## Microwave Assisted Synthesis of Alkaline Earth Phosphates Nanospheres

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Statement of Purpose: Alkaline earth phosphates have a wide range of biomedical applications. Of these, calcium phosphate (CaP) is the most well-known, being a major constituent of bone [1]. Magnesium phosphate (MgP) has attracted research interests in recent years [2]. Strontium doped calcium phosphate can fight against osteoclast and stimulate osteoblast activity [3], while an excess strontium content can inhibit cell proliferation on contrast [4]. Additionally, strontium can provide radio-opacity and antimicrobial activity [5, 6]. This study demonstrates the possibility to produce alkaline earth phosphate nanospheres via a rapid microwave assisted synthesis process. There are several highlights of this work: 1) it is an efficient way to produce highly active alkaline earth phosphate in the form of nanospheres; 2) it is easy to control the composition of alkaline earths in synthesized nanospheres; 3) it provides a possibility to systematically study the combined effects of alkaline earth elements on cell behavior and tailor the optimum composition of alkaline earth phosphate.

Methods: The synthesis technique uses an aqueous solution containing alkaline earth elements ions (Mg<sup>2+</sup>,  $Ca^{2+}$ ,  $Sr^{2+}$ ) and phosphate ions (PO<sub>4</sub><sup>3-</sup>). To proceed with microwave-assisted process, beaker with 100 ml prepared aqueous solution was placed into a household 800 W microwave oven for 5 min maximum power heating. At the end of microwave heating, the beaker was moved to a cold water bath to cool down. Finally, the precipitates were collected and dried in 37°C oven overnight. Two important aspects in this approach are: 1) solution needs to be transparent before microwave heating; and 2) a suitable pH should be present in which the synthesized alkaline earth phosphate nanospheres are stable. The precipitates were characterized using XRD, SEM, and TEM. Their activity and biocompatibility were also evaluated.

Results: As shown in Fig. 1, the as-synthesized materials are nanospheres. CaMgP, CaSrP, and MgSrP can all be synthesized with varied molar ratio of alkaline earth elements. Additionally, Mg<sup>2+</sup> was observed to stabilize the spherical structure of alkaline earth phosphates instead of forming nanoneedles at the nanosphere/solution interface during the cooling. The result is the loss of crystallinity of the as-synthesized materials (Fig. 1). The nanospheres can be converted into mature apatite once in contact with simulated body fluid (SBF) or other medium. Such phenomenon suggested the synthesized nanospheres can be precursors of matured alkaline earth phosphates apatite. The *in vitro* studies show the combination of Ca<sup>2-</sup> and  $Mg^{2+}$  is beneficial to osteoblast cells proliferation, and the combination of  $Mg^{2+}$  to  $Sr^{2+}$  can significantly reduce the toxicity of  $Sr^{2+}$  to osteoblast cells (Fig. 2). After sintering at 900 °C, the as-synthesized nanospheres can fuse together to generate porous structure (Fig. 3).

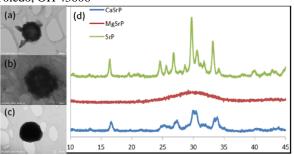


Figure 1. TEM images of (a) SrP, (b) CaSrP, (c) MgSrP, and (d) their related XRD patterns

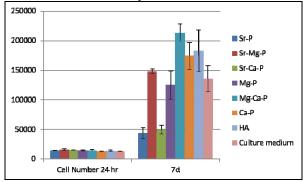


Figure 2. Results of 7 days MC3T3 preosteoblast cell culture on synthesized nanospheres, HA and blank well used as control

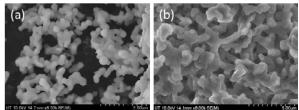


Figure 3. SEM of (a) sintered CaMgP and (b) sintered MgP nanospheres

**Conclusions:** This microwave assisted synthesis route is able to synthesize alkaline earth phosphate nanospheres. It also allows studying the interactions of different alkaline earth ions in crystals formation and surrounding cells activity. The root cause of the success of this method is the presence of as-synthesized nanospheres that are energetically the most stable structure under microwave irradiation. These nanospheres with optimized compositions are expected to have potential applications in tissue engineering.

## **References:**

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