Synopsis of Original Research Paper

Development of Functional Hydrophilic Colloids Containing Many Water Molecules

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Hydrophilic-gels and -nanoparticles are paid much attention in medicinal and cosmetic fields. Especially in the field of contrast agents such MRI, fluorescence and RI, the functional nanoparticles, which form approximately 100 nm size in solutions, are passively accumulated in tumor tissues, thus many researchers have reported the tumor-accumulating nanoparticles based on the 100 nm. This tumor-accumulating behavior utilizing the nanoparticles is known as Enhanced Permeability Retention (EPR) effect. Moreover, there is a deep relationship between MRI contrast agents and water molecules; the high contrast ability is derived from presence of many water molecules around the contrast agents. Thus, the hydrophilic nanoparticles, in which many water molecules are taken the core of the particle into, are promising as MRI contrast agents with a high contrast ability. We have studied on the MRI contrast agents utilizing the organic radical. Because the typical MRI contrast agents in clinical, which are consisted of Gadolinium ions (Gd) as a metal spin source, have some issues; renal disorder and brain accumulation by an excess usage. Accordingly, instead of Gd ion, the metal free contrast agents consisting of organic radical are planned. This time, three nanoparticles consisted of radical species are prepared and the physical parameters such rotational correlation time (τ_R) bases on the ESR signal intensity and width, T_1-weighed image with T_1-relaxation time, hydrodynamic diameter (D_H) by a dynamic light scattering (DLS), and morphology observations of nanoparticles using a transmission electron microscopy (TEM). Due to checks of the hydrophilicity of the nanoparticles, ClogP values of the nanoparticles were calculated by a ChemDraw Professional 16.0.

Three nanoparticles with organic radicals, **RNP-OTHP**, **-OH**, and **OAc**, were prepared according to a previous our report. In the DLS of the aqueous solutions, D_H values for all **RNP-X** showed the similar 100 - 200 nm size-distribution. In contrast, TEM images of **RNP-OH** and **-OTHP** showed the different morphology; film-like particles and spherical particles, for **RNP-OTHP** and –**OH**, suggesting that the former and latter are vesicle-like and micelle-like particles, respectively. In the contrast agent ability, the relaxivities (r_1) of **RNP-OH** and **-OAc**, which are calculated by a slope of the plot of inverse T_1 relaxation times vs concentration of contrast agents, showed 0.17 and 0.31 $mM^{-1}s^{-1}$, respectively, indicating that the latter is more than 1.7 time larger than that of the former, and the highest value among the radical nanoparticles reported by our group. To reveal the relationship between r_1 value and hydrophilicity, ClogP values were estimated to be -0.38 and 1.4 for **RNP-OH** and **-OAc**, respectively. In the previous our report, the micelle-like nanoparticle, PRO2, possesses the smaller ClogP (-0.037) and r_1 (0.17 $mM^{-1}s^{-1}$) values rather than those of **RNP-OAc**. The above-mentioned results indicate that the morphology of the nanoparticles are control by the ClogP value: the value of approximately 1.0 as a borderline, the nanoparticles with the smaller and larger ClogP value rather than 1.0, would form the micelle and vesicle-like morphology. Accordingly, the vesicle-like nanoparticle based on own ClogP value caused the high r_1 value of **RNP-OAc**.

Considering the above-mentioned results, by controlling the suitable ClogP value, the construction of the metal-free MRI contrast with the high contrast ability (relaxivity: r_1) is underway.