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Determining the key parameters to reach synergistic effects between magnetic hyperthermia and ROS production in $Zn_xFe_{3-x}O_4$ magnetic Nanoparticles.

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Current challenges in the field of cancer research have gradually shifted their focus from monotherapy to combination therapy for enhanced treatment effectiveness [1]. In this way, the fast evolution in the field of nanozymes has led to the promising combination between nanocatalytic or chemodynamic therapy (CDT) with other kinds of therapies such as phothermal therapy (PTT) [2], photodynamic therapy (PDT) [3] and Magnetic Fluid Hyperthermia (MFH) [4] to improve their therapeutic results.

When talking about nanocatalytic therapies, the main idea is to use of the hydroxyl radical (·OH), the most toxic of the reactive oxygen species (ROS), to induce initial oxidative damage to the cell membrane, improving the permeability of the cell membrane and making it more sensitive to heat. This radical is produced by the disintegration of hydrogen peroxide (H2O2) through a Fenton reaction with a metal ion. In this way, great therapeutic effects have been reported to threaten breast cancer and osteosarcoma cell lines [4, 5]. However, it is imperative to study how the intrinsic parameters of magnetic nanoparticles (MNPs) used as nanozymes affect the ROS production and heat release, to find the best relationship between them and improve the synergy between the therapies. In this work, a series of $Zn_xFe_{3-x}O_4$ MNPs with mean diameters $<d>$ between 11-32 nm were studied. A detailed characterization study, including Proton-Induced X-ray emission (PIXE), Transmission Electron Microscopy (TEM), SQUID Magnetometry, Ferromagnetic Resonance (FMR), Electron Paramagnetic Resonance (EPR) and Specific Loss Power (SLP) was performed, unravelling a compromise between the heating efficiency of the MNPs and their ROS production. Values of SLP up to 1440 w/g and concentration up to 1000 nM of hydroxyl radical (·OH) were obtained. The optimal size of the MNPs for the combination therapy is in the range of 20-25 nm.

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