Cracked Iron Oxide Nanoprticles as T2 Contrast Agents for Magnetic Resonance Imaging

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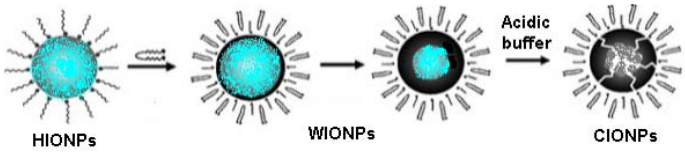
ABSTRACT

Metal [Fe, Mn, Gd, and Co] oxide nanoparticles water suspension as magnetic resonance imaging (MRI) contrast agents has a variety of characteristics that penetrate effectively biological membranes, circulate for a long time in blood vessel, and conjugate with targeted receptors. Especially, nanoparticles with small size and large surface provide magnetic resonance image with high sensitivity and specificity at low imaging-agent concentration.[1] Metal oxide nanoparticles with hollow spheres can incorporate therapeutic agents into their payloads, enabling simultaneous MRI diagnosis and delivery of drugs to targeted sites. There have very recently been developed a novel and facile synthesis of hollow manganese oxide nanoparticles (HMONs) and their potential application as multifunctional agents for simultaneous MR imaging and drug delivery.[2] HMONs have strong relaxivities due to their large surface. Iron oxide nanoparticles as T_2 contrast agents are employed to image tumors, stem cell migration, and cancer metastases. Iron ions are usually safer than potentially toxic metal ions such as Gd^{3+} and Mn^{2+} in the body. Herein, we report a facile synthesis of nontoxic cracked iron oxide nanoparticles (CIONPs) from hydrophobic FeO nanoparticles (HIONPs) *via* 3 steps. With complex surface structure, CIONPs showed improved r_2 relaxivities compared to hydrophobic FeO nanoparticles (HIONPs). We expect that CIONPs have the potential application as a drug or chemical delivery vehicle because of their cracked spheres. In addition, cellular and in vivo MR imaging study with CIONPs will be tested.

EXPERIMENT



Scheme 1. Formation of CIONPs (FeO-: sky blue, Fe_3O_4-: black, oleate: ~, poly(ethylene glycol) phospholipid, ~)

Procedure for formation of 14 nm CIONPs

(1) Synthesis of hydrophobic FeO nanoparticles (HIONPs) – Thermolysis of $Fe(acac)_3$ with surfactants such as OA (oleic acid) and OAm (oleylamine)
(2) Synthesis of hydrophilic iron oxide nanoparticles (WIONPs) - PEG-phospholipid coating
(3) Oxidation under distilled water and formation cracked Fe_3O_4 nanoparticles (CIONPs) under acidic buffers (pH 2.6~4.6)

RESULTS

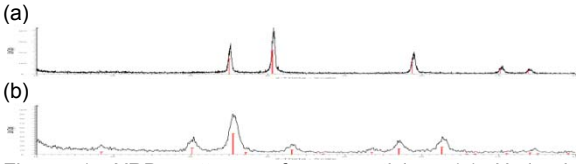


Figure 1. XRD patterns of nanoparticles. (a) Hydrophobic FeO nanoparticles spectrum (black pattern : hydrophobic Hydrophobic FeO nanoparticles, red line ; reference FeO nanoparticles. (b) Cracked Fe_3O_4 nanoparticles spectrum (black pattern : cracked Fe_3O_4 nanoparticles, red line : reference Fe_3O_4 nanoparticles).

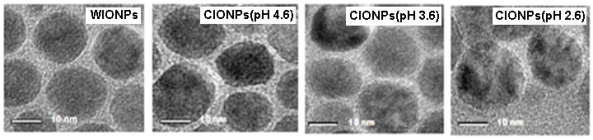


Figure 2. TEM image of WIONPs, CIONPs (pH 4.6), CIONPs (pH 3.6), and CIONPs (pH 2.6)

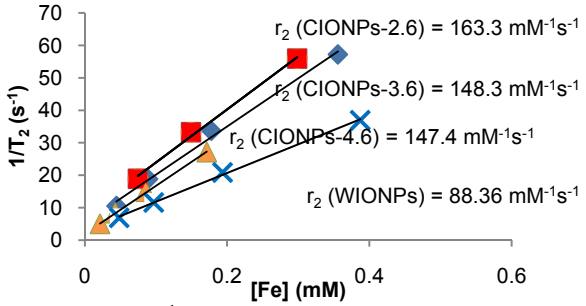


Figure 3. Plots T_2^{-1} versus Fe concentration for WIONPs (x), CIONPs-4.6 (▲), CIONPs-3.6 (◆), and CIONPs-2.6 (■).

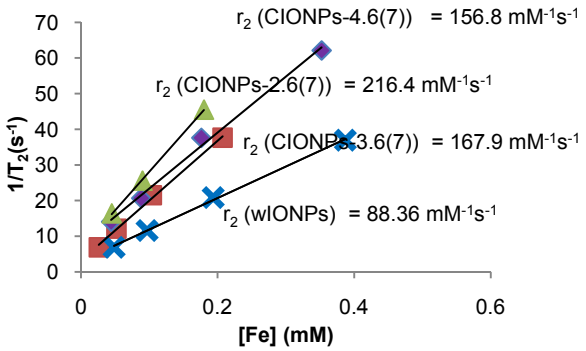


Figure 4. Plots T_2^{-1} versus Fe concentration for WIONPs (x), CIONPs-4.6 (7)(◆), CIONP-3.6(7) (■), and CIONP-2.6(7) (▲).

Table 1. Relaxation of nanoparticles at 4.7 T MRI

Nanoparticles	T_2[a][ms]	r_2[$s^{-1}mM^{-1}$]
WIONPs	122	88.4
CIONPs-4.6[b]	69	147.7
CIONPs-3.6[b]	65	148.3
CIONPs-2.6[b]	51	163.3
CIONPs-4.6(7)[c]	55	156.8
CIONPs-3.6(7)[c]	49	167.9
CIONPs-2.6(7)[c]	38	216.4

[a] Measured at 0.08 mM (as measured by ICP-AES).
[b] Formatted using WIONPs under water for 1 day with acidic buffer.
[c] Formatted using WIONPs under water for 7 days with acidic buffer.

CONCLUSIONS

1. Cracked iron oxide nanoparticles (CIONPs) are generated form monodispersed hydrophobic FeO nanoparticles (HIONPs) *via* 3 steps, such as surface coating with PEG-phospholipid, oxidation under water, and getting FeO phase off using acidic buffers.
2. CIONPs have good T_2 relaxivities and potential applications, such as vectors for drug delivery and chemical storage.

REFERENCES

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2.J. Shin, R. M. Anisur, M. K. Ko, G. H. Im, J. H. Lee, I. S. Lee, *Angew. Chem. Int. Ed.* **2009**, *48*, 321.