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Research Paper

Effects of high-energy ball-milling on injectability and strength of β-tricalcium-phosphate cement

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ABSTRACT

Calcium phosphate cement (CPC) offers many advantages as a bone-substitution material. The objective of this study is to develop a new CPC that simultaneously exhibits fine injectability, a short setting time, and high strength. β-tricalcium phosphate (β-TCP, control) powder was ball-milled for 24 h to produce a new cement powder. The modified β-TCP after 24 h milling (mβ-TCP-24 h) exhibited excellent injectability even 1 h after mixing. The mechanical properties of the set cement (compact) were evaluated using compressive strength (CS) and diametral tensile strength (DTS) testing. The CS and DTS values of the mβ-TCP-24 h compacts were 8.02 MPa and 2.62 MPa, respectively, at 5 h after mixing, and were 49.6 MPa and 7.9 MPa, respectively, at 2 weeks after mixing. All the CS and DTS values of the mβ-TCP-24 h compacts were significantly higher than those of the control for the same duration after mixing. These results suggest that the mechano-chemically modified β-TCP powder dissolves rapidly and accelerates hydroxyapatite precipitation, which successfully shortens the cement setting time and enhances the strength. This study supports that mβ-TCP-24 h is a promising candidate for use in injectable CPCs with improved strength.

1. Introduction

Self-setting calcium–phosphate cements (CPCs) were first developed in 1980s by Brown and Chow (1983) (Gruninger et al., 1984) and have been widely used commercially for bone repair and bone augmentation (Bohner et al., 2005; Dorozhkin, 2010b, 2013; Zhang et al., 2014). One of the remaining problems of CPC is its poor injectability (Baroud et al., 2005; Bohner and Baroud, 2005; Habib et al., 2012; Habib et al., 2008, 2010), which is insufficient for cement paste injection into bone defects through minimally invasive surgery (Alshaaer et al., 2013; Fatimi et al., 2012; Matassi et al., 2011). A basic and effective method to improve the

Abbreviations: CPC, calcium phosphate cement; β-TCP, β-tricalcium phosphate; mβ-TCP-24 h, modified β-TCP after 24 h milling; CS, compressive strength; DTS, diametral tensile strength; SEM, scanning electron microscopy

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injectability is decreasing the calcium–phosphate powder-to-mixing-liquid ratio (P/L ratio) (Baroud et al., 2005; Bohner and Baroud, 2005; Gbureck et al., 2004b; Montufar et al., 2013). However, the mechanical properties of cement after setting decrease because of a reduction in the P/L ratio, and the set cement (compact) might be ruptured easily (Dorozhkin, 2013). In contrast, the setting time of CPCs increases with decreasing P/L ratio (Barralet et al., 2004; Bigi et al., 2004). These two reverse dependencies of injectability and setting time on the P/L ratio limit the range of the P/L ratio of commercial CPCs (Dorozhkin, 2013). Decreasing the particle size of the CPC powder is the another effective approach to improve the injectability (Dorozhkin, 2013). Although a smaller particle size results in more liquid for mixing, the injectability and cohesion of the compact are generally excellent (Bigi et al., 2004; Bohner, 2001; Dorozhkin, 2013). Several processes have been developed to produce small-particle-size calcium–phosphate powder: wet-chemical processes, sol–gel synthesis, hydrothermal synthesis, and dry processes (Alves Cardoso et al., 2012). The particles produced using these processes exhibit an amorphous phase with various calcium-to-phosphate molar ratios (Ca/P ratios) (Dorozhkin, 2010a). Because the Ca/P ratio is one of the effective factors in controlling CPC properties such as the setting time and compressive strength (Bermudez et al., 1994a, b; Driessens et al., 2002; Guo et al., 2009), the uncertain Ca/P ratio of calcium–phosphate powders makes controlling the CPC properties difficult. To produce amorphous calcium–phosphate powders with a controlled Ca/P ratio, a dry process of ball-milling can maintain the chemical composition of the starting calcium–phosphate and thus produce CPC powders with a specific Ca/P ratio (Dorozhkin, 2010a; Gbureck et al., 2004a; Gbureck et al., 2003). Therefore, a planetary ball-milling process is employed in the present study.

The starting calcium–phosphate for amorphous CPC powders also significantly affects the CPC properties. Popular calcium–phosphates utilized in commercial CPCs are dicalcium–phosphate anhydrous (DCPA, Ca/P ratio=1.0), dicalcium–phosphate dihydrate (DCPD, Ca/P ratio=1.0), α-tricalcium–phosphate (α-TCP, Ca/P ratio=1.5), β-tricalcium-phosphate (β-TCP, Ca/P ratio=1.5), calcium-deficient hydroxyapatite (CDHA, Ca/P ratio=1.5–1.67), hydroxyapatite (HA, Ca/P ratio=1.67) and tetracalcium–phosphate (TTCP, Ca/P ratio=2.0) (Dorozhkin, 2013). In the present study, β-TCP is employed as the single starting CPC powder because the solubility of β-TCP is lower than that of other calcium–phosphates except HA (Dorozhkin, 2013). Although the starting calcium–phosphate transforms into HA or brushite after setting (Dorozhkin, 2013), a part of the starting powders might remain without reaction (Cheng et al., 2013; Grover et al., 2013; Sariibrahimoglu et al., 2013), and some types of calcium–phosphate might dissolve and cause inflammation around the cement (Prudhommeaux et al., 1996). To reduce the risk of inflammation, a neutral calcium–phosphate with lower solubility is a better reactant, and β-TCP has been reported to be a promising candidate (Dorozhkin, 2013; Theiss et al., 2005).

The mixing liquid is also an important reactant affecting the setting and mechanical properties of CPCs. Popular liquids of CPCs are water or phosphate solutions, for instance, a solution of Na_2HPO_4, NaH_2PO_4 and H_3PO_4 (Barinov and Komlev, 2011; Dorozhkin, 2013; Ginebra et al., 2010). A potential problem concerning phosphate mixing liquids is that the total Ca/P ratio of the CPC must be smaller than that of the CPC powder. In previous studies, a CPC with a smaller Ca/P ratio exhibited a lower compressive strength than that with a Ca/P ratio close to 1.5 (Bermudez et al., 1994a, b; Driessens et al., 2002). Therefore, an additional calcium compound without phosphate is required to maintain the total Ca/P ratio at 1.5, that of β-TCP in the present study, or higher. Popular additional calcium compounds without phosphate for the CPC are $CaCO_3$ powder and $Ca(OH)_2$ solution (Dorozhkin, 2013). The addition of $CaCO_3$ powder increases the P/L ratio of the CPC and might reduce the injectability. The basic $Ca(OH)_2$ solution increases the pH of the mixing solution and might increase the setting time because of the increase of the saturated concentration of calcium phosphate (Dorozhkin, 2013). A previous study suggested that α-TCP mixed with $CaCl_2$ solution and NaH_2PO_4 solution consecutively resulted in rapid transformation to HA compare with that mixed only with phosphate solution (Kon et al., 1998). The advantages of the $CaCl_2$ solution are that the pH is near neutral and might be less effective on the setting time. An additional effect of the consecutive mixing of the $CaCl_2$ solution and NaH_2PO_4 solution is that HA crystals precipitate in the solution (Ehrlich et al., 2005; Sobhana et al., 2009) and will be nuclei of HA formation during the CPC setting (Dorozhkin, 2013). Although the starting powder of CPC in the present study is not α-TCP, $CaCl_2$ solution and NaH_2PO_4 solution are employed as the mixing liquids for these reasons. The calcium concentration in the mixing liquids also affects the Ca/P ratio and thus the properties of the CPC. To set the Ca/P ratio of the CPCs consisting of TCP powder to 1.5 or higher, the Ca/P ratio of the mixing liquid must be 1.5 or higher. In the present study, the Ca/P ratio of the mixing liquid is set to be 1.67, resulting in the maximum diametral tensile strength (DTS) of the compact (Kon et al., 1998).

The objective of the present study is to investigate the effects of planetary ball-milling of β-TCP powder on the injectability and mechanical properties of CPC. In previous studies investigating the ball-milling effects on β-TCP powder, the maximum milling time was 24 h using agate balls (Gbureck et al., 2003), and the maximum milling time was 30 min using ZrO_2 balls (Baroud et al., 2005). Because the density of ZrO_2 is larger than that of agate, ZrO_2 ball-milling should result in higher milling energy. In addition, a longer milling time should provide the powder with more milling energy. In the present study, the effects of longer milling time using planetary ZrO_2 ball-milling on the injectability and mechanical properties of β-TCP-powder-based CPC are evaluated.

2. Materials and methods

2.1. β-TCP powder preparation and characterization

β-TCP cake (Taihei Chemical Industrial Co. Ltd., Osaka, Japan) was an ingredient of the CPC powder in the present study. The cake was first crushed with a pestle and then ground in an automortar (ANM-200, Nitto Kagaku Co. Ltd., Nagoya, Japan) for 30 min (120 rpm). The ground powder is called cβ-TCP (control β-TCP) in the present study. Ball-milling of 8 g cβ-TCP was performed to reduce the particle size using a planetary ball-mill (Pulverisette 7, Fritsch GmbH, Idar-Oberstein, Germany) at