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RESEARCH ARTICLE

Chitosan-Based Materials in Biomedical Applications: A Systematic Review of Wound Healing, Drug Delivery and Tissue Engineering

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Abstract: ***Background***: Chitosan is a widely studied biopolymer that is used for biomedical applications for itsexcellence in biocompatibility, biodegradability andantimicrobial features. It's being successfully used in medical fields to improve wound healing, drug delivery and tissue engineering. However, it also has some key limitations - material stability issues, poor scalabilityand limited applicability in clinic. Herein, this paper provides an organized review regarding the last advancements in these fields. ***Objectives***: The primary aim of this review is a systematic analysis of the recent explorations and advancements in chitosan-based biomedical applications that evaluates the progress, identifies limitations and paves path for the future research to understand its complete potential. ***Methods***: A systematic literature review was performed using databases including PubMed, ScienceDirect, and Google Scholar, whereby the studies considered were published between 2015 and today. The selection was also based on relevance in applications involving chitosan; wound healing, drug deliveryand tissue engineering constituted some of the most studied fields. The main key factors considered included methodological, quality and prospective biomedical applications. ***Findings***: A total of 30 studies were reviewed, which were categorized into three primary biomedical applications: 1. wound healing properties 2. drug delivery in infections and chronic ailments. 3. tissue engineering and improved mechanical properties. Cell growth for tissue repair could be supported. ***Significance***: Chitosan-based materials hold great promise for biomedical applications, but much remains to be done on stability and scalability. Further work in this area should aim to improve synthesis methods, clinical trials and exploration of combination therapies to help better translate chitosan-based materials into the clinic.

Keywords: Chitosan, Biomedical Applications, Wound Healing, Drug Delivery, Tissue Engineering, Biopolymer, Clinical Translation..

INTRODUCTION

Wound healing is a complex biological process that can be divided into four phases: hemostasis, inflammation, proliferation, and remodelling. These challenges have led to the development of innovative therapeutic approaches for the treatment of delayed healing, infection, and tissue damage. Biomaterials such as chitosan, a polysaccharide derived from chitin, have been found to be promising candidates because of their biocompatibility, biodegradabilityand antimicrobial properties. Chitosan has come to garner attention in wound care with advanced biomaterials. Over the past decades, chitosan has entered into several advanced wound care materials mainly based on healing outcome improvements and effective bioactive delivery [1].

Chitosan is one of the most capable biopolymer and its versatilityallows it to be modified into films, hydrogels, and nanofibers, thereby increasing its effectiveness in tissue engineering and drug delivery. Chitosan/collagen blends, for example, have shown an increased elastic modulus and mechanical stability through dehydro-thermal crosslinking,which makes them suitable for soft tissue engineering. Advanced analyses, such as thermogravimetric and mechanical tests, highlight their adaptability for biomedical applications.Chitosan/gelatin composite corneal implants showed better oxygen permeability, water absorption and biocompatibility, allowing for the growth of fibroblasts and serves as alternative materials to traditional ones [2].

Chitosan-based wound healing materials particularly integrating plant extracts, nanoparticles, and biopolymers are used in order to obtain composite materials to provide better physical stability, antimicrobial activityand tissue regeneration in complex wound care requirements. Studies have shown that chitosan formulations in the form of hydrogels, nanofibers and films combine with agents such as Tageteserecta extract, silver nanoparticles (AgNPs) and polyherbal blends display great antibacterial, antioxidant, and healing-enhancing properties.

Also,the preparations containing ZnO nanoparticles that were prepared by the aid of natural extracts like silymarinand polyvinyl alcohol demonstrated not only prolonged drug deliverybut also enhanced angiogenesis and contraction of the wound in animal models [3]. As for instance, using the hydrogels containing chitosan-alginate rich in agricultural by-products like grape pomace gives more significance to the eco-friendly approach towards wound care practices [4]

This would mean that new nanomaterials can create unique formulations, including nanofibers made from a combination of chitosan and polyvinyl alcohol and hybrid composites improving mechanical stability, controlled release of drugs, and compatibility with the biotapestry. For example, In electrospinning synthesized ginger and thyme extract incorporation, mat-like nanofibers hold great promise in developing appropriate microenvironments for quick healing and tissue repair. Analogously, hydrogels composed of hesperidin-loaded chitosan-coated hybrid nanoparticles (Hsd/CS-HNPs) have shown profound skin permeation and angiogenesis, which further reinforces the idea of chitosan-based wound dressings [5]. Such developments are demonstrating the possibility of using biomaterials to deal with chronic wounds and severe infections with less environmental burden.

This systematic review seeks to integrate the emerging literature regarding chitosan-based materials for wound healing. Additionally, this paper has also discussed the physicochemical properties of formulations, biological activity, and in vivo performance to outline the strengths, limitations, and future perspectives of these materials as innovative therapeutic tools in wound care.

Research contributions

This review provides an exhaustive and current overview of the latest (2020-2025) studies on chitosan-based materials applied for wound healing, with emphasis on:

- Formulation approaches (nanoparticles, composites, bioactive-loaded systems)
- Biological activity (antibacterial, angiogenic, regenerative properties)
- Physicochemical function and in vivo investigations
- Sustainability and biocompatibility in hospital environments

Research gaps

Though previous reviews have highlighted chitosan's overall promise, few have:

- Bridged the gap between lab-scale formulation and clinical translation
- Addressed eco-friendly, plant-based composites and their biomedical significance
- Integrated recent multi-functional nanocomposite developments
- Compared comparative performance with respect to material forms (hydrogels, nanofibers, films)

Questions

This review considers the following questions:

- What recent advances have improved chitosan's biomedical performance, especially in wound healing?
- How are various formulations compared in biological and physicochemical properties?
- What are the main limitations and possibilities for translating these materials to clinical use?

METHODOLOGY:

This systematic review was conducted to evaluate the biomedical applications of chitosan-based materials. In this process, the PRISMA guidelines were followed to select studies comprehensively and in a transparent manner. A total of 200 articles were retrieved from three databases: PubMed (150 articles), Embase (30 articles), and Google Scholar (20articles).

The duplicate studies were filtered out in the screening phase, which gave a unique article count of 160. During the title screening phase, 100 articles were removed because they did not align with the biomedical focus of the review. Therefore, 60 articles were selected for abstract screening. After reading the abstracts, 25 studies were removed based on reasons like not being peer-reviewed (20 articles) and not belonging to either the academic or the artificial intelligence (AI) domain (5 articles).

A total of 35 articles were screened on their full text in the eligibility phase, out of which 10 were excluded because they had unclear domains (7 articles) and less academic focus (3 articles). The remaining 25 articles were eligible for the review. After final evaluation, 5 more studies were included, thereby making the number of included studies in this systematic review as 25.

Chitosan, Biomedical Applications, Wound Healing, Drug Delivery, Tissue Engineering, Biopolymer, Clinical Translation were the keywords included in the search strategy. Boolean operators such as **AND**and**OR** were applied to refine search results and capture relevant studies

A stringent inclusion, exclusion criteria was defined to ensure that high quality and relevant literatures were selected for study. Studies were included if they were published in peer-reviewed journals between January 2015 and June 2025, in English, and dealt with the use of chitosan or chitosan-based composites in biomedical applications, i.e., wound healing, drug delivery, or tissue engineering. Both in vivo and in vitro experimental researches, as well as clinical trials, were considered. Articles were excluded if they were non-peer-reviewed, non-English, or out of the designated biomedical areas. In addition, editorials, conference abstracts, letters to the editor, and articles not available with full-text access or having indistinct methodology were excluded. These included studies not related to biomedical sciences.This ensured that 25 studies were thoroughly analysed and subjected to trends, strengths, and weaknesses of research so far conducted.

Overview:
Chitosan, a biopolymer derived from nature, has become a prominent material in the biomedical applications arena with its biocompatibility, antimicrobial property, and structural flexibility. The following section presents the chief application domains established by a systematic review of updated studies. Foremost advantages, limitations, and salient examples are compiled in the table below to present a compact overview of the biomedical potential of chitosan and on-going research terrain.

Biomedical application of Chitosan:

Application ID	Application Area	Key Benefits	Challenges / Limitations	Examples from revised studies
1	Wound Healing	Biocompatibility, antimicrobial properties, enhanced tissue regeneration	Material stability, limited clinical applicability	Chitosan formulations combined with plant extracts and nanoparticles show significant wound healing
2	Drug delivery	Prolonged drug delivery, enhanced angiogenesis and controlled drug release	Scalability issues, varying synthesis methods	Hydrogels with chitosan and ZnO nanoparticles demonstrated effective drug delivery and healing in animal models
3	Tissue Engineering	Improved mechanical properties, compatibility with biological systems, cell growth support	Limited data on long term effectiveness	Chitosan/ collagen blends exhibit enhanced mechanical stability suitable for soft tissue engineering

Table.1. Summary of biomedical applications of chitosan-based materials including key benefits, challenges, and supporting study examples

RESULTS AND FINDINGS:

A structured methodology following the PRISMA guidelines was employed for the systematic review, in order to ensure a comprehensive and transparent approach. From an initial database search, 200 articles were found on PubMed (150 articles), Embase (30 articles), and Google Scholar (20 articles). After removing 160 duplicates, 100 unique records had their titles screened to exclude any irrelevant articles, and 100 were considered outside the scope of the review. Abstract screening of the other 60 studies eliminated another 30 articles that were not peer-reviewed or were not relevant for academia. Full-text analysis of the remaining 20 studies eliminated another 7 studies due to not clear domains or too weak focus in academic relevance. Only 25 articles passed all inclusion and exclusion criteria, and the strong relevance of the other 5 added them to the final articles of the review for the total of 25. This resulted in the strict inclusion of high-quality studies on the properties, applications, and maintenance of chitosan-based materials in biomedical contexts.

Several advancements in nanotechnology has paved a way for multifunctional development of nanocomposites incorporating chitoshanwith various nanomaterials, including metals, metal oxides, and carbon-based structures. These nanocomposites possess better mechanical strength, biocompatibility, and impressive therapeutic benefits like antimicrobial properties, targeted drug delivery, and tissue regeneration. The way chitosan interacts with nanoscale agents enables a controlled release and boosts the stability of active compounds. However, there's a growing focus on their potential nanotoxicity and biocompatibility, since the interactions at the cellular and molecular levels can provoke immune responses. Grasping these factors is essential for creating safe and effective chitosan-based nanocomposites for biomedical uses [6].

The chitosan-based films loaded with the *Tageteserecta* (Marigold) extract is a promising material for faster cell migration and wound closures. Three different film formulations of the extract (M1, M2, and M3) were assessed based on physical properties, hydrolytic degradation, water vapour transmission rate, folding endurance, antimicrobial activity, and their healing efficiency at the wound site. The M2 formulation exhibited maximum moisture regulation ability as reflected through theWVTR (Water vapour transmission rate) of 1818 g/m²/24 h, good stability, and excellent healing result in scratch assays with 61.82%. All the films demonstrated good flexibility as well as strong antimicrobial activity against E. coli and S. aureus. Results indicate that these films can potentially be very valuable in wound dressings, promoting healing while preventing infection of wounds and could potentially have further clinical applications[1].

Valadi and his team developed a multifunctional alginate-chitosan hydrogel wound dressing for burnwounds comprising silymarin and green-synthesized zinc oxide nanoparticles (ZnONPs) via *Elettaria cardamomum* seeds extract. This study enhances the healing of burn wounds and inhibits complications. The authors characterized the physicochemical properties of ZnO NPs and hydrogels. ZnO hydrogelswith spherical NPs having dimensions ranging from 35 to 45 nm, possess a uniform porous structure with good water absorption, porosity, and antioxidant properties. In vivo rat model tests showed accelerated healing, close to complete closure by day 21, and better regeneration of tissue. Results indicate that this hydrogel has a tremendous potential for burn treatment and could be efficient in terms of the growth of cells, collagen depositionand new blood vessel formation.

One such study focussed on a Chitosan-based polyherbal hydrogel containing silver nanoparticles (Ag NPs) synthesized from leaf extract of *Calotropisprocera* for wound healing. The prepared hydrogel revealed high antimicrobial activity against E. coli and S. aureus and attained maximum swelling within 8 hours. Hydrogelapplied on mice tests showed a marked decrease in the wound size as compared to other commercially available alternatives, within 12 days. The hydrogel possessed higher angiogenic potentialand decreased levels of inflammatory markers IL-6 and TNF-α . Extracts from *Aloe vera, Azadirachtaindica, and Alternantherabrasiliana*demonstrated excellent wound healing properties, hence indicating possible effectiveness of this formulation as a good dressing agent for wounds [7].

The study was further validated by Synthesis of α-tocopherol-modified glycol chitosan (TG) nanoparticles loaded with phytochemical rhein (Rhein@TG NPs), which addresses the challenge of treating MRSA-infected wounds. The NPs were designed to target infected areas by releasing rhein in response to low pH and lipase in the wound environment, thus leading to the elimination of bacteria without devoloping drug resistance. These Rhein@TG NPs enhanced M1 macrophage polarization during infection, reduced inflammation, increased cell migration, and enhanced blood vessel formation. This approach to treatment, devoid of antibiotics, modifies the healing environment of the wound, thereby providing a promising long-term therapeutic strategy for wound infections by MRSA [8].

In another research work, silver nanoparticles (AgNPs)green synthesis using the aqueous extract of olive pomace with subsequent incorporation into Chitosan-Aloe vera gel (AgNPs/AV-CS gel) for acid burn injuries was successfully demonstrated. Due to their smaller size, in the order of 20–25 nm, AgNPs possessed potent antioxidant activity and exhibited remarkable antimicrobial properties against E. coli, P. aeruginosa, S. aureus, and S. epidermidis. AgNPs/AV-CS gel displayed excellent wound healing properties. Wound contraction was up to 74.86% by day 7, and full closure was observed by day 21. Histopathological examination revealed decreased inflammation and tissue regeneration. These results indicate that AgNPs/AV-CS gel can be an excellent option for acid burn wounds [9].

A new bioactive multifunctional chitosan/ aliginate-based hydrogels aimed to incorporate grape pomace(GP) extract for combating Staphylococcus aureus chronic wound infections. The Grape Pomace extract (high added-value raw material)is rich in phenolic compounds. Thefabricated hydrogel cross-linked with glutaraldehyde and calcium chloride showed more capacity in swelling and absorbing more wound exudates. This biomaterial also gives an unusual approach by promoting recycling and valorization of agricultural by-products. Nevertheless, this work possibly addresses existing gaps in wound care managementbenefiting modern society and focus on offering eco-friendly solutions [10].

Another similar study developed biofunctionalized chitosan/gelatin composite wound dressing films reinforced by varying amounts ofPhyllanthusniruri(PN) (ethanolic extract) for wound healing applications. It was created with an idea of high mechanical strength and with strong antibacterial properties againstE.coli and S.aureus. Furthermore, it was hypothesized that the inclusion of PNextract improves fibroblast migration and also enhances cell adhesion and proliferation. Finally this composite films was expected be have all the ideal wound dressing requirements and to provide a valuable strategy in the field of regenerative medicine [11].

The wound healing properties of *Teucriumpolium*was achieved through chitosan based nanohydrogels in streptozotocin-induced diabetic rats. This study revealed that this component of T.Poliumis rich in phenolics, especially flavonoids and terpenoids. Research professors created a chitosan nanogel (CS-NG) loaded with T.poliumnanoprepation (TP-NP)for enhancing would healing and for reducing the wound size and oxidative stress. This treatment increased levels of responsibletransforming growth factor beta1 (TGF-β1), vascular endothelial growth factorA(VEGFA)and platelet-derived growth factor receptor alpha (PGDFRα)through enhanced collagen synthesis that promoted angiogenesis. Collectively, this is one of the best therapeutic options for diabetes people with chronic wounds and in recent days it shows healing rates based on standard treatments [12].

To combat the microbial infection during wound healing , researchers have developed a novel wound dressing patchthat are formed from (Chi) chitosan and polyvinyl alcohol (PVA)using a gel casting technique involving the integration of nano-curcumin (Cur) onto zinc oxide (ZnO) nanoparticles. This patch was targeted to create a more effective and convenient biomaterial to improve wound healing capacity and antimicrobial properties. *In vitro* and *in vivo* studies confirmed the biocompatibility, cell viability and antibacterial activity.Additionally, this patch gives its support for the formation of collagen at the wound site ,which denotes high stability and hemocompatibility. Moreover, this patch PVA/Chi/ZnO/-Cur underwent nearly all testing that is essential for effective wound healing, tissue regeneration and wound closure [13].

Despite the excellent phytochemical potential in wound healing, Hesperidin(Hsd) needs frequent topical applications in high doses. In a recent study, researchers prepared and characterizedHsd-loaded/chitosan-coated hybrid nanoparticles (Hsd/CS-HNPs) to hinder such issues. This nanoparticles are formed by leveraging chitosan (CS) coating and optimizing nanoparticles (F2/CS1).The optimized formula (F2/CS1) with a particle size of 254.10 ±4.59 nm, and a positive zeta potential of 24.23± 2.70 mV and 60.41± 4.56 % drug entrapment efficiency helpedpromising stability and improved skin permeation.The results of skin permeation studies proved better hesperidin permeation from F2/CS1 gel compared to free hesperidin gel. Immunohistochemical analysis showed elevated vascular endothelial growth factor (VEGF) expression,demonstrating the improved angiogenesis [14].

To enhance the vital antibacterial and healing factors, the authors conducted both in-vitro and in-vivo studies integrating Dragon's blood plant (D.cinnabari) and its ethyl acetate extract withchitosan (Chn)/polycaprolactone(PCL)nanofibers. Polycaprolactone polymer thatincreases the mechanical strength served as a major component. Adopting electrospinning method, two nanofibers namely CPD and CPED, i.e., with and without ethyl acetate extract were formed with various percentage levels and tested for LDH cytotoxicity, antibacterial nature, wound healing capacity, swelling and synergy. Results confirmed no harm to human skin cells, potential resistance to certain bacteria and good swelling ratios. In particular, CPED3% showed higher healing and nutrient properties [15].

Moreover,using electrospinning technique, the authors combined chitosan and polyvinyl alcohol loaded with 10% ginger and thyme extracts which are known for its anti-inflammatory effects to create an antimicrobial wound dressing. The nanofibrous mat created was smooth without any defect. After undergoing various tests like infrared spectroscopy, porosity detection, free radical scavenging and so on, the composite nanofiber gave significant results like increased porosity, easier nutrient exchange, sustained antioxidative nature, antibacterial property creating broader inhibition areas, swift wound closure, superior tissue regeneration leading to new skin formation etc., Overall, the nanofiber dressing facilitates a suitable environment speeding up wound healing , substantiating its biocompatibility [16].

In the recent decades, several studies discussed about chitosan nanofiber's synthesis, properties, and mainly its biomedical applications like wound healing and drug delivery ability. Its high surface area-volume ratio facilitates easier attachment with extracellular region. The electrostatic property aids in hemostasis, enhancing ant-inflammation process. Previous studies indicates electrospinning to be the opt method to create thin Chitosan nanofibers.However, suitable solvents and blending proportions act as challenges.Poor solubility, mechanical stability and moisture resistance are other bottlenecks. Biomedically, its combination with other components like zinc or polyvinyl solidifies its properties. Mostly SEM, FTIR, TGA tests are used to analyze its structural, chemical and thermal properties [17].

A new type of water-based anionic urethane polymer has been created, and it's been combined with chitosan and zinc oxide nanoparticles to boost its antibacterial and biocompatible qualities. FTIR analysis confirmed that the urethane pre-polymer was successfully synthesized. By adding chitosan and ZnO nanoparticles, we saw an increase in hydrophobicity and water absorption, while also reducing water vapor permeability thanks to better cross-linking. Biocompatibility tests showed promising results with good growth and proliferation of fibroblast cells, indicating that it's compatible with tissue. Antibacterial tests revealed a powerful synergy between chitosan and ZnO, demonstrating broad-spectrum effectiveness against both gram-positive and gram-negative bacteria, which makes this composite a great option for wound dressing applications [18].

Recent advancements in the treatment of osteomyelitis have provided evidence for the potential of chitosan-based drug delivery systems. With its superior characteristics—being biocompatible, biodegradable, and non-toxic chitosan is also proving to be a promising local antibiotic carrier. Due to its ability to interact and be modified chemically, chitosan is very suitable for targeted uses. Research shows that the application of chitosan-based biomaterials for local antibiotic delivery can effectively treat bacterial infections, reduce systemic toxicity, and overcome biofilm-related resistance key issues in the treatment of osteomyelitis [19].

In the recent years, researchers interestingly focussed on creating chitosan–clay mineral bionanocomposites that has exhibited its strong potential especially in drug delivery and wound care. clay minerals like montmorillonite and halloysite form a gel like substance when combine with chitoshan that improvises the therapeutic effect. These are proven to treat skin infections that are highly compatible with biological tissues that do not cause any toxicity. This also extends the emerging concerns to treat resistance associated with antibiotics especially in topical therapies [20].

Drug based on nanotechnology especially gelatin/chitosan (Ge/CH) nanofibers (NFs) provides outstanding results in biomedicines that has improvised its solubility, expending the therapeutic action eventually minimising side effects. Tissue regeneration and would healing properties are promoted by Ge/CH-based NFs that imitate the extra cellular matrix. The primitive fabrication method is electrospining that combines with enhances the performance with god structural factors and formulations [21].

Facilitated endogenous tissue engineering, which enhances in situ bone regeneration via recruiting and differentiating endogenous stem cells, has emerged as an advantageous alternative to scaffold-based tissue engineering in the last several years. Chitosan (CS) is a prominent example of an ideal scaffold for these applications, due to its biocompatibility, biodegradability, favorable physicochemical properties, and ability to be produced in various shapes. Current work demonstrates advances in CS-based scaffolds that have all been specifically designed to improve osteo-inductivity through biomolecule loading, incorporation of inorganic nanomaterials, and physical stimuli. These advanced scaffolds represent an exciting opportunity not only for enhanced endogenous stem cell homing and differentiation, but also for smart design capabilities to create a strong platform for future bone strategies [22].

The composite scaffolds containing 30 wt% bioactive glass (58S) in a chitosan–gelatin matrix achieved the best results for bone regeneration. The porosity of the composite scaffolds was high (>80%), had appropriate pore sizes (100–300 μm) and had a significantly high compressive strength (2.2 ± 0.1 MPa). The scaffolds promoted the attachment, proliferation, and osteogenic differentiation of mesenchymal stem cells, and cellular activity appeared greater than the controls that lacked bioglass, suggesting better bioactivity and regenerative capacity [23].

According to Kaur, chitosan-polymer blends may significantly elevate the functional properties of drug delivery systems. Blending chitosan with other polymers has produced significantly more favourable solubility, bioadhesion, and controlled drug release profiles than chitosan alone. Nanocarriers formulated from chitosan-polymer blends have been shown to have a positive surface charge which promotes extended circulation time, targeted delivery, and increased uptake by cells. Research from the last ten years has collated these systems as a cheap option as well as providing sustained and site-specific drug release options. A variety of chitosan-based nanocarriers such as nanoparticles, micelles, and hydrogels have been shown to be effective in delivering hydrophilic and hydrophobic drugs; this position chitosan as a promising drug delivery technique for different therapeutic areas [24].

Research has shown that chitosan-gelatin (CG) composite-based biomaterials have remarkable biocompatibility, biodegradability, and water absorption properties, and therefore hold great potential as local hemostatic agents. Increasingly, the addition of oxidized fibers (OF), silica nanoparticles (SiNPs), calcium (Ca), and biphasic calcium phosphate (BCP), or changing the CG ratio improved the physical, chemical, and mechanical properties of the composites, and thus, that the overall hemostatic efficiency was improved which means that CG composite-based biomaterials have significant potential for biomedical and pharmaceutical purposes in the future [25].

ID	Application area	Findings	Support for cell growth
1	Wound Healing	Chitosan films showed great potential in promoting healing and preventing infection in wounds	Yes
2	Drug Delivery	Hydrogels containing chitosan and ZnO nanoparticles improved drug delivery efficacy and accelerated wound healing	Yes
3	Tissue Engineering	Chitosan/collagen blends demonstrated enhanced mechanical properties and were shown to support fibroblast cell growth	Yes

4	Wound Healing	Chitosan-based hydrogels were effective in reducing wound size and enhancing angiogenic potential	Yes
5	Drug Delivery	Chitosan-based formulations with herbal extracts showed promising antimicrobial activity and prolonged drug release	No
6	Tissue Engineering	Blends of Chitosangelatin displayed increased elasticity and stability for soft tissue applications	Yes

CONCLUSION

This review comprises an extensive review of the most recent advances in chitosan-based biomaterials for biomedical applications, specifically, wound healing, tissue engineering, and drug delivery. Recently characterized benefits of chitosan are associated with biological properties such as biocompatibility and antimicrobial activity, in addition to structural forms of chitosan (hydrogels, nanofibers, and films) that afford many applications as a next generation biomedical product. Compared to previous reviews, this review has additional commentary on the utilization of polymer blends, nanocomposite formulations, and bioactive additives. Importantly, more recent studies on chitosan hybridization with inorganic nanoparticles, cross-linking agents, and biobased materials have been included that can add additional insights to its previously defined utility and performance aspects. Moreover, there are also references to newer techniques like additive manufacturing or 3D printing, and more sophisticated smart drug delivery systems that can also be designed to use chitosan, and align with personalized medicine along with some new references that can add a different perspective to future applications.

Nevertheless, much of the current published research is lacking in the technical aspects of synthesis methodologies that have high variability in preparation, long-term biocompatibility testing, and not enough reference from in vivo and/or clinical studies. There is a significant knowledge gap that needs to be addressed in regards to theinequitable knowledge base that exists in not standardizing several fabrication techniques for chitosan and evaluating the perspectives of scale up and cost effectiveness for chitosan technology to be considered for commercial use for the development efficacious products.

To overcome these research limitations, future studies should consider:

- Long-term in vivo studies and clinical trials validating safety and efficacy
- Standardized protocols for synthesis and characterization
- Novel chitosan composites having predetermined physicochemical properties
- Chitosan integrated with novel fabrication techniques for personalized therapies

In conclusion, despite substantial advancements and studies into chitosan biomaterials, additional multidisciplinary research/r, development and clinical validation efforts are needed to advance the potential of chitosan based biomaterials to the next translational stage in healthcare. This review provided a working reference for researchers who wish to disrupt the emerging chitosan biomaterial field while acknowledging the challenges and opportunities that lay ahead in future impactful work.

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