Hydroxyapatite (HAp) based nanocomposites for controlled drug delivery and water purification

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ABSTRACT

This dissertation is concerned with the investigation of hydroxyapatite nanocomposites in potential applications such as drug delivery, antibacterial and water purification. Current cancer treatment protocols result in harmful side effects. Consequently, there is an increasing demand to develop targeted drug delivery systems that can destroy cancer cells without damaging healthy cells. This study focuses on investigating the possibility of improving the efficacy of drug molecules by encapsulating them in nanoparticles. Therefore, preparation of a novel drug carrier using iron oxide nanoparticles (IONPs), combined with polymers (Sodium alginate and Carboxymethyl cellulose) and hydroxyapatite (HAp) for targeted (pH sensitive) and slow release of drug molecules was investigated. Nanocarriers were characterized using XRD, FT-IR, SEM, TEM, TGA and AAS. The best carrier system was identified as the NaAlg/HAp@IONP. This, system was utilized to load doxorubicin, curcumin, 6-gingerol and their combinations to understand the effectiveness as a drug carrier. These systems exhibited 95-98% (w/w) drug loading efficiency with a preferential slow release of drug molecules at lower pH (5.3) over 4-7 days. *In-vitro* anti-proliferative activity of drug loaded nanocarriers were tested on MCF-7 and HEpG2 cancer cells and exhibited low IC_{50} values compared with the previously reported work. Fluorescence images for these cancer cells treated with drug loaded nanoparticles indicated that these particles can induce apoptosis as many of the cells were undergoing drastic morphological and nuclear changes after 24 hours of incubation. This was further confirmed using flow cytometry. To ensure the safer application of these nanoparticles in targeted delivery, the effect of them on erythrocytes, rat bone marrow cells and epithelial kidney cells (Vero- non cancerous) was investigated. The results implied that the drug loaded systems have less impact on these non-cancerous cells. These drug loaded systems were further tested for their antibacterial property. The antibacterial effect of curcumin loaded NaAlg/HAp@IONPs and 6-gingerol loaded NaAlg/HAp@IONPs was tested on *Staphylococcus aureus* and it was found that the antibacterial effect of these two systems was sustained for four days, whereas with the positive control (gentamicin) showed the complete disappearance of the antibacterial effect.

In a separate investigation, morphologically different polymer and metal based HAp systems were synthesized and employed in water purification applications. The removal of Pb(II) and an azo dye was investigated using these systems. Carboxymethylcellulose (CMC) incorporated nano HAp (CMC@HAp) system and chitosan incorporated nano HAp (CTS@HAp) system were found to adsorb Pb(II) with adsorption capacities of 625 mg/g and 909 mg/g respectively. Also, these systems recorded the adsorption capacities of 200 mg/g (CMC@HAp) and 303 mg/g (CTS@HAp) for the azo dye and these adsorption values were the highest recorded.

The results highlighted the versatile behavior of the synthesized HAp nanosystems. It provided a novel biocompatible, pH sensitive, slow release and targeted drug delivery system with profound anti-proliferative effect on breast and liver cancer cells. In addition, polymer based HAp nanocomposites can be potentially employed in point-of-use water filters due to high adsorption capacities observed.

Key words: Iron oxide, hydroxyapatite, water purification, targeted, pH sensitive, apoptotic