Materials and Design 109 (2016) 547–555

Contents lists available at ScienceDirect

Materials and Design

journal homepage: www.elsevier.com/locate/matdes

Fast route for synthesis of stoichiometric hydroxyapatite by employing the Taguchi method

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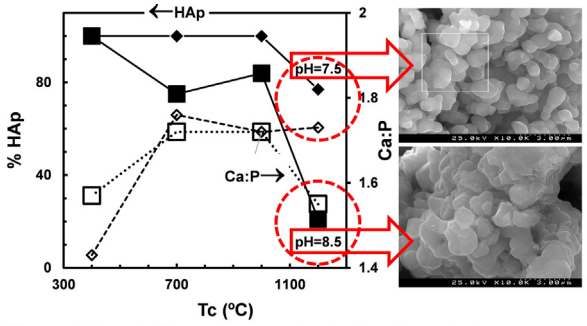
HIGHLIGHTS

- Taguchi methods used for simultaneous effects of 5 processing parameters on phase purity and properties of hydroxyapatite.
- The five different parameters were pH, synthesis temperature, synthesis time, drying temperature and calcination temperature.
- Logarithmic scales used for linear multivariate regression based on kinetic models, giving meaningful regression coefficients.
- Comprehensive analysis of effects of processing parameters on 4 properties: crystallite size, surface area, Ca/P ratio and mol% HAp.
- Calcination temp had greatest impact on morphology, crystallite size & surface area; pH had greatest influence on Ca:P ratio.

GRAPHICAL ABSTRACT



Effects of T_c and pH on phase purity, Ca:P ratio and microstructures

ARTICLE INFO

Article history:
Received 19 May 2016
Received in revised form 14 July 2016
Accepted 17 July 2016
Available online 19 July 2016

Keywords:
Hydroxyapatite
Nanoparticles
Nanosynthesis
Biomaterials
Biocompatibility
Taguchi method

ABSTRACT

The Taguchi experimental design method is an elegant and efficient way of deriving optimum conditions for processes from the minimum number of experiments. We correlated various relevant synthesis parameters in the precipitation synthesis of single-phase pure hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAp) nanoparticles, via a rapid wet precipitation method, without any aging time. Taguchi planning was used for a systematic study of the combined effects of five different parameters: pH, synthesis temperature, synthesis time, drying temperature and calcination temperature. Using T\aguchi methods, we were able to evaluate the effects of four variations (levels) in each of these five parameters, with just 16 experiments (an L_{16} (1024) orthogonal array). We assessed the impact of these parameters on four distinct properties, namely crystallite size, surface area, Ca/P atomic ratio and mol% of HAp. Calcination temperature exerted the greatest impact on hydroxyapatite morphology, corresponding to crystallite size and specific surface area, for which the role of other processing parameters was not significant. On the contrary, the Ca:P ratio was affected mainly by pH. These findings were confirmed by microstructural, structural and spectroscopic characterisation. FTIR spectra, revealing the conditions to retain a pure or prevailing hydroxyapatite phase, and also to indicate favourable conditions for A-type substitutions of carbonate for hydroxide groups, or B-type substitution for phosphate groups.

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http://dx.doi.org/10.1016/j.matdes.2016.07.083
0264-1275/

1. Introduction

Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, HAP) is a major component of bone, and has been used as a synthetic biomaterial for implants and a wide range of biomedical applications. It can also be used as a filter or membrane, creating unique chromatography tools [1,2]. HAp is classified as a bioactive, biocompatible and osteoconductive material, which aids local osteosynthesis when used in implants, owing to its high compatibility with the composition of natural bone mineral [3]. It is an important substitute in the treatment of bone disorders, and is also an optimum restoration material for dental decay. It can also be used as a surface coating to improve the biocompatibility of other implants [4], and is used as a biomaterial with functionalised nanostructure as a carrier for therapeutics [5].

Among several methods for HAp synthesis [2–4,6–8], precipitation from solution is the most widely used, this being a convenient low cost method for obtaining HAp powder [9]. The bioactivity of synthetic HAp is governed by several factors, such as pH and temperature of synthesis, and thermal treatment including drying and calcination [4]. Starting materials also influence the morphology and crystallinity of the product, and the mode of addition of the reactants effects the subsequent growth of HAp when prepared by precipitation [10]. It was reported previously that changing the stirring time and synthesis temperature leads to highly crystalline HAp [11], while changing pH affects the morphology and the particle size of the synthesised HAp [12].

Almost all previous studies have focused on the effect of only one to three parameters at a time, applying various methods [13–16]. This investigation will uniquely focus on the simultaneous influence of five different parameters on the synthesis of HAp, namely: i) pH; ii) synthesis temperature; iii) time of synthesis reaction; and iv) drying temperature; v) calcination temperature. This is achieved through the application of a simple, fast, low cost and highly efficient analysis process, using Taguchi methods [17]. Taguchi methods are statistical methods that were originally developed after the Second World War to improve the quality of manufactured goods, and are finding increasing application in the engineering and biotechnology sectors to improve procedures [18]. Taguchi methods have been used to investigate and optimise various inorganic syntheses and ceramic processes, such as the hydrothermal synthesis of titania nanoparticles [8], the formation of SiAlON and mullite oxide/non-oxide ceramic composites [19], the synthesis of superhydrophobic polyvinylidene fluoride (PVDF)/zinc oxide composites [20], and for a wide variety of different applications such as photocatalytic zinc oxide nanoparticles [21], ceria nanoparticles for catalyst supports [22], sol-gel applied anti-corrosion titania nanocoatings [21], biomaterials [23,24], etc.

The Taguchi method is an experimental design method, used to find solutions for complex problems with a large number of variables and levels using relatively few actual experiments [25]. In the Taguchi method, orthogonal arrays are used to efficiently determine the effect of variables and levels to achieve a robust design, greatly lowering the number of trials and the subsequent cost in time, manpower and resources. Based on Taguchi experimental design, the optimised experimental conditions can be determined by comparing a mean of the means [8,18]. In the case of our study, we studied the five parameters listed above, with four levels of variation for each one. Applying fractional factorial design and the Taguchi statistical method, the 1024 ($=4^5$) separate experiments required to reproduce every possible combination can be reduced to only 16 experiments (an L_{16} (1024) orthogonal array), as shown in Table 1. Each of the experiments gives a unique combination of factors, which can be analysed to give the optimum synthesis conditions for HAp. In addition, Taguchi planning allows one to measure the impact of those processing parameters on four distinct properties, namely crystallite size (nm), specific surface area (m^2/g), Ca/P atomic ratio and mol% of HAp phase present, and analyse these results to determine the optimum conditions.

Table 1
L_{16} orthogonal array of experiments, accompanied by the results of crystallite size (D), specific surface area (A), Ca:P ratio and % Hap. The five parameters studied were: pH; synthesis temperature T_s/K; stirring time t_s/min; drying temperature T_d/K and calcination temperature T_c/K.

	pH	T_s (K)	t_s (min)	T_d (K)	T_c (K)	D (nm) (nm)	A (m^2/g)	Ca:P	Hap (%)
E1	7.5	318	30	333	673	0	105	1.43	100
E2	7.5	333	60	343	973	19	38	1.76	100
E3	7.5	348	90	353	1273	9	19	1.72	100
E4	7.5	363	120	363	1473	1	4	1.73	77
E5	8.5	318	60	353	1473	103	4	1.55	21
E6	8.5	333	30	363	1273	54	13	1.72	84
E7	8.5	348	120	333	973	27	18	1.72	75
E8	8.5	363	90	343	673	9	83	1.57	100
E9	9.5	318	90	363	973	57	19	1.88	51
E10	9.5	333	120	353	673	1	92	1.69	100
E11	9.5	348	30	343	1473	42	4	1.69	47
E12	9.5	363	60	333	1273	62	8	1.67	66
E13	5.5	318	120	343	1273	81	4	1.87	86
E14	5.5	333	90	333	1473	73	4	1.74	52
E15	5.5	348	60	363	673	1	69	1.97	100
E16	5.5	363	30	353	973	21	19	1.87	48

2. Experimental

2.1. Experimental design

Taguchi planning was selected because its performance has been widely demonstrated in many technical and scientific fields. Five variable parameters (factors) with 4 levels were chosen for the synthesis of hydroxyapatite, as shown in Table 1. To reduce the total number of experiments, fractional factorial design was employed. An L_{16} orthogonal array of experiments was chosen to evaluate the effect of pH, synthesis temperature, stirring time, drying temperature and calcination temperature on the crystallite size, specific surface area, Ca/P molar ratio, and the percentage of HAp phase of the nano particles (NPs). This method is an efficient way to assess simultaneous effects of several different parameters, also at different levels, without undue experimental effort, cost and time. The conventional approach to vary every single parameter independently would imply enormous efforts, as demonstrated on comparing the actual number of experiments for 5 independent variables at 4 different levels (16) to the corresponding number of experiments for all the combinations of variables and their levels ($4^5 = 1024$). This enormous economy in cost and time allows simultaneous inspection of several relevant properties, as demonstrated in the actual study of effects of synthesis conditions (pH, temperature and time), and processing steps (drying and calcination temperatures) on crystallite size, specific surface area, Ca:P ratio and hydroxyapatite content of the resulting materials. This planning also allows further insight on mechanisms involved by complementary structural, microstructural and spectroscopic characterisation, even if this information is only qualitative.

2.2. Synthesis procedure

Nanostructured HAp may be synthesised via precipitation in aqueous media, such as in reference [26]. However, in this work a new, easy and very fast route was implemented to synthesis HAp. Analytical grade calcium acetate monohydrate ($Ca(CH_3CO_2)_2 \cdot H_2O$) and orthophosphoric acid (H_3PO_4) were used as starting precursors for calcium and phosphorous respectively, maintaining the stoichiometric ratio of reactants at a Ca:P molar ratio of 1.67. Ammonia (NH_3) was used as a buffer to keep the pH near constant at a designated value (between 5.5 and 9.5). All reagents were purchased from Sigma Aldrich, Germany, and were ACS grade. The reactants were added to distilled water at a fixed stirring rate for all experiments. After the necessary synthesis time, the product was dried using a rotary evaporator for 1 h. Then all samples were subjected to heat treatment at predefined temperature