Investigaciones Medicoquirúrgicas
ÓRGANO OFICIAL DEL CIMEQ

2025; 16: e925

Review article

Effects of chitosan on wound and burn healing

Efectos del quitosano en el proceso de cicatrización de heridas y quemaduras

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SUMMARY

Introduction: Wound healing is a complex and constantly evolving technique, vital for tissue restoration and function. To reduce the impact of wounds and their care, an understanding of the healing mechanism is necessary. The use of natural polymers for biomedical applications is beneficial due to their high biocompatibility, biodegradation kinetics and easy manipulation of chemical properties, among which is chitosan.

Objective: To delve deeper into the effects of chitosan on wound and burn healing.

Methods: A documentary review was conducted that included articles from journals indexed in PubMed/Medline, SciElo, Scopus databases and the Google Scholar search engine, in the period from March to December 2024, related to the effects of chitosan on wound and burn healing. 40 original articles were reviewed in the period 2018-2024, in Spanish and

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English, and 30 were referenced. The search terms included biomaterials, properties and effects of chitosan on wound and burn healing.

Development: Chitosan, a biopolymer derived from chitin, is an emerging biomaterial in wound and burn healing due to its biocompatibility, biodegradability, affinity with biomolecules and wound healing activity. It exhibits healing capacity by accelerating the development of new skin cells, reducing inflammation and preventing infections.

Conclusions: Chitosan is an effective biomaterial for healing and repairing tissue in wounds and burns.

Keywords: chitosan; healing; wounds; burns.

RESUMEN

Introducción: La cicatrización de heridas es una técnica compleja y en constante evolución, vital para la restauración y la función de los tejidos. Para reducir el impacto que tienen las heridas y su cuidado, es necesario la comprensión del mecanismo de cicatrización. El uso de polímeros naturales para aplicaciones biomédicas es beneficioso debido a su alta biocompatibilidad, su cinética de biodegradación y su fácil manipulación de propiedades químicas, dentro de los que se encuentra el quitosano.

Objetivo: Profundizar en los efectos del quitosano en la cicatrización de heridas y quemaduras.

Métodos: Se realizó una revisión documental que incluyó artículos de revistas indexadas en bases de datos PubMed/Medline, SciElo, Scopus y el motor de búsqueda Google académico, en el período de marzo a diciembre del 2024, relacionados con los efectos del quitosano en la cicatrización de heridas y quemaduras. Se revisaron 40 artículos originales en el período 2018-2024, en idiomas español e inglés y fueron referenciados 30. Los términos para la búsqueda incluyeron, biomateriales, propiedades y efectos del quitosano en la cicatrización de heridas y quemaduras.

Desarrollo: El quitosano, un biopolímero derivado de la quitina, constituye un biomaterial emergente en la cicatrización de heridas y quemaduras por su biocompatibilidad, biodegradabilidad, afinidad con las biomoléculas y la actividad cicatrizante. Exhibe capacidad de curación al acelerar el desarrollo de nuevas células cutáneas, reducir la inflamación y prevenir infecciones.

Conclusiones: El quitosano es un biomaterial eficaz como cicatrizante y reparador de tejidos en heridas y quemaduras.

Palabras clave: quitosano; cicatrización; heridas; quemaduras.

Received: 01/14/2025

Accepted: 01/22/2025

INTRODUCTION

Healing is a dynamic multicellular process that aims to restore the barrier represented by the skin. For proper wound healing, it is necessary to control the conditions in the damaged tissue. In burns, recovery time is delayed, more control is required, and more exudate is produced, which creates an environment conducive to bacterial proliferation. [(1)]

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Wound healing is a complex and constantly evolving technique that is vital for restoring tissue integrity and function. To reduce the impact of wounds and their care, an understanding of the wound healing mechanism is necessary, which requires the search for new therapeutic approaches and the continued development of technologies for their treatment. [2, 3, 4]

In the last decade, wound care has made progress, from the use of conventional treatments such as ointments and gauze to the use of dressings, tissue substitutes, hyperbaric chambers, etc. The use of natural polymers for biomedical applications is highly beneficial due to their high biocompatibility, their biodegradation kinetics and their easy manipulation of chemical properties, among which are chitosan, Aloe vera, among others. [2, 3, 4, 5]

Chitosan, a biopolymer derived from chitin, has emerged as an emerging biomaterial in the field of wound healing due to its distinctive features, including biocompatibility, biodegradability, affinity to biomolecules, and wound-healing activity. This natural polymer exhibits excellent healing capabilities by accelerating the development of new skin cells, reducing inflammation, and preventing infections. Due to its distinctive biochemical characteristics and innate antibacterial activity, chitosan has been widely investigated as an antibacterial wound dressing; [6,7,8] It is an effective choice for a biomaterial as it is versatile and can be easily adjusted to change its structure or properties.

The aim of this review is to delve deeper into the effects of chitosan on wound and burn healing.

DEVELOPMENT

Currently, efforts are being made to develop therapies and biomaterials that promote the healing process in a wound. In this sense, the use of dressings has been a field studied for hundreds of years, going from being materials that covered the wound to avoid dehydration and prevent infections, to materials that improve and enhance tissue engineering. [3,4,9] In an attempt to reduce the impact of wounds and their care, efforts have focused on understanding the healing mechanism in search of new therapeutic approaches and the development of technologies for their treatment. Biomaterials deal with biological systems, including active cells, tissues and body systems; they are an important contribution in medical, pharmaceutical and biotechnological applications. [3, 4]

The therapeutic use of biomaterials in wound healing has gained momentum and different products are being tested. The fundamental characteristic of biomaterials in tissue repair is to stimulate cell adhesion, expansion and separation, as well as to regulate the shape and size of the restored tissue. There are numerous options for constructing a particular biomaterial to be used as a scaffold, including organic biomaterials, synthetic biomaterials and various composites. [3]

For the manufacture of wound dressings, biopolymers and synthetic polymers are most commonly used. Chitosan is a natural biopolymer obtained from chitin which can be found in the shells of crustaceans such as shrimp and crabs, as well as in the cell walls of some fungi. It is formed by deacetylation of chitin, a process that involves the removal of acetyl groups from chitin molecules. The versatility of chitosan, as well as its distinctive features, resulted in its widespread adoption in various sectors, making it valuable and sustainable with a wide variety of possibilities. [3, 4]

Chitosan dissolves in acidic solutions, allowing it to react with other useful materials to form compounds [10] and could be used to create scaffolds, membranes, gels, nanofibers, microparticles, and sponges. Chitosan possesses a wide range of biological actions and health benefits, including its ability to reduce the occurrence of gastric ulcers, is anti-inflammatory, offers protection against genotoxic effects, fights cancer, among others. It also has a positive impact on faster recovery at various stages of wound healing, including fibroplasia and collagen synthesis. [11]

Chitosan is a biodegradable and non-toxic polymer, biocompatible, with minimal immunological reactions, mucoadhesive qualities and promotes absorption. Due to the biological properties of chitosan, which include stimulation of blood coagulation, fibroblast proliferation and collagen deposition, wound healing can be improved. Their biocompatibility, biodegradability and antimicrobial properties make them valuable components in the field of biomaterials. [10, 11]

Antibacterial activity of chitosan

The cell walls of Gram-negative bacteria are characterized by their hydrophilicity and negative charge compared to those of Gram-positive bacteria. Using chitosan, increased contact with Gram-negative bacteria was demonstrated, which increased its antibacterial efficacy. The antibacterial properties of chitosan help reduce the spread of diseases and the emergence of problems that delay wound healing. [12]

Anti-inflammatory activity

The components in the structure of the chitosan molecule, independent of the MV (viscosity average molecular weight), contribute the most to its anti-inflammatory effect. (13) Chitosan favors the treatment of acid indigestion and peptic ulcers because it is alkaline and has free amino acid groups that can eliminate digestive acids and produce a protective barrier in the intestines. Glucosamine hydrochloride or its production of phosphate, sulfate and other salts through salt transformation, as well as acid hydrolysis of chitosan, are responsible for the anti-inflammatory mechanism of chitosan. [13]

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Antioxidant activity

Its antioxidant effect is given by scavenging extremely persistent DPPH radicals used in experimental studies, as well as oxygen radicals, including superoxide, hydroxyl and alkyl. Low molecular weight chitosan samples showed an increased capacity to scavenge various radicals. Bioadhesive and bacteriostatic chitosan also functions as an antioxidant, chelating agent and hemostatic agent. [14]

Antitumor activity

Both in vitro and in vivo, the intrinsic anticancer activity of chitosan and its low molecular weight variants has been confirmed. Its antitumor effect was evidenced against several strains of tumor cells under laboratory conditions and it is used to combat tumors due to its high molecular weight, biodegradability and biocompatibility. Chitosan's different molecular weights and degree of deacetylation (DDA) have been linked to tumor growth inhibitory actions in clinical mice, its anticancer action seems to depend on its chemical structure and molecular size. [15]

In the various phases of the wound healing process (hemostasis, inflammation, proliferation and remodelling), chitosan plays an important role in tissue repair. The inflammatory phase is characterised by haemostasis and inflammation, produced when exposed collagen resulting from wound development and blood clot components release cytokines and growth factors to initiate the inflammatory phase.

The key process in wound healing is the dynamic shift from the inflammatory phase to the proliferative phase. Fibroplasia, re-epithelialization, epithelial-mesenchymal interaction, angiogenesis and peripheral nerve repair are hallmarks of the proliferative phase and are led by macrophages, with a predominance in the inflammatory phase. [15]

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- Actions of chitosan in the phases or stages of wound healing

Hemostasis phase: Chitosan, due to its strong positive charge from the presence of its amino group (-NH2), attracts and binds with negatively charged components, such as red blood cells at the wound site, and when combined with a procoagulant, forms a blood clot to stop bleeding quickly.

Inflammatory phase: Chitosan and its byproducts accelerate wound healing by enhancing the capabilities of cells associated with inflammation, such as macrophages, polymorphonuclear leukocytes (PMN), osteoblasts and fibroblasts. [(16)] It may serve to eliminate bacteria from the injury area through the process of the inflammation stage.

The anti-inflammatory characteristics of chitosan help modify the immune system response and inflammation by decreasing the production of pro-inflammatory chemokines and cytokines. (16) The immunomodulatory effects of chitosan produce cytokines, in addition to decreasing the accumulation of fluid and edema at the wound site and the movement of inflammation-related cells, necessary for the production of development factors and pro-inflammatory substances during the initial stages of the healing process. It is also able to enter the nucleus of microorganisms, which is where it binds to DNA, as well as preventing the creation of mRNA and proteins. [(16)]

Proliferative phase: Chitosan has the ability to stimulate the release of platelet-derived growth factor (PDGF) and transforming growth factor (TGF), provides a non-protein matrix for 3D tissue development, and stimulates macrophages to engage in tumor healing functions. [(18)] It acts as a carrier of growth factors or cytokines that stimulate cell movement, growth, and differentiation and the construction of new vessels in the bloodstream (angiogenesis), which provide nutrients and oxygen for proliferating cells. [(17)]

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Skin remodeling phase: Chitosan precipitation in the dermis helps injured cells to heal by forming a system that connects cells and stimulates collagen production and preserves adequate oxygen penetration. Chitosan has great biodegradability, biocompatibility, hemostatic, anti-inflammatory and antibacterial activity, favors the absorption of exudate and promotes tissue rejuvenation, as well as the formation of collagen fibers in the skin. It is used as a component in a wide spectrum of dermatological treatments. [18]

Due to its biological suitability, biodegradable and low toxicity properties, it is useful in the medical and pharmaceutical area. Chitosan can be used as a coating for common biomedical materials and has an accelerating effect on wound healing. When chitosan is present, the promotion of platelet adhesion by extracellular matrix and plasma proteins has a favorable impact on wound healing. [19]

Chitosan action in treating burns has been shown to induce fibroblast proliferation and angiogenesis in second-degree burn areas in rats, while chitosan coatings healed second-degree burns in humans in in vivo trials. Chitosan hydrogels have been shown to heal third-degree burns without causing irritation or injury. [20]

Chitosan membranes act as a physical barrier over burn wounds and control external contaminants, debris, and infections. In situ, injectable chitosan hydrogels show changes from inflammation to proliferative phase in third-degree burn wounds in Wistar albino rats. [21]

Chitosan has chelating capacity, antimicrobial effects against gram-positive and negative bacteria and fungi; it also has self-adhesive, analgesic and hemostatic properties, rapid degradation, is non-toxic, biodegradable and promotes cell union and tissue regeneration due to its cytosine component. It promotes the formation of granulation tissue with angiogenesis. [22, 23, 24]

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Due to its dermogenerative action, it is useful for the treatment of burns and wounds, as well as in the cosmetics industry. Its accelerating effects on the healing of wounds and burns are based on its modulating effects on the functions of some inflammatory cells, such as PMN, macrophages and fibroblasts, which results in the activation of the repair and remodeling of damaged tissue and, due to its antimicrobial effects, prevents the proliferation of bacteria that slow down the healing process. [25] It is an option to accelerate healing and treat mild burns and to recover the elasticity and tone of the skin after superficial treatments such as laser or peeling. [26]

Chitosan is approved by the US Food and Drug Administration (FDA) and several studies have shown that it has antimicrobial, wound healing, anti-inflammatory, antioxidant effects and hemostatic activity. The muco-bioadhesive properties increase its potential in topical and local applications and in formulations intended for skin and mucous membranes. These characteristics are useful for materials intended to treat mucosal surfaces and infected, inflamed and damaged skin. [27, 28, 29]

Chitosan emerges as a therapeutic alternative due to its properties of accelerating the healing process and its antimicrobial effect. It is a natural polysaccharide composed of glucosamine units linked by a glycosidic bond. Its implementation is necessary as an alternative for wound healing. [30]

Chitosan is biocompatible, biodegradable, non-toxic, antimicrobial, hemostatic and moisturizing. It will gradually depolymerize to release N-acetyl-D-glucosamine which gives way to fibroblast proliferation, helps collagen deposition and stimulates a higher level of natural hyaluronic acid synthesis at the wound site. Due to this relationship, its topical use is recommended in the treatment of skin diseases. [30]

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Chitosan is an effective biomaterial for healing and repairing tissue. It has an accelerating effect on the wound healing process and acts as a physical barrier to burns. Its properties of biological suitability, biodegradable and low toxicity make it useful in the medical and pharmaceutical fields.

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Conflicts of interest

There are no conflicts of interest.