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Review

Biphasic, triphasic and multiphasic calcium orthophosphates

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ABSTRACT

Biphasic, triphasic and multiphasic (polyphasic) calcium orthophosphates have been sought as biomaterials for reconstruction of bone defects in maxillofacial, dental and orthopedic applications. In general, this concept is determined by advantageous balances of more stable (frequently hydroxyapatite) and more resorbable (typically tricalcium orthophosphates) phases of calcium orthophosphates, while the optimum ratios depend on the particular applications. Therefore, all currently known biphasic, triphasic and multiphasic formulations of calcium orthophosphate bioceramics are sparingly soluble in water and, thus, after being implanted they are gradually resorbed inside the body, releasing calcium and orthophosphate ions into the biological medium and, hence, seeding new bone formation. The available formulations have already demonstrated proven biocompatibility, osteoconductivity, safety and predictability in vitro, in vivo, as well as in clinical models. More recently, in vitro and in vivo studies have shown that some of them might possess osteoinductive properties. Hence, in the field of tissue engineering biphasic, triphasic and multiphasic calcium orthophosphates represent promising biomaterials to construct various scaffolds capable of carrying and/or modulating the behavior of cells. Furthermore, such scaffolds are also suitable for drug delivery applications. This review summarizes the available information on biphasic, triphasic and multiphasic calcium orthophosphates, including their biomedical applications. New formulations are also proposed.

1. Introduction

Calcium orthophosphates are of special significance for humans because they represent the inorganic part of normal (bones, teeth and deer antlers) and pathological (i.e. those appearing due to various diseases) calcified tissues in mammals [1,2]. Therefore, due to chemical similarity to biological calcified tissues the majority of artificially prepared calcium orthophosphates possess remarkable biocompatibility and bioactivity. Materials scientists use this property to construct artificial bone grafts that are either entirely made of or surface coated by biologically relevant calcium orthophosphates [3,4]. The available calcium orthophosphates, with the chemical formulae, standard abbreviations and solubility data, are listed in Table 1 [5–8]. As can be seen from Table 1, the solubility values of individual calcium orthophosphates vary over a wide range.

It has been known since the mid 1980s that the existing calcium orthophosphates listed in Table 1 might form biphasic [9,10], triphasic and multiphasic (polyphasic) combinations, in which the individual components frequently cannot be separated from each other. Obviously, the individual phases in such formulations are homogeneously and intimately "mixed" at the submicron (<1 μm) level and, therefore, are strongly integrated with each other. Nevertheless, the presence of each individual phase is easily seen by X-ray diffraction (XRD) (Fig. 1), which clearly indicates that they remain unchanged. However, the sharp and well-defined diffraction peaks show that the dimensions of particle of the individual phases of hydroxyapatite (HA) and β-tricalcium phosphate (β-TCP) in such formulations exceeds ∼50 nm (otherwise the diffraction peaks become broader). Thus, roughly speaking, biphasic, triphasic and multiphasic calcium orthophosphates consist of the individual phases with particle dimensions between 50 and 500 nm.

Concerning the properties of such biphasic, triphasic and multiphasic calcium orthophosphates, as a rule of a thumb one can say that, in general, they are between of those of the constituent phases and depend on the relative amounts of the ingredients. Furthermore, by changing the ratio of more stable and more soluble calcium orthophosphates it is possible to prepare biphasic, triphasic and multiphasic formulations possessing adjustable properties. Such bioceramics can be applied to large bone defects, in some load bearing areas and as customized pieces which will maintain their shape over long periods of time [13,14].

The main biomedical idea behind the biphasic, triphasic and multiphasic calcium orthophosphate formulations is a proper balance of more stable calcium orthophosphate phases and more soluble ones [15,16] such that the major biomedical properties

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