Biomimetic Mineralisation – Nature-inspired Strategy for Promising Hard Tissue Regenerative Materials Development

Lin Xue ZHANG[1#], Zuo Ying YUAN[2#], Yu Ming ZHAO[1], Yun Fan ZHANG[3]

Biomineralisation is a remarkable biological process in which living organisms exert precise control over the nucleation and growth of inorganic crystalline phases, resulting in the formation of hierarchically structured biocomposites that exhibit exceptional mechanical and functional properties. Since damage to bone and teeth directly affect everyday life, various biomimetic mineralised materials have been engineered for use in biomedical applications. While bioinspired materials typically demonstrate superior mechanical properties and biological functions, significant disparities remain between biomimetic constructs and their natural counterparts, especially concerning mechanical performance and multiscale structural organisation. This review initially describes the dynamic reciprocity between type I collagen fibrils, amorphous calcium phosphate phases and multifunctional non-collagenous protein within mineralisation microenvironments. Furthermore, it evaluates recent progress in advanced biomaterials based on biomimetic mineralisation strategies and seeks to spark innovative and promising solutions for investigators exploring biomineralisation principles in regenerative medicine and hard tissue reconstruction. Existing problems and future directions are discussed.
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As load-bearing systems in vertebrates, dental and skeletal tissues demonstrate evolutionarily optimised structural integration of organic-inorganic components.[1,2] The exceptional mechanical performance of hard tissue arises from mineralisation-driven architectural features, including spatially ordered hydroxyapatite (HA) deposition, organic matrix-guided crystallographic alignment and interfacial bonding between collagen fibrils and mineral phases.[3] Biomineralisation is a natural biosynthetic process whereby organisms fabricate hierarchical organic-inorganic composites to maintain life, support growth and drive biological evolution.[4] Following the identified mechanisms of biomineralisation, biomimetic mineralisation materials have shown

1 Department of Pediatrics, Peking University School and Hospital of Stomatology, National Center for Stomatology, National Clinical Research Center for Oral Diseases, National Engineering Research Center of Oral Biomaterials and Digital Medical Devices, Beijing Key Laboratory of Digital Stomatology, Research Center of Engineering and Technology for Computerized Dentistry Ministry of Health, NMPA Key Laboratory for Dental Materials, Beijing, P.R. China
2 Center of Basic Medical Research, Institute of Medical Innovation and Research, Peking University Third Hospital, Beijing, P.R. China
3 Department of Geriatric Dentistry, Peking University School and Hospital of Stomatology, Beijing, P.R. China
# Equal contribution.

Corresponding authors: Dr Yu Ming ZHAO, Department of Pediatrics, Peking University School and Hospital of Stomatology, 22# Zhongguancun South Avenue, Haidian District, Beijing 100081, P.R. China. Tel: 86-13522240011. Email: yuming_zhao@hotmail.com.

Dr Yun Fan ZHANG, Department of Geriatric Dentistry, Peking University School and Hospital of Stomatology, 22# Zhongguancun South Avenue, Haidian District, Beijing 100081, P.R. China. Tel: 86-13661042504. Email: YunfanZhang@bjmu.edu.cn.

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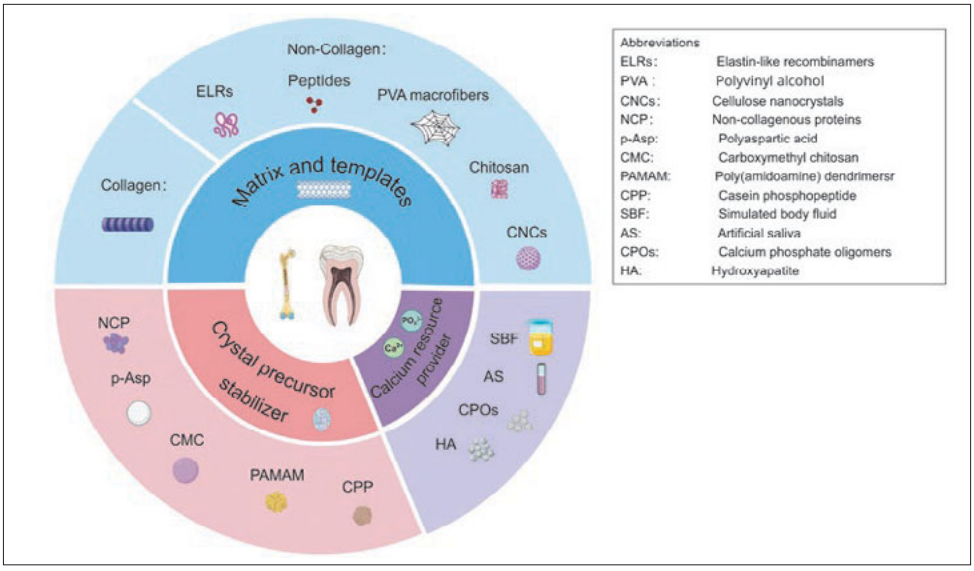

Fig 1 Illustration of strategies for biomimetic mineralised materials development.

promising mechanical properties in laboratory settings. Collaborative efforts have been made to engineer biomimetic osteoconductive scaffolds, with the goal of enhancing bioactive interface compatibility and integrating robust mechanical properties and superior biological functionalities and synchronised resorption rates with neo-osteogenesis timelines. In repairing bone defects, the closer the engineered scaffold mimics the natural bone properties, the higher the likelihood of its acceptance by the body and its ability to promote new tissue growth.[5] Subsequently, contemporary biomimetic mineralisation strategies focus accordingly on recapitulating the dynamic mineralisation microenvironment of hard tissue through controlled deposition of calcium phosphate phases within engineered collagen matrices.[6]

This review describes cutting-edge advancements in template-based biomimetic mineralisation strategies for hard tissue regeneration (Fig 1), elucidating the current research status of biomimetic mineralisation and discussing future development trends.

Synthesis and assembly process of biomineralised tissue (collagen-based) in natural conditions

Biomineralisation is a biological phenomenon characterised by organisms' precise regulation of biomineral formation, wherein mineral nucleation occurs through spatially organised processes that yield defined crystalline architectures under biomolecular orchestration.[7,8] It is important to provide a brief introduction to the collagen-based biomineralisation of hard tissues-with a hierarchical structure containing inorganic carbonated HA nanocrystals embedded within organic type I collagen matrices.[9,10]

Biomineralisation modalities are categorised as intrafibrillar and extrafibrillar based on mineral-collagen spatial orchestration. Intrafibrillar mineralisation, which exemplifies biological regulation of inorganic crystallisation with mineral nanocrystals aligned along the long axis of a single fibril, governs the biomechanical competence of bone through crystal alignment within the supramolecular confinement of collagen, simultaneously enabling hierarchical assembly and osteogenic functionality.[11-17] Extrafibrillar mineralisation manifests through ectopic deposition of mineral phases external to the supramolecular architecture of collagen, generating HA-collagen composites with disordered spatial configurations.[18] This process features micrometre-scale HA aggregates localised at fibrillar interfaces or inter-fibrillar gaps, contrasting with intrafibrillar crystallisation patterns.[19]

Biomineralisation begins with the conversion of calcium and phosphate ions into amorphous calcium phosphate (ACP) nano-precursors. Subsequently, mineral nucleation is templated at specific sites on the collagen substrate, guiding the formation of the biomineral structure under the mediation of non-collagenous proteins (NCPs).

The scaffolds and templates, collagen molecules, are secreted by osteoblasts, which assemble into amino acid triplets predominantly composed of proline (Pro), hydroxyproline (Hyp) and glycyl (Gly).[20,21] Their molecular structures contain carboxyl groups, which can form carboxylates under physiological conditions. The binding of calcium ions to the negatively charged car-

boxylate groups of collagen is a pivotal factor in initiating the nucleation of HA crystals.[22] The fibrillogenesis in osseous tissues is initiated with synthesis of triple helical polypeptide chains (predominantly two α1 and one α2 chains) that undergo supramolecular assembly to establish the characteristic hierarchical architecture.[23]

During mineralisation, ACP, providing calcium recourse, undergoes thermodynamically favoured transition, ultimately recrystallising into carbonated HA nanocrystals aligned with collagen's axial periodicity, which finally transform into HA, thereby imparting anisotropic mechanical reinforcement.[24-28]

Notably, NCPs demonstrate multifaceted functionality in orchestrating mineralisation dynamics through initiation of crystal nucleation, stabilisation of amorphous precursors, modulation of morphogenesis and suppression of uncontrolled calcification.[29-31] These acidic macromolecules, including mineral-binding proteoglycans bone sialoprotein (BSP), osteonectin, osteopontin (OPN) and osteocalcin (OCN), dentine phosphoprotein (DPP), dentine matrix protein 1 (DMP1), bone sialoprotein, osteocalcin and bone morphogenetic protein (BMP-2), enriched with aspartic/glutamic acid residues bearing ionisable carboxyl moieties, demonstrate high-affinity calcium chelation capacities, a critical determinant of their mineralisation regulatory functions.[32-34]

Given the intricate orchestration of biomineralisation in natural tissues, the development of biomimetic mineralisation strategies has emerged as a promising avenue to replicate these processes artificially. By harnessing the principles of biomineralisation, researchers aim to design advanced synthetic materials that closely mimic the hierarchical structure and functionality of natural bone, thereby enhancing their potential for biomedical applications such as bone repair and regeneration.

Strategy for development of biomimetic mineralised materials

The mechanical behaviour of the collagen-mineral composite in bone is critically dependent on the nanomechanical heterogeneity of mineral and collagen components, as well as their hierarchically staggered nanostructure, which enables the bone to dynamically adapt to varying mechanical demands.[5,14,35] Thus, the goal of biomimetic mineralisation is to recapitulate the cross-linking chemistry and molecular packing structure of collagen, the characteristics of mineral particles and their interaction.

Matrix and templates

The nucleation, growth and morphology of hierarchical mineralised structures are influenced significantly by the charge distribution, conformational changes, supramolecular assembly and post-translational crosslinking of biomacromolecules within the templates.[36] Artificial biomaterials have been engineered as scaffolds to emulate the structural organisation and composition of biominerals, with the goal of replicating their biological functionality.

Collagen

Mineralised collagen is the most basic building block of natural bone and dentine.[37,38] Its integrin α2β1-binding domains mediate cellular adhesion while orchestrating calcium phosphate nucleation through spatial confinement effects, directing nanocrystalline alignment.[38,39] The conventional method of mineralising collagen involves simulating the composition of hard tissue, which means directly blending minerals and collagen solution or immersing preformed collagen scaffolds in the solutions of mineral ions.[38,40,41] Researchers have used a freeze-dried collagen solution to fabricate collagen-based bone regeneration scaffolds and achieved bone repair.[8,42-44] Merely simulating the composition of bone is insufficient, as the intricate structures of bone play a crucial role in its overall functionality and mechanical properties.

Extrafibrillar mineralisation has been primarily reported to develop mineralised collagen to stimulate the construction of hard tissue. However, the limitation of extrafibrillarly mineralised collagen (EMC) is its inadequate mechanical strength. This deficiency arises because the populations of HA aggregates within the extrafibrillar spaces inhibit the transport of precursors to the inside of the matrix and prevent further mineralisation throughout its depth and fail to replicate the multi-scale design of hard tissue.[45] Then, strategies adopted for biomimetic intrafibrillar mineralisation have been introduced, which can be roughly categorised into two types. In one, NCP-stabilised amorphous precursors infiltrate collagen's supramolecular confinement, then transform into the crystalline phase to initiate mineralisation.[25,46,47] Liu et al[48,49] created a hierarchical intrafibrillar mineralised collagen scaffold that mimics the periodic nano-architectures of native bone, utilising polyacrylic acid as mineralisation regulator.

In the other, synchronised apatite crystallisation and collagen organisation occur in a cooperative self-assem-

bly process through liquid crystalline phase transitions, which only requires amorphous primary particles and organic macromolecules without NCPs or their polymeric analogues.[22,50-52] The concentration of calcium ions could strongly influence the mineral distribution in collagen matrices and the size and direct 3D orientation of apatite crystals, in a manner similar to that found in fresh untreated bone.[50,51,53] The formation of a bio-inspired mineralisation of collagen matrix on graphene oxide (GO) nanosheet surfaces by changing the concentration of collagen has been reported in the absence of calcium-binding polymer or NCP.[54] Giraud-Guille et al[55] also found that intact, 300-nm-long collagen molecules could form typical liquid crystalline domains in viscous collagen solution after sonication. Additionally, self-assembly collagen/apatite scaffold can also be synthesised by changing the main mechanical microenvironment, such as solution pH optimisation and the application of a small amount of fluid shear stress (FSS) (less than 2 Pa, especially within 1.5 Pa) to induce the assembly of collagen molecules.[56-58]

Non-collagen

Current methodologies rely predominantly on animal-derived collagen. However, naturally extracted collagen is difficult to optimise and modify, and its structural domains are often suboptimal in vitro to obtain sufficient mechanical properties for hard tissue engineering. Replacing collagen with engineered organic matrices allows systematic control over structural and process-directing parameters, thereby elucidating their individual contributions to biomineralisation mechanisms.[31,59]

Notably, Li et al[26,60] achieved intrafibrillar mineralisation of self-assembled elastin-like recombinamers (ELRs) utilising a bioinspired polymer-induced liquid precursor (PILP) mineralisation method, by which polyaspartate-stabilised amorphous calcium phosphates infiltrated preferentially into the fibrils and then crystallised into HA crystals with their axes aligned parallel to the long axis of the ELR fibril. Similarly, Yu et al reported a biomineralisation-inspired technique for the synthesis of hybrid materials mimicking the hierarchical structure of spider silk fibres, composed of polyvinyl alcohol (PVA) and sodium alginate (Alg), with HA uniformly mineralised along PVA to reinforce PVA macrofibres with their excellent mechanical properties and exhibit remarkable mechanical properties.[61]

Cellulose nanocrystals (CNCs) can also be used as versatile templates for engineering hierarchical 3D architectures owing to their exemplary mechanical robustness, biocompatible nature, reduced mass density and minimal cytotoxic/ecotoxic potential.[62] The anionic surface characteristics of CNCs facilitate electrostatic stabilisation of inorganic nanoparticles (e.g., Ag, Au, Pt, Pd) in aqueous suspensions, enabling biomimetic nucleation of calcium phosphate phases.[63-65] Ribeiro et al[63] have developed nanocomposites using hierarchical-mineralised CNCs (mCNCs) modified with platelet lysate providing cell binding sites to mimic the nucleation of calcium phosphates, successfully reconstructing a nanostructured biomimetic mineralisation microenvironment that emulates extracellular matrix.

Chitosan (CS), a partially or fully deacetylated chitin derivative, exhibits structural homology and biomimetic functionalities analogous to extracellular matrix components during biomineralisation.[66,67] Guo et al[68] fabricated a hybrid nanostructured HA-CS composite scaffold by alkaline solution treatment to recapitulate the hierarchical mineralisation dynamics of osseous apatite. Carboxymethyl CS (CMCS) is a water-soluble derivative of CS with the ability to chelate Ca^{2+} and regulate the nucleation and growth of apatite. CMCS nanofibres mineralised by HA have shown the enhancement of the adhesion, proliferation and differentiation behaviours of BMSCs and the promotion of new bone formation and maturation.[69] Beyond conventional CS/calcium phosphate composites, silica-incorporated hybrid biomimetic mineralised CS scaffolds shave also exhibited accelerated calcium phosphate deposition with preserved cytocompatibility, demonstrating superior in vitro osteogenic bioactivity compared to pristine CS architectures.[70,71]

Synthetic polymers are also widely used as scaffolds for bone tissue engineering. Buschmann et al[72] developed a hybrid of poly(lactic-co-glycolic acid) (PLGA) and HA, replicating both compositional and ultrastructural features of collagen-apatite complexes inherent to cortical bone extracellular matrices.[73]

Moreover, there are many ways to enhance biomineralisation, such as strategic integration of magnesium-based compounds (MgO, $MgCO_3$) into biomaterials to promote the proliferation and osteogenic differentiation of BMSCs.[74] Controlled release of silicate ions could promote massive collagen secretion and accelerate polydopamine surface functionalisation to provide nucleation sites for apatite deposition.[75-77] Another example of successful biomimetic mineralisation of analogues of materials is the gelatine methacryloyl (GelMA)-polylactide (PLA) composite scaffolds, where the hydrophobic PLA component emulates cortical bone mechanics while GelMA hydrogels mimic cancellous bone microenvironments, achieving dual-phase structural biomimicry.[78,79]

Calcium resource provider

ACP constitutes a metastable ionic assembly of calcium and phosphate ions, functioning as a transient precursor phase for apatite crystallisation.[80-84] Considering the ACP fluid precursor is transient and unstable, ACP nanoparticles (NACP) and casein phosphopeptide-ACP (CPP-ACP) paste were promoted, which could enhance mechanical integrity and dentine remineralisation through increased surface area and efficient ion release.[85,86] Clinically, however, the most commonly used calcium-containing mineralising medium is calcium phosphate mineralising solution, including simulated body fluid (SBF) and calcium/phosphate-enriched artificial saliva (AS) to replicate physiological conditions for HA deposition.[3-17,26,27,87-90]

In addition, calcium phosphate oligomers (CPOs), engineered nanoscale clusters of calcium phosphate ions, bioactive glass and calcium chloride solution, could also be employed as calcium resource provider.[91-94]

Crystal precursor stabiliser

Since the thermodynamic instability of ACP often leads to its transformation into more stable HAP crystals, which cannot infiltrate collagen fibrils, much attention has been drawn to NCPs.[29,80] NCPs with a high degree of anionic character due to the presence of a considerable number of carboxylate groups along their backbone could inhibit bulk crystallisation and instruct ions to be sequestered to form stabilised ACP precursor, thereby achieving intrafibrillar mineralisation. instructing ions to be sequestered and form stabilised ACP precursor.[47,95-99] Due to their limited availability, high cost and difficulty to extract and purify natural NCPs, however, numerous researchers have dedicated their efforts to identifying and engineering synthetic analogues capable of replicating the functional roles of NCPs within biomineralisation.[90]

Many researchers are committed to identifying and developing analogues that can effectively replicate the role of NCPs in the biomineralisation process. Polyanionic synthetic polymers including polyaspartic acid (p-Asp), polyacrylic acid (PAA) and polyvinyl phosphonic acid (PVPA) mimic charge distribution. Polyaspartic acid (p-Asp) has the capacity to stabilise ACP clusters by capillary action. Deshpande et al[100] employed poly-l-aspartic acid as a non-collagenous analogue, resulting in the deposition of ribbon-shaped apatite crystals within fibrils with aligned c-axes, replicating native bone/dentine organisation. Poly (acrylic acid) (PAA) may mimic the calcium phosphate-binding sites of DMP1, while poly(vinylphosphonic acid) (PVPA) simulates the collagen-binding function of DMP1, guiding the recruitment of nano-precursors to the collagen matrix.[81,101-107] Hu et al[107] leveraged the ionotropic properties of PAA to align HA nanocrystals along collagen's longitudinal axis, emulating bone's anisotropic mineralisation pattern.

Further studies revealed that polyallylamine hydrochloride (PAH), a polycationic compound, could also induce intrafibrillar mineralisation.[108,109] The positive charge of PAH-ACP drives cations out of the collagen fibres, causing water to exit and create negative pressure, which is then alleviated as PAH-ACP electrostatically interacts with collagen to allow fluid ACP to enter the fibres.[110]

Moreover, CMC, a zwitterionic polymer with abundant carboxyl groups, could bind strongly with Ca^{2+} and acts as a water-soluble chelator to synthesise ACP precursors, forming nanocomplexes that penetrate collagen fibrils and facilitate intrafibrillar mineralisation.[111,112]

Beyond polyelectrolytes, casein phosphopeptides (CPPs) containing phosphoryl residues can bind with calcium and phosphate ions, preventing the aggregation or precipitation of ACP nano-precursors. This interaction subsequently promotes crystal nucleation and growth along the phosphorylated dentine collagen fibres.[86]

Branched polymers such as PAMAM dendrimers have been reported to exhibit sequestration and templating functions similar to those of NCPs.[84] In solution, PAMAM dendrimers, including diverse terminal groups such as carboxyl-terminated (PAMAM-COOH), hydroxy-terminated (PAMAM-OH), amine-terminated (PAMAM-NH2) and phosphate-terminated (PAMA-PO3H2) can inhibit mineralisation and stabilise ACP nanoprecursors, thereby preventing phase transformation.[13,113-116]

Except polymers, amino acids, such as glutamic acid (Glu) at appropriate concentrations, can also induce the aggregation of HA with spherical morphology in a hierarchical structure.[117] Periodic FSS alone can complete intrafibrillar mineralisation and promote the transformation of ACP into apatite crystals, accelerating the formation of highly orientated hierarchical intrafibrillar mineralised collagen.[57,118]

In addition, some small molecules, such as citrate and fluoride, have been found to affect intrafibrillar mineralization. Citrate molecules could reduce the interfacial energy between the collagen matrix and ACP precursors significantly, thus regulating the heterogeneous mineralisation behaviour.[119] Saxena et al[120] also found that the fluoride concentration could influence the morphology of the crystals and the mineralisation site and increase the amount of inter-/extrafibrillar mineral.

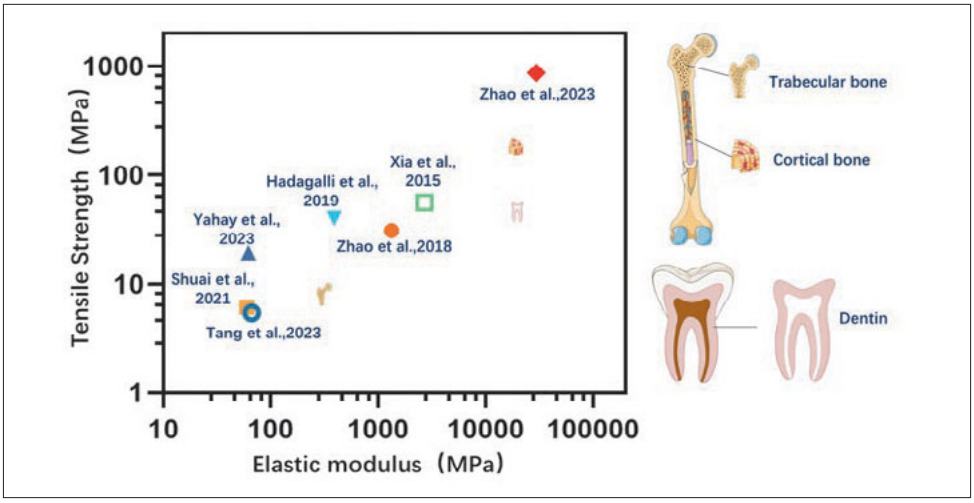

Fig 2 Mechanical properties (including elastic modulus and tensile strength) of biomimetic mineralisation materials compared with natural bone and dentin(log10).[130-139]

Furthermore, biomimetic mineralisation can occur independently of NCPs or their counterparts.[121] Wang et al[50] successfully demonstrated spontaneous collagen self-assembly alongside the initiation and alignment of carbonate apatite mineral growth, all without the requirement of any additional vertebrate extracellular matrix molecules typically involved in calcifying tissues.

Clinical application

Biomimetic mineralisation materials offer significant advantages in clinical applications, particularly hard tissue regeneration, due to their optimal mechanical properties, biodegradability and architecture for cell colonisation and organisation.[122] Their mechanical properties can be tailored to match those of natural bone, making them suitable for load-bearing applications.[50,53,96] Biomimetically engineered materials exhibit superior regulation of degradation kinetics relative to inorganic calcium phosphate (CaP) counterparts, owing to their programmed architectural configurations that enable rather controllable degradation rate.[123] Furthermore, they could promote vascularisation and tissue integration, which are critical for repairing large bone defects.[44,56,75,76,78,124]

However, several challenges hinder the widespread clinical adoption of biomimetic mineralisation materials.[72,125] Collagen scaffolds, while biocompatible, suffer from poor mechanical properties and insufficient structural stability because collagen may swell readily when implanted in vivo due to its high hydrophilicity.[126] Moreover, the degradation of synthetic materials used as scaffolds and crystal precursor stabilisers, like synthetic polymers, may negatively affect the osteogenic microenvironment because the degradation process may release acidic byproducts during hydrolysis, inducing localised pH reduction, thereby compromising cellular osteogenic capacity. Additionally, significant gaps in mechanical properties and biological performance persist compared to natural mineralised tissues (Fig 2), primarily due to several key limitations. These include the lack of precise control over the nucleation, growth and assembly of HAP crystals in vitro, the inability to effectively replicate the natural organic-inorganic combination mechanisms and the challenge of forming appropriate hierarchical microstructures.[11]

For clinical application, demand for biodegradable and sustainable materials is also urgent due to environmental concerns. Both natural and synthetic biodegradable materials could offer promising solutions for clinical applications while addressing environmental sustainability. Biomaterials of natural origin (e.g. collagen and silk) are processed via eco-friendly aqueous methods and degrade without releasing cytotoxic by-products.[127] Meanwhile, synthetic polymers, including PLA and PLGA, could degrade through simple chemical hydrolysis to form lactic acid and glycolic acid, which are safely removed via normal metabolic pathways.[128,129]

Conclusion

Natural bone and dentine are organic-inorganic composites primarily composed of collagen and HA, arranged in hierarchical structures spanning from the atomic to macroscopic scales. To deepen understanding of collagen biomineralisation and offer guidance for the design of mineralised collagen-based materials, this

review provides a comprehensive summary of the current mechanisms underlying collagen mineralisation and recent biomimetic strategies for bone regeneration and tooth repair. Future research should extend to the need for predesigned templates with multiscale ordered structures and manufacturing scalability which can be addressed through advanced technologies like 3D printing and biomanufacturing.

Conflicts of interest

The authors declare no conflicts of interest related to this study.

Author contribution

Dr Lin Xue ZHANG contributed to the manuscript draft; Dr Zuo Ying YUAN contributed to the conceptualisation and manuscript editing; Dr Yu Ming ZHAO contributed to the study design; Dr Yun Fan ZHANG contributed to the conceptualisation, manuscript draft and revision.

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References

1. Abou Neel EA, Aljabo A, Strange A, et al. Demineralization-remineralization dynamics in teeth and bone. Int J Nanomedicine 2016;11:4743–4763.
2. Ma L, Sun Y, Cheng Q, et al. Silk protein-mediated biomineralization: From bioinspired strategies and advanced functions to biomedical applications. ACS Appl Mater Interfaces 2023;15:33191–33206.
3. Cheng Q, Jiang L, Tang Z. Bioinspired layered materials with superior mechanical performance. Acc Chem Res 2014;47:1256–1266.
4. Nie Z, Zhang Y, Tang R, Wang X. Biomimetic mineralization: An emerging organism engineering strategy for biomedical applications. J Inorg Biochem 2022;232:111815.
5. Wu X, Walsh K, Hoff BL, Camci-Unal G. Mineralization of biomaterials for bone tissue engineering. Bioengineering (Basel) 2020;7:132.
6. Fu Y, Liu S, Cui SJ, et al. Surface chemistry of nanoscale mineralized collagen regulates periodontal ligament stem cell fate. ACS Appl Mater Interfaces 2016;8:15958–15966.
7. Elsharkawy S, Al-Jawad M, Pantano MF, et al. Protein disorder–order interplay to guide the growth of hierarchical mineralized structures. Nat Commun 2018;9:2145.
8. Tang S, Dong Z, Ke X, Luo J, Li J. Advances in biomineralization-inspired materials for hard tissue repair. Int J Oral Sci 2021;13:42.
9. Depalle B, McGilvery CM, Nobakhti S, Aldegaither N, Shefelbine SJ, Porter AE. Osteopontin regulates type I collagen fibril formation in bone tissue. Acta Biomater 2021;120:194–202.
10. Scott JE, Haigh M. Proteoglycan-type I collagen fibril interactions in bone and non-calcifying connective tissues. Biosci Rep 1985;5:71–81.
11. Wu S, Chen Y, Guo X, Wu Y. Collagen mineralization and its applications in hard tissue repair. Mater Chem Front 2021;5:7071–7087.
12. Kim HD, Amirthalingam S, Kim SL, Lee SS, Rangasamy J, Hwang NS. Biomimetic materials and fabrication approaches for bone tissue engineering. Adv Healthc Mater 2017;6:1700612.
13. Xie H, Sun J, Xie F, He S. Intrafibrillar mineralization of type I collagen by micelle-loaded amorphous calcium phosphate nanoparticles. RSC Adv 2023;13:11733–11741.
14. Liu Y, Liu S, Luo D, et al. Hierarchically staggered nanostructure of mineralized collagen as a bone-grafting scaffold. Adv Mater 2016;28:8740–8748.
15. Christoffersen J, Landis WJ. A contribution with review to the description of mineralization of bone and other calcified tissues in vivo. Anat Rec 2005;230:435–450.
16. Hu C, Zhang L, Wei M. Development of biomimetic scaffolds with both intrafibrillar and extrafibrillar mineralization. ACS Biomater Sci Eng 2015;1:669–676.
17. Zhou Y, Hu Z, Jin W, et al. Intrafibrillar mineralization and immunomodulatory for synergetic enhancement of bone regeneration via calcium phosphate nanocluster scaffold. Adv Healthc Mater 2023;12:e2201548.
18. Beniash E. Biominerals--Hierarchical nanocomposites: The example of bone. Wiley Interdiscip Rev Nanomed Nanobiotechnol 2011;3:47–69.
19. Chen L, Zeng Z, Li W. Poly(acrylic acid)-assisted intrafibrillar mineralization of type I collagen: A review. Macromol Rapid Commun 2023;44:e2200827.
20. Yu L, Wei M. Biomineralization of collagen-based materials for hard tissue repair. Int J Mol Sci 2021;22:944.
21. Sorushanova A, Delgado LM, Wu Z, et al. The collagen suprafamily: From biosynthesis to advanced biomaterial development. Adv Mater 2019;31:e1801651.
22. Cui FZ, Li Y, Ge J. Self-assembly of mineralized collagen composites. Mater Sci Eng R-Rep 2007;57:1–27.
23. Oosterlaken BM, Vena MP, de With G. In vitro mineralization of collagen. Adv Mater 2021;33:e2004418 [erratum 2023;35:e2305203].
24. Liu Y, Li N, Qi YP, et al. Intrafibrillar collagen mineralization produced by biomimetic hierarchical nanoapatite assembly. Adv Mater 2011;23:975–980.
25. Jehannin M, Rao A, Cölfen H. New horizons of nonclassical crystallization. J Am Chem Soc 2019;141:10120–10136.
26. Li Y, Chen X, Ribeiro AJ, et al. Hybrid nanotopographical surfaces obtained by biomimetic mineralization of statherin-inspired elastin-like recombinamers. Adv Healthc Mater 2014;3:1638–1647.
27. Hu D, Ren Q, Li Z, Zhang L. Chitosan-based biomimetically mineralized composite materials in human hard tissue repair. Molecules 2020;25:4785.
28. Capulli M, Paone R, Rucci N. Osteoblast and osteocyte: Games without frontiers. Arch Biochem Biophys 2014;561:3–12.
29. Zhu WEI, Robey PG, Boskey AL. The regulatory role of matrix proteins in mineralization of bone. In: Marcus R, Feldman D, Nelson DA, Rosen CJ (eds). Osteoporosis, ed 3. San Diego: Academic Press; 2008:191–240.
30. Sreenath T, Thyagarajan T, Hall B, et al. Dentin sialophosphoprotein knockout mouse teeth display widened predentin zone and develop defective dentin mineralization similar to human dentinogenesis imperfecta type III. J Bio Chemi 2003;278:24874–24880.
31. de Melo Pereira D, Habibovic P. Biomineralization-inspired material design for bone regeneration. Adv Healthc Mater 2018;7:e1800700.

32. Oldberg A, Franzén A, Heinegård D. Cloning and sequence analysis of rat bone sialoprotein (osteopontin) cDNA reveals an Arg-Gly-Asp cell-binding sequence. Proc Natl Acad Sci U S A 1986;83:8819–8823.
33. Chien YC, Tao J, Saeki K, et al. Using biomimetic polymers in place of noncollagenous proteins to achieve functional remineralization of dentin tissues. ACS Biomater Sci Eng 2017;3:3469–3479.
34. Ruiz-Agudo C, Cölfen H. Exploring the potential of nonclassical crystallization pathways to advance cementitious materials. Chem Rev 2024;124:7538–7618.
35. Fratzl P, Gupta HS, Paschalis EP, Roschger P. Structure and mechanical quality of the collagen–mineral nano-composite in bone. J Mater Chem 2004;14:2115–2123.
36. Athanasiadou D, Carneiro KMM. DNA nanostructures as templates for biomineralization. Nat Rev Chem 2021;5:93–108.
37. Wang W, Yeung KWK. Bone grafts and biomaterials substitutes for bone defect repair: A review. Bioact Mater 2017;2:224–247.
38. Zhang D, Wu X, Chen J, Lin K. The development of collagen based composite scaffolds for bone regeneration. Bioact Mater 2018;3:129–138.
39. Sayin E, Rashid RH, Rodríguez-Cabello JC, Elsheikh A, Baran ET, Hasirci V. Human adipose derived stem cells are superior to human osteoblasts (HOB) in bone tissue engineering on a collagen-fibroin-ELR blend. Bioact Mater 2017;2:71–81.
40. Li Z, Du T, Ruan C, Niu X. Bioinspired mineralized collagen scaffolds for bone tissue engineering. Bioact Mater 2020;6:1491–1511.
41. Fox K, Tran PA, Tran N. Recent advances in research applications of nanophase hydroxyapatite. Chemphyschem 2012;13:2495–2506.
42. Levingstone TJ, Matsiko A, Dickson GR, O'Brien FJ, Gleeson JP. A biomimetic multi-layered collagen-based scaffold for osteochondral repair. Acta Biomater 2014;10:1996–2004.
43. Cholas R, Kunjalukkal Padmanabhan S, Gervaso F, et al. Scaffolds for bone regeneration made of hydroxyapatite microspheres in a collagen matrix. Mater Sci Eng C Mater Biol Appl 2016;63:499–505.
44. Zhang Z, Li Z, Zhang C, et al. Biomimetic intrafibrillar mineralized collagen promotes bone regeneration via activation of the Wnt signaling pathway. Int J Nanomedicine 2018;13:7503–7516.
45. Kim D, Lee B, Thomopoulos S, Jun YS. In situ evaluation of calcium phosphate nucleation kinetics and pathways during intra- and extrafibrillar mineralization of collagen matrices. Cryst Growth Des 2016;16:5359–5366.
46. Palmer LC, Newcomb CJ, Kaltz SR, Spoerke ED, Stupp SI. Biomimetic systems for hydroxyapatite mineralization inspired by bone and enamel. Chem Rev 2008;108:4754–4783.
47. Yu L, Martin IJ, Kasi RM, Wei M. Enhanced intrafibrillar mineralization of collagen fibrils induced by brushlike polymers. ACS Appl Mater Interfaces 2018;10:28440–28449.
48. Liu Y, Luo D, Yu M, et al. Thermodynamically controlled self-assembly of hierarchically staggered architecture as an osteoinductive alternative to bone autografts. Adv Funct Mater 2019;29:1806445.
49. Liu Y, Kim YK, Dai L, et al. Hierarchical and non-hierarchical mineralisation of collagen. Biomaterials 2011;32:1291–1300.
50. Wang Y, Azaïs T, Robin M, et al. The predominant role of collagen in the nucleation, growth, structure and orientation of bone apatite. Nat Mater 2012;11:724–733.
51. Silver FH, Landis WJ. Deposition of apatite in mineralizing vertebrate extracellular matrices: A model of possible nucleation sites on type I collagen. Connect Tissue Res 2011;52:242–254.
52. Zhang W, Liao SS, Cui FZ. Hierarchical self-assembly of nano-fibrils in mineralized collagen. Chem Mater 2003;15:3221–3226.
53. Liu Y, Luo D, Wang T. Hierarchical structures of bone and bioinspired bone tissue engineering. Small 2016;12:4611–4632.
54. Yue C, Ding C, Du X, Wang Y, Su J, Cheng B. Self-assembly of collagen fibrils on graphene oxide and their hybrid nanocomposite films. Int J Biol Macromol 2021;193(Pt A):173–182.
55. Giraud-Guille MM. Liquid crystallinity in condensed type I collagen solutions. A clue to the packing of collagen in extracellular matrices. J Mol Biol 1992;224:861–873.
56. Niu X, Fan R, Guo X, et al. Shear-mediated orientational mineralization of bone apatite on collagen fibrils. J Mater Chem B 2017;5:9141–9147.
57. Du T, Niu X, Hou S, et al. Highly aligned hierarchical intrafibrillar mineralization of collagen induced by periodic fluid shear stress. J Mater Chem B. 2020;8:2562–2572.
58. Romero-Castillo I, López-Ruiz E, Fernández-Sánchez JF, Marchal JA, Gómez-Morales J. Self-assembled type I collagen-apatite fibers with varying mineralization extent and luminescent terbium promote osteogenic differentiation of mesenchymal stem cells. Macromol Biosci 2021;21:e2000319.
59. Farokhi M, Mottaghitalab F, Samani S, et al. Silk fibroin/hydroxyapatite composites for bone tissue engineering. Biotechnol Adv 2018;36:68–91.
60. Li Y, Rodriguez-Cabello JC, Aparicio C. Intrafibrillar mineralization of self-assembled elastin-like recombinamer fibrils. ACS Appl Mater Interfaces 2017;9:5838–5846.
61. Yu Y, He Y, Mu Z, et al. Biomimetic mineralized organic–inorganic hybrid macrofiber with spider silk-like supertoughness. Adv Funct Mater 2019;30:1908556.
62. Domingues RMA, Gomes ME, Reis RL. The potential of cellulose nanocrystals in tissue engineering strategies. Biomacromolecules 2014;15:2327–2346.
63. Ribeiro JP, Domingues RMA, Babo PS, et al. Highly elastic and bioactive bone biomimetic scaffolds based on platelet lysate and biomineralized cellulose nanocrystals. Carbohydr Polym 2022;292:119638.
64. Moon RJ, Martini A, Nairn J, Simonsen J, Youngblood J. Cellulose nanomaterials review: Structure, properties and nanocomposites. Chem Soc Rev 2011;40:3941–3994.
65. Islam MS, Chen L, Sisler J, Tam KC. Cellulose nanocrystal (CNC)–inorganic hybrid systems: Synthesis, properties and applications. J Mater Chem B 2018;6:864–883.
66. Zheng B, Mao C, Gu T, et al. Phosphorylated chitosan to promote biomimetic mineralization of type I collagen as a strategy for dentin repair and bone tissue engineering. New J Chem 2019;43:2002–2010.
67. Wen B, Dai Y, Han X, et al. Biomineralization-inspired mineralized hydrogel promotes the repair and regeneration of dentin/bone hard tissue. NPJ Regen Med 2023;8:11.
68. Guo YP, Guan JJ, Yang J, Wang Y, Zhang CQ, Ke QF. Hybrid nanostructured hydroxyapatite-chitosan composite scaffold: Bioinspired fabrication, mechanical properties and biological properties. J Mater Chem B 2015;3:4679–4689.
69. Zhao X, Zhou L, Li Q, Zou Q, Du C. Biomimetic mineralization of carboxymethyl chitosan nanofibers with improved osteogenic activity in vitro and in vivo. Carbohydr Polym 2018;195:225–234.
70. Pipattanawarothai A, Suksai C, Srisook K, Trakulsujaritchok T. Non-cytotoxic hybrid bioscaffolds of chitosan-silica: Sol-gel synthesis, characterisation and proposed application. Carbohydr Polym 2017;178:190–199.

71. Salama A, Hesemann P. Synthesis and characterization of N-guanidinium chitosan/silica ionic hybrids as templates for calcium phosphate mineralization. Int J Biol Macromol 2020;147:276–283.
72. Buschmann J, Härter L, Gao S, et al. Tissue engineered bone grafts based on biomimetic nanocomposite PLGA/amorphous calcium phosphate scaffold and human adipose-derived stem cells. Injury 2012;43:1689–1697.
73. Soheilmoghaddam M, Padmanabhan H, Cooper-White JJ. Biomimetic cues from poly(lactic-co-glycolic acid)/hydroxyapatite nano-fibrous scaffolds drive osteogenic commitment in human mesenchymal stem cells in the absence of osteogenic factor supplements. Biomater Sci 2020;8:5677–5689.
74. Yuan Z, Wei P, Huang Y, et al. Injectable PLGA microspheres with tunable magnesium ion release for promoting bone regeneration. Acta Biomater 2019;85:294–309.
75. Wan Z, Yuan Z, Li Y, et al. Hierarchical therapeutic ion-based microspheres with precise ratio-controlled delivery as microscaffolds for in situ vascularized bone regeneration. Adv Funct Mater 2022;32:2113280.
76. Wei PF, Yuan ZY, Jing W, et al. Regenerating infected bone defects with osteocompatible microspheres possessing antibacterial activity. Biomater Sci 2019;7:272–286.
77. Wei P, Yuan Z, Cai Q, Mao J, Yang X. Bioresorbable microspheres with surface-loaded nanosilver and apatite as dual-functional injectable cell carriers for bone regeneration. Macromol Rapid Commun 2018;39:e1800062.
78. Zhang J, Tong D, Song H, et al. Osteoimmunity-regulating biomimetically hierarchical scaffold for augmented bone regeneration. Adv Mater 2022;34:e2202044.
79. Shi Z, Zhong Q, et al. Nanohydroxyapatite, nanosilicate-reinforced injectable, and biomimetic gelatin-methacryloyl hydrogel for bone tissue engineering. Int J Nanomedicine 2021;16:5603–5619.
80. Lotsari A, Rajasekharan AK, Halvarsson M, Andersson M. Transformation of amorphous calcium phosphate to bone-like apatite. Nat Commun 2018;9:4170.
81. Nudelman F, Pieterse K, George A, et al. The role of collagen in bone apatite formation in the presence of hydroxyapatite nucleation inhibitors. Nat Mater 2010;9:1004–1009.
82. Boonrungsiman S, Gentleman E, Carzaniga R, et al. The role of intracellular calcium phosphate in osteoblast-mediated bone apatite formation. Proc Natl Acad Sci U S A 2012;109:14170–14175.
83. Nitiputri K, Ramasse QM, Autefage H, et al. Nanoanalytical electron microscopy reveals a sequential mineralization process involving carbonate-containing amorphous precursors. ACS Nano 2016;10:6826–6835.
84. Yang Q, Zheng W, Zhao Y, et al. Advancing dentin remineralization: Exploring amorphous calcium phosphate and its stabilizers in biomimetic approaches. Dent Mater 2024;40:1282–1295.
85. Huang Q, Liang Z, Li J, Bai Y, He J, Lin Z. Size dependence of particulate calcium phosphate fillers in dental resin composites. ACS Omega 2021;6:35057–35066.
86. Cao Y, Mei ML, Xu J, Lo EC, Li Q, Chu CH. Biomimetic mineralisation of phosphorylated dentine by CPP-ACP. J Dent 2013;41:818–825.
87. Leung VW, Darvell BW. Artificial salivas for in vitro studies of dental materials. J Dent 1997;25:475–484.
88. Zhao Y, Xiong Y, Zheng J, et al. A multifaceted biomimetic periosteum with a lamellar architecture and osteogenic/angiogenic dual bioactivities. Biomater Sci 2023;11:3878–3892.
89. Tsai SW, Hsu FY, Chen PL. Beads of collagen-nanohydroxyapatite composites prepared by a biomimetic process and the effects of their surface texture on cellular behavior in MG63 osteoblast-like cells. Acta Biomater 2008;4:1332–1341.
90. Cao CY, Mei ML, Li QL, Lo EC, Chu CH. Methods for biomimetic remineralization of human dentine: A systematic review. Int J Mol Sci 2015;16:4615–4627.
91. Liang K, Zhao C, Song C, et al. In situ biomimetic mineralization of bone-like hydroxyapatite in hydrogel for the acceleration of bone regeneration. ACS Appl Mater Interfaces 2023;15:292–308.
92. Shao C, Jin B, Mu Z, et al. Repair of tooth enamel by a biomimetic mineralization frontier ensuring epitaxial growth. Sci Adv 2019;5:eaaw9569.
93. Vollenweider M, Brunner TJ, Knecht S, et al. Remineralization of human dentin using ultrafine bioactive glass particles. Acta Biomater 2007;3:936–943.
94. Wang Q, Wang XM, Tian LL, Cheng ZJ, Cui FZ. In situ remineralizaiton of partially demineralized human dentine mediated by a biomimetic non-collagen peptide. Soft Matter 2011;7:9673–9680.
95. Fisher LW, Torchia DA, Fohr B, Young MF, Fedarko NS. Flexible structures of SIBLING proteins, bone sialoprotein, and osteopontin. Biochem Biophys Res Commun 2001;280:460–465.
96. Qi Y, Ye Z, Fok A, al. Effects of molecular weight and concentration of poly(acrylic acid) on biomimetic mineralization of collagen. ACS Biomater Sci Eng 2018;4:2758–2766.
97. Kim YK, Gu LS, Bryan TE, et al. Mineralisation of reconstituted collagen using polyvinylphosphonic acid/polyacrylic acid templating matrix protein analogues in the presence of calcium, phosphate and hydroxyl ions. Biomaterials 2010;31:6618–6627.
98. Jee SS, Thula TT, Gower LB. Development of bone-like composites via the polymer-induced liquid-precursor (PILP) process. Part 1: Influence of polymer molecular weight. Acta Biomater 2010;6:3676–3686.
99. He G, George A. Dentin matrix protein 1 immobilized on type I collagen fibrils facilitates apatite deposition in vitro. J Biol Chem 2004;279:11649–11656.
100. Deshpande AS, Beniash E. Bio-inspired synthesis of mineralized collagen fibrils. Cryst Growth Des 2008;8:3084–3090.
101. Olszta MJ, Cheng X, Jee SS, et al. Bone structure and formation: A new perspective. Mater Sci Eng R Rep 2007;58:77–116.
102. Ping H, Wagermaier W, Horbelt N, et al. Mineralization generates megapascal contractile stresses in collagen fibrils. Science 2022;376:188–192.
103. Gower LB. Biomimetic model systems for investigating the amorphous precursor pathway and its role in biomineralization. Chem Rev 2008;108:4551–4627.
104. Tay FR, Pashley DH. Guided tissue remineralisation of partially demineralised human dentine. Biomaterials 2008;29:1127–1137.
105. Thula TT, Svedlund F, Rodriguez DE, Podschun J, Pendi L, Gower LB. Mimicking the nanostructure of bone: Comparison of polymeric process-directing agents. Polymers (Basel) 2011;3:10–35.
106. Tanimoto S, Nishii I, Kanaoka S. Biomineralization-inspired fabrication of chitosan/calcium carbonates core-shell type composite microparticles as a drug carrier. Int J Biol Macromol 2019;129:659–664.
107. Hu C, Zilm M, Wei M. Fabrication of intrafibrillar and extrafibrillar mineralized collagen/apatite scaffolds with a hierarchical structure. J Biomed Mater Res A 2016;104:1153–1161.

108. Cantaert B, Kim Y, Ludwig H, Nudelman F, Sommerdijk NAJM, Meldrum FC. Think positive: Phase separation enables a positively charged additive to induce dramatic changes in calcium carbonate morphology. Adv Funct Mater 2012;22:907–915.
109. Niu LN, Jee SE, Jiao K, et al. Collagen intrafibrillar mineralization as a result of the balance between osmotic equilibrium and electroneutrality. Nat Mater 2017;16:370–378.
110. Ma YX, Hoff SE, Huang XQ, et al. Involvement of prenucleation clusters in calcium phosphate mineralization of collagen. Acta Biomater 2021;120:213–223.
111. Zhang Q, Guo J, Huang Z, Mai S. Promotion effect of carboxymethyl chitosan on dental caries via intrafibrillar mineralization of collagen and dentin remineralization. Materials (Basel) 2022;15:4835.
112. Wang Y, Van Manh N, Wang H, Zhong X, Zhang X, Li C. Synergistic intrafibrillar/extrafibrillar mineralization of collagen scaffolds based on a biomimetic strategy to promote the regeneration of bone defects. Int J Nanomedicine 2016;11:2053–2067.
113. Liang K, Gao Y, Li J, et al. Biomimetic mineralization of collagen fibrils induced by amine-terminated PAMAM dendrimers – PAMAM dendrimers for remineralization. J Biomater Sci Polym Ed 2015;26:963–974.
114. Liang K, Gao Y, Li J, et al. Effective dentinal tubule occlusion induced by polyhydroxy-terminated PAMAM dendrimer in vitro. RSC Adv 2014;4:43496–43503.
115. Li J, Yang J, Li J, et al. Bioinspired intrafibrillar mineralization of human dentine by PAMAM dendrimer. Biomaterials 2013;34:6738–6747.
116. Chen M, Yang J, Li J, et al. Modulated regeneration of acid-etched human tooth enamel by a functionalized dendrimer that is an analog of amelogenin. Acta Biomater 2014;10:4437–4446.
117. Bu H, Yang H, Shen L, Liu W, Li G. Glutamic acid concentration dependent collagen mineralization in aqueous solution. Colloids Surf B Biointerfaces 2020;190:110892.
118. Niu X, Wang L, Tian F, et al. Shear-mediated crystallization from amorphous calcium phosphate to bone apatite. J Mech Behav Biomed Mater 2016;54:131–140.
119. Shao C, Zhao R, Jiang S, et al. Citrate improves collagen mineralization via interface wetting: A physicochemical understanding of biomineralization control. Adv Mater 2018;30:1704876.
120. Saxena N, Cremer MA, Dolling ES, et al. Influence of fluoride on the mineralization of collagen via the polymer-induced liquid-precursor (PILP) process. Dent Mater 2018;34:1378–1390.
121. Jin HE, Jang J, Chung J, et al. Biomimetic self-templated hierarchical structures of collagen-like peptide amphiphiles. Nano Lett 2015;15:7138–7145.
122. Zhou Y, Liu K, Zhang H. Biomimetic mineralization: From microscopic to macroscopic materials and their biomedical applications. ACS Appl Bio Mater 2023;6:3516–3531.
123. Félix Lanao RP, Leeuwenburgh SC, Wolke JG, Jansen JA. Bone response to fast-degrading, injectable calcium phosphate cements containing PLGA microparticles. Biomaterials 2011;32:8839–8847.
124. Chen L, Wu C, Chen S, et al. Biomimetic mineralizable collagen hydrogels for dynamic bone matrix formation to promote osteogenesis. J Mater Chem B 2020;8:3064–3075.
125. Hong MH, Lee JH, Jung HS, Shin H, Shin H. Biomineralization of bone tissue: calcium phosphate-based inorganics in collagen fibrillar organic matrices. Biomater Res 2022;26:42.
126. Ferreira AM, Gentile P, Chiono V, Ciardelli G. Collagen for bone tissue regeneration. Acta Biomater 2012;8:3191–3200.
127. Stoppel WL, Ghezzi CE, McNamara SL, Black LD 3rd, Kaplan DL. Clinical applications of naturally derived biopolymer-based scaffolds for regenerative medicine. Ann Biomed Eng 2014;43:657-680 [erratum 2015;43:2023].
128. Oleksy M, Dynarowicz K, Aebisher D. Advances in biodegradable polymers and biomaterials for medical applications—A review. Molecules 2023;28:6213.
129. Liu X, Ma PX. The nanofibrous architecture of poly(l-lactic acid)-based functional copolymers. Biomaterials 2010;31:259–269.
130. Bowen Rl, Rodriguez MS. Tensile strength and modulus of elasticity of tooth structure and several restorative materials. J Am Dent Assoc 1962;64:378–387.
131. Hadagalli K, Panda AK, Mandal S, Basu B. Faster biomineralization and tailored mechanical properties of marine-resource-derived hydroxyapatite scaffolds with tunable interconnected porous architecture. ACS Appl Bio Mater 2019;2:2171–2184.
132. Shuai Y, Lu H, Lv R, et al. Biomineralization directed by prenucleated calcium and phosphorus nanoclusters improving mechanical properties and osteogenic potential of antheraea pernyi silk fibroin-based artificial periosteum. Adv Healthc Mater 2021;10:e2001695.
133. Yahay Z, Moein Farsani N, Mirhadi M, Tavangarian F. Fabrication of highly ordered willemite/PCL bone scaffolds by 3D printing: Nanostructure effects on compressive strength and in vitro behavior. J Mech Behav Biomed Mater 2023;144:105996.
134. Xia S, Wang Z, Chen H, et al. Nanoasperity: Structure origin of nacre-inspired nanocomposites. ACS Nano 2015;9:2167–2172.
135. Reilly DT, Burstein AH. The elastic and ultimate properties of compact bone tissue. J Biomech 1975;8:393–405.
136. Keller TS, Mao Z, Spengler DM. Young's modulus, bending strength, and tissue physical properties of human compact bone. J Orthop Res 1990;8:592–603.
137. Zhao X, Chen X, Zhang L, et al. Preparation of nano-hydroxyapatite coated carbon nanotube reinforced hydroxyapatite composites. Coatings 2018; 8:1395–1406.
138. Tang M, Xu K, Shang H, et al. Biomineralization of bone-like hydroxyapatite to upgrade the mechanical and osteoblastic performances of poly(lactic acid) scaffolds. Int J Biol Macromol 2023;226:1273–1283.
139. Zhao X, Chen Z, Zhuo H, et al. Ultra-strong and transparent biomimetic nanocomposite through orientation effects and in situ biomineralization. Adv Funct Mater 2024;34:2310094.