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The growth of calcium phosphate on ceramic surfaces

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Calcium phosphate ceramics are very important materials for prosthetic applications because of their excellent biocompatibility. The chemical composition of the ceramics is determining, both with respect to their capability of inducing calcium phosphate formation and regarding the crystalline phase formed. From a series of porous ceramics based on hydroxyapatite (HAP) containing metal oxides, it was found that only those containing ZrO_2 stabilized with 8% Y_2O_3 were able to induce calcium phosphate formation upon introduction into calcium phosphate supersaturated solutions. The overgrowing phase was increasingly crystalline, did not show any other characteristic X-ray peaks and infrared bands than those pertinent to a-tricalcium phosphate and had a molar Ca : P ratio of 3 : 2. Kinetics analysis with respect to $Ca(PO_4)_2$ yielded an apparent order of reaction of 5.0 ± 0.5, suggesting polynuclear nuclei above nuclei growth. The surface energy calculated from the kinetics data for the crystalline overgrowth was found to be 88 mJ m^{-2}.

1. Introduction

Calcium phosphate ceramics are an attractive category of prosthetic materials because of their osteophylic character. The properties of these materials depend on their composition, the presence of trace impurities and physical characteristics such as porosity and particle size [1, 2]. Because of their excellent conformity with biocompatibility requirements, tricalcium phosphate, tetracalcium phosphate and hydroxyapatite have been used for implantation applications [3]. Investigations concerning the relationship between the calcium to phosphate molar ratios in the solid implant materials, revealed that resorbability of the material increased at lower ratios [4]. More recent studies, however, have suggested that it is not necessary for an equilibrium to be established between the surface of the calcium phosphate ceramic and the surrounding biological aqueous medium [5]. The large specific surface area, usually shown by porous materials is another characteristic that may be decisive in the enhancement of overgrowth of bone-like material [6]. The method of preparation of the ceramic materials is very important for their final chemical composition, which in turn influences their behaviour as effective nucleators of the bone mineral [7].

In the present work we have attempted to synthesize and characterize ceramic materials based on synthetic hydroxyapatite. Subsequently we have examined their capability of inducing calcium phosphate precipitation. The kinetics and the stoichiometry of the crystalline overgrowth were also investigated.

2. Experimental procedure

2.1. Ceramic materials preparation

Hydroxyapatite (HAP; Sigma Co.), designated type 1, was used in our preparations. 22.0 g HAP were mixed with 8.1 g polyvinylchloride (PVC) and 7.2 g ZrO_2 (stabilized with Y_2O_3, 8%). The three components were thoroughly ground in a mortar and the powder was subsequently made into pellets using an infrared die. The pellets, 280 mg each, were made by applying a pressure of 1400 MPa. Next, the pellets were heated at 900° C at a heating rate of 10° C min^{-1}, for 12 h. Following the heating period, the pellets were brought back to room temperature again at 10° C min^{-1} and they were submitted to dry impregnation with 0.1 N HNO_3. The pellets were again heated to 250° C for 1 h, at a constant heating rate of 10° C min^{-1} in a chromatographic oven. Finally, the pellets were again heated at 1200° C for 2 h and following cooling (again at 10° C min^{-1}) they were ready for use in the crystallization experiments. The specific surface area (SSA), determined by a multiple point BET method (Sorptometer, Perkin Elmer model 212D) in a specific cell, was found to be 0.92 m^{2}g^{-1}. The pore size distribution, as estimated from the particle size distribution of PVC done by optical microscopy, was found to be 59 ± 30 μm. The porosity in the pellets used for the crystal growth experiments was found to be 0.65 ml g^{-1}.

Another batch of ceramic pellets consisting of 30 g HAP I, 15 g PVC and 10 g TiO_2 subjected to the same process, was also prepared. The BET SSA of this sample was found to be 0.89 m^{2}g^{-1} and its porosity 0.61 ml g^{-1}.

Finally, 30 g HAP powder were subjected to the same treatment and were made pellets.

Powdered samples of all materials prepared were examined by infrared spectroscopy (Perkin Elmer 137), X-ray diffraction (Phillips 1300/00) and by

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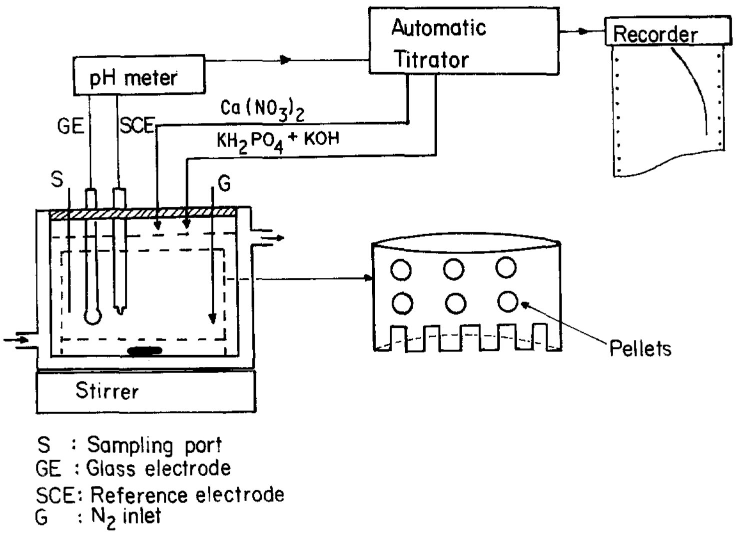

Figure 1 Experimental procedure for the investigation of the mineralization of ceramic pellets under conditions of sustained supersaturation.

chemical analysis for calcium by atomic absorption spectroscopy (Varian 1200) and for phosphate by a modified vanadomolybdate method [8] spectrophotometrically (Varian, Cary 219).

2.2. Crystallization experiments

All experiments were done at 25.0 ± 0.1° C, in a thermostatted double walled pyrex vessel of 0.250 dm^3 total volume. Stock solutions of calcium nitrate were prepared from solid reagent (Merck, Puriss) and standardized as described in detail elsewhere [9]. Standard phosphate solutions were prepared from potassium dihydrogen phosphate (Riedel de Häen, Purum), following drying at 105° C. Potassium hydroxide solution was made from standard solutions (Merck, Titrisol). All solutions were made using triply distilled, CO_2-free water and were filtered through 0.1 μm (Gelman) membrane filters. The supersaturated solutions were prepared in the double walled vessel by mixing equal volumes of calcium and phosphate solutions up to a total volume of 0.200 dm^3. Presaturated nitrogen at 25° C was bubbled through the solutions throughout the experiments. The pH was adjusted to 7.40. The stability of the solutions used was verified by the constancy of pH over several hours (at least 4 h), following which, a polyethylene holder with 20 pellets mounted by means of an inert wax was introduced. The total surface area of the pellets used was 2.9 m^2 for each experiment.

Upon introduction of the pellet holder with the pellets, into the supersaturated solutions, the crystallization process started without any appreciable induction period only for the HAP/ZrO_2 (Y_2O_3) ceramic. The initiation of the precipitation process resulted in proton release which, in turn, triggered the addition of titrants from two mechanically coupled burettes of an appropriately modified pH-state (Metrohm). The solution pH was monitored by a combination glass/saturated calomel electrode (Metrohm), calibrated before and after each experiment with NBS buffer solutions [9]. The calcium phosphate and potassium hydroxide titrants had the stoichiometry of hydroxyapatite ($Ca_5(PO_4)_3OH$, HAP) 5:3:1. The volume of titrants added as a function of time was

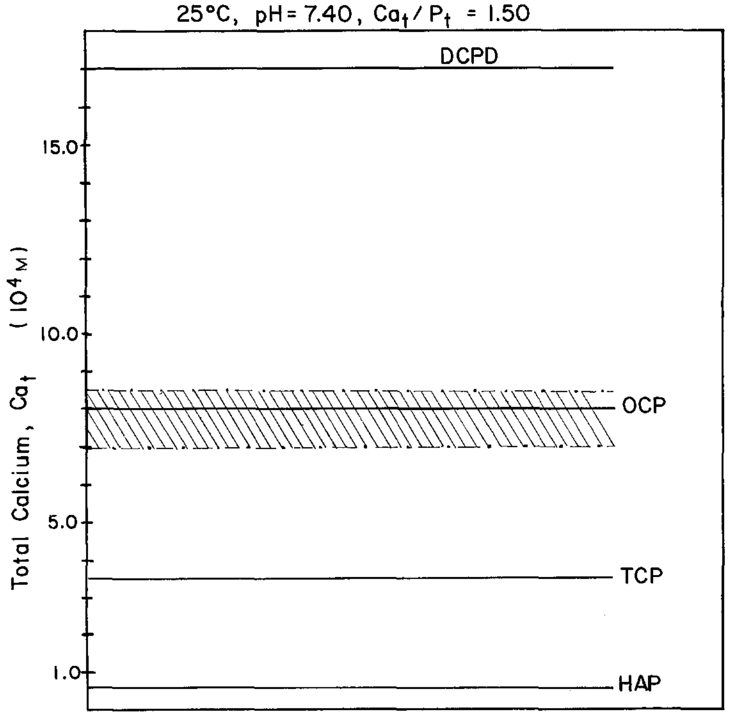

Figure 2 Experimental conditions for the mineralization of the ceramic pellets.

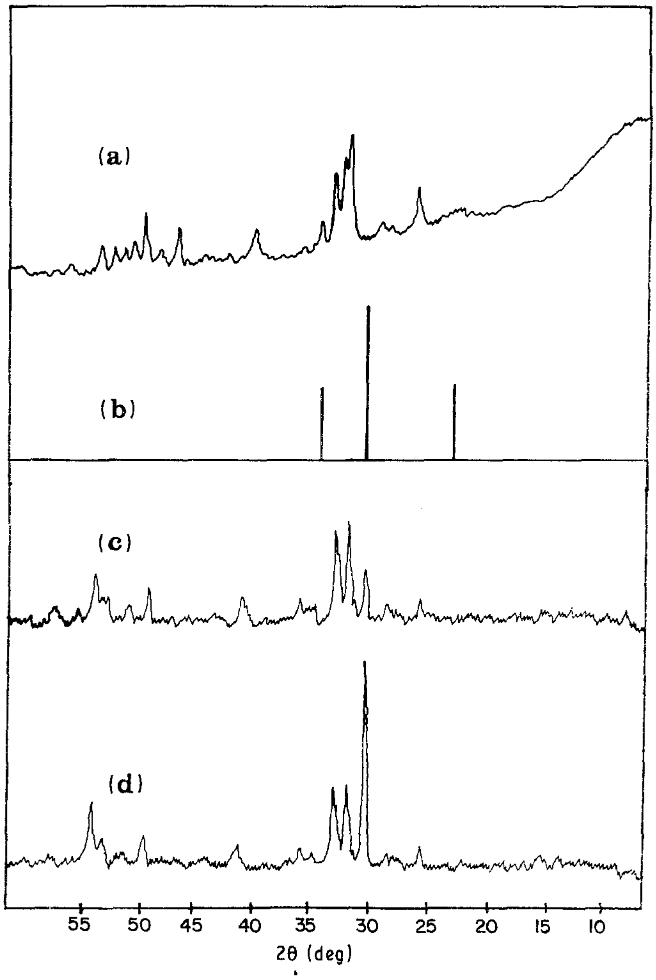

Figure 3 Powder X-ray diffraction spectra of (a) HAP, (b) a-TCP ASTM File no. 29-359, (c) heated HAP/ZrO_2 (8% Y_2O_3) ceramic used as matrix for overgrowth, (d) heated HAP/ZrO_2 (8% Y_2O_3) ceramic after the overgrowth of $Ca_3(PO_4)_2$.

recorded and the rates were measured directly from the slope of the linear plots. Samples were withdrawn randomly from the solution, filtered through membrane filters (Gelman, 0.1 μm) and the filtrates were analysed for calcium and phosphate, in order to ensure constancy of the solution supersaturation. The experimental layout is shown schematically in Fig. 1.

3. Results and discussion

The experiments in the present work were done under conditions such that the supersaturated solutions were mainly supersaturated with respect to HAP and *b*-tricalcium phosphate (*b*-$Ca_3(PO_4)_2$, TCP). The experimental conditions correspond to the shaded area of Fig. 2. In all cases when the ceramic materials consisting of either calcium phosphate 2 (HAP/TiO_2 heated to 1200° C), or calcium phosphate 3 (HAP heated to 1200° C) was employed, no reaction was observed. It is interesting to note that the powder X-ray diffraction spectra of the calcium phosphate 2 and calcium phosphate 3 did not show the characteristic 4 4 1, 1 7 0 peak of a-TCP, shown in calcium phosphate 1, as may be seen in the spectra of Fig. 3. The high-temperature a-TCP is probably stabilized by the presence of ZrO_2.

The supersaturation calculations were done by an iterative procedure of successive approximations for the ionic strength, taking into account the appropriate equilibria, mass balance and the electroneutrality conditions [10, 11]. The driving force for the formation of each of the calcium phosphate polymorphs, x, is the Gibbs free energy change, ΔG_x, for the transfer from the supersaturated solution to equilibrium

$$\Delta G_x = -\frac{RT}{v}\ln\left(\frac{IP}{K_s^0}\right)_x = -\frac{RT}{v}\ln\Omega_x \quad (1)$$

where $(IP)_x$ is the activity product at the experimental conditions and $K_{s,x}^0$ the activity product of the polymorph at equilibrium; Ω_x is the saturation ratio of the polymorph x, consisting of v ions. The experimental conditions are detailed in Table I. As may be seen, the calcium phosphate ceramic 1 (HAP/$ZrO_2(Y_2O_3)$, or

TABLE I Initial conditions for the crystallization of tricalcium phosphate on calcium phosphate-ZrO_2 pellets at 25° C; molar ratio of total calcium to phosphate = 1.50, pH 7.40; total volume of working solution 200 ml

Expt. no.	T_{Ca} (mM)	ΔG_{HAP} (kJ mol^{-1})	ΔG_{TCP} (kJ mol^{-1})	ΔG_{OCP} (kJ mol^{-1})	ΔG_{DCPD} (kJ mol^{-1})	Growth rate (10^9 mol min^{-1} m^{-2})
1	0.850	−4.91	−1.80	−0.12	+1.23	1.319
2	0.800	−4.81	−1.79	−0.02	+1.34	0.913
5	0.775	−4.75	−1.63	+0.04	+1.40	0.637
3	0.750	−4.69	−1.57	+0.09	+1.46	0.548
4	0.700	−4.58	−1.44	+0.20	+1.59	-

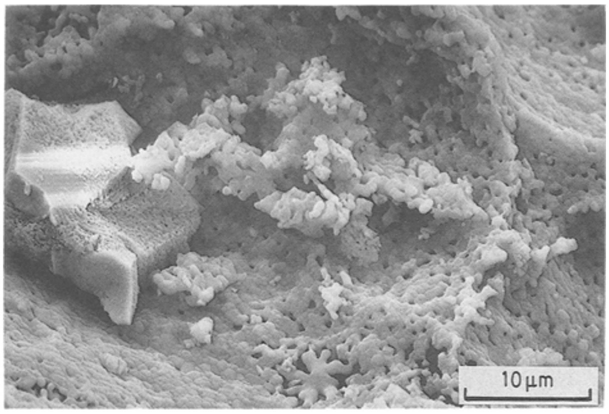

Figure 4 Scanning electron micrograph of the ceramic material after the mineral deposition.

TABLE II Growth of TCP on calcium phosphate–ZrO_2 ceramic; pH 7.40, T = 298.15 K, Ca/P = 1.5

Expt. no.	Time (h)	T_{Ca} (mM)	T_P (mM)	Amounts of TCP deposited (mg)
1	0	0.850	0.567	0
	20	0.860	0.561	1.25
	46	0.860	0.573	3.15
2	0	0.800	0.533	0
	21	0.804	0.523	0.96
	46	0.801	0.525	2.24

CPC1), induced the precipitation of crystalline calcium phosphate on the pellets, the rates of precipitation increasing with supersaturation. As we anticipated the formation of HAP, we prepared the titrants according to the stoichiometry for this salt, i.e. Ca : P : OH = 5 : 3 : 1, as described in Section 2. However, the solution composition could not be kept constant in all of the crystallization experiments, thus suggesting that a phase other than apatite might be forming. As a result, we changed the titrant solution and the Ca : P ratio in the working supersaturated solutions to 3 : 2, which is the case for tricalcium phosphate. Fig. 4 shows a scanning electron micrograph of the ceramic material following the mineral deposition. Under these conditions, analyses showed that the solution supersaturation was maintained for extended periods of time, as may be seen in Table II. Subsequent kinetics analysis was done with respect to *b*-TCP, according to Equation 2 [12]

$$R = ks\{[(Ca^{2+})^3(PO_4^{3-})^2]^{1/5} - (K_s^0)^{1/5}\}^n \quad (2)$$

In Equation 2 k is a specific rate constant, s a constant depending on the active growth sites, n the apparent order of reaction and the parentheses denote activities. Logarithmic plots of the rate R as a function of the left-hand side of Equation 2 yielded a linear plot, shown in Fig. 5. From the slope of the resulting straight line, an apparent order of $n = 5.0 \pm 0.5$ is obtained. This high value for the apparent order of the precipitation process, is typical for the polynuclear nuclei above nuclei crystal growth model [13]. Using this model, the surface energy of the overgrowing phase estimated from kinetics data, according to Equation 3

$$R = A\sigma_x^{5/6} \exp(-B/\sigma_x) \quad (3)$$

where $\sigma_x = (\Omega_x^{1/5} - 1)$, A is a constant and B is a function of the surface energy of the overgrowth, σ_v, given by Equation 4

$$B = 4\pi/3\,(\alpha^2\sigma_v/kT) \quad (4)$$

α is taken equal to 0.3 nm. The value of σ_v = 88 mJ m^{-2} estimated from the straight line resulting from logarithmic plots according to Equation 3, shown in Fig. 6, is typical for sparingly soluble salts [14].

Examination of the solid material of the pellets before and after deposition by infrared and powder X-ray spectroscopy gave the spectra seen in Figs 7 and 3. Examination of the infrared spectra at 615 to 500 cm^{-1}, shows that the powder thermal treatment resulted in conversion of HAP to a-TCP [15]. Following growth, infrared spectra did not reveal the formation of any other crystalline phase. It is possible that the initially formed a-TCP which forms upon heating HAP (at 1125° C or even at 600° C [15]) favours the overgrowth of a mixture of non-stoichiometric apatite and a-TCP which cannot be distinguished further due to the limited extent of the crystal growth process in

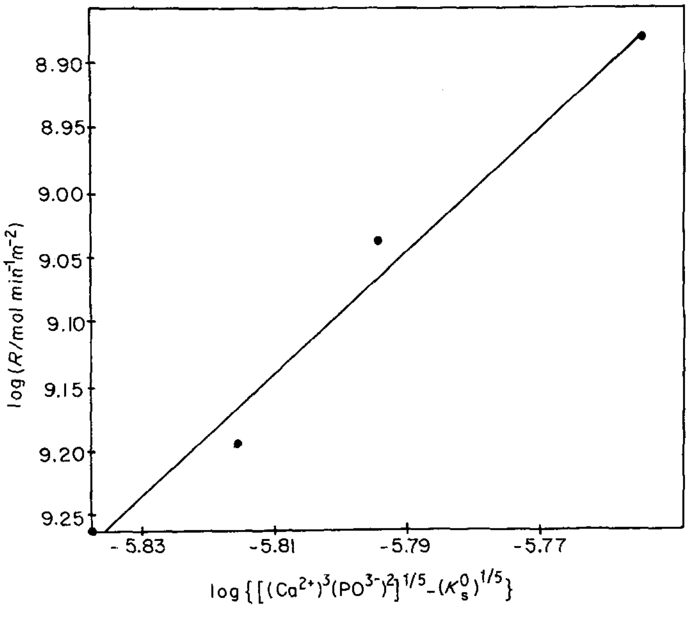

Figure 5 Kinetics plots for the growth of $Ca_3(PO_4)_2$ on heated HAP/ZrO_2 (8% Y_2O_3) ceramic pellets.

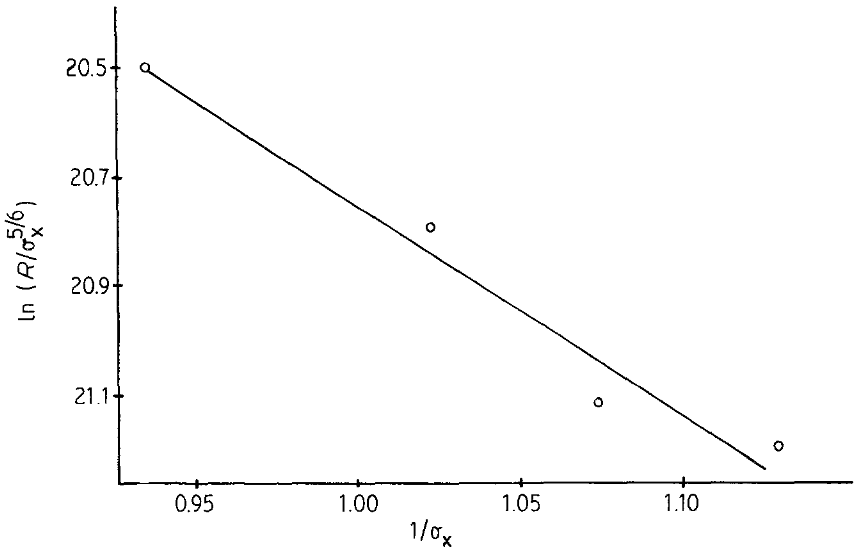

Figure 6 Logarithmic plot for the growth of $Ca_3(PO_4)_2$ on heated HAP/ZrO_2 (8% Y_2O_3) ceramic pellets according to nuclei above nuclei model.

the samples examined. The powder X-ray diffraction spectra shown in Fig. 3, show that as a result of the crystallization process the 4 4 1, 1 7 0 peak, if the a-TCP was present in the starting ceramic pellets is enhanced. This is supporting evidence that a crystalline phase similar to a-TCP is being deposited. Because a-TCP is a calcium phosphate polymorph, unstable in aqueous solutions [16] there is no reliable thermodynamic solubility product available. Therefore the supersaturation of the solutions under our experimental conditions could not be evaluated.

Although the limited extent of growth precludes a definite direct analysis of the overgrowth with the means available in our laboratory, we may conclude that:

(1) the ceramic material prepared was made active with respect to the induction of the growth of calcium phosphate by the presence of ZrO_2 stabilized by Y_2O_3;

(2) the calcium phosphate phase growing on this material has a molar Ca : P ratio at 3 : 2, showing characteristic peaks of a-TCP in the X-ray spectra and at the 500 to 630 cm^{-1} bands of the infrared spectra.

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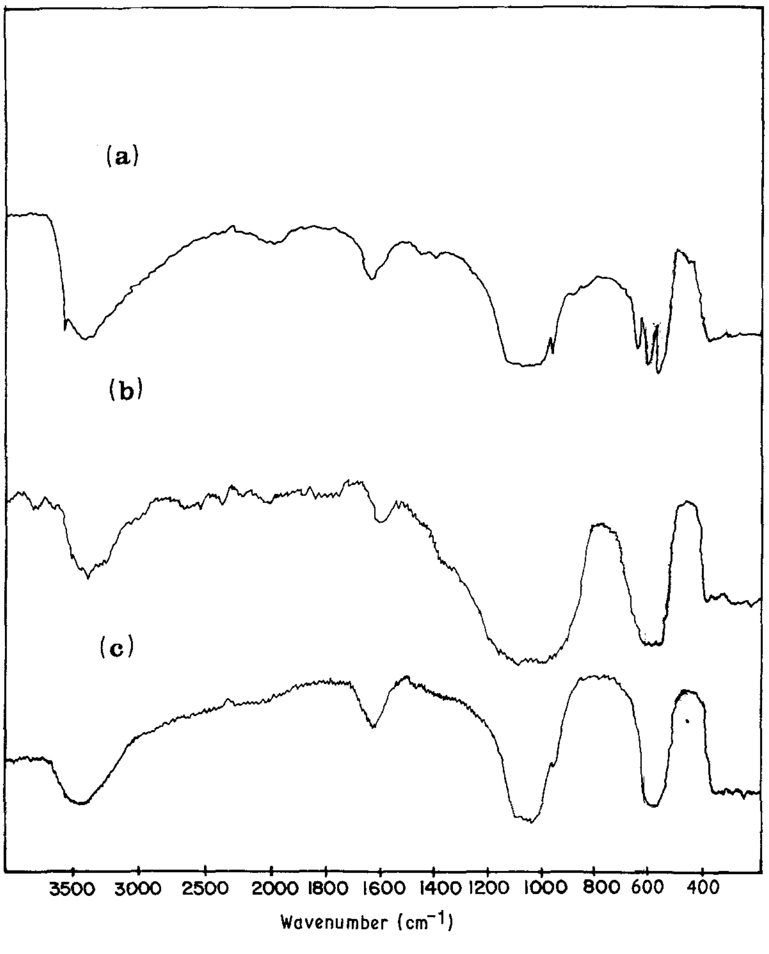

Figure 7 Infrared spectra of (a) apatite (Sigma Co. I), (b) heated HAP/ZrO_2 (8% Y_2O_3) ceramic before mineral deposition, (c) heated HAP/ZrO_2 (8% Y_2O_3) ceramic following crystallization of $Ca_3(PO_4)_2$.

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