Biomedical Applications of Ceramic Nanocomposites

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Abstract

Bioceramics and bioceramic composites have been widely used for biomedical applications for the last 50 years. This chapter discusses the advantages of using ceramic nanocomposites. The application of both inert and bioactive ceramics for orthopaedic and dental implants, as well as in the novel field of tissue engineering, is discussed and future trends are presented.

Keywords: Bioceramic nanocomposites, inert ceramics, bioactive ceramics, bone tissue engineering, orthopaedic and dental implants

1. Introduction

Over the past 50 years significant progress has been made in the use of bioceramics and bioceramic composites for biomedical applications. The first attempts at implantation of ceramics in the biomedical sector started in the late 18th century, with the use of porcelain for crowns in dental applications. A hundred years later, in the late 19th century, there were studies of the use of plaster for bone repair according to Chevalier and Gremillard (2009). Soon after, in 1920, TCP (tricalcium phosphate), a bioresorbable ceramic, was proposed for use to fill gaps in bone. Some 10 years later, Rock (1933) was the first to consider the use of alumina ceramics as joint replacements. However, it was not until 30 years later (Sandhaus, 1967) when an alumina material, Degussit AL 23, was first patented for hip joints. According to Rieger (2001), this alumina material can be considered as the ancestor of today’s high-tech ceramics. Other Biomedical applications of ceramic nanocomposites ceramics were introduced in the following years, including hydroxyapatite (HAp) and TZP (tetragonal zirconia polycrystals) in the 1970s.

Over the past 50 years, therefore, there has been a significant move forward in the use of bioceramics for biomedical applications. The development of bioceramics can be classified into three generations (Vallet-Regi, 2010). The first generation would correspond to bioinert bioceramics, such as alumina and zirconia, which are mostly used for inert orthopaedic and dental implants. The second generation comprises bioactive and bioabsorbable ceramics, such as calcium phosphates or bioglasses. Finally, scaffolds for tissue engineering are the third generation; these aim to drive the regeneration of living tissues. In the meantime, many studies have demonstrated that better and unusual material properties can be achieved by manipulating ceramic length scales in the nano range. For that reason, during the last two decades, nanostructured materials have been widely studied and significant steps forward have been made in their understanding in recent years.

Nanostructured materials are defined as solid materials with at least one characteristic structural length in the order of a few nanometres (1 nm = 10^{-9} m) (Gleiter, 1995). Although some authors (e.g. Meyers *et al.*, 2006) define an upper limit of 250 nm for considering a material as nanometric, in general the nanometric grain size is meant to be below 100 nm (Nazarov and Mulyukov, 2002; Narayan *et al.*, 2004; Tjong and Chen, 2004; Liu and Webster, 2007; Kim and Estrin, 2008). Over this limit, the terms ultrafine grained materials or submicrometric materials (100-300 nm) are used.

This chapter discusses the advantages of using ceramic nanocomposites for biomedical applications. A material is defined as nanocomposite when at least one of the solid phases is in the nanometric range. First, the improvements achieved using nanocomposites are described. The next section focuses on inert ceramic nanocomposites for orthopaedic and dental implants. The applications of bioactive ceramics, such as calcium phosphates, in bone tissue engineering are then reviewed and future trends are presented.

2. Why ceramic nanocomposites are usedin biomedical applications

Ceramics are broadly used in a large variety of technological applications requiring both structural and functional properties. They have received significant attention as candidate materials for use as structural materials under conditions of high loading rates, high temperature, wear and chemical etching too severe for metals. In this sense, bone-related biomedical applications are the most demanding of bioceramics. However, their inherent brittleness derived from their low fracture toughness has prevented their use in some applications. Moreover, the presence of flaws or defects in the material can lead to catastrophic failure during mechanical loading. Therefore, new kinds of materials have been studied for increasing the performance of ceramic matrix materials. For ceramics used in biomedical applications, which are extensively called bioceramics, this problem still remains. Nanophased ceramics are being investigated as a way of solving some of the structural and bio-related problems. For example, nanometric features in the surface of a prosthesis seem to reduce the risk of rejection and enhance the proliferation of osteoblasts (bone-forming cells). Nanophased or nanostructured ceramics can be obtained either by nanocrystalline materials or with nanocomposites.

Nanocrystalline materials are solids with a nanometric microstructure, consisting of polycrystals with one or several nanometric phases (Gleiter, 2000). Nanocomposites are materials with at least one of the solid phases in the nanometric range. Both nanomaterials are structurally characterized by a large volume fraction of grain boundaries, which can significantly alter their physical, mechanical and chemical properties.

3. Nanocrystalline ceramics

In the case of nanocrystalline ceramics, as the grain size is reduced, the grain volume at grain boundaries is increased (Meyers *et al*., 2006). Thus, due to the high density of interfaces, an important fraction of atoms will be at the interface. This fact allows nanocrystalline materials to offer unusual and improved properties when compared to microscale materials.

There are studies (Webster *et al*., 1999) that provide evidence that nanophase ceramics could promote osseointegration, which is critical for the clinical success of orthopaedic/dental implants. Webster *et al*. (2000) synthesized dense nanophase alumina (Al_2O_3) materials and showed a significant increase in protein absorption and osteoblast adhesion on the nano-sized ceramic materials compared to traditional micron-sized ceramic materials. Other studies (Du *et al*., 1999) have suggested that better osteoconductivity would be achieved if synthetic HAp could more resemble bone minerals in composition, size and morphology.

The use of nanocrystalline materials can thus offer advantages for use in biomedical applications, such as:

- increased resistance/hardness
- improved toughness
- lower elastic modulus and lower ductility
- reduced risk of rejection
- enhanced proliferation of osteoblasts
- promotion of ossointegration

With ceramic nanocomposites, even greater improvements can be achieved and the use of new ceramic matrix nanocomposites has been suggested (Gleiter, 1995; Narayan *et al*., 2004; Meyers *et al*., 2006; Liu and Webster, 2007).

4. Ceramic nanocomposites

Nanocomposites based on ceramic materials have been studied in order to improve mechanical properties and alter functional properties. The ceramic nanocomposites reported until now are either a ceramic nanophase in a ceramic matrix, a carbonaceous nanophase in a ceramic matrix or a ceramic nanophase in a polymer matrix.

Enhancements in stability, hardness, strength, toughness and creep resistance compared to the unreinforced matrix material have been reported in nanocomposites (Narayan *et al.*, 2004). Moreover, the combination of properties can lead to a new generation of medical devices and implants combining mechanical properties with bioactive properties. Some examples of ceramic-based nanocomposite materials are as follows.

- **Alumina-based nanocomposites:** with the addition of several nano-reinforcements, alumina matrix materials with improved mechanical properties (higher resistance, hardness, wear resistance and fracture toughness) have been obtained.
- **Alumina/silicon carbide nanocomposites:** the incorporation of SiC nanoparticles to an alumina matrix increases wear resistance.
- **Alumina/zirconia nanocomposites:** also known as zirconia-toughened alumina (ZTA) nanocomposites, they consist of a fine-grained alumina matrix reinforced with zirconia particles. The addition of the zirconia nanoparticles is intended to increase the toughness of the alumina matrix.
- **Alumina/titania nanocomposites:** increased hardness, fracture toughness and fracture resistance have been achieved.
- **Zirconia/alumina nanocomposites:** also known as alumina-toughened zirconia (ATZ), they consist of a zirconia matrix reinforced with alumina nanoparticles. They show exceptional resistance and extraordinary toughness.
- **Silicon nitride/silicon carbide nanocomposites:** the obtained results are controversial.
- **Ceramic/carbon nanofibre composites:** widely used, there is an improvement in properties (Pace *et al.*, 2002).
- **Ceramic/carbon nanotube (CNT) composites:** mechanical and electrical properties are enhanced, but biocompatibility issues are still contro- versial (Streicher *et al.*, 2007; Garmendia *et al.*, 2008, 2009, 2010, 2011).
- **Ceramic in polymer composites:** especially relevant for tissue engineering applications.

5. Orthopaedic and dental implants

Ceramics such as zirconia (ZrO_2) and alumina (Al_2O_3) appear to be ideally suited for the fabrication of orthopaedic implants because of their hardness, low wear rates and excellent biocompatibility. For dental applications, where aesthetic requirements (colour, translucency) are also essential, the use of zirconia is preferred.

6. Bearing materials for orthopaedic implants

Alumina and zirconia ceramic materials have been used as joint substitutes for over 30 years as an alternative to CoCr-UHMWPE bearing pairs. These ceramics have crystal structures where atoms are joined by the combination of strong ionic and covalent bonds. Due to the existence of these bonds they show exceptional mechanical properties (high compressive strength, elastic modulus and hardness) and they are chemically inert *in vivo*. Their biocompatibility is also related to their high chemical stability, which confers resistance to corrosion and reliability in the *in vivo* behaviour during the lifetime of the implant (Rahaman and Yao, 2007). Also, the surfaces of these oxides present polar hydroxyl groups (OH^-), which promote interaction with aqueous body fluids, providing a lubricating layer. In addition, ceramics can be polished to tight tolerances and, due to the hardness of the material, they are not affected by the wear particles than can be generated due to the wear of bone cement, for example (Skinner, 2006). The drawback of alumina and zirconia ceramics is their intrinsic brittleness, which can lead to catastrophic failure *in vivo* and limits their use in orthopaedic applications. However, the incidence of brittle failures decreases with improvements in the quality of materials, manufacturing techniques and implant design. Nevertheless, their low fracture toughness, combined with their susceptibility to failure due to slow crack growth under stresses below their fracture resistance, remains a problem regarding the reliability of ceramic bearings (Rahaman and Yao, 2007).

The use of ceramics in joint prostheses began in the early 1970s. It was observed that the low production of polyethylene wear debris in contact with the ceramic solved the problem of loss of the prosthesis as a result of osteolysis or bone loss. Boutin in France and Mittelmeier in Germany began using aluminum oxide or alumina (Al_2O_3) as a constituent material of the bearing surfaces of total hip prostheses. Alumina shows a resistance, as measured by bending tests, of more than 550 MPa and a Vickers hardness of more than 1800-2000 HV. These hardness values are much higher than those offered by metals such as CoCr or titanium alloys used in orthopaedics, with hardness values bellow 500 HV. Currently, the most widely used ceramic in total hip arthroplasty is alumina. It is estimated that by the year 2005 more than five million Al_2O_3 femoral heads had already been implanted worldwide. But, together with its many advantages, alumina presents some drawbacks. In addition to its low fracture toughness (~ 4 MPa $m^{1/2}$), it is very sensitive to the surface finish and the sphericity of the bearing surfaces, to the tolerance between them and to the orientation of the components. It is also sensitive to fracture due to fatigue if the assemblage of the metal components is irregular or if there is not perfect adaptation of the dimensions.

7. Alumina–zirconia nanocomposites

There is a critical zirconia grain size below which no tetragonal to monoclinic phase transformation occurs. When the grain size is above 1 μm, the material behaves unstably and is susceptible to spontaneous tetragonal to monoclinic transformation. When the grain size is below 0.5 μm, a slow transformation occurs. With grain sizes under 0.2 μm, the martensitic transformation is not promoted, therefore reducing the possibility of cracking (Evans and Heuer, 1980; Gutknecht *et al*., 2007). Therefore, by reducing the zirconia grain size, aging resistance is increased. But, on the other hand, the transformation toughening mechanism that gives zirconia its exceptional mechanical properties will be lost. With the development of zirconia–alumina nanocomposites, the combination of both aging resistance and enhanced mechanical properties is promising. During recent years, several zirconia-alumina composites and nanocomposites have been developed and have shown significant improvement in toughness, strength and aging resistance (Menezes and Kiminami, 2008; Nevarez-Rascon *et al*., 2009).

Two kinds of composites can be prepared in the zirconia-alumina system (De Aza, 2002): an alumina matrix reinforced with zirconia particles (zirconia-toughened alumina, ZTA) or a phase-stabilized zirconia matrix reinforced with alumina particles, known as alumina-toughened zirconia (ATZ). Composites with high fracture toughness are suitable in the ATZ system while composites with high hardness and relatively low fracture toughness belong to the ZTA system (Nevarez-Rascon *et al*., 2009).

8. Future trends

Current load-bearing implants with osteconductive surfaces or tissue engineering based on natural or synthetic biodegradable scaffolds offer a significant increase in the quality of bone repair and improved mechanical properties. However, they still present limitations and hence there is potential for major advances to be made in the field. Bone can actually heal itself when it is broken or removed. However, this capability is impaired in situations where substantial loss of bone has occurred due to a trauma or tumour resection, leading to non- or delayed unions. This inability in bone healing is also related to disease or old age (Graus, 2006).

Most of the current limitations in this field are related to the lack of ‘smart’ biomaterials with the capability to elicit specific responses at molecular and cellular level. These biomaterials act as structural support and delivery vehicles, providing cells and bioactive molecules necessary for the formation of new bone tissue. Ideal biomaterial must possess mechanical properties adequate to support growing bone tissue, good biocompatibility and high porosity (Sitharaman *et al.*, 2008). In addition, it should be able to avoid rejection (e.g. associated with infections), react to changes in the immediate environment and stimulate specific regenerative events at the molecular level, directing cell proliferation, cell differentiation, and extracellular matrix production and organization.

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