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Water Based Sol-Gel Synthesis of Hydroxyapatite

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The hydroxyapatite (HA) bioceramic was synthesized using a sol-gel processing route of calcium nitrate with trimethyl phosphate and diethyl phosphite. The formation of hydroxyapatite and other compounds during the heat-treatment cycle were identified and characterized using ^{1}H NMR, FTIR, X-ray diffraction spectroscopy. Aging effect on the phase evolution of water-based sol-gel process to synthesize hydroxyapatite was studied in terms of aging time and using different phosphorus precursors. The use of diethyl phosphite has improved the sol-gel procedure by eliminating the aging period that was required for trimethyl phosphate.

Keywords: bioceramics, hydroxyapatite, calcium nitrate, diethyl phosphite, trimethyl phosphate, sol-gel synthesis.

INTRODUCTION

Ceramic materials that are specially developed for use as medical and dental implants are termed bioceramics. Bioceramics can have structural functions as joint or tissue replacements, can be used as coatings to improve the biocompatibility and corrosion resistance [1] of metal implants, and can function as resorbable lattices, which provide temporary structures and a framework that is dissolved, replaced as the body rebuilds tissue. Hydroxyapatite (HA, $Ca_{10}(PO_4)_6(OH_2)$ ceramics belongs to a class of phosphate-based materials, which have been widely used as bone substitutes. Recently, HA has been used for a variety of biomedical applications [2 – 4], including matrices for drug release control [5]. Due to the chemical similarity between HA and mineralized bone of human tissue, synthetic HA exhibits strong affinity to bone hard tissue. Formation of chemical bond with the host tissue offers HA a greater advantage in clinical applications than most other bone substitutes. HA coatings on metallic substrates, offer great improvement in orthopaedic and dental applications and are used in successful clinic practices.

A number of methods have been used for HA powder synthesis. Calcium phosphates can be synthesised by hydrothermal [6, 7], solid state [8] or wet chemical reactions [9, 10]. One of the earliest techniques developed of the synthesis of hydroxyapatite involved the hydrothermal conversion of fluoroapatite to hydroxyapatite under a pressure 5000 p.s.i. and temperature range of 920 – 1230 °C. HA as a final product may be preceded by the formation of intermediate products such as β-calcium pyrophosphate or calcium monohydrogen phosphate depending upon the applied temperature and pressure. Most biomaterial applications use hydroxyapatite prepared via the wet chemical method involves an aqueous solution of Ca salts and phosphates. Different calcium phosphates will precipitate from the system depending on its pH values. In order to obtained the required Ca/P ratio phase, this method usually needs long time (days) for complete reaction. The precipitated powder is usually calcinated at 400 – 600 °C or even at 1200 °C. However, fast precipitation during phosphate titration leads to chemical inhomogeneity in the final products. Slow titration and diluted solutions must be used to improve chemical homogeneity and stoichiometry of the resulting hydroxyapatite, careful control of the solution condition is critical in the wet precipitation.

Sol-gel synthesis of HA ceramics has recently attracted much attention [11 – 16]. The sol-gel method offers a molecular-level mixing of the calcium and phosphorus precursors, which capable of improving extent, in comparison with conventional methods. Besides, the so-gel approach provides significantly milder conditions for the synthesis of HA powders or films. In the sol-gel synthesis of HA, calcium alkoxides or salts are frequently using as calcium precursors. In most cases, phosphorus compounds – oxide, triethylphosphate and triethylphosphite are employing as phosphorus precursors in water or organic solvents phase. However a long period of the sol-gel preparation time, 24 h or longer is commonly reported in literature as required to form desirable product. This is because of slow reaction between calcium and phosphorus precursors in the sol phase. Obviously, the reactivity depends on the chemical nature of the precursors. Phosphate esters, being very stable towards water, can not be hydrolyzed easily and the hydrolysis may be possible in the presence of metal ion-containing catalysts. The phosphite esters have the larger hydrolysis rate constants, then corresponding phosphate esters compounds [17].

In this investigation calcium nitrate, and phosphorus compounds – trimethyl phosphate and diethyl phosphite were selected as Ca and P precursors for HA synthesis, respectively. Aging effect on the phase evolution of sol-gel process was studied in terms of aging time for those phosphorus precursors.

EXPERIMENTAL

The solutions pH values were determinate with Mettler Toledo MP 200 pH meter. IR spectra of the materials were recorded in KBr powders using Perkin-Elmer Spectrum

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BX FT-IR spectrometer. The HA phase derived from all types of gel was detected using an X-ray diffractometer DRON-3M. The XRD patterns were recorded using radiation of Cu Kα generated at 34 kV and 26 mA.

The precursors used in this study of sol-gel processing of hydroxyapatite were calcium nitrate tetrahydrate $(Ca(NO_3)_2\,4{\cdot}H_2O$ as a source of calcium ions and trimethyl phosphate $((CH_3O)_3PO)$ and diethyl phosphite $((C_2H_5O)_2POH)$ as the phosphorus precursors. The molar ratio of precursors Ca/P was 1.67. The flow chart of the synthesis is depicted in Fig. 1. The solution of phosphorus precursor (0.03 mol trimethyl phosphate or diethyl phosphite in 5 ml distilled water) was added drop-wise to the stirred calcium nitrate solution (0.05 mol in the 25 ml distilled water). After mixing the sol-gels were aged 2 h, 24 h or 72 h hours at room temperature. After aging the slow evaporation process was done in the oil bath for 24 h at 60 °C. The dried gels were further calcinated at 250 °C for 6 h at air atmosphere. The dried sol-gels were calcinated at 400, 500, 750 and 1000 °C for 3 h respectively.

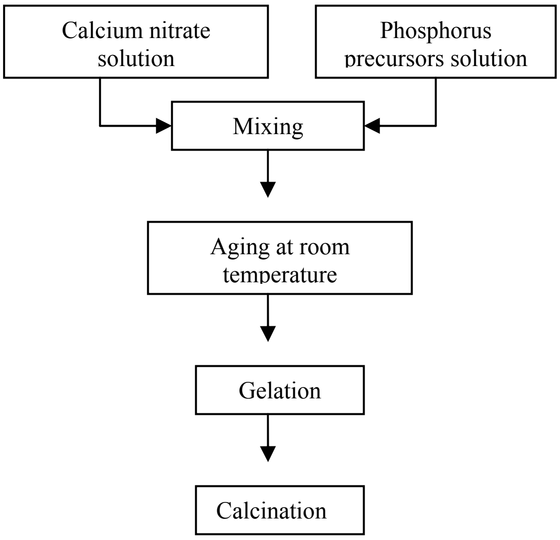

Fig. 1. Flow chart of hydroxyapatite preparation by the sol-gel route

The pH values of solutions after mixing and after aging were recorded. Fourier transform infrared (FTIR) transmission mode was used to examine the possible structural variations and reactions in those aged sols, dried and calcinated gels. The gels heated at 1000 °C were crushed into fine powder and they were examined by X-ray diffraction techniques to determine the phases formed.

RESULTS

In the sol-gel process of the HA the calcium compounds and phosphorus precursors are converted thought hydrolysis and condensation reactions to the amorphous gels, which are further transformed to ceramics when heated at relatively low temperature. The hydrolysis and polycondensation are not separated in time, but take place simultaneously.

Phosphorus derivatives of various esters functional groups exhibit characteristics of hydrolysis upon exposure to water molecules. The hydrolysis can be monitored by testing its pH values. The sol-gel samples after different aging time 2 h, 24 h, and 72 h were investigated. The pH values of aging precursors during aging are summarized in Table 1.

Table 1. pH values of reaction mixtures

No.	Reaction mixture	pH after mixing	pH after aging		
			2 h	24 h	72 h
1	$(CH_3O)_3PO$ $Ca(NO_3)_2$	2.98	2.83	2.58	1.08
2	$(C_2H_5O)_2POH$ $Ca(NO_3)_2$	1.61	1.55	1.28	–

The decrease in pH values due to the aging step is manifest irrespective of the phosphorus precursor hydrolysis step, indicating hydrolysis of trimethyl phosphate and diethyl phosphites. The hydrolysis products form a complex with calcium ions dissolved in the solution. Upon aging, the hydrolyzed phosphorus sol interacted with Ca sol, possibly in the form of ions Ca^{2+} in water, to form oligomeric derivatives containing Ca-O-P bonds. For the aqueous-based process, an ionic derivative may be developed as follows:

$$OP(OR)_3 + Ca^{2+} + NO_3^- \rightarrow (NO_3)^-(OH)\text{-}Ca\text{-}O\text{-}PHO(OR)_2 + H^+ + ROH + H_2O$$

$$HOP(OR)_2 + Ca^{2+} + NO_3^- \rightarrow (NO_3)^-(OH)\text{-}Ca\text{-}O\text{-}PHOOR + H^+ + ROH + H_2O$$

The release of protons seems to account for a decreased pH level of the sol as experimentally observed. Further heating causes removal of the solvents, accompanied by accelerated thermal dehydration and polymerization, condensation between these derivative units, resulting in the formation of more (-Ca-O-P-) containing bonds in the dry gels. Calcium nitrate often used in HA sol-gel processes, is not only Ca precursor, but it is known that oxidizing agent such as nitrate anions presented in the sol-gel precursor will help organics to be decomposed more easily. Therefore, processing temperature as well as residual organics in calcinated coating will be lower. Slow evaporation of solvent provides not only intimate interaction but also thermal energy for reactants.

Both sols transformed into clear, viscous liquid after approximately 3/4 of the solvents were removed upon heating at 60 °C. Upon cooling to ambient temperature, a remarkable increase in viscosity was observed for both the viscous sol. Extended heating of viscous sol at 60 °C resulted in a white solid gel.

In order to determine the formation temperature of hydroxyapatite, samples of dried gel were heated at 400, 500, 750 and 1000 °C. After heated treatment, the samples were air-quenched to room temperature, and the formed phases were examined using FTIR spectral and X-ray diffraction characterization techniques. Fig. 2 and Fig. 3 illustrates FTIR spectra of the samples of the trimethyl phosphate and Fig. 4 spectra of the diethyl phosphite The all samples of the trimethyl phosphate (after aging 24 h, 72 h) diethyl phosphite (after aging 2 h, 24 h), and were heated at 500 °C still exhibit amorphous materials bands. The bands at 1420 and 1465 cm^{-1} correspond to the vibration of the carbonate ion. The first indication of the formation of hydroxyapatite is the form of broad IR band centred at about 1050 cm^{-1} at 500 °C (Fig. 2, 3, 4). The spectrum of sample from the trimethyl phosphate (Fig. 2) after aging 24 h and heated at 1000 °C, shows the bands corresponding to hydroxyapatite, carbonate anions and calcium hydroxide (3645 cm^{-1}). The calcium oxide cannot be detected as bands corresponding to the Ca-O stretching modes would lie in the near IR region at wave numbers below 400 cm^{-1}, which is below the detection threshold of the instrument used. The X-ray diffraction spectra data confirm the presence of calcium oxide.

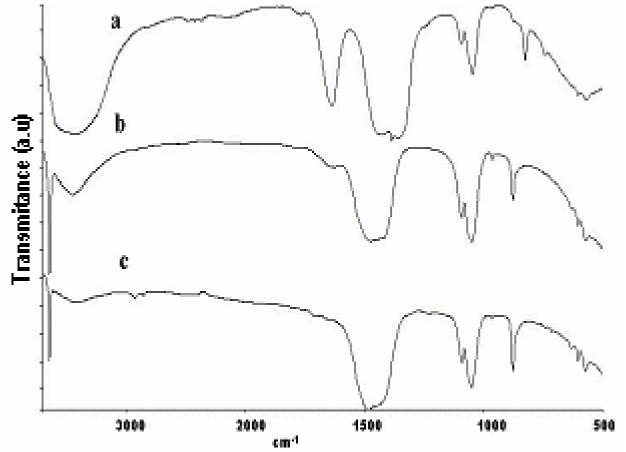

Fig. 2. IR spectra of powders obtained from precursors calcium nitrate and trimethyl phosphate after aging 24 h and calcinated at a) 500 °C, b) 750 °C, c) 1000 °C

Formation of hydroxyapatite occurs at a relatively low temperature of about 500 °C. The spectra of samples of the fully hydrolysed trimethyl phosphate and diethyl phosphite (Fig. 3 and Fig. 4) and heated at 750 °C show a significant increase in the intensity of the bands at about 1048 cm^{-1} and 1090 cm^{-1}.

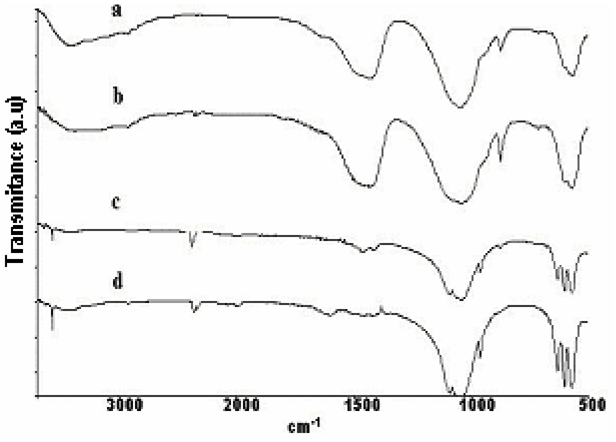

Fig. 3. IR spectra of powders obtained from precursors calcium nitrate and trimethyl phosphate after aging 72 h and calcinated at a) 400 °C, b) 500 °C, c) 750 °C, d) 1000 °C

These bands arise due to factor group splitting of the v_3 fundamental vibrational mode of the PO_4^{3-} tetrahedral. This fundamental mode corresponds to the triply degenerate asymmetric P-O stretching modes. The band at about 960 cm^{-1} corresponds to v_1 symmetric P-O stretching vibration of the PO_4^{3-} ion. The distinguishable presence of these bands together with the bands at about 604 and 570 cm^{-1} corresponding to the triply degenerate v_4 bending vibration of the PO_4^{3-} indicate the increased quantity of hydroxyapatite in the batch at this temperature. The bands 1420 and 1465 cm^{-1} of the heated samples at 750 °C and 1000 °C show a decrease in intensity while the bands assigned to the stretching and absorption band of hydroxyapatite (3570 cm^{-1} and 636 cm^{-1}) are observed

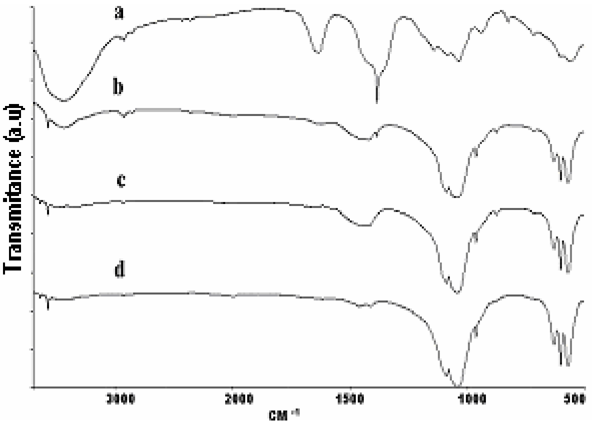

Fig. 4. IR spectra of powders from precursors calcium nitrate with diethyl phosphite after aging 2h and calcinated at a) 400 °C, b) 500 °C, c) 750 °C, d) 1000 °C

On examining Fig. 5 we observe, that the pattern representative of the samples of the trimethyl phosphate (after aging 24 h) is hydroxyapatite characterized by very strong X-ray peaks at 31.5° 2*θ*, corresponding to the strongest intensity (84 %) reflection, and two peaks at 32.1° and 33° both having equal intensity (55 %). The peak at 28.5° 2*θ* together, with a peak at 34° 2*θ* are characteristic of calcium hydroxide (portlantide). The peak at 37.5° 2*θ* correspond to reflection from calcium oxide (lime).

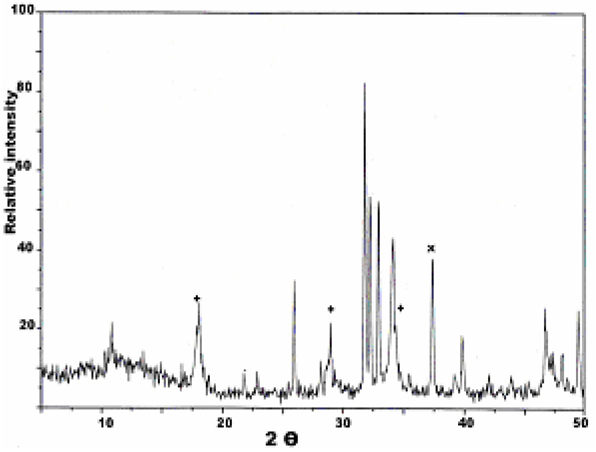

Fig. 5. XRD patterns of powders from precursors calcium nitrate and trimethyl phosphate, after aging 24h calcinated at 1000 °C. CaO (x), Ca $(OH)_2$ (+), other HA

XRD results of the fired gel of trimethyl phosphate after aging 72 h is given in Fig. 6. The major phase for both aging periods 24 h and 72 h was hydroxyapatite with accompanying phases of CaO and Ca $(OH)_2$. Over the 72 h aging period, XRD indicate a slight lowering of intensity of the CaO peak and absence of the calcium hydroxide with respect to hydroxyapatite intensity. The reason being thought for the presence of calcium oxide and hydroxide phases is lack of stoichiometry between the starting precursors due to low trimethyl phosphate hydrolysis rate.

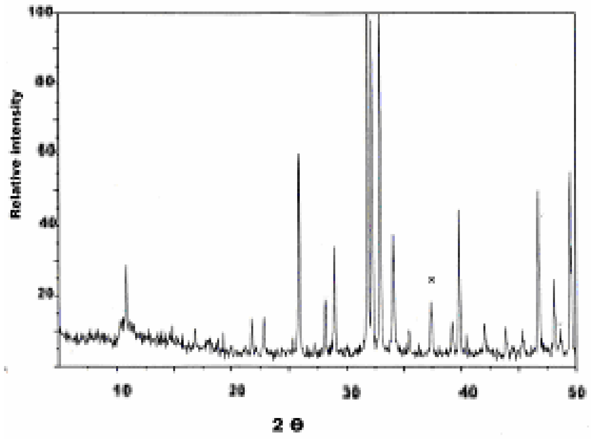

Fig. 6. XRD patterns of powders from precursors calcium nitrate and trimethyl phosphate after aging 72 h calcinated at 1000 °C. CaO(x), other HA

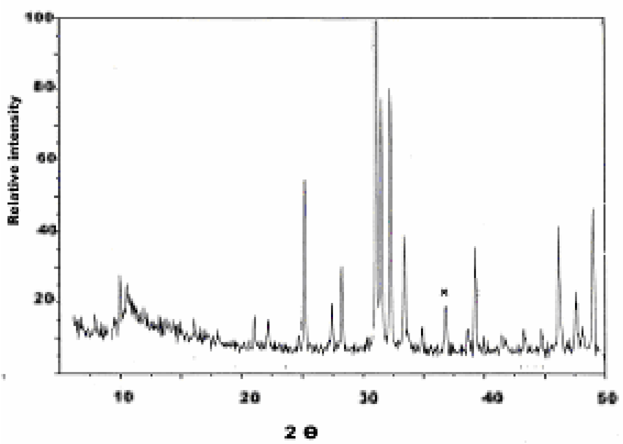

Fig. 7. XRD patterns of powders from precursors calcium nitrate and diethyl phosphite after aging 2 h calcinated at 1000 °C. CaO (x), other HA

XRD patterns (Fig. 7) of the sample of the reaction mixture from calcium nitrate and diethyl phosphite (after aging 2 h) show intense hydroxyapatite peaks and very weak calcium oxide peaks, indicating that most part of the phosphorus precursor diethyl phosphite was combined by calcium ions after 2 h aging. The composition of the sample of diethyl phosphite after aging 24 h is similar as after 2 h, and it did not showed here. The higher hydrolysis rate of the diethyl phosphite is the main reason, which allows reducing the aging period of so-gel.

CONCLUSIONS

Hydroxyapatite was synthesized using the sol-gel route with calcium nitrate and trimethyl phosphate or diethyl phosphite as precursors. The gel formed as colloidal gel, and hence difficulties associated with the slow rates of hydrolysis of trimethyl phosphate were overcome. Different batches made calcium nitrate with trimethyl phosphate and diethyl phosphite after aging 2 h, 24 h, and 72 h. Aging effect on the phase evolution of water-based sol-gel process to synthesize hydroxyapatite was studied in terms of aging time and using different phosphorus precursors. The use of diethyl phosphite has improved the sol-gel procedure by eliminating the aging period that was required for trimethyl phosphate.

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