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Green and scalable aqueous synthesis of biocompatible magnetite nanoparticles for cancer treatment by magnetohyperthermia

Laudemir Carlos Varanda[1], Natália Mariana dos Santos[1], Fillipe Vieira Rocha[2], Tamara Teixeira[3]

[1]Instituto de Química de São Carlos - Universidade de São Paulo (*Físico-Química*) , [2]Univerdade Federal de São Carlos (*Química*) , [3]Universidade Federal de São Carlos (*Química*)

e-mail: lvaranda@iqsc.usp.br

Challenges for magnetic iron oxide nanoparticle (SPIONs) applications in cancer treatment via magnetohyperthermia include the costs of large-scale production and its surface functionalization for biocompatibility, increased circulation time, and tissue recognition [1]. Here, a new one-pot synthesis of functionalized SPIONs in an aqueous medium is described. The reduction-precipitation method [2,3] uses $FeCl_3$ and Na_2SO_3 to promote the in situ stoichiometric reduction of Fe^{3+} to Fe^{2+}, followed by precipitation in an alkaline medium (NaOH). This method reduces costs and does not need deaeration or an inert atmosphere, resulting in SPIONs with an average of 25±4 nm. This meets the precepts of Green Chemistry with a high yield (~2.1 g/100 mL of solution) scaled in a chemical reactor using a solution volume of up to 2000 mL. SPIONs structure by Mössbauer spectroscopy revealed a non-stoichiometric magnetite phase (oxygen vacancies, $\square$), $Fe^{3+}[Fe^{2.5+}_{1.44}Fe^{3+}_{0.47}\square_{0.09}]O_4$. The method allows the SPIONs functionalization with 3-(mercaptopropyl)trimethoxysilane (MPTMS) inside the reactor (SPIONS@MPTMS). The SPIONs@MPTM has a hydrodynamic diameter of 125 nm, zeta potential of -30 mV, saturation magnetization of 60 emu/g, and high hyperthermal efficiency (heat generation in alternating magnetic field). No cytotoxicity was observed in different tumors and healthy cell lines. The MPTMS onto the SPION surface allows simple additional functionalization via disulfide bonding with polymers, drug loading and tissue recognition molecules, e.g., folic acid. Our results show a simple, green, low-cost, and large-scale synthesis route for MPTMS-functionalized SPIONs with high potential for cancer treatment via magnetohyperthermia.

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