Effect of polymeric additions on the properties of calcium salt cements

Raúl García Carrodeguas, Luci Cristina de Oliveira,* Luis Alberto dos Santos,* Eliana C. da Silva Rigo,* Anselmo Ortega Boschi* y Sussette Padilla Mondéjar.

Departamento de Cerámicas y Composites, Centro de Biomateriales, Universidad de La Habana, Avenida Universidad s/n, Ciudad de La Habana, C.P. 10400, Cuba. *Universidade Federal de São Carlos, Departamento de Engenharia de Materiais, Laboratório de Biocerámicas, São Carlos, SP, Brasil.

Recibido: 10 de enero de 1999. Aceptado: 8 de octubre de 1999.

Palabras clave: cementos de fosfatos de calcio, cementos óseos, alginato de sodio, ácido poliacrílico.
Key words: calcium phosphate cements, bone cements, sodium alginate, polyacrylic acid

RESUMEN. En los últimos tiempos se ha prestado considerable atención a los cementos basados en sales de calcio, debido a sus ventajas sobre las biocerámicas de fosfatos de calcio convencionales empleadas en reparaciones óseas, en lo que respecta a la capacidad de manipulación y conformación *in situ*. Sin embargo, la resistencia mecánica de los cementos de sales de fosfatos de calcio es relativamente baja, especialmente durante la primera etapa de implantación y los tiempos de fraguado frecuentemente son demasiado cortos o largos para aplicaciones clínicas. El objetivo de este trabajo fue la mejora de las propiedades de tres cementos de sales de calcio. Se estudió el efecto de la adición de alginato de sodio (SA) y ácido poliacrílico (PAA) a las formulaciones anteriores de cementos de sales de calcio, teniendo en cuenta que ambos aditivos poliméricos contienen grupos carboxílicos capaces de interactuar con los iones Ca^{2+}, Mg^{2+} y H^{+}, pudiéndose esperar un efecto reforzante sobre la masa de los cementos. Se determinaron el pH inicial, el tiempo de fraguado, la resistencia a la compresión, la composición de fases y la microestructura de los cementos sin y con aditivos, encontrándose que la presencia de 4,8 % (m/m) de SA en el cemento F1 produjo una disminución de su tiempo de fraguado de 14 a 12 min y un aumento de su resistencia a la compresión inicial de 4,9 a 7,2 MPa . Además, la adición de SA a F1 disminuyó la pérdida en resistencia a la compresión después de inmersión en fluido corporal simulado. Una explicación posible a este efecto reforzante del SA en F1 pudiera ser la formación de ácido algínico fibroso capaz de actuar como fibra de refuerzo de la matriz inorgánica del cemento. Para el resto de combinaciones de cementos y aditivos estudiados siempre se encontró un efecto deletéreo sobre sus propiedades.

ABSTRACT. Recently, great attention has been paid to calcium salts cements, because of their advantages in comparison with conventional calcium phosphate bioceramics employed for bone repairing, regarding in situ handling, and shaping abilities. Nevertheless, the strength of calcium salts cements is relatively low, especially during the early stages of implantation, and their setting times are often too short or too long for clinical application. The aim of this work was the improvement of the properties of three calcium salts cements. The effect of the addition of sodium alginate (SA) and polyacrylic acid (PAA) to the above formulations of calcium salt cements was studied. Both SA and PAA content pendant carboxylic groups able to interact with Ca^{2+}, Mg^{2+}, and H^{+} ions thus reinforcing the cement mass. Initial pH, setting time, compressive strength, phase composition and microstructure of cements with and without additives were determined. The presence of 4.8 wt-% SA in the cement F1 decreased its setting time from 14 to 12 min. and increased its initial compressive strength from 4.9 to 7.2 MPa. Furthermore, the addition of SA diminished the decay in compressive strength of this cement after 1-week immersion in simulated body fluid. A possible explanation for the reinforcing effect of SA in F1 cement is the formation of fibrous alginic acid, which would act as a reinforcing fiber in the inorganic cement matrix. For the rest of combinations of cements and additives studied, a deleterious effect on their properties was always found.

INTRODUCTION

Calcium salt cements (CSC) have attracted much attention in medicine and dentistry because of their excellent biocompatibility and bone-replacing behavior over long periods combined with the abilities to be molded, injected, and set *in situ*.[1,2] However, their low mechanical strength and too long or too short setting time limit wider clinical applications of these cements. A promising solution to these problems could be the addition of polymeric modifiers to the CSC.[3,4]

Several kinds of CSC have been reported with different biological, physicochemical and mechanical properties. Thus, composites of hydroxyapatite (HA) and gypsum have been proposed as a partially biodegradable bone-replacing material.[5] Lemaitre *et al.* found that combinations of β-tricalcium phosphate (β-TCP) and monocalcium phosphate monohydrate (MCPM) resulted in cements with dicalcium phosphate dihydrate (DCPD) as the resulting phase.[6] MCPM can be substituted by orthophosphoric acid with similar results.[7] Driessens *et al.* carried out an exploratory study that indicated that there were about 15 different formulations resulting in the formation of CSC.[8]

The selected polymeric modifiers in this work were sodium alginate (SA) and polyacrylic acid (PAA). They are macromolecules with car-

boxylic groups on their chains. SA reacts with calcium ions forming an insoluble 3-dimensional network and with hydrogen ions precipitating fibrous alginic acid. PAA could interact too with the ionic species existing in the cement mass. Both are biocompatible and have been used as components of implant devices.

Accordingly, in this work the effects of the addition of SA and PAA on the mechanical strength and other properties of CSC were studied.

MATERIALS AND METHODS

Different formulations of cements were studied (Table 1).

All chemicals were of analytical grade except the β-TCP and the sintered hydroxyapatite (SHA). β-TCP (12 wt-% HA) was synthesized as described elsewere.[9] SHA was APA-FILL-G®, particle size < 100 mm (BIOMAT, Cuba). The employed additives were SA (Sigma, Cat. No. A2033, Medium Viscosity), and PAA obtained by polymerization of acrylic acid in chloroform at 60 °C, followed by precipitation in diethyl ether. PAA thus obtained had a M_v of 90 000.

Cement pastes were prepared by mixing liquid and powder during 1 min. The setting time was determined by the Vicat method (ASTM C472-90a). Cylinders (12-mm H x 6-mm D) were molded and conditioned 24 h at 100 % RH and room temperature. Compressive strength was measured after the 24 h conditioning period and after 1-week immersion in simulated body fluid (SBF) at 37 °C (Universal Testing Machine Instron 1127; 1 mm · min^{-1}).

Cylinders after conditioning for 24 h at 100 % HR were immersed 24 h in water (W/S volume ratio = 10) at 37 °C and pH was measured. Porosity was determined by the Archimedes method. The phase composition and microstructure were studied by X-Ray Diffraction (powdered samples, X-ray diffractometer D 5000, Siemens, 2°/min, CuK_α, Ni filter, 40 kV, 40 mA) and Scanning Electron Microscopy (gold-covered fracture surfaces of dried pieces remaining from compressive strength test; Philips XL30 TMP D6615 scanning electron microscope).

RESULTS AND DISCUSSION

Some chemical transformations during setting and immersion in SBF of the studied cement formulations were expected to happen (Table 2).

Equations 1 y 2 represent the reactions that occur during the mixture of liquid and powder components of F1 cements and they were confirmed by X-Ray Diffraction Analysis (Fig. 1a). Equation 3 corresponds to the hydrolysis of the DCPD obtained in reaction 1 and Equation 4 to the hydrolysis of unreacted β-TCP. Both could have taken place during the immersion period in SBF.[1] No evidences of them were found in the X-ray diffractograms (Fig. 1b). According to the peaks intensities in the X-ray diffraction patterns (Figures 2a and b), the addition of SA seemed to partially inhibit the completion of the reaction between β-TCP and H_3PO_4 in F1 series. On the other hand, PAA favored the formation of dicalcium phosphate anhydrous (DCPA) instead of DCPD (Figures 2c and d).

For F2 cements the setting reaction is the formation of calcium phosphate dihydrate (CSD) by hydration of CSH as confirmed the X-Ray Diffraction Analysis (Fig. 1c and d). The SHA only acts as non-degradable biocompatible filler, in a readily biodegradable SCD matrix.

Table 2. Expected chemical reactions during setting and immersion in SBF.

Cement	Chemical reactions
F1	(1) $Ca_3(PO_4)_2 + H_3PO_4 + 6H_2O = 3CaHPO_4 \cdot 2H_2O$
	(2) $CaSO_4 \cdot ½H_2O + 1½H_2O = CaSO_4 \cdot 2H_2O$
	(3) $5CaHPO_4 \cdot 2H_2O = Ca_5(PO_4)_3OH + 2H_3PO_4 + 9H_2O$
	(4) $5Ca_3(PO_4)_2 + 3H_2O = 3Ca_5(PO_4)_3OH + H_3PO_4$
F2	(2) $CaSO_4 \cdot ½H_2O + 1½H_2O = CaSO_4 \cdot 2H_2O$
F3	(5) $2Ca_3(PO_4)_2 + 2CaHPO_4 \cdot 2H_2O + H_2O = Ca_8H_2(PO_4)_6 \cdot 5H_2O$
	(6) $Ca_3(PO4)_2 + NaH_2PO_4 + 7H_2O = 3CaHPO_4 \cdot 2H_2O + NaOH$
	(7) $5Ca_8H_2(PO_4)_6 \cdot 5H_2O = 8Ca_5(PO_4)_3OH + 6H_3PO_4 + 17H_2O$
	(8) $CaO, MgO + NaH_2PO_4 = (Ca, Mg)NaPO_4 \cdot 6H_2O$

Table 1. Solid and liquid components of the studied formulations.

Formulation	Solid components (wt-%)								Liquid and mixing ratio (mL/g)
	β-TCP	CSH	SHA	DCPD	CaO	MgO	SA	PAA	
F1	85.7	14.3	—	—	—	—	—	—	H_3PO_4 2 mol/L 0.69
F1 + SA	81.6	13.6	—	—	—	—	4.8	—	H_3PO_4 2 mol/L - 0.69
F1 + PAA	81.6	13.6	—	—	—	—	—	4.8	H_3PO_4 2 mol/L - 0.69
F2	—	33.3	66.7	—	—	—	—	—	H_2O - 0.74
F2 + SA	—	31.7	63.5	—	—	—	4.8	—	H_2O - 0.81
F2 + PAA	—	31.7	63.5	—	—	—	—	4.8	H_2O - 0.81
F3	66.6	—	9.5	12.2	6.7	5.0	—	—	NaH_2PO_4 2 mol/L - 0.60
F3 + SA	63.4	—	9.0	11.6	6.4	4.8	4.8	—	NaH_2PO_4 2 mol/L - 0.60
F3 + PAA	63.4	—	9.0	11.6	6.4	4.8	—	4.8	NaH_2PO_4 2 mol/L - 0.60

CSH Calcium sulfate hemihydrate.

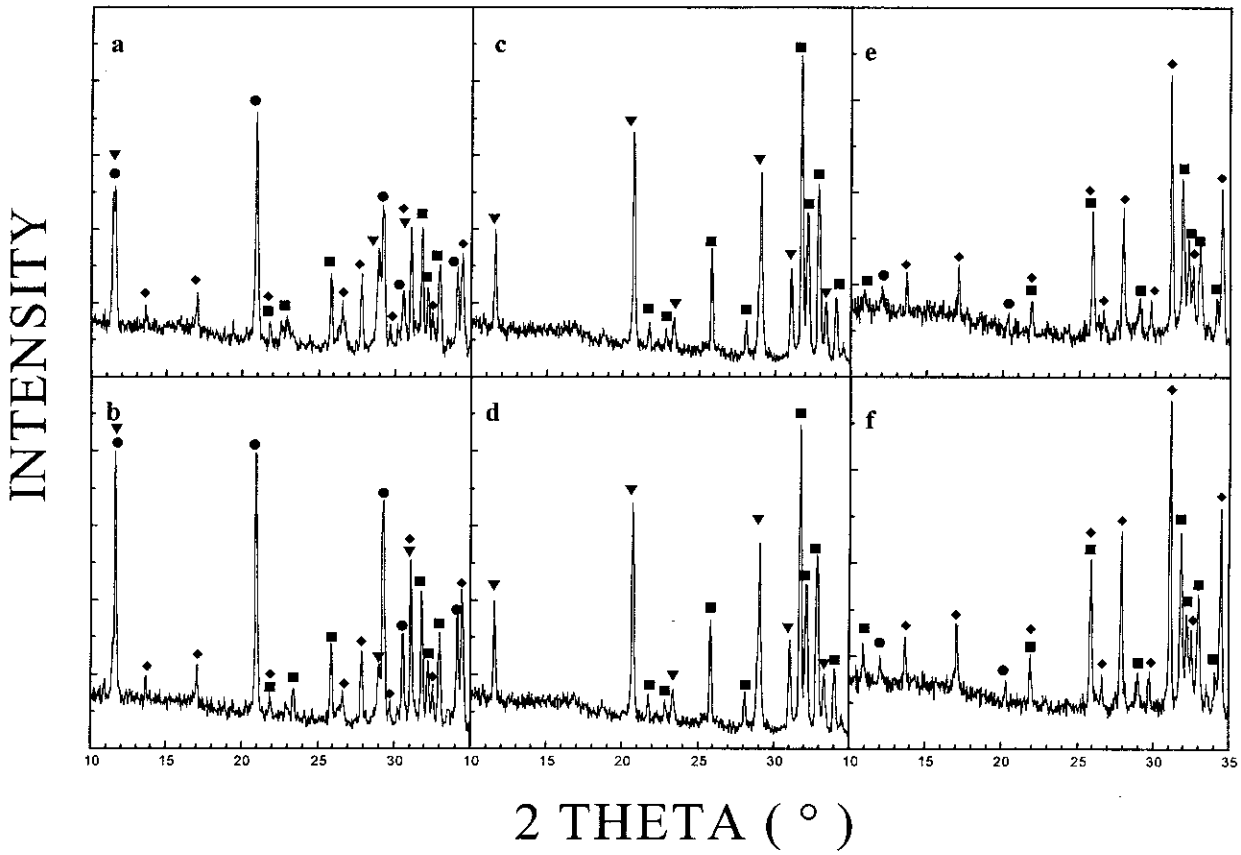

Fig. 1. X-ray diffraction patterns of cements F1, F2 and F3.
a) F1 after 24 h-conditioning at 100 % RH. b) F1 after immersion in SBF for 7 d. c) F2 after 24 h-conditioning at 100 % RH. d) F2 after immersion in SBF for 7 d. e) F3 after 24 h-conditioning at 100 % RH. f) F3 after immersion in SBF for 7 d. ●DCPD; ▼CSD; ■HA; ◆ β-TCP.

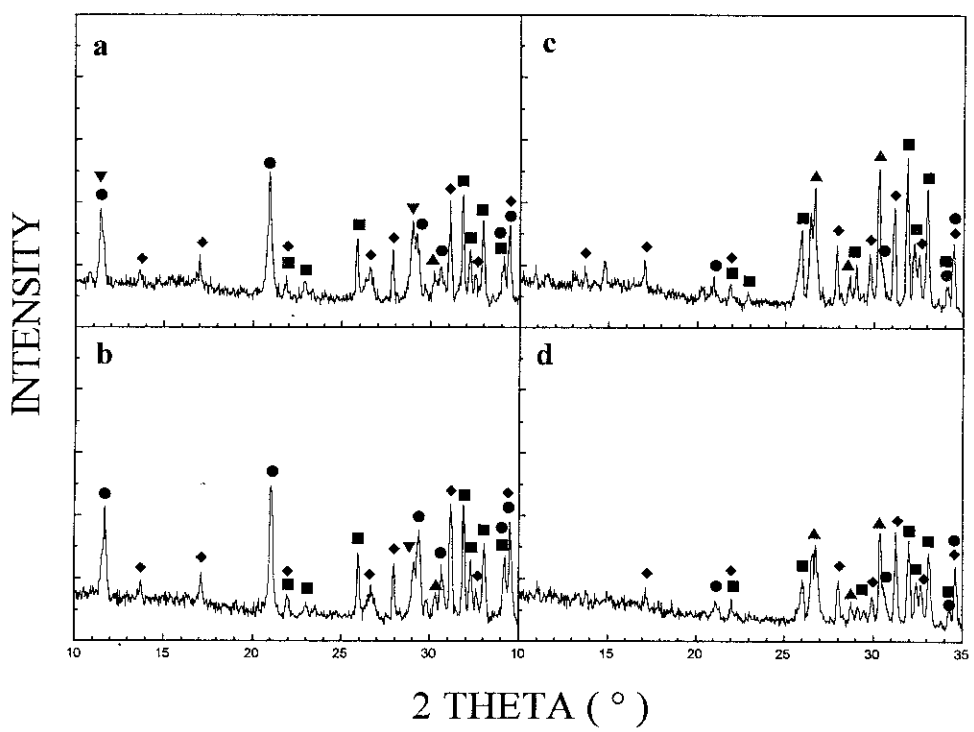

Fig. 2. X-ray diffraction patterns of cements F1 + SA and F1 + PAA.
a) F1 + SA after 24 h-conditioning at 100 % RH. b) F1 + SA after immersion in SBF for 7 d. c) F1 + PAA after 24 h-conditioning at 100 % RH. d) F1 + PAA after immersion in SBF for 7 d. ●DCPD; ▼CSD; ▲DCPA; ■HA; ◆ β-TCP.

In the F3 series the picture is more complex and several reactions (5, 6, 7, and 8) can occur, being those represented by Equations 5, 6, and 8 the most probable during the setting. Immersion in SBF can evoke the reaction of Equation 7. However, X-Ray Diffraction Analysis did not show any evidence of formation of new crystal phases after mixing and conditioning for F3 (Fig. 1e and f).

Table 3 displays the values of setting time, pH, compressive strength, and porosity obtained for the cements.

The presence of 4.8 wt-% SA and PAA in F1 cement did not influence remarkably on the setting time. The same additions on F2 and F3 caused a considerable increasing in setting times.

Values of pH for F1 and F2 cements with and without additives were slightly low. However, the buffer capacity of biological fluids could probably compensate the slight acidity of these cements. On the other hand, F3 cement had a pH frankly alkaline that could evoke necrosis during *in vivo* applications.

Cements F2 and F3 completely decayed after 1-week immersion in SBF, and F2 + SA, F2 + PAA, F3 + SA, F3 +PAA had non-measurable compression strength.

The highest compressive strength was obtained for F1 + SA, after conditioning at 100 % RH, and after 1-week immersion in SBF. As expected, compressive strength directly correlated to porosity for F1 series.

Figure 3a and b displays the SEM images of fracture surfaces of F1 cement, before and after soaking in SBF for 7 d, respectively. Large plate-like crystals of DCPD and CSD needles surrounding particles of unreacted β-TCPare observed. More soluble CSD needles are less abundant after the treatment in SBF. The same CSD needles are present in figures 1 c and d, corresponding to cement F2. SHA particles are visible among the CSD crystalline entanglement. The same effect of CSD dissolution after immersion in SBF is detected. In figures 1 e and f, corresponding to F3, an amorphous phase and large particles of SHA are the unique constituents detected.

The SEM photography of the fracture surface of the F1 + SA is presented in figures 4a and b. A drastic change in fracture surface morphology is evident when comparison with figures 1a and b is made. The crystalline size of the constituent phases and porosity diminished considerably. The lower peak intensities in figure 2a and b in comparison to those in figures 1a and b, and the porosity values (Table 3), confirm the SEM findings.

Table 3. Setting time (ST), pH, compressive strength (σ_c), and porosity (P) of the cements.

Cement	ST	pH	σ_c (MPa)		P (%)	
	(min)		24 h 100 % RH	1 week SBF	24 h 100 % RH	1 week SBF
F1	14	5.94	4.9 (0.2; 5)	2.8 (0.3; 5)	47.4 (2.2; 5)	53.0 (1.2; 4)
F1+SA	12	5.18	7.2 (0.8; 5)	5.2 (0.5; 5)	43.5 (0.8; 3)	50.9 (1.0; 3)
F1+PAA	15	5.19	3.4 (1.0; 5)	1.7 (0.3; 5)	49.4 (1.5; 3)	62.1 (1.8; 3)
F2	20	5.78	1.5 (0.06; 5)	NM	63.7 (1.7; 5)	64.0 (0.2; 3)
F2+SA	> 60	6.80	NM	NM	ND	ND
F2+PAA	> 60	6.43	NM	NM	ND	ND
F3	20	11.28	0.3 (0.06; 5)	NM	51.4 (1.4; 3)	53.8 (0.3; 3)
F3+SA	> 60	ND	NM	NM	ND	ND
F3+PAA	> 60	ND	NM	NM	ND	ND

ND Non-determined. NM Non-measurable.
Standard deviations and number of replicas in parentheses.

For F1 + PAA (Figures 4c and d) a similar picture is observed but in this is case porosity is greater than for F1 + SA (Table 3).

A possible explanation for the reinforcing effect of SA in F1 cement is the formation of fibrous alginic acid that would act as a reinforcing fiber in the inorganic cement matrix. In fact, in figure 2a crystals and pores seem to be partially covered by an amorphous substance, possibly alginic acid. This is supported by the fact that the reinforcing effect was only observed for F1 cement with lower pH and for SA whose corresponding acid is insoluble in water, and not for the soluble PAA. Further work should be conducted to elucidate the current reinforcing mechanism for this system.

This reinforcing effect apparently overcomes the inhibiting effect on the transformation of β-TCP into DCPD, suggested by the X-Ray Diffraction results (Fig. 1).

CONCLUSIONS

The addition of SA to F1 cement seems to be a promising way to improve the mechanical strength. To elucidate the reinforcing mechanism further work needs to be conducted. PAA has deleterious effect on the properties of F1, F2, and F3 cements.

ACKNOWLEDGEMENTS

This work was financially supported by the National Research Council (CNPq) RHAE Grant No. 460.461/96-6, the Third World Network of Scientific Organizations (TWNSO) Joint Research Project No. 18/95, and the Cuban Ministry of Science, Technology and Environment Project No. 00409047. This work is part of the activities of the Joint Project CYTED VIII.6 "Biomateriales compuestos con carga de hidroxiapatita".

BIBLIOGRAPHY

1. Chow L.C. Calcium phosphate cements: Chemistry and applications, in LeGeros R.Z. and LeGeros J.P, eds., Bioceramics, Vol. 11 (Proceedings of the International Symposium on Ceramics in Medicine), New York, World Scientific, 45-49, 1998.
2. Driessens F.C.M., Fernández E., Ginebra M.P., Boltong M.G., Planell J.A. Calcium phosphates and ceramic bone cements vs. acrylic cements, **Anal. Quim. Int. Ed., 93**, S38, 1997.
3. Khairoun I., Driessens F.C.M., Boltong M.G., Planell J.A. and Wenz R.A. Addition of cohesion promotors to calcium phosphate cements, **Biomaterials, 20**, 393, 1999.
4. Cherng A., Takagi S. and Chow L.C. Effects of hydroxypropyl methylcellulose and other gelling agents on the handling properties of calcium phosphate cement, **J. Biomed. Mater. Res., 35**, 273, 1997.
5. Parsons J.R., Rici J.L., Alexander H., Bajpai P.K. Osteoconductive composite grouts for orthopedic use, **Ann. N. Y. Acad. Sci., 523**, 190, 1988.
6. Lemaitre J., Mirtchi A.A., Mortier A. Calcium phosphate cements for medical use: State of the art and perspectives of developmen, **Sil. Ind. Ceram. Sci. Technol., 52**, 141, 1987.

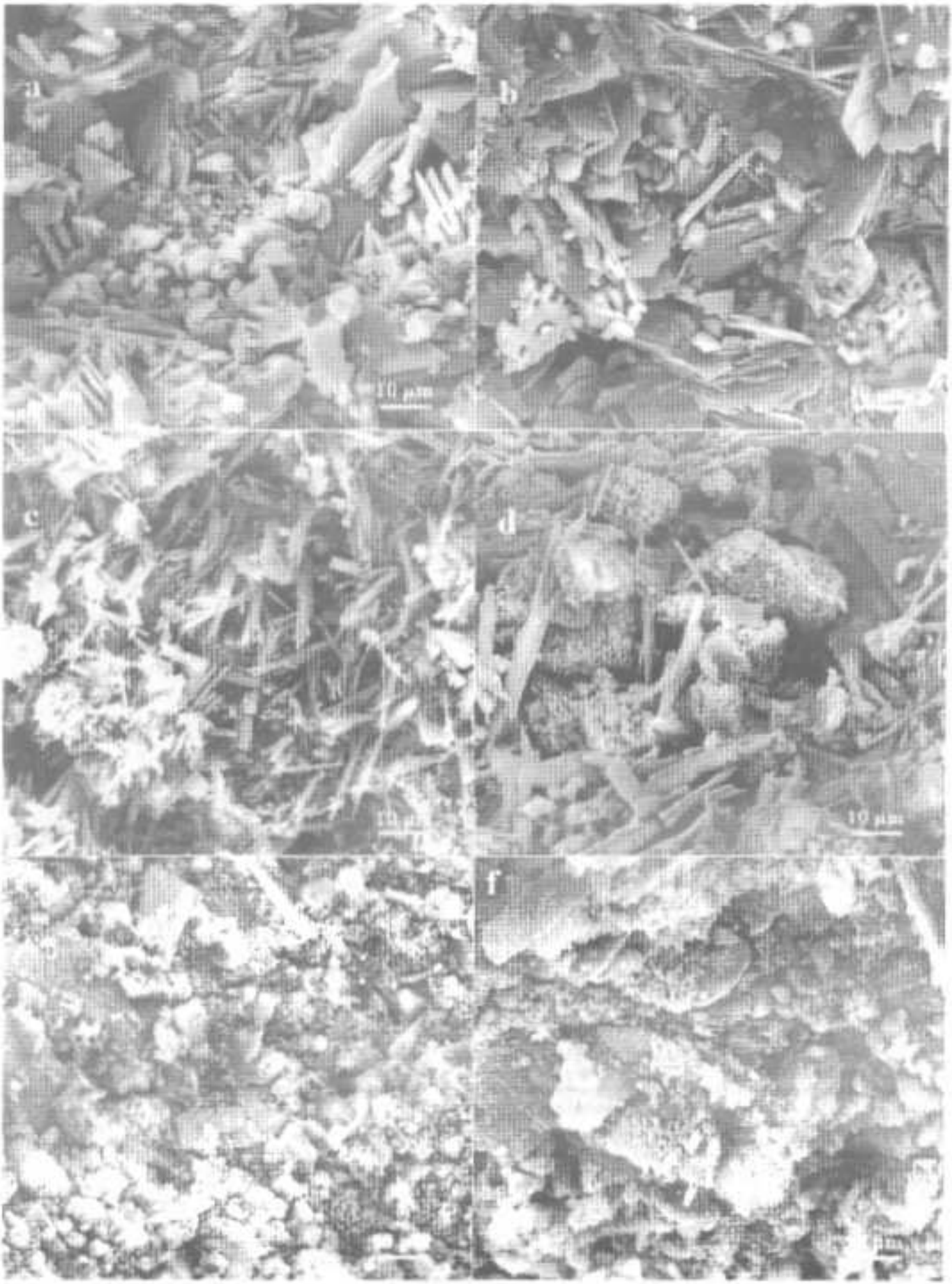

Fig. 3. SEM images of fracture surfaces of cements F1, F2 and F3.
a) F1 after 24 h-conditioning at 100 % RH. b) F1 after immersion in SBF for 7 d. c) F2 after 24 h-conditioning at 100 % RH. d) F2 after immersion in SBF for 7 d. e) F3 after 24 h-conditioning at 100 % RH. e) F3 after immersion in SBF for 7 d. 1 000 X.

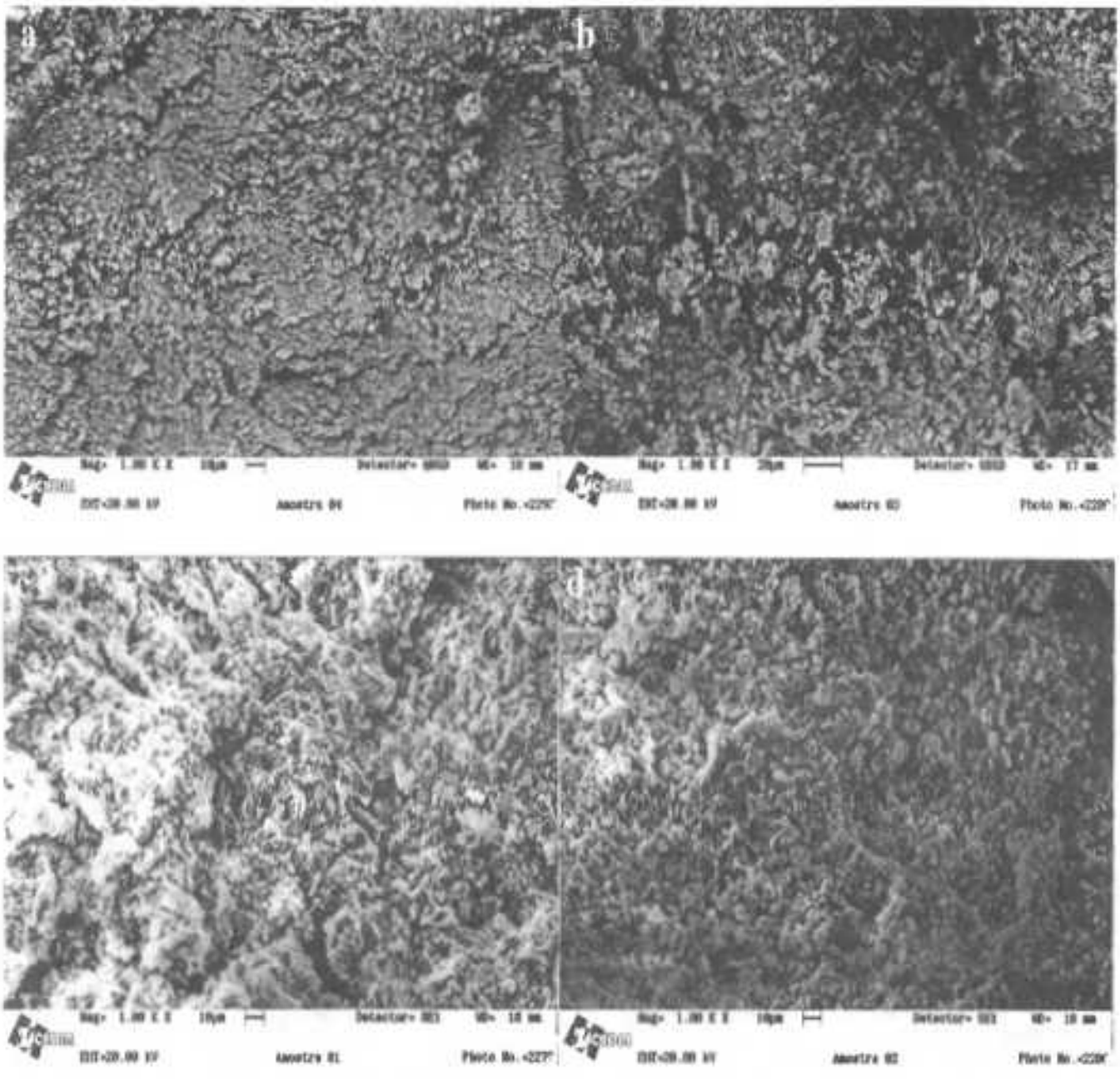

Fig. 4. SEM images of fracture surfaces of cements F1 + SA and F1 + PAA.
a) F1 + SA after 24 h-conditioning at 100 % RH. b) F1 + SA after immersion in SBF for 7 d. c) F1 + PAA after 24 h-conditioning at 100 % RH. d) F1 + PAA after immersion in SBF for 7 d. 1 000 X.

7. Frayssinet P., Gineste L., Conte P., Fages J. and Rouquet N. Short-term implantation effects of a DCPD-based calcium phosphate cement, **Biomaterials**, 19, 971, 1998.

8. Driessens F.C.M., Boltong M.G., Bermúdez O., Planell J.A., Ginebra M.P., Fernández E. Effective formulations for the preparation of calcium phosphate bone cements. **J. Mater. Sci. Mater. Med.**, 5, 164, 1994.

9. Bohner M., Lemaitre J., Ring T.A. Effect of sulfate, pyrophosphate, and citrate ions on the physichochemical properties of cements made of β-TCP - H_3PO_4-H_2O mixtures, **J. Am. Ceram. Soc.**, 79, 1427, 1996.