



DESENVOLVIMENTO DE NOVOS BIOMATERIAIS PARA REGENERAÇÃO ÓSSEA GUIADA

MACHADO, Gabriela Moraes; KASPER, Rafaela Hartmann; MAURMANN Natasha; PRANKE, Patricia; BAVARESCO, Caren; BREW, Myrian Camara.

Palavras-chave: Odontologia, biomateriais, regeneração óssea.

O objetivo desse estudo foi desenvolver biomateriais em forma de pó particulado e de membrana para regeneração óssea guiada, bem como comparar a membrana produzida por eletrofiação com uma membrana de colágeno comercialmente utilizada. O biomaterial particulado foi obtido e avaliado na forma de quitosana, bem como dos complexos quitosana/ASAP e quitosana/ASAP/ β -TCP. As partículas foram caracterizadas por Espectroscopia no Infravermelho por Transformada de Fourier (FTIR) e tamanho e potencial zeta. Foi realizado o ensaio de viabilidade celular brometo de 3-(4,5-dimetiltiazol-2-il)-2,5-difeniltetrazolio (MTT), colorações das células vivas com fluoresceína diacetato (FDA) e ensaio nuclear com 4',6'-diamino-2-fenil-indol (DAPI). As membranas foram desenvolvidas pelo método de eletrofiação, onde a membrana de policaprolactona (PCL) 14% p/v foi tratada com ASAP 300 μ g/ml. Esses materiais foram caracterizados por ângulo de contato e foi realizada análise de viabilidade celular (MTT) e de coloração com FDA. A análise estatística foi realizada por ANOVA, pelo teste Post Hoc Bonferroni. Os resultados do FTIR sugerem que houve processo de complexação entre quitosana e ASAP. O valor médio do tamanho das partículas no grupo complexo quitosana/ASAP/ β -TCP foi de 416,2 nm, o grupo apenas quitosana foi de 465,5nm, o grupo de quitosana/ASAP 784,6 nm, o grupo β -TCP 233,1 nm e o grupo ASAP 62,67 nm. O potencial zeta demonstrou a boa estabilidade do biomaterial particulado experimental. Na avaliação da viabilidade celular, pode-se observar biocompatibilidade e bioatividade dos biomateriais particulados quitosana/ASAP/ β -TCP e quitosana/ASAP. A adsorção de ASAP na membrana com PCL aumentou sua hidrofilicidade. Em termos de viabilidade celular, todas as amostras foram biocompatíveis e a viabilidade celular das membranas foi comparável com as membranas de colágeno. Sendo assim, o complexo quitosana/ASAP/ β -TCP e a membrana com ASAP adsorvida são biomateriais promissores para a regeneração óssea guiada. Entretanto, são necessários mais estudos para aplicação clínica destes biomateriais.

Alenezi A, Chrcanovic B, Wennerberg A. Effects of Local Drug and Chemical Compound Delivery on Bone Regeneration Around Dental Implants in Animal Models: A Systematic Review and Meta-Analysis. *Int J Oral Maxillofac Implants*. 2018; 33(1):e1-e18.

Anitha A, Sowmya S, Kumar PTS, Deepthi S, Chennazhi KP, Ehrlich H et al. Chitin and chitosan in selected biomedical applications. *Prog. Polym. Sci.* 2014; 39(9):1644–1667.

Beth-Tasdogan NH, Mayer B, Hussein H, Zolk O. Interventions for managing medication-related osteonecrosis of the jaw. *Cochrane Database Syst Rev*. 2017;10(10):CD012432.

Bottezini PA. Efeito da remoção seletiva de tecido cariado nas características imunofenotípicas apresentadas por células-tronco mesenquimais da polpa de dentes deciduos humanos [dissertação]. Programa de Pós-Graduação em Odontologia da Universidade Federal do Rio Grande do Sul (UFRGS). Porto Alegre: 2019.

Bujnáková Z, Dutková E, Zorkovská A, Baláž M, Kováč J, Kello M et al. Mechanochemical synthesis and in vitro studies of chitosan-coated InAs/ZnS mixed nanocrystals. *J. Mater. Sci.* 2017;52(2):721–735.

Bunyaratavej P, Wang HL. Collagen membranes: a review. *J Periodontol*. 2001 Feb;72(2):215-29.



- Buser, Dula DK, Hirt HP, Schenk RK. Lateral Ridge Augmentation Using Autografts and Barrier Membranes: A Clinical Study With 40 Partially Edentulous Patients. *J OralMaxillofac Surg.* 1996; 54(4): 420-32.
- Caballé-Serrano J, Abdeslam-Mohamed Y, Munar-Frau A, Fujioka-Kobayashi M, Hernández-Alfaro F, Miron R. Adsorption and release kinetics of growth factors on barrier membranes for guided tissue/bone regeneration: A systematic review. *Arch Oral Biol.* 2019;100:57-68.
- Cicciù M, Fiorillo L, Cervino G. Chitosan Use in Dentistry: A Systematic Review of Recent Clinical Studies. *Mar Drugs.* 2019; 17(7):417-432.
- Claesson PM, Ninham BW. pH-dependent interactions between adsorbed chitosan layers. *Langmuir*, v. 8, n. 5, p. 1406-1412, 1992.
- Cucchi A, Vignudelli E, Napolitano A, Marchetti C, Corinaldesi G. Evaluation of complication rates and vertical bone gain after guided bone regeneration with non-resorbable membranes versus titanium meshes and resorbable membranes. A randomized clinical trial. *Clin Implant Dent Relat Res.* 2017 Oct;19(5):821-832. doi: 10.1111/cid.12520.
- DePhillipo NN, Aman ZS, Kennedy MI, Begley JP, Moatshe G, LaPrade RF. Efficacy of Vitamin C Supplementation on Collagen Synthesis and Oxidative Stress After Musculoskeletal Injuries: A Systematic Review. *Orthop J Sports Med.* 2018;6(10):2325967118804544.
- Gamzazade AI & Nasibov SM. Formation and properties of polyelectrolyte complexes of chitosan hydrochloride and sodium dextran sulfate. *Carbohydrate Polymers.* 2002; 50(3): 339-343.
- Gautam S, Dinda A, Mishra N. Fabrication and characterization of PCL/gelatina composites nanofibrous scaffolds for tissue engineering applications by electrospinning method. *Mater Sci Eng C Mater Biol Appl.* 2013; 33(3):1228-35.
- Gruber R, Stadlinger B, Terheyden H. Cell-to-cell communication in guided bone regeneration: molecular and cellular mechanisms. *Clinical Oral Implants Research.* 2016; 28(9):1-8.
- Hoxha A, Gillam DG, Bushby AJ, Agha A, Patel MP. Layered Double Hydroxide Fluoride Release in Dental Applications: A Systematic Review. *Dent J (Basel).* 2019; 2;7(3). pii: E87.
- Huang ZM, Zhang YZ, Kotaki M, Ramakrishna S. A review on polymer nanofibers by electrospinning and their applications in nanocomposites. *Composites Science and Technology.* 2003; 63(15): 2223-2253.
- Ji J, Wu D, Liu L, Chen J, Xu Y. Preparation, characterization, and in vitro release of folic acid-conjugated chitosan nanoparticles loaded with methotrexate for targeted delivery. *Polym. Bull.* 2012;68(6):1707-1720.
- LeGeros RZ. Calcium phosphate-based osteoinductive materials. *Chem Rev.* 2008; 108(11):4742-53.
- Li Z, Tang H, Liu X, Xia Y, Jiang J. Preparation and characterization of microporous poly(vinyl butyral) membranes by supercritical CO₂-induced phase separation. *J. Membr. Sci.* 2008; 312:115-124.
- Matins MIP, Borges JP. Desenvolvimento de hidrogéis à base de quitosano/fosfatos de cálcio para aplicações ortopédicas [dissertação]. Faculdade de Ciências e Tecnologia. Universidade de Lisboa: Monte de Caparica, 2012.
- Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate-induced exposed bone (osteonecrosis/osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. *J Oral Maxillofac Surg.* 2005; 63(11):1567-75.
- Mason C & Dunnill P. A brief definition of regenerative medicine. *Regen. Med.* 2010; 17:5-6.
- Maurmann N, Pereira DP, Burguez D, Pereira SFDA, Neto PI, Rezende RA et al. Mesenchymal stem cells cultivated on scaffolds formed by 3D printed PCL matrices, coated with PLGA electrospun nanofibers for use in tissue engineering. *Biomedical Physics & Engineering Express.* 2017; 3(4): 045005.
- Miroshnichenko S, Timofeeva V, Permykova E, Ershov S, Kiryukhantsev-Korneev P, Dvořáková E, Shtansky DV, Zajíčková L, Solovieva A, Manakhov A. Plasma-Coated Polycaprolactone Nanofibers with Covalently Bonded Platelet-Rich Plasma Enhance Adhesion and Growth of Human Fibroblasts. *Nanomaterials (Basel).* 2019 Apr 19;9(4):637. doi: 10.3390/nano9040637. PMID: 31010178; PMCID: PMC6523319.
- Nicola, F.C ; MARQUES, M. R. ; ODORCYK, F. ; ARCEGO, D. M. ; PETENUZZO, L. ; ARISTIMUNHA, D. ; VIZUETE, A. ; SANCHES, E.F. ; PEREIRA, D. P. ; MAURMANN, NATASHA ; DALMAZ, C. ; PRANKE, Patricia ; Netto, C.A. . Neuroprotector effect of stem cells from human exfoliated deciduous teeth transplanted after traumatic spinal cord injury involves inhibition of early neuronal apoptosis. *BRAIN RESEARCH*, v. 1663, p. 95-105, 2017.
- Ngiam M, Liao S, Chan C, Ramakrishna S. Cell-based nanocomposites and biomolecules for bone tissue engineering. *Advanced Biomaterials.* 2010; 551-588.
- Pighinelli L, Guimaraes MF, Paz RL. Properties of Hydrochloric Chitosan Solutions Modified With Nano-Calcium Phosphate Complex. *J Tissue Sci Eng.* 2015; 6: 155.
- Rasperini G, Pilipchuk SP, Flanagan CL, Park CH, Pagni G, Hollister SJ et al. 3D-printed Bioresorbable Scaffold for Periodontal Repair. *Journal of Dental Research.* 2015; 94(9_suppl), 153S-157S.



- Reynolds EC, Wong A. Effect of adsorbed protein on hydroxyapatite zeta potential and streptococcus mutans Adherence. *Infection and Immunity*. 1983; 39(3): 1285-1290.
- Rickert D, Vissink A, Slot WJ, Sauerbier S, Meijer HJ, Raghoebar GM. Maxillary sinus floor elevation surgery with BioOss mixed with a bone marrow concentrate or autogenous bone: test of principle on implant survival and clinical performance. *Int J Oral Maxillofac Surg*. 2014; 43:243-247.
- Ruggiero SL, Mehrotra B, Rosenberg TJ, Engroff SL. Osteonecrosis of the jaws associated with the use of bisphosphonates: a review of 63 cases. *J Oral Maxillofac Surg*. 2004; 62(5):527-34.
- Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B et al. American Association of Oral and Maxillofacial Surgeons Position Paper on Medication-Related Osteonecrosis of the Jaw.. *Journal of Oral and Maxillofacial Surgery* 2014; 72(10):1938-56.
- Sanz M, Donos N, Alcoforado G, Balmer M, Gurzawska K, Mardas N, et al. Therapeutic concepts and methods for improving dental implant outcomes. Summary and consensus statements. The 4th EAO Consensus Conference 2015. *Clin Oral Implants Res*. 2015;26(11):202- 06.
- Sapountzi E, Braiek M, Farre C, Arab M, Chateaux JF, Jaffrezic-Renault N et al. One-Step Fabrication of Electrospun Photo-Cross-Linkable Polymer Nanofibers Incorporating Multiwall Carbon Nanotubes and Enzyme for Biosensing. *Journal of The Electrochemical Society*. 2015; 162 (10): B275-B281.
- Sela M, Kohavi D, Krausz E, Steinberg D, Rosen G. Enzymatic degradation of collagens membranes by periodontal bacteria. *Clin Oral Implants Res*. 2003 Jun; 14(3):263-68.
- Tang J, Saito T. Biocompatibility of Novel Type I Collagen Purified from Tilapia Fish Scale: An In Vitro Comparative Study. *Biomed Res Int*. 2015;2015:139476. doi:10.1155/2015/139476.
- Tsutsumi K, Fujikawa H, Kajikawa T, Takedachi M, Yamamoto T, Murakami S. Effects of L-ascorbic acid 2-phosphate magnesium salt on the properties of human gingival fibroblasts. *J Periodontal Res*. 2012 Apr;47(2):263-71. doi: 10.1111/j.1600-0765.2011.01430.x. Epub 2011 Nov 9. PMID: 22066831.
- Telles C, Silva AD, Wiltgen A, Kijner M, Camassola M, de Borba P. Isolation and characterization of dental pulp stem cells from permanent third molars. *Stomatos*. 2016; 22(42): 32-41.
- Thakur VK & Voicu SI. Recent advances in cellulose and chitosan based membranes for water purification: A concise review. *Carbohydr Polym*. 2016; 146:148-65.
- Wessing B, Lettner S, Zechner W. Guided Bone Regeneration with Collagen Membranes and Particulate Graft Materials: A Systematic Review and Meta-Analysis. *Int J Oral Maxillofac Implants*. 2018; 33(1):87–100.
- Xu R. Progress in nanoparticles characterization: Sizing and zeta potential measurement. *Particuology*. 2008; 6(2):112-115.
- Xu x, Magdalena W & Hecke, Kristof & Buyst, Dieter & Mara, Dimitrije & Vervaet, Chris & Herman, Karen & Wynendaele, Evelien & De Spiegeleer, Bart. (2020). Structural study of L-ascorbic acid 2-phosphate magnesium, a raw material in cell and tissue therapy. *JBIC Journal of Biological Inorganic Chemistry*. 2020; 26(5): 10.1007/s00775-020-01801-3.
- Yang L, Wang Q, Peng L, Yue H, Zhang Z. Vascularization of repaired limb bone defects using chitosan- β -tricalcium phosphate composite as a tissue engineering bone scaffold. *Mol Med Rep*. 2015 Aug;12(2):2343-7. doi: 10.3892/mmr.2015.3653. Epub 2015 Apr 21. PMID: 25902181.
- Yang SJ, Lin FH, Tsai KC, Wei MF, Tsai HM, Wong JM, et al. Folic acid-conjugated chitosan nanoparticles enhanced protoporphyrin IX accumulation in colorectal cancer cells. *Bioconjugate Chem*. 2010;21(4):679–689.
- Zargarian SS, Haddadi-Asl V, Azarnia M, Kafrashian Z, Seyedjafari E. Surfactant-assisted-water-exposed versus surfactant-aqueous-solution-exposed electrospinning of novel super hydrophilic Polycaprolactone-based fibers: Cell culture studies. *J Biomed Mater Res A*. 2019 Jun;107(6):1204-1212. doi: 10.1002/jbm.a.36616. Epub 2019 Feb 8. PMID: 30672114.
- Zhang X, Hamadeh IS, Song S, Katz J, Moreb JS, Langaaee TY et al. Osteonecrosis of the jaw in the United States Food and Drug Administration's Adverse Event Reporting System (FAERS). *Journal of Bone and Mineral Research*. 2016; 31(2):336-40.
- Zhao, Mitomo, Nagasawa, Yoshii, & Kume, 2003) Zhao, L., Mitomo, H., Nagasawa, N., Yoshii, F., & Kume, T. (2003). Radiation synthesis and characteristic of the hydrogels based on carboxymethylated chitin derivatives. *Carbohydrate Polymers*, 51, 169-175.
- Zotarelli Filho IJA, Cornélio ML, Fett-Conte AC. Investigação do potencial de utilização em terapia celular de células tronco mesenquimais cultivadas em matrizes de quitosana-colágeno-genipina, em petacas e após criopreservação [tese]. Pós-graduação em Biofísica Molecular. Universidade Estadual Paulista Julio de Mesquita Filho. Campus de São José do Rio Preto: São Paulo, 2018
- Zitzman N, Naef R, Scherer P. Resorbable versus non-resorbable membranes in combination with Bio-Oss for guided bone regeneration. *Int J Oral and Maxillofac Implants*. 1997 Dec; 12(6):220-238.