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Original Research Paper

Continuous microwave assisted flow synthesis and characterization of calcium deficient hydroxyapatite nanorods

Aneela Anwar *, Samina Akbar

Department of Basic Sciences and Humanities, University of Engineering and Technology, KSK Campus, GT Road, Lahore 39020, Pakistan

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ABSTRACT

Synthetic calcium deficient hydroxyapatite (CDHA) nanorods (<100 nm) were rapidly prepared with the help of a new continuous microwave assisted flow synthesis (CMFS) reactor in 5 min only from aqueous solution of calcium hydroxide and orthophosphoric acid at pH 8.5. The effect of various reaction parameters like, pH, concentration, temperature, residence time, degree of crystallinity and particle surface area were studied in detail. The phase purity, particle size and morphology of the powder samples were characterised by techniques such as X-ray diffraction analysis, transmission electron microscopy, scanning electron microscopy and FTIR and Raman spectroscopy. With the help of X-ray photoelectron spectroscopy, the chemical analysis was completed. Measurements were taken into account to estimate the particle size following the dynamic light scattering. The results showed that the employed synthesis procedure offered an efficient and economical route to achieve high quality nano-sized products with suitable size and low level of impurities.

1. Introduction

In the past couple of decades, substantial work has been made on the synthesis of nanoscale ceramic materials for biomedical applications. Among a large variety of biomaterials, calcium phosphates (CaPs) are famous for their usage as reinforcements in biomedical composites, coatings on metal implants, as injectables, and for dental restoration because of their exceptional biocompatibility [1–3]. Different forms of CaP structures, which generally form a class of compounds termed as 'apatites' of which $Ca_{10}(PO_4)_6(OH)_2$, demonstrates high biocompatibility and low solubility in aqueous media for its rich calcium content. Nano-bioceramics, used as scaffold materials, are favoured to promote new bone growth for osteoinductive coatings and as a bulk bone filler. Though, bone mineral is basically calcium deficient hydroxyapatite [CDHA] with Ca:P molar ratio of 1.5, which structurally resembles to stoichiometric hydroxyapatite with Ca:P ratio 1.67 but compositionally to tricalcium phosphate (TCP) [4–6].

CDHA has gained a paramount importance as element of bone cements for controlling particle properties in order to regulate cement setting behaviour. CDHA has greater dissolution rate compared to stoichiometric HA in physiological body fluids. Natural The bones in our body comprises of calcium deficient HA (Ca:P < 1.67) and has excessive power for various cation exchange. Furthermore, It acquired high specific surface area than TCP and pure HA that might be advantageous for bone regeneration applications and rapid seeding efficacy. CDHA has become a potential candidate for acquiring good electrical properties in gas sensing and electrical conductivity [7–11]. Consequently, CDHA is exceptionally beneficial for their use as an ion-exchange media for water distillation [3,12].

Multiple methods have been formulated for the preparation of CDHA and majority of them involve longer reaction times, stirring, aging and drying etc. The most adopted procedures are wet chemical precipitation [13,14], microwave synthesis [4,11] and continuous hydrothermal flow synthesis [15,16]. Many of the above reactions are not necessarily suitable for manufacture in the third world due to the poor availability of the reagents. Hence there is a need for simplified production methods that operate under ambient conditions and use affordable and readily available reagents. Recently, the synthesis of calcium phosphate nanoceramic using the continuous hydrothermal flow synthesis (CHFS) at supercritical conditions of high temperature and pressure (400 °C and 24 MPa) was extended [15]. Unfortunately, owing to corrosion of the reactor at the high temperature and pressure, products from continuous hydrothermal processes tend to be contaminated with trace amounts of metals (*e.g.* iron and chromium from stainless steel),

* Corresponding author.
E-mail address: a.anwar@uet.edu.pk (A. Anwar).

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therefore they may be unacceptable for clinical applications. Furthermore, the nano-HA produced by continuous hydrothermal processes is relatively large and on a similar scale to those obtained using more conventional routes. Smaller and smarter nanoparticles in the discipline of nanoworld may open up new applications, *e.g.* those requiring rapid dissolution *in vitro*, injectables or hard filler components for bone replacement and dental restoration.

Our group has expertise in low temperature synthesis (60–100 °C) procedures for the preparation of phase pure [17], surface modified [18] and ion substituted [19,20] calcium phosphate nanoscale bioceramic materials. Our recently patented continuous plastic flow synthesis (CPFS) system has successfully adopted for the rapid production of various phase pure calcium phosphates bioceramics for biomedical applications [18,19]. It has been learnt through experiments that the particles properties, crystallinity and nature depended significantly on the reaction time, pH, temperature and variation in Ca/P ratio.

In the continuation of our extensive studies in the field of nanoscale bioceramics, we have recently introduced a unique, most efficient microwave assisted version of continuous flow synthesis process in order to obtain, phase pure, highly dispersed, very fine bioceramic nanoparticles. Continuous microwave flow synthesis procedure offers several advantages over others including faster synthesis in shorter time period, quick energy transformation and throughout the volume heating. It operates through an internally produced heat within the materials molecules unlike external heating system. Thus the proposed system is a facile, quick, green process and plays an essential role in reactions performing in aqueous media. This latest methodology describes the production of synthetic CDHA with most advantageous properties which resemble natural bone ingredients.

2. Materials and methods

2.1. Reagents and materials

Analytical grade Calcium hydroxide [$Ca(OH)_2$, 98%] and Phosphoric acid [H_3PO_4, 97%] were bought from Sigma Aldrich Chemical Company. VWR International supplied Ammonium hydroxide solution (NH_4OH (aq.), 28 vol%). In all the experiments deionised (DI) water was used.

2.2. Synthesis methodology

2.2.1. Continuous microwave assisted flow synthesis of CDHA nanoparticles

CDHA nanoparticles were prepared at room temperature using a single step, cost effective microwave assisted continuous flow synthesis reactor as shown in Fig. 1. In this process, 0.3 M orthophosphoric acid H_3PO_4 and 0.45 M calcium hydroxide Ca $(OH)_2$ solutions were continuously pumped at the flow rate of 10 mL min^{-1} using peristaltic pumps, to meet at a T-piece mixer through a straight union reducer (see Table 1).

This reaction mixture was connected to 400 cm long Teflon tubing (ID: 0.60 cm), placed inside a 800 W household microwave oven (Samsung ME-732 K). The flow rates were maintained for pump 1 and 2 respectively to give a total retention time of 5 min in order to obtain the phase pure reaction product.

The following equation can illustrate the precipitation of CDHA.

$$10[Ca(OH)_2] + 6H_3PO_4 \rightarrow [Ca_10(PO_4)_6(OH)_2] + 18H_2O$$

To form CDHA powder, the obtained precipitates were first filtered under vacuum and dried in freeze drier for about 22 h. Filter cakes (freeze-dried) were grounded in a pestle and mortar to get very fine white nanopowder of CDHA with ~85% yield. It was seen that by increasing reaction concentration, the particle size increased too with almost the identical product yield (~85%).

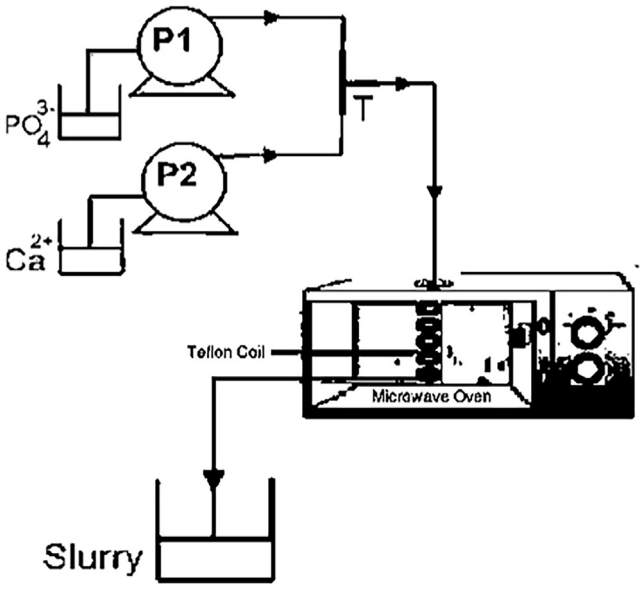

Fig. 1. Schematic diagram of continuous microwave assisted flow synthesis of CDHA nanoparticles.

Table 1
Reaction conditions for the synthesis of phase pure calcium deficient hydroxyapatite nanoparticles made via continuous microwave flow synthesis.

Heating source	**Initial pH of solution 1**	**Initial pH of solution 2**
800 W Microwave	$Ca(OH)_2 \sim 13$	$H_3PO_4 \sim 3$
Dropping Mechanism	**Flow rate**	**Retention time**
Peristaltic pumps	10 mL min^{-1}	5 min
Ca:P ratio	**Drying method**	**Tubing**
1.50	Freeze drying	Teflon (ID: 0.6 cm)

2.3. Characterization methods

2.3.1. Transmission electron microscopy (TEM)

JEOL JEM-2100 electron microscope was used to get TEM images. Suspension was made by scattering a meagre sample (<10 mg) into methanol followed by ultrasonification for 10 min. Image J software was used for evaluating particle sizes.

2.3.2. Scanning electron microscopy (SEM)

A JEOL JS-6301F SEM was used to analyse CDHA samples. The SEM was operated at 20 kV and in vacuum samples having gold coating with thickness ~250 Å were obtained using ion-sputtering device.

2.3.3. Powder x-ray diffraction (PXRD)

Powder X-ray diffraction technique (Bruker AXS D8) to find out the phase transformation in CDHA was employed. The data was documented in the 2θ range from 20 to 80° with a step size of 0.02° using Cu-Kα radiation. The crystallite size was figured by using the Debye-Sherrer equation [21].

2.3.4. Dynamic light scattering (DLS)

The particle size was determined through dynamic light scattering measurement while polydispersity index (PDI) using a Malvern Instruments Zetasizer. The sample slurry was produced with solid content of approximately ~1% by volume and diluted with methanol. This suspension was afterwards moved to ultrasonic bath for

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