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Magnesium Nanoparticles for Photothermal Therapy

Authors : E. Locatelli, I. Monaco, R. C. Martin, Y. Li, R. Pini, M. Chiariello, M. Comes Franchini

Abstract : Despite the many advantages of application of nanomaterials in the field of nanomedicine, increasing concerns have been expressed on their potential adverse effects on human health. There is urgency for novel green strategies toward novel materials with enhanced biocompatibility using safe reagents. Photothermal ablation therapy, which exploits localized heat increase of a few degrees to kill cancer cells, has appeared recently as a non-invasive and highly efficient therapy against various cancer types; anyway new agents able to generate hyperthermia when irradiated are needed and must have precise biocompatibility in order to avoid damage to healthy tissues and prevent toxicity. Recently, there has been increasing interest in magnesium as a biomaterial: it is the fourth most abundant cation in the human body, and it is essential for human metabolism. However magnesium nanoparticles (Mg NPs) have had limited diffusion due to the high reduction potential of magnesium cations, which makes NPs synthesis challenging. Herein, we report the synthesis of Mg NPs and their surface functionalization for the obtainment of a stable and biocompatible nanomaterial suitable for photothermal ablation therapy against cancer. We synthesized the Mg crystals by reducing MgCl2 with metallic lithium and exploiting naphthalene as an electron carrier: the lithium–naphthalene complex acts as the real reducing agent. Firstly, the nanocrystal particles were coated with the ligand 12-ethoxy ester dodecanehydroxamic acid, and then entrapped into water-dispersible polymeric micelles (PMs) made of the FDA-approved PLGA-b-PEG-COOH copolymer using the oil-in-water emulsion technique. Lately, we developed a more straightforward methodology by introducing chitosan, a highly biocompatible natural product, at the beginning of the process, simultaneously using lithium–naphthalene complex, thus having a one-pot procedure for the formation and surface modification of MgNPs. The obtained MgNPs were purified and fully characterized, showing diameters in the range of 50-300 nm. Notably, when coated with chitosan the particles remained stable as dry powder for more than 10 months. We proved the possibility of generating a temperature rise of a few to several degrees once MgNPs were illuminated using a 810 nm diode laser operating in continuous wave mode: the temperature rise resulted significant (0-15 °C) and concentration dependent. We then investigated potential cytotoxicity of the MgNPs: we used HN13 epithelial cells, derived from a head and neck squamous cell carcinoma and the hepa1-6 cell line, derived from hepatocellular carcinoma and very low toxicity was observed for both nanosystems. Finally, in vivo photothermal therapy was performed on xenograft hepa1-6 tumor bearing mice: the animals were treated with MgNPs coated with chitosan and showed no sign of suffering after the injection. After 12 hours the tumor was exposed to near-infrared laser light. The results clearly showed an extensive damage to tumor tissue after only 2 minutes of laser irradiation at 3Wcm-1, while no damage was reported when the tumor was treated with the laser and saline alone in control group. Despite the lower photothermal efficiency of Mg with respect to Au NPs, we consider MgNPs a promising, safe and green candidate for future clinical translations.

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