Control of Clustered Iron Oxide Interparticle Spacing and Their Magnetic Properties

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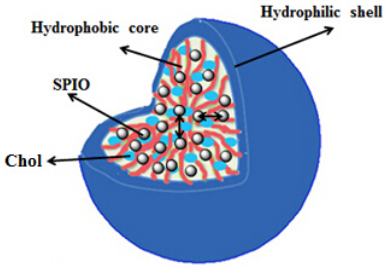
Purpose: Superparamagnetic iron oxide (SPIO) has been widely used in clinical medicine as magnetic resonance (MR) contrast agents for the diagnosis of diseases, cellular trafficking, angiogenesis imaging, etc [1]. But, the development of the high sensitive probe is still an urgently problem to be solved. It is reported that the aggregation degree of SPIO nanoparticle are related to different values of T_2 relaxivity, higher aggregation degree usually leads to a better signal contrast enhancement [2]. There are, however, less known about the mechanism behind this phenomenon. In this study, we directly controlled the interparticle spacing of SPIO nanoparticles though self-assemble to determine the relationship between T_2 relaxivity and SPIO nanoparticels interparticle distance of the aggregate.

Materials & Methods: We exploited self-assembly of SPIO nanoparticles doping rigid cholesterol (Chol) to mediate interparticle spacing with the help of diblock copolymer mPEG2k-b-PCL2k or mPEG2k-b-PLA2k, while keep the total amount of SPIO and Chol unchanged. The copolymer/Chol-SPIO formation is illustrated in Scheme 1. Small-angle X-ray scattering (SAXS, λ = 1.24 Å, Shanghai Synchrotron Radiation Facility) was used to quantify directly the SPIO average interparticle spacing in micelles which have the slight differences in the size distribution.



Scheme 1. Schematic illustration of copolymer/Chol-SPIO micelle formation.

Results: In copolymer/SPIO composite assemblies, we observed a clear increase of the average interparticle spacing with the increasing mass ratio of Chol to SPIO (Fig. 1). The interparticle spacing values attained for mPEG2k-PCL2k/Chol-SPIO micelles showed a regular trend of edge-to-edge spacing from 0.27 nm for the absence of Chol to 0.73 nm for Chol/SPIO = 6 (Table 1). The average interparticle spacing of SPIO piled in mPEG2k-PLA2k/Chol-SPIO micelles have similar tendency (Fig. 1b). More surprising, the SPIO averaged interparticle spacing of the lyophilized micelles is smaller than that of the pellet in water. It decreased about 0.23 nm when self-assemble of Chol/SPIO = 6.

Fig. 2 diaplays T_2 relaxivity of nanoparticle-loaded micelles is decreased dramatically with the increase of the

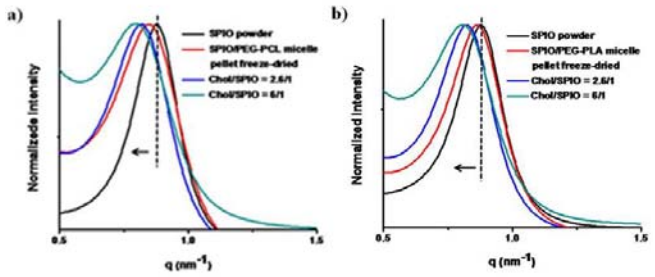


Fig. 1 SAXS plots shown after background subtraction and normalization. (a) Chol/SPIO assembled with mPEG2k-PCL2k micelles pellet freeze-dried. (b) Chol/SPIO assembled with mPEG2k-PLA2k micelles pellet freeze-dried micelle.

Table 1 Spacing values and increased spacing values of SPIO nanocrystals assembled with Chol using polymer mPEG2k-PCL2k.

Sample	q* (nm^{-1})	ND (nm)	Increased ND (nm)
SPIO powder	0.88	7.15	---
SPIO/PEG-PCL micelles pellet freeze-dried	0.85	7.42	0.27
Chol/SPIO = 2.6/1	0.82	7.64	0.49
Chol/SPIO = 6/1	0.80	7.88	0.73

q* values taken from SAXS plots and spacing values (ND) obtained using d (nm) = 2π/q

interparticle spacing. SPIO-loaded mPEG2k-PCL2k micelles have a T_2 relaxivity of 448 mM^{-1} s^{-1}. When Chol/SPIO = 6, nanocrystal containing micelles only have a T_2 relaxivity of 214 mM^{-1} s^{-1}.

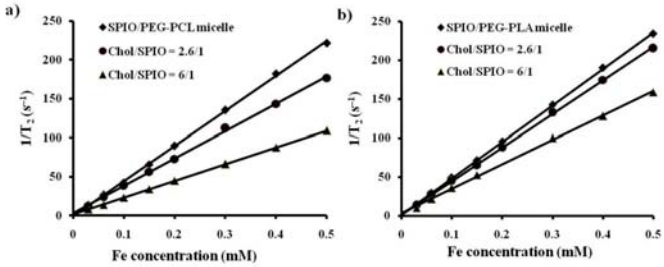


Fig. 2 T_2 relaxation rate (1/ T_2, s^{-1}) as a function of iron concentration (mM) for Chol-SPIO loaded micelles at 1.5 T. (a) mPEG2k-PCL2k micelles (b) mPEG2k-PLA2k micelles.

Conclusion: An understanding of the relationship between interparticle spacing and changes in relaxivity is critical for designing MRI probes for molecular imaging applications using.

Reference: 1. J Xie, G Liu, H Ai and XY Chen, Acc Chem Res. 2011, 44: 883-892. 3. HY Su, YH Liu, D Wang and H Ai, Biomaterials, 2013, 34: 1193-1203.