

SPIRULINA-LOADED CHITOSAN-BASED COMPOSITE SPONGES FOR WOUND DRESSING – A REVIEW

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ABSTRACT

Wound healing is a complex biological process involving hemostasis, inflammation, proliferation, and tissue remodeling. Impairment of these coordinated events, particularly in chronic, diabetic, infected, and highly exudative wounds, can result in prolonged inflammation, excessive oxidative stress, microbial colonization, and delayed tissue regeneration. Consequently, considerable attention has been directed toward multifunctional wound dressings capable of simultaneously controlling bleeding, managing exudate, reducing microbial burden, and promoting tissue repair. Chitosan-based porous sponges are promising wound-dressing materials because of their biocompatibility, biodegradability, intrinsic hemostatic activity, antimicrobial properties, and high fluid-absorption capacity. The incorporation of natural bioactive compounds can further enhance their therapeutic potential. Spirulina, commercially associated primarily with *Arthrospira platensis*, is a valuable source of proteins, phycobiliproteins, carotenoids, phenolic compounds, vitamins, minerals, and essential fatty acids. Among its bioactive constituents, C-phycocyanin has attracted particular attention because of its antioxidant, anti-inflammatory, antibacterial, and wound-regenerative activities. Experimental evidence indicates that C-phycocyanin can promote fibroblast proliferation and migration, reduce oxidative stress, and support tissue repair. Importantly, porous chitosan sponges loaded with C-phycocyanin have demonstrated high encapsulation efficiency and controlled release, providing direct evidence for the feasibility of combining Spirulina-derived bioactives with chitosan sponge matrices. Recent studies have further demonstrated the potential of Spirulina protein–chitosan-based biomaterials for infected wound healing. This review summarizes the biological requirements of an ideal wound dressing, the physicochemical and biological characteristics of chitosan, the wound-healing potential of Spirulina-derived compounds, and the rationale for their incorporation into porous composite sponges. Fabrication strategies, structure–property relationships, therapeutic mechanisms, characterization methods, current limitations, and future research opportunities are critically discussed. The available evidence suggests that Spirulina-derived bioactives incorporated into chitosan-based porous sponges represent a promising platform for next-generation multifunctional wound dressings. However, systematic studies using standardized whole-Spirulina extracts or purified bioactive fractions, together with comprehensive in vitro, in vivo, and clinical validation, remain essential for successful translation.

KEYWORDS: *Arthrospira platensis*; Spirulina; chitosan; C-phycocyanin; composite sponge; wound dressing; wound healing; tissue regeneration.

1. INTRODUCTION

The skin is the largest protective organ of the human body and functions as a barrier against physical damage, microbial invasion, dehydration, and environmental stress. Following injury, tissue repair proceeds through coordinated stages of hemostasis, inflammation, proliferation, extracellular matrix deposition, re-epithelialization, and remodeling^[1, 2]. Chronic wounds may become arrested in prolonged inflammatory states, particularly in the presence of diabetes, infection, vascular insufficiency, and oxidative stress.^[1-3]

Conventional dressings such as cotton gauze mainly provide physical coverage and may have limited capacity for active exudate management, antimicrobial protection, and biological stimulation of tissue repair.^[3,4] Advanced wound dressings are therefore increasingly designed to maintain moisture, absorb excess exudate, control bleeding, reduce microbial contamination, and support tissue regeneration.^[4,5]

Chitosan is a particularly attractive natural polymer because of its biocompatibility, biodegradability, hemostatic activity, antimicrobial properties, and structural versatility.^[5-8] It can be fabricated as films, hydrogels, membranes, fibers, powders, and porous sponges. Porous sponges are especially suitable for bleeding and highly exudative wounds because of their interconnected architecture and high fluid-absorption capacity.^[7-9]

Spirulina, commonly associated with *Arthrospira platensis*, is a valuable source of proteins, phycobiliproteins, carotenoids, polysaccharides, vitamins, and other antioxidant compounds.^[10-12] C-phycocyanin is particularly relevant because of its antioxidant, anti-inflammatory, and regenerative activities.^[13-15] The combination of chitosan with Spirulina-derived bioactives therefore provides a rational route toward multifunctional wound dressings capable of combining structural and biological functions.

2. Biological Requirements of an Advanced Wound Dressing

An advanced wound dressing should provide complementary physical and biological functions. It should absorb excess wound exudate while maintaining an appropriate moist environment, permit gas exchange, reduce microbial colonization, support hemostasis, protect regenerating tissue, and possess adequate mechanical integrity.^[3-5] For chronic wounds, antioxidant and anti-inflammatory functions are particularly important because excessive reactive oxygen species and persistent inflammation can impair fibroblast activity and extracellular matrix formation.^[2,3]

Porous sponge systems can address several of these requirements because their interconnected pore network supports fluid uptake and provides a high internal surface area for therapeutic loading. However, pore structure and porosity must be balanced against mechanical stability and controlled bioactive release.

Table 1: Essential properties of an ideal multifunctional wound dressing.

Property	Functional importance
Biocompatibility	Prevents cytotoxicity and adverse tissue responses
Hemostatic activity	Supports rapid control of bleeding
High fluid absorption	Manages blood and wound exudate
Moisture retention	Maintains a favorable environment for cell migration
Gas permeability	Supports oxygen exchange
Antimicrobial activity	Reduces microbial colonization and infection
Antioxidant activity	Reduces excessive reactive oxygen species
Anti-inflammatory activity	Prevents prolonged inflammatory damage
Mechanical stability	Allows handling and maintains wound coverage
Controlled bioactive release	Provides sustained local therapeutic activity

3. Chitosan as a Multifunctional Wound-Dressing Biomaterial

Chitosan is produced by partial deacetylation of chitin and contains β -(1 $\rightarrow$ 4)-linked D-glucosamine and N-acetyl-D-glucosamine units. Its molecular weight and degree of deacetylation influence solubility, degradation, viscosity, mechanical behavior, and biological performance.^[5,6]

The positively charged amino groups of chitosan facilitate interactions with negatively charged biological surfaces. These interactions contribute to its hemostatic and antimicrobial properties. In wound applications, chitosan can promote aggregation of erythrocytes and platelets and can support clot formation independently of some conventional coagulation mechanisms.^[7,8]

Chitosan also exhibits antimicrobial activity through interactions with microbial cell surfaces, potentially affecting membrane integrity and cellular functions.^[5,6] Its reactive amino and hydroxyl groups further allow crosslinking and composite formation, making chitosan highly suitable for porous multifunctional wound-dressing systems.

4. Spirulina as a Source of Wound-Healing Bioactives

Spirulina is a commercially important cyanobacterial biomass generally associated with *Arthrospira* species, particularly *Arthrospira platensis*. Its composition includes proteins, amino acids, phycobiliproteins, carotenoids, fatty acids, minerals, vitamins, and bioactive polysaccharides.^[10–12]

C-phycocyanin is among the most extensively studied Spirulina-derived bioactive molecules. It has demonstrated antioxidant and anti-inflammatory activity and has been investigated for its ability to reduce oxidative stress and regulate inflammatory processes.^[13,14] Experimental studies have also shown that C-phycocyanin can promote fibroblast proliferation and migration, supporting its relevance to tissue regeneration.^[15]

Recent animal-based evidence indicates that *Arthrospira*-derived materials can support wound closure, tissue regeneration, vascularization, and epithelialization. Nevertheless, clinical evidence remains limited, highlighting the need for standardized formulations and translational studies.^[16]

Table 2: Major Spirulina-derived constituents relevant to wound healing.

Bioactive component	Proposed biological activity	Potential wound-healing relevance
C-Phycocyanin	Antioxidant; anti-inflammatory; regenerative	Reduces oxidative stress and supports fibroblast migration
Carotenoids	Antioxidant	Protect against oxidative injury
Proteins and peptides	Nutritional and biological activity	May support cellular metabolism and matrix interactions
Phenolic compounds	Antioxidant and anti-inflammatory	May reduce oxidative and inflammatory stress
Essential fatty acids	Membrane and inflammatory modulation	May support tissue repair
Polysaccharides	Immunomodulatory activity	Potential contribution to tissue regeneration

5. Scientific Rationale for Spirulina–Chitosan Composite Sponges

Chitosan and Spirulina-derived bioactives provide complementary therapeutic functions. Chitosan contributes structural integrity, fluid management, hemostatic activity, antimicrobial effects, and biodegradability. Spirulina-derived compounds may provide antioxidant, anti-inflammatory, and regenerative activity.

Direct evidence supporting this concept has been reported for C-phycoerythrin-loaded chitosan sponges. Porous chitosan materials have demonstrated high encapsulation efficiency and effective loading of C-phycoerythrin, followed by controlled release^[18]. More recent Spirulina protein–carboxymethyl chitosan systems have demonstrated antibacterial, antioxidant, and wound-healing potential in infected wound models.^[17]

Together, these findings provide a strong scientific basis for developing porous composite sponges containing standardized Spirulina extracts, protein isolates, or purified C-phycoerythrin.

Table 3: Complementary functions of Spirulina-derived bioactives and chitosan.

Component	Principal contribution
Chitosan	Hemostasis, antimicrobial activity, biodegradability, structural matrix
Porous sponge architecture	Blood absorption, exudate management, high surface area
C-Phycocyanin	Antioxidant, anti-inflammatory, regenerative activity
Spirulina protein fraction	Potential structural and biological activity
Carotenoids and phenolics	Antioxidant protection
Composite formulation	Tunable mechanical properties and controlled release

6. Fabrication Strategies for Spirulina-Loaded Chitosan Composite Sponges

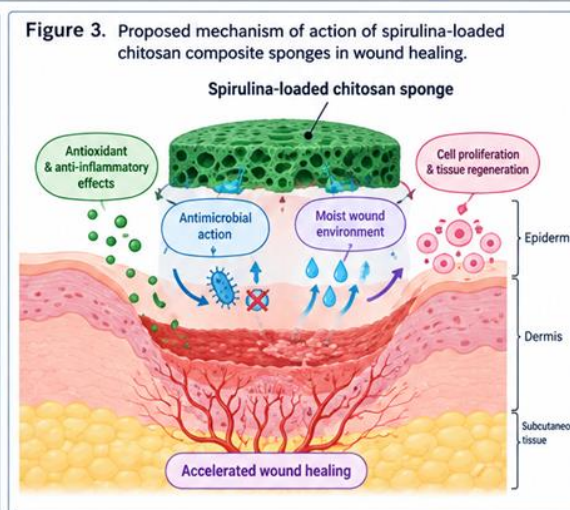
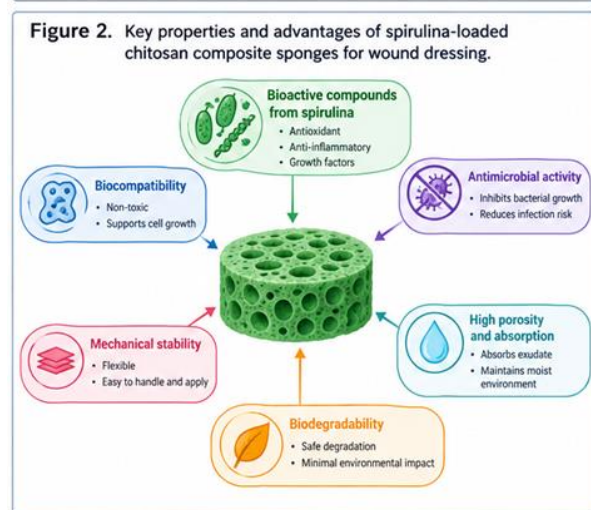
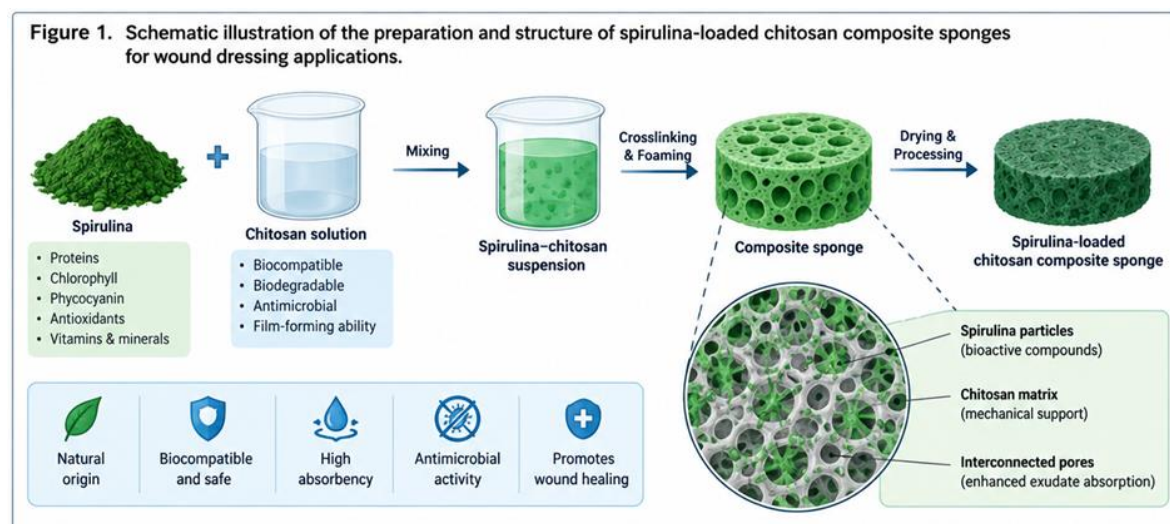
Freeze-drying is one of the most suitable approaches for producing porous chitosan sponges. Chitosan is dissolved in an appropriate acidic medium and combined with Spirulina biomass, standardized extract, protein isolate, or purified C-phycoerythrin. The mixture is frozen, allowing ice crystals to function as temporary pore templates. Lyophilization subsequently removes the frozen solvent and produces an interconnected porous structure.

Crosslinking can improve mechanical integrity and regulate swelling and degradation. Potential approaches include ionic interactions, genipin-mediated crosslinking, Schiff-base chemistry, and composite polymer interactions. Secondary biopolymers such as gelatin, collagen, alginate, cellulose derivatives, silk fibroin, and hyaluronic acid may also improve mechanical and biological properties.

The fabrication process should be optimized to preserve Spirulina-derived bioactivity while achieving suitable porosity, swelling capacity, mechanical stability, and controlled release.

Table 4: Recommended characterization strategy for Spirulina-loaded chitosan composite sponges.

Evaluation category	Recommended methods	Key outcome
Chemical characterization	FTIR; UV–Vis spectroscopy	Polymer–bioactive interactions
Morphology	SEM	Pore size and architecture
Structural properties	XRD	Crystallinity and structural changes
Fluid management	Swelling and absorption studies	Exudate-handling ability
Mechanical properties	Compression/tensile testing	Handling and structural integrity
Bioactive loading	Protein/C-phycoerythrin analysis	Encapsulation and loading capacity
Release behavior	In vitro release study	Release kinetics
Antioxidant activity	DPPH; ABTS; ROS assays	Oxidative-stress reduction potential
Cytocompatibility	MTT; Alamar Blue or equivalent	Cellular safety
Cell migration	Scratch assay	Regenerative potential
Antimicrobial testing	CFU reduction/inhibition studies	Infection-control potential
Hemostatic evaluation	Clotting and blood absorption assays	Bleeding-control performance



7. Proposed Mechanisms of Action in Wound Healing

Following application, a Spirulina-loaded chitosan sponge may influence multiple stages of wound healing. The porous matrix absorbs blood and wound fluid, while chitosan promotes aggregation of blood components and supports hemostasis^[7-9]. Chitosan also contributes antimicrobial activity.

Spirulina-derived antioxidants, particularly C-phycocyanin, may reduce excessive reactive oxygen species and limit oxidative damage to regenerating cells. Anti-inflammatory activity may help prevent prolonged inflammatory responses and facilitate progression toward the proliferative phase.^[13-15]

C-phycocyanin-associated stimulation of fibroblast proliferation and migration may support granulation tissue formation and wound contraction.^[15] Together, these mechanisms may contribute to extracellular matrix deposition, re-epithelialization, and tissue remodeling.

8. Characterization and Biological Evaluation

A comprehensive evaluation strategy is essential for biomedical development. Physicochemical characterization should include FTIR, XRD, SEM, porosity analysis, swelling capacity, fluid absorption, water-vapor transmission, mechanical testing, and degradation studies.

Bioactive characterization should include total protein analysis, C-phycocyanin concentration and purity, encapsulation efficiency, loading capacity, antioxidant activity, storage stability, and release kinetics.

Biological evaluation should include cytocompatibility with fibroblasts and keratinocytes, cell proliferation, scratch-wound migration assays, antimicrobial testing, hemolysis analysis, blood-clotting studies, reactive oxygen species assays, inflammatory biomarkers, and collagen-associated markers. Preclinical validation should preferably include full-thickness, infected, and diabetic wound models.

9. Current Limitations and Research Gaps

Whole *Spirulina* biomass may vary according to strain, cultivation conditions, nutrient availability, harvesting, and processing. Standardization is therefore essential for reproducible biomedical applications.

C-phycocyanin is sensitive to environmental conditions, including temperature and pH. Fabrication and sterilization procedures must preserve its structural integrity and biological activity. Direct evidence for chitosan sponge systems is currently stronger for purified C-phycocyanin than for whole *Spirulina* biomass.

Mechanical weakness is another challenge associated with highly porous sponges. Increasing crosslinking may improve stability but can reduce porosity and fluid absorption. Finally, the majority of evidence remains preclinical, and human clinical trials are required before clinical translation can be established.^[16]

10. Future Perspectives

Future studies should compare whole *Spirulina* biomass, standardized extracts, protein isolates, and purified C-phycocyanin to identify the most effective therapeutic formulation. Advanced composite designs may incorporate secondary polymers to improve mechanical stability and regulate bioactive release.

Stimuli-responsive materials that respond to wound pH, bacterial enzymes, or oxidative conditions may further improve therapeutic precision. Multifunctional designs combining hemostatic, antimicrobial, antioxidant, anti-inflammatory, and regenerative functions may be particularly valuable for diabetic and infected wounds.

Standardized in vitro, in vivo, and clinical evaluation frameworks will be essential for translating *Spirulina*–chitosan composite sponges into clinically relevant wound-care products.

11. CONCLUSION

Spirulina-loaded chitosan-based composite sponges represent a promising strategy for the development of multifunctional wound dressings. Chitosan provides a versatile and biodegradable matrix with intrinsic hemostatic and antimicrobial properties, while porous architecture supports exudate management and localized delivery of therapeutic compounds.

Spirulina contributes bioactive molecules with antioxidant, anti-inflammatory, and regenerative potential. Evidence demonstrating successful loading and controlled release of C-phycocyanin from chitosan sponges provides direct proof of concept, while recent *Spirulina* protein–chitosan systems further strengthen the rationale for this biomaterial combination.

Further research should focus on standardization of Spirulina-derived bioactives, preservation of biological activity, mechanical optimization, controlled release, sterilization, and clinical validation. With systematic development, Spirulina–chitosan composite sponges may emerge as an important platform for next-generation wound-care technologies.

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