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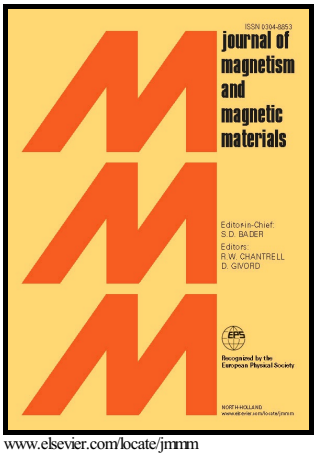

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Simultaneous hyperthermia and doxorubicin delivery from polymer-coated magnetite nanoparticles

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ABSTRACT

In this work, the hyperthermia response, (i.e., heating induced by an externally applied alternating magnetic field) and the simultaneous release of an anti-cancer drug (doxorubicin) by polymer-coated magnetite nanoparticles have been investigated. After describing the setup for hyperthermia measurements in suspensions of magnetic nanoparticles, the hyperthermia (represented by the rate of suspension heating and, ultimately, by the specific absorption rate or SAR) of magnetite nanoparticles (both bare and polymer-coated as drug nanocarriers) is discussed. The effect of the applied ac magnetic field on doxorubicin release is also studied, and it is concluded that the field does not interfere with the release process, demonstrating the double functionality of the investigated particles.

KEYWORDS

Doxorubicin; drug release; magnetic hyperthermia; magnetic nanoparticles; polymeric stabilization; PEGylation

1. INTRODUCTION

The number of biomedical applications of magnetic nanoparticles has grown exponentially in recent years [1-3]. Three main fields can be mentioned, and their combinations thereof. One is contrast enhancement in magnetic resonance imaging (MRI) [1], while drug delivery and magnetic hyperthermia are also active research areas. In the latter, taking advantage of the fact that an alternating magnetic field applied to a ferrofluid produces heating in it, local temperature elevations can be produced in a site of the body where the particles have been injected (a tumor, say), without the need of physical contact. If a temperature of 42 ºC can be reached and maintained during at least half an hour, death of the tumor cells and, eventually, the disappearance of the tumor itself can be achieved [4-6]. The topic in this work is the possibility of employing the magnetic fluid with the double target of releasing antitumor drug while inducing hyperthermia. The method has been applied to a number of magnetic nanoparticle/drug combinations [7-9].

In the present work, we extend our previous investigation on the hyperthermia performance of magnetite nanoparticles (MNPs) with different stabilizing coatings [10] to include drug delivery. Magnetite particles are coated with a layer-by-layer assembly of the polyelectrolytes poly(ethyleneimine) (PEI) and poly(styrenesulfonate) (PSS) (P-MNPs hereafter), and an additional layer of poly(ethylene glycol) (PEG-MNPs). Doxorubicin (DOX), well known for its chemotherapeutic application in the treatment of different tumors [11], is then loaded by adsorption on the particles. The release rate of the drug from the nanoparticle vehicles is investigated in three different conditions: healthy body temperature, 42 ºC (the hyperthermia target) in a thermostatted bath, and also during the hyperthermia experiments themselves. Overall, the results indicate that