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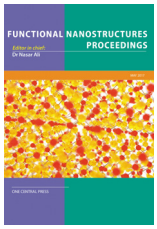

Calcitriol Nanoencapsulation as a New Approach for its Use in Chemotherapy

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ABSTRACT

The clinical use of calcitriol as an anticancer agent is limited by the occurrence of hypercalcemia due to the supraphysiological doses required for such an application [1]. Calcitriol vectorization is an interesting strategy to overcome these limitations and to enhance its efficiency by targeting and extending its activity in cancer cells [2]. In this line, biodegradable polymeric nanoparticles (NP) were chosen as delivery systems and formulation studies were carried out by varying polymer:oil mass ratio in order to develop a long-acting form. NP of around 200 nm presenting a high encapsulation efficiency of calcitriol (>70%) were obtained. Their growth inhibitory efficiency was evaluated in vitro on human breast adenocarcinoma cells (MCF-7) using an MTT assay. We found that formulation variables directly impact calcitriol release from NP, and hence its biological activity in vitro. Incubation for 24 hours with 10−7 M of calcitriol showed a significantly higher antiproliferative activity of the NP formulation presenting the most sustained release profile (polymer:oil ratio of 1:2) compared to free calcitriol at day 7, and 33% and 93% of cell viability were respectively found at day 10. Preliminary in vivo toxicity assays were performed by administering calcitriol-loaded NP to mice. A good tolerance of treatment was found as the initial calcemia (10.5mg/dL) was recovered at day 7, allowing repeated dose administration to go forward with in vivo efficacy evaluations of developed system on a xenograft mouse model.
In conclusion, our developed system enhanced and extended calcitriol antiproliferative activity in vitro and will be confirmed in vivo.

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