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Effect of mechanical grinding of MCPM and CaO mixtures on their composition and on the mechanical properties of the resulting self-setting hydraulic calcium phosphate cements

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Calcium bis-dihydrogenophosphate monohydrate (or monocalcium phosphate monohydrate, MCPM) is often used as the acid calcium phosphate in hydraulic calcium phosphate cement formulations. But commercial MCPM is not pure; it contains a small amount of orthophosphoric acid and moisture. Consequently, MCPM is difficult to mill and the powder is sticky and presents aggregates. Because granularity influences the mechanical properties of the hardened cements, a possible way to get around this difficulty that has been proposed is to premix it with other materials before grinding. We therefore ground commercial MCPM with CaO. A rapid decrease in the amount of MCPM was observed during mechanical grinding by a solid-solid reaction with calcium oxide. The final products were anhydrous or dihydrate dicalcium phosphate and/or hydroxyapatite or calcium-deficient hydroxyapatite depending on the initial calcium-to-phosphate (Ca/P) ratio. The mechanical properties (compressive strength and setting time) of cements made from MCPM and CaO were affected whatever the Ca/P ratio as a consequence of the change in composition of the starting materials. Storage at different temperatures of MCPM and CaO mixtures manually ground in a mortar for only 2 min and without mechanical grinding did not affect their composition, but a decrease was observed in the compressive strength of cements made from these mixtures.

1. Introduction

Calcium phosphate cements (CPCs) have attracted much attention in medicine and dentistry because of their excellent biocompatibility and bone-replacing behaviour over long periods of time [1, 2]. CPCs are obtained by an acid-base reaction in water between an acid calcium phosphate and a basic calcium phosphate (or another basic calcium salt), giving a calcium phosphate with intermediate basicity such as dicalcium phosphate dihydrate $CaHPO_4 \cdot 2H_2O$ (DCPD) or anhydrous $CaHPO_4$ (DCPA), octacalcium phosphate $Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$ (OCP), stoichiometric hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ (OHAp) or calcium-deficient hydroxyapatite $Ca_{(10-x)}(HPO_4)_x(PO_4)_{(6-x)}(OH)_{(2-x)}$ with $0 < x \leq 1$ (CDOHAp). In a previous paper [3] we reported results on a CPC obtained from calcium bis-dihydrogenophosphate monohydrate $Ca(H_2PO_4)_2 \cdot H_2O$ (or monocalcium phosphate monohydrate MCPM) and calcium oxide CaO.

It is well known that the particle size of the starting materials influences the mechanical properties (setting time and compressive strength) of hydraulic cements and the conversion rate to the final product via their dissolution rate which is faster with small particles [4, 5]. Therefore, we investigated the influence of grinding of starting materials on the final mechanical properties of MCPM-CaO cements we developed. However commercial MCPM is not pure; it contains a small amount of orthophosphoric acid (≈ 5 wt %) and moisture (3–4 wt %) . Consequently, ground MCPM is not homogeneous; the powder is sticky and presents aggregates. Indeed, grinding MCPM for 5 h, we only obtained a particle size around 20 μm. To get around this problem, some authors premix MCPM before grinding with the desired amount of CaO [6]. By grinding a MCPM and CaO mixture for 5 h in order to obtain a finer particle size, we surprisingly observed a strong decrease in the compressive strength of cement samples after storage for 24 h at 37 °C, 100% relative humidity (RH). The X-ray diffraction (XRD) analysis of the starting mixture after grinding revealed that the powder had been transformed into hydroxyapatite. Thus, we studied the

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variation in the composition of the starting materials as a function of grinding time and its influence on the setting time and the final compressive strength.

2. Materials and methods

2.1. Chemicals and materials

All chemicals were analytical reagent grade purchased from Aldrich (CaO, OHAp), Fluka (MCPM, DCPD, DCPA, NaH_2PO_4, $Na_2HPO_4 \cdot 12H_2O$, $Ca(OH)_2$) or Prolabo (H_3PO_4). Commercial CaO was heated at 900° C for 2 h to remove H_2O and CO_2 and stored in a vacuum desiccator. The CaO particle size was around 7 µm (d_{10}–d_{90}: 2–40 µm; specific area: $1.3\,m^2\,g^{-1}$, Mastersizer, Malvern Instruments). The commercial MCPM used in this work contained 3.8 ± 0.3% moisture (determined by thermogravimetry) and 6 ± 0.5% free H_3PO_4 (determined by acidimetry and phosphate titration with ammonium molybdate); the particle size was approximately 230 µm (50–700 µm; specific area: $0.06\,m^2\,g^{-1}$). The commercial powder was pulverized for 5 h in a rotating micromill (Retsch Instruments) before use to obtain a final particle size of about 20 µm (5–130 µm; specific area: $0.60\,m^2\,g^{-1}$) and was first used without other treatment. In a second time, to eliminate the orthophosphoric acid contaminant, commercial MCPM was washed for 1 h with anhydrous ethanol then dried for 24 h at 60 °C or ground with 5 wt % DCPA. Water was doubly distilled on quartz after deionization on an ion-exchange resin.

Powder XRD patterns were obtained with an automatic Philips Diffractometer controlled by an IBM PC (36 acquisitions, 3–35 °θ, 3200 points or 5 or 36 acquisitions, 2–20 °θ, 900 points, acquisition delay 500 ms) using an anti-cathode CuK_α (0.1542 nm) with a nickel filter.

2.2. Grinding procedure

MCPM and CaO in the desired ratio were mixed for 2 min in a mortar for homogenization. Then 10–15 g of the homogeneous powder was placed in a 500-ml porcelain mortar with five porcelain balls (27 mm in diameter) and ground in a rotating micromill (Retsch Instrument) at 300 ± 15 rpm. At different intervals (0.25, 0.5, 1, 1.5, 2, 3, 4 and 5 h) 50 mg powder was taken for XRD analysis to evaluate the kinetics of change in the powder and 1 g to prepare cement samples for compressive strength and setting time measurements. Four mixtures were ground with calcium-to-phosphate ratios (Ca/P) of 1.1, 1.35, 1.5 and 1.67 corresponding to powders that, after setting, theoretically gave DCPD, OCP, CDOHAp or OHAP as final product respectively.

2.3. Stability of MCPM—CaO mixtures

Appropriate amounts of MCPM and CaO were manually mixed by crushing in a mortar for 2 min and stored in closed recipients at different temperatures (0, 20, 30, 37, 50 and 60 °C). At regular intervals (0, 1, 2, 3, 4, 6.5, 10 and 13 weeks), powder samples were analysed by XRD and cement samples were prepared for compressive strength measurements.

2.4. Preparation of calcium phosphate cements

The cement powder was prepared by weighing appropriate amounts of the two components to obtain the desired final calcium-to-phosphate ratio (Ca/P). At this stage, when phosphate buffer was used as the liquid phase, the amount of phosphate in the buffer was taken into account. The liquid phase was either pure water or 0.45 M or 1 M sodium phosphate buffer, pH 7. The powder-to-liquid ratio (P/L) was $1.8\,g\,ml^{-1}$. The powder was incorporated into the liquid by successive fractions as for dental zinc phosphate cements; 1/6 of the powder was added every 15 s. It was kneaded with the aid of a spatula between each addition to produce a paste of workable consistency. After a total mixing time of two minutes, carried out on a glass plate at 20 ± 1 °C, the paste was loaded into the moulds.

2.5. Mechanical strength and setting time measurements

After mixing for 2 min, the paste was loaded into Teflon molds (4 mm diameter × 6 mm h) using a spatula with periodic packing by means of a stainless steel rod. The top and bottom surfaces of the molds were then covered tightly with two Plexiglas plates, clamped and stored in a 37 °C, 100% RH box for 24 h. The hardened CPC specimens were then removed from the molds after polishing their top and bottom planes, and the compressive strength (CS) was measured. At least five specimens were used for each determination. The diameter and length of each specimen were first measured at ± 0.02 mm. The CS was determined on an Erweka TB 24 testing machine with a 2.5 MPa s^{-1} loading rate.

The setting time of the CPC samples was measured as previously described [3] with a Vicat needle with a tip diameter of 1 mm and a weight load of 400 g (International Standard ISO 1566 for dental zinc phosphate cements). Our values corresponded to the final setting time F described by Driessens *et al.* [7].

3. Results

3.1. Influence on the composition of starting materials

XRD patterns showed that, after a few minutes of grinding, DCPD, DCPA, $Ca(OH)_2$ and OHAp (or CDOHAp, calcium-deficient hydroxyapatite) appeared. Their respective amounts in the powder as a function of grinding time were estimated from the diffraction peak intensities: diffraction planes 0.1.0 ($\theta = 3.70°$), $\bar{1}.\bar{2}.1$ ($\theta = 11.44°$) and $\bar{1}.2.1$ ($\theta = 12.10°$) mean value for MCPM; 0.2.0 ($\theta = 5.82°$) for DCPD; 0.2.0 ($\theta = 13.24°$) for DCPA; 0.0.2 ($\theta = 12.98°$) for OHAp; 2.0.0 ($\theta = 18.75°$) for CaO and 1.0.1 ($\theta = 17.13°$) for $Ca(OH)_2$ for which there is not quite an overlap. Peak intensity was used for these quantitative determinations instead of peak area for simplicity as commonly done [8–11] and because we showed that the results obtained in this way were confirmed by other analytical techniques on the condition to repeat measurements [3]. Mixtures of MCPM and CaO with Ca/P ratios of 1.67, 1.5, 1.35 and 1.1 were studied. Fig. 1 shows the variations of MCPM,

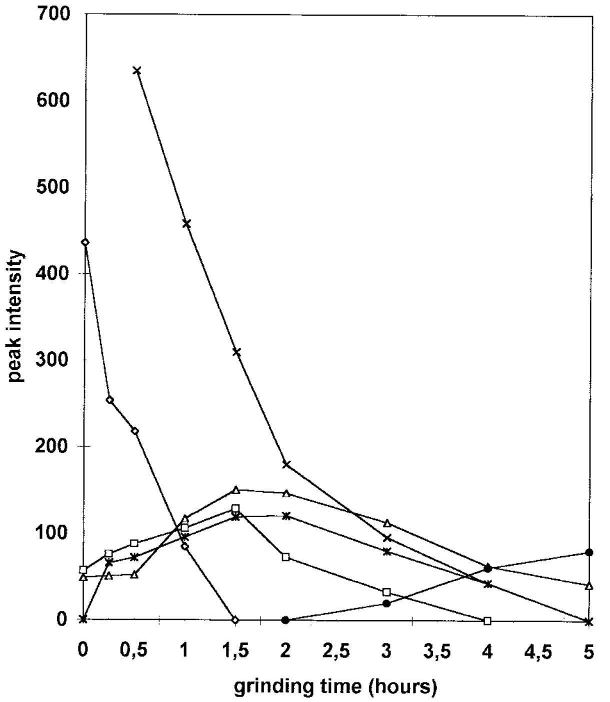

Figure 1 Variations in the amounts of MCPM (◇), DCPD (□), DCPA (△), CaO (x), $Ca(OH)_2$ (*) and OHAp (•) from a MCPM-CaO mixture with a Ca/P ratio of 1.67 as a function of the mechanical grinding time, measured by XRD.

DCPD, DCPA, OHAp (or CDOHAp), CaO and $Ca(OH)_2$ amounts with grinding time for a ratio $Ca/P = 1.67$. Similar profiles were obtained for the other Ca/P ratios. The presence of OCP and/or β-TCP was not observed whatever the Ca/P ratio. After a 5-h grinding time, the final products were: DCPD + DCPA for a Ca/P ratio of 1.1 and a mixture of DCPA and poorly crystallized OHAp (or CDOHAp) for the other Ca/P ratios. The disappearance of MCPM with grinding time for the different Ca/P ratios is represented in Fig. 2. For clarity the standard deviations of each point (2–4 measurements) are not represented in these figures. XRD patterns after 2-h grinding showed the appearance of OHAp (or CDOHAp).

3.2. Stability of the powder after mixing

After a manual crushing in a mortar for 2 min, whatever the temperature of storage (from 0 up to 60 °C), the shape of the XRD patterns was unchanged for up to 3 months indicating no change in the powder composition (Fig. 3). A possible decrease in crystallinity of the compounds is suggested by the decrease of the intensity of the diffraction peaks throughout the storage. The low intensity peaks at 5.80 °θ, 10.52 °θ and 13.24 °θ indicate the presence of small amounts of DCPD and DCPA, resulting from the reaction of orthophosphoric acid (which is present in commercial MCPM) with CaO, which remained constant with time at low storage temperatures but DCPA was preferentially observed at 50 or 60 °C storage. A minor fraction of CaO was hydrated during mortaring into $Ca(OH)_2$ (diffraction peak at 9.07 °θ).

3.3. Influence of the grinding time and storage time on compressive strength and setting time

The influence of grinding time on compressive strength was studied for different Ca/P ratios in the powder and with pure water or 0.45 M or 1 M sodium phosphate buffer (pH 7) as liquid phase. The results are summarized in Table I. The compressive strength was also measured

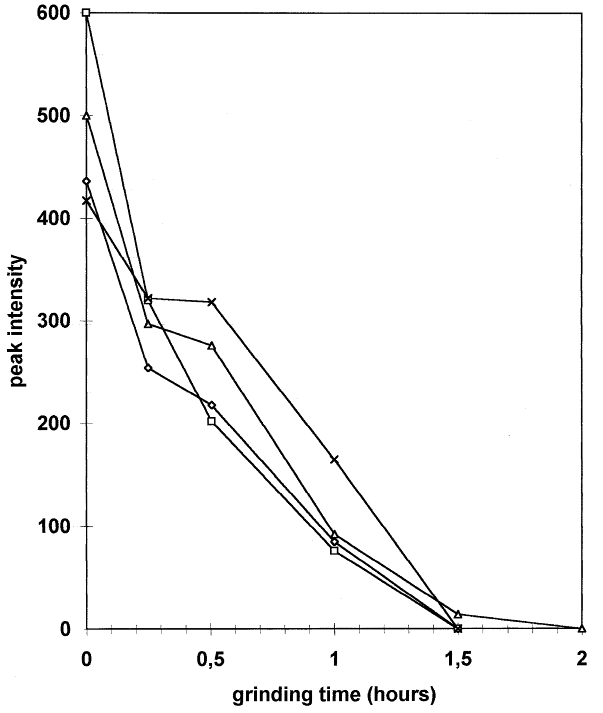

Figure 2 Variations in the amount of MCPM from MCPM-CaO mixtures with different Ca/P ratios (◇, 1.67; □, 1.50 ; △, 1.35 ; x, 1.1) as a function of the mechanical grinding time, measured by XRD.

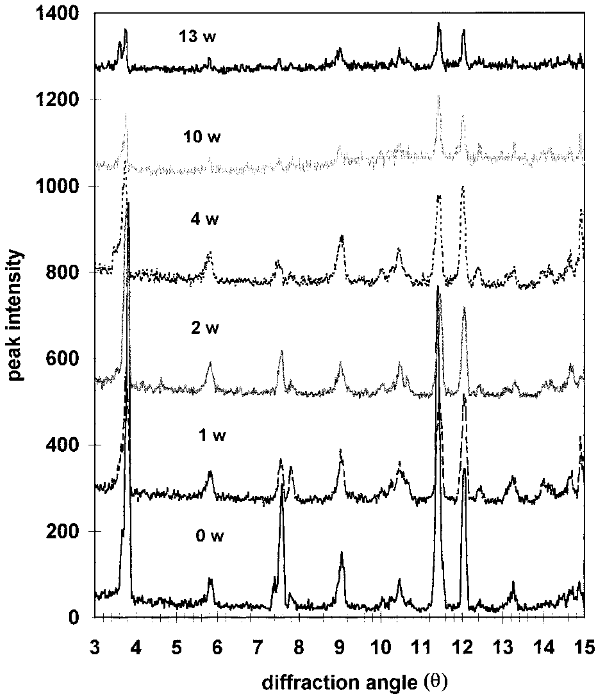

Figure 3 XRD patterns after 0, 1, 2, 4, 10 and 13 weeks of storage at 20 °C of a mixture of MCPM and CaO ($Ca/P = 1.67$) mortared for only 2 min.

TABLE I Influence of the grinding time on the compressive strength of CPCs obtained with water or sodium phosphate buffers as liquid and different calcium-to-phosphate ratios (Ca/P). Values in parentheses denote standard errors on five measurements

Sodium phosphate buffer (M)	Compressive strength (MPa)					
	Time of grinding (min)					Reference values [6]
	0	15	30	60	90	
Ca/P = 1.67						
0	4.5 (0.5)	3.5 (0.2)	3.1 (0.3)	1.8 (0.2)	0.6 (0.1)	0.5
0.45	16.7 (1.7)	18.8 (1.2)	17.3 (1.3)	16.8 (1.8)	9.5 (0.9)	
1	26.3 (0.5)	25.9 (0.6)	25.2 (1.4)	19.1 (1.0)	6.6 (0.4)	
Ca/P = 1.50						
0	8.8 (1.4)	7.2 (0.6)	7.8 (1.0)	3.3 (0.4)	0.9 (0.2)	1
0.45	14.5 (0.9)	14.0 (1.0)	15.3 (0.9)	8.0 (0.7)	5.8 (0.3)	
1	14.2 (1.3)	14.1 (1.2)	11.6 (1.6)	9.2 (1.5)	7.5 (1.6)	
Ca/P = 1.35						
0	10.5 (0.3)	10.2 (0.5)	10.7 (0.4)	8.6 (0.3)	2.9 (0.3)	5.2
0.45	10.1 (0.8)	10.3 (1.1)	11.7 (0.7)	8.7 (0.6)	5.7 (0.4)	
1	9.9 (1.1)	12.8 (0.8)	15.0 (0.8)	11.2 (0.6)	5.6 (0.2)	
Ca/P = 1.1						
0	3.2 (0.2)					0.2
0.45	ND[a]		Experiments not performed			
1	3.5 (0.3)					

[a] Samples broke when they were removed from the molds.

on samples prepared with powders that were stored for different times at different temperatures (20 and 50 °C). After storage for one day, whatever the temperature, the CS value decreased to 16 ± 1 MPa when 1 M sodium phosphate buffer (pH 7) was used as liquid phase and remained constant up to 3 months, therefore longer storage times were not investigated. The setting time of the cements was also affected by the grinding time of the initial mixtures of the materials (Table II).

3.4. Influence of the orthophosphoric acid contaminant on compressive strength

Cement samples were prepared with MCPM from which the orthophosphoric acid contaminant was eliminated (i) by washing with ethanol or (ii) by grinding with 5 wt % DCPA. Other samples were prepared with commercial MCPM ground with 5 wt % H_3PO_4. The compressive strength values of cements obtained with water, 0.45 M and 1 M sodium phosphate buffer as liquid phase are shown in Table III.

4. Discussion

These results clearly show: (i) that MCPM reacts with CaO during mechanical grinding, and the final products are hydroxyapatite (or calcium-deficient hydroxyapatite) and dihydrate and/or anhydrous dicalcium phosphate depending on the initial Ca/P ratio; (ii) when MCPM and CaO powders are placed in contact for 2 min by manual grinding in a mortar to ensure a homogeneous mixture of the products, no reaction is observed even after storage for 3 months, whatever the temperature. The origin of the small peaks at 5.82 and $10.52\,^{\circ}\theta$ and $13.24\,^{\circ}\theta$ (Fig. 3 and Fig. 4 curve 1) observed after manual mixing corresponded to DCPD and DCPA respectively, and they resulted from the orthophosphoric acid-CaO reaction. This was confirmed by mixing CaO and MCPM first ground with 5 wt % DCPA or MCPM first washed with ethanol and dried. In these ways MCPM was orthophosphoric acid free and consequently DCPA and DCPD were not observed on the XRD patterns (Fig. 4 curves 2 and 3) and the hydration of CaO was less important (Fig. 4, diffraction peak at $9.07\,^{\circ}\theta$).

During mechanical grinding, under the impacts of the balls, intimate contacts arose between reactants, and the energy provided by the shocks allowed the reaction to take place, which was not when the powders were just placed in contact.

The change in composition of the initial substances during grinding affects the mechanical properties (compressive strength and setting time) of the cement made from the powder after different grinding times as shown in Tables I and II. Whatever the Ca/P ratio, the compressive strength remains constant for up to 30 min of grinding and decreases for longer grinding times. In a

TABLE II Influence of the grinding time on the setting time of CPCs obtained with 1 M sodium phosphate buffer as liquid for two calcium-to-phosphate ratios (Ca/P). Values in parentheses denote standard errors on three measurements

Ca/P	Setting time (min)				
	Time of grinding (min)				
	0	15	30	60	90
1.67	9.0 (0.3)	6.7 (0.3)	6.5 (0.3)	5.5 (0.3)	5.2 (0.3)
1.50	13.5 (0.5)	13.5 (0.3)	11.2 (0.3)	8.0 (0.5)	6.5 (0.5)

TABLE III Influence of the orthophosphoric acid in MCPM on the compressive strength after 24 h of CPCs obtained with water or sodium phosphate buffers as liquid and a calcium-to-phosphate ratio of 1.67. Values in parentheses denote standard errors on five measurements

MCPM		Compressive strength (MPa)		
Treatment	Solubility ($g\,l^{-1}$)	Sodium phosphate buffer (M)		
		0	0.45	1
Untreated (commercial)	110	4.5 (0.5)	16.7 (1.7)	26.3 (0.5)
Washed with ethanol and dried	6.9	4.7 (0.3)	9.0 (0.7)	11.9 (1.1)
Ground with 5 wt % DCPA	18	5.0 (0.2)	13.5 (1.3)	14.0 (1.0)
Ground with 5 wt % H_3PO_4	210	4.2 (0.2)	16.5 (1.3)	11.8 (0.9)

previous paper [3], we showed that the first step of the cement setting reaction was the formation of DCPD from the reaction of MCPM with a part of the CaO. Attempts to obtain good quality cement directly from DCPD and CaO were unsuccessful; the cement was ten times less resistant than that made with MCPM. After grinding for 30 min, about 50% of the MCPM was transformed into DCPD and DCPA, consequently we should have observed a decrease in compressive strength, which was not the case. The specific area of the powder (Ca/P = 1.67) was 0.9, 1.1, 1.4 and 1.6 $m^2\,g^{-1}$ after grinding for 0, 5, 15 and 30 min, respectively. Thus, for short grinding times, the increase in specific area (which is known to enhance the compressive strength [4, 5, 12]) counterbalanced the effect of the transformation of MCPM into DCPD and DCPA. In their experiments with MCPM and CaO, Bermudez *et al.* [6] ground the MCPM-CaO mixture for 60 to 90 min [13]. This explains the differences observed between the compressive strength values we reported (Table I, first column, and in [3]) and theirs (Table I, last column and in [6]) that we noted in a previous paper and which we attributed initially to a difference in the powder-to-liquid mixing procedure which also influences the final compressive strength [3]. The CS values that we obtained for grinding times of 60 to 90 min (Table I) correspond to those reported in [6] whatever the Ca/P ratios.

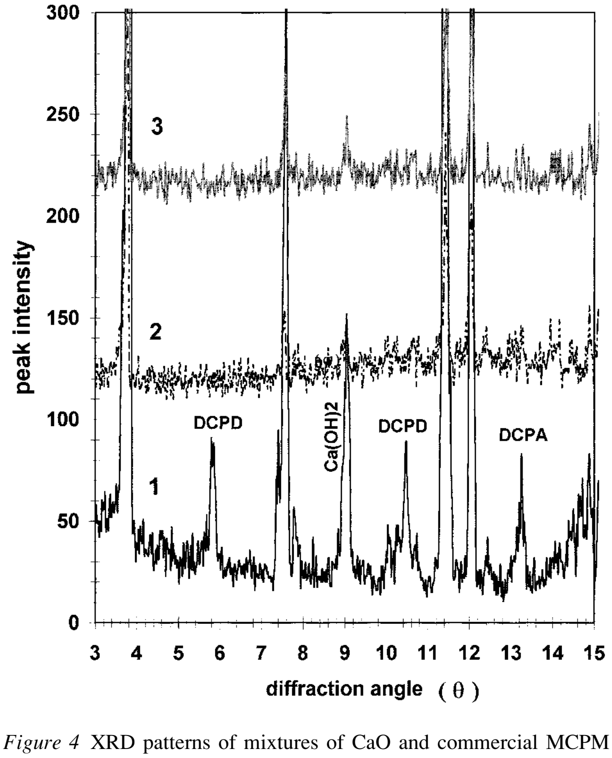

Figure 4 XRD patterns of mixtures of CaO and commercial MCPM (curve 1) or MCPM ground with 5 wt % DCPA (curve 2) or MCPM washed with ethanol and dried (curve 3), (Ca/P = 1.67) mortared for only 2 min.

As expected, the setting time (Table II) decreased as the grinding time increased, due to an increase in the specific area which enhanced the dissolution rate and as such supersaturation was reached more rapidly.

Given the fact that commercial MCPM cannot be correctly ground, the orthophosphoric acid contaminant and moisture were removed by washing commercial reagent with anhydrous ethanol [14]. In this way, after grinding, the powder was not sticky and presented a finer particle size (by subjective filling between the finger tips). The compressive strength value of the cement obtained with this material and a Ca/P ratio of 1.67 was the same as with commercial MCPM when water was used as the liquid phase (Table III) but only half that with 1 M phosphate buffer (12 ± 1 MPa). This low value could be a result of washing with ethanol which could deactivate the powder. Thus the orthophosphoric acid contaminant was removed by using another procedure, namely, grinding commercial MCPM with 5 wt % DCPA which reacted with the H_3PO_4 contaminant to give MCPM. Whatever the liquid phase used, we obtained the same results as with the ethanol washing procedure. The commercial MCPM we used had a solubility of 110 $g\,l^{-1}$; after ethanol washing or grinding with DCPA the solubility fell to 7 and 18 $g\,l^{-1}$, respectively. This can explain the decrease in compressive strength. Since the presence of orthophosphoric acid increases the solubility of MCPM, we added 5 wt % H_3PO_4 to the commercial MCPM. The results were again the same as those obtained with washed MCPM, i.e. the same compressive strength value with water as liquid phase and half that value with 1 M phosphate buffer (Table III) in spite of the solubility of MCPM increased up to 210 $g\,l^{-1}$. Finally, commercial MCPM was the best starting material. At this point, it should be noted that the amounts of orthophosphoric acid contaminant and moisture can vary batch to batch; this influences the powder-to-liquid ratio (P/L) which in turn influences the compressive strength. Indeed, in our previous study [3], the P/L ratio of 1.53 $g\,l^{-1}$ (MCPM, batch Fluka 354489/1 796) gave the best CS; in the present work this value was 1.80 $g\,l^{-1}$ (MCPM, batch Fluka 354489/1 44996).

5. Conclusion

During the grinding step, to obtain a fine and homogeneous particle size distribution, MCPM reacts with CaO and this affects the mechanical properties of the resulting cements, whatever the Ca/P ratio. Commercial MCPM, without any other treatment than grinding, appears to give the best results because of its high solubility. From a practical point of view, for a clinician, it would be preferable to have at one's disposal a single powder ready to be mixed with the liquid phase. The powder should be homogeneous, have a constant granularity, and be stable over a long period. The mechanical properties of the cement must be independent of the duration and temperature of storage. Unfortunately, this seems to be impossible for the present formulation, given the solid-solid reaction between MCPM and CaO during grinding and the deterioration of the mechanical properties of the resulting cements after storage. Powders will have to be separated for storage if the main property of the cement desired is hardness. Because the final product of the MCPM-CaO solid-solid reaction is OHAp or CDOHAp via the DCPD or DCPA-CaO solid-solid reaction, it is probable that such reactions occur during grinding between other acid and basic calcium phosphates commonly used in the formulations of CPCs. This investigation is presently in progress and the first results seem to support this hypothesis.

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