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Advancements in Chitosan and Its Derivatives for Enhanced Wound Healing

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Abstract: In recent years, the academic community has continued to explore effective methods to promote wound healing and prevent scar hyperplasia. This research area is both challenging and has attracted significant attention. Wound healing is a complex and orderly process involving the precise coordination of various growth factors, inflammatory cells, and repair cells. To optimize this intricate process, researchers have developed a series of innovative synthetic dressings designed to improve the wound healing environment. Among these dressings, the natural polymer chitosan has emerged as a preferred material due to its cost-effectiveness, renewable nature, and exceptional biocompatibility and biodegradability, as demonstrated in the biomedical field, particularly in the area of wound dressings.

Keywords: Chitosan; Wound healing; Derivatives

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1. Introduction

Chitosan, a natural polymer polysaccharide, is derived from the shells of crustaceans through the deacetylation of chitin, resulting in a linear polysaccharide chain. Due to its excellent biocompatibility, biodegradability, and multiple biological functions, chitosan is widely applied in various industries, including medicine, food, cosmetics, and agriculture [1]. Its unique properties make it an indispensable material in these fields. Enterprises are encouraged to actively respond to national initiatives by efficiently utilizing chitosan and its derivatives, thereby enhancing their value and promoting their broader application.

2. The role of chitosan derivatives in wound healing

2.1. Antimicrobial properties of chitosan derivatives in wound healing

Wound infection is a significant obstacle in the healing process, and chitosan derivatives exhibit excellent antimicrobial properties, which are essential for effective wound healing [2]. These derivatives inhibit bacterial growth and reproduction through multiple mechanisms. First, the positive charge of chitosan derivatives interacts with the negatively charged bacterial cell membrane, altering its permeability and thereby suppressing bacterial growth. Additionally, chitosan derivatives can penetrate bacterial cells, bind to intracellular DNA and RNA, and disrupt normal physiological functions, further inhibiting bacterial proliferation.

2.2. Promotion of wound healing by chitosan derivatives

Chitosan derivatives also play a crucial role in accelerating wound healing by stimulating the proliferation and migration of cells surrounding the wound and promoting the synthesis and secretion of collagen [3]. Collagen, an essential structural protein in wound healing, facilitates tissue repair and reconstruction. By enhancing collagen synthesis and secretion, chitosan derivatives create an optimal repair environment, contributing to the rapid recovery of wound tissues.

2.3. Potential of chitosan derivatives in reducing scar formation

Scar formation is a common outcome of wound healing, but excessive scar tissue can negatively affect both appearance and function. Chitosan derivatives effectively regulate collagen arrangement and tissue distribution, inhibit abnormal scar tissue proliferation, and result in smoother and more aesthetically pleasing wound surfaces after healing [4]. Additionally, chitosan derivatives possess the ability to inhibit melanin production and accumulation, which mitigates pigmentation-related issues, further enhancing the overall outcome of wound healing.

3. New synthetic dressing forms based on chitosan

Chitosan nanofibers are distinctive in the tissue engineering field for dressing preparation. Their unique properties, including high porosity, excellent permeability, and an ideal surface-area-to-volume ratio, make them highly similar to the structure of the human skin extracellular matrix. This structural resemblance provides favorable conditions for cell adhesion and proliferation during wound repair, thereby effectively promoting wound healing [5]. Compared with other dressing forms, the preparation methods for chitosan nanofibers are relatively straightforward, including separation techniques, self-assembly methods, and electrospinning.

In the field of liquid dressings, the primary component derived from chitosan is acrylate copolymer, which forms a physical barrier on the wound surface and maintains a moist environment conducive to healing. This form of dressing is user-friendly, non-irritating, and can rapidly form a dry film after spraying, allowing easy observation of the wound while reducing allergic reactions, alleviating pain, and improving patient comfort. The incorporation of chitosan not only facilitates wound healing in a moist environment but also exhibits anti-inflammatory properties and prevents scar hyperplasia [6].

Hydrogels, composed of high-molecular-weight materials, contain numerous hydrophilic groups that can absorb substantial amounts of water. This absorption provides a cooling effect for the wound, reducing the temperature of inflamed tissues. Hydrogels also demonstrate excellent cell adhesion, enabling direct contact with the wound to minimize fluid loss and prevent secondary infections [7].

4. Application of chitosan derivatives in wound healing

Chitosan is derived from the natural deacetylation of chitin and is widely distributed, making it a resourcerich material. However, its insolubility in water and most solvents has posed a significant barrier to its broader application across various fields. Nevertheless, the rich hydroxyl (-OH) and amino (-NH_2) functional groups within chitosan molecules—due to their high reactivity—offer opportunities for chemical modification, resulting in the generation of more versatile derivatives [8]. These modified derivatives often exhibit enhanced physical and chemical properties, while retaining the superior characteristics of chitosan.

Through chemical modification techniques, chitosan derivatives have demonstrated substantial potential for application in the medical field. These derivatives are not only biocompatible and biodegradable but are also non-toxic, antibacterial, and possess excellent hemostatic properties. It is important to note that the hemostatic properties are not inherent in chitosan itself but are introduced through chemical modifications that promote platelet activation, activate the complement system, and induce red blood cell aggregation. This makes chitosan derivatives particularly valuable in the development of hemostatic materials.

Despite the broad application potential of chitosan, certain challenges remain, particularly in the medical field. One key challenge is the high crystallinity and extensive hydrogen bonding in its molecular structure, which results in its extremely low solubility, making it almost insoluble in water [9]. In clinical practice, the exudate from hypertonic wounds is typically abundant, highlighting the urgent need to improve chitosan's water solubility. To address this issue, several strategies have been employed: first, optimizing the deacetylation process of chitin; second, introducing hydrophilic groups into chitosan molecules to disrupt the hydrogen bond structure and achieve chemical modification; and third, utilizing enzyme degradation technology to break down chitosan into smaller molecular substances, thereby enhancing its solubility [10]. These strategies provide a solid foundation for expanding the use of chitosan in the medical field.

4.1. Alkylated chitosan: Multifunctional application and research progress

The application of alkylated chitosan in wound healing has become a prominent focus in medical research in recent years. Chitosan, derived from the deacetylation of chitin, is a unique biopolysaccharide polymer with excellent biocompatibility, biodegradability, antibacterial activity, and thermal stability. These properties make chitosan a highly promising material in the field of biomedicine, particularly in wound treatment. Alkylated chitosan is a derivative of chitosan, created through a specific chemical modification that introduces alkyl groups, thereby enhancing its properties [11]. This modification not only improves the stability of chitosan but also endows it with superior characteristics for specific applications.

In wound healing, alkylated chitosan plays a significant role in promoting cell regeneration, accelerating wound healing, reducing scar formation, and exhibiting antibacterial properties. First, alkylated chitosan demonstrates an effective hemostatic action. The positive charge on its surface allows it to adhere to and aggregate with the negative charge on the surface of red blood cells, resulting in electrostatic neutralization and blood coagulation. It can also neutralize the negative charge generated on the surface after platelet activation, facilitating the rapid formation of blood clots and contributing to hemostasis. The unique molecular structure of alkylated chitosan enables it to bind with plasma proteins and key clotting factors, enhancing the firmness of blood clots and effectively controlling wound bleeding.

Second, alkylated chitosan promotes cell regeneration and accelerates the healing process. It serves as a positive chemotactic agent for macrophages, activating and inducing various growth factors that stimulate surrounding defective cells to proliferate and enhance cytophagocytosis to clear degraded debris. Additionally, alkylated chitosan inhibits the production of type I collagen at the wound site, promoting the secretion of type III collagen and the formation of granulation tissue and epithelial tissue. This contributes to the reduction of wound contraction and scar formation [12].

Third, alkylated chitosan exhibits notable antibacterial activity. Its antibacterial effects are influenced by its positive charge and molecular weight. Low-molecular-weight alkylated chitosan can penetrate bacterial cell membranes, interact with bacterial cellular components, disrupt normal physiological functions, inhibit bacterial growth and reproduction, and ultimately lead to bacterial cell death.

4.2. Carboxylate chitosan: Revolutionary application and multifunctional research

Carboxylate chitosan is a functional derivative of chitosan that combines the core advantages of chitosan, including biocompatibility, biodegradability, and antibacterial properties. As a result, it has emerged as a promising biomedical material. With its unique physical and chemical properties and biological activities, carboxylate chitosan has brought about a revolutionary shift in the field of wound healing.

In the complex process of wound healing, the positive and negative charge distribution on its surface interacts with red blood cells and platelets, providing strong support for rapid coagulation [14]. When in contact with blood, carboxylate chitosan can quickly activate the clotting system, promoting the aggregation and activation of platelets to form a stable blood clot, thereby effectively controlling wound bleeding. This mechanism relies not only on the physical adsorption properties of carboxylate chitosan but also on its ability to activate the endogenous clotting pathway, accelerate the conversion of prothrombin to thrombin, achieve efficient hemostasis, and create favorable conditions for subsequent wound repair.

As a bioactive polysaccharide, carboxylate chitosan can activate and induce a variety of growth factors, such as fibroblast growth factor (FGF) and epidermal growth factor (EGF), which play crucial roles in cell proliferation, differentiation, and tissue repair. By promoting the release and activity of these growth factors, carboxylate chitosan accelerates the proliferation and differentiation of surrounding defective cells, enhances the formation of granulation and epithelial tissues, and ultimately speeds up the wound-healing process.

Moreover, carboxylate chitosan can regulate the synthesis and distribution of collagen, inhibit the excessive production of type I collagen, and promote the secretion of type III collagen. These actions help reduce scar formation, resulting in a smoother, more aesthetically pleasing wound after healing. Carboxylate chitosan can be incorporated into various wound dressings, providing effective hemostatic, antibacterial, and healing properties. Additionally, it helps maintain a moist environment at the wound site, facilitates material exchange between the wound and the external environment, promotes rapid recovery, and improves patient comfort by ensuring better adherence to the wound and reducing discomfort during treatment.

4.3. Quaternary ammonium chitosan biocolloid solution: Curative effect study in incision care

Postoperative incision care following acute appendicitis surgery is a critical aspect of surgical treatment. Incision infections are among the most common postoperative complications, which not only extend the hospital stay of patients and increase medical costs but can also adversely affect patient prognosis. Therefore, the search for an effective material to reduce the risk of infection and promote wound healing has become a significant focus in surgical research.

Chitosan, as a natural polymer material, exhibits good biocompatibility, degradability, and certain antibacterial properties, which makes it widely used in wound dressings. However, with the continuous advancement of medical technology and evolving patient needs, a single chitosan formulation has proven insufficient to meet clinical requirements [15]. As a derivative of chitosan, quaternary ammonium chitosan enhances its antibacterial activity and broadens its antibacterial spectrum through a quaternization reaction, thus providing a promising new option for wound care.

In a clinical study aimed at preventing and treating appendicitis incision infections and promoting wound healing, patients with acute appendicitis were randomly assigned to experimental and control groups. Patients in the experimental group received treatment with the quaternary ammonium chitosan biocolloid solution, while the control group was treated with traditional iodophor disinfection. The results demonstrated that the incision infection rate, dehiscence rate, induration rate, and redness rate in the experimental group were significantly lower than those in the control group. Furthermore, the rates of good and excellent incision healing in the experimental group were also significantly higher compared to the control group. These findings suggest that the quaternary ammonium chitosan biocolloid solution not only effectively prevents incision infections but also significantly accelerates the wound healing process.

5. Concluding remarks

This paper provides a comprehensive discussion of the specific mechanisms by which chitosan and its derivatives promote wound healing. Additionally, it systematically examines various forms of new synthetic dressings and their practical effects in medical applications. The aim is to contribute valuable insights to researchers by analyzing the combined application of chitosan and its derivatives with new synthetic dressings. This analysis is intended to support the rapid development of the medical industry and elevate the standard of healthcare in China.

Disclosure statement

The author declares no conflict of interest.

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