

Control of the injectability of calcium carbonate-calcium phosphate mixed cements for bone reconstruction

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Keywords: injectability, bone cement, co-grinding

Abstract. The purpose of this study was to improve injectability and cohesiveness of original calcium carbonate-calcium phosphate mixed (CaCO₃-CaP) self-setting paste for bone filling and repair. With this aim in view dry co-grinding was implemented on the solid phase (vaterite and dicalcium phosphate dihydrate) of this cement. A protocol designed to quantify paste injectability has been established and pointed out the synergistic positive effects of solid phase co-grinding treatment on injectability, cohesiveness and setting time of the paste. The improvement of these properties are related to close and homogeneous association of reactive powders and to the decrease of specific surface area favoring the powders hydration process enhancing setting reaction rate. In addition, the particle size decrease and morphology modification improved flowability of the paste which results in a low and constant (320 g) force level to extrude the paste.

Introduction

With the development of minimally invasive surgery techniques, injectable biomaterials have attracted much attention in recent years. Fast-setting calcium phosphate cements for bone reconstruction are good candidates due to their excellent biocompatibility and bioactivity properties and their ease of use as mouldable and injectable self-setting pastes [1]. However two phenomena, “filter-pressing” (solid particles separate from liquid within the syringe and plug the tip of the canula while the liquid passes through) and “cement washout” (disintegration of the paste on contact with tissue or fluids) affect paste cohesion and greatly limit their implantation using an injection process [2-3]. Several groups have explored the possibility to improve cement paste cohesiveness during injection using the rheological properties of natural and synthetic polymer additives [4-5]. Another approach consists in controlling reactive powders particle size and particle size distribution which are determining factors affecting paste cohesiveness, hydration process and mechanical properties of cements [2, 6-7]. However little attention has been paid to the use of co-grinding treatment of solid phase mixtures for biomedical cements.

Recently, calcium carbonate-calcium phosphate mixed (CaCO₃-CaP) cements have been presented as promising resorbable bone cements [8] and the rheological properties of these original cement compositions are just beginning to be explored. The objective of this study is to set up a protocol for injectability characterization of CaCO₃-CaP cement paste and to improve its cohesiveness and injectability by controlling the powder particle size and morphology using grinding or co-grinding processes.

Materials and Methods

The reactive powders (CaCO₃ vaterite and dicalcium phosphate dihydrate (DCPD, CaHPO₄, 2 H₂O) constituting the solid phase (S) of the cement were synthesized by precipitation at ambient temperature, following protocols described previously [8]. The precipitates were filtered, washed

with deionized water, lyophilized and stored in a freezer to avoid any evolution of these metastable powders before their use.

In order to reach the smallest particle size and intimate powders mixture, dry batch grinding and co-grinding experiments were performed using a laboratory tumbling ball mill. It consists in a ceramic cylindrical chamber, 1 L in capacity, rotating around its horizontal axis, and containing ceramic balls of different diameters: 19, 9.2 and 5.6 mm. The rotating speed of the chamber was fixed at 100 rpm, i.e. at 75 % of the critical speed, while the ball loading volume represented 20 % of the whole volume of the chamber. The powder filling rate represents 10 % of the void space between the balls. The DCPD powder was ground separately during a period ranging from 1 to 30 minutes, but also together with vaterite powder (co-grinding period from 1 to 20 minutes). Powder samples were taken from different regions of the chamber at various times to be analyzed. The removed sample mass was small enough, so as not to modify significantly the powder proportion in the mill.

SEM observations after silver plating (LEO 435 VP), FTIR spectroscopy (Nicolet 5700), X-ray diffraction (INEL CPS 120), laser diffraction granulometry (Malvern, Mastersizer 2000), and specific surface area analyses (Monosorb MS22, Quantachrom) were carried out to characterize the powders before and after (co)grinding treatment.

Cement paste was prepared by mixing equal quantities of vaterite and DCPD (unground, ground or co-ground) with the liquid phase (L) composed of deionized water ($L/S = 0.5$). Injectability was measured using a TAXT2 texture analyzer (Stable Micro Systems) equipped with a specific syringe system and following a protocol designed to measure the force needed to extrude a volume of paste corresponding to a displacement of 15 mm of the syringe piston (surface = 64 mm^2). Measurements were performed 5 min after paste preparation.

The setting rate of the cement was followed using the same texture analyzer fitted with a cylindrical needle (surface = 0.785 mm^2). The setting time was considered to be reached when the paste developed a resistance to needle penetration over 600 g/mm^2 .

Results and Discussion

Table 1 gives the specific surface area and the particle mean size (d_{50} is the mean particle diameter corresponding to cumulated volume fractions of 50 %) of vaterite and DCPD powders obtained by precipitation. Because of its small particle size ($d_{50} = 1.7 \text{ }\mu\text{m}$), vaterite do not require grinding treatment, whereas crystals of DCPD can be ground until particle size reaches $2.8 \text{ }\mu\text{m}$; the corresponding optimal grinding time (offering the smallest mean size while avoiding agglomeration phenomena) has been determined equal to 27 minutes.

Table 1: Mean size (d_{50}) and specific surface area (S_{BET}) of the reactive powders used to prepare cements.

	vaterite	DCPD	ground DCPD
$d_{50} [\mu\text{m}]$	1.7	9.2	2.8
$S_{\text{BET}} [\text{m}^2/\text{g}]$	36.8	1.8	2.3

The reference solid phase was prepared by mixing unground vaterite with unground DCPD and was compared with two other solid phases: one is composed of a mixture of vaterite with ground DCPD and the other one of co-ground reactive powders (13 minutes was determined as the optimal co-grinding time for the solid phase).

Figure 1.b shows that after co-grinding, most of lentil-like vaterite particles are stuck on DCPD crystals, which have been broken during grinding. In addition, when compared with unground solid phase (fig 1.a), powders are more intimately and homogeneously mixed; furthermore, the contact surface between the two reactive components has increased using co-grinding process.

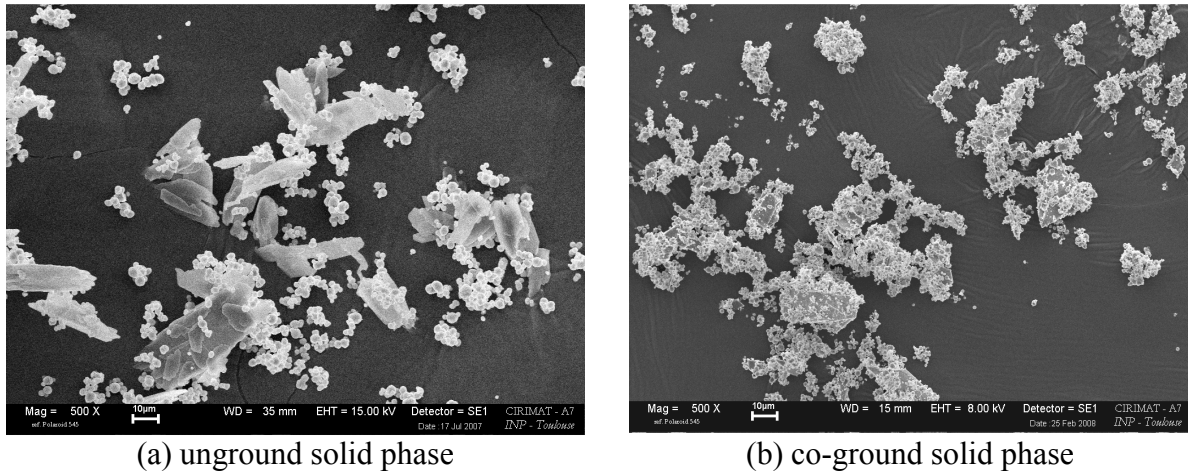


Fig. 1: SEM micrographs of cement solid phase before and after co-grinding process.

XRD patterns of hardened cements prepared with the 3 different solid phases are presented on figure 2. It showed that grinding and co-grinding have no effect on the cement setting reaction: in all cases, the hardened cement is composed of poorly crystalline apatite (A) and excess vaterite (V). This result was confirmed by FTIR spectroscopy analyses (data not presented).

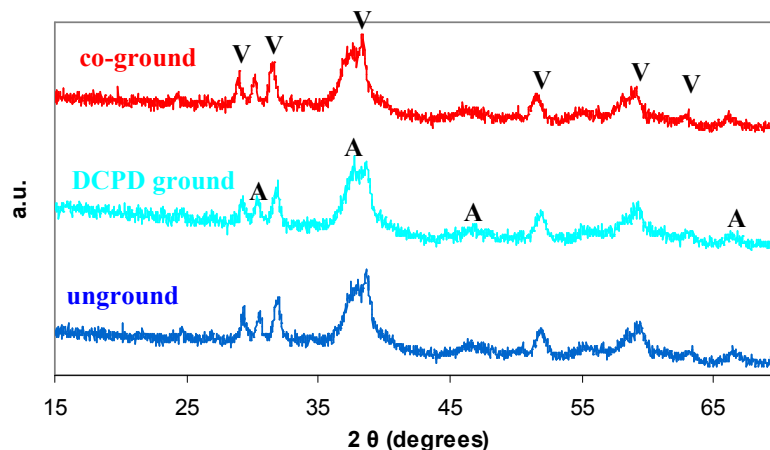


Fig. 2: XRD patterns of hardened cements prepared with unground, DCPD ground and co-ground solid phases.

In addition, co-grinding the reactive powders has a strong influence on the paste setting time which is nearly divided by two when using co-ground powders ($t_{\text{setting}} = 75$ min) compared to reference cement ($t_{\text{setting}} = 140$ min). The increased specific surface and contact area between reactive powders speed up the hydration process necessary for the setting reaction.

We can see on figure 3 that the force needed to extrude the reference paste (unground powders) from a syringe increases almost linearly all along the extrusion, up to 33 kg whereas its increase is strongly attenuated (7 kg) when using ground DCPD and is no more occurring for co-ground powders. The co-grinding process greatly improves the injectability of the paste nearly by a factor 100 and prevents the “filter pressing” phenomenon: with co-ground reactive powders the force level to extrude the paste remains low and constant (320 g) during the paste extrusion underlining the determinant effect of particles size and morphology on the paste flowability. We can assume that, because of their morphology, platelet particles of DCPD hinder the paste flow more or less depending on their orientation towards flow direction. Ground DCPD particles are greatly smaller and closer to spherical morphology and should therefore obstruct the path less than unground particles.

Moreover, the cohesion of the paste can be checked by observing how it is extruded: disjointed spaghettis can be seen using unground powders whereas a long homogeneous spaghetti is obtained

using co-ground powders; these observations indicate how solid phase co-grinding treatment could possibly lead to a decrease of paste “washout” phenomenon *in vivo*.

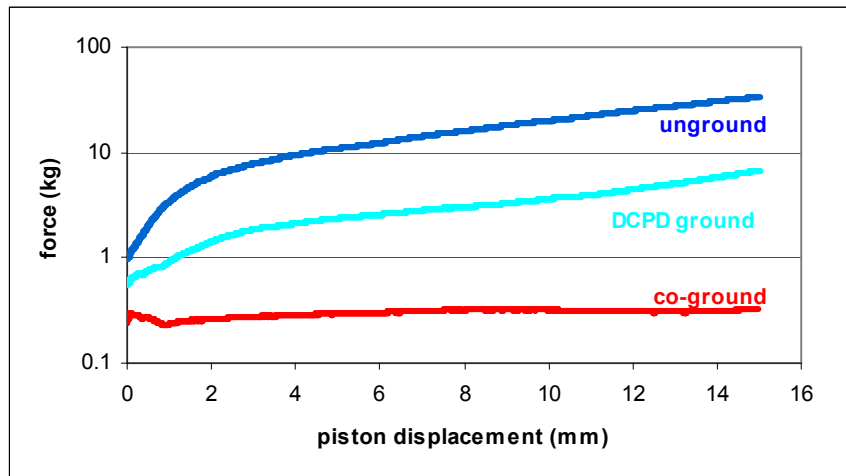


Fig. 3: Evolution of the force needed to extrude a determined volume of paste prepared with unground, DCPD ground only or co-ground reactive powders.

In the case of CaCO_3 -CaP mixed cement, co-grinding favors fragmentation of DCPD large platelet-crystals and close association of the two reactive powders allowing a satisfactory flowability of the paste and faster rate of setting chemical reaction. The improvement of the latter is probably related to better powder hydration enhancing the formation of an apatite analogous to bone mineral through dissolution-precipitation process and reaction between carbonate ions from vaterite and hydrogenphosphate ions from DCPD to give phosphate of apatite.

Co-grinding treatment of the solid phase leads therefore to synergistic positive effects resulting in better paste injectability, cohesiveness and cement setting time.

Conclusions

We demonstrated that the protocol we have designed for the injectability measurements of CaCO_3 -CaP mixed cement paste is quantitative, reliable and discriminating; interestingly a low and constant (320 g) force level to extrude the paste can be obtained using co-ground reactive powders. This study pointed out the usefulness of the co-grinding process to improve and control powders reactivity and paste rheological properties which constitute a decisive advantage for ease of use of CaCO_3 -CaP self-setting pastes.

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