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# Facile synthesis of lithium carbonate nanoparticles with potential properties for bone repair applications

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ABSTRACT

Lithium carbonate nanoparticles were synthesized by facile chemical route in the presence of organic capping agents. Nanosized $Li_2CO_3$ particles of ~86 nm in size were produced from LiOH solution and preferably using PVA as a capping agent. FTIR-ATR analysis revealed that $Li_2CO_3$ phase is formed during calcination of the freeze-dried synthesis product. *In vitro* tests shown that nanoparticle concentrations up to 600 μg/mL do not disturb cell viability and promote the osteogenic differentiation of stem cells by $Li^+$ ions (9.7 mM) leached from the nanoparticle. The biological properties exhibited by the $Li_2CO_3$ nanoparticles make of them attractive for bone repair applications.



## 1. Introduction

Lithium, a key ingredient for batteries, is also a therapeutic element with properties to stimulate the cellular mechanisms of bone tissue formation [1]. Local application of $Li^+$ ions enhances bone healing by increasing bone mineral density or accelerating the bone formation process [2]. Likewise, bioceramics such as calcium phosphate cement [3] and microbioactive glass [4,5] have shown a superior osteogenic and angiogenic [6] properties when doped with lithium.

Elements produced in nanoparticle form offer greater surface area for biological interactions, a more controlled release of ions, and the possibility of designing nanocomposite materials. Bioactive nanoparticles in powder are also demanded in bone reconstruction and tissue engineering. The synthesis of zero-valent lithium 5 nm – colloidal nanoparticles has been reported by chemical reduction of $Li^+$ ions [7], which however requires sophisticated separation methods [8]. In this respect, lithium carbonate ($Li_2CO_3$) nanoparticles can be produced in their powder form as demonstrated by Lu et al. [9] by precipitation reactions in a membrane microreactor.

In this work, we reported the synthesis of powdered $Li_2CO_3$ nanoparticles by using facile chemical routes and studied the influence of different capping agents on particle size. The cytocompatibility and ability of the nanoparticles to enhance the alkaline phosphatase (ALP) activity in stem cells is also demonstrated.

## 2. Materials and methods

### 2.1. Synthesis of nanoparticles

Nanoparticles were synthesized from a lithium hydroxide (LiOH) solution in the presence of polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), or cetyltrimethylammonium bromide (CTA) as capping agents. Briefly, 0.5 g of capping agent compound was dissolved in 50 mL distilled water at room temperature for 1.5 h. Then, 1 g of LiOH was added and the reacting solution was kept under stirring at room temperature for 1 h. Afterward, the suspension was frozen at −80 °C, lyophilized and calcined at 700 °C in air for 5 h at a heating rate of 4 °C/min to obtain a fine white powder.

### 2.2. Nanoparticle characterization

The particle size and morphology of the synthesized products were analyzed by scanning electron microscopy (SEM) with a Jeol JSM-IT300LV microscope equipped with energy dispersive X-ray detector Aztec EDS (Oxford Instruments) for microanalysis. Particle size distribution was estimated by using the analysis tools of the microscope software. The data were analyzed using One-way ANOVA analysis and Tukey's multiple comparison tests in Graph Pad Prism software at $p < 0.05$.

The percentage yield of the synthesis process was estimated by dividing the mass of the synthesis product by the mass of LiOH used in the reaction according to the following expression: % Yield = (mass of synthesized product/LiOH mass) × 100.

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**Table 1**
Mean particle size of products and synthesis yields.

| | Particle size (nm) | Yield (%) |
|---|---|---|
| PVA/nLi | 86.6 ± 10.8 | 86 |
| PVP/nLi | 108.5 ± 19.3 | 71 |
| CTA/nLi | 101.9 ± 17.5 | 48 |

A selected nanoparticle product was further analyzed by attenuated total reflectance with Fourier transform infrared spectroscopy (ATR-FTIR) on an Agilent Cary 630 ATR-FTIR spectrometer. X-ray diffraction (XRD) pattern was measured on a Siemens D 5000 diffractometer using CuKα radiation within a 2$\theta$ range of

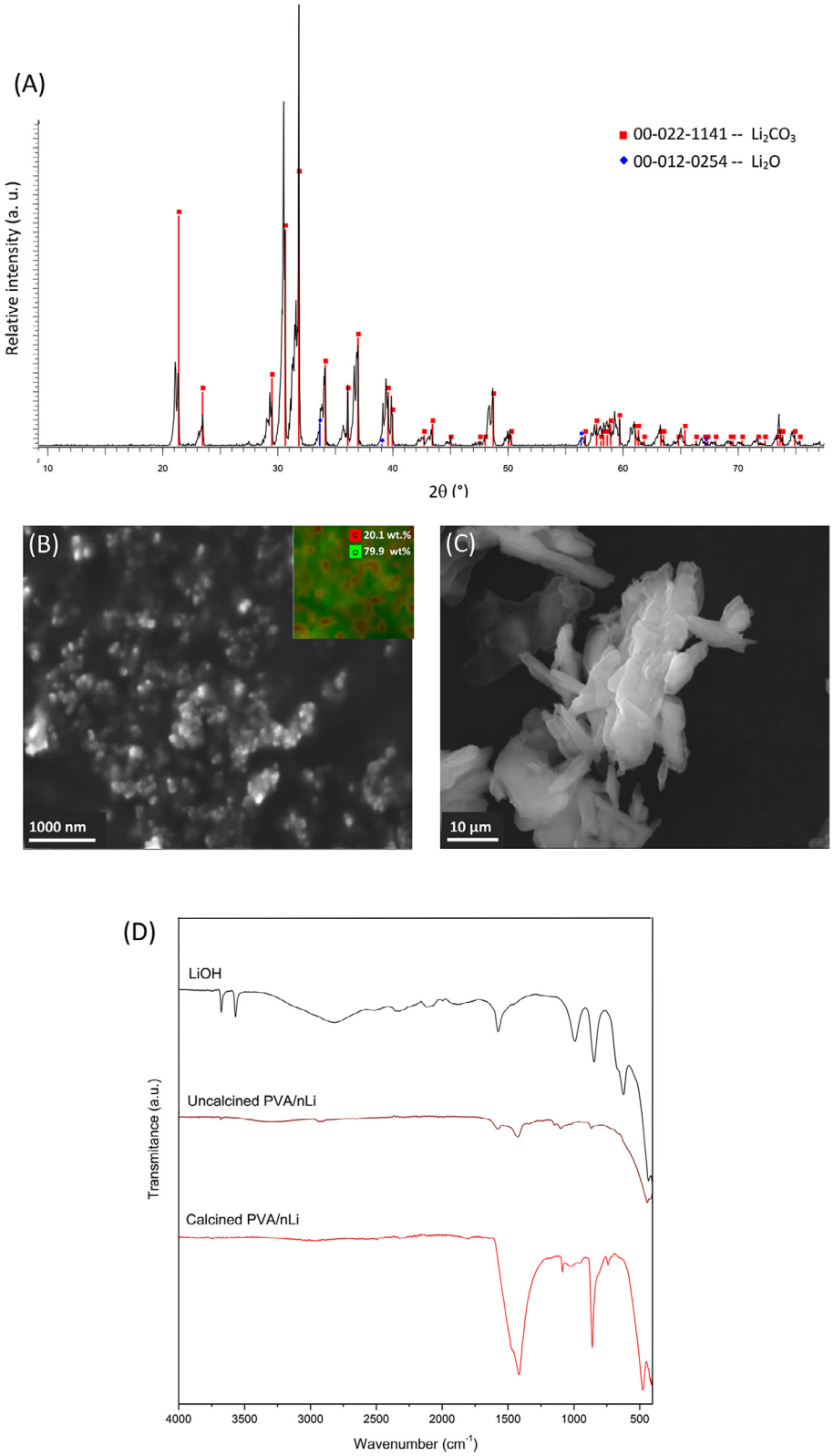


**Fig. 1.** XRD analysis (A) and SEM image (B) of PVA/nLi particles. SEM image of traditional $Li_2CO_3$ microparticles (C). FTIR-ATR analysis of PVA/nLi synthesis products (D).