Digest Journal of Nanomaterials and Biostructures Vol. 3, No.2, June 2008, p. 99 - 102

# THE HEATING STUDY OF TWO TYPES OF COLLOIDS WITH MAGNETITE NANOPARTICLES FOR TUMOURS THERAPY

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Magnetic microparticles and nanoparticles have a large variety of applications in biomedicine such as hyperthermic treatment of tumors, magnetically targeted drug delivery by magnetic carriers. Also, non-targeted biomedical magnetic microparticles and nanoparticles are available for use as contrast agents (MRI) and as drug reservoirs that can be activated by a magnet applied outside the body. In this work, the heating influence of two magnetic colloids for applications in hyperthermia treatment of tumors is discussed. One colloid with magnetite in poly(ethylene glycol) and sodium dodecylsulphate, and another one with magnetite in mono(ethylene glycol) were heated inside an induction coil with a power of P = 0.5 kW and P = 0.4 kW, respectively. Frequence used was ν = 315 kHz. The temperature of the two colloids was measured with a thermometer as a function of time.

(Received May 3, 2008; accepted May 12, 2008)

*Keywords*: Magnetic particle, Magnetic suspension, Heating, Hyperthermia

## 1. Introduction

In the last years nanomaterials are frequently used in biomedical applications. In this study we will focus on the magnetic particles, rather on application in hyperthermia with magnetic particles knowed as the *magnetic hyperthermia*. In the first place, these particles can be manipulated using a external magnetic field. They can generate heat in this AC magnetic field and can be used as the agents for malignant cell destruction and implicit the tissue from do they belongs.

Although it is possible to determine the manner in which behave magnetic particles finded out in suspension in vitro under the act of an external AC magnetic field [1], it is not clear yet their behaviour in physiological systems because they are submissive influences of physiological supplementary factors such as *the haematic flow*, *reticuloendothelial system* and high dynamic *tissue microenvironment* where can operate cellular receptors and cellular absorbtion.

Physical factors which must be controlled are *heat generation* [2] and *temperature distribution*. A special importance is given to relations among the heat response at nanoscale level and the heat disengagement at macroscopic level. It is very important to understand the heating mechanism at microscopic level to prevent the heating and destruction of adjacent healthy cells.

In this work are studied the heating processes of magnetic particles in biocompatible environments: aqueous suspensions of biocompatible polymers.

## 2. Experimental

Colloid I (Magnetite in PEG + SDS): used materials are $FeSO_4$ 2M in HCl 2M (x), $FeCl_3$ 1M in HCl 2M (y), 1.0M $NH_3$ in water as a precipitation agent, polyethylene glycol (PEG) 25% and sodium dodecyl sulphate (SDS) as an anionic surfactant.

*Preparation method*: in a 100 ml vessel were added x and y solutions, they were titrated under magnetic stirring with 40 ml $NH_3$ until mixture gives rise to a black precipitate (magnetite). Then magnetic precipitate is separated, is washing with water until pH = 5.5 (neuter). 2 ml PEG 25% is added to precipitate and after that mixture is immersed in SDS.

Colloid II (Magnetite + MEG): $FeSO_4$ 2M in HCl 2M, $FeCl_3$ 1M in HCl 2M, 1.0M $NH_3$ and monoethylene glycol (MEG). It is used same method as to the colloid I with the difference that after washing the precipitate was immersed in 30 ml MEG.

Figure 1 is a sketch of experimental device [1]. The colloid is entered into the testing tube which is in a magnetic field created by an inductor of 70 mm diameter, to a frequency of 315 kHz. It is used a power of 0.5 kW for the colloid I and 0.4 kW for the colloid II. The sample temperature was measured with an alcohol thermometer in order to don't influence the heating level of the particles. All heating studies of particles were repeated three times for each sample.

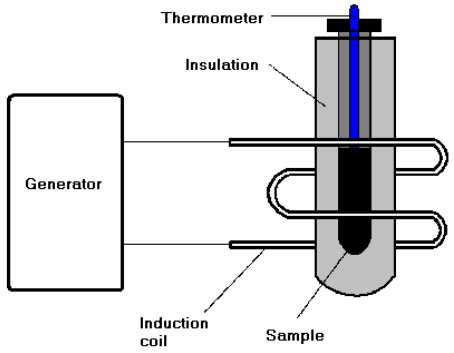


*Fig. 1. The sketch of the experimental device. The sample was put in an field created by an induction coil conected to a AC power source. The temperature was measured with an alcohol thermometer through direct reading.*

## 3. Results

In this work was studied the heating behaviour in vitro of two magnetic colloids. Figure 2 and 3 presents the temperature variations depending on the time of maintaining in the colloid concentration. In both colloids, the magnetic particles are in homogeneous suspension. The temperature variation was situated in the range: 36°C (minimum temperature of human organism) and 46°C (maximum temperature of the tumoral cells necrosis). This range was preferred because it encompasses all the transformations that suffers the ferrofluid in organism under the action of the AC magnetic field.

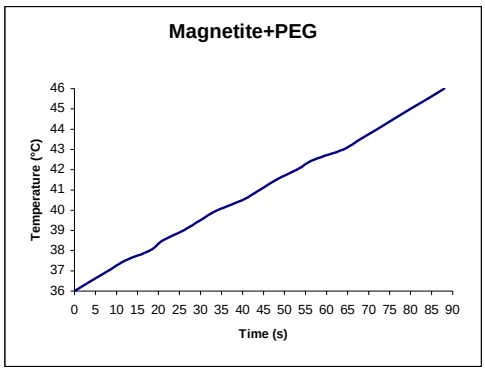


*Figure 2. Temperature evolution (°C) depending on time (s) in colloid I.*

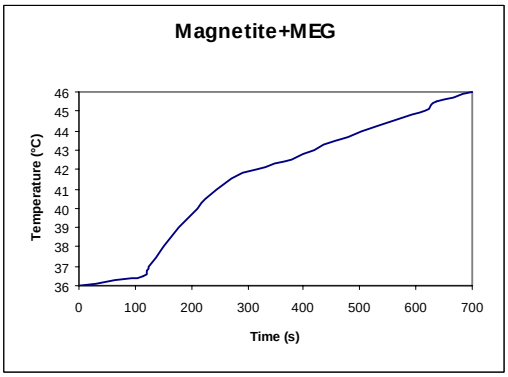


*Fig. 3. Temperature evolution(°C) depending on time (s) in colloid II.*

For each sample were used 2 ml from each colloid.

## 4. Discussion

The first colloid (Fig. 2) has a heating behaviour with the time almost linear at a power P = 0.5 kW, the temperature having a quick growth in 36°C - 46°C interval for 90s. This quick breeding is explained through the fact that the brownian agitation of the particles into the colloid it is accelerated by the presence of surfactant SDS (sodium dodecyl sulphate) at the surfaces of magnetite particles.

The second colloid has a heating behaviour much slower at a power P = 0.4 kW. The abrupt variations occurs after nearly 100 s from the begining of experiment at 36.5°C (temperature which corresponds to the normal temperature of human body) and after 300 s from the begining of experiment at 42°C (temperature which coincides with necrosis temperature of tumoral cells).

The heating time is longer because the surfactant is missing from the surface of the magnetite particles and due to the fact that used power has a lower value.

The heating behaviour of magnetite particles depends on frequency, application time and, also, on particle size and suspension medium.

In the case of colloid I, the endurance developed by viscosity against brownian relaxation it is smaller by reason of the presence of surfactant, whiles at colloid II, because of lake of surfactant, the suspension medium is much viscous whence results that the phenomenon of brownian relaxation is make heavier, therefore the heating time will be much longer [3-6].

The phenomenon of brownian relaxation which generates the heat is characterized by the brownian constant of time:

$$\tau_B = {3\eta V_B}/{k_B T} \tag{1}$$

where $V_B$ is the hydrodynamic volume, i.e. the total volume of a particle coated with surfactant and/or polymer, $\eta$ is the viscosity of the suspension medium, and $k_B T$ is the thermal energy.

The particle heating occurs by Néel mecanism, too [3-6]. This phenomenon is explained through the motion of magnetic moments inside the particle in the magnetic field of the coil. This mechanism is characterized by the Néel time constant:

$$\tau_N = \tau_0 \exp\left({\Delta E}/{k_B T}\right) \tag{2}$$

where $\Delta E = KV$ is the activation energy, and $\tau_0 = 10^{-9} s$.

## 5. Conclusions

In this work were studied the heating beaviour *in vitro* of two types of magnetic colloids for their utilization *in vivo*. It was observed that the particles beaviour through induction heating strongly depends on the amount of magnetic colloid and particle size, but mainly depends on the suspension medium (viscosity, thermal conductivity).

There are some problems that must be mentioned. Because the particles are polydispersed in the ferrofluid, the power generated is not uniform for all the particles and depends on their size. Another problem is the temperature measured at macroscopic level that is not the same with temperature measured at nano level. Therefore it is necessary to develop models for correlation of the two temperatures in order to use the particles in suspension media *in vitro*, as *in vivo* in organic environments, as well as in the sanguin medium or other types of tissues, chiefly the tumoral ones.

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