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Effective formulations for the preparation of calcium phosphate bone cements

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In the system $CaO–P_2O_5–H_2O$ 13 different solids with varying Ca/P ratios are known. In addition calcium phosphates containing other biocompatible constituents like Na, or K, or Mg or Cl or carbonate, are known. Therefore, a large number of combinations of such compounds is possible which might result in the formation of calcium phosphate cements upon mixing with water. However, the number of calcium phosphates possibly formed by precipitation at room or body temperatures is limited to 12, which should limit the number of suitable combinations. In this study more than 450 different combinations of reactants have been investigated. The results were evaluated on the basis of the following criteria: (a) was the intended reaction product formed? (b) was the final setting time shorter than 60 min? (c) was the compressive strength after soaking for 1 day in Ringer's solution at 37 °C higher than 2 MPa? We found that 15 formulations satisfied all of these criteria. The distribution of cements synthesized in this way was 3 DCPD type, 3 CMP type, 6 OCP type and 3 CDHA type cements. The DCPD type cements were acidic during setting and remained that for a long time afterwards. CDHA type cements were neutral or basic during setting, and remained neutral after completion of the reaction. The OCP type cements were neutral both during and after setting. Two CMP type cements were basic both during and after setting. In this study compressive strengths were found up to 90 MPa. Also, in the literature values up to 90 MPa have been reported for this type of cement. Taking into account the excellent biocompatibility and the good osteoconductivity of calcium phosphates and the fact that these calcium phosphate cements can be injected into the site of operation, it may be expected that these materials will become the materials of choice for bone replacement and augmentation. Their suitability for the fixation of metal endoprostheses for joint replacement should be investigated as well.

1. Introduction

The best known bone cement at the moment is that based on poly (methyl methacrylate) PMMA. The annual number of surgical hip and knee replacements amounts to about 700 000 now and this number increases annually by more than 10%. A few of these surgical treatments result in complications [1].

However, when the surgery is successful, the service life of a cemented prosthesis is between 10 and 15 years, mostly limited by the ageing of the cement and the formation of a layer of fibrous tissue as a foreign body reaction between the cement and the bone structure. This layer allows for micromovements and may lead ultimately to mechanical breakdown of the bone cement and to the formation of particulate debris. Such a debris often results in an agressive foreign-body reaction leading to bone lysis [2]. Therefore, although the orthopaedic surgery of hip and knee replacement has been very successful in moving up the morbidity of elderly populations to a higher age, the need for revision of old prostheses increases by the year due to the limited service life of the surgical device, especially that part of it consisting of the classical PMMA bone cement.

About 10 years ago an alternative way of implantations was developed: metal endoprostheses were covered with a thin layer of calcium phosphates before implantations, e.g. by plasma spraying [3, 4]. The prosthesis is fixed initially by press fit. Secondary fixation is obtained by ongrowth of bone [5]. Although the initial fixation with this technique is not as good as that in the cementation technique, it is not clear yet whether the average service life of these prostheses is better or worse than that of the cemented prostheses. The final fixation is certainly better than in the case of cemented prostheses, because removal of the prostheses and revisional treatment is practically impossible. So the state of the art of joint replacement is such that in general the classical cementation technique results in good initial fixation but poor final fixation of metal endoprotheses, whereas the press-fit and coating technique results in poor initial fixation and good final fixation.

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The solution to this problem might be found in the development and application of more appropriate bone cements. Some investigators have proposed trying glass ionomer cements as alternative bone cements. Apart from the fact that their mechanical properties may be too low for this application, it is known that such materials release constituents like silicate and aluminate which might accumulate in soft tissues like liver, kidneys and brain.

On the other hand, ceramics made of calcium phosphates like hydroxyapatite or α-tertiary calcium phosphate are extremely well accepted by the living tissues upon implantation [6–9]. They may even be called osteoconductive in their efficiency of replacing and augmenting bond tissue [10–14]. For this reason attempts have been made to synthesize calcium phosphate cements which can be prepared at room or body temperature and which can be moulded during the operation on the patient. Such materials seem to be ideal for bone reconstruction or augmentation from the surgical and biological point of view.

The first successful attempt has been made by Brown and Chow [15]. They made mixtures of dicalcium phosphate dihydrate (DCDP) with tetracalcium phosphate (TTCP) and of dicalcium phosphate (DCP), TTCP and hydroxyapatite (HA) and reported setting times between 8 and 22 min as measured with a Vicat needle. The compressive strength was up to 34 MPa. Others found compressive strength values of only 21 [16] and 9 [17] MPa for these products. The reaction product in these cements appeared to be apatitic.

Lemaitre *et al.* [18–20] formed a DCPD (dicalcium phosphate dihydrate) cement by mixing a powder of α-tertiary calcium phosphate (α-TCP) with an aqueous solution of monocalcium phosphate monohydrate (MCPM). Its setting time was 1 to 2 min and its diametral tensile strength about 1 MPa. Another brushite cement was formed by Constantz *et al.* [21] by reaction of a mixture of MCPM and TTCP in an aqueous slurry.

Monma *et al.* [17] reported that they obtained octocalcium phosphate (OCP) cements by reaction of α-TCP with DCDP. Setting times varied from 9 to 30 min and the compressive strength was 17 MPa.

Constantz *et al.* [22, 23] used appropriate mixtures of anhydrous phosphoric acid or MCPM with TTCP, made pastes with an aqueous lubricant and claimed to have obtained HA as a reaction product. They reported setting times from 6 to 11 min and compression strengths from 15 up to 92 MPa.

Brown and Chow [15] and later Fukase *et al.* [24] claimed that their powder mixture of DCP and TTCP reacted upon mixing with water to stoichiometric hydroxyapatite. However, more recent investigations [25–27] have shown that only the first nuclei consist of nearly stoichiometric hydroxyapatite, whereas further growth of these nuclei occurs in the form of calcium deficient hydroxyapatite (CDHA) with a Ca/P ratio near 1.5. The same may apply to the cements made by Constantz *et al.* [22, 23].

The purpose of the present study was to repeat most of these studies as mentioned in the literature [15–23] and to develop also other calcium phosphate cement formulations giving: (a) the intended reaction product; (b) physical setting within 60 min; and (c) bodies with a substantial strength after immersion for at least 1 day in Ringer's solution at 37 °C.

2. Materials and methods

Solids occurring in the system Ca $(OH)_2$–H_3PO_4–H_2O around room and body temperature are listed in Table I. Not all of them come into consideration as reaction product in calcium phosphate cements. In the physiological range of pH only octocalcium phosphate OCP, calcium deficient hydroxyapatite CDHA and precipitated hydroxyapatite PHA are stable or

TABLE I Solids occurring in the system Ca $(OH)_2$–H_3PO_4–H_2O around room and body temperature

Ca/P	Formula	Abbreviation	Remarks
0.5	$Ca(H_2PO_4)_2 \cdot H_2O$	MCPM	Stable below pH 2
1	$CaHPO_4 \cdot 2H_2O$	DCPD	Stable between pH 2 and 4, nucleates rapidly and may grow rapidly even up to pH 6.5
1.33	$Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$	OCP	Nucleates rapidly and grows between pH 6.5 and 8, more stable than DCPD or ACP in that range
1.5	$Ca_3(PO_4)_2 \cdot xH_2O$	ACP	This substance occurs as the first phase when precipitation is at high concentrations between a pH of 4 and 8, but it transforms rapidly into DCPD, OCP or CDHA. When it incorporates Mg ions, it is stabilized so that it becomes even more stable than CDHA
1.5	$Ca_9(HPO_4)(PO_4)_5OH$	CDHA	This hydroxyapatite is calcium deficient. It does not precipitate spontaneously at room or body temperature but has either DCPD or OCP as precursors. However, it may be in metastable equilibrium with aqueous solutions indefinitely
1.67	$Ca_{10}(PO_4)_6(OH)_2$	PHA	Precipitated hydroxyapatite is the most stable compound in this system at a pH higher than 4. It precipitates directly only above pH 8. However, at lower pH its nucleation can be initiated by fluoride
2.0	$Ca(OH)_2$		This solid is stable only in aqueous solutions not containing any phosphate with a pH higher than about 12

TABLE II Compounds in the system $CaO-P_2O_5-H_2O$ which are stable at higher temperatures

Ca/P	Formula	Abbreviation	Remarks
1.0	$CaHPO_4$	DCP	It is formed by precipitation at higher temperatures and is slightly more stable than DCPD
1.5	$Ca_3(PO_4)_2$	β-TCP	Is stable up to 1180 °C. In water it is more stable than DCPD or OCP but less than CDHA in the range between pH 6 and 8
1.5	$Ca_3(PO_4)_2$	α-TCP	Forms by heating above 1180 °C and keeps its structure when quenched to room temperature. In water it is less stable than DCPD or OCP
1.67	$Ca_{10}(PO_4)_6(OH)_{2-2x}O_x$	SHA	Sintered hydroxyapatite forms by heating between about 700 and 1400 °C. In water it is as stable as CDHA
2.0	$Ca_4(PO_4)_2O$	TTCP	Forms by heating at temperatures above 1420 °C and keeps its structure when cooling in the furnace to room temperature. In water it is less stable than SDHA, CDHA, DCPD or OCP
∞	CaO		Forms by heating $CaCO_3$ at temperatures higher than about 450 °C

TABLE III Other calcium and/or phosphate containing compounds suitable in principle as reactants for the synthesis of calcium phosphate cements or as reaction products

Component	Compounds
Sodium	$CaNaPO_4$ (α or β), $Ca_{10}Na(PO_4)_7$ (α or β) orthophosphates of Na
Potassium	$CaKPO_4$, orthophosphates of K
Magnesium	MgO, $MgCO_3$, $MgCl_2$, orthophosphates of Mg
Chloride	Ca_2PO_4Cl, $Ca_{10}(PO_4)_6Cl_2$, $CaCl_2$
Carbonate	$CaCO_3$, $Ca_{8,5}Na_{1,5}(PO_4)_{4,5}(CO_3)_{2,5}$, $Ca_9K(PO_4)_5(CO_3)_2$

metastable. Of course, products like monocalcium phosphate monohydrate MCPM, dicalcium phosphate dihydrate DCPD and calcium hydroxide come into consideration for use as reactants.

There are other calcium phosphates which can be formed at higher temperatures (see Table II). Only sintered hydroxyapatite SHA is stable in the physiological range, whereas β-TCP is metastable. The other products like dicalcium phosphate DCP, α-tertiary calcium phosphate α-TCP, tetracalcium phosphate TTCP and calcium oxide can be used as reactants to obtain calcium phosphate cements.

In fact, other oligo-elements like Na, K, Mg, Zn, carbonate and chloride are known [28], which enlarges the group of compounds suitable, in principle, as reactants for the synthesis of calcium phosphates (see Table III). Some of these compounds may also play a role as reaction products.

Table IV gives a summary of calcium phosphates which contain only biocompatible constituents and which are reported to be formed directly or indirectly by precipitation from aqueous solutions [28]. This means that the possible reaction products of calcium phosphate cement formulations are limited to this group of compounds.

The ingredients and/or reactants mentioned in Table V were available directly on the market. Other reactants prepared from the ingredients and their method of synthesis are mentioned in Table VI.

In this study 466 different mixtures of the indicated reactants were prepared by proportioning and subsequent milling in an agate ball mill. Pastes were prepared by mixing at the most suitable water/powder W/P ratio. Initial setting time I and final setting time F (min) were determined with Gilmore needles.

Cylinders with a height of 12 mm and a diameter of 6 mm were prepared. They were soaked for 1 day in Ringer's solution at 37 °C. Then their compressive strength C and their diametral tensile strength T were determined (MPa) using a Instron Universal Testing machine Type 4507 at a compression rate of 1 mm min^{-1}.

The identity of the reaction products was established by X-ray diffraction. Also, the pH of the cement pastes was measured from the start of mixing with water up to at least 1 day.

3. Results

The formulations were evaluated on the basis of the following criteria:

(a) Was the intended reaction product (see Table IV) formed?
(b) Did the final setting time F not exceed 60 min?
(c) Was the compressive strength C after soaking for 1 day in Ringer's solution at 37 °C higher than 2 MPa?

There were not even 15 formulations which met all three of these criteria strictly (see Table VII). Formulations deviating from the compositions mentioned in this table gave inferior results which indicates that it is not useful to try formulations leading to any mixture of two or more reaction products, like those mentioned in Table IV. Products containing only one of the possible reaction products turned out to be superior. For comparison, mixtures which did not react at all, did not have any final setting time, whereas their compressive strength C was as low as 0.2 MPa after soaking for 1 day in Ringer's solution.

The pH of the cement pastes during setting and after 1 day is presented in Fig. 1, 2 and 3. It is observed that DCPD cements are acidic having a pH near 4.

TABLE IV Calcium phosphates which contain only biocompatible constituents and which are thought to be precipitated directly from aqueous solutions [28] around room or body temperature

Ca/P	Formula	Abbreviation	Name
0.5	$CaZn_2(PO_4)_2$	CZP	Calcium zinc phosphate
0.67	$Ca_4Mg_5(PO_4)_6$	CMP	Calcium magnesium phosphate
1.0	$CaHPO_4 \cdot 2H_2O$	DCPD	Dicalcium phosphate dihydrate
1.28	$Ca_9Mg(PO_4)_6(HPO_4)$	MWH	Magnesium whitlockite
1.28	$Ca_9Zn(PO_4)_6(HPO_4)$	ZWH	Zinc whitlockite
1.33	$Ca_8(HPO_4)_2(PO_4)_4 \cdot 5H_2O$	OCP	Octocalcium phosphate
1.5	$Ca_9(HPO_4)(PO_4)_5OH$	CDHA	Calcium deficient hydroxyapatite
1.67	$Ca_{10}(PO_4)_6(OH)_2$	PHA	Precipitated hydroxyapatite
1.67	$Ca_{10}(PO_4)_6F_2$	FA	Fluorapatite
1.8	$Ca_{8 \cdot 5}Na_{1 \cdot 5}(PO_4)_{4 \cdot 5}(CO_3)_{2 \cdot 5}$	SCCA	Sodium and carbonate containing apatite
1.89	$Ca_9K(PO_4)_5(CO_3)_2$	PCCA	Potassium and carbonate containing apatite
2.0	$Ca_9(PO_4)_{4 \cdot 5}(CO_3)_{1 \cdot 5}(OH)_{1 \cdot 5}$	HCHA	Heavily carbonated hydroxyapatite

TABLE V Raw chemicals used either directly or after milling as basic materials or used as chemicals to prepare other basic materials

Name	Formula	Brand	Catalogue number
Calcium hydrogen phosphate	$CaHPO_4$	Merck[a]	2144
Calcium carbonate	$CaCO_3$	Merck	2076
Calcium chloride anhydrous	$CaCl_2$	Merck	2388
Calcium hydrogen phosphate dihydrate	$CaHPO_4 \cdot 2H_2O$	Merck	2146
Tricalcium phosphate[b]	$Ca_3(PO_4)_2$	Merck	2143
Sodium carbonate anhydrous	Na_2CO_3	Merck	6392
Calcium hydroxide	$Ca(OH)_2$	Merck	2047
Potassium carbonate	K_2CO_3	Merck	4924
Calcium oxide from marble	CaO	Merck	2109
Calcium phosphate monobasic-1-hydrate	$Ca(H_2PO_4)_2 \cdot H_2O$	Panreac[c]	141225
Magnesium oxide	MgO	Merck	5867
Magnesium hydrogen phosphate trihydrate	$MgHPO_4 \cdot 3H_2O$	Merck	5872
Zinc oxide	ZnO	Merck	8846

[a] E. Merck, Darmstadt, Germany
[b] This product appeared to be a precipitated hydroxyapatite PHA
[c] Montplet y Esteban S. A., Barcelona, Spain

TABLE VI Basic products prepared by heating appropriate mixtures of $CaHPO_4$, $CaCO_3$, Na_2CO_3, K_2CO_3 and/or $CaCl_2$ in a furnace at high temperatures

Abbreviation	Basic product	Formula	Conditions of preparation applied
α-TCP	α-tertiary calcium phosphate	$Ca_3(PO_4)_2$	Heating for 6 h at 1300 °C and quenching in air to room temperature
TTCP	Tetracalcium phosphate	$Ca_4(PO_4)_2O$	Heating for 12 h at 1500 °C and cooling down in furnace to room temperature
β-TCP	β-tertiary calcium phosphate	$Ca_3(PO_4)_2$	Heating for 4 h at 1100 °C and cooling down in furnace to room temperature
SHA	Sintered hydroxyapatite	$Ca_{10}(PO_4)_6OH_{2-2x}O_x$	Heating for 10 h at 1100 °C and cooling down in furnace to room temperature
SP	Spodiosite	Ca_2PO_4Cl	Heating for 6 h at 700 °C and cooling down in furnace to room temperature
CPP	Calcium potassium phosphate	$CaKPO_4$	Heating for 6 h at 900 °C and cooling down in furnace to room temperature
SWH	Sodium whitlockite	$Ca_{10}Na(PO_4)_7$	Heating for 6 h at 1000 °C and cooling down in furnace to room temperature
CA	Chloroapatite	$Ca_{10}(PO_4)_6Cl_2$	Heating for 6 h at 800 °C and cooling down in furnace to room temperature
RH	Rhenanite	$CaNaPO_4$	Heating for 6 h at 900 °C and cooling down in furnace to room temperature

TABLE VII Calcium phosphate cements complying to the criteria of intended reaction, sufficiently fast setting and substantial strength

N	Reaction product	Components	Additives	W/P	*I*	*F*	*C*	*T*
1	DCPD[a]	MCPM + β-TCP	–	0.50	1	2	2.7	0.8
2	DCPD[a]	MCPM + TTCP	–	0.40	5	10	2.1	0.5
3	DCPD[b]	MCPM + CA + SWH	–	0.30	4	15	6.0	1.5
4	$CaMg_2(PO_4)_2$[b]	MCPM + MgO	–	0.50	3	8	3.0	0.7
5	$CaMg_2(PO_4)_2$	DCP + MgO + $MgHPO_4 \cdot 3H_2O$	–	0.35	3	6	11	2.0
6	$CaMg_2(PO_4)_2$	DCPD + MgO + $MgHPO_4 \cdot 3H_2O$	–	0.40	2	4	5.1	1.0
7	OCP	MCPM + CaO	PHA	0.52	4	28	6.1	1.6
8	OCP	DCPD + TTCP	PHA	0.30	4	24	10	3.0
9	OCP	DCP + α-TCP	PHA	0.30	8	48	30	4.5
10	OCP	MCPM + α-TCP	PHA	0.50	12	52	11	2.3
11	OCP	MCPM + TTCP	PHA	0.45	20	80	6.9	2.0
12	OCP	MCPM + CPP	PHA	0.60	3	8	6.5	1.5
13	CDHA	α-TCP	PHA	0.35	12	43	44	11
14	CDHA	MCPM + CaO + α-TCP	PHA	0.52	3	14	6.3	1.3
15	CDHA[+]	DCP + TTCP	PHA	0.30	8	29	12	2.1

[a] These cements have been mentioned in the literature
[b] The fluid was water containing 50% glycerol in order to adjust the setting times
N = number
W/P = water/powder ratio (g/g)
I = initial setting time (min)
F = final setting time (min)
C = compressive strength (MPa)
T = diametral tensile strength (MPa)

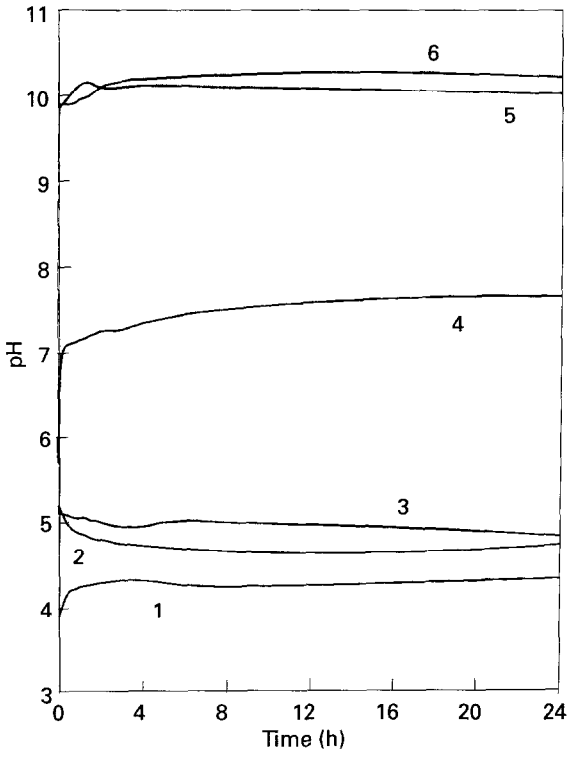

Figure 1 The pH of the pastes of the DCPD cements 1–3 and the CMP cements 4–6 measured from the start of mixing the solid ingredients with water.

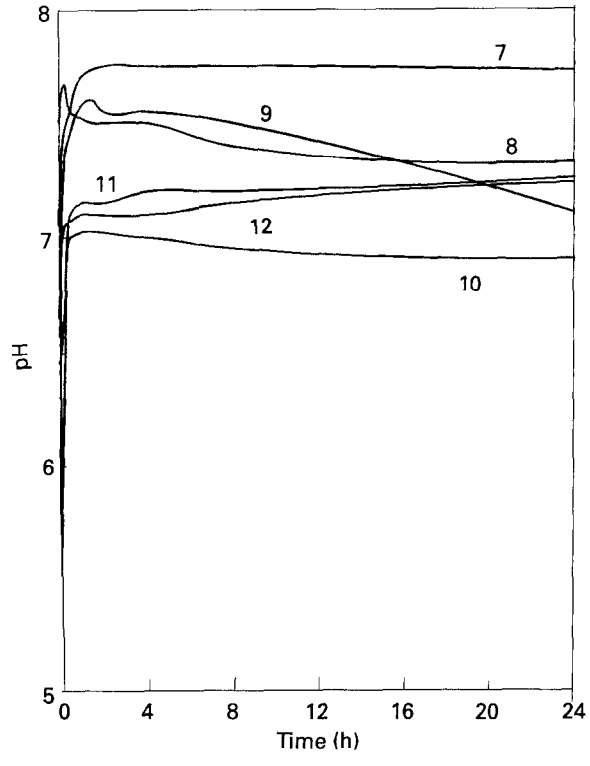

Figure 2 The pH of the pastes of the OCP cements 7–12 measured from the start of mixing the solid ingredients with water.

Even after several weeks these cements appeared to have the same acidity.

CDHA cements are neutral or basic during their setting with a pH up to 11. However, once they are set, the pH goes to neutral. OCP, and one of the CMP cements are neutral, even during their setting. The other two CMP cements are basic and remain so for at least three days.

4. Discussion

As mentioned earlier [29], the method of measuring the setting time of these cement pastes is probably the

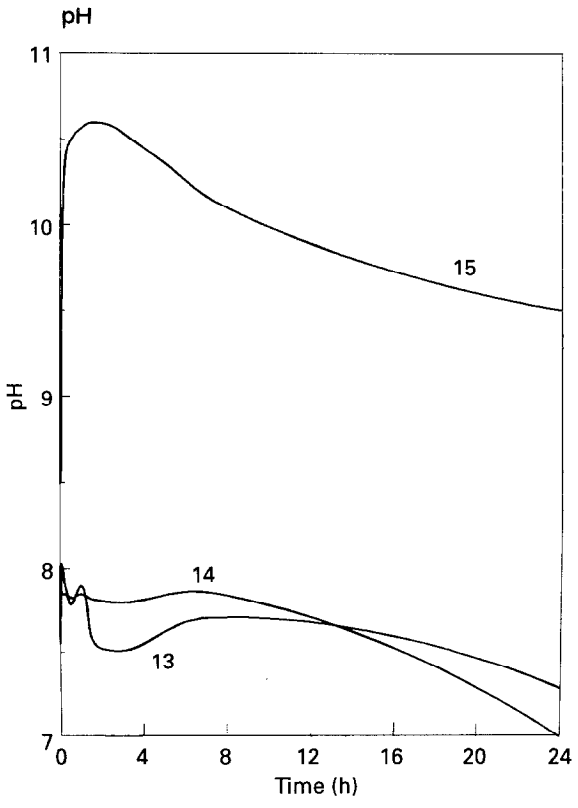

Figure 3 The pH of the pastes of the CDHA cement 13–15 measured from the start of mixing the solid ingredients with water.

fastest way to determine whether a reaction occurs upon making a paste of the mixture of reactants with water. Sometimes a minimum is found in the setting times at that composition of reactants which is 'stoichiometric' in the sense of the reaction product [17, 30]. However, in other cases a plateau has been found in the setting times as a function of the Ca/P ratio of the components [31]. Setting times are shorter for lower water/powder ratio's, as expected in analogy with gypsum [32].

The same analogy with gypsum [33] teaches us that a precipitation reaction will lead only to a considerable strength in these materials on the following two conditions: (a) the precipitate grows in the form of clusters of crystals which have a fair degree of rigidity; (b) the morphology of the crystals of the precipitate enables entanglement of the clusters. As shown already elsewhere [29], about 40% of the formulations investigated in this study gave a final setting time shorter than 60 min. However, only part of these formulations led to cement bodies having a considerable strength after soaking for 1 day in Ringer's solution at 37 °C. It was consistently found in this and other studies [30, 31, 34] that the strength values, both for compressive and for diametral tensile strength, were maximum for 'stoichiometric' compositions with respect to the reaction products.

X-ray diffraction on the resultant cements of these maxima confirmed the identity of the reaction products as far as the patterns appeared to be the same as some published pattern. However, the diffraction peak for OCP at $d = 1.86$ nm was not found, probably due to a slight deviation from stoichiometry of the precipitated phase [35]. Similarly, the relative intensity of other peaks of OCP was considerably different from that of published single crystal data [36].

That the DCPD cements had a pH near 4 may be a consequence of the fact that DCPD in contact with water has the tendency to hydrolyze into HA, whereas there is a triple point in the system Ca $(OH)_2$–H_3PO_4–H_2O for the combination of DCPD, HA and their aqueous solution at pH = 4.1 [37]. Hence, it is not strange either that the pH of these cements remains near 4 even long after setting, because the hydrolysis of DCPD into HA is a very slow process. The decrease in strength of cement number 1 as a function of the time of soaking, reported by Mirtchi *et al.* [19] may have resulted from this hydrolysis. Hence, with respect to applications DCPD cements have two disadvantages: (1) their acidity which probably evokes inflammation of living tissues upon implantation; (2) loss of strength due to gradual transformation of DCPD into HA upon implantation.

Whether the basic character of some CDHA cements during setting has any deleterious histological effects, is still to be investigated. However, this basicity is limited to the period of reaction. For cement number 14 this period may be as long as 35 h [34]. However, addition of 4% of PHA to the reactant resulted in a shortening of the reaction period for that cement down to 14 h. The neutral cements are not likely to give any histological problem.

In the case of gypsum the reactant besides water is calcium sulfate hemihydrate and the reaction product is calcium sulphate dihydrate. If instead of water a solution of potassium sulphate is used, the setting of gypsum is much faster [38]. This effect is known as the common ion effect of sulphate additives. A similar phenomenon may occur in the systems producing calcium phosphate cements. This is indicated by the fact that the setting times of cement number 12 are much shorter than those of the other OCP cements numbers 7 to 11 in Table VII. The latter group reacts like sulphate hemihydrate whereby the setting reaction consumes some water. However, the setting reaction of cement number 12 proceeds as follows: $4Ca(H_2PO_4)\cdot H_2O$ (s) + $20CaKPO_4$(s) + $11{*}H_2O$ (1) → $3Ca_8(HPO_4)(PO_4)_4\cdot 5H_2O$ (s) + $20K^+$ (1) + $10HPO_4^{2-}$ (1). In this reaction (s) means solid and (1) liquid. Thus one can imagine that the reaction itself leads to increasing phosphate ion concentrations in the aqueous phase of the cement and, hence, to a common ion effect. If this occurs generally in our systems, this common ion effect might be used to decrease the setting times and thus the setting periods of our materials to more practical values, especially of the CDHA cements and the other OCP cements. This will be the subject of a follow-up study.

In a separate study the behaviour of OCP cements number 7 and 9 during implantation has been investigated [39]. Both cements were transformed into bone mineral having the apatite structure and containing Na, Mg and carbonate. This behaviour is as expected from that of natural bone, in which the initial mineral phase is OCP and in which the same transformation occurs [28, 40]. However, despite this transformation the implants retained their strength [39]. Therefore it

seems that OCP cements have at least the following advantages for use as biomaterials: (a) they retain their strength; (b) while they are transformed into bone. The *in vivo* behaviour of CDHA and CMP cements has still to be investigated.

The fact that calcium phosphates have such a high biocompatibility and a perfect osteoconductivity, means that calcium phosphate cements will be as useful as HA or β–TCP ceramic for bone replacement or bone augmentation. However, the fact that calcium phosphate cements are injectable makes them preferable over calcium phosphate ceramics for those purposes.

Calcium phosphate ceramics are used for non-load bearing situations with the exception of HA coatings on metal endoprostheses. Even these coatings, and also the traditional PMMA bone cements, can be replaced by calcium phosphate cements when made suitable for load bearing conditions. Constantz [23] has shown that compressive strength values as high as 90 MPa can be reached with these materials. In this respect the strength values reported in Table VII must not be considered as the ultimate values which can be reached with the cements mentioned: optimization of these formulations must still be done. It may be expected that the use of calcium phosphate cements for fixation of metal endoprostheses will result not only in good initial fixation, but also in a durable final fixation due to the gradual transformation of these cements into bone, a transformation which appears to occur without loss of strength [39].

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