Colloids and Surfaces B: Biointerfaces 149 (2017) 243–249

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

journal homepage: www.elsevier.com/locate/colsurfb

Tuning the non-covalent confinement of Gd(III) complexes in silica nanoparticles for high T_1-weighted MR imaging capability

Svetlana V. Fedorenko[a], Svetlana L. Grechkina[b], Asiya R. Mustafina[a], Kirill V. Kholin[a], Alexey S. Stepanov[a,b,*], Irek R. Nizameev[a,c], Ildus E. Ismaev[d], Marsil K. Kadirov[a], Rustem R. Zairov[a,b], Alfia N. Fattakhova[b], Rustem R. Amirov[b], Svetlana E. Soloveva[a]

[a] A.E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center of Russian Academy of Sciences, Arbuzov str., 8, 420088, Kazan, Russia
[b] Kazan (Volga region) Federal university, Kremlyovskaya str., 18, 420008, Kazan, Russia
[c] Kazan National Research Technological University, Kazan 420015, Russia
[d] A.N. Tupolev Kazan National Research Technical University, 10, K. Marx St., Kazan, 420111, Russia

ARTICLE INFO

Article history:
Received 29 June 2016
Received in revised form 6 September 2016
Accepted 13 October 2016
Available online 14 October 2016

Keywords:
Positive contrast agents
Silica nanoparticles
MRI
Gd(III) complexes
Cytotoxicity
Interfaces

ABSTRACT

The present work introduces deliberate synthesis of Gd(III)-doped silica nanoparticles with high relaxivity at magnetic field strengths below 1.5 T. Modified microemulsion water-in-oil procedure was used in order to achieve superficial localization of Gd(III) complexes within 40–55 nm sized silica spheres. The relaxivities of the prepared nanoparticles were measured at 0.47, 1.41 and 1.5 T with the use of both NMR analyzer and whole body NMR scanner. Longitudinal relaxivities of the obtained silica nanoparticles reveal significant dependence on the confinement mode, changing from 4.1 to 49.6 mM^{-1} s^{-1} at 0.47 T when the localization of Gd(III) complexes changes from core to superficial zones of the silica spheres. The results highlight predominant contribution of the complexes located close to silica/water interface to the relaxivity of the nanoparticles. Low effect of blood proteins on the relaxivity in the aqueous colloids of the nanoparticles was exemplified by serum bovine albumin. T_1- weighted MRI data indicate that the nanoparticles provide strong positive contrast at 1.5 T, which along with low cytotoxicity effect make a good basis for their application as contrast agents.

1. Introduction

Positive contrast agents (CAs) have gained great attention during recent decades due to their great impact in medicine [1–6]. Mononuclear Gd(III) complexes have got a wide application, although shortcomings of commercial CAs leave a room for improvement. Relaxivity enhancement due to slow tumbling of Gd(III) centres is a reason for increasing interest for nanoparticulate Gd(III)-based MRI CAs [5–12]. Silica coating of ultrasmall Gd(III) oxide or citrate nanoparticles, as well as mononuclear Gd(III) complexes is rather promising route to make nanoparticulate Gd(III)-based MRI contrast agents [13–18]. Silica coating provides hydrophilization of Gd_2O_3 nanoparticles [13–15] or silica nanoparticles serve as supports for surface immobilization by Gd(III) mononuclear complexes [16–21]. The extraction of Gd(III) ions by silica templates is one of possible immobilization ways [18], although a covalent silica surface functionalization by Gd(III) complexes is more widely represented in literature [16,17,19–21] for the immobilization. However, silica surface decoration by target peptides is required for selective binding with biotarget, which is exemplified by report [22] representing silica surface decoration by both gadolinium complexes and cell-penetrating peptides along with fluorophores. Nevertheless, simple noncovalent incorporation of mononuclear complexes into silica through a sol-gel method is worth noting for its advantage in remaining silica surface open for further decoration by biorelevant anchor groups [23–25].

The works of Caravan [26,27] highlight that subtle combination of rotation correlation times and water exchange rates is required for high r_1 and r_2 values at low fields (below 1.5 T). This tendency points to an impact of silica coating thickness in relaxivity of silica coated Gd(III) complexes. The importance of silica coating thickness in relaxivity is well documented for aqueous colloids of silica coated iron oxide nanoparticles [28,29]. Diffusion rate of water molecules through silica matrix to iron oxide cores is documented as main factor influencing relaxivity of the nanoparticles in aqueous col-

* Corresponding author at: A.E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Scientific Center of Russian Academy of Sciences, Arbuzov str., 8, Kazan, 420088, Russia.
E-mail address: aleksestepanov@yandex.ru (A.S. Stepanov).

http://dx.doi.org/10.1016/j.colsurfb.2016.10.025
0927-7765/