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Thin hydroxyapatite coatings via sol–gel synthesis

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Production of hydroxyapatite coatings using an alkoxide-based sol–gel route requires control of solution aging time and heating schedule. ^{31}P nuclear magnetic resonance spectroscopy was used to investigate the changes during aging of the sol and thermal gravimetric analysis employed to study the behavior of the xerogels as a function of temperature, while final products were determined using X-ray diffraction. Results from ^{31}P nuclear magnetic resonance spectroscopy and thermal analysis revealed that sols must be aged for at least 24 h to complete the reaction of the two reactants. Deposition of the sol for coating production will then yield monophasic hydroxyapatite. Coatings produced from sols aged for less than 24 h yielded calcium oxide in addition to hydroxyapatite. Prefiring is necessary to remove most of the residual organic materials. Final heating up to 800 °C produces crystallization at 550 °C and removal of the remaining organic constituents for the formation of a thin hydroxyapatite layer. *© 1998 Kluwer Academic Publishers*

1. Introduction

Hydroxyapatite coatings continue to be used as bioactive surfaces on titanium-based alloys for stronger bone bonding and stimulation of bone growth towards the implant surface. Thermal spraying has been the main technique used for coating production and has been faced with challenges of producing a controllable resorption response in clinical situations. While thermally sprayed coatings are continually being improved, other technologies capable of producing thinner coatings are being investigated. This is being driven by the finding on sputtered hydroxyapatite coatings that a submicrometre coating thickness is sufficient to stimulate carbonate apatite deposition under *in vivo* conditions [1].

Coating processes capable of producing thin coatings include pulsed-laser deposition [2] and sputtering [3] which, like thermal spraying, involves high-temperature processing. Other technologies such as *in vitro* methods [4], electrodeposition [5] and sol–gel [6–11] utilize lower temperatures and avoid the challenges associated with the structural instability of hydroxyapatite at elevated temperatures [12].

Sol–gel processing is classed as an intermediate temperature technique which, like other techniques, can produce either an amorphous or crystalline coating, but more importantly results in stoichiometrically homogeneous coating. The lower processing temperature is an advantage insofar that it avoids the 883 °C phase transition that occurs in the titanium alloys used in biomedical devices.

A major processing stage involves solution chemistry, whereby a sol is produced from suitable alkoxides or salts to yield a hydroxyapatite composition upon heating. The chemical phase purity of the coating is thus determined early in the process and is dictated by the purity of the precursor materials and the aging time of the solution. Firing of the coating then involves removal of the organic constituent to produce hydroxyapatite. This work will discuss the changes occurring during the aging period and also upon heating to produce a uniform hydroxyapatite coating.

2. Materials and methods

2.1. Xerogel preparation

Solution preparation was conducted in a moisture-free atmosphere owing to the hygroscopic nature of the reactants based on the method outlined by Masuda *et al.* [13]. High-purity calcium diethoxide (200 mg, Kojundo Chemical Laboratory, Saitama, Japan) was dissolved with the aid of a magnetic stirrer in a vial containing ethanol (BDH, Kilsyth, Australia) and ethane diol (BDH, UK). A quantity of 153 mg triethyl phosphite (Sigma Chemical Co., St. Louis, MO, USA) was added to another vial consisting of ethanol and ethanediol. The phosphite solution was then added dropwise to the calcium-containing solution to obtain a Ca:P molar ratio of 1.67:1, and the resultant mixture was stirred for a period of 10 min at ambient temperature. This solution was allowed to age for periods up to 24 h. The course of the reaction

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was followed with ^{31}P nuclear magnetic resonance spectroscopy to determine the changes taking place during the maturing stage.

Another set of solutions was prepared with comparable aging times, removed from the dry box, and hydrolyzed at 70 °C in an oven for about 48 h until dry. These xerogels were analyzed with thermal analysis and pyrolysis gas chromatography to investigate the thermal behavior and evolved gases upon heating.

2.2. Characterization of sols and xerogels

High-field nuclear magnetic resonance (NMR) spectra were obtained on a 300 DRX Bruker (Bruker-Spectrospin, Sällanden, Switzerland) spectrometer operating at 121.495 MHz for ^{31}P using a 60606 Hz sweep width and a 90° (8.1 μs) pulse. Data was collected in 16 K points using 16 scans. Pulse delay was 2 s with an acquisition time of 0.135 s. All ^{31}P spectra were taken with proton decoupling and data acquired at 300 K. Orthophosphoric acid (85 vol%) was chosen as an external reference. Both the triethyl phosphite (containing $\leqslant 1\%$ triethyl phosphate $[(C_2H_5O)_3P(O)]$ and $\leqslant 1\%$ diethyl phosphite $[(C_2H_5O)_2P(O)H]$), and the hydroxyapatite sol, were examined by ^{31}P NMR.

The gels were crushed in a mortar and pestle and analyzed with thermogravimetric analysis and differential thermal analysis using an SDT 2960 simultaneous thermal analyzer (TA Instruments, Newcastle, USA). The powder was heated at 10 °C min^{-1} to 500 °C, held for 15 min at that temperature and subjected to heating at a slower rate (3.3 °C min^{-1}) to 1000 °C in a stagnant air atmosphere.

Gas pyrolysis chromatography using a Hewlett Packard 5890 GC coupled to 5970 series mass selective detector was used to determine the volatile species evolved in the heating process up to the temperature range used for coating synthesis. The dried gel was pyrolyzed at 500 and 800 °C and the evolved gases analyzed with a mass spectrometer.

2.3. Coating production

Square titanium coupons ground and polished to a surface finish of 0.05 μm were used as substrates. Before coating, the coupons were ultrasonically cleaned twice with acetone and then twice in ethanol. A quantity of 0.05 ml aged unhydrolyzed solution was taken from the vial and placed on the polished coupon surface. A spin coater (Headway Research, Garland, USA) was used at a speed of 2500 r.p.m. for 10 s to produce the coating. The applied layer was hydrolyzed in an oven at 70 °C for 10 min and then prefired at 500 °C for 5 min. A total of seven layers were deposited before final firing to 600, 700, 800 and 900 °C for 10 min.

2.4. Characterization of coatings

Coatings were analyzed using X-ray diffraction with a grazing angle attachment and an incident angle of 1°. The crystallization temperature determined in differential thermal analysis was confirmed with X-ray diffraction on a Siemens (Karslruhe, Germany) D-5000 diffractometer with Cu$K\alpha$ radiation. The diffraction pattern was collected over the 2θ range of 20°–40° with an acquisition time of 10 s at each step of 0.02°.

Scanning electron microscopy was performed in a Jeol JSM-6300 using a field emission gun as the electron source. Coatings fired to different temperatures were coated with carbon before analysis.

3. Results and discussion

Fig. 1 shows the ^{31}P NMR spectra of the sol–gel solution as a function of aging time following initial mixing. The bottom spectrum labeled "No age" was recorded within one hour of mixing: it displays a sharp and intense peak at a chemical shift of +139 p.p.m. The "no age" spectrum is similar to that observed for the unreacted $P(OEt)_3$ blank with the +139 p.p.m. peak in agreement with the literature assignment for this compound [14, 15]. As the solution ages, a broad doublet peak with maxima at −99 and −105 p.p.m. grows in intensity. No further changes in the spectra were observed between 1 and 7 d aging. The doublet is assigned to phosphorous in the chemical state $[Ca–O–PO_3]_n$, where two of the oxygen atoms in the PO_3 are bound to additional phosphorous or calcium atoms in the sol [16]. The shift in the primary phosphorous peak from +139 to near −100 p.p.m. is consistent with a change in oxidation state from P(III) to P(V). The NMR data indicate that aging is required by the kinetics of the reaction between the two alkoxide precursors and condensation steps of the sol–gel synthesis. This aging period is typical for sol–gel systems [17].

Also observed in Fig. 1 for the aged solutions is a peak appearing at +135 p.p.m. This peak suggests the formation of a $EtO–Ca–O–P(OEt)_2$ compound in

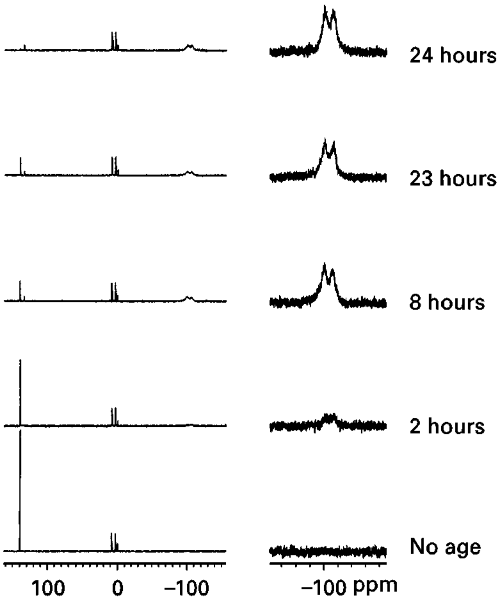

Figure 1 ^{31}P Nuclear magnetic resonance spectra of solutions after 0, 2, 8, 23 and 24 h aging showing a decrease in sharp peak intensity at 139 p.p.m. and the appearance of a broad doublet at − 100 p.p.m. with time. An enlarged view of the broad doublet is shown.

solution, which corresponds to the combination of the two alkoxides. When the 24 h aged solution is heated in steps from 300–340 K during the NMR measurement, the peak intensity at 135 p.p.m. increases at the expense of the broad doublet peak at −100 p.p.m. (data not shown). When the solution is cooled, it displays the original NMR spectrum of the 24 h aged solution, Fig. 1. This temperature dependence indicates that the combination of the calcium and phosphorous diethoxides is the rate-limiting step in the aging of hydroxyapatite sols, whereas the condensation step is rapid and reversible. The merging of the doublet with increased temperature further indicates rearrangement of the sol particle in solution.

The peaks from −1 to +10 p.p.m. correspond to phosphorous impurities in the $P(OEt)_3$ reagent and intermediates in the sol–gel reaction. Previous ^{31}P NMR experiments on titanium phosphate sol–gel reactions attributed peaks in this region to $O{=}P(OEt)_{3-x}(OH)_x$ compounds [18]. These compounds may also exist as intermediates in the synthesis of the calcium phosphate sol–gel. The chemical shifts of these small peaks change upon addition of calcium ethoxide; however, the intensities of the peaks in the region of −1 to +10 p.p.m. remain constant over the complete time period.

The thermal gravimetric analysis of the xerogels aged for different times showed a decrease in the overall weight loss with aging, Fig. 2a. After 24 h aging, the weight loss at temperatures greater than 800 °C equates to a value of 28–30 wt%. Previous work has shown that this is the critical time for aging of the solution to obtain a product consisting only of hydroxyapatite [19].

The weight loss occurring before 24 h can be attributed to the unreacted calcium diethoxide. Upon exposure to air, the hygroscopic nature of calcium diethoxide induces a transformation to calcium hydroxide. Heating then produces calcium carbonate. This is supported by the X-ray diffraction pattern of the powder heated to 450 °C, Fig. 3. The large weight loss at about 600 °C represents the decomposition of calcium carbonate to form calcium oxide. This has been found as the only accompanying phase in insufficiently aged solutions [19]. By assuming that the difference in weight loss, relative to the aged sample, above 800 °C is attributed to the decomposition of calcium carbonate to calcium oxide, the calcium oxide content can be shown to decrease with time up to 24 h where it is no longer detectable by X-ray diffraction, Fig. 2b. Unaged samples thus contain calcium diethoxide or calcium hydroxide as the hydrolysis product. Unreacted phosphorous may be incorporated in the hydroxyapatite lattice to form a calcium-deficient hydroxyapatite or form a phosphorous-rich compound. Further work is required to ascertain the location of the phosphorous species.

Differential thermal analysis of the aged samples shows an endotherm followed by three exotherms positioned at 220, 400 and 550 °C, Fig. 2c. The endothermic reaction at low temperature is believed to be related to the desorption of alcohols and adsorbed water [20]. The first two exotherms correspond to polycondensation and the release of organics thus requiring a prefiring temperature of 500 °C. The exothermic peak at 550 °C suggests crystallization of

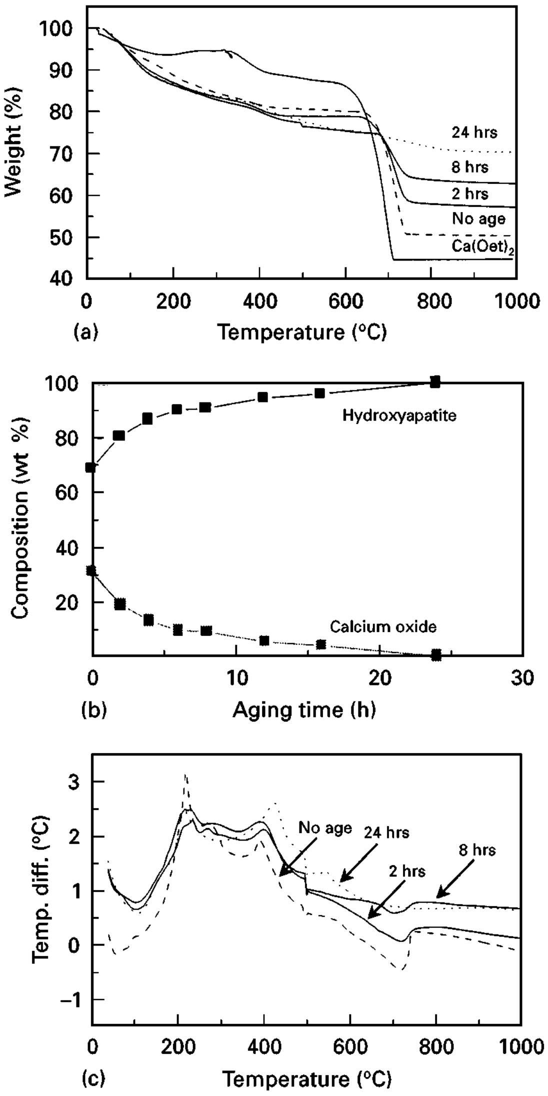

Figure 2 Thermal analysis showing (a) thermal gravimetric analysis of calcium diethoxide and solutions aged for 0, 2, 8 and 24 h, (b) the amount of hydroxyapatite, calculated from the weight loss above 800 °C assuming a conversion from calcium carbonate to calcium oxide, and (c) differential thermal analysis of solutions aged for 0, 2, 8 and 24 h.

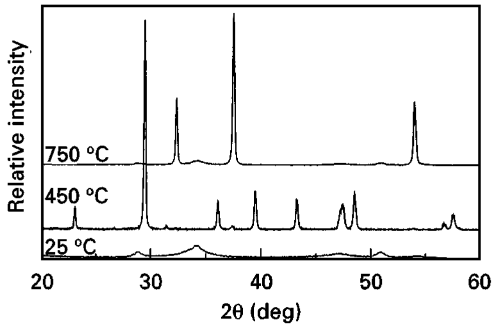

Figure 3 X-ray diffraction of calcium diethoxide after exposure to air and heated to 450 and 750 °C. The X-ray diffraction patterns correspond to calcium hydroxide at 25 °C, calcium carbonate at 450 °C and calcium oxide at 750 °C.

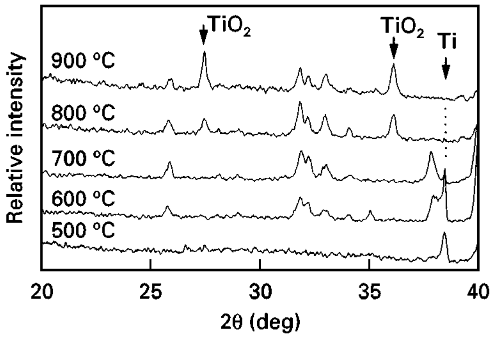

Figure 4 X-ray diffraction of sol–gel coatings prefired to 500 °C on titanium substrates and then fired at various temperatures.

an amorphous calcium phosphate. Coatings fired to temperatures between 500 and 900 °C and analyzed by X-ray diffraction indicate that crystallization occurs between 500 and 600 °C, Fig. 4. The release of heat on crystallization is small, suggesting that a small rearrangement of the atomic arrangement of the calcium and phosphate species is required for crystallization. This crystallization temperature is in agreement with the findings on other sol–gel [21] plasma sprayed [22, 23], sputtered [24] and pulsed-laser deposited [25] coatings and is a characteristic of amorphous calcium phosphates within atmospheres of different partial water vapor pressure [22].

Most of the organics are released prior to about 500 °C, within the prefiring stage of the gel, Fig. 2a. The gases evolved upon pyrolysis at temperatures ranging from 200–700 °C indicated the release of water, carbon monoxide and carbon dioxide. It is believed that these gases may become incorporated into the hydroxyapatite lattice to form carbono-apatite, and Fourier transform–infrared spectroscopy should reveal this. If heavier molecular weight gases such as alcohols were evolved, they were not detected with pyrolysis gas chromatography.

X-ray diffraction of the coatings heated to the various temperatures indicated that initially the titanium substrate was observed which oxidized at temperatures starting at 800 °C. Based on the possible phase transformation in the metallic substrate, the occurrence of oxidation and very little loss after 800 °C, it is suggested that this temperature is suitable for manufacturing sol–gel hydroxyapatite coating. The resulting microstructure is a nanograined hydroxyapatite coating with an average grain size of 50 nm, Fig. 5. Densification of the coating can then be obtained with a longer firing temperature at 800 °C.

The combined use of thermal gravimetry, ^{31}P nuclear magnetic resonance and X-ray diffraction have revealed that a time of 24 h is necessary for complete combination of the calcium and phosphite ethoxides to produce a hydroxyapatite coating. Preparation of a homogeneous coating then required a prefire at 500 °C to remove most of the organics followed by a final firing at 800 °C.

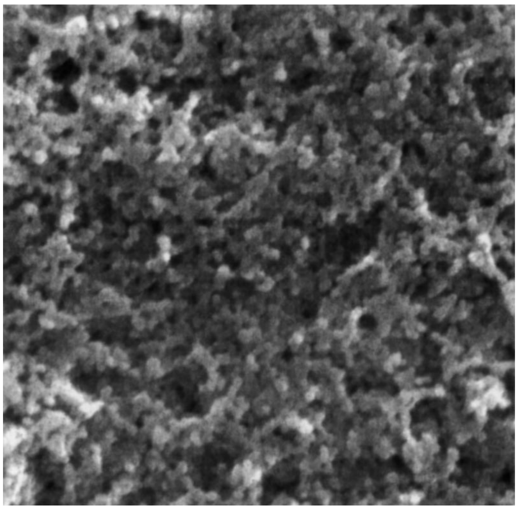

Figure 5 A scanning electron micrograph of a coating fired to 800 °C for 10 min. The field of view is 250 nm × 250 nm.

4. Conclusion

The production of sol–gel hydroxyapatite coatings on titanium substrates using alkoxide precursors requires control of the aging time and firing temperature. ^{31}P nuclear magnetic resonance spectroscopy and previously reported X-ray diffraction work indicate that the reaction between the reactants is complete after 24 h. At shorter times, unreacted calcium diethoxide undergoes conversion to calcium oxide which is included in the coating. A final firing temperature of 800 °C is required to remove most of the organic material and produce a thin homogeneous hydroxyapatite coating.

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