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骨替代材料BCP应用于种植体骨再生的研究进展

胡志钊[1,2*]，葛艇蕊[3]，胡　杨[1,2#]

[1]新疆医科大学第一附属医院(附属口腔医院)修复种植科，新疆 乌鲁木齐
[2]新疆维吾尔自治区口腔医学研究所，新疆 乌鲁木齐
[3]新疆医科大学第六附属医院口腔科，新疆 乌鲁木齐

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摘　要

双相磷酸钙(biphasic calcium phosphate, BCP)是由*β*-磷酸三钙(*β*-tricalcium phosphate, *β*-TCP)和羟基磷灰石(hydroxyapatite，HA)组成的种植体牙周骨替代材料。种植体牙周骨量、骨质密度和牙槽骨结构决定着种植义齿修复的稳定性。近年来随着研究的不断深入，发现BCP具有着一定的骨诱导能力有利于种植体牙周骨再生，并且具有极佳的骨传导性、生物相容性、生物活性等特点，所以利用BCP来恢复种植体牙周水平及垂直骨量不足是目前口腔临床治疗领域中一大研究热点。本文旨在通过梳理国内外相关文献资料，对牙周骨替代材料BCP的组成及优点、BCP复合材料的研究新进展、BCP在种植体骨再生领域的研究现状等进行综述，以期为口腔临床诊疗及应用提供参考。

关键词

骨替代材料，BCP，种植体骨再生，*β*-TCP，HA

Research Progress on the Use of Bone Substitute Material BCP for Bone Regeneration in Implants

Zhizhao Hu[1,2*], Tingrui Ge[3], Yang Hu[1,2#]

[1]Department of Prosthetics and Implantology, The First Affiliated Hospital of Xinjiang Medical University (Affiliated Stomatology Hospital), Urumqi Xinjiang
[2]Xinjiang Uygur Autonomous Region Institute of Stomatology, Urumqi Xinjiang
[3]Department of Stomatology, The Sixth Affiliated Hospital of Xinjiang Medical University, Urumqi Xinjiang

*第一作者：胡志钊，男，1998年生，住院医师，硕士研究生，主要从事口腔修复种植学相关研究。
#通讯作者。

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Abstract

Biphasic calcium phosphate (BCP) is a material used to replace periodontal bone in implants. It consists of *β*-tricalcium phosphate (*β*-TCP) and hydroxyapatite (HA). The stability of implant denture restorations is determined by the amount of implant periodontal bone, bone density, and alveolar bone structure. In recent years, research has shown that BCP has osteoinductive ability and is beneficial for implant periodontal bone regeneration. Additionally, BCP has excellent osteoconductivity, biocompatibility, and bioactivity. Therefore, using BCP to restore implant periodontal horizontal and vertical bone volume is a major research focus in oral clinical treatment. The aim of this paper is to review the composition and benefits of periodontal bone replacement material BCP, recent advances in BCP composite research, and the current research status of BCP in the field of implant bone regeneration. Relevant domestic and foreign literature will be combined to provide a reference for dental clinical diagnosis, treatment, and application.

Keywords

Bone Substitute Material, BCP, Implant Bone Regeneration, *β*-TCP, HA

1. 引言

BCP 是由 HA 和 *β*-TCP 按照一定比例混合的种植体牙周骨替代材料，因此其同时具有两种材料在种植体骨再生领域的性质。HA 的无机成分和骨组织相似，其降解速率低可为骨再生提供一定稳定性，目前在骨再生工程中主要应用于大面积骨缺损[1]。*β*-TCP 材料性能和 HA 相似，但其与骨组织之间的生物学特性更为显著，不足之处在于其骨诱导性不佳[2]。目前 BCP 已经应用于口腔临床治疗中并已取得不错的成效，为使 BCP 性能被口腔临床医师更广泛地认知，本文就 BCP 骨替代材料在种植体骨再生领域的应用进行综述。

2. BCP 骨移植材料的优势及构成

口腔种植学植骨材料中“自体骨”的成骨性能最为稳定，但其存在取骨区二次创伤、术后并发症高、取骨数量有限等缺点。其他植骨材料例如“同种异体骨”、“异种骨”在临床中也有使用，但其存在传播疾病以及性能单一性等缺点。随着对植骨材料的不断深入，BCP 因其良好的理化性能被广大骨替代材料的口腔基础研究者所知晓，将 BCP 复合材料与 3D 打印技术结合起来，在口腔种植体牙周骨再生工程中已广泛应用[3] [4] [5]。

BCP 是一种生物陶瓷类的种植体骨替代材料，其主要合成方法为机械混合法、化学沉淀法等。通过调节 BCP 材料中 HA 与 *β*-TCP 的构成比，可取得较稳定的骨再生率及降解率，其中 HA 主要影响着 BCP 的降解速率，HA 比例较高则 BCP 材料吸收速率更稳定[6]。BCP 作为种植体骨替代材料较常用于上颌窦提升术中，Bouwman W F 等[7]经过对比研究得出当 HA：*β*-TCP 分别为 0:100、60:40、20:80 时，当比例

为 60:40 时种植体牙周垂直丧失骨量最低；同时 Cha J K 等[8]研究人员则发现 HA：β-TCP = 60:40 时 BCP 吸收速率及骨再生率稳定。

3. BCP 复合材料新进展

在种植体牙周骨替代材料领域中，BCP 与各种微量元素或其他材料共同促进种植体牙周骨再生是近年研究的热点。BCP 和 Mg 构成的复合材料在骨再生工程领域中也有着不错的成效。例如：Ballouze R 等[9]研究人员对掺镁双相磷酸钙(Mg-BCP)进行研究，体外实验结果表明 Mg-BCP 具有生物活性且无细胞毒性。经过体内实验的结果显示，Mg-BCP 物质在生物体内表现出了良好的相容性，同时还展现出了出色的骨骼再生能力。然而与其他生物陶瓷一样，Mg-BCP 支架的最佳理化性质尚未确定，因此 Mg-BCP 在种植体牙周骨组织工程中的应用需要进一步深入研究。Padmanabhan V P 等[10]研究银(Ag)纳米粒子(NPs)与 BCP 复合材料结合用于骨再生领域的有效性。实验对复合材料的各种理化性质进行了表征研究，包括结晶度、晶体结构、孔隙率、表面电荷、形貌和热稳定性等，同时还测试了 Ag-BCP 的抗菌性能。最后研究结果显示该复合材料保持了 BCP 的结构框架，同时在不影响其基本特性的情况下形成了多孔网络结构。当 Ag 粒子被引入时，BCP 材料的抗压强度和热稳定性都得到了改善。根据实验结果可知，Ag-BCP 复合材料将成为理想的骨替代材料。Yoo K H 等[11]研究者在经过文献查阅后知晓锂离子(Li)是在骨再生过程中发挥作用的微量元素。通过共沉淀法合成了不同掺杂水平(0、5、10、20 at%)的掺锂 BCP 粉末，通过一系列实验结果得出结论 BCP 中最有效的锂掺杂水平约为 10%。因为睾酮(T)被认为是一种有前途的骨整合剂，da Costa K J R 等[12]研究评估 PLGA、PCL 和 BCP 的睾酮复合物的活性和骨再生性，并评估组织对复合材料植入的反应。最后结果表明睾酮与聚合物复合材料的组合能够增加成骨细胞的活力，增加细胞外基质的产生和矿化。此外该支架具有良好的生物相容性，可引起细胞粘附和血管生成，这说明从复合材料在骨替代材料领域具有着研究潜力。在骨组织领域，骨移植材料是否能够保持足够的机械强度和维持组织体积是较为关键的一个因素。Choi J B 等[13]将 BCP 应用于 GelMA 中制备出复合水凝胶。采用红外光谱仪(FTIR)、X 射线衍射仪(XRD)和力学测试仪对制备的水凝胶进行了分析。结果确认其成功地与水凝胶结合。同时检查细胞的增殖和分化能力，为了评估细胞活力。分析结果表明，应用了 BCP 的复合水凝胶具有较高的细胞活力和较高的骨分化能力。这一实验结果表明 BCP 与 GelMA 复合水凝胶是理想的骨替代材料。通过上述实验研究可知 BCP 复合材料作为骨替代材料应用于种植体骨再生领域是有效的策略。

4. BCP 作为种植体骨移植材料的应用

BCP 因其的良好理化性能目前已广泛应用于各类型种植体骨再生工程中[14]。Andrli M 等[15]对可注射双相磷酸钙(IBCP)进行研究，实验组中 21 名患者在牙槽嵴保存术中用 IBCP，对照组 20 名患者用牛异种骨移植物(BX)。手术后进行了 6 个月的定性和定量组织学分析。分析结果显示，无论是使用的哪种骨移植物，均表现出了良好的骨传导性和生物相容性，没有引起炎症组织反应。而且，术后 6 个月内，牙槽嵴的新骨形成得到了有效保护。这项研究表明 IBCP 在牙槽嵴保存术以及解决种植体牙周骨量不足领域具有潜在意义。Klimecs V 等[16]用 HA 和 β-TCP 比例为 90:10 的 BCP 颗粒(0.5~1.0 mm)用于 18 例种植体周围炎患者的牙周骨再生术。经过至少五年的随访，进行了临床检查和 3D 锥形束计算机断层扫描。临床结果确认种植体的稳定性良好，并且周围没有任何炎症迹象。影像学检查显示种植体所在的牙槽骨的放射密度与正常的牙槽骨非常相似。Allinson 等[17]将 BCP 应用于 10 例上颌窦提升术中并且从组织形态学和免疫学等多个方面进行研究。术后 6 个月通过锥形束计算机断层扫描进行了放射性分析测量所得患者牙周骨量平均增加 8.03 ± 1.72 mm。从组织学来看 BCP 是一种适合用于上颌窦提升手术的骨移植材

料，并且具有一定的成血管作用。Toledano-Serrabona J 等[18]比较双相磷酸钙(BCP)和脱蛋白牛骨(DBB)用于上颌窦提升术中的临床和组织学结果。实验对种植体成功率、种植失败率、种植体周围边缘骨丧失、骨再生量和残留骨替代材料进行研究。从系统回顾和数据分析结果表明，BCP 可以被认为是上颌窦底增强术中 DBB 的合适替代方案。林奕真博士[19]对 BCP 结合重组人骨形态发生蛋白 2 (rhBMP2)体外及体外成骨性能进行研究。首先探讨两者结合对小鼠成骨前体细胞系 MC3T3-EI 体外成骨能力的影响，结果显示 rhBMP2 能增强 MC3T3-E1 細胞的迁移募集能力，并且与 BCP 结合后，细胞的迁移募集能力没有改交，而且能显著的增加 MC3T3-E1 细胞的增殖能力以及成骨分化能力。体内成骨性能研究表明 rhBMP2 结合 BCP 对于大鼠的骨缺损区城具有良好的骨形成能力。这一研究为 BCP 与 rhBMP2 在种植体牙周骨再生领域提供了一定实验基础。BCP 已广泛应用于牙槽嵴保存术、上颌窦提升术、种植体周围炎等种植体骨增量手术并且取得了良好的临床效果，对种植义齿的长期稳定性具有重大意义。

5. 总结与展望

BCP 生物陶瓷类骨替代材料同时具有 HA 及 β-TCP 优异的理化性能，并且通过两材料配比可达到稳定的骨形成率以及吸收率，其中 HA 材料的比重决定着 BCP 复合材料吸收速率，BCP 复合材料在种植体牙周骨再生各领域的最佳比例仍有待后续研究。已有临床病例表明 BCP 在上颌窦提升术、拔牙术后牙槽嵴保存术、种植体周围炎等多领域发挥着重要的作用，但是目前 BCP 应用于上颌窦提升植骨术中较为常见[20]-[60]。

BCP 作为种植体骨替代材料的基础研究较为缺乏。先天性免疫细胞特别是巨噬细胞，在组织修复和防御中发挥双重作用。尽管 BCP 已被证实是一种优良的骨免疫调节生物材料，但 BCP 的离子释放是否直接影响巨噬细胞极化以及 BCP 离子释放参与骨免疫调节的机制尚不清楚。Zhao Q 等[61]通过研究表明 BCP 持续释放的钙离子形成了有利于成骨的微环境，同时强调了巨噬细胞在骨再生中的关键作用，并阐明了钙离子介导的生物材料骨诱导的分子机制。种植体植入后种植体表面直接与牙槽骨及血液直接接触，种植体涂层的性质决定着种植体骨结合能力。Tabrizi R 等[62]对双相磷酸钙涂层(BCPC)与喷砂酸蚀(SLA)种植体稳定性进行对比研究。数据分析表明，在 ISQ 测量方面，BCPC 种植体在种植后两个月内的继发稳定性可能高于 SLA 种植体。BCP 在种植体骨再生工程的生物分子机制仍未阐明，以及 BCP 在种植体涂层领域的应用仍有待后续进一步研究。

参考文献

[1] Li, X., Zhou, Q., Wu, Y., *et al.* (2022) Enhanced Bone Regenerative Properties of Calcium Phosphate Ceramic Granules in Rabbit Posterolateral Spinal Fusion through a Reduction of Grain Size. *Bioactive Materials*, **11**, 90-106. https://doi.org/10.1016/j.bioactmat.2021.10.006

[2] Lima, F.B., Pereira, R.S., Junior, S.M.L., *et al.* (2017) Prospective Randomised Clinical Trial Using Autogenous Bone or Beta-Tricalcium Phosphate in Maxillary Sinus Lifting: Histological and Tomographic Results. *International Journal of Oral and Maxillofacial Surgery*, **46**, 266. https://doi.org/10.1016/j.ijom.2017.02.897

[3] Bouler, J.M., Pilet, P., Gauthier, O., *et al.* (2017) Biphasic Calcium Phosphate Ceramics for Bone Reconstruction: A Review of Biological Response. *Acta Biomaterialia*, **53**, 1-12. https://doi.org/10.1016/j.actbio.2017.01.076

[4] Ebrahimi, M. and Botelho, M. (2017) Biphasic Calcium Phosphates (BCP) of Hydroxyapatite (HA) and Tricalcium Phosphate (TCP) as Bone Substitutes: Importance of Physicochemical Characterizations in Biomaterials Studies. *Data in Brief*, **10**, 93-97. https://doi.org/10.1016/j.dib.2016.11.080

[5] Kim, S.E. and Park, K. (2020) Recent Advances of Biphasic Calcium Phosphate Bioceramics for Bone Tissue Regeneration. In: Chun, H., Reis, R., Motta, A. and Khang, G., Eds., *Biomimicked Biomaterials*: *Advances in Tissue Engineering and Regenerative Medicine*, Springer, Singapore, 177-188. https://doi.org/10.1007/978-981-15-3262-7_12

[6] 沈红裕, 宋珂. 双相磷酸钙陶瓷在口腔种植的应用及研究进展[J]. 口腔医学研究, 2022, 38(5): 404-407.

[7] Bouwman, W.F., Bravenboer, N., Ten Bruggenkate, C.M., *et al.* (2021) Tissue Level Changes after Maxillary Sinus

Floor Elevation with Three Types of Calcium Phosphate Ceramics: A Radiological Study with a 5-Year Follow-Up. *Materials*, **14**, Article 1471. https://doi.org/10.3390/ma14061471

[8] Cha, J.K., Kim, C., Pae, H.C., *et al.* (2019) Maxillary Sinus Augmentation Using Biphasic Calcium Phosphate: Dimensional Stability Results after 3 - 6 Years. *Journal of Periodontal & Implant Science*, **49**, 47-57. https://doi.org/10.5051/jpis.2019.49.1.47

[9] Ballouze, R., Marahat, M.H., Mohamad, S., *et al.* (2021) Biocompatible Magnesium-Doped Biphasic Calcium Phosphate for Bone Regeneration. *Journal of Biomedical Materials Research Part B*: *Applied Biomaterials*, **109**, 1426-1435. https://doi.org/10.1002/jbm.b.34802

[10] Padmanabhan, V.P., Sivashanmugam, P., Kulandaivelu, R., *et al.* (2022) Biosynthesised Silver Nanoparticles Loading Onto Biphasic Calcium Phosphate for Antibacterial and Bone Tissue Engineering Applications. *Antibiotics*, **11**, Article 1780. https://doi.org/10.3390/antibiotics11121780

[11] Yoo, K.H., Kim, Y., Kim, Y.I., *et al.* (2022) Lithium Doped Biphasic Calcium Phosphate: Structural Analysis and Osteo/Odontogenic Potential *in Vitro*. *Frontiers in Bioengineering and Biotechnology*, **10**, Article 993126. https://doi.org/10.3389/fbioe.2022.993126

[12] Da Costa, K.J.R., Gala-García, A., Passos, J.J., *et al.* (2019) Testosterone Improves the Osteogenic Potential of a Composite *in Vitro* and *in Vivo*. *Cell and Tissue Research*, **376**, 221-231. https://doi.org/10.1007/s00441-018-2970-3

[13] Choi, J.B., Kim, Y.K., Byeon, S.M., *et al.* (2021) Fabrication and Characterization of Biodegradable Gelatin Methacrylate/Biphasic Calcium Phosphate Composite Hydrogel for Bone Tissue Engineering. *Nanomaterials*, **11**, Article 617. https://doi.org/10.3390/nano11030617

[14] Titsinides, S., Agrogiannis, G. and Karatzas, T. (2019) Bone Grafting Materials in Dentoalveolar Reconstruction: A Comprehensive Review. *Japanese Dental Science Review*, **55**, 26-32. https://doi.org/10.1016/j.jdsr.2018.09.003

[15] Andrli, M., Tomas, M., Karl, M., *et al.* (2022) Comparison of Injectable Biphasic Calcium Phosphate and a Bovine Xenograft in Socket Preservation: Qualitative and Quantitative Histologic Study in Humans. *International Journal of Molecular Sciences*, **23**, Article 2539. https://doi.org/10.3390/ijms23052539

[16] Klimecs, V., Grishulonoks, A., Salma, I., *et al.* (2018) Bone Loss around Dental Implants 5 Years after Implantation of Biphasic Calcium Phosphate (HAp/*β*-TCP) Granules. *Journal of Healthcare Engineering*, **2018**, Article ID: 4804902. https://doi.org/10.1155/2018/4804902

[17] Olaechea, A., Mendoza-Azpur, G., *et al.* (2019) Biphasic Hydroxyapatite and *β*-Tricalcium Phosphate Biomaterial Behavior in a Case Series of Maxillary Sinus Augmentation in Humans. *Clinical Oral Implants Research*, **30**, 336-343. https://doi.org/10.1111/clr.13419

[18] Toledano-Serrabona, J., Romeu-I-Fontanet, A., Gay-Escoda, C., *et al.* (2021) Clinical and Histological Outcomes of Maxillary Sinus Floor Augmentation with Synthetic Bone Substitutes for Dental Implant Treatment: A Meta-Analysis. *Journal of Oral Implantology*, **48**, 158-167. https://doi.org/10.1563/aaid-joi-D-20-00202

[19] 林奕真. 双相磷酸钙(BCP)结合重组人骨形态发生蛋白-2 (RhBMP2)成骨性能的研究&病例报告[D]: [博士学位论文]. 武汉: 武汉大学, 2018.

[20] Fadeeva, I.V., Deyneko, D.V., Forysenkova, A.A., *et al.* (2022) Strontium Substituted *β*-Tricalcium Phosphate Ceramics: Physiochemical Properties and Cytocompatibility. *Molecules* (*Basel*, *Switzerland*), **27**, Article 6085. https://doi.org/10.3390/molecules27186085

[21] Ito, Y., Kato, H., Umetsu, M., *et al.* (2023) Preparation and Evaluation of Cements Using Spherical Porous *β*-Tricalcium Phosphate Granules. *Journal of the Japan Society of Powder and Powder Metallurgy*, **70**, 242-247. https://doi.org/10.2497/jjspm.70.242

[22] Ortiz, C.H., Caicedo, J.C. and Aperador, W. (2022) Physical Properties Evolution of *β*-Tricalcium Phosphate/Hydroxyapatite Heterostructures in Relation to the Bilayer Number. *Thin Solid Films*, **752**, Article 139256. https://doi.org/10.1016/j.tsf.2022.139256

[23] Fu, Q., Guo, Z., Bo, D., *et al.* (2023) Multi-Drug Delivery and Osteogenic Performance of *β*-Tricalcium Phosphate/Alginate Composite Microspheres. *International Journal of Polymeric Materials and Polymeric Biomaterials*.

[24] Malherbi, M.S., Dias, L.C., Lima, M.S.Z., *et al.* (2022) Electrically Stimulated Bioactivity in Hydroxyapatite/*β*-Tricalcium Phosphate/Polyvinylidene Fluoride Biocomposites. *Journal of Materials Research and Technology*, **20**, 169-179. https://doi.org/10.1016/j.jmrt.2022.06.151

[25] Tanaka, T., Komaki, H., Kumagae, Y., *et al.* (2022) Repair of Large Bone Defects Using Beta-Tricalcium Phosphate. *Biomedical Journal of Scientific & Technical Research*, **44**, 5457-35463. https://doi.org/10.26717/BJSTR.2022.44.007044

[26] 陈凯歌, 陈仁吉, 郭思远, 等. 人工骨材料 *β*-磷酸三钙在牙槽嵴裂骨缺损修复中的应用[J]. 口腔疾病防治, 2023, 31(4): 252-256.

[27] Stipniece, L., Skadins, I. and Mosina, M. (2022) Silver- and/or Titanium-Doped *β*-Tricalcium Phosphate Bioceramic with Antibacterial Activity against *Staphylococcus aureus*. *Ceramics International*, **48**, 10195-10201. https://doi.org/10.1016/j.ceramint.2021.12.232

[28] Wang, Y., Yuan, X. and Ye, J. (2022) Effects of Zinc/Gallium Dual Doping on the Physicochemical Properties and Cell Response of 3D Printed *β*-Tricalcium Phosphate Ceramic Scaffolds. *Ceramics International*, **48**, 28557-28564. https://doi.org/10.1016/j.ceramint.2022.06.169

[29] Bi, G., Mo, L., Liu, S., *et al.* (2022) DLP Printed *β*-Tricalcium Phosphate Functionalized Ceramic Scaffolds Promoted Angiogenesis and Osteogenesis in Long Bone Defects. *Ceramics International*, **48**, 26274-26286. https://doi.org/10.1016/j.ceramint.2022.05.310

[30] Putri, T.S., Ratnasari, A., Sofiyaningsih, N., *et al.* (2022) Mechanical Improvement of Chitosan-Gelatin Scaffolds Reinforced by *β*-Tricalcium Phosphate Bioceramic. *Ceramics International*, **48**, 11428-11434. https://doi.org/10.1016/j.ceramint.2021.12.367

[31] Kim, H.Y., Kim, B.H. and Kim, M.S. (2022) Amine Plasma-Polymerization of 3D Polycaprolactone/*β*-Tricalcium Phosphate Scaffold to Improving Osteogenic Differentiation *in Vitro*. *Materials*, **15**, Article 366. https://doi.org/10.3390/ma15010366

[32] Jing, T., Liu, Y., Xu, L., *et al.* (2022) The Incorporation of *β*-Tricalcium Phosphate Nanoparticles within Silk Fibroin Composite Scaffolds for Enhanced Bone Regeneration: An *in Vitro* and *in Vivo* Study. *Journal of Biomaterials Applications*, **36**, 1567-1578. https://doi.org/10.1177/08853282211065621

[33] Liu, Y., Wu, H., Bao, S., *et al.* (2023) Clinical Application of 3D-Printed Biodegradable Lumbar Interbody Cage (Polycaprolactone/*β*-Tricalcium Phosphate) for Posterior Lumbar Interbody Fusion. *Journal of Biomedical Materials Research. Part B, Applied Biomaterials*, **111**, 1398-1406. https://doi.org/10.1002/jbm.b.35244

[34] Putri, T.S., Sunarso., Hayashi, K., *et al.* (2022) Feasibility Study on Surface Morphology Regulation of *β*-Tricalcium Phosphate Bone Graft for Enhancing Cellular Response. *Ceramics International*, **48**, 13395-13399. https://doi.org/10.1016/j.ceramint.2022.02.200

[35] Zhou, J., Sun, S., He, Y., *et al.* (2022) Role of Magnesium-Doped Calcium Sulfate and *β*-Tricalcium Phosphate Composite Ceramics in Macrophage Polarization and Osteo-Induction. *Odontology*, **110**, 735-746. https://doi.org/10.1007/s10266-022-00708-6

[36] Ningsih, H.S., Tannesia, L., Animut, T.Y., *et al.* (2022) Characterization of Mesoporous in *β*-Tricalcium Phosphate Using Electron Microscopy. *Journal of the Australian Ceramic Society*, **58**, 1445-1454. https://doi.org/10.1007/s41779-022-00781-8

[37] Xu, Z., Sun, Y., Dai, H., *et al.* (2022) Engineered 3D-Printed Polyvinyl Alcohol Scaffolds Incorporating *β*-Tricalcium Phosphate and Icariin Induce Bone Regeneration in Rat Skull Defect Model. *Molecules* (*Basel, Switzerland*), **27**, Article 4535. https://doi.org/10.3390/molecules27144535

[38] Nakagawa, S., Okada, R., Kushioka, J., *et al.* (2022) Effects of rhBMP-2-Loaded Hydroxyapatitegranules/Beta-Tricalcium Phosphate Hydrogel (HA/*β*-TCP/Hydrogel) Composite on a Rat Model of Caudal Intervertebral Fusion. *Scientific Reports*, **12**, Article No. 7906. https://doi.org/10.1038/s41598-022-12082-y

[39] 金合, 李晋玉, 俞兴, 等. 可注射骨修复材料结合骨碎补总黄酮修复极量颅骨缺损的实验研究[J]. 生物骨科材料与临床研究, 2012, 9(1): 26-29.

[40] Hallmann, L. and Gerngro, M.D. (2022) Chitosan and Its Application in Dental Implantology. *Journal of Stomatology, Oral and Maxillofacial Surgery*, **123**, e701-e707. https://doi.org/10.1016/j.jormas.2022.02.006

[41] Canas, E., Orts, M.J., Sanchez, E., *et al.* (2022) Deposition of Bioactive Glass Coatings Based on a Novel Composition Containing Strontium and Magnesium. *Journal of the European Ceramic Society*, **42**, 6213-6221. https://doi.org/10.1016/j.jeurceramsoc.2022.05.064

[42] Rahnejat, B., Hassanzadeh, N.N., Sadrnezhaad, S.K., *et al.* (2023) Promoting Osteoblast Proliferation and Differentiation on Functionalized and Laser Treated Titanium Substrate Using Hydroxyapatite/*β*-Tricalcium Phosphate/Silver Nanoparticles. *Materials Chemistry and Physics*, **293**, Article 126885. https://doi.org/10.1016/j.matchemphys.2022.126885

[43] Sharma, A., Emery, R.J.H., Pitsillides, A.A., *et al.* (2022) OC10: RAMAN Spectroscopy Exposes Sex-Specific Bone Matrix Signatures Coupled to Pro-Angiogenic Vascular Phenotypes. *Microcirculation*, **29**, e12739.

[44] Xue, Z., Wang, X. and Xu, D. (2022) Molecular Investigations of the Prenucleation Mechanism of Bone-Like Apatite Assisted by Type I Collagen Nanofibrils: Insights Into Intrafibrillar Mineralization. *Physical Chemistry Chemical Physics*, **24**, 18931-18942. https://doi.org/10.1039/D2CP02573F

[45] Silambarasan, I. and Rajalakshmi, A.N. (2022) A Review on Freeze-Drying: A Stability Enhancement Technique. *Research Journal of Pharmacy and Technology*, **15**, 4841-4846.

[46] Boonsirikamchai, W., Phisalprapa, P., Kositamongkol, C., *et al.* (2023) An Effectiveness and Economic Analyses of

Tricalcium Phosphate Combined with Iliac Bone Graft versus RhBMP-2 in Single-Level XLIF Surgery in Thailand. *BMC Musculoskeletal Disorders*, **24**, Article No. 503. https://doi.org/10.1186/s12891-023-06590-9

[47] Maruyama, K., Cheng, J., Ishii, H., *et al.* (2022) Activation of NLRP3 Inflammasome Complexes by Beta-Tricalcium Phosphate Particles and Stimulation of Immune Cell Migration *in Vivo*. *Journal of Innate Immunity*, **14**, 207-217. https://doi.org/10.1159/000518953

[48] Zhang, Y., Yan, M., Niu, W., *et al.* (2022) Tricalcium Phosphate Particles Promote Pyroptotic Death of Calvaria Osteocytes through the ROS/NLRP3/Caspase-1 Signaling Axis in Amouse Osteolysis Model. *International Immunopharmacology*, **107**, Article 108699. https://doi.org/10.1016/j.intimp.2022.108699

[49] Ali, A., Hasan, A. and Negi, Y.S. (2022) Effect of Cellulose Nanocrystals on Xylan/Chitosan/Nanoβ-TCP Composite Matrix for Bone Tissue Engineering. *Cellulose*, **29**, 5689-5709. https://doi.org/10.1007/s10570-022-04607-5

[50] Funayama, T., Noguchi, H., Shibao, Y., *et al.* (2023) Unidirectional Porous Beta-Tricalcium Phosphate as a Potential Bone Regeneration Material for Infectious Bony Cavity without Debridement in Pyogenic Spondylitis. *Journal of Artificial Organs*, **26**, 89-94. https://doi.org/10.1007/s10047-022-01335-2

[51] Jing, T., Liu, Y., Xu, L., *et al.* (2022) The Incorporation of Beta-Tricalcium Phosphate Nanoparticles Within Silk Fibroin Composite Scaffolds for Enhanced Bone Regeneration: An *in Vitro* and *in Vivo* Study. *Journal of Biomaterials Applications*, **36**, 1567-1578. https://doi.org/10.1177/08853282211065621

[52] Kabilan, N., Karthikeyan, N., Dinesh Babu, K., *et al.* (2023) Third-Order Nonlinear Optical Properties of Mono and Biphasic Beta-Tricalcium Phosphate in Continuous Wave Regime. *Journal of Materials Science*: *Materials in Electronics*, **34**, Article No. 885. https://doi.org/10.1007/s10854-023-10256-6

[53] Eldeeb, D.W., Hommos, A.M., Taalab, M.R., *et al.* (2023) Immuno-Histologic and Histomorphometric Evaluation of Angelica Sinensis Adjunctive to β-Tricalcium Phosphate in Critical-Sized Class II Furcation Defects in Dogs. *BDJ Open*, **9**, Article No. 23. https://doi.org/10.1038/s41405-023-00150-y

[54] Kim, S.M., Yoo, K.H., Kim, H., *et al.* (2022) Simultaneous Substitution of Fe and Sr in Beta-Tricalcium Phosphate: Synthesis, Structural, Magnetic, Degradation, and Cell Adhesion Properties. *Materials*, **15**, Article 4702. https://doi.org/10.3390/ma15134702

[55] Alves, A.P.N., Arango-Ospina, M., Oliveira, R.L.M.S., *et al.* (2023) 3D-Printed β-TCP/S53P4 Bioactive Glass Scaffolds Coated with Tea Tree Oil: Coating Optimization, *in Vitro* Bioactivity and Antibacterial Properties. *Journal of Biomedical Materials Research*. *Part B*, *Applied Biomaterials*, **111**, 881-894. https://doi.org/10.1002/jbm.b.35198

[56] Sundar, R., Rai, A., Jayakumar, N., *et al.* (2022) Calvarial Bone Defect Regeneration Using Beta-Tricalcium Phosphate: A Translational Research Study in Rat Animal Model. *International Journal of Research in Medical Sciences*, **10**, 2420-2426. https://doi.org/10.18203/2320-6012.ijrms20222836

[57] Autefage, H., Briand-Mésange, F., Cazalbou, S., *et al.* (2009) Adsorption and Release of BMP-2 on Nanocrystalline Apatite-Coated and Uncoated Hydroxyapatite/β-Tricalcium Phosphate Porous Ceramics. *Journal of Biomedical Materials Research Part B*: *Applied Biomaterials*, **91B**, 706-715. https://doi.org/10.1002/jbm.b.31447

[58] Zhang, Z., Liu, D., Chen, Z., *et al.* (2022) Fabrication, *in Vitro* and *in Vivo* Properties of β-TCP/Zn Composites. *Journal of Alloys and Compounds*, **913**, Article 165223. https://doi.org/10.1016/j.jallcom.2022.165223

[59] Qiu, X., Li, S., Li, X., *et al.* (2022) Experimental Study of β-TCP Scaffold Loaded with VAN/PLGA Microspheres in the Treatment of Infectious Bone Defects. *Colloids and Surfaces*, *B*. *Biointerfaces*, **213**, Article 112424. https://doi.org/10.1016/j.colsurfb.2022.112424

[60] 王婧. 3D 打印载淫羊藿苷的 PVA/β-TCP 复合支架成血管性能的研究[D]: [硕士学位论文]. 长春: 吉林大学, 2022.

[61] Zhang, J., Wu, Q., Yin, C., *et al.* (2021) Sustained Calcium Ion Release from Bioceramics Promotes CaSR-Mediated M2 Macrophage Polarization for Osteoinduction. *Journal of Leukocyte Biology*, **110**, 485-496. https://doi.org/10.1002/JLB.3MA0321-739R

[62] Tabrizi, R., Sadeghi, H.M., Ghasemi, K., *et al.* (2022) Does Biphasic Calcium Phosphate-Coated Surface Increase the Secondary Stability in Dental Implants? A Split-Mouth Study. *Journal of Maxillofacial and Oral Surgery*, **21**, 557-561. https://doi.org/10.1007/s12663-020-01448-2