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Synthesis of Magnetic Iron Oxide Nanoparticles for Biomedical Applications

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Abstract

Magnetic iron oxide nanoparticles have been synthesized by an hydrothermal method using three different iron precursors. The yield of synthesis was determined for all samples and found to be dependent on the iron precursor, solution pH and reaction time. The synthesized nanoparticles will be characterized by transmission electron microscopy and X-ray diffraction analysis and their suitability for biomedical applications, with particular focus on the hyperthermia method, will be studied.

1. Introduction

In the last decade the progress achieved on the synthesis of inorganic nanostructures has been accompanied by the parallel exploitation of these systems in various fields, such as biology and medicine. In particular, magnetic nanoparticles are used in a variety of biomedical applications, including hyperthermia, drug delivery, bioseparation and magnetic resonance imaging [1]. Drug delivery using magnetic nanoparticles is a promising application since it is a noninvasive technique where a high efficiency can be achieved. When the size of the particles is lower than 50 nm they become supermagnetic due to the thermal relaxing phenomenon. The particles supermagnetism is particularly important for their application in magnetic hyperthermia, a method used to treat cancerous tissues and that is based on the increasing temperature of nanoparticles when they are in contact with the damaged tissues under a magnetic field.

Iron oxide is the most investigated material for biomedical techniques, due to its superior biocompatibility when compared with other magnetic materials based on oxides. Several types of iron oxides exist in nature and can be prepared in the laboratory. In this work, carried out under the framework of the Biomedical Engineering Project of the under-graduated Biomedical Engineering Course of Polytechnic Institute of Bragança, the main objective is to synthesize and characterize magnetic iron oxide nanoparticles for assessment of their possible

application in biomedical areas, namely for the hyperthermia process.

2. Methods

Preparation of iron oxide nanoparticles

The iron oxide magnetic nanoparticles were synthesized by a hydrothermal process at 180°C, adapting the procedures described elsewhere [2, 3]. Different metallic precursors ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ and $\text{K}_4\text{Fe}(\text{CN})_6 \cdot 3\text{H}_2\text{O}$), solution pH (acid or basic) and reaction times (3 or 6 h) were considered, aiming to understand the influence of these parameters on the synthesis yield, nanoparticle size, morphology and composition. In a typical procedure of synthesis, 0.01 mol of the metallic precursor was dissolved in 50 mL of distilled water. When required, the pH was adjusted with a 25% ammonia aqueous solution that was slowly dropped to the iron solution. The resulted solution was then placed in a Teflon-sealed vessel inside a stainless steel autoclave (Fig. 1) and maintained at 180°C in autogeneous pressure during the desired reaction time.

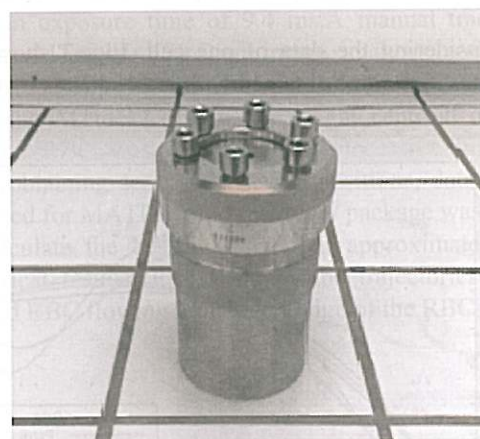


Fig. 1. Stainless Steel reaction autoclave.

At the end of the reaction, the autoclave was cooled down to room temperature and the obtained products were then recovered by filtration through a 0.45 μm cellulose nitrate membrane, washed with water and

dried overnight at 40°C. Depending on the reaction conditions used, dark or light brown/orange powders were obtained. All the produced samples and the respective synthesis conditions are gathered in Table 1.

3. Results and Discussion

Table 1 shows the yields obtained in each experiment, calculated according to the following equation:

$$\text{Yield (\%)} = \frac{\text{Mass of iron in the precursor}}{\text{Mass of iron in the nanoparticles}} \times 100$$

Table 1. Synthesis conditions and respective yield of iron oxide nanoparticles.

Sample Reference	Precursor	pH	Time (h)	Yield (%)
CA3	FeCl ₃ .6H ₂ O	1.7	3	10.8
CB3		9.2*	3	68.2
CB6		8.2*	6	86.5
NA3	Fe(NO ₃) ₃ .9H ₂ O	1.5	3	86.3
NB3		8.1*	3	53.4
NB6		9.2	6	74.6
HB3	K ₄ Fe(CN) ₆ .3H ₂ O	8.4	3	19.9
HB6		8.4	6	33.1

* Addition of ammonia solution (25%)

Table 1 shows that the best reaction yields are obtained using the FeCl₃.6H₂O precursor with an alkaline pH of 8.2 and 6 hours of reaction at 180°C, or as alternative by using the Fe(NO₃)₃.9H₂O precursor at the natural solution pH (1.5) during 3 hours at 180°C. In both cases, the yield is higher than 86.0%. A more detailed analysis reveal that the influence of pH on the reaction yield depends on the precursor used. This yield is clearly increased when FeCl₃.6H₂O is used as precursor and the reaction takes place in alkaline conditions. For instance, the yield obtained at acid pH was the lowest (10.8% for sample CA3), while at basic pH the yield increased to 68.2 or 86.5% for pH values of 9.2 (sample CB3) or 8.2 (sample CB6), respectively. When Fe(NO₃)₃.9H₂O is used as precursor, the reverse occurs, i.e., the highest yield was obtained at acid pH (86.3% for sample NA3) and the reaction yield decreases at basic pH (53.4 and 74.6% for samples NB3 and NB6, respectively). Regarding the reaction time, the influence of this parameter is evident, the yield increasing more than 25% (66% in the case of sample HB6), regardless of the metallic precursor used.

4. Conclusions and Future Directions

From the work done so far, it is possible to conclude that the better conditions to use regarding the maximization of the nanoparticles reaction yield is either using the FeCl₃.6H₂O precursor at basic pH and 6 h of reaction time or the Fe(NO₃)₃.9H₂O precursor at natural pH (acid) and 3 h of reaction time. The

synthesized nanoparticles will be further characterized by transmission electron microscopy and by X-ray diffraction analysis in order to understand the influence of the studied parameters on the nanoparticles size, morphology and phase composition. These new data will allow to take definitive conclusions about the best reaction conditions needed to assure the optimum properties of the developed nanoparticles for biomedical applications.

To extend the time of circulation in blood vessels, the nanoparticles are usually involved by a biocompatible polymer. Future work also considers the study of the encapsulation of the nanoparticles with a biocompatible polymer (e.g., chitosan). A final stage of this work will consider the study of the biocompatible magnetic nanoparticles injected in physiologic serum (normal saline), to simulate blood, using a circulation simulator (microchannels) subjected to a magnetic field to render conclusions about the suitability of the nanoparticles to be used in the hyperthermia process. Micro-flow visualization techniques will be applied at this stage, as described elsewhere [4].

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