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Brief/Technical Note

Magnetite Content Evaluation on Magnetic Drug Delivery Systems by Spectrophotometry: A Technical Note

Érica Lira Silva-Freitas,[1] Juliana Fernandes Carvalho,[1] Thales R. F. Pontes,[1] Rafael P. Araújo-Neto,[1] Artur Silva Carriço,[2] and Eryvaldo Socrates Tabosa Egito[1,3]

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INTRODUCTION

Magnetic polymer particles have been widely used in a large number of biotechnology and biomedicine applications (1–3). In modern pharmacy, basic investigations for the manufacturing and characterization of new dosage forms are frequently performed using magnetic fillers and drug carriers, which can be classified as the artificial sources of magnetic fields. These sources are most typically based on magnetite, iron (III) γ-oxide, and barium ferrite (4).

Magnetite is an iron ferrite with the general formula Fe_3O_4 and a crystal lattice of the inverse spinel type. The octahedral crystal structure is a characteristic feature of magnetite. In the inverse spinel structure, the tetrahedral sites are occupied by Fe^{3+} ions and the octahedral sites are shared between equal amounts of Fe^{3+} and Fe^{2+} ions (5). Part of the qualitative analysis of magnetic components in biological objects may be performed using the techniques of superconducting quantum interference device magnetometry and ferromagnetic resonance (6).

An important point in the preparation of magnetic polymer particles, especially for biomedical applications, is the evaluation of the magnetic content (7). The quantitative composition determination of magnetic substances is commonly performed by a variety of methods such as titration (8), thermogravimetric techniques (7,9), and X-ray diffraction (10). Nowadays, spectrophotometric methods have often been applied for even metal trace determination (11), due to advantages such as accuracy and good precision, low cost, and simple operation.

The objective of the present work is to report a simple, yet accurate, manner for the determination of the magnetite content in magnetic polymeric microparticles, by the association of spectrophotometry, via the complexation of iron ions with sulfossalycilic acid dihydrate (SSA), and magnetometry.

MATERIAL AND METHODS

Materials

Ferric chloride hexahydrate (Acros Organics, Brazil; P.A.); ferrous sulphate heptahydrate (Acros Organics, USA; 99%), sodium hydroxide (NaOH; Vetec chemical, Brazil; 99%), hydrochloric acid (HCL; Vetec Chemical, Brazil; 37%), Amoxicillin (Galena, Brazil; 97%), Eudragit®S100 (Rohm Gmbh & Co. KG, German; methacrylic acid—methyl methacrylate copolymer 1:2, 100%), SSA (Sigma, German, 99%) and ammonia solution (Vetec chemical, Brazil, 28–30%) were of pharmaceutical grade and used as received without further purification.

[1] Departamento de Farmácia, Universidade Federal do Rio Grande do Norte, Rua Gustavo Cordeiro de Farias s/n, Petropolis, Natal, Rio Grande do Norte CEP: 59010–180, Brazil.
[2] Departamento de Física Teórica e Experimental, Universidade Federal do Rio Grande do Norte, Natal, Rio Grande do Norte, Brazil.
[3] To whom correspondence should be addressed. (e-mail: socrates@ufrnet.br)

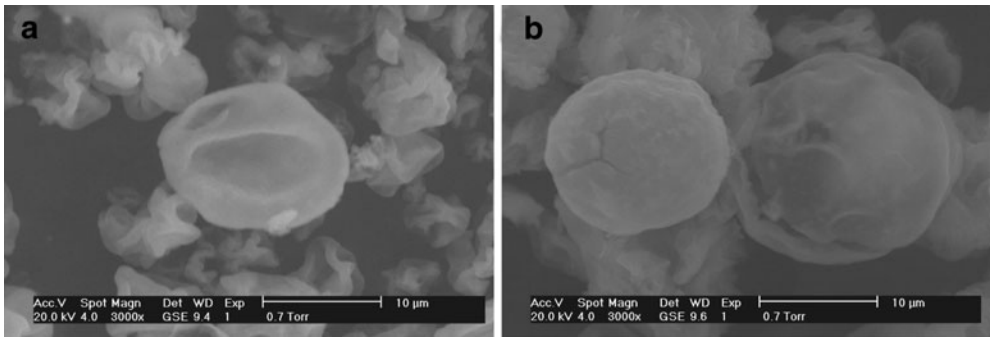

Fig. 1. Scanning electron microscopy image **a** MagAmox 13% and **b** MagAmox 22%

Synthesis of Magnetite Particles

The magnetite microparticles synthesis was based on the coprecipitation method (12,13). For the magnetite particles synthesis, 0.1 M ferric chloride hexahydrate ($FeCl_3 \cdot 6H_2O$) and 0.05 M ferrous sulphate heptahydrate ($FeSO_4 \cdot 7H_2O$) were prepared by dissolving iron salts in 0.1 M HCl solutions, respectively. Therefore, these solutions were combined and a homogenous mixture was formed. In a typical experimental procedure, 9 ml of the mixture of ferrous and ferric salts was added drop-wise into 450 ml of NaOH 1 M under ultrasonic bath (Unique USC 1800, 40 kHz, Brazil) and vigorous mechanical stirring at 154 g (IKA RW-20, Germany) for 30 min at room temperature (25°C). The solution color could be seen to alter from orange to black, leading to a black precipitate. The supernatant was discarded by decantation. Distilled water was then added to wash the precipitates.

Production of Polymeric Magnetic Particles with Amoxicillin

Polymeric magnetic microparticles with amoxicillin were produced by the spray-drying technique. Two samples were prepared starting with suspensions with different amounts of magnetite. The MagAmox13% was prepared by feeding the sprayer with a suspension containing 50 mg of magnetite, 100 mg of amoxicillin and 250 mg of Eudragit®S100. MagAmox22% was prepared with a larger content of magnetite, using a suspension of 100 mg of magnetite, 100 mg of amoxicillin, and 250 mg of Eudragit®S100. Ninety milliliters of the preparations were fed (Mini Spray-dryer Büchi B191, Germany) at 1.2 ml/min (inlet temperature 120°C) by means of a peristaltic pump and sprayed in the drying chamber of the instrument by means of a flow of compressed air. The solvent evaporation by a flow of heated air aspirated by a pump induced the formation of solid microparticles from the drops.

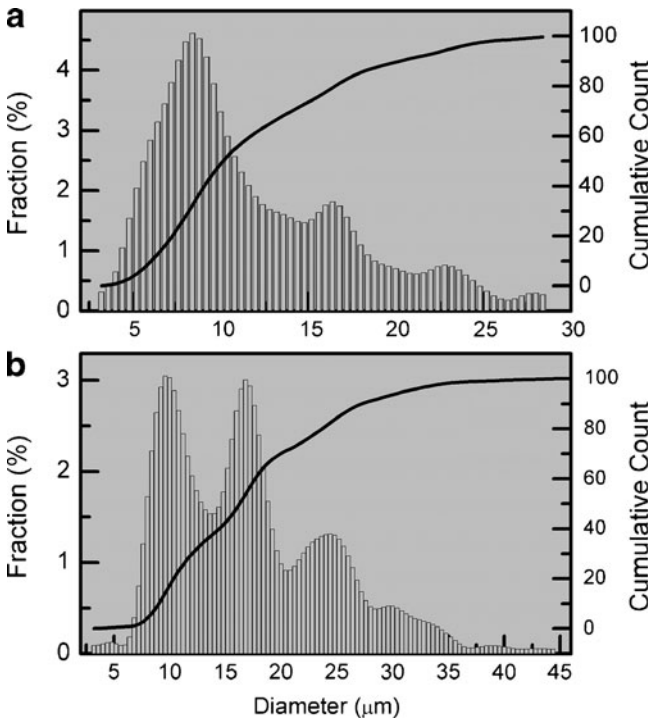

Fig. 2. Size distribution of **a** magnetite particles and **b** MagAmox 22%

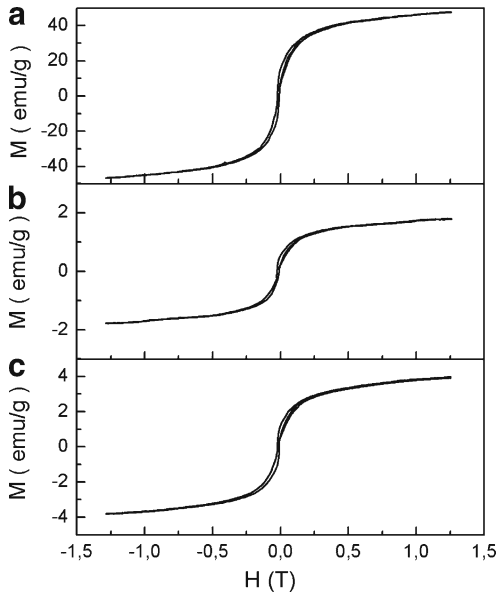

Fig. 3. Magnetization curves of **a** magnetite microparticles, **b** MagAmox 13%, and **c** MagAmox 22%

Magnetite Quantification

The quantitative composition of the composite particles was evaluated by measuring the magnetite content in a two-stage process. First, 100 mg of the polymeric magnetic particles was added to a 100-ml volumetric flask and ethanol was used to dissolve Eudragit®S100, stirring for 30 min and sonicated in an ultrasonic bath for 15 min. The magnetite microparticles were separated by centrifugation at 2,050×*g* for 5 min. Second, in order to measure the magnetite content, the precipitate was resuspended and dissolved in 0.1 N HCL solution under stirring during 9 days to ensure total dissolution (4). The total iron released determination was performed by complexation with SSA (14,15). A 5 mL of the supernatant from the magnetite dissolution was used in a 25 mL volumetric flask, with @@@750 μL of SSA solution 10% (*w*/*v*). After stirring for 2 min, 750 μL of ammonia solution 25% (*w*/*v*) was added and the flask volume was completed with distilled water in order to evaluate the spectra for total iron complex at 425 nm, against a blank (14,15). The spectrophotometric results were compared with magnetic measurements.

Magnetization measurements were performed using a homemade vibrating sample magnetometer, previously used for the characterization of polymerized microparticle samples (16–18). The amoxicillin was quantified by a spectrophotometer analysis at a wavelength of 233 nm (19) from the supernatant. The absorbance results were correlated with the amoxicillin concentration through a calibration curve previously determined. The Eudragit content was calculated from the difference among the constituents.

SIZE AND MORPHOLOGY STUDIES

The magnetite microparticles and polymeric magnetic microparticles were subjected to particle size analysis using optical microscopy (Leica microscopic) and according to Ferret's diameter (20). Morphology analysis of polymeric magnetic microparticles was conducted by microscopy on a scanning electron microscope (XL 30 ESEM, Philips, the Netherlands) at ×3,000 magnification.

RESULTS AND DISCUSSION

Polymeric amoxicillin microparticles were found to be roughly spherical in shape (Fig. 1), with a mean diameter of 17.2 μm, and a magnetic core made of magnetite superparamagnetic particles, with a mean diameter of 11.8 μm, were prepared by spray drying (Fig. 2).The magnetite content of the polymeric particles was evaluated from the total iron content, as measured from the absorption at 425 nm (14,15). The original mass composition of the suspensions to prepare MagAmox22% and MagAmox13% corresponded to 22.2% and 12.5% of magnetite, respectively. The magnetite content of the polymeric particles was found to be smaller than the original composition of the suspension used to feed the spray drier. This is a well-known feature of spray drying, and is due to differences in the physical properties of the components of the suspension, which control the impact of the operating parameters of the spray drier on the final yield (7).

As seen in Fig. 3, the increase by a factor of about two in the magnetite content of the formulations (from MagAmox13% to MagAmox22%) leads to a corresponding change in the initial susceptibility. Most interestingly, the saturation magnetization of MagAmox13% (1.8 emu/g) and MagAmox22% (3.9 emu/g), correspond to 3.8% and 8.2% of the saturation magnetization of the magnetite (47.68 emu/g) used to make the polymeric magnetic particles. This confirms the final content evaluation of magnetite by spectrophotometry. The final compositions were found to be: MagAmox22% (4.0% amoxicillin, 87.0% Eudragit, and 9.0% magnetite) and MagAmox13% (3.9% amoxicillin, 92.1% Eudragit, and 4.0% magnetite). Also, we have shown that the magnetite content of the polymeric particles is controllable by the initial composition of the suspension.

CONCLUSIONS

The results suggest that the association of magnetometry and spectrophotometry provide a satisfactory manner to evaluate the magnetite content and might be helpful in the description of key properties of magnetic systems for drug targeting.

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