation and penetration of β-arbutin fabricated in chitosan nanoparticles as the delivery system, Cosmetics 9(6) (2022) 114.
[25] D. Szopa, K. Pstrowska, A. Witek-Krowiak, Chitosan-Coated Alginate Matrices with Protein-Based Biostimulants: A Controlled-Release System for Sustainable Agriculture, Materials 18(3) (2025) 591.
[26] D. Yu, F. Ye, S. Dobretsov, J. Dutta, Antifouling activity of PEGylated chitosan coatings: Impacts of the side chain length and encapsulated ZnO/Ag nanoparticles, International Journal of Biological Macromolecules 281 (2024) 136316.
[27] S. Ghattavi, A. Homaei, E. Kamrani, D. Saberi, M. Daliri, Fabrication of antifouling coating based on chitosan-melanin hybrid nanoparticles as sustainable and antimicrobial surface, Progress in Organic Coatings 174 (2023) 107327.
[28] B. Yang, K. Gu, S. Wang, Z. Yi, Y. Zhou, C. Gao, Chitosan nanofiltration membranes with gradient cross-linking and improved mechanical performance for the removal of divalent salts and heavy metal ions, Desalination 516 (2021) 115200.
[29] Q. Long, Z. Zhang, G. Qi, Z. Wang, Y. Chen, Z.-Q. Liu, Fabrication of chitosan nanofiltration membranes by the film casting strategy for effective removal of dyes/salts in textile wastewater, ACS Sustainable Chemistry & Engineering 8(6) (2020) 2512-2522.
[30] K. Chen, Y. Ni, X. Shi, Z. Jia, H. Qiu, G. Portale, Green fabrication of chitosan microcapsules via double emulsion-simple coacervation and their application in fabrics, Cellulose 30(18) (2023) 11875-11887.
[31] S. Peers, A. Montembault, C. Ladavière, Chitosan hydrogels for sustained drug delivery, Journal of Controlled Release 326 (2020) 150-163.
[32] I.N. Khan, S. Navaid, W. Waqar, D. Hussein, N. Ullah, M.U.A. Khan, Z. Hussain, A. Javed, Chitosan-based polymeric nanoparticles as an efficient gene delivery system to cross blood brain barrier: in vitro and in vivo evaluations, Pharmaceuticals 17(2) (2024) 169.
[33] M. Rinaudo, Chitin and chitosan: Properties and applications, Progress in polymer science 31(7) (2006) 603-632.
[34] J. Berger, M. Reist, J. Mayer, O. Felt, N. Peppas, R. Gurny, Structure and interactions in covalently and ionically crosslinked chitosan hydrogels for biomedical applications, European journal of pharmaceutics and biopharmaceutics 57(1) (2004) 19-34.
[35] S.A. Agnihotri, N.N. Mallikarjuna, T.M. Aminabhavi, Recent advances on chitosan-based micro-and nanoparticles in drug delivery, Journal of controlled release 100(1) (2004) 5-28.

[36] Q. Wang, X. Wang, Y. Feng, Chitosan hydrogel as tissue engineering scaffolds for vascular regeneration applications, Gels 9(5) (2023) 373.
[37] J. Kumirska, M.X. Weinhold, J. Thöming, P. Stepnowski, Biomedical activity of chitin/chitosan based materials—influence of physicochemical properties apart from molecular weight and degree of N-acetylation, Polymers 3(4) (2011) 1875-1901.
[38] A.J. da Silva Lucas, E.Q. Oreste, H.L.G. Costa, H.M. López, C.D.M. Saad, C. Prentice, Extraction, physicochemical characterization, and morphological properties of chitin and chitosan from cuticles of edible insects, Food Chemistry 343 (2021) 128550.
[39] P. Chen, C. Zhao, H. Wang, Y. Li, G. Tan, Z. Shao, Y. Nishiyama, T. Hu, J. Wohlert, Quantifying the contribution of the dispersion interaction and hydrogen bonding to the anisotropic elastic properties of Chitin and Chitosan, Biomacromolecules 23(4) (2022) 1633-1642.
[40] H. El Knidri, R. Belaabed, A. Addaou, A. Laajeb, A. Lahsini, Extraction, chemical modification and characterization of chitin and chitosan, International journal of biological macromolecules 120 (2018) 1181-1189.
[41] P. Sahariah, M. Másson, Antimicrobial chitosan and chitosan derivatives: A review of the structure–activity relationship, Biomacromolecules 18(11) (2017) 3846-3868.
[42] M. Chen, J. Liu, J. Lin, K. Zhuang, Y. Shan, S. Tiwari, L. Jiang, J. Zhang, Progress in Polysaccharide-Based Hydrogels for Preventing Postoperative Adhesions: A Review, Gels 11(3) (2025) 188.
[43] L.I. Moura, A.M. Dias, E. Carvalho, H.C. de Sousa, Recent advances on the development of wound dressings for diabetic foot ulcer treatment—A review, Acta biomaterialia 9(7) (2013) 7093-7114.
[44] S. Islam, M.R. Bhuiyan, M. Islam, Chitin and chitosan: structure, properties and applications in biomedical engineering, Journal of Polymers and the Environment 25 (2017) 854-866.
[45] V. Sinha, A.K. Singla, S. Wadhawan, R. Kaushik, R. Kumria, K. Bansal, S. Dhawan, Chitosan microspheres as a potential carrier for drugs, International journal of pharmaceutics 274(1-2) (2004) 1-33.
[46] H. Ibrahim, E. El-Zairy, Chitosan as a biomaterial—structure, properties, and electrospun nanofibers, Concepts, compounds and the alternatives of antibacterials 1(1) (2015) 81-101.
[47] S. Khattak, F. Wahid, L.-P. Liu, S.-R. Jia, L.-Q. Chu, Y.-Y. Xie, Z.-X. Li, C. Zhong, Applications of cellulose and chitin/chitosan derivatives and composites as antibacterial materials: current state and perspectives, Applied microbiology and biotechnology 103 (2019) 1989-2006.
[48] A. Jiang, R. Patel, B. Padhan, S. Palimkar, P. Galgali, A. Adhikari, I. Varga, M. Patel, Chitosan based biodegradable composite for antibacterial food packaging application, Polymers 15(10) (2023) 2235.
[49] M. Wang, Y. Wang, G. Chen, H. Gao, Q. Peng, Chitosan-Based Multifunctional Biomaterials as Active Agents or Delivery Systems for Antibacterial Therapy, Bioengineering 11(12) (2024) 1278.
[50] W.A. Sarhan, H.M. Azzazy, I.M. El-Sherbiny, Honey/chitosan nanofiber wound dressing enriched with Allium sativum and Cleome droserifolia: enhanced antimicrobial and wound healing activity, ACS applied materials & interfaces 8(10) (2016) 6379-6390.
[51] N. Ardila, N. Medina, M. Arkoun, M.-C. Heuzey, A. Ajji, C.J. Panchal, Chitosan–bacterial nanocellulose nanofibrous structures for potential wound dressing applications, Cellulose 23 (2016) 3089-3104.
[52] Y. Pilehvar-Soltanahmadi, A. Akbarzadeh, N. Moazzez-Lalaklo, N. Zarghami, An update on clinical applications of electrospun nanofibers for skin bioengineering, Artificial cells, nanomedicine, and biotechnology 44(6) (2016) 1350-1364.
[53] W.F. de Oliveira, P.B.S. Albuquerque, N.E.R. Rodrigues, P.M. dos Santos Silva, J.F. Kennedy, M.T. dos Santos Correia, L.C.B.B. Coelho, Pharmaceutical applications of chitosan on medical implants: a viable alternative for construction of new biomaterials?, Carbohydrate Polymer Technologies and Applications 7 (2024) 100407.
[54] X. Che, T. Zhao, J. Hu, K. Yang, N. Ma, A. Li, Q. Sun, C. Ding, Q. Ding, Application of chitosan-based hydrogel in promoting wound healing: a review, Polymers 16(3) (2024) 344.
[55] P. Kassal, J. Kim, R. Kumar, W.R. de Araujo, I.M. Steinberg, M.D. Steinberg, J. Wang, Smart bandage with wireless connectivity for uric acid biosensing as an indicator of wound status, Electrochemistry Communications 56 (2015) 6-10.
[56] H.P. Felgueiras, M.T.P. Amorim, Functionalization of electrospun polymeric wound dressings with antimicrobial peptides, Colloids and Surfaces B: Biointerfaces 156 (2017) 133-148.
[57] D.W. Song, S.H. Kim, H.H. Kim, K.H. Lee, C.S. Ki, Y.H. Park, Multi-biofunction of antimicrobial peptide-immobilized silk fibroin nanofiber membrane: Implications for wound healing, Acta biomaterialia 39 (2016) 146-155.
[58] N. Monteiro, M. Martins, A. Martins, N.A. Fonseca, J.N. Moreira, R.L. Reis, N.M. Neves, Antibacterial activity of chitosan nanofiber meshes with liposomes immobilized releasing gentamicin, Acta biomaterialia 18 (2015) 196-205.
[59] Y. Tang, X. Lan, C. Liang, Z. Zhong, R. Xie, Y. Zhou, X. Miao, H. Wang, W. Wang, Honey loaded alginate/PVA nanofibrous membrane as potential bioactive wound dressing, Carbohydrate polymers 219 (2019) 113-120.
[60] C.-H. Yao, C.-Y. Lee, C.-H. Huang, Y.-S. Chen, K.-Y. Chen, Novel bilayer wound dressing based on electrospun gelatin/keratin nanofibrous mats for skin wound repair, Materials Science and Engineering: C 79 (2017) 533-540.
[61] L.A. Nazar, S. sameer Al-salman, S.H. Torki, M.H. Al-Musawi, A. Najafinezhad, P. Noory, E.S. Rajab, N. Khosravi, S. Talebi, F. Azamian, 3D printed PHB-dextran-whitlockite porous construct coated with sildenafil-loaded nanofibers: a hybrid scaffold for craniofacial reconstruction, International Journal of Biological Macromolecules (2025) 144352.
[62] Y.C. Shin, D.M. Shin, E.J. Lee, J.H. Lee, J.E. Kim, S.H. Song, D.Y. Hwang, J.J. Lee, B. Kim, D. Lim, Hyaluronic acid/PLGA core/shell fiber matrices loaded with EGCG beneficial to diabetic wound healing, Advanced healthcare materials 5(23) (2016) 3035-3045.
[63] D. Chouhan, B. Chakraborty, S.K. Nandi, B.B. Mandal, Role of non-mulberry silk fibroin in deposition and regulation of extracellular matrix towards accelerated wound healing, Acta biomaterialia 48 (2017) 157-174.
[64] T. Zhou, N. Wang, Y. Xue, T. Ding, X. Liu, X. Mo, J. Sun, Electrospun tilapia collagen nanofibers accelerating wound healing via inducing keratinocytes proliferation and differentiation, Colloids and Surfaces B: Biointerfaces 143 (2016) 415-422.
[65] M. Séon-Lutz, A.-C. Couffin, S. Vignoud, G. Schlatter, A. Hébraud, Electrospinning in water and in situ crosslinking of hyaluronic acid/cyclodextrin nanofibers: Towards wound dressing with controlled drug release, Carbohydrate polymers 207 (2019) 276-287.
[66] Y. Chen, J. Chen, K. Chen, H. Qiu, Preparation and properties of antibacterial composite hydrogels based on polyvinyl alcohol, chitosan, and nano-metal oxide, Cellulose 31(6) (2024) 3607-3622.
[67] S. Ranjbar, A. Bakhtiari, N. Khosravi, S.J. Ashkavandi, F. Azamian, M. Alijaniha, M. Karbalaee, Silver nanoparticles: biomedical applications and future perspectives, Journal of Composites and Compounds 6(20) (2024).
[68] S. Nasra, S. Pramanik, V. Oza, K. Kansara, A. Kumar, Advancements in wound management: Integrating nanotechnology and smart materials for enhanced therapeutic interventions, Discover nano 19(1) (2024) 159.
[69] A. Alberts, D.-I. Tudorache, A.-G. Niculescu, A.M. Grumezescu, Advancements in Wound Dressing Materials: Highlighting Recent Progress in Hydrogels, Foams, and Antimicrobial Dressings, Gels 11(2) (2025) 123.
[70] R. Jayakumar, M. Prabaharan, P.S. Kumar, S. Nair, H. Tamura, Biomaterials based on chitin and chitosan in wound dressing applications, Biotechnology advances 29(3) (2011) 322-337.
[71] M. Wang, Q. Yang, J. Long, Y. Ding, X. Zou, G. Liao, Y. Cao, A comparative study of toxicity of TiO2, ZnO, and Ag nanoparticles to human aortic smooth-muscle cells, International Journal of Nanomedicine (2018) 8037-8049.
[72] Y. Song, R. Guan, F. Lyu, T. Kang, Y. Wu, X. Chen, In vitro cytotoxicity of silver nanoparticles and zinc oxide nanoparticles to human epithelial colorectal adenocarcinoma (Caco-2) cells, Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis 769 (2014) 113-118.
[73] F. Dong, S. Li, Wound dressings based on chitosan-dialdehyde cellulose nanocrystals-silver nanoparticles: mechanical strength, antibacterial activity and cytotoxicity, Polymers 10(6) (2018) 673.
[74] R. Ahmed, M. Tariq, I. Ali, R. Asghar, P.N. Khanam, R. Augustine, A. Hasan, Novel electrospun chitosan/polyvinyl alcohol/zinc oxide nanofibrous mats with antibacterial and antioxidant properties for diabetic wound healing, International journal of biological macromolecules 120 (2018) 385-393.
[75] P. Kassal, M. Zubak, G. Scheipl, G.J. Mohr, M.D. Steinberg, I.M. Steinberg, Smart bandage with wireless connectivity for optical monitoring of pH, Sensors and Actuators B: Chemical 246 (2017) 455-460.
[76] D. Jankowska, M. Bannwarth, C. Schulenburg, G. Faccio, K. Maniura-Weber, R. Rossi, L. Scherer, M. Richter, L. Boesel, Simultaneous detection of pH value and glucose concentrations for wound monitoring applications, Biosensors and Bioelectronics 87 (2017) 312-319.
[77] H. Adel Alawadi, K. Andarzbakhsh, A. Rastegari, Z. Mohammadi, M. Aghsami, F. Saadatpour, Chitosan–Aloe Vera Composition Loaded with Zinc Oxide Nanoparticles for Wound Healing: In Vitro and In Vivo Evaluations, IET nanobiotechnology 2024(1) (2024) 6024411.
[78] R. Cassano, P. Perri, E. Scarcello, P. Piro, R. Sole, F. Curcio, S. Trombino, Chitosan hemostatic dressings: properties and surgical applications, Polymers 16(13) (2024) 1770.
[79] H. Li, X. Wei, X. Yi, S. Tang, J. He, Y. Huang, F. Cheng, Antibacterial, hemostasis, adhesive, self-healing polysaccharides-based composite hydrogel wound dressing for the prevention and treatment of postoperative adhesion, Materials Science and Engineering: C 123 (2021) 111978.
[80] X. Zhang, Y. Liang, S. Huang, B. Guo, Chitosan-based self-healing hydrogel dressing for wound healing, Advances in Colloid and Interface Science (2024) 103267.
[81] F. Mushtaq, M. Ashfaq, F. Anwar, B.T. Ayesha, H.S. Latif, S. Khalil, H.S. Sarwar, M.I. Khan, M.F. Sohail, I. Maqsood, Injectable chitosan–methoxy polyethylene glycol hybrid hydrogel untangling the wound healing behavior: in vitro and in vivo evaluation, ACS omega 9(2) (2023) 2145-2160.
[82] F.M. Aldakheel, D. Mohsen, M.M. El Sayed, K.A. Alawam, A.S. Binshaya, S.A. Alduraywish, Silver nanoparticles loaded on chitosan-g-PVA hydrogel for the wound-healing applications, Molecules 28(7) (2023) 3241.
[83] A.C. Alavarse, F.W. de Oliveira Silva, J.T. Colque, V.M. da Silva, T. Prieto, E.C. Venancio, J.-J. Bonvent, Tetracycline hydrochloride-loaded electrospun nanofibers mats based on PVA and chitosan for wound dressing, Materials Science and Engineering: C 77 (2017) 271-281.

[84] H. Adeli, M.T. Khorasani, M. Parvazinia, Wound dressing based on electrospun PVA/chitosan/starch nanofibrous mats: Fabrication, antibacterial and cytocompatibility evaluation and in vitro healing assay, International journal of biological macromolecules 122 (2019) 238-254.
[85] B.P. Antunes, A. Moreira, V. Gaspar, I. Correia, Chitosan/arginine–chitosan polymer blends for assembly of nanofibrous membranes for wound regeneration, Carbohydrate polymers 130 (2015) 104-112.
[86] K. Azuma, T. Osaki, T. Wakuda, S. Ifuku, H. Saimoto, T. Tsuka, T. Imagawa, Y. Okamoto, S. Minami, Beneficial and preventive effect of chitin nanofibrils in a dextran sulfate sodium-induced acute ulcerative colitis model, Carbohydrate Polymers 87(2) (2012) 1399-1403.
[87] K. Azuma, T. Osaki, S. Ifuku, H. Saimoto, T. Tsuka, T. Imagawa, Y. Okamoto, S. Minami, α-Chitin nanofibrils improve inflammatory and fibrosis responses in inflammatory bowel disease mice model, Carbohydrate polymers 90(1) (2012) 197-200.
[88] I. Ito, T. Osaki, S. Ifuku, H. Saimoto, Y. Takamori, S. Kurozumi, T. Imagawa, K. Azuma, T. Tsuka, Y. Okamoto, Evaluation of the effects of chitin nanofibrils on skin function using skin models, Carbohydrate polymers 101 (2014) 464-470.
[89] F. Notario-Pérez, A. Martín-Illana, R. Cazorla-Luna, R. Ruiz-Caro, M.D. Veiga, Applications of chitosan in surgical and post-surgical materials, Marine drugs 20(6) (2022) 396.
[90] A.Z. Pathan, S. Aijaz, S. Sheikh, S. Sattar, Randomized trial comparing radial hemostasis techniques; catechol conjugated chitosan pad (InnoSEAL) versus pneumatic compression band, Catheterization and Cardiovascular Interventions 98(2) (2021) E181-E187.
[91] J.S. Roberts, J. Niu, J.A. Pastor-Cervantes, Comparison of hemostasis times with a chitosan-based hemostatic pad (Clo-SurPlus Radial™) vs mechanical compression (TR band®) following transradial access: A pilot study, Cardiovascular Revascularization Medicine 20(10) (2019) 871-874.
[92] M.A. Khan, M. Mujahid, A review on recent advances in chitosan based composite for hemostatic dressings, International journal of biological macromolecules 124 (2019) 138-147.
[93] J. Shah, D. Patel, D. Rananavare, D. Hudson, M. Tran, R. Schloss, N. Langrana, F. Berthiaume, S. Kumar, Recent Advancements in Chitosan-Based Biomaterials for Wound Healing, Journal of Functional Biomaterials 16(2) (2025) 45.
[94] J.P. Winebrake, A. Mahrous, A. Kacker, A. Tabaee, J.I. Levinger, A.N. Pearlman, M.G. Stewart, G.J. Lelli Jr, Postoperative bioresorbable chitosan-based dressing for endoscopic middle meatal dacryocystorhinostomy with balloon dilation, Ear, Nose & Throat Journal 100(6) (2021) 425-429.
[95] Z. Zheng, W. Zhang, W. Sun, X. Li, J. Duan, J. Cui, Z. Feng, H.M. Mansour, Influence of the carboxymethyl chitosan anti-adhesion solution on the TGF-β1 in a postoperative peritoneal adhesion rat, Journal of Materials Science: Materials in Medicine 24 (2013) 2549-2559.
[96] M. Madrazo-Jiménez, Á. Rodríguez-Caballero, M.-Á. Serrera-Figallo, R. Garrido-Serrano, A. Gutiérrez-Corrales, J.-L. Gutiérrez-Pérez, D. Torres-Lagares, The effects of a topical gel containing chitosan, 0, 2% chlorhexidine, allantoin and despanthenol on the wound healing process subsequent to impacted lower third molar extraction, Medicina oral, patologia oral y cirugia bucal 21(6) (2016) e696.
[97] Y. Huang, J. Zheng, G. Zeng, H. Xu, Y. Lv, X. Liang, L. Jin, X. Jiang, Chitosan-crosslinked polyvinyl alcohol anti-swelling hydrogel designed to prevent abdominal wall adhesion, Materials Today Bio 24 (2024) 100931.
[98] B.T. Iber, N.A. Kasan, D. Torsabo, J.W. Omuwa, A review of various sources of chitin and chitosan in nature, Journal of Renewable Materials 10(4) (2022) 1097.
[99] P. Baharlouei, A. Rahman, Chitin and chitosan: prospective biomedical applications in drug delivery, cancer treatment, and wound healing, Marine Drugs 20(7) (2022) 460.
[100] S. Kumari, R. Kishor, Chitin and chitosan: origin, properties, and applications, Handbook of chitin and chitosan, Elsevier2020, pp. 1-33.
[101] L.H. Zoe, S.R. David, R. Rajabalaya, Chitosan nanoparticle toxicity: A comprehensive literature review of in vivo and in vitro assessments for medical applications, Toxicology Reports 11 (2023) 83-106.
[102] J. Li, S. Zhuang, Antibacterial activity of chitosan and its derivatives and their interaction mechanism with bacteria: Current state and perspectives, European Polymer Journal 138 (2020) 109984.
[103] C. Dias, L. Commin, C. Bonnefont-Rebeix, S. Buff, P. Bruyère, S. Trombotto, Comparative Evaluation of the In Vitro Cytotoxicity of a Series of Chitosans and Chitooligosaccharides Water-Soluble at Physiological pH, Polymers 15(18) (2023) 3679.
[104] J. Frigaard, J.L. Jensen, H.K. Galtung, M. Hiorth, The potential of chitosan in nanomedicine: An overview of the cytotoxicity of chitosan based nanoparticles, Frontiers in pharmacology 13 (2022) 880377.