Field-controlled magnetoelectric core-shell-shell nanoparticles as remote magnetic hyperthermia and on-demand drug release

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This study presents the design of innovative magnetoelectric nanoparticles (MENPs) consisting of a bimagnetic core (Fe_3O_4@$CoFe_2O_4$) and a piezoelectric shell ($BaTiO_3$). The aim is to harness the quantum exchange coupling of bimagnetic nanoparticles alongside the magnetoelectric effect of the core-shell-shell structure under external magnetic fields for cancer therapy applications. The nanoparticles heating capability under high-frequency magnetic fields enables inductive magnetic hyperthermia, while the intrinsic magnetoelectricity of MENPs coupled with low-frequency magnetic fields, allow for the remote, controlled release of a drug model (e.g., paclitaxel, PTX) in a biological medium.

Keywords: magnetoelectric nanoparticles; magnetic hyperthermia; drug release

1. Introduction

Exchange-coupled bimagnetic nanoparticles have demonstrated remarkable properties for inductive hyperthermia applications, owing to the quantum synergism between the magnetic core and a magnetically thin shell [1]. The heating efficiency of these particles is quantified by the specific absorption rate (SAR), an extrinsic parameter that is influenced by the physicochemical properties of the particles. Additionally, the magnetoelectric effect (ME) provides a unique capability for field-triggered drug release, enabling controlled, on-demand drug delivery by breaking chemical bonds under the influence of an electromagnetic stimulus [2].

2. Results and discussion

In this study, a magnetoelectric core-shell-shell architecture (Fe_3O_4@$CoFe_2O_4$@$BaTiO_3$), designated as IO@CFO@BTO, was synthesized using a solvothermal method followed by an organosol route. Magnetically core-shell nanoparticles were produced via one-pot thermal decomposition, while the piezoelectric shell was grown on the surface of the seed nanoparticle using a sol-gel process in a lipophilic solvent system. The shape, size, and shell thickness of the nanoparticles were controlled through the composition, surfactant molar ratio of precursors, heating rate, and reaction time.

The structural and morphological characteristics of the nanostructures were characterized using techniques such as X-ray diffraction (XRD), Raman spectroscopy, X-ray photoelectron spectroscopy (XPS), selected area electron diffraction (SAED), and scanning electron microscopy (SEM). Magnetic inductive measurements were performed to evaluate the heating capacity (i.e., specific absorption rate (SAR)) of the colloidal nanoparticles under an alternating magnetic field (AMF) (ν = 488 kHz, B = 24 mT). To ensure water-based colloidal stability, the surface of the magnetic nanoparticles was modified by silane coupling, resulting in a zeta potential range of -26.4 mV to -23.3 mV. The SAR results of IO@CFO@BTO nanoparticles (52 W/g) showed slightly lower heating properties compared to the bimagnetic core counterpart (64 W/g). This reduction is primarily attributed to the presence of the ferroelectric outer shell, which leads to a decrease in mass magnetization and an increase in the average hydrodynamic diameter of the nanoparticles, from 133 nm to 196 nm.

The drug loading capacity onto the functionalized MENPs was determined via UV-Vis spectroscopy, yielding a value of 81% (78 µg/mg MENPs). PTX release in PBS medium was evaluated under low-frequency AC fields (ν = 1 kHz, B = 2.6 mT). After successive therapy protocols (60 min/day for 3 days), the cumulative release rates were over 64%, 85%, and 95% of the drug, respectively. These results demonstrate that relatively low AC fields can effectively trigger paclitaxel release on demand while maintaining safe delivery conditions. ME of the core-shell-shell architecture provides a physical mechanism for remotely modulating the binding forces between the oppositely charged MENPs and the polarized PTX drug molecule.

Thus, an approach integrating magnetic inductive hyperthermia with on-demand drug release, triggered by a non-invasive external stimulus, holds great promise for advancing cancer therapy.

References

[1] J.H. Lee et al., Nat. Nanotechnol. **6** (2011), 418–422.
[2] V. Andre et al., Nanoscale Horiz. **10** (2025), 699-718.

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