Modelling and Validation of Nano Hydroxyapatite Formation for Medical Applications

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In this study, a wet chemical synthesis of Nano-hydroxyapatite HAP [$Ca_{10}(PO_4)_6(OH)_2$] was investigated through a kinetic model derived based on the classical nucleation theory. The model mapped the nucleation rate from synthesis variables, supersaturation, temperature, and interfacial tension. During the study, the effect of supersaturation for nano formation of hydroxyapatite particles was experimentally studied keeping the other two variables constant. Since a direct measurement is not possible to measure the nucleation rate, the induction time, which is inversely proportional to the nucleation rate, was introduced to the model. The model simply suggests that the induction time will decrease with increased supersaturation. Also, it indirectly predicted the finer particles for lower induction times caused by higher supersaturations. Then the model was subjected to the validated process with a proper experimental design. During the experiment, the nano-hydroxyapatite powder was synthesized using $Ca(OH)_2$ and H_3PO_4 as precursors at five different supersaturations while the temperature for the whole study remained the same as 30^0C. The supersaturation for hydroxyapatite was caused by changing the concentration of precursors maintaining the constrained Ca/P molar ratio near 1.6-1.7 between Calcium and Phosphorus. The H_3PO_4 was added to the $Ca(OH)_2$ suspension at a constant acid addition rate of 4 ml/min using a burette under vigorous stirring having maintained the final pH at 10.

During the synthesis reaction, the variation of pH of the mixed precursor suspension was measured and analyzed. The main parameter obtained from the experiment was the induction time. This induction time was marked by the onset of the first and more significant pH drop in the final mixture. After 48 hrs. of aging, the precipitate was separated by centrifuging at room temperature. Then the resulting wet powder samples were dried and characterized. First, the predicted model validity was investigated through a linear regression model and the regression/ kinetic constants

were determined. In statistical validation, 95.84% variability could be described by the predicted model according to R_2-test. In addition, the validated model could be applied to describe the nucleation process with the critical radius approach for each sample. With laser particle analyzer results, it was obvious that there was a significant reduction in the particle size when the supersaturation was higher. The model predicted this was caused by the higher nucleation density with increased supersaturation. In that scenario, the nucleation mechanism would be dominant compared to the growth of hydroxyapatite. The morphological and chemical analysis with SEM revealed that the formation of hydroxyapatite in solution is not a single-step process and it takes place via some amorphous intermediates with a time-dependent Ca/P molar ratio. In nano-sized form, hydroxyapatite is extensively used for a variety of extended medical applications. Finally, this model was experimentally validated by Laser Particle Analyzer and SEM studies. FTIR studies showed the characteristic peaks in hydroxyapatite and a trace amount of carbonate incorporation was observed in the lattice due to the synthesis in atmospheric conditions.

Keywords: Nano-hydroxyapatite, wet chemical precipitation, Supersaturation