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CHITOSAN FROM NATURAL BIOLOGICAL SOURCES FOR WOUND-HEALING APPLICATIONS: HISTORICAL BACKGROUND, PHARMACEUTICAL PROPERTIES AND FUTURE PERSPECTIVES

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ABSTRACT

Background: Natural biological materials have historically played an important role in wound management and the development of medicinal preparations. The medical heritage of Abu Ali ibn Sina (Avicenna) describes the rational use of natural substances of plant, mineral and animal origin, including materials intended for wound cleansing, protection and tissue recovery. Although chitosan as a defined chemical polymer was discovered centuries later, modern pharmaceutical research provides an opportunity to reinterpret this historical experience using contemporary biomaterial science. **Objective:** This review analyzes the relationship between traditional concepts of natural wound-healing agents and the modern pharmaceutical application of chitosan, with emphasis on chitosan derived from crustacean shells and its potential use in wound dressings and drug-delivery systems. **Main findings:** Chitosan is a biodegradable, biocompatible and cationic polysaccharide characterized by mucoadhesive, film-forming, sorption and hemostatic properties. These characteristics support its application in wound dressings, hydrogels, films, sponges, nanoparticles and controlled drug-delivery systems. Pharmaceutical performance is strongly influenced by molecular weight, degree of deacetylation, purity and solubility. Crustacean shells represent a major biological source of chitin and chitosan, and the utilization of local freshwater crayfish shells may provide both pharmaceutical and environmental benefits. Integration with natural bioactive compounds may further enhance functionality, although such combinations require adequate physicochemical, microbiological, pharmacological and toxicological evaluation. **Conclusion:** Chitosan derived from natural biological sources is a promising biomaterial for modern wound-care and pharmaceutical applications. The rational use of natural medicinal resources described in Ibn Sina's medical tradition can be regarded as a historical conceptual background rather than evidence of direct chitosan use. Combining traditional knowledge with modern polymer and pharmaceutical

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technologies may support the development of sustainable, locally sourced and biologically compatible wound-care materials.

Keywords: chitosan; chitin; wound healing; wound dressing; natural biomaterials; crustacean shells; drug delivery; pharmaceutical technology; Avicenna; freshwater crayfish

1. INTRODUCTION

Natural products have served as important sources of therapeutic agents throughout the history of medicine. Long before the development of modern pharmaceutical chemistry, substances of plant, mineral and animal origin were used for the management of wounds, inflammatory conditions and other pathological processes. Among the most influential historical medical systems, the works of Abu Ali ibn Sina (Avicenna) occupy a prominent position because of their systematic approach to drug selection, preparation, dosage and therapeutic application [1,2].

In The Canon of Medicine, Ibn Sina described numerous naturally derived medicinal substances and emphasized that therapeutic effectiveness depended not only on the identity of a material but also on its origin, quality, dose, method of preparation and conditions of use. His pharmacotherapeutic approach included principles related to wound cleansing, control of bleeding and inflammation, application of dressings and protection of damaged tissues [1-3]. These concepts represent an early systematic formulation of several principles that remain relevant to contemporary wound management.

Modern pharmaceutical science has substantially expanded the use of natural biological materials by isolating, characterizing and modifying their functional components. One of the most promising examples is chitosan, a partially deacetylated derivative of chitin. Chitin is widely distributed in crustacean and insect exoskeletons and in fungal cell walls. Industrial chitin production is still largely based on crustacean shells, where chitin occurs in association with proteins, minerals and pigments [4,6,7].

Chitosan has attracted pharmaceutical interest because of its biodegradability, biocompatibility, cationic character, mucoadhesive properties, sorption capacity, film-forming behavior and ability to be processed into fibers, sponges, hydrogels and nanoscale delivery systems [4,5,8]. These properties support its investigation as a matrix for wound dressings, hemostatic materials, topical formulations and controlled drug-delivery systems [8-12]. The functional behavior of chitosan is closely related to its molecular weight, degree of deacetylation, purity, solubility and distribution of acetylated and deacetylated units along the polymer chain [4-6]. Consequently, standardization of both biological raw materials and extraction technology is essential when chitosan is intended for pharmaceutical use.

Particular interest may be directed toward locally available freshwater crayfish shells as a potential raw material for chitin and chitosan production. Crustacean shells are complex natural composites containing calcium carbonate, proteins, pigments and chitin. Sequential demineralization and deproteinization permit the isolation of chitin, followed by conversion into chitosan through deacetylation [6,7]. Utilization of such biological waste may simultaneously provide a source of functional pharmaceutical polymers and contribute to resource-saving and waste-reduction strategies.

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Accordingly, this review examines chitosan as a natural biomaterial for wound-healing applications, focusing on its biological sources, production, physicochemical characteristics, pharmaceutical properties and incorporation into advanced wound-care and drug-delivery systems. Particular attention is given to the conceptual relationship between the historical use of natural medicinal materials described by Ibn Sina and modern strategies for the development of biologically derived pharmaceutical polymers.

2. HISTORICAL BACKGROUND: AVICENNA AND NATURAL WOUND-HEALING AGENTS

Ibn Sina's medical writings systematized knowledge about simple and compound medicines and placed considerable emphasis on the rational use of natural medicinal raw materials. The second book of The Canon of Medicine discusses simple drugs of plant, mineral and animal origin, whereas the fifth book is devoted to compound formulations and their preparation and therapeutic use [1,2]. The value of this historical framework lies not in direct correspondence with modern pharmaceutical substances but in its methodological attention to material origin, quality, formulation and clinical purpose.

Animal-derived materials, including honey, wax and other natural products, were incorporated into preparations intended for external application. Historical descriptions of wound care also addressed bleeding control, reduction of inflammation and edema, wound cleansing and the use of protective dressings [3]. In modern terms, these functions correspond to several core objectives of wound management: hemostasis, protection from contamination, control of exudate, maintenance of a favorable local environment and support of tissue repair.

It is important to distinguish historical continuity from anachronistic attribution. The term chitosan, its chemical definition and its isolation technology emerged centuries after Ibn Sina. Therefore, it would be scientifically incorrect to claim that he used chitosan itself. A more defensible interpretation is that historical use of animal-derived materials and the broader principle of rational utilization of natural medicinal resources provide a conceptual background for present-day research on biopolymers derived from biological raw materials. This distinction preserves historical accuracy while allowing meaningful scientific comparison between traditional material-based medicine and contemporary pharmaceutical biomaterials.

3. NATURAL SOURCES AND PRODUCTION OF CHITOSAN

3.1. Biological sources of chitin and chitosan

Chitin is one of the most abundant natural polysaccharides and occurs in a wide range of organisms, including crustaceans, insects, mollusks and fungi [6,7]. Commercial chitosan is produced predominantly by deacetylation of chitin isolated from shrimp, crab and related shell waste. Alternative sources, particularly fungal biomass, are increasingly investigated because they may offer advantages in terms of seasonal availability, mineral content and allergen control [6]. Nevertheless, crustacean shells remain attractive because they are generated in large quantities by food-processing activities and contain substantial amounts of recoverable chitin.

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The composition of crustacean shells varies with species, age, season and habitat. In general, the shell matrix includes chitin, proteins, calcium carbonate and pigments, together with smaller amounts of lipids and other components [6,7]. These associated materials must be removed in a controlled manner because harsh extraction conditions can influence polymer chain length, acetylation pattern, color, residual mineral content and ultimately the pharmaceutical performance of the resulting chitosan.

3.2. Conventional production from crustacean shells

Conventional processing of crustacean shells typically includes demineralization, deproteinization, optional decolorization or bleaching, and deacetylation [6,7]. Demineralization is commonly performed with an acid to remove calcium salts, while deproteinization uses alkaline treatment to remove proteins. The isolated chitin is subsequently exposed to concentrated alkali at elevated temperature to remove acetyl groups and generate chitosan. The final material requires thorough washing, neutralization, drying and characterization before pharmaceutical use.

Chemical processing is relatively simple and scalable, but it can consume substantial quantities of acid and alkali and generate saline effluents. Furthermore, excessively severe conditions may reduce molecular weight or alter other structural parameters. Biological and enzyme-assisted approaches, ionic liquids and deep eutectic solvents have therefore been explored as more sustainable alternatives [6,7]. At present, however, the choice of method must balance yield, purity, reproducibility, environmental impact and the intended final application.

3.3. Local freshwater crayfish as a potential raw material

Freshwater crayfish shells represent a potentially useful local source of chitin and chitosan. Their value is twofold. First, conversion of shell residues into a pharmaceutical biopolymer can increase the value of locally available biological resources. Second, it can reduce the volume of organic waste requiring disposal. For regions where freshwater crayfish are readily available, systematic evaluation of shell composition, extraction yield, degree of deacetylation, molecular weight, ash content, protein residues and microbiological purity would be necessary to determine suitability for pharmaceutical applications.

Local sourcing should not be interpreted as evidence of pharmaceutical equivalence. Chitosan intended for wound-care products must meet reproducible quality specifications regardless of origin. Therefore, future studies on local freshwater crayfish should compare extracted material with established pharmaceutical-grade chitosan using validated physicochemical and biological methods.

4. PHYSICOCHEMICAL AND PHARMACEUTICAL PROPERTIES OF CHITOSAN

4.1. Molecular weight and degree of deacetylation

Molecular weight and degree of deacetylation are among the most important variables governing chitosan behavior. The degree of deacetylation determines the proportion of free amino groups, whereas molecular weight influences viscosity, chain mobility, mechanical behavior and processing characteristics [4-6]. Together, these

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parameters affect solubility, mucoadhesion, antimicrobial action, degradation rate and interactions with drugs or biological tissues. For this reason, publications that report chitosan-based formulations should provide adequate characterization of the polymer used rather than referring to chitosan as a chemically uniform material.

4.2. Solubility, cationic character and mucoadhesion

Chitosan is a weak polybase with amino groups that become protonated under acidic conditions. Protonation gives the polymer a positive charge and permits dissolution in dilute organic acids such as acetic or lactic acid. In neutral and alkaline media, native chitosan has limited solubility, which can restrict formulation options [8,9]. The positively charged polymer can interact electrostatically with negatively charged biological surfaces, proteins and mucins, accounting for its strong mucoadhesive behavior and its ability to increase residence time at mucosal or wound surfaces.

The amino and hydroxyl groups of chitosan also provide reactive sites for cross-linking and chemical modification. Carboxymethylation, quaternization, thiolation and other modifications have been used to improve solubility, mechanical properties or functional activity. Such modifications can broaden pharmaceutical use but introduce additional requirements for characterization and safety assessment.

4.3. Biocompatibility, biodegradability, antimicrobial activity and hemostasis

Chitosan is widely investigated as a biomedical polymer because it is generally biodegradable and has favorable biocompatibility when appropriately purified and formulated [4,8,12]. Enzymatic degradation produces smaller saccharide fragments that can be metabolized or cleared. However, biocompatibility is not solely an intrinsic property of the polymer; it can be influenced by molecular weight, deacetylation, residual proteins, endotoxins, processing reagents and the concentration used in a formulation.

The antimicrobial activity of chitosan is commonly associated with its polycationic nature. Electrostatic interaction with negatively charged microbial cell surfaces can alter membrane permeability and cellular function. The magnitude of this effect depends on polymer characteristics, pH, microorganism type and formulation conditions [12,15,16]. Chitosan is also of interest as a hemostatic material. Its interaction with cellular blood components and its ability to form adhesive barriers have supported the development of hemostatic dressings, although performance can differ substantially among products and formulations [14,17].

5. CHITOSAN-BASED WOUND-HEALING SYSTEMS

An ideal wound dressing should protect the wound from external contamination, manage exudate, maintain a moist environment, minimize trauma during dressing changes and, when possible, contribute actively to hemostasis, infection control and tissue repair. Chitosan is attractive because it can be processed into several dosage forms and can function both as a structural biomaterial and as a carrier for active substances [10-16].

5.1. Films and membranes

Chitosan films and membranes provide a flexible barrier over damaged tissue and can be produced by casting, coating or related techniques. Their transparency may facilitate visual inspection of the wound, while their polymer network can be modified to

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control water-vapor transmission, swelling and mechanical strength. Native chitosan films may be brittle under certain conditions, so plasticizers or polymer blends are often introduced to improve flexibility. Films can also incorporate antimicrobial agents, plant-derived compounds or other therapeutic substances for localized delivery [13,15].

5.2. Hydrogels and sponges

Hydrogels are three-dimensional polymer networks capable of retaining large amounts of water and wound exudate. Chitosan-based hydrogels can be created through physical or chemical cross-linking and can provide a moist environment that is favorable for tissue repair [10]. Their soft structure makes them suitable for irregular wound surfaces, and they can serve as reservoirs for drugs, growth factors or natural bioactive compounds. Sponges and porous matrices, in contrast, can absorb fluid rapidly and provide a three-dimensional structure for cell attachment and tissue infiltration. These properties are particularly relevant when a combination of exudate management and hemostatic action is required.

5.3. Nanoparticles and controlled drug-delivery systems

Chitosan can be formulated into nanoparticles, microparticles and other carrier systems for controlled or targeted delivery. Its cationic character enables interaction with anionic compounds and permits ionic gelation strategies that avoid harsh organic solvents. Chitosan-based carriers have been investigated for oral, transdermal, nasal, ocular and local drug delivery [8,9]. In wound care, nanoparticles can be incorporated into hydrogels, films or dressings to prolong local retention of antimicrobials, anti-inflammatory substances or other bioactive agents.

The main pharmaceutical advantage of a carrier-based approach is the possibility of protecting active substances from degradation and modulating their release. However, nanoparticle size distribution, surface charge, encapsulation efficiency, release kinetics, stability and sterilization compatibility must be controlled. A promising laboratory formulation cannot be considered clinically translatable without reproducible manufacturing and appropriate toxicological evaluation.

Table 1. Principal chitosan-based wound-care formats and their pharmaceutical functions

Format	Potential function	Key development issues
Films/membranes	Protective barrier; local drug loading; adjustable permeability	Brittleness, moisture balance, adhesion to wound
Hydrogels	Moist environment; exudate uptake; sustained release	Mechanical weakness; cross-linker safety; sterilization
Sponges/foams	High porosity; fluid absorption; hemostatic support	Structural stability; reproducible pore architecture
Fibers/nanofibers	High surface area; ECM-	Manufacturing complexity;

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	like architecture; active-agent delivery	scale-up
Nanoparticles	Controlled/local delivery; protection of active compounds	Aggregation, batch variability, safety characterization
Composite dressings	Combination of chitosan with other polymers or bioactives	Compatibility, interactions, standardization

6. COMBINATION WITH NATURAL BIOACTIVE COMPONENTS

A particularly attractive strategy is to combine chitosan with natural bioactive substances. Honey, plant extracts, phenolic compounds and other natural products may provide complementary antimicrobial, antioxidant or anti-inflammatory effects, whereas chitosan can act as a structural matrix and release-controlling carrier [13]. This concept is consistent with the broader historical tradition of combining natural materials for wound management while applying modern pharmaceutical principles of standardization and controlled delivery.

Nevertheless, biological plausibility alone is insufficient to justify a new combination. Each formulation must be evaluated for compatibility, stability, release profile, antimicrobial activity, cytocompatibility and, where relevant, pharmacological efficacy. Natural extracts can vary with species, harvest conditions, extraction procedure and storage. Their incorporation therefore increases rather than decreases the importance of analytical standardization.

7. SAFETY, STANDARDIZATION AND TRANSLATIONAL CHALLENGES

The transition from laboratory-scale chitosan research to a reproducible pharmaceutical or medical product requires careful control of raw-material and process variables. Relevant specifications may include identity, degree of deacetylation, molecular weight distribution, viscosity, moisture, ash, residual protein, residual solvents or reagents, microbial contamination and endotoxin burden. For formulations containing active substances, drug content, uniformity, release profile and stability must also be established.

Sterilization represents another challenge because heat, irradiation or chemical sterilants may change molecular weight or mechanical properties. The selected method should therefore be validated for the specific formulation. Packaging must preserve hydration state, sterility and functional performance over the intended shelf life.

Clinical evidence also requires cautious interpretation. A systematic review of randomized studies concluded that available clinical data on chitosan dressings were limited and heterogeneous, with only some trials showing clear advantages over conventional dressings [17]. Thus, strong mechanistic rationale and promising in vitro data should not be presented as proof of clinical superiority. Well-designed comparative studies remain necessary for each specific formulation and indication.

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8. ENVIRONMENTAL AND ECONOMIC SIGNIFICANCE

The use of crustacean shell waste as a chitin source aligns with principles of circular use of biological resources. Instead of treating shells exclusively as waste, the mineral, protein and polysaccharide fractions can potentially be recovered and valorized. Chitin extraction and chitosan production may therefore contribute to waste reduction and the creation of value-added biomaterials [6,7].

For local freshwater crayfish, such a strategy may be particularly relevant if sufficient raw material is available in a reproducible manner. However, economic feasibility depends on collection logistics, preprocessing, reagent consumption, waste-water treatment, quality-control requirements and market demand. Environmental benefits should therefore be assessed using actual process data rather than assumed solely from the biological origin of the polymer.

9. FUTURE PERSPECTIVES

Future work should prioritize reproducibility, pharmaceutical-grade characterization and clinically relevant formulation design. For locally derived chitosan, comparative studies should determine how source and extraction conditions affect molecular weight, deacetylation, purity, viscosity and biological performance. Establishing specifications for raw shells and intermediate chitin would improve batch consistency.

A second priority is the development of multifunctional dressings that combine physical protection with hemostatic, antimicrobial and controlled-release properties. Hydrogels, porous sponges, electrospun fibers and nanoparticle-loaded composite systems are especially promising, but they should be designed with realistic manufacturing and sterilization constraints from the outset [10-17].

A third direction is the rational incorporation of standardized natural bioactive compounds. Such systems may provide a modern pharmaceutical interpretation of the long-standing use of natural materials in wound care. However, future studies should clearly distinguish historical inspiration from experimental evidence and should define the contribution of each component using appropriate controls.

Finally, translation requires a complete evidence chain: chemical characterization, formulation optimization, stability testing, in vitro biological evaluation, microbiological testing, in vivo safety and efficacy studies, and ultimately appropriately designed clinical investigations. This sequence is essential if chitosan from local biological sources is to move beyond an interesting raw material and become a reliable pharmaceutical or medical product.

10. CONCLUSION

Chitosan is a versatile natural biopolymer with physicochemical and biological properties that support its use in wound dressings, hemostatic materials, hydrogels, films, sponges and drug-delivery systems. Its pharmaceutical performance depends strongly on molecular weight, degree of deacetylation, purity, solubility and formulation conditions. Crustacean shells, including potentially local freshwater crayfish shells, represent valuable sources of chitin and chitosan and may offer environmental advantages through the valorization of biological waste.

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The medical heritage of Ibn Sina provides a historically important example of rational use of natural medicinal materials and compound preparations. Scientifically, this heritage should be presented as a conceptual background rather than as evidence that chitosan itself was known or used in medieval medicine. When this historical distinction is maintained, the connection between traditional natural-resource use and modern pharmaceutical biomaterials becomes both defensible and informative.

Further progress will depend on standardized extraction, detailed polymer characterization, formulation-specific safety testing and stronger clinical evidence. Combining locally sourced chitosan with contemporary pharmaceutical technologies may provide a practical pathway toward sustainable and biologically compatible wound-care materials.

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