



## Liposomes loaded with hydrophilic magnetite nanoparticles: Preparation and application as contrast agents for magnetic resonance imaging

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### ABSTRACT

Magnetic fluid-loaded liposomes (MFLs) were fabricated using magnetite nanoparticles (MNPs) and natural phospholipids via the thin film hydration method followed by extrusion. The size distribution and composition of MFLs were studied using dynamic light scattering and spectrophotometry. The effect of ranges of magnetite concentration in MNPs hydrosol and MFLs for contrasting at both  $T_2$  and  $T_1$  relaxation times were determined. On  $T_2$  weighted images, the MFLs effectively increased the contrast if compared with MNPs hydrosol, while on  $T_1$  weighted images, MNPs hydrosol contrasting was more efficient than that of MFLs. *In vivo* magnetic resonance imaging (MRI) contrasting properties of MFLs and their effects on tumor and normal tissues morphology, were investigated in rats with transplanted renal cell carcinoma upon intratumoral administration of MFLs. No significant morphological changes in rat internal organs upon intratumoral injection of MFLs were detected, suggesting that the liposomes are relatively safe and can be used as the potential contrasting agents for MRI.

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## 1. Introduction

Theranostics, a new area in biomedical science combining both diagnostic and therapeutic functions in a single entity, is attracting researchers' attention worldwide [1]. Theranostics is focused on fabrication of functional tools combining the diagnostic and therapeutic functions. The concept of theranostics is fully met by nanosized magnetic particles, which have been demonstrated to be a potent means for tumor tissue targeting, local hyperthermia-based therapy [2] and for MRI diagnostics [3–5].

Particularly, the remote heating of magnetic nanoparticles in tissues can be induced by the alternating magnetic field at a few hundreds kilohertz [6]. Among others, magnetite nanoparticles are the promising nanomaterial for biomedical applications, since they exhibit both the high values of magnetic permeability and the relatively high biocompatibility, and have been actively used in

inorganic composite fabrication [7]. Noteworthy, the synthesis and surface modification of magnetite nanoparticles can be achieved through the easy and straightforward facile techniques [8]. Normally, the magnetite nanoparticles change transverse relaxation time  $T_2$  and significantly increase the targeted tissue contrast in MR images [5,9].

The increase of nanoparticle circulation time in blood vessels facilitates the biomedical applications of MNPs through the accumulation of the therapeutic dose in the target tissue and implementing the targeted and controllable delivery. Incorporation of magnetic nanoparticles into liposomes can be an effective route to promote the MNPs-based vehicles for targeted delivery and MRI-enhancing agents [10].

Typically, two types of magnetic liposomes are produced: the classical small-sized magnetic liposomes containing the magnetic “core” (~15 nm) covered with the (phospho) lipid bilayer, and the large unilamellar magnetic liposomes (~100–500 nm) bearing the magnetic nanoparticles in the internal aqueous compartment (magnetic fluid-loaded liposomes or MFLs) [1,11]. The large unilamellar liposomes are more susceptible for directed navigation

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