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Biological effects of chitosan in Dentistry

Efectos biológicos del quitosano en Odontología

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Abstract:

Current research in the world has focused on biomaterials studies in the medical area, leaving an emerging research model in dentistry, with little information available. In this sense, there are several biomaterials with potential to be used in various areas of dentistry, mainly in endodontics. Chitosan is a versatile biomaterial from its production to its multiple properties, applications and benefits; it is a biomolecule with an average molecular weight of 100 to 500 kDa, obtained from the exoskeleton of arthropods such as crabs, shrimp, lobsters and mollusks (squid, oysters, cuttlefish). Its chemical structure is similar to that of cellulose, formed by amino and hydroxyl functional groups in its polymeric structure, soluble in aqueous media. Several studies have considered it a safe product for biomedical use. It is currently used in the food industry for its fat absorption capacity, helping in weight loss for the control of overweight-obesity, as well as in food preservation, cosmetics manufacturing, antioxidants, among others. Some of its properties in the medical area include its potent bactericidal, hemostatic and tissue regenerative effect. Giving better results thanks to its great properties of biocompatibility, biodegradability, low toxicity and great antimicrobial potential. However, more clinical studies are needed to know its benefits and what its use implies in the clinical area. Therefore, this manuscript aims to provide existing information on chitosan for the research and development of new, safer and more effective dental materials.

Keywords:

Chitosan, chitin, nanoparticles, dentistry

Resumen:

La investigación actual en el mundo se ha centrado en estudios de biomateriales en el área médica, dejando un modelo de investigación emergente en odontología, con poca información disponible. En este sentido, existen varios biomateriales con potencial para ser utilizados en diversas áreas de la odontología, principalmente en endodoncia. El quitosano es un biomaterial versátil desde su producción hasta sus múltiples propiedades, aplicaciones y beneficios; es una biomolécula con un peso molecular medio de 100 a 500 kDa, que se obtiene del exoesqueleto de artrópodos como cangrejos, gambas, langostas y moluscos (calamares, ostras, sepias). Su estructura química es similar a la de la celulosa, formada por grupos funcionales amino e hidroxilo en su estructura polimérica, soluble en medios acuosos. Varios estudios lo han considerado un producto seguro para uso biomédico. Actualmente se utiliza en la industria alimentaria por su capacidad de absorción de grasas, ayudando en la pérdida de peso para el control del sobrepeso-obesidad, así como en la conservación de alimentos, fabricación de cosméticos, antioxidantes, entre otros. Algunas de sus propiedades en el área médica incluyen su potente efecto bactericida, hemostático y regenerador de tejidos. Dando mejores resultados gracias a sus grandes propiedades de biocompatibilidad, biodegradabilidad, baja toxicidad y gran potencial antimicrobiano. Sin embargo, son necesarios más estudios clínicos para conocer sus beneficios y lo que implica su uso en el área clínica. Por ello, el presente manuscrito pretende aportar la información existente sobre el quitosano para la investigación y desarrollo de nuevos materiales dentales más seguros y eficaces.

***Palabras Clave*:**

Quitosano, quitina, nanopartículas, odontología

INTRODUCTION

In the last decade, advances in the scientific and healthcare fields have increased the quality of medical and dental care, mainly in terms of the techniques, protocols and materials used. This has

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provided guidelines for the creation and development of increasingly precise and effective bionanomaterials. Biotechnology is fundamental to the development of medicine. Thus, it has been pointed out that medicine combined with these materials significantly improves the success of treatments.[1-3] Natural polysaccharides such as chitosan, alginate, pectin, dextran, starch, etc., are among the preferred biomaterials in the Health Sciences.[1-2,4] This review will be exclusively addressed to the therapeutic applications of chitosan in dentistry. Chitosan is a macromolecule obtained from repeating D-glucosamine that has different functions, reliably and effectively used in various fields of dentistry.[1]

BIOPOLYMERS

Biopolymers have emerged as a valuable tool for surgical materials and the treatment of post-surgical complications.[5] These biopolymers are natural macromolecules that can be obtained from plant, animal or microbial sources. On the other hand, biomaterials can be classified according to their origin as natural or synthetic; in turn, natural biomaterials are classified as marine and terrestrial. According to the National Institute of Statistics and Geography, Mexico has approximately 11,000 km of coastline in the Pacific Ocean, 8,475 km in the Gulf and 3,117 km in the Caribbean Sea. There are 176 protected natural areas, 68 of which are in marine and coastal ecosystems. There are effective applications of biomaterials of marine origin in surgical, orthopedic, reconstructive plastic, aesthetic and dental biomaterials. Some examples of biomaterials of natural origin are silk, cellulose, rubber, chitosan, collagen, alginate, among others. [4,6] Proteins such as elastin, hyaluronic acid and fibrin are also considered biomaterials. [3,4] The exploitation of all these natural resources, based on sustainable development and research into new materials, promotes the economic and technological development of the country and modified polymers have also been developed that provide additional benefits to these materials.[5, 7-8]

NANOPARTICLES

The influence of nanoparticles in the field of dentistry is progressing rapidly. Bionanomaterials have recently gained importance in technological advances due to their superior physical, mechanical, chemical and biological properties. Nanometer-sized antibacterial agents are preferable, as they have a higher surface-to-volume ratio, also favoring the absorption and bioavailability of many drugs, leading to a reduction in the dose and frequency of their administration, and curing some oral diseases such as oral cancer. The nano scale equivalent to one billionth of a meter (1/1,000,000,000,000) or one thousandth of a micron (1/1,000); which according to its Greek etymology "νανος"(nano), means small or tiny.[9] These properties have resulted in better performance compared to their conventional counterparts, treating and curing some oral diseases.[10]

In terms of enamel and dentin regeneration, the combination of tissue bioengineering; along with the development of genetically engineered trigger nanoparticles and nanoparticles that are biomimetic with mineralized tissues, have begun to bear fruit in the fabrication of dental organs in vitro.[11,12]

CHITIN

Chitin is the second most abundant natural polymer, a natural chemical substance that functions as a structural component of the exoskeleton of arthropods, the shells of crabs and the cuticles of insects.[13,17] Chitin may also be present in the mycelium of fungi of the family Mucoracea such as Absidia, Mucor and Rhizopus, forming part of their cell wall. It should be noted that shrimps or prawns are the most important source of chitin. The performance comes from the type of species, there being more than 300 different species in the world (Figure 1).[4,13]

Figure 1. Chitin may also occur in certain fungi of the family mucoracea, a structural component of the exoskeleton of arthropods.[4,13]

The chitin extraction process consists of 3 steps:

1. The removal of proteins inherent to invertebrate tissue. To do this, an alkaline aqueous solution is used.

2. Removal of the biomineral layer covering the exoskeleton of marine species (mainly hydroxyapatite and calcium carbonates) by means of an acid solution.

3. The final extraction is carried out by alkaline treatment at temperatures of 50-80 °C.

Since it comes from natural and renewable resources, it is not only an abundant and economical natural biopolymer, but also environmentally friendly.[4, 13,18,19]

CHITOSAN

In 1859, Rouget discovered chitosan by treating chitin with a hot potassium hydroxide solution. In 1894, Gilson confirmed the presence of glucosamine in chitin and at the same time it was given the name chitosan. Chitosan, a linear biopolymer consisting of 2-amino-2-deoxy-β-D-glucose (60-100%) and 2-acetamino -2-deoxy-β-D-glucoside (0-50%), bound together by ß (1→4) bonds, occurs naturally in the cell walls of fungi, soil and sediments, where it is produced from the degradation of chitin. Commercial chitosan is derived from the deacetylation of chitin contained in the shells of various marine crustaceans, such as shrimp, a rich source of dietary fiber, is used as a dietary supplement, has an effect on protein aggregation, emulsifying capacity, induces film formation and also exhibits antimicrobial and antioxidant activities. (Figure 2)[8,13]

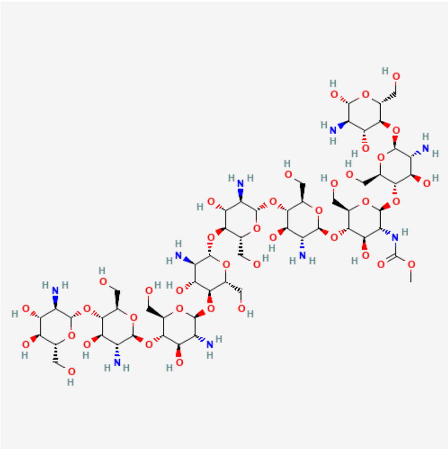

Figure 2. Representation of the chemical structure of chitosan.[8, 13]

With an average molecular weight of 100 to 500 kDa. It is derived from the alkaline deacetylation of chitin, obtained from the shells of marine crustaceans (crabs and shrimp). It is a fiber, chemically similar to cellulose.[14-15]

Considered the number one among the most abundant organic materials of natural origin in the world, due to its physicochemical properties, capable of associating with various biomolecules, it has antifungal and hemostatic effects, due to its polysaccharide nature, has low toxicity and is biocompatible in humans. Approved as safe by the US FDA (Food and Drug Administration) and the EU (European Union) for dietary use and wound dressing applications. No published data have been found showing human toxicity of chitosan-based formulations or questioning the safety of chitosan for human use. However, there are several animal toxicity studies that report good safety in vivo and in vitro, it is biodegradable, has no irritant effects, among others (Figure 3)[2, 5, 16-17]

Shrimps Crabs Lobsters

Figure 3. Most important source for obtaining chitin.[2, 5, 16-17]

CHITOSAN MECHANISM OF ACTION

Chitosan has received much attention in the pharmaceutical, food, agricultural, textile, and tissue engineering industries due to its biocompatibility, biodegradability, and low toxicity.[20] chitosan contains antioxidant, healing, and mucoadhesive properties, the ability to form films and gels.[21 ,22] It also has anti-adhesion activity, resulting in bacterial surface modifications, alterations in the expression levels of bacterial surface ligands. These characteristics are responsible for the bactericidal and bacteriostatic properties of chitosan.[17, 23] it has been found to have no antigenic response, it has anti-inflammatory properties modifying prostaglandin E2 levels. The hemostatic effect of chitosan is also a notable feature, mainly because it can induce platelet adhesion and aggregation and activate endogenous blood coagulation. Chitosan controls bleeding by adsorption of plasma and coagulation of red blood cells.[17, 24]

The interaction of cationic chitosan with the anionic cell surface, increased membrane permeability and leakage of cellular material from the cell may be the antibacterial mechanism of chitosan. Chitosan can also interfere with mRNA production and protein incorporation. Chitosan has a high affinity for proteins, binds to mucosa and demonstrates antifungal effects; therefore, it is an ideal material for biomedical applications.[14, 24, 25.]

It has different processing forms (solution, mixture, sponge, film, gel, paste, tablet, mesh, membrane, suture, fiber, nanoparticle, etc.).[2,12,26.]

Due to its outstanding characteristics such as absorbency, malleability and cohesive concentration threshold to store and gradually release drugs with optimal resorption, it has been previously used as a transport system for local drug delivery, mucoadhesives, multiparticulate parenterals and floating orals.[24]

Chitosan has immunomodulatory properties, stimulating macrophages to release IL-1, which in turn stimulates fibroblast and collagen proliferation. It promotes effective wound healing and regeneration of soft, bone and nerve tissues. [26-28]

BIOLOGICAL EFFECTS OF CHITOSAN IN DENTISTRY

Chitosan, as a natural polysaccharide, with multiple properties, has been used in different areas of dentistry, such as modification of restorative dental materials, dentin bonding and adhesion, dental repair, enamel modification and toothpaste. Applied to different areas of the dental discipline. The use of this compound, bonded to synthetic dental materials, could improve their characteristics.[29]

1. In conservative dentistry it has been used for caries prevention, has remineralizing properties, hardens dental tissues. It works as a desensitizer when added to toothpastes. Mouthwash is the effective chemical plaque control mechanism practiced worldwide. However, long-term use of chlorhexidine has been associated with a variety of side effects, including discoloration of the teeth and tongue, a temporary change in taste perception, an increase in calculus deposits, a stinging sensation, and genotoxicity of oral epithelial cells. Both chitosan and chlorhexidine have been found to be effective in effectively controlling

microbial growth and postoperative inflammation in oral implantology, as well as protecting and helping to repair the gums and oral mucosa in periodontal and peri-implant treatments, in the study by Vilasan et al. in the 3-month oral evaluation of 3 different groups subjected to mouth rinses; Group1: Chitosan, Group2: Chlorhexidine and Group3: Combination of chitosan and chlorhexidine, the combination of both substances showed a statistically significant reduction ($p<0.05$) in plaque indices at time intervals compared to chlorhexidine or chitosan alone. A combination of both provides better results.[17,18,30]

2. In endodontics, studies have shown that chitosan increases the bond strength between root canal sealer and dentinal tubules. Chitosan is considered an alternative to ethylenediaminetetraacetic acid (EDTA) due to its antibacterial and physicochemical properties, such as its high chelating capacity under acidic conditions. A combination of chitosan and silver nanoparticles can further enhance the antimicrobial activity in endodontic treatment. The possibility of incorporating natural compounds with a potent ability to fight endodontic infections is paramount and deserves further investigation, with the primary goal of providing a fully biocompatible approach that eradicates infection and induces healing of periapical tissue. Chitosan in combination with glass ionomer cement has demonstrated hemostatic effects in root canal treatment in children.[31-35]

3. Poor oral hygiene in orthodontic patients and surface porosities are two factors that lead to the accumulation of residual food and microorganisms, such as *Streptococcus mutans* and *Candida albicans*. The accumulation of these microorganisms increases the incidence of caries and oral diseases and compromises the effectiveness of orthodontic treatments. When incorporated into different materials such as cements and bactericidal media, it reduces the bacterial load, increasing the success of the treatment. It promotes remineralization after orthodontic treatment.[30, 32]

4. In periodontology, a specific application of chitosan within bone regeneration is periodontal bone repair. Periodontal regeneration includes not only alveolar bone regeneration, but also regeneration of cementum, periodontal ligament and gingiva.[8, 28]

5. In implantology, they have been used as coatings for titanium implants, dental membranes and hemostatic dressings. Hydrogels composed of hyaluronate acid and chitosan loaded with dexamethasone for the treatment of peri-implatitis.[5,8,26]

6. In the field of oral surgery, the use of chitosan facilitates surgical healing of post-extraction oral wounds. It has been used to repair the alveolus after tooth extraction, in guided bone regeneration, hemostasis of surgical wounds in oral reconstruction, repair of temporomandibular joint discs.[13, 14, 24,26]

7. In prosthetic dentistry, it is used for the modification of glass ionomer restoratives and the antibacterial activity of dental adhesive and the modification of lithium disilicate glass-ceramic luting procedures.[6, 20, 29]

8. In dental therapeutics, it facilitates their use for drug delivery. Biodegradable chitosan films have been fabricated to deliver effective concentrations of local anesthetics such as tetracaine, lidocaine and benzocaine. They can provide prolonged anesthetic treatments and pain relief. Chitosan- and glycerophosphate-based thermosensitive hydrogels are developed as injectables loaded with anti-inflammatories and antibiotics (i.e., metronidazole and moxifloxacin) or growth factors, to enhance biomineralization. The use of polymeric drug vehicles proved to be a very successful technique to formulate micro- and nanoparticles with controlled or targeted drug release in the oral cavity. [24,25,37]

9. In pediatric dentistry, chitosan is used to prevent mucoadhesion of cariogenic bacteria. It is used in conjunction with chewing gums and mouthwashes due to its antibacterial and anti-plaque effects. These innovative strategies have the potential to provide an improved therapeutic approach for the prevention and treatment of various oral diseases not only for adults, but also in pediatric dental practice.[11-12]

CONCLUSION

In conclusion, the results examined in this narrative review show that chitosan is a reliable biopolymer to administer, with no reported side effects, with several positive properties for applications in dentistry. It is expected to promote the development of the use of chitosan in dentistry, considering their physicochemical properties, bioactivity and multifunctionality. Therefore, it is necessary to deepen in its properties and benefits of this nanomaterial

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