REVIEW PAPER

Chitosan-A Versatile Biopolymer: Fabrications, Properties, and Clinical Promise

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ABSTRACT

Chitosan, a versatile biopolymer, shows great promise in advanced wound dressing applications. The overall capabilities of chitosan lie in its inherent biocompatibility, biodegradability, haemostatic action, antimicrobial activity, and mucoadhesive properties. This review summarizes the source of chitosan, the extraction procedure, molecular characteristics, and biological functions of chitosan. It primarily focuses on the performance of chitosan and how variations in molecular weight, degree of deacetylation, and chemical changes affect it. This review also enlightens the different manufacturing processes for chitosan-based dressings like films, hydrogels, sponges, nano-fibers, scaffolds, and composites, along with their physicochemical characteristics and biological effects. Finally, it highlights the clinical applicability of chitosan in modern wound care, which can be emphasized by elaborating on in vivo and in vitro evaluation methodologies, which are used to evaluate its efficacy by comparing it with existing commercial products, limitations of these dressings, and providing useful information on future trends and smart dressing technologies.

Keywords: *chitosan, biopolymer, wound healing,*

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INTRODUCTION

The biological skin repair process is a convoluted, signal-driven process divided into four phases. These include remodelling (structural refinement), proliferation (tissue growth), inflammation (immune response), and haemostasis (stopping blood flow). Chronic conditions, like diabetic ulcers, fluctuate as the healing gets delayed due to disruption in the physiological cycles. On the other hand, healthy bodies complete these processes successfully to heal acute wounds [1]. Conventional dressings like cotton, gauze, and bandage serves as a preliminary barrier against impurities. These traditional dressings do not possess the ability to heal actively. As a result, they are unable to manage exudates, prevent infection, or promote tissue regeneration effectively [2]. Some work even reveals that regular dressing changes can cause discomfort for patients and further impede the growth of new tissue. Keeping all these in mind, it resulted in the creation of sophisticated wound dressings that actively help in the process of healing, which is achieved by preserving the moisture, controlling gaseous exchange, absorbing exudates, inhibiting the growth of microorganisms, and delivering therapeutic agents like stem cells, growth factors, or antimicrobial peptides. Chronic wound care is still a major clinical concern in cases of diabetic wounds, burns, or trauma because efficient wound care is required in these cases. The cost of wound care is also an obstacle to efficient treatment involving the above cases. Biopolymers have emerged as an attractive material for advanced wound care due to their biodegradability, biocompatibility, and close resemblance to the natural extracellular matrix (ECM) [3]. Among several biopolymers, chitosan and alginate are the two varieties of polysaccharide-based polymers that have initiated maximum interest. Chitosan has natural antibacterial, haemostatic, and adhesive properties. In addition to these, they encourage collagen synthesis and immune modulation. Chitosan, being cationic in nature, supports wound healing by increasing the clot formation, cell proliferation, and tissue remodelling, and reducing inflammation. Moreover, the antimicrobial and immune-modulatory properties help to reduce infection and inflammatory response. Without triggering the intrinsic coagulation pathway, chitosan causes platelets and RBC aggregation. It controls inflammation by scavenging reactive oxygen species, decreasing pro-inflammatory

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cytokines, and encouraging macrophage polarization towards M2 phenotype [4]. Alginates, on the other hand, are derived from marine algae and can absorb large amounts of fluid. They can also form soft gel, which is well-suited for wounds with heavy exudates. Along with these two biopolymers, bacterial cellulose, collagen, and silk fibroin also find a place as wound dressing materials due to their mechanical strength, ECM mimicry, and biocompatibility [5]. Bioengineering innovations have produced smart dressings that monitor wounds, respond to pH or temperature cues, and control drug release. Porous matrices can be helpful for better drug and cell delivery using fabrication techniques like 3D bio-printing. It is seen that though biopolymers possess several benefits, they also have some drawbacks, like inconsistent degradation rates, variable mechanical strength, and increased production costs [6]. The present review employs an integrated framework that integrates fabrication methods, physicochemical characteristics, and biological outcomes in contrast to earlier reviews that was more focused on material characterization or biological performance separately. In conjunction with fabrication-property-function correlation, this work offers a unique evaluation matrix that connects tests for films, hydrogels, sponges, scaffolds, and composites. Ultimately, this review stands out as a thorough and translational resource for wound care research as it discusses chemical modifications like carboxymethyl and quaternized chitosan. It also discusses smart dressing innovation, biocompatibility assay (MTT, haemolysis, and histology), commercial products, and regulatory perspectives [7, 8].

Sources and extraction of chitosan

Chitin was first identified in the year 1884 from the diverse groups of arthropods like crabs, lobsters, shrimp, krill, and barnacles. All these contribute in the biological ecosystem and are a plentiful source of chitosan as they contain a high amount of chitin. The total chitin content from all these sources can vary from 2% to 12%. Seasonal variability and chemical waste prompted exploration of alternative sources, mainly fungi and insects. Fungi such as Mucor rouxii, Aspergillus niger, and Rhizopus oryzae are used because they are less allergenic than crustacean-derived chitosan [9, 10]. On the other hand Beetles, silkworms, mealworms, and crickets reported as new chitosan sources derived from insects [11]. With advancement in biotechnology, chitosan synthesized via genetic engineering or enzymatic processes can be an alternative source of chitosan, which is still under development and not yet commercialized. De-proteinization followed by demineralization and finally de-acetylation are the critical steps to extract chitosan from chitin (Table 1) [12, 13].

Table 1. Extraction process of chitosan

Method	Steps	Factors
Deproteinization	Critical step involving removal of tightly bound proteins using NaOH (1%-5%) at 65°C - 100°C [14]. Advanced techniques used to save time include Ultrasound-assisted and microwave-assisted de-proteinization [15].	Process efficiency depends on alkali concentration, temperature, reaction time and source.
Demineralization	Helps to remove inorganic components like calcium carbonate from chitin and purify them before conversion by removing $CaCO_3$ using HCl (0.1–2 M) at room temperature for 30 min–2 h [16].	Reaction parameter includes acid concentration, time, temperature, and solid-liquid ratio.
De-acetylation	The final step is performed by treating with concentrated NaOH, at elevated temperatures (80–120°C) for several hours. Degree of de-acetylation (DD > 50%) defines chitosan [16].	Biological activity, solubility, and functional activity depend upon the DD.

Molecular structure and degree of de-acetylation

Chitosan is a polysaccharide composed of N-acetyl-D-glucosamine (GlcNAc) and β-(1→4) linked D-glucosamine (GlcN) units. Its physiochemical properties, including viscosity, charge density, solubility, and crystallinity of chitosan are all significantly affected by DD. Commercial chitosan generally exhibits DD values between 60 and 95%, with industrial grade material exceeds 70% [17,18]. Deacetylation is achieved by treating chitin with with strong alkali, such as NaOH at elevated temperature, to remove acetyl groups ($-COCH_3$) from the N-acetyl-D-glucosamine units of chitosan and increase free amino groups ($-NH_2$). After purification and drying [19] chitosan usually has a molecular weight ranges from 300 to 1000 kDa. DD is determined by methods such as FTIR (e.g., band ratios at ~1320/1420 cm^{-1}), ^1H NMR, UV-VIS, and titration. Increased protonable amino groups improve solubility in diluted acids, and chain flexibility through intra-molecular hydrogen bonding [20,21].

Biocompatibility of chitosan

A biocompatible substance fosters haemostasis, lowers inflammation, speeds up cell proliferation, and assists in tissue repair by supporting tissue integration and cellular functions without causing immunological or toxic reactions. In vitro and in vivo studies assessing cytotoxicity, inflammatory response, and long-term

interactions in compliance with FDA, EMA, and ISO 10993 guidelines confirm biocompatibility, which is essential for implants, drug-delivery systems, and tissue engineering. Strong tissue interactions are rendered possible by chitosan's structural and cationic qualities, which improve fibroblast, osteoblast, and keratinocyte adhesion, proliferation, and migration. As a result, chitosan's scaffolds, hydrogels, films, and nanoparticles are extremely biocompatible [22,23]. The degree of de-acetylation (ideally 70–85%), molecular weight (MW), purity, and source all impact biocompatibility; chitosan derived from fungi provides higher purity and fewer allergenic issues [24]. By influencing the solubility, rate of degradation, and interaction with cells, chitosan's MW has a major impact on its biocompatibility. Low molecular weight chitosan (LMWC), improves cellular uptake and lowers cytotoxicity as it has increased solubility and decreased viscosity. This property makes it appropriate for wound dressings. On the other hand, high molecular weight chitosan offers lower permeability and slower biodegradation, which impede cell growth [25,26]. The difference in the source of chitosan, purity, acetylation level, and residual protein content makes a substantial impact on the biocompatibility. For instance, crustacean-derived chitosan contains allergic proteins which are capable of triggering immune responses, while fungal-derived chitosan is free from it offering greater consistency and purity and being more biocompatible. Fungal chitosan also exhibits lower cytotoxicity and better cell compatibility [27,28]. PEGylation or carboxymethylation also refines chitosan's biocompatibility. In a review done by Frigaard et al. several in vitro and in vivo assessments were observed. Theses includes cytotoxicity assay, haemocompatibility tests, cell adhesion and proliferation test, animal model studies, histological examinations, degradation and immune response study of chitosan. It was concluded that haemolysis and coagulation tests establish general haemocompatibility and safety of chitosan, while MTT and LDH assays are done to evaluate cytotoxicity using L929, HeLa or NIH-3T3 cells [29].

Biodegradability of Chitosan

Chitosan is broken down by enzymes, which makes it biodegradable and beneficial for wound healing, drug delivery, biomedical devices, and eco-friendly packaging. In addition to environmental factors like pH, temperature, enzymes, and microbial activity, intrinsic factors like DD, MW, crystallinity, and crosslinking additionally influence its degradation (Figure 1).

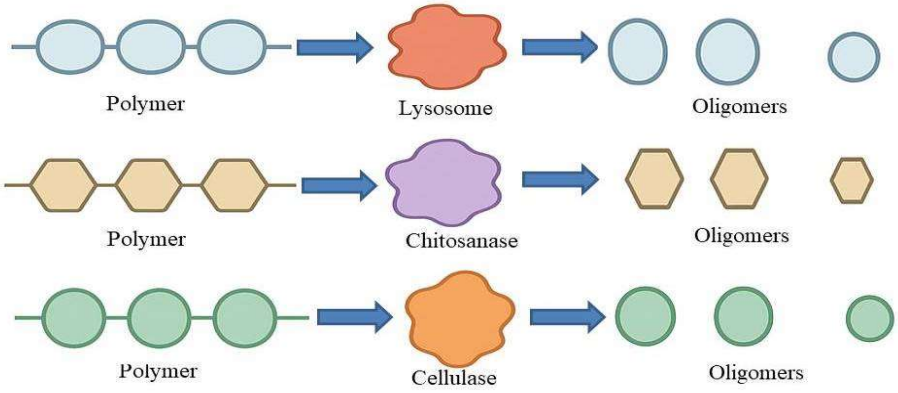


Figure 1. Enzymatic degradation of chitosan

The DD of partially acetylated chitosan is an essential element in biodegradation because the β-(1→4) linkages between N-acetyl-D-glucosamine and D-glucosamine are broken by lysozyme, which exists in human tears and mucosal fluids [30]. Chitosan with DD above 80% degrades faster due to increased amino groups, hydrophilicity, and enzyme accessibility, whereas lower DD and higher crystallinity slow degradation. Like DD kinetics of degradation are also influenced by MW; low MW chitosan breaks rapidly compared to its higher counterpart. Since microbial chitinases facilitates chiotosan to biodegrade in soil and water, it can be used as an eco-friendly substitute for synthetic polymers [31,32]. Derivatives of chitosan, like carboxymethyl chitosan (CMCh) and quaternized chitosan (QTCh) exhibits variable rates of degradation (Table 2) [33].

Table 2. Analysis of biodegradability of chitosan

Method	Purpose	Description
Gravimetric analysis	Measures mass loss over time	Determines degradation rate by quantifying the weight reduction of the sample over a defined time period.
Gel Permeation Chromatography (GPC)	Evaluates molecular weight changes	Tracks polymer degradation through reductions in molecular weight and polydispersity.
Scanning Electron	Observes morphological	Provides high-resolution images of surface

Microscopy (SEM)	changes	erosion, pore formation, cracks, and overall structural breakdown.
Fourier Transform Infrared Spectroscopy (FTIR)	Detects chemical/structural changes	Identifies alterations in functional groups and chemical bonds during degradation.
Enzyme assays (lysozyme, chitosanase)	Measures enzymatic degradation	Quantifies degradation kinetics in the presence of biological enzymes [34].
In vivo studies	Determines biodegradation in living organisms	Implantation in animal models followed by histological, biochemical, and morphological evaluation over weeks to months [35,36].

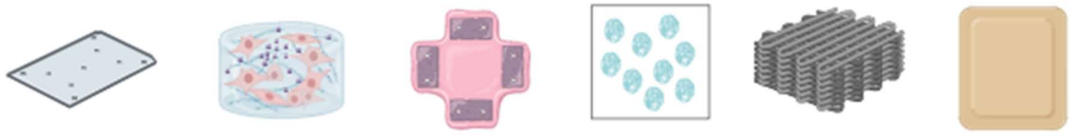


Figure 2. Chitosan based dressing materials. a. Film b. Hydrogel c. Sponge d. Nano-fiber e. Scaffold f. Composite dressings

Films

Chitosan-based films have drawn interest as efficient wound dressings because of their inherent bioactivity, tunable properties, and ease of fabrication. The positive charge of chitosan allows it to interact strongly with negatively charged cell membranes and microbial surfaces, producing natural haemostatic and antibacterial effects that are helpful in the early management of wounds. These films produce a moist, protective layer that shields tissue from contamination and mechanical damage while absorbing light exudate. Their muco-adhesive, film-forming properties reduce scar formation while increasing cell migration and re-epithelialization [37]. Khor et al. and Li et al. in their independent reviews, showed that chitosan films are frequently blended, cross-linked, or integrated with bioactive agents to overcome limitations in mechanical strength and solubility. This allows for improved mechanics, regulated drug release, and customized degradation [38,39]. Pramanik et al. in their recent review, explored chitosan-based smart films featuring antioxidant activity, stimuli-responsive delivery, and wound monitoring properties. Chitosan films exhibit better biocompatibility and healing, but more clinical trials, purity, and scalability are required to validate next-generation wound care applications [40].

Hydrogels

The reactive amino and hydroxyl groups of chitosan enable simple crosslinking and chemical modification, which impart biodegradability, biocompatibility, and intrinsic haemostatic and antimicrobial actions. In this regard, chitosan-based hydrogels have become a multipurpose wound care system. These systems help in re-epithelialization, angiogenesis, and matrix reconstruction by retaining moisture, absorbing exudates, conforming to intricate wound shapes, and offering sustained release of medications, growth factors or antimicrobials [41]. It is also observed that by the incorporation of silver or other metal nanoparticles, antioxidants, antibiotics, or blending with polymers like PVA or PEG, the mechanical stability, release profiles, and antibacterial activity are also enhanced. Silver or copper nanoparticles loaded chitosan hydrogels dramatically reduce the bacterial burden and enhance the healing property in diabetic, immune-compromised, and infected wound models when compared with controls. Self-healing systems, thermo-sensitive, chemically modified, and injectable hydrogels further support the clinical use. The other factors helping in the use of the hydrogel systems include source, DD, residual impurities, sterility, and controlled biodegradation of chitosan [42].

Sponges

Chitosan based sponges have increasingly made a mark in wound management due to their higher biocompatibility, adjustable porosity, and innate haemostatic and antimicrobial properties. They possess a positive charge and, as a result, are effective in controlling bleeding and heavy exudate wounds by increasing the clotting. These sponges are manufactured by breeze-drying, gas foaming, or porogen leaching, which enhances their mechanical and pharmacological properties. Altering the polymer content, crosslinking, or building dual-network “super-porous” structures increases the permeability and quick shape recovery for irregular wounds, mechanical strength, elasticity, and pore dimensions of the system [43]. Numerous studies have shown that to increase antimicrobial activity, some additives, growth factors, tannic acid, AgNPs, or metal-organic frameworks (Zn-MOFs) are incorporated in the system. Variability in formulation and nanoparticle dose raises concerns about cytotoxicity and long-term scarring, despite preclinical data showing decreased bleeding, infection, and faster closure [44,45].

Nano-fibers

Chitosan-based nano-fibers have emerged as an adaptable and highly intriguing class of wound-dressing materials because they combine the natural biological activity of chitosan with the structural advantages of nano-scale fibrous scaffolds. Electrospinning is the most popular method for producing chitosan-based nano-fibers because it generates high surface-area mats with ECM-like porosity that facilitate fluid handling, cell adhesion and migration, and gas/nutrient exchange. These characteristics urge the formation of granulation tissue and re-epithelialization while acting as physical barriers against microbes [46]. Chitosan can be blended with natural or synthetic polymers, such as gelatine or silk fibroin, as well as PLC, to enhance mechanical strength and ease of processing while preserving its biological activity. Functionalization increases the therapeutic potential of nano-fibers. The spatial separation of structural and bioactive functions, such as a polymeric core for extending drug release and an outer chitosan-rich shell for instant antibacterial action, is made possible by coaxial and core-shell electro-spinning. In-vivo and in-vitro studies demonstrate that such structures improve collagen deposition, reduce inflammation, and increase wound closure rates. Incorporating bioactive phytochemicals like curcumin, metal nanoparticles like silver, and growth factors improves the antimicrobial efficacy, suppresses inflammatory responses, and promotes quicker re-epithelialization. Safety profile, like AgNp accumulation causing toxicity, is still considered an unresolved challenge in this system [47].

Scaffolds

Chitosan based scaffolds are now widely recognized as an essential dressing material for effective wound healing. Chitosan scaffolds can be designed in many different forms, such as hydrogels, films, membranes, porous or lyophilized sponges, and electro-spun nano-fibrous mats, allowing them to be tailored to suit different kinds of wounds and the specific stages of the healing process. These scaffold formats facilitate modular design; integrating chitosan with collagen, alginate, PCL, PVA, or hyaluronic acid increases mechanical integrity and handling for different types of wounds. Blending chitosan with growth factors, zinc oxide, silver nanoparticles, or antimicrobial peptides creates synergistic scaffolds that are particularly effective for treating chronic or infected wounds. Addressing this issue is critical for effective antimicrobial functionalization. Recent studies also look into composite scaffolds that include stimuli-responsive (pH, enzyme) chitosan hydrogels for on-demand release and pro-angiogenic agents to accelerate the proliferative stage. Many novel composite scaffolds are still in the preclinical stage, despite the fact that there are several chitosan dressings on the market. This suggests that translation to clinical devices is encouraging but not yet finished [48].

Composite dressings

Combination with collagen, alginate, or AgNPs is used to produce composite dressings. This system improves the mechanical strength, fluid handling capacity, and cell adhesiveness to optimise wound healing. A Chitosan-alginate composite utilizes electrostatic interaction between positively charged chitosan and negatively charged carboxylates of alginates to form a complex. This system improves the overall mechanical and pharmacological attributes. Additionally, layered or porous chitosan/alginate membranes support staged healing and infection control by enabling controlled medication release [49]. Chitosan-collagen composites target to combine the antibacterial and haemostatic characteristics of chitosan. This is achieved by natural ECM signalling and the superior cell-adhesion pattern of collagen. Moreover, these improve fibroblast attachment, proliferation, and organized matrix deposition in preclinical models by accelerating granulation and re-epithelialization. These composites mimic the biochemistry and ECM mechanism, thus finding their relevance in both acute and chronic wounds. Like other systems, silver nanoparticles are incorporated here to enhance the antimicrobial spectrum of the composite. Various preclinical research indicates that chitosan-AgNP composites increase the healing metrics and decrease infection more rapidly, despite the need for careful control of AgNP size, dosage, and release kinetics [50].

Processing Pathways: converting chitosan into functional healing mats

Chitosan dressings are made using unique fabrication methods (Figure 3) chosen according to the requirements of the wound, the required porosity, strength, and bioactive incorporation.

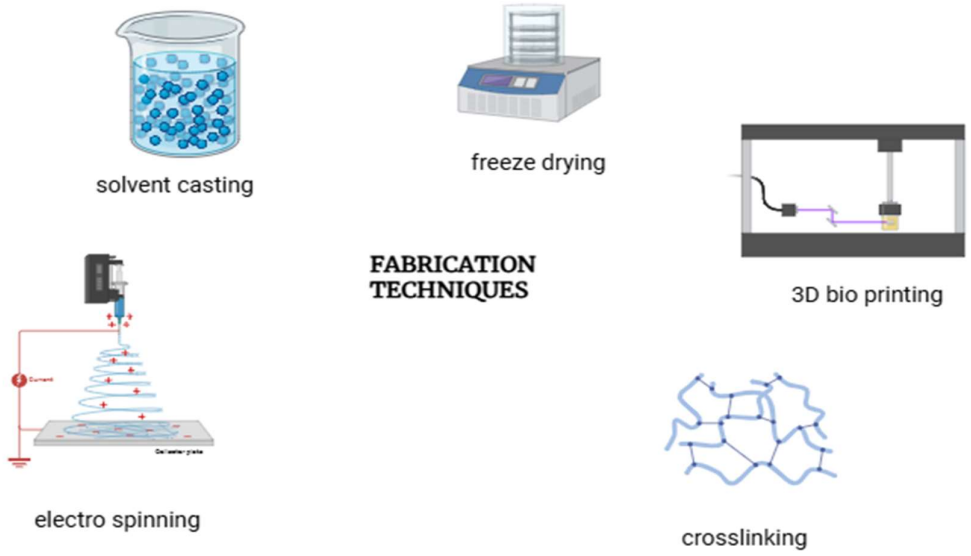


Figure 3: Fabrication techniques of chitosan-based dressing material

Solvent Casting

Solvent-casting is one of the most straightforward and most prevalent methods for producing chitosan films and contact-layer dressings (Figure 4).

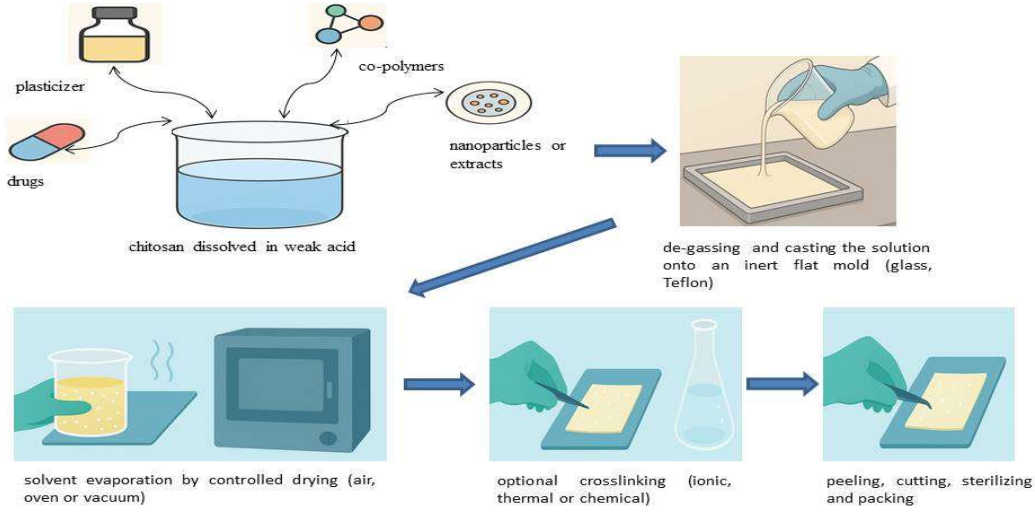
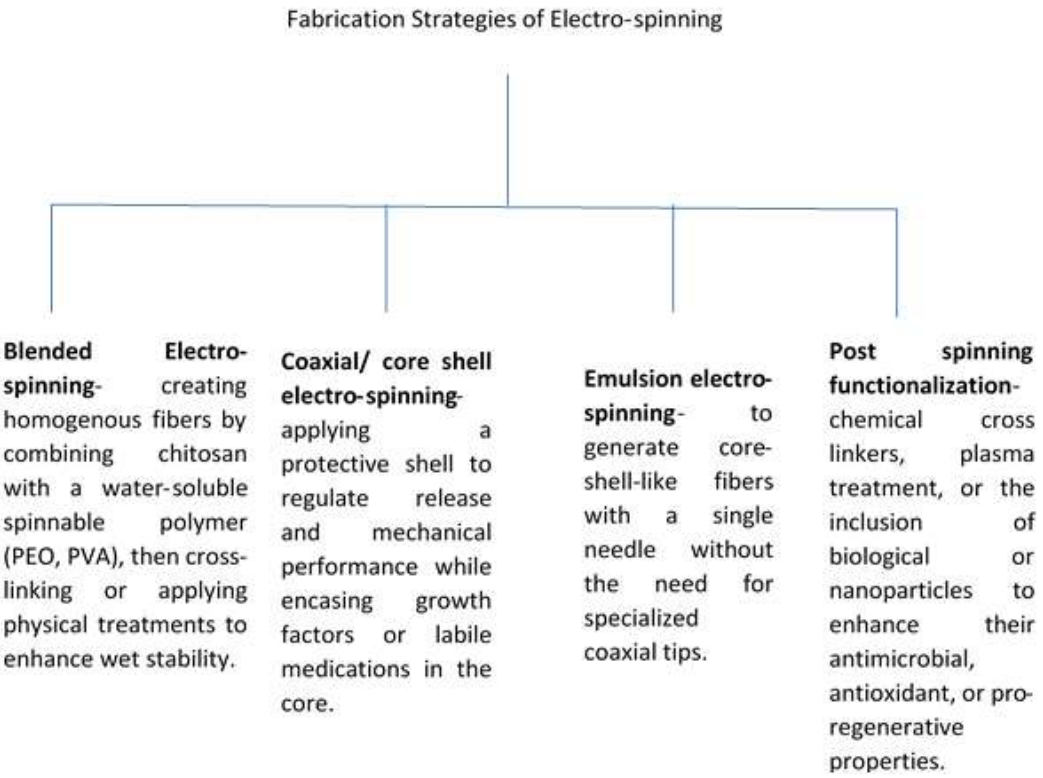


Figure 4: Solvent casting method

Film mechanics, hydration, permeability, drug release, and biocompatibility are all affected by polymer concentration, chitosan molecular weight and de-acetylation, solvent type and acidity, viscosity, degassing, cast volume, drying conditions, and post-treatments. Researchers like Khubiev et al. frequently add plasticizers for flexibility, blend with hydrophilic polymers for easier handling, and add antimicrobial agents. The preferred solvent is still acetic acid. Bubbles are reduced by degassing, and thickness variation is constrained by regulated humidity. To prevent contamination from slow drying or cracking from rapid loss, drying must be balanced. Low-cost equipment, small-batch scalability, adaptable loading and thickness, transparency, bioactive compatibility, and multilayer options are all benefits of solvent-casting dressings. Factors like variability, leftover solvents, lengthy drying times, and restricted toughness are disadvantages of this process. Sterility, release tests, and consistent physicochemical specifications are required for clinical use [51].

Electro-spinning

Versatile nano-fibers are generated by electro-spinning, and the resulting surface's adjustable structure and functionality make them suitable for wound dressings.



Partovi et al. in their study showed that to improve healing and antimicrobial activity, electro-spun chitosan nano-fibers can be functionalized with substances like drugs, extracts, or nanoparticles. Lu et.al in their review concluded that stability is increased by coatings, hydrophobic blending, or crosslinking. Although encouraging in vitro and in animals, there are still issues with sustaining bioactivity, attaining wet-stability, expanding production, and fulfilling clinical validation standards [52].

Freeze drying

Freeze-drying, sometimes referred to as lyophilisation, is a prevalent manufacturing technique to create porous, highly absorbent chitosan dressings suitable for wound care (Figure 5).

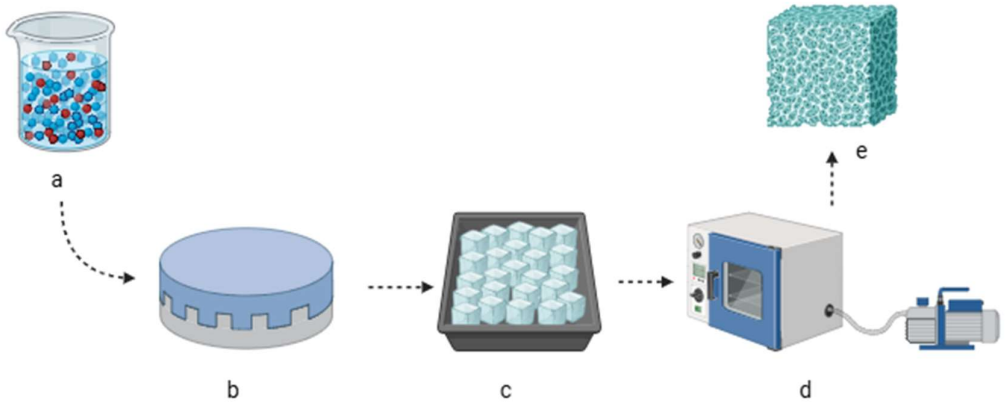


Figure 5: Typical workflow of freeze drying. a. acidic chitosan solution (or chitosan blended with other polymers/additives). b. mold or formed beads/gels. c. frozen ice crystals. d. sublimation under vacuum to remove ice. e. interconnected porous scaffold

Important processing variables include solvent/polymer concentration, freezing temperature, and cooling rate. Ice-templating is crucial because it controls the formation of ice crystals and, consequently, pore size, porosity, and connectivity. While freeze-gelation and post-crosslinking enhance strength without hindering porosity, directed

solidification or regulated cooling aligns pores. Although freeze-drying has long cycles, scale-up problems, and low wet strength, it offers bioactive compatibility, high drainage, and adjustable pores. In general, requirements determine the best approach, and hybrid strategies are frequently the best [53].

Crosslinking

Soluble chitosan is transformed into stable dressings with unique mechanical behaviour and degradation through crosslinking. During covalent crosslinking, its hydroxyl and amine groups react with small-molecule reagents. Glutaraldehyde, genipin, and carbodiimide systems are common agents (EDC/NHS). While glutaraldehyde creates quick, robust crosslinks but is more cytotoxic, genipin, a natural and low-toxicity alternative, creates long-lasting, biocompatible networks with a distinctive blue hue. By forming amide bonds, EDC/NHS is frequently used to attach chitosan to proteins or other polymers. When longer stability, greater stiffness, less swelling, or slower enzymatic degradation is needed, covalent networks are favoured [54]. Protonated chitosan and multivalent ions such as sulphated polysaccharides, Ca2+, Fe3+, or TPP interact electrostatically to form ionic crosslinking. Although they have less mechanical strength, these gentle, reversible interactions facilitate the encapsulation of delicate biomolecules. Chemical-ionic hybrid systems improve responsiveness and robustness. Nam et al. in their review concluded that Tyrosinase, TG, and HRP are examples of enzymatic methods that allow for mild in-situ gelation with tuneable kinetics. This results in the formation of biocompatible chitosan composites, which are appropriate for sophisticated dressings and injectables. Thermo-sensitive or enzymatically cross-linked hydrogels support minimally invasive use, while porous, moderately cross-linked sponges are suitable for highly exudative deep wounds. Efficient healing can be achieved by dual cross-linked designs like ionic + covalent, chitosan + collagen, hyaluronic acid, or inorganic fillers, which help in balancing the adhesion, strength, degradation, and bioactivity [55].

3D Bio-printing

Patient-specific chitosan-based hydrogels with regulated porosity and drug release are now possible due to 3D printing and bio-printing. Chitosan supports adjustable rheology for extrusion, photo-curing, or inkjet printing when it's modified (carboxymethylated, methacrylated, amphiphilic) or combined with polymers such as alginate, gelatin, PCL, or nano-cellulose. Multifunctional dressings are produced by crosslinking and the addition of bio-actives (Table 3). Regulatory approval, standardized bio-inks, and improved mechanics are still required despite promising in-vitro/in-vivo results (Table 4) [56,57].

Table 3: Characterization of chitosan-based dressing materials with their chemical and biological parameters

Chitosan based dressings	Physical, structural, and mechanical parameters	Chemical parameters
Films	Surface topography, porosity, and homogeneity by AFM and scanning electron microscopy (SEM). Crystallinity and thermal transitions by X-ray diffraction (XRD) and differential scanning calorimetry (DSC) Tensile testing (Young's modulus, tensile strength, elongation) to observe the withstand handling and attachment to tissue. Hydrophilicity and fluid management by contact angle and swelling tests [58].	Polymer identity, crosslinking, and interactions with incorporated actives by Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), differential scanning calorimetry / thermo gravimetric analysis (DSC/TGA), X-ray photoelectron spectroscopy (XPS), and degree-of-de-acetylation (DD) [59].
Hydrogels	Functional assays by swelling, gelation time, and crosslink density, zeta-potential. Surface topography, porosity, and homogeneity by SEM. Viscosity and gelation time are measured to obtain the mechanical strength.	Confirm composition, cross-linking and functional groups are observed by FTIR, NMR. Crystallinity by XRD. Thermal stability by TGA/DSC. Molecular weight/distribution by GPC. Degree of de-acetylation and substitution by titration/FTIR.
Sponges	Porosity (%) and pore size distribution are estimated by SEM. Water absorption capacity and Density measurement. Mechanical strength of the sponge is measured by the compression modulus and the resilience test	Functional groups are observed by FTIR. Crystallinity by XRD. Thermal stability by TGA/DSC.
Nano-fibers	Fiber diameter distribution and porosity by SEM, TEM. Surface roughness by AFM. Tensile testing (Young's modulus, tensile strength, elongation) to observe the withstand handling and attachment to	Surface elemental composition by XPS. Confirm composition, cross-linking, and functional groups are observed by FTIR. Crystallinity by

	tissue.	XRD.
Scaffolds	Porosity & interconnectivity by Micro-CT, SEM. Pore size distribution, swelling capacity and degradation rate in simulated fluids. Compression/tensile tests and dynamic mechanical analysis (DMA)	Functional groups are observed by FTIR. Crystallinity by XRD. Thermal stability by TGA/DSC.
Composite Dressings	Surface/topography by SEM, AFM. Thickness & density measurement. Water vapour permeability. Contact angle (hydrophilicity/hydrophobicity). Tensile strength, elongation, flexibility & folding endurance.	FTIR. XRD. EDS for elemental mapping for nanoparticles.

Table 4: In-vivo and In-vitro testing of chitosan-based dressings

In-vitro study	In-vivo study
Scratch wound closure. Cell adhesion. MTT. Live/Dead proliferation. CCK-8. Fibroblast/ keratinocyte proliferation and migration. Haemocompatibility/haemolysis tests, Macrophage polarization. Cytokine assays. Antimicrobial activity- Zone of inhibition, CFU count.	Full-thickness dorsal excisional models of mice and rats. In-Vivo wound-closure studies. Histology and immunohistochemistry for measuring collagen deposition. Neovascularization and re-epithelialization [60]. Haemolysis. Clotting time. Cytokine profiling. Wound-closure kinetics, Histology (H&E, Masson's trichrome). Immunohistochemistry for angiogenesis (VEGF, CD31) and inflammation (CD68). Haemostasis time (tail amputation and minor liver laceration for small animals) (swine femoral artery and standardized liver-injury systems for larger animals).

Advantages and disadvantages of chitosan based dressing material

Some major advantages of chitosan based dressings are as follows:

The cationic nature of the chitosan helps in interaction with negatively charged bacterial membranes, showing intrinsic antimicrobial activity. Interaction with blood components and promotion of platelet aggregation favours rapid haemostasis [61]. Favourable biocompatibility and biodegradability marks advantageous then other biopolymers. Chitosan is very easy to modify chemically, which allows for the incorporation of therapeutic agents and functional tailoring. Its versatility also helps to produce films, sponges, hydrogels, nano-fibers, foams, or composite dressings. Finally, its ability to load growth factors, antimicrobials, nanoparticles, or antioxidants for targeted or customized therapies (e.g., diabetic, infected, or burn wounds). Some limitations were also recorded after several studies. These include pure chitosan dressing material, which often lacks tensile strength and durability, necessitating blending or crosslinking due to their variable physical properties and mechanical weakness. Variations in molecular weight, DD, and source material result in batch-wise variation in biological reactions, solubility, and degradation. Limited antimicrobial strength against resistant pathogens often requires modification to enhance antimicrobial property. Unmodified chitosan's poor water solubility makes processing and use more difficult. Depending on the biological source of chitosan, it may cause immunogenicity or allergic reactions. Despite encouraging preclinical data, there are few large-scale clinical trials, which limit clinical translation [62].

Future Trends

Commercial dressings with antimicrobial activity and quick haemostasis include HemCon®, ChitoGauze, ChitoFlex, and CeloxTM. Through conductive, stimuli-responsive matrices, 3D-printed patient-specific scaffolds, sustainable production, and hybrid hydrogels or nano-fibers that enable controlled drug delivery, future chitosan-based dressings are anticipated to provide multifunctional, intelligent, and customizable therapy. Next-generation chitosan wound care will be further improved by developments in real-time wound sensing, integration of regenerative biologics, and comprehensive clinical testing [60].

CONCLUSION

Chitosan-based wound dressings are an adaptable, bioactive class of materials that connect contemporary multifunctional therapies with conventional passive dressings. Multiple stages of healing, like cell growth, angiogenesis, matrix remodelling, rapid clotting, and infection control, are supported by their intrinsic biocompatibility, biodegradability, antimicrobial action, haemostatic capacity, and mucoadhesion. Due to their protonated amino groups and structural similarity to natural glycosaminoglycans, chitosan materials interact with cells, growth factors, and tissue matrices, thus promoting healing. It can be formed into films, hydrogels, sponges, scaffolds, nano-fibers, and complex composites. This can be achieved by adjusting the porosity, mechanics, degradation rates, and drug-release behaviour with advancements in the fabrication techniques like electro-spinning, solvent casting, freeze drying, crosslinking and 3D bio-printing. Other biopolymers (alginate, collagen), bioactive molecules (antimicrobials, antioxidants), or nanomaterials (silver, zinc) can be added to enhance the performance while diminishing the drawbacks like

inconsistent quality, low solubility at physiological pH, and restricted mechanical strength. Modifying chitosan based dressing material can increase the release kinetics and decrease the trauma in dressing removal. The natural ability of chitosan to break down helps in easier waste management. Animal studies reveal that, in comparison to traditional dressings, these treatments lead to enhanced wound closure, decreased bacterial infection, improved tissue formation, and better-looking scars. Studies also reveal that these dressings can be used in burn wounds, diabetic ulcers, traumatic wounds, and surgical sites. Challenges still remain in regulation, scalability, and standardization, limiting the use in mass. Further studies are predicted to evolve a "smart" chitosan system that can detect wound conditions and release treatments when needed, combining bioengineering, nanotechnology, and regenerative medicine to furnish next-generation wound care solutions.

Conflict of interest statement
The authors declare no potential conflict of interest.

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