



Review paper

Calcium orthophosphate bioceramics

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Abstract

Various types of grafts have been traditionally used to restore damaged bones. In the late 1960s, a strong interest was raised in studying ceramics as potential bone grafts due to their biomechanical properties. A bit later, such synthetic biomaterials were called bioceramics. In principle, bioceramics can be prepared from diverse inorganic substances but this review is limited to calcium orthophosphate (CaPO₄)-based formulations only, which possess the specific advantages due to the chemical similarity to mammalian bones and teeth. During the past 40 years, there have been a number of important achievements in this field. Namely, after the initial development of bioceramics that was just tolerated in the physiological environment, an emphasis was shifted towards the formulations able to form direct chemical bonds with the adjacent bones. Afterwards, by the structural and compositional controls, it became possible to choose whether the CaPO₄-based implants remain biologically stable once incorporated into the skeletal structure or whether they were resorbed over time. At the turn of the millennium, a new concept of regenerative bioceramics was developed and such formulations became an integrated part of the tissue engineering approach. Now CaPO₄-based scaffolds are designed to induce bone formation and vascularization. These scaffolds are usually porous and harbor various biomolecules and/or cells. Therefore, current biomedical applications of CaPO₄-based bioceramics include bone augmentations, artificial bone grafts, maxillofacial reconstruction, spinal fusion, periodontal disease repairs and bone fillers after tumor surgery. Perspective future applications comprise drug delivery and tissue engineering purposes because CaPO₄ appear to be promising carriers of growth factors, bioactive peptides and various types of cells.

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1. Introduction

One of the most exciting and rewarding areas of the engineering discipline involves development of various devices for health care. Some of them are implantable. Examples comprise sutures, catheters, heart valves, pacemakers, breast implants, fracture fixation plates, nails and screws in orthopedics, various filling formulations, orthodontic wires, total joint replacement prostheses, *etc.* However, in order to be accepted by the living body without any unwanted side effects, all implantable items must be prepared from a special class of tolerable materials, called biomedical materials or biomaterials, in short. The physical character of the majority of the available biomaterials is solids [1,2].

From the material point of view, all types of solids are divided into 4 major groups: metals, polymers, ceramics and various blends thereof, called composites. Similarly, all types of solid biomaterials are also divided into the same groups: biometals, biopolymers, bioceramics and biocomposites. All of them play very important roles in both replacement and



Fig. 1. Several examples of the commercial CaPO₄-based bioceramics.

regeneration of various human tissues; however, setting biometals, biopolymers and biocomposites aside, this review is focused on bioceramics only. In general, bioceramics comprise various polycrystalline materials, amorphous materials (glasses) and blends thereof (glass-ceramics). Nevertheless, the chemical elements used to manufacture bioceramics form just a small set of the Periodic Table. Namely, bioceramics might be prepared from alumina, zirconia, magnesia, carbon, silica-contained and calcium-contained compounds, as well as from a limited number of other chemicals. All these compounds might be manufactured in both dense and porous forms in bulk, as well as in the forms of crystals, powders, particles, granules, scaffolds and/or coatings [1–3].

As seen from the above, the entire subject of bioceramics is still rather broad. To specify it further, let me limit myself by a description of CaPO₄-based formulations only. Due to the chemical similarity to mammalian bones and teeth, this type of bioceramics is used in a number of different applications throughout the body, covering all areas of the skeleton. The examples include healing of bone defects, fracture treatment, total joint replacement, bone augmentation, orthopedics, cranio-maxillofacial reconstruction, spinal surgery, otolaryngology, ophthalmology and percutaneous devices [1–3], as well as dental fillings and periodontal treatments [4]. Depending upon the required properties, different types of CaPO₄ might be used. For example, Fig. 1 displays some randomly chosen samples of the commercially available CaPO₄ bioceramics for bone graft applications. One should note that, in 2010, only in the USA the sales of bone graft substitutes were valued at ~\$1.3 billion with a forecast of ~\$2.3 billion by 2017 [5]. This clearly demonstrates an importance of CaPO₄-based bioceramics.

A list of the available CaPO₄, including their standard abbreviations and major properties, is summarized in Table 1 [6]. To narrow the subject further, with a few important exceptions, bioceramics prepared from undoped and un-substituted CaPO₄ will be considered and discussed only. Due to this reason, CaPO₄-based bioceramics prepared from biological

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