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PROPERTIES OF CHITOSAN MATRIX COMPOSITES WITH HYDROXYAPATITE AND CARBON NANOTUBES, AND THEIR USE IN BONE TISSUE ENGINEERING

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Abstract: There is a growing demand for bone grafts by various clinical sectors, such as aesthetic procedures, treatment of injuries and dentistry, the use of synthetic materials is shown to be good due to the availability and the reduction of risks that their use brings, among the materials that are used in the clinic can be cited the chitosan matrix composites (CHI) with hydroxyapatite (HA) and carbon nanotubes (CNTs), which uses materials that are already used in the clinic HA and CHI with an innovative material in the sector the CNTs. The aim was to analyze and compare data from the current state of the art of CHI matrix composites with HA and CNTs applied in bone tissue engineering. This study is based on a review of the specialized literature on articles in online scientific journals, with thematic issues related to the properties of the biocomposite on board. The influence of the use on the composite properties generated by the use of CNTs together with the HA in the CHI matrix, for biomedical applications, more specifically in bone tissue engineering, was observed. It was observed that with subtle increases of CNTs in the CH composite Ha composites, the bioactivity, osteoconduction, antibacterial activity, mechanical properties of the composites, changes in the nanotexturas, and a homogeneous distribution of the materials occur, potentiality of its use in more than one application within bone tissue engineering. In the present study it was possible to observe that CHI matrix composites with HA and CNTs present a combination of properties highlighting the potential for application in bone tissue engineering.

Keywords: Bone tissue engineering. Hydroxyapatite. Chitosan. Carbon nanotubes.

1 INTRODUCTION

Bone tissue has the ability to regenerate within a limit, when due to the extension, or the nature of the bone lesion if it exceeds that limit, or when the time required for the full recovery of the injured part of the system is too long, a intervention in the procedures for recovery of bone tissue, one of the techniques used are the bone grafts.

The bone graft may be a fragment of bone taken from another site of the same patient and placed in the injured site, a procedure called "autograft", however even then the patient's lesion may be of a proportion where one does not remove a fragment of body due to the size required.[1] Another factor taken into account in the autograft is the need to perform two or more of two surgical procedures in the same patient, which results in a longer time required for the procedure, can lead to unwanted scars, and exposure to undesirable risks common to the procedures surgical.

The grafts can also be made from a bone fragment of a donor, a procedure called allograft, but donors are not always available, and in these procedures there is possibility of transmission of infectious diseases, and in both cases (autograft and allograft) there are chances of a biological response from the body of the graft recipient, such as inflammation, which often causes the recipient to have to undergo anti-inflammatory drug treatment. One of the factors that contribute to this risk of inflammation is the fact that along with the bone tissue fragments of other tissues may appear as muscle and adipose.[1]

Despite their limitations autografts continue to be good candidates for orthopedic transplants, bone tissue engineering proposes new strategies. This includes the development of new biomaterials, polymer composites and synthetic ceramics to support tissue production.[2]

A technique that has a lower chance of rejection and greater availability, is the filling of bone lesions with artificial materials with bone-like properties, which can be shaped for the lesion of the patient, being called scarffolds, thus requiring less time surgical. The need for bone grafts has been increasing due to surgeries due to traumas, tumors, craniosynostosis and surgeries with aesthetic purposes.[3]

These materials that present biocompatibility with human organisms, are classified by the science of materials as biomaterials, and can not present any biological degenerative response of the organism. Some biomaterials can be absorbed by the human body over time, and may stimulate the formation of bone tissue simultaneously, the ideal for these materials is that the rate of degradation of the implanted material coincides with the bone tissue neoformation that the even stimulates, a possible intervention that facilitates the regeneration and adoption of *scaffolds* to fill the defects and support the natural loads of the fabric.[3-4]

Such materials must still have other characteristics so that their use is feasible, in addition to biocompatibility. The success of a biomaterial implant depends on bone-like mechanical properties, simulating the loads that are inserted naturally into the tissue in the most diverse daily activities, ranging from standing still to running. Biocomposites should be exposed to a simulated physiological environment, where parameters of temperature, humidity, acidity, and frequency of loading are established. For the study of these materials are made test specimens submitted to tests in a simulated physiological environment.[5]

Several composite materials are studied in the academic and commercial environments in order to obtain bone grafts with optimum dosages and conditions of porosity of the materials, allowing a faster and more efficient recovery of patients with bone lesions, with lower patient risks. The part of engineering that studies the applicability of biomaterials in bone tissue reconstruction is called bone tissue engineering.

The composites based on Hydroxyapatite, Carbon Nanotubes with Biopolymers are excellent candidates for application in bone grafts and coating of bone prostheses, due to their mechanical properties, to promote osteogenesis and reduce bacterial fixation.[6-9]

The purpose of the manuscript is to analyze and compare data from the current state of the art of CHI matrix composites with HA and CNTs applied in bone tissue engineering. The aim was to study and understand the main parameters and form of application used in the studies found, according to the parameters that were varied, in the final shape of the composite and the composition of the composites, and the influence of the composition on the properties.

2 MATERIAL AND METHODS

This study is based on a review of the specialized literature, conducted between March and June 2018, in which a consultation was conducted with online books and periodicals, by scientific articles selected through search in the database of SciELO platforms and CAPES (Coordination for the Improvement of Higher Education Personnel), ELSEVIER. A total of 17 articles were selected, most of which were published in the last 6 years, but older articles were used in a timely manner to bring fundamental concepts about the theme. The search in the databases was performed using the terminologies registered in the Descriptors in Health Sciences created by the Virtual Health Library developed from the Medical Subject Headings of the US National Library of Medicine, which allows the use of common terminology in Portuguese, English and Spanish. The keywords used in the search were Bone Tissue Engineering, Hydroxyapatite, Chitosan, Carbon Nanotubes. The inclusion criteria for the studies found were the approach focused on the influence of the properties and function of the variation of the composite materials of the composite. We excluded studies that reported the use of other materials. Afterwards, the aim was to study and understand the main parameters and form of application used in the studies found, according to the parameters that were varied, in the final shape of the composite and the composition of the composites, and the influence of the composition on the properties.

3 RESULTS

The results presented are obtained from 9 articles. Some materials that have biocompatibility are not ideal for use in bone tissue engineering individually but have potential for use in combination with other materials in the form of biocomposites. The creation of three-dimensional frameworks with only biopolymers is not feasible, since they do not have ideal properties, but when these biopolymers are increased, for example hydroxyapatite has improved its mechanical properties, degradation, biocompatibility and biofunctionality.[10-11]

The use of CHI combined with HA for the production of superporous hydrogels has resulted in a promising material for the production of three-dimensional frameworks for bone tissue engineering due to its high resemblance to the bone matrix.[12]

CNTs significantly influence the mechanical properties of three - dimensional frameworks made of polymeric nanocomposites, increasing the compression modulus of the shells, preferentially lining the surface of the polymeric composite. Thus, a nanotexture is formed that improves the binding with the cells, and improves the protein adsorption.[13]

Composites of HA / CNTs prepared to have foam consistency, ended up having better mechanical properties, microstructural and degree of interconnection, the frameworks ended up having a mixture of large pores of 1-2 mm and small pores of 20-300 µm, that favored the osteoconduction and formation of bone tissue.[14]

In a comparison between pure CHI, CHI plus HA and CHI plus HA and CNTs, it was found that both HA and CNTs are uniformly distributed in the polymer matrix, and that the composites gave twice as much support for development and cell proliferation than pure CHI, somewhat similar to what Leung and Naguib[11] later stated in 2012.[7] Increasing by only 0.5% CNTs increased the hardness of a composite of polymer matrix HA by 10 times, and in comparison, generated more bone tissue neoformation in vivo in the correction of skull defects than the composite without CNTs. Highlighting the combined effects of increased mechanical strength and osteogenicity that CNTs generate on biocomposites and the possibility of their use in the healing of large extensions of bone tissue.[8]

Upon being introduced into the surface of biomedical implants in the form of a coating, CHT-modified CNTs having as their content the medical antiseptic ZnO (Zinc Oxide), it was found that CNTs proved to be a material that strengthens antibacterial activity against *Escherichia Coli and Staphylococcus Aureus* and regulates the osteogenesis of osteoblasts.[9]

The use of a nanocomposite of CHI, HA and graphene oxide in the form of titanium substrate surface coating by electrodeposition resulted in a uniformly distributed biocompatible coating that, in simulated body fluid assays, provided effective protection against corrosion of the substrate, exhibited good biocompatibility during cell incubation and decreased staining of Staphylococcus Aureus bacteria.[15]

Some of the challenges in the use of prostheses in patients are the differences in thermal dilation between the bone matrix and the prosthesis, and the need for cushioning between bone and prosthesis in the joints. CHI nanocomposite reinforced with single wall CNTs in thin films, presented high elastic energy storage capacity, and proved to be a good thermal stabilizer with good thermal barrier.[16]

The use of nanotubes must be done within ideal ranges of use that science is trying to map through successive experimental approaches. When evaluating the use of multiple wall CNTs as a reinforcement of gelatinous composites of CHI and HA at the rates of 0.1 and 0.2 or 0.4% by mass of CNTs with respect to the matrix, showed that due to the agglomeration of the CNTs in the matrix, the worst result of mechanical resistance came from the higher utilization rate, still having better properties than the pure matrix.[10] As for biocompatibility the formation of a bone-like apatite layer on the surface of the supports after immersion in simulated body fluid.

4 DISCUSSION

It is observed that in both the studies,[6-8,17] with only subtle increments of CNTs, mechanical properties of CHI polymer matrices can be substantially improved, and that both HA and CNTs are evenly distributed in CHI matrix.

Subtle increments of carbon nanotubes in polymer matrices used in bone grafts significantly improve the mechanical properties of the matrix. The incorporation of only 0.8% by weight of multiple wall CNTs in the CHI matrix improved the mechanical properties, including the tensile modulus and strength, by more than 90% when compared to pure chitosan, in addition to CNTs were dispersed homogeneously in the CHI matrix.[17] Combining the properties of the carbon nanotubes and the versatility and biocompatibility of chitosan, a composite material is obtained that presents potential for biological applications.[14]

It can be observed in nanocomposites of CNTs, HA and CHI, a uniform distribution of HA and CNTs in the CHI matrix, where in the study, the percentage of CNTs was varied as a function of the mass of QUI, varying from 0% to 5% , and it was observed that in subtle additions the nanotubes substantially improve the mechanical properties of the matrix, doubling its modulus of elasticity and almost tripling its resistance to compression.[6]

It is possible to emphasize the possibility of making prosthetics with polymer matrix having CNTs in their composition,[9,15] since they tend to distribute homogeneously on the surface of this type of matrix in the form of nanotexturas, which would be positive in bacterial control.

The use of synthetic composites has the advantage, besides the ease of molding them according to the patient's injury in the shape of scaffolds, to require less surgical time. In addition, it is possible to improve their properties depending on the processing used in the manufacture, such as the final configuration of the biomaterial that can be in the form of hydrogels and foams, in its finish that can be nanotexturized, and by obtaining pre-established parameters such as porosity and pore sizes.

5 CONCLUSION

With the present work it was possible to carry out studies that verify the current state of the art of chitosan matrix composites with hydroxyapatite and carbon nanotubes, and its applicability in bone tissue engineering, where its potentiality can be evidenced in applications such as bone grafts , prosthesis coating and matrix of bone prostheses due to the fact that these composites present a combination of mechanical, biocompatible, antibacterial properties, and the most adequate proportions for each of these applications, which is of paramount importance in the scientific environment, methodologies to obtain this composite, proportions of the composite forming materials and their respective properties, improving the understanding of the interference of each material in the set of properties of the composite.

The composites of HA / CNTs in CHI matrix present potential for use in bone grafts and bone prosthesis coating, having as homogeneity in the distribution of HA / CNTs in the CHI matrix, superficial nanotextures formed by CNTs and nanopores that favor osteogenesis, fixation of osteoblasts and osseointegration, and also, make bacterial fixation difficult.

CONFLICT OF INTEREST

There were no conflicts of interest.

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REFERENCES

1. Garcia CD, Pereira JD, Garcia VD. Doação e transplante de órgãos e tecidos. 1. ed. São Paulo: Segmento Farma editores Ltda; 2015.

2. Grémare A, Guduric V, Bareille R, Heroguez VL, Heureux SLN, Fricain JC, *et al*. Characterization of printed PLA scaffolds for bone tissue engineering. J. Biomed. Mater. Res. 2018; 106(4):887-94.

3. Maia M, Klein ES, Monje TV, Pagliosa C. Reconstrução da estrutura facial por biomateriais: revisão de literatura. Rev Bras Cir Plást. 2010; 25(3):566-72.

4. Mercuri EGF, Daniel AL, Machado RD. Modelo numérico micromecânico para scaffold de hidroxiapatita com cultura celular. 10th World Congress Computational Mechanics; 2014; 1(1). São Paulo: 2014.

5. Caselis JLV, Cervantes ER, Rosas ER. Crecimiento en fluido fisiológico simulado de hidroxiapatita sobre películas de PMMAsílice-CaO. Sociedad Mexicana de Ciencia y Tecnología de Superficies y Materiales. 2011; 24(3):92-5.

6. Shen G, Hu X, Guan G, Wang L. Surface Modification and Characterisation of Silk Fibroin Fabric Produced by the Layer-by-Layer Self-Assembly of Multilayer Alginate/Regenerated Silk Fibroin. The National Natural Science Foundation of China. 2015; 10(4):1-19.

7. Venkatesan J, Qianb ZJ, Ryua B, Kumar NA, Kim SK. Preparation and characterization of carbon nanotube-grafted-chitosan – Natural hydroxyapatite composite for bone tissue engineering. Carbohydr Polym. 2011; 83(2):569-77.

8. Jing Z, Wu Y, Su W, Tian M, Jiang W, Cao L, *et al*. Carbon Nanotube Reinforced Collagen/Hydroxyapatite Scaffolds Improve Bone Tissue Formation *In vitro* and In Vivo. Ann Biomed Eng. 2017; 45(9):2075-87.

9. Zhu Y, Kelvin Xl, Yeung Wk, Chuc Pk, Wua S. Biofunctionalization of carbon nanotubes/chitosan hybrids on Ti implants by atom layer deposited ZnO nanostructures. Appl Surf Sci. 2017; 400(3):14-23.

10. Mesgar As, Mohammadi Z, Khosrovan S. Improvement of mechanical properties and *in vitro* bioactivity of freeze-dried gelatin/chitosan scaffolds by functionalized carbon nanotubes. Int J Polym Mater Po. 2018; 67(5):267-76.

11. Leung LH, Naguib HE. Viscoelastic properties of poly(«-caprolactone) – hydroxyapatite micro- and nano-composites. Polym Adv Technol. 2012; 24(2):144-50.

12. Beskardes IG, Demirtas TT, Durukan MD, Gümüsderelioglu M. Microwave-assisted fabrication of chitosan-hydroxyapatite superporous hydrogel composites asbone scaffolds. J Tissue Eng Regen Med. 2015; 2015(9):1233-46.

13. Chen L, Hu J, Shen X. Synthesis and characterization of chitosan–multiwalled carbon nanotubes/hydroxyapatite nanocomposites for bone tissue engineering. J Mater Sci Mater Med. 2013; 24(8):1843-51.

14. Liu Y, Tang J, Chen X, Xin Jh. Decoration of carbon nanotubes with chitosan. Carbon. 2005; 43(15):3178-80.

15. Shi YY, Li MG, Liu Q, Jia JZ, Xu XC, Cheng Y, Zheng YF.Electrophoretic deposition of graphene oxide reinforced chitosan–hydroxyapatite nanocomposite coatings on Ti substrate. J Mater Sci Mater Med. 2016; 27(48):1-13.

16. Venugopal, G, Veetil JC, Raghavan N, Singh V, Kuma A, Mukkannan A. Nano-dynamic mechanical and thermal responses of single-walled carbon nanotubes reinforced polymer nanocomposite thinfilms. J Alloy Compd. 2016; 668(b):454-9.

17. Wang FW, Shen L, Zhang WD, Tong YJ. Preparation and Mechanical Properties of Chitosan/Carbon Nanotubes Composites. Biomacromolecules. 2005; 6(6):3067-72.