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Synthesis and Characterization of Calcium Phosphate Bioceramic Powders using Thiourea as an Additive for biomedical applications

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Abstract

In this research work, hydrothermal method was employed for the synthesis of thiourea assisted tricalcium phosphate nanoparticles that could be potentially used for biomedical applications. In order to obtain bioceramic powders with phase composition represented by tricalcium phosphate (β-Ca3(PO4)2 and/or α-Ca3(PO4)2), calcium and phosphate precursors with a Ca/P molar ratio of 1.5 was used. Thiourea was used as an growth regulating agent and as an internal fuel to promote self-combustion. The HAP powders thus obtained by thiourea (TU) asssited tricalcium phosphate was characterized using various analytical techniques like FTIR, XRD, TGA and SEM. FTIR studies has revealed that calcium phosphate powders were successfully formed and the purity of the tricalcium phosphate was confirmed by XRD analysis while the thermogravimetric analysis proved the thermal stability of the powders. Morphological study was done by SEM studies which had shown that the particles have average diameters of 100-300 nm. The biocompatibility studies of the as-obtained calcium phosphate powders are yet to be done.

Keywords: Tricalcium phosphate, thiourea, hydrothermal method, nanoparticles, biomedical applications.

1 Introduction

For many years, materials based on tricalcium phosphate $Ca_3(PO_4)_2$ remain in the focus of researchers in the field of inorganic medical materials science [1]. Among ceramic materials, calcium phosphate bioceramics are recognized as an attractive biomaterial because they have similar chemical composition to the mineral component of bone. Moreover, they possess bioactive, biodegradable and osteoinductive properties. Among the ceramics of calcium phosphate, beta-tricalcium phosphate (β-TCP) $[Ca_3(PO_4)]_2$ stands out for its osteoconductive activity [2]. Calcium phosphate materials consisting of β-$Ca_3(PO_4)_2$ and/or α $Ca_3(PO_4)_2$, for which the Ca/P molar ratio is 1.5, can be obtained using various synthesis methods, primarily related to the preparation of the initial powder or components of the original powder mixture. [3]. Tricalcium phosphate (β-TCP) is an active factor that has recently been introduced which acts as a remineralizing source [4] since it dissociates into Ca^{2+} and PO_4^{3+} ions, essential for dental remineralization, making them available in the environment as single ions or their agglomerates [5]. Tricalcium phosphate (TCP) possesses a crystalline structure and chemical makeup similar to bone, making it a biocompatible and bioabsorbable material. Interestingly, when compared to other bone replacements, its rate of biodegradation is higher than that of hydroxyapatite (HA) [6]

Different synthesis routes can produce TCP, e.g., mechanosynthesis, wet methods, microwave irradiation, sol–gel, etc. Each of these methods provides specific characteristics to the TCP, such as particle size, mechanical properties, morphology and crystalline structures [7]. TCP is distinguished by its unique crystalline and physical characteristics, as well as by its very pure and homogeneous chemical makeup [8]. Additionally, additive manufacturing processes are amenable to the base calcium phosphate particle being structurally altered [9] or doped with additional bioactive ions, to improve osteo-inductivity [10]

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or mechanical strength [11,12]. Hence novel materials have been fabricated through biomimetic synthesis of nano calcium phosphate using SBF which could not be achieved by conventional methods [13]. In the present work, tricalcium phospahate powders were successfully synthesized through hydrothermal method with the addition of thiourea which has contributed to the enhanced purity and quality of the powders.

2. Experimental method

2.1 Chemicals and Reagents

Calcium nitrate tetrahydrate $Ca(NO_3)_2.4H_2O$ (Merck, India) and diammonium hydrogen phosphate $(NH_4)_2HPO_4$ were used as calcium and phosphate precursors respectively and thiourea was used as an additive. The reaction was conducted in presence of basic medium using ammonia (NH_3) solution. All the reagents were purchased in Merck, India and used without further purification. All the chemicals were of analar grade (AR) and deionized water was used throughout the experimental process.

2.2 Preparation of tricalcium phosphate

The tricalcium phosphate was synthesized using hydrothermal method by the following process. 0.5M of $Ca(NO_3)_2.4H_2O$ and 0.3 M $(NH_4)_2HPO_4$ was mixed together and to this mixture thiourea solution (0.1 M & 0.2 M) was used as an additive which was dissolved in 50 ml of deionized water is added. The pH of the above solution is maintained at 10 by adding ammonia solution. Then the mixed solution was strongly stirred for 1 hour at 600rpm. Then reaction mixture was transferred into the hydrothermal reactor and heated in the hot air oven for 3 hours at 120 ^oC. The obtained precipitate was washed with water and ethanol in the ratio of 1:1, filtered followed by drying in the oven at 80 ^oC. The obtained powder was calcined and sintered to get the tricalcium phosphate powder. The synthesized powder was characterized by different techniques.

2.3 Characterization

To analyze the functional groups, specifically the phosphate groups within the tricalcium phosphate, Fourier transform infrared spectroscopy (FTIR) was performed using a Perkin Elmer instrument. The infrared spectrum was recorded across a wavenumber range of 4000 to 350 cm^{-1} with a specific resolution. The crystal phase of the synthesized tricalcium phosphate sample was identified using X-ray diffraction (XRD) with a Bruker (AXS D2 PHASER,) system. Powder XRD patterns were obtained by scanning over a 2θ range of 10-70°. The crystallite size was then calculated using the well-known Debye-Scherrer equation. The surface morphology of the tricalcium phosphate was investigated through scanning electron microscopy (SEM) using a Carel Zeiss Evo 18. Finally, thermogravimetric analysis (TGA) was conducted using a Simultaneous Thermal Analyzer STA 600 (Perkin Elmer). The sample was heated from 50°C to 900°C at a heating rate of 20°C per minute.

3. Results and Discussion:

3.1 Fourier transform infrared spectroscopic studies

Fourier transform infrared spectroscopy (Perkin Elmer FTIR, India) was employed to identify the functional groups present in the synthesized TCP reveals the presence of functional groups such as phosphate. **Fig. 1 (a–c)** displays the FTIR spectra of the obtained TCP powder and the tricalcium phosphate powder synthesized with thiourea assistance. In this spectrum, the phosphate bands at 1126 and 1041(υ3) cm^{-1}, as well as 595 and 552(υ4) cm^{-1} which are characteristic peaks of tricalcium phosphate [14]. The two sharp peaks at 619 and 547 cm^{-1} are characteristic of the pure β-TCP and absence of any strong absorbance peak at 1400–1600 cm 1 and at about 875 cm^{-1} suggests that no carbonate group is present in any sample [20]. The faint shoulder on the $\upsilon_3(PO_4)$ band at 969 cm^{-1} corresponds to the $\upsilon_1(PO_4)$band [15]. Based on the FTIR spectrum analysis, all the characteristic peaks expected for tricalcium phosphate were identified. These corresponding wavenumber values are detailed in **Table 1.**

Table 1: FTIR spectral assignment of the functional groups.

Functional group and vibrational frequency	Wavenumber (cm^{-1})		
	TCP	0.1 M TU	0.2 M TU
Phosphate (PO_4^{3-})			
υ_1	987	975	969
υ_2	493	493	493
υ_3	1041 & 1114	1047 & 1126	1041& 1126
υ_4	552 & 607	547 & 607	547 & 619

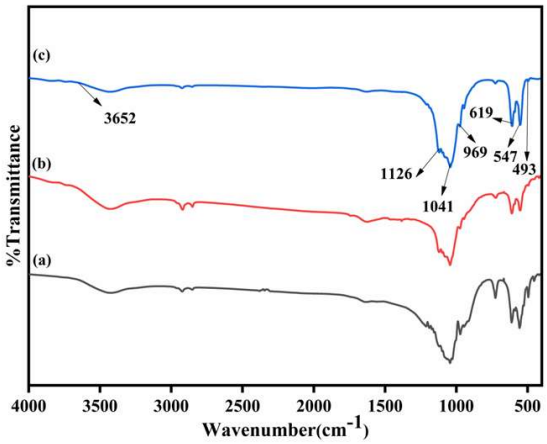

Fig. 1 FTIR spectra of TCP powder prepared at different thiourea concentrations: (a) TCP, (b) 0.1 M TU and (c) 0.2 M TU.

3.2 X-Ray Diffraction (XRD)

The formation of the crystalline TCP phase, both with and without the additive, was confirmed using XRD analysis. Fig. 2(a–c) illustrates the synthesized tricalcium phosphate powders via hydrothermal method with varying thiourea (TU) concentrations of 0.1 M and 0.2 M respectively. The prominent diffraction peaks observed in Fig. 2(a-c) at 2θ values of 27.76°, 31.02°, 34.37°, 46.03°, and 52.61° closely align with the characteristic peaks of standard β-TCP (JCPDS No. 09-0169) [16], corresponding to the (214), (210), (220), (410), and (330) crystallographic planes, respectively. The calculated average grain size of TCP powders using Scherer's equation $D=K\lambda / (\beta \cos \theta)$ is shown in Table 2 [17].

Table 2 Calculated average grain size of TCP powders using Scherer's equation

Sample code	hkl values	Average grain size (nm)
TCP	(214), (210), (220), (410), (330)	22
TCP & TU (0.1 M)	(214), (210), (220), (410), (330)	19
TCP & TU (0.2 M)	(119), (210), (220), (413), (330)	15

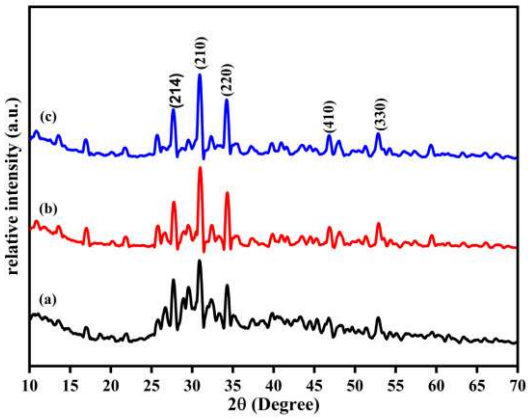

Fig. 2 XRD pattern of TCP powder prepared at different thiourea concentrations: (a) TCP, (b) 0.1 M TU and (c) 0.2 M TU.

3.3 Scanning Electron Microscope analysis

Fig. 3 (a–c) presents the surface morphology of the tricalcium phosphate powder synthesized via the hydrothermal method using different concentrations of thiourea (0.1 M and 0.2 M, respectively). The images demonstrate that the synthesized tricalcium phosphate (TCP) powders, assisted by thiourea, possess a spherical morphology. This spherical shape is particularly beneficial for biomedical applications, as it enhances the compatibility and integration between the implant material and the surrounding biological tissues. The presence of thiourea plays a crucial role in this outcome, as it not only promotes the formation of TCP but also serves as a filling agent during synthesis, thereby aiding in the production of uniform nano-sized TCP powders. The average particle size of the TCP, TCP & 0.1M TU and TCP & 0.2 M TU is 264.65 nm, 220.68 nm and 180.58 nm respectively. It is proved that the average particle size of the thiourea assisted powder is decreased when the concentration of thiourea is increased due to structure directing and surface functionalizing agent.

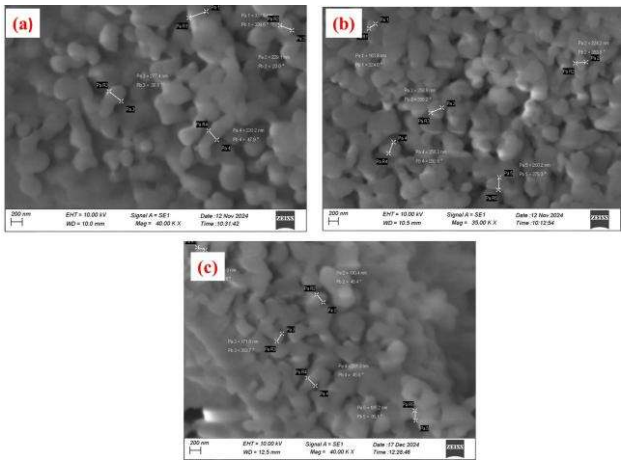

Fig. 3 SEM images of TCP powder prepared at different thiourea concentrations: (a) TCP, (b) 0.1 M TU and (c) 0.2 M TU.

3.4 Thermal analysis of TCP

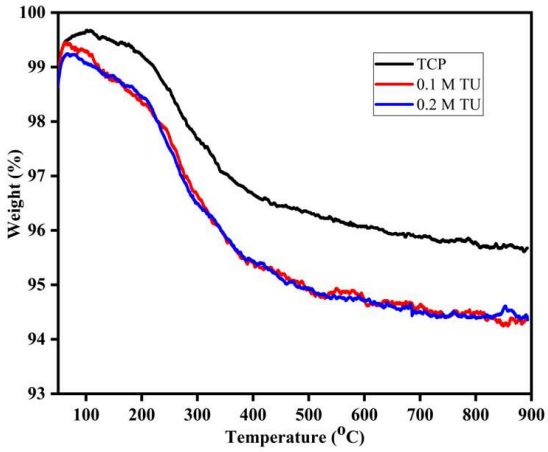

Fig. 4 (a–c) displays the thermogravimetric analysis (TGA) curves of the prepared HAP samples within the temperature range of 50–900 °C. The TGA plots provide insights into the thermal stability of the samples and indicate chemical decomposition or vaporization events. The curves do not show any loss in weight indicating that no decomposition has occurred in the sample proving a very good thermal stability of the as-synthesized powders.

Fig. 4 TGA graph of TCP powder prepared at different thiourea concentrations: (a) TCP, (b) 0.1 M TU and (c) 0.2 M TU.

4. Conclusion

In this research work, tricalcium phosphate (TCP) powder was successfully synthesized using the hydrothermal method with thiourea as an additive. The results confirmed the purity of the synthesized powders, as no impurity peaks were observed in the FTIR analysis. XRD studies revealed that the powders were well-crystallized. SEM analysis demonstrated effective control over particle size and morphology, resulting in spherical-shaped TCP particles. TGA analysis shows that there is no weight loss in the sample and hence it proved the thermal stability of the synthesized powder. These characteristics suggest that the synthesized TCP powder holds strong potential for biomedical applications.

5. Conflict of interest:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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