

Applications of Cubic Spinel Ferrite Nanoparticles for an *in-vivo* Hyperthermia Agent in Biomedicine

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In recent, as *in-vivo* hyperthermia therapy, a modality of malignant cancer treatment inside the human body, has been paid considerable attentions, the interest of applying nano-size controlled cubic spinel ferrite magnetic particles for an *in-vivo* hyperthermia agent are remarkably increased [1-2]. In this work, self heating temperature rising characteristics, bio-compatibility including cell cytotoxicity, and magnetic and physical properties of cubic spinel ferrite nanoparticles were primarily investigated to confirm the effectiveness for an *in-vivo* hyperthermia agent in biomedicine. Three kinds of cubic spinel ferrites (Mg, Ni, and Co-ferrite) were considered as a hyperthermia agent in order to explore the effects of magnetic susceptibility (permeability) on the physical natures of self-heating temperature rising characteristics and to indirectly verify the contribution of Néel rotations of the magnetic spins to the self-heated temperature. The cytotoxicity of three cubic spinel ferrite nanoparticles was investigated by MTT (Methylthiazol Tetrazolium bromide Test) method using JB6-C141 normal mouse epidermal cells and WB-F344 normal rabbit liver cells. The biophysiological properties of three ferrite nanoparticles associated with the deleterious physiological response during self-heating for *in-vivo* hyperthermia treatment were evaluated by determining $H_b \cdot f_{applied}$ values under different applied magnetic fields and frequencies. Effects of disordered surface spin structures on the temperature rising characteristics were explored by measuring the self-heating temperature at both in a solid and in an agar states. Fig. 1 (a) and (b) show the self-heating temperature rising characteristics of three ferrite nanoparticles with 30 ~ 35 nm particle sizes in solid state at a fixed frequency of 110 kHz. As can be seen in Fig. 1(a), Mg, and Ni-ferrite had very promising self-heating characteristics. In addition, among three ferrite nanoparticles, Mg ferrite particles showed the maximum self-heated temperatures. The highest self-heating temperature of Mg ferrite is thought to be due to a higher initial magnetic susceptibility (Fig. 1-(b)) and a larger hysteresis loss. This result indicates that both hysteresis loss and the Néel rotations of the magnetic spins are mainly involved in contributing to the self-heating temperature rising. According to the MTT testing results, all the three ferrite magnetic nanoparticles had a high enough biocompatibility to be used as an *in-vivo* hyperthermia treatment agent. In addition, it was revealed that the maximum self-heating temperature of solid-state Mg and Ni-ferrite nanoparticles is easily controlled in the biological safety and physiological tolerance ranges.

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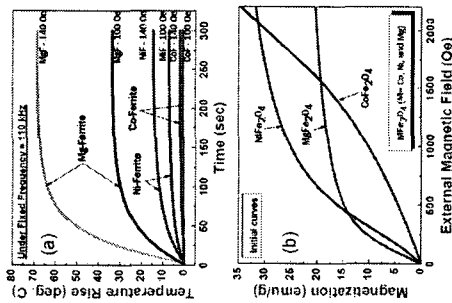


Fig. 1. Self-heating characteristics and magnetic properties of ferrite nanoparticles.

Analysis of Trace Oligonucleotide with Novel Bio-bar Code Assay and Nano Magnetic Particles

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In this research, the method for analyzing DNA of the extremely low concentration by using the bio-bar code assay (BCA) and nano magnetic particles (NMP) is described. The BCA originally proposed is the method for securing the signal which is amplified by using the combined bar code DNA for the gold nano particle probe. The bio-bar code assay is a recently developed system utilizing short oligonucleotides as detection strands and signal amplifier in both protein and DNA detection(2). One of the systems originally suggested by Mirkin Group of Northwestern University (1) is consist of two types of particles. One is the magnetic particles for the separation and attachments of the target of interest attached. The other is gold or polymeric particles, which has binding sites for the attachment of the target and oligonucleotide, which can make a hybridized structure. However, the method for presenting in this research is the method for obtaining the high sensitivity by analyzing magnetic nano particle (MNPP) instead of the bar code DNA itself. This method is elementarily comprised of the particle for the separating a target from a sample and the analysis particle uniting with the bar code DNA and the MNPP. Moreover, at the same time, the analysis particle has the partially complementary sequence with not only target DNA but also the Bio-bar code Probe DNA. The micro-size particle for a separation and the other polymeric particle have Probe DNA1 and Probe DNA2 which are partially complementary with the target DNA (Fig 1). Since being the mode which directly does not analyze the target DNA but measures the number of the nano magnetic particle conjugated bio-bar code DNA amplified, the analysis becomes possible to analysis very low concentration of the target DNA. The results suggested that bio-sensor system combing the BCA with NMP could be employed as the alternatives of conventional DNA detection system.

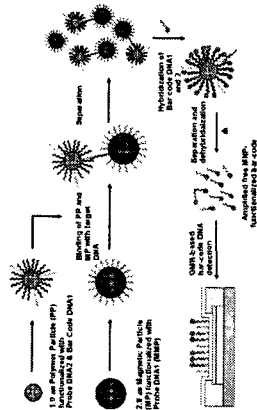


Fig. 1. Basic Scheme of the BCA employed.

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