

## The Fe<sub>3</sub>O<sub>4</sub>-PAA-(HP-γ-CDs) Biocompatible Ferrimagnetic Nanoparticles for Increasing Efficacy and Reducing Toxicity in Superparamagnetic Hyperthermia: A Promising Approach for Alternative Cancer Therapy

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In this paper we present the obtaining of Fe<sub>3</sub>O<sub>4</sub>-PAA-(HP-γ-CDs) ferrimagnetic nanobioconjugates in a hybrid core-shell biostructure (core: inorganic Fe<sub>3</sub>O<sub>4</sub> nanoparticles, and shell: organic PAA-(HP-γ-CDs)) and their use in superparamagnetic hyperthermia without cellular toxicity and with increased efficacy for future alternative cancer therapy. In order to design the optimal experimental conditions for obtaining nanobioconjugates and then superparamagnetic hyperthermia (SPMHT), we used the study techniques by molecular docking simulation and computational assessment of maximum specific loss power (SLP) that leads to nanoparticles heating. The nanoparticles and nanobioconjugates obtained were studied and characterized by X-ray diffraction (XRD), transmission electron microscopy (TEM), Fourier transformed - infrared spectroscopy (FT-IR), dynamic light scattering (DLS) and magnetic measurements (MM). The cell viability of the nanoparticles and nanobioconjugates was assessed by means of a colorimetric test entitled 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay using human immortalized keratinocytes (HaCaT) cell line. Superparamagnetic hyperthermia with nanoparticles and nanobioconjugates was obtained experimentally in a magnetic field of 15.92 kA/m and frequency of 312.2 kHz for magnetic nanoparticles core with a (average) diameter of 15.8 nm, which give the maximum hyperthermic effect that lead to the temperature of ~42.5 °C necessary in the therapy of tumors in a short time so as not to affect the healthy tissues. The biological screening of Fe<sub>3</sub>O<sub>4</sub>-PAA nanoparticles and PAA-(HP-γ-CDs) nanobioconjugates showed no cytotoxic effect on HaCaT cells for a time interval of 24 h, both under standard (37 °C) and hyperthermia conditions (42.5 °C). Thus, Fe<sub>3</sub>O<sub>4</sub>-PAA-(HP-γ-CDs) ferrimagnetic nanobioconjugates can be used successfully in superparamagnetic hyperthermia without toxicity and with increased efficiency due to the small layer thickness of PAA-(HP-γ-CDs) shell which is suitable in this alternative therapeutic technique.

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