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Nanoceramics in Bone Tissue Engineering: The Future Lies Ahead

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Abstract Nanoceramics are composed of ceramics and are classified as inorganic, heat-resistant, nonmetallic solids made of both metallic and nonmetallic compounds. Bone tissue engineering applies bioactive scaffolds, host cells and osteogenic signals for restoring damaged or diseased tissues. Composites of bioactive ceramics closely match the properties of bone. In the present review paper, an attempt has been made to emphasize the suitability of nanoceramics in the field of bone tissue engineering. Toxicity of these synthesized nanomaterials should be checked before their real application. Nanoceramics, in future, will surely prove to be important nanomaterials in the field of tissue engineering.

Keywords: *Nanoceramics, composites, bone tissue engineering, scaffolds*

Nanoceramics

Nanoceramic is a type of nanoparticle which is composed of ceramics and are classified as inorganic, heat-resistant, nonmetallic solids made of both metallic and nonmetallic compounds. Nanoceramics have received significant attention as candidate materials due to their capability to demonstrate improved and unique properties in comparison with conventional bulk ceramic materials. Nanoceramics exhibit unique processing, mechanical, and surface characteristics such as superplasticity, machinability, strength, toughness, and bioactivity due to the fine grain size, abundant grain boundaries, and controllable crystallinity[1]. Applications of nanoceramics and their composites are numerous. Solid state lighting ceramics, electroceramic sensors, thermoelectric nanoceramics, nanoceramics for energy, environments, and healthcare, advanced ceramic coatings, structural nanoceramics with improved hardness, strength, fracture toughness, thermal shock, oxidation resistance are the fields which will open the gateways for future research. Ceramics is one of the fields where nanoscience and nanotechnology have shown remarkable progress, producing a variety of advanced materials with unique properties and performance. Nanoceramics is a term used to refer to ceramic materials fabricated from ultrafine particles which are less than 100 nm in diameter. There is increasing interest in the use of nanoparticles as fillers in polymer matrices to develop biomaterials which mimic the mechanical, chemical and electrical properties of bone tissue for orthopaedic applications[2].

Bone, a highly dynamic connective tissue, consist of a bio-organic phase comprising osteogenic cells and proteins which lies over an inorganic phase predominantly made of $CaPO_4$ (biological apatite). Injury to bone can be due to mechanical, metabolic or inflammatory agents also owing pathological conditions like fractures, osteomyelitis, osteolysis or cysts may arise in enameloid, chondroid, cementum, or chondroid bone which forms the intermediate tissues of the body[3]. Bone tissue engineering is based on the understanding of bone structure, bone mechanics, and tissue formation as it aims to induce new functional bone tissues. Bone tissue engineering aims to induce new functional bone regeneration via the synergistic combination of biomaterials, cells, and factor therapy[4]. Bone tissue engineering applies bioactive scaffolds, host cells and osteogenic signals for restoring damaged or diseased tissues. Various bioceramics used in bone tissue engineering can be bioactive (like glass ceramics and hydroxyapatite bioactive glass), bio-resorbable (like tricalcium phosphates) or bio-inert (like zirconia and alumina)[3]. Composites of biodegradable polymers and bioactive ceramics are candidates for tissue-engineered scaffolds that closely match the properties of bone. Figure 1 (Reprinted from Amini *et al.*[4]) shows three steps in bone tissue engineering.

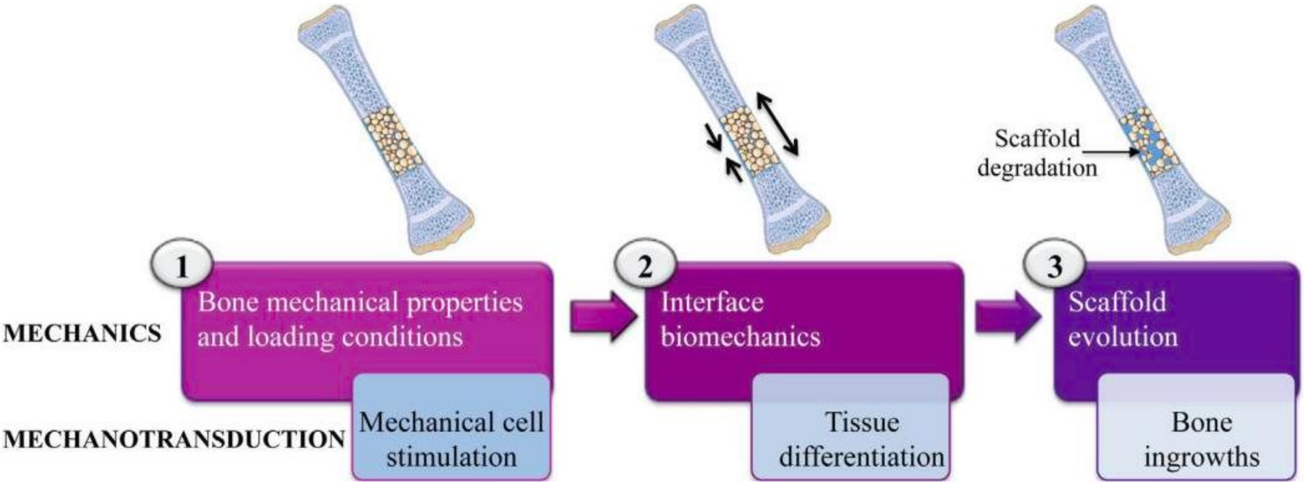

Figure 1: Three-step biomechanical paradigm in bone tissue engineering (Reprinted from Amini *et al.[4]*)

Synthesis

Systems of metal oxides, carbides, borides and nitrides compose most of the important ceramic materials[5]. A new porous hydroxyapatite ceramic was prepared by cold isostatic pressing and sintering of the flaky powder, that was synthesized through two-stage hydrolysis of brushite; (1) a structural change into the apatite structure and (2) a compositional increase in Ca/P ratio[6]. This powder consisted of fine needle crystals, which had a tendency to grow into the larger grains, but the powder was highly resistant to sintering under the usual heating conditions at 1200 degrees C. The product showed a 70% apparent porosity with spherical pores, ranging from 100-200 microns in size, and most pores were interconnected.

Mechanochemical synthesis involves mechanical activation of solid-state displacement reactions. This process has been successfully used recently to make nanoceramic powders such as Al_2O_3 and ZrO_2. It involves the milling of precursor powders (usually a salt and a metal oxide) to form a nanoscale composite of the starting materials which react during milling, and subsequent heating, if necessary, to form a mixture of dispersed nanoparticles of the desired oxide within a soluble salt matrix. Nanoparticles of Al_2O_3 (10-20 nm), for example, can be prepared by milling $AlCl_3$ with CaO[5]. In a study, Indialite ceramic was prepared using fly ash and magnesium carbonate powder as precursors[7]. X-ray diffraction results indicated that the formation of indialite was achieved by solid-state sintering reactions at 1200 degrees C for 4 h. With increasing amounts of LiOH . H2O, the viscosity decreased and beta-spodumene, spinel phases started to develop at the expense of indialite. Scanning electron microscopy observations revealed that the surface of the sintered samples became smoother with higher porosity losses and grain size reduction[7].

Nanoceramics in Bone Tissue Engineering

Nanoceramics have been used in bone tissue engineering[5,6]. The improvisation of the treatment procedures for treating the various kind of bone defects such as, bone or dental trauma and for diseases such as osteoporosis, osteomyelitis etc., need the suitable and promising biomaterials with resemblance of bone components[10]. Mimicking of natural structure of bone, like the use of nanomaterials, is an attractive approach for generating scaffolds for bone regeneration[11].

Chitin and chitosan based nanocomposite scaffolds have been widely used for bone tissue engineering. These chitin and chitosan based scaffolds have been reinforced with nano-components viz. Hydroxyapatite (HAp), Bioglass ceramic (BGC), Silicon dioxide (SiO2), Titanium dioxide (TiO2) and Zirconium oxide (ZrO2) to develop nanocomposite scaffolds[12]. Macroporous bioceramic scaffolds are often fabricated via the foam replica technique, based on polymeric foam impregnation with a glass slurry, followed by slow heat treatment to allow for drying, polymeric burnout, and sintering of the glass particles. Scaffolds produced by rapid vacuum sintering exhibited an excellent degree of sintering while scaffolds produced by slow sintering were incompletely sintered. The mean compressive strength was significantly higher for the RVS groups[8]. In another study, the feasibility of using indirect selective laser sintering (SLS) to produce parts from glass-ceramic materials for bone replacement applications has been investigated[9]. A castable glass based on the system SiO_2 x Al_2O_3 x P_2O_5 x CaO x CaF_2 that crystallizes to a glass-ceramic with apatite and mullite phases was produced, blended with an acrylic binder, and processed by SLS. An increase in strength was achieved by infiltrating the brown parts with a resorbable phosphate glass, although this altered the crystal phases present in the material.

Formulation and biological actions of nano-bioglass ceramic particles doped with Calcarea phosphorica for bone tissue engineering were investigated[10]. Bioactive glass ceramic (BGC) has recently acquired great attention as the most promising biomaterials; hence it has been widely applied as a filler material for bone tissue regeneration. Because it elicts specific biological responses after implantation in addition more potential in formation of strong interface with both hard and soft tissues by dissolution of calcium and phosphate ions[10]. The SEM and DLS were shown the size of the particles at nano scale, also the EDS, and FT-IR investigations indicated that the Calcarea phosphorica was integrated with nBGC particles and also the crystalline nature of particles was confirmed by XRD studies.

Another study evaluated the potential of raloxifene combined with BioGran(R) through the sonochemical method in the repair of critical bone defects in the calvaria of rats[13]. Hypothesis was that the homogenization of raloxifene to Biogran at the 20% concentration would improve the bone repair at the grafted site and results reported that BioGran(R) alone or in an 80/20 mass concentration with raloxifene can lead to favourable bone formation[13]. Use of Nano-biphasic calcium phosphate ceramic for the repair of bone defects has also been evaluated in another recent study. evaluate the effect of nanonization on the biphasic calcium phosphate (BCP) ceramic in the repair of bone cavities in the canine mandible. Results depicted that the rate of resorption increased significantly after nanonization even though the nano-sized BCP failed to make a superior regeneration than the ordinary BCP[11].

Zirconium has been employed in different research studies on bone tissue engineering[11,12,14]. Zirconium oxide nanoparticles (ZrO2 NPs) were incorporated for the first time in organic-inorganic hybrid composites containing chitosan, poly(ethylene glycol) and nano-hydroxypatite (CS-PEG-HA) to develop bone-like nanocomposites for bone tissue engineering application. These nanocomposites were characterized by FT-IR, XRD, TEM combined with SAED. SEM images and porosity measurements revealed highly porous structure having pore size of less than 1mum to 10mum. The mechanical strengths and porosities were similar to that of human spongy bone. Strong antimicrobial effects against gram-negative and gram-positive bacterial strains were also observed[14]. Due to the controllable mechanical properties and degradation rate, calcium silicates such as akermanite (Ca2MgSi2O7) with Ca-Mg and Si- containing bio-ceramics have received much more attention. In addition, the piezoelectric effect plays an important role in bone growth, remodeling and defect healing[15]. Inter-connected pore channel was observed in the SEM images. The manipulation flexibility of this method indicated the potential for the customized needs in the application of bone substitutes. Another study prepared poly(-caprolactone) (PCL) nanocomposites incorporating three different perovskite ceramic nanoparticles, namely, calcium titanate (CT), strontium titanate (ST) and barium titanate (BT)[2]. The tensile strength and modulus of the composites increased with the addition of nanoparticles. Scanning electron microscopy indicated that dispersion of the nanoparticles scaled with the density of the ceramics, which in turn played an important role in determining the enhancement in mechanical properties of the composite. Induction coupled plasma-optical emission spectroscopy indicated the release of small quantities of Ca^{+2}, Sr^{+2}, Ba^{+2} ions from the scaffolds. Piezo-force microscopy revealed that BT nanoparticles imparted piezoelectric properties to the scaffolds[2].

Conclusion

Nanoceramics exhibit unique mechanical and surface characteristics. Bone tissue engineering applies bioactive scaffolds, host cells and osteogenic signals for restoring damaged or diseased tissues. Composites of bioactive ceramics are candidates for tissue-engineered scaffolds that closely match the properties of bone. In the present review paper, nanoceramics have been seen to provide a broad platform to the field of bone tissue engineering. Toxicity of these synthesized nanomaterials should be checked before their real application. Nanoceramics, in future, will surely prove to be important nanomaterials in the field of tissue engineering.

Conflict of Interest

None declared

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