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Multifunctional Nanocomposites Based on Mesoporous Silica: Potential Applications in Biomedicine

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1. Introduction

In the last decade, significant research efforts were devoted to obtaining materials with well-defined nanostructures for a wide range of applications (Hamley, 2003; Soler-Illia et al., 2002; Paul & Sharma, 2006). Mesoporous silica materials like M41S, HMS, SBAn, FSM, and MSU, among others, are a fairly new type of material that has pores in the mesoscopic range of 2–50 nm (Wan et al., 2007). The characteristic features of ordered mesoporous materials are their monodispersed and adjustable pore size in an inert and biocompatible matrix with an easily modified surface.

Procedures to obtain ordered mesoporous silicates rely on the micelle-forming properties of a surfactant, whose chemical composition, size, and concentration control the structural dimensions of the final material (Zhao et al., 1998). In most cases, ionic and neutral surfactants have been employed as templates to direct mesophase formation based on the electrostatic and hydrogen-bonding interaction. Polymerization of the inorganic precursor and further removal of the surfactants result in a rigid silica shell that delimits the structural shape of the mesopores. In such processing routes, the resultant material presents an ordered hexagonal arrangement of unidirectional mesoporous channels and a high surface area, above 800 m^2/g, depending on the synthesis conditions. Figure 1 shows the scheme of structure formation mediated by inorganic mesoporous structure-directing agent.

The intrinsic uniform porous structure of this class of compounds with their large specific surface area and pore volume, associated with surface silanol groups, give these materials a significant potential for applications as matrices of many chemical species, such as organic molecules, metals, and polymeric materials. The combination of different materials to obtain nanocomposites is of great research interest due to their potential medical applications, such as tissue engineering, drug delivery devices, and hyperthermia, among others (Vallet-Regi et al., 2008; Souza et al., 2010).

In this work, the recent developments in nanocomposites based on mesoporous materials (also referred to as hybrid materials) will be overviewed. Two categories of nanocomposites

will be described: (1) mesoporous silica with magnetic nanoparticles and (2) mesoporous silica with polymers included. The recent progress and applications of each one of these materials in the biomedical field will be reported.

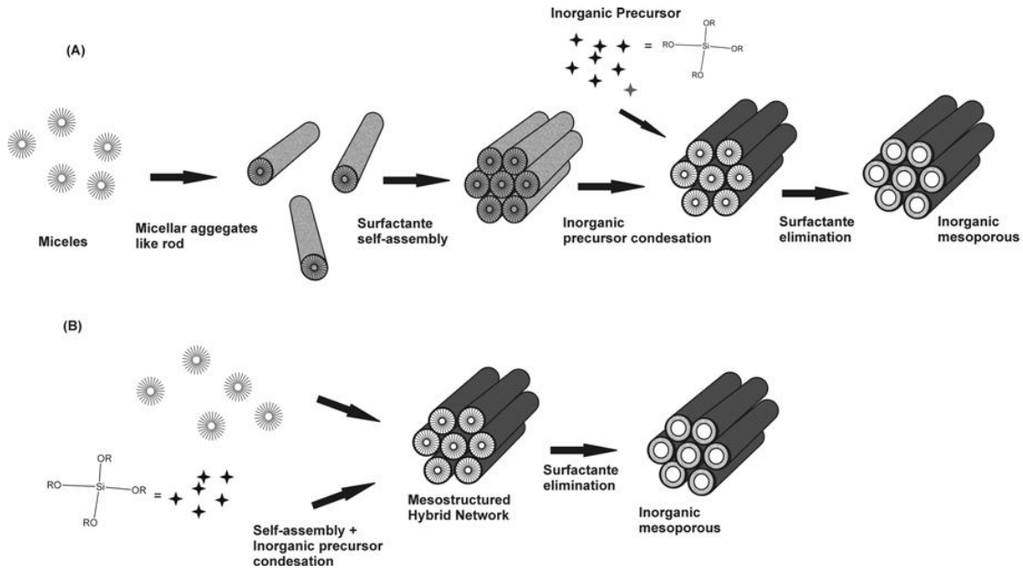


Fig. 1. Scheme of structure formation mediated by inorganic mesoporous structure-directing agent. (A) Formation of liquid crystal from surfactant and (B) self-organizing cooperative process.

2. General aspects

The performance of these materials in many fields of applications depends directly on the silica network porosity. Because of their large pores, high hydrothermal stability, and easy preparation, SBA-15 materials have been considered very promising for hosting and further delivery under appropriate conditions of a variety of molecules of pharmaceutical interest (Sousa et al., 2004). The delivery of these molecules was once considered difficult, because of the difficulty associated with the diffusion of large molecules through the materials of conventional drug delivery systems (DDS). These organic substances are normally very large in size and mesoporous silica is a potential candidate to encapsulate such molecules by utilizing ordered mesopores. Indeed, the properties of the formed solids are extremely dependent on the synthesis temperature, and the properties of surfactants used as templates in the synthesis are reflected in several properties of the final solid. In this way, structural characteristics such as pore size and porosity can be altered by change in some of the synthesis parameters. Consequently, the release kinetics from the matrix, due to its well-arranged structure, can be altered by change in the textural characteristics. Nevertheless, there is one major problem for the mesoporous systems as far as drug release is concerned, and that is the limited control of the drug release whose major mechanism is diffusion. The need to create new materials with optimized, predetermined characteristics has spurred an increasing interest in hybrid materials, especially in organic and inorganic nanocomposites.

The development of new delivery systems has proven to be of great interest for pharmaceutical technology. Ceramic materials generally release drugs by the following

mechanisms: (i) diffusion, (ii) chemical reaction, or (iii) solvent activation. Beyond these, some systems can by externally activated to release more drugs when necessary, using external forces such as magnetism or temperature.

In the case of magnetism as an external force, the first type of nanocomposites that will be presented in this chapter, small magnetic beads are uniformly dispersed within a matrix. When these nanoparticles are exposed to a biological system, normal diffusion of the drug occurs due to a concentration gradient. However, upon exposure to an external oscillating magnetic field, larger quantities of drug can be released quickly. This nanocomposite combines the special structural characteristics of mesoporous silica matrix with the advantages of the unique magnetic properties of magnetic nanoparticles, because the unprotected magnetic nanoparticles can easily form aggregates and react with oxygen present in the air. Therefore, a suitable coating with mesoporous silica is essential to prevent such limitation. These materials seem suited for numerous *in vivo* applications, such as tumor hyperthermic treatment and magnetic drug targeting (Souza et al., 2009; Souza et al., 2010). Magnetic drug targeting allows the release of drugs at a defined target site with the aid of a magnetic field. The concept of hyperthermia is to heat a region of the body affected by cancer to temperatures between 43 and 45 ^{o}C. At these temperatures, the growth of cancerous cells can be halted.

In the case of temperature as an external force for diffusion, which is the second category that will be presented in this chapter, the systems are hybrid. Several studies have reported the encapsulation of polymers into mesoporous silica hosts. Encapsulation of stimuli-responsive polymers has been of particular interest in the drug delivery area. Among these stimuli-responsive polymers, temperature-responsive hydrogels such as poly(*N*-isopropylacrylamide) [P(*N*-iPAAm)] are a well-studied class of drug delivery systems, as they can respond strongly to temperature changes. In water, P(*N*-iPAAm) exhibits a phase transition at a lower critical solution temperature (LCST) of approximately 33^{o}C (Freitas & Cussler, 1987). Below the LCST, the hydrogel incorporates water and swells, whereas the release of water in response to an increase in temperature causes shrinkage. Thus, the development of hybrid functional nanosystems based on silica-P(*N*-iPAAm) has drawn much attention to the control of molecular transport, including drug release, because self-regulated delivery allows for drug release when it is needed (Sousa et al., 2010).

3. Magnetic nanocomposites and bioapplications

The nanostructured silica has gained importance for biomedical applications and has been studied extensively. Silica has well established chemistries that allow surface modification with various functional groups (e.g., amine, thiol, carboxyl, and methacrylate). These nanoparticles can be further modified with biomolecules such as enzymes, proteins, DNA molecules, etc., for biological applications. The surface modification with biomolecules allows for the specific recognition of immobilized and free species, can provide diagnostic information, and serve as part of a purification or separation process (Jin et al., 2003).

Another type of material that gained prominence in biological applications is magnetic nanoparticles. The synthesis of nanostructured magnetic materials has been intensively pursued because of their broad applications, including in magnetic storage media, catalysis, ferrofluids, contrast materials for magnetic resonance imaging, magnetic bioseparation, and magnetic carriers for drug targeting (Pankhurst et al., 2003), among others.

The application of the different forms of iron oxides for diagnostic procedures has gained wide acceptance in radiological practice, but therapeutic applications are still under investigation. Such applications have exploited two major advantages of iron oxides: their low toxicity to humans and the possibility of controlling their magnetization. For example, many of the particles used are superparamagnetic that can be easily magnetized with an external magnetic field, and when the field is removed, they do not exhibit residual magnetization. If exposed to an alternating magnetic field, the iron oxide particles become powerful heat sources by transforming the energy from the magnetic field into heat (Chastellain et al., 2004; Jordan et al., 1997). The most important characteristic of magnetic nanoparticles for heat generation is particle size (Kalambur et al., 2005). The greatest difficulty in the synthesis of ultrafine particles is size control on the nanometric scale. Thus, the research of easy and flexible magnetic synthetic routes to produce nanoparticles with desired sizes and acceptable size distribution without particle aggregation is of extreme importance to fulfill the potential of these materials in biomedical applications.

Iron oxide (either Fe_3O_4 or γ-Fe_2O_3) can be synthesized through the co-precipitation of Fe^{2+} and Fe^{3+} aqueous salt solutions by addition of a base. The control of size, shape, and composition of nanoparticles depends on the type of salts used (e. g. chlorides, sulphates, nitrates, perchlorates, etc.), Fe^{2+} and Fe^{3+} ratio, pH, and ionic strength of the media (Gupta & Gupta, 2005).

Other methods to prepare magnetite nanoparticles are microemulsion (Liu & Wang, 2004a), electrochemical synthesis (Franger et al., 2004), pyrolysis (Gun'ko et al., 2001), and hydrothermal synthesis (Wu et al., 2005). However, most methods present some synthesis problems, such as difficulties in the prevention of flocculation, the control of Fe^{2+} and Fe^{3+} ratio in the co-precipitation process, and the removal of surfactants in the micron-emulsion process. Recently, an oxidation-precipitation method for the preparation of magnetite nanoparticles has been used by some researchers (Thapa et al, 2004). The formation of Fe_3O_4 follows the nucleation-growth mechanism when the $Fe(OH)_2/Fe(OH)_3$ molar ratio is 1:2, which is the characteristic value of the magnetite structure. However, it does require the careful adjustment of the solution pH value for particle formation and stabilization, and it is difficult to control particle size and size distribution.

As discussed, for an efficient performance, the particles must remain non-aggregated, be stable against oxidation, and display high magnetization during application. Thus, appropriate nanoparticle coating is essential to overcome this limitation. Silica/iron oxide nanocomposites are of particularly interest, since the protective layer afforded by silica can prevent dipolar magnetic attraction between magnetite particles, and consequently produce quite uniform particle dispersion.

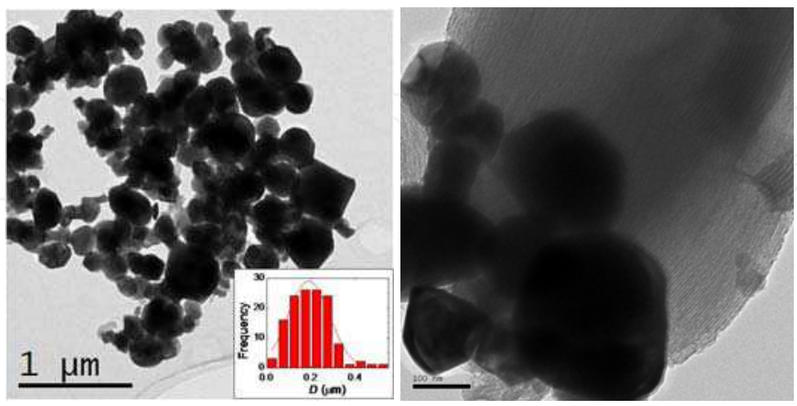
The approaches for the synthesis of SiO_2–Fe_2O_3 nanocomposites are varied (Ma et al., 2006; Chen et al., 2008). Such nanocomposites are composed of magnetic nanoparticles embedded or encapsulated in an inorganic oxide matrix. In addition, to coat the surface of magnetic nanoparticles, silica is obtained by classical sol–gel methods, but in this case, the final product may present a wide pore size distribution (Singh, 2008). The new class of nanocomposites, which combine special structural characteristics of mesoporous silica matrix with the advantages of the unique magnetic properties of iron nanoparticles, seems suited for numerous *in vivo* applications, such as tumor hyperthermic treatment and drug delivery. Most importantly, particle growth can be effectively confined to the channels of mesoporous silica, limiting particle size to the nanoscale.

Studies concerning the growth of Fe_3O_4 and γ-Fe_2O_3 nanoparticles inside mesoporous silica MCM-41 and MCM-48, using an ionic surfactant as a template, have also been reported (Köhn et al., 2003; Fellenz et al., 2006a). More recently, Fe_3O_4 nanoparticles modified covalently with triethoxysilane having a quaternarydicetylammonium ion were used as building blocks and incorporated in the structure (Alvaro et al., 2006). The surface of these nanoparticles was modified to become compatible with the structure-directing agent (cetyltrimethylammonium). However, these approaches result in materials presenting two main limitations: (i) due to the use of ionic surfactants, they present typical wall thicknesses around 1 nm (Doadrio et al., 2006) and consequently, low stability; (ii) the functionalization of the mesoporous surface and nanoparticle surface leads to a decrease in the pore size and surface area (Alvaro et al., 2006), facts that could affect the applicability of such materials in adsorption systems, like drug delivery systems.

In this context, we reported the synthesis of mesoporous SiO_2-coated Fe_3O_4 nanoparticles by using a neutral surfactant and without the application of any functionalization method (Souza et al., 2008). To accomplish this, the Fe_3O_4 nanoparticles were synthesized by oxidation–precipitation and coated with mesoporous silica (SBA-15) by using nonionic block copolymer surfactants as the structure-directing agent. We observed that the magnetite nanoparticles were completely and homogeneously coated by well-ordered mesoporous silica with stable (~8 nm thick) pore walls, Figure 2. The applied synthesis route did not affect the structural and magnetic properties of the Fe_3O_4 nanoparticles.

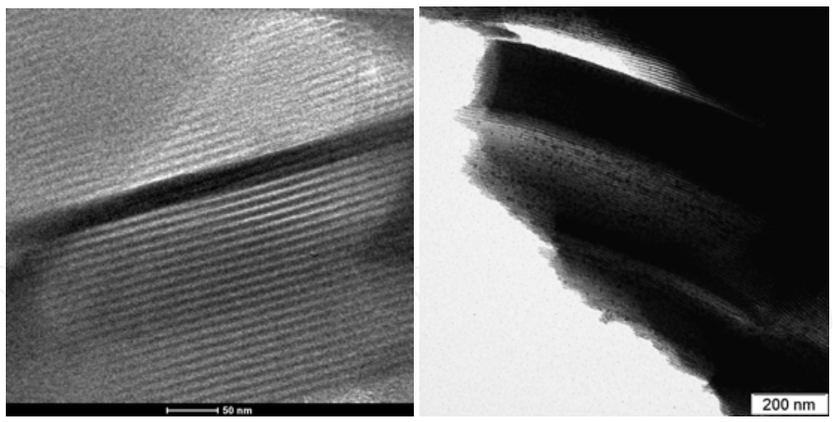
In the other report, we presented a wet impregnation method which proved efficient to obtain well-dispersed Fe_3O_4 nanoparticles inside the pores of silica (Souza et al. 2010). The proposed method involved the preparation of an iron oxide precursor in ethanol and its subsequent transfer to SBA-15 mesoporous hexagonal silica. Iron oxide was formed inside the porous structure to obtain a magnetic material, Figure 3. The sample was heated to 550 ^oC for 2 h in air for the formation of iron oxide and then was heated to 550 ^oC for 8 h in an N_2 atmosphere to obtain Fe_3O_4.

The main methods of synthesis of composites using magnetic oxides dispersed in silica matrix and their various applications will be discussed below, having in mind the growing interest in using these materials in the biological area.



(a) (b)

Fig. 2. Transmission electron micrographs: (a) Low resolution and (b) high resolution images showing the magnetite nanoparticles (dark region) covered by the mesoporous silica; the inset in (a) is the quantification of the size distribution of the Fe_3O4 particles.



(a) (b)

Fig. 3. TEM of unidirectional canals of the open mesoporous structure, and image showing the magnetite nanoparticles (dark region) covered by mesoporous silica.

3.1 Bioseparation

Magnetic separation provides a convenient method for the removal of magnetizable particles by applying an appropriate magnetic field. In 1973 Robinson et al. used magnetic separation for the first time in a biotechnology context. In their work, silica-coated magnetic iron oxide and cellulose-coated magnetic iron oxide were used to immobilize two enzymes, α-chymotrypsin and β-galactosidase, for applications in bioreactors. Since then, magnetic separation has become an increasingly popular tool for the separation of biological molecules and cells (Bruce et al., 2004).

If the magnetic material surface is selective for a specific protein, it will be able to connect to this surface, and its separation from the biological environment could be done by using a magnet (Figure 4). Once the surface has been modified, a system comprised of a magnetic core coated with silica can be used for bioseparation.

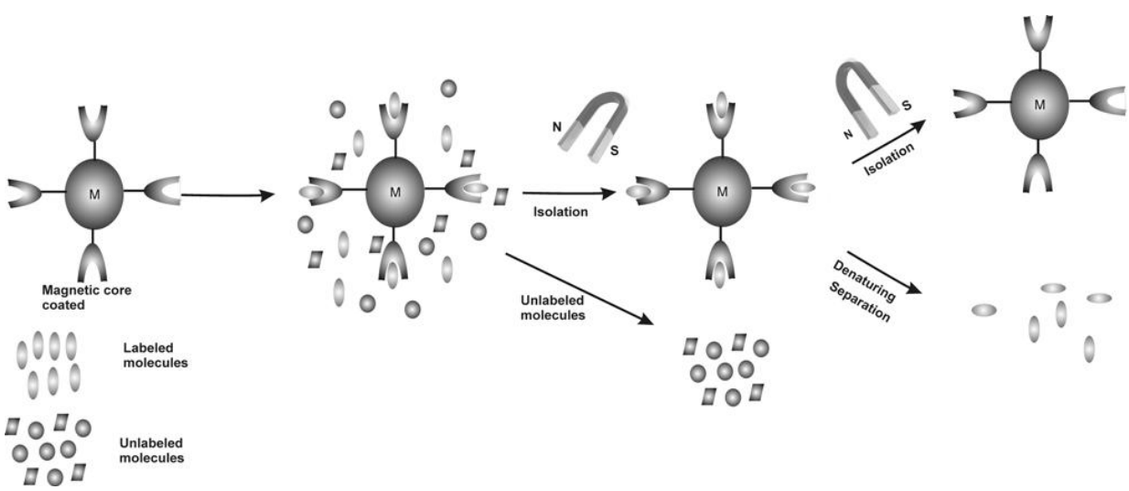


Fig. 4. Scheme illustrating steps involved in the extraction of biomolecules using magnetic bioseparation agents.

The first bioseparation work onto a functionalized silica support was performed by Zhao and coworkers in 2003 (Zhao et al., 2003). The authors developed a novel genomagnetic nanocapturer (GMNC) for the collection, separation, and detection of trace amounts of DNA/RNA molecules with one single-base difference. The GMNC was constructed by bioconjugating molecular beacon DNA probes onto magnetic nanoparticle surfaces. The method showed an excellent ability to differentiate single-base mismatched DNA/mRNA samples by combining the exceptional specificity of molecular beacons and the separation power of magnetic nanoparticles.

Later, Liu and coworkers synthesized magnetite (Fe_3O_4) nanoparticles by the coprecipitation method and coated their surface with silica, obtaining well dispersed magnetic silica nanospheres of about 50–80 nm in diameter. The surface of these nanospheres was functionalized with amino-silane coupling agent, *N*-(2-aminoethyl)-3-aminopropyltrimethoxysilane (AEAPS) (Liu et al., 2004b). The functionalized silica has undergone a series of experiments performed to investigate the protein immobilization in a magnetic matrix. Bovine serum albumin (BSA) was chosen as a model protein and was covalently immobilized onto the amino-silane modified magnetic silica supports. The result shows that such amino-silane modified magnetic silica is a well-dispersed and effective superparamagnetic support for bioseparation with maximum BSA immobilization capacity (up to 86 mg/g), presenting, thus, potential use as immune-magnetic support for protein purification.

Sen et al. (2006) reported the template-assisted fabrication of a magnetic mesoporous silica-magnetite nanocomposite and its potential for application in magnetic bioseparations, evaluating its ability (i) to bind and elute DNA and (ii) to extract RNA from bacterial cells. Magnetite nanoparticles previously synthesized were used as a core material for the fabrication of a mesoporous magnetic nanocomposite. Both core magnetite and silica-magnetite nanocomposite demonstrated a high capacity for binding the DNA. Nearly 100% recovery of DNA was obtained from the surface of the nanocomposite, whereas <10% was recovered from the magnetite core. It was possible to bind and elute approximately the same quantity of DNA using half the amount of the mesoporous silica-magnetite composite, as compared to classical amorphous silica-magnetite materials (Bruce et al., 2004).

Specifically in enzyme immobilization, it is known that because of the low enzyme loading on the conventional magnetic beads, more and more attention was paid to the magnetic mesoporous support. Magnetite mesoporous silica hybrid support was fabricated by depositing magnetite and MCM-41 nanoparticles onto polystyrene beads using the layer-by-layer (LBL) method. The incorporation of magnetite gives an additional magnetic property to the hollow mesoporous silica shells. This perfect combination of mesoporous material properties with a magnetic property improves the enzyme immobilization (Xie et al., 2009).

Another field of interest in applications that has gained prominence in the biological area is the use of these systems in studies of drug delivery.

3.2 Controlled release of drugs

The idea of controlled release of biologically active substances began to be used in the 1950s with the advent of polymeric materials. The potential advantages of controlled release systems include: (i) localized release of drugs in a particular compartment of the body, thereby decreasing the systemic level of the drug, (ii) maintaining constant levels of drug in the body, resulting in greater efficiency in the use of the agent (i.e., it is necessary to lower the concentration of the drug to produce the same effect as in conventional systems), (iii)

preservation of the medicines that are quickly destroyed by the body (this is particularly important for biologically sensitive molecules such as proteins), (iv) lower frequency of administration of the active agent, enhancing patient comfort and effectiveness of treatment (Langer, 1990; Ogawa & Plepis, 2002). Besides the polymeric matrix, other controlled release systems based on different materials have been intensively studied in recent years, such as bioceramic and composites. Some examples are antibiotics like gentamicin, released from the matrix composed of calcium phosphates and poly(DL-lactide) (PLA) (Baro et al., 2002) and from the composite of hydroxyapatite/collagen (Martins & Goissis, 2000), and anti-neoplastic agents like cisplatin, released from calcium phosphate (CaP) nanoparticles (Barroug et al., 2004).

The porosity of conventional matrices is highly heterogeneous due to complex chemical composition, which presents as a great disadvantage the difficulty of ensuring homogeneous drug distribution through the matrix, affecting the release rate. Therefore, the need to address this disadvantage has led to improvements in this field through the use of ordered mesoporous materials, chemically homogeneous, which have well defined porosity.

In this context, we have reported the influence of magnetic nanoparticles on drug release kinetics of three model drugs: cisplatin, carboplatin, and atenolol under *in vitro*. In this work (Souza et al., 2009), magnetic nanoparticles embedded into mesoporous silica were prepared in two steps: first, magnetite was synthesized by oxidation-precipitation method, and next, the magnetic nanoparticles were coated with mesoporous silica by using nonionic block copolymer surfactants as structure-directing agents. The SEM images of magnetite in Figure 5 show that the material has uniform morphology and particle size distribution. In addition, some particle clusters may be observed due to the magnetic interaction between the particles. The regular octahedral morphology indicates that the particles are well crystallized. Figure 5.b shows the morphology of SBA-15. It consists of vermicular-shaped particles. In contrast, the nanocomposite presents spherical morphology. This may be attributed to the presence of the magnetite silica-coated nanoparticles. The average size of the spherical particles varied from 0.139 to 0.476 μm. Particles smaller than the human body capillary diameter (8 μm) are suitable for intravenous drug-delivery injection. The desired particle size range for a specific application may be selected by nanoparticle centrifugation at a controlled rate.

Drug release was studied with and without a magnetic field in two experiments: a) with a constant magnetic field and b) with an alternating magnetic field. To simulate drug release in the presence of a magnetic field, a NdFeB magnet (0.250 T) was used in the first experiment, and in the second one, a low-frequency alternating magnetic field was obtained

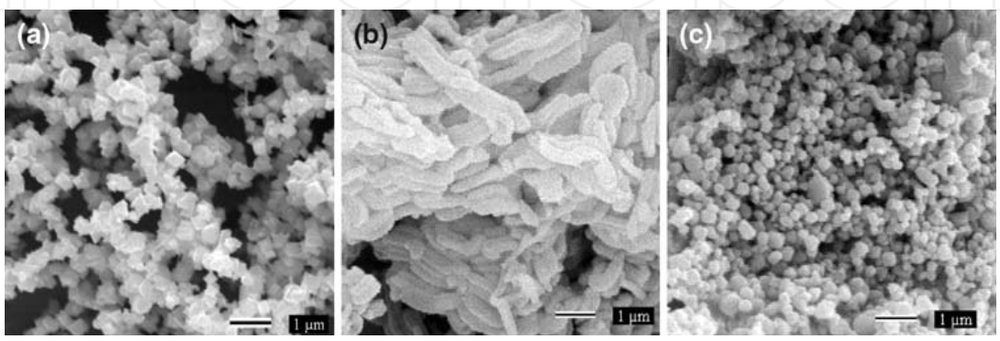


Fig. 5. SEM of (a) magnetite, (b) pure SBA-15, and (c) SBA- 15/Fe_3O4

with a magnetic cavity composed of a Helmholtz coil connected to a direct current source coupled to a frequency generator and a Hall probe for measuring the magnetic field. The following frequencies were used: 15, 30, 45, 60, 100, and 300 Hz with a 17 mT magnetic field. The application of an alternating magnetic field provokes the vibration of the magnetic particles and the quick release of large quantities of drugs. The measures presented here are designed to assess the influence of the application of low frequency (≤300 Hz) alternating magnetic fields (170 Oe) on drug release. Figure 6a shows the release profiles of cisplatin without a magnetic field, with a constant magnetic field, and an alternating magnetic field up to 300 Hz. Drug release was more effective and faster in the alternating magnetic field, Figure 6. The alternating magnetic field showed a large influence on the cisplatin release profile. These results can be explained by the possible interaction of the drugs with the magnetite nanoparticles, possibly due to the incorporation of cisplatin into the mesopores and its interaction with the surface of the magnetic nanoparticles.
Another promising application for these materials is in magnetic hyperthermia.

3.3 Magnetic hyperthermia

Hippocrates (460–370 BC) believed that any disease could be cured by heating the patient's body (Ito et al., 2005). Since 1957, hyperthermia, a modality of cancer treatment with an elevated temperature between 41 and 45 ºC with a treatment time of at least 30 min, has received considerable attention due to its clinical efficacy, such as minimizing clinical side effects and the possibility of selectively destroying a localized or a deeply seated malignant cancer tumor (Bae et al., 2009).
Cancer cells generally perish at around 43 ºC because their oxygen supply via the blood vessels is not sufficient, whereas normal cells are not damaged at even higher temperatures. In addition, tumors are more easily heated than the surrounding normal tissues, since the blood vessels and nervous systems are poorly developed in the tumor. Therefore, hyperthermia is expected to be a very useful cancer treatment with few side effects. Various techniques for heating the tumors, such as treatments with hot water, infrared rays, ultrasound, and microwaves have been attempted. However, deep-seated tumors cannot be heated effectively and locally using these techniques (Kawashita et al., 2005).

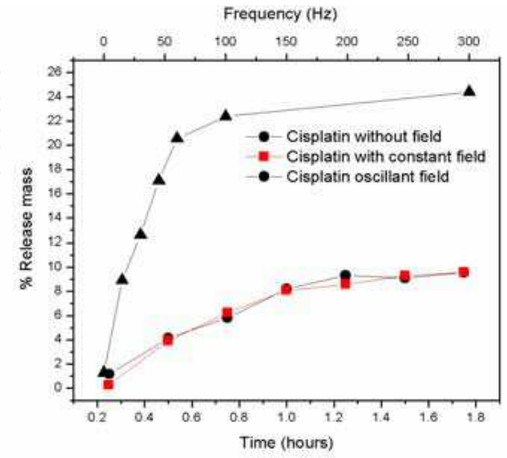


Fig. 6. Release profile of the nanocomposite/cisplatin system without a field, in a constant field, and in an alternating field.

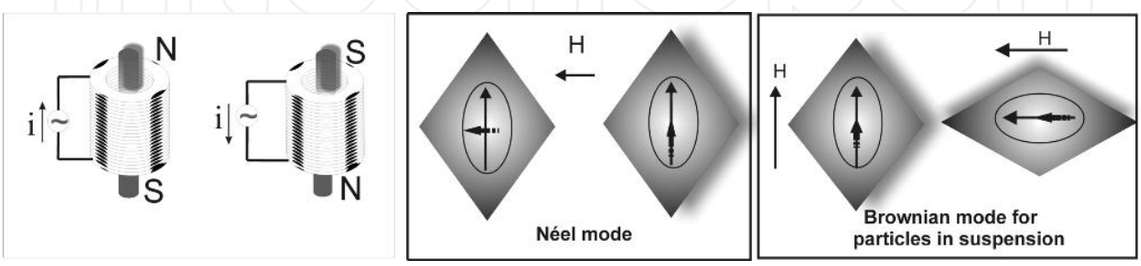
The biggest problem with this treatment is that it is not selective, i.e., when subjected to hyperthermia for tumor treatment, it also affects normal cells adjacent to the tumor. Thus, there is a need to develop a tumor-specific hyperthermia for tumor cells.

Some researchers have proposed the concept of "intracellular" hyperthermia and have developed submicron magnetic particles for inducing hyperthermia. This concept is based on the principle that under an alternating magnetic field (AMF), a magnetic particle can generate heat by hysteresis loss (Ito et al., 2005).

There are at least three different mechanisms by which magnetic materials can generate heat in an alternating field (Kalambur et al., 2005): (i) generation of eddy currents in bulk magnetic materials, (ii) hysteresis losses in bulk and multi-domain magnetic materials, and (iii) relaxation losses in 'superparamagnetic' single-domain magnetic materials. The mechanisms (i) and (ii) contribute very little to the heating system of particles with a single-domain. The mechanism that contributes to significant heating of these particles, therefore, is the relaxation mechanism (iii). Relaxation losses in single-domain magnetic nanoparticles fall into two modes: rotational (Brownian) mode and Néel mode (Figure 7). In the Néel mode, the magnetic moment originally locked along the crystal easy axis rotates away from that axis towards the external field. The Néel mechanism is analogous to the hysteresis loss in multi-domain magnetic particles, whereby there is an 'internal friction' due to the movement of the magnetic moment in an external field that results in heat generation. In the Brownian mode, the whole particle oscillates towards the field with the moment locked along the crystal axis under the effect of a thermal force against a viscous drag in a suspending medium. This mechanism essentially represents the mechanical friction component in a given suspending medium.

Kawashita and coworkers (Kawashita et al., 2005) studied magnetite microspheres with capacity heat generation. Two kinds of microspheres were synthesized: (a) magnetite microspheres formed by melting powders in high-frequency induction thermal plasma, and (b) silica glass microspheres formed by precipitation from an aqueous solution. In case (a), the magnetite microsphere diameter was 20 to 30 μm, with heat generation capacity of 10 W/g, under 300 Oe and 100 kHz; in case (b), the silica glass microspheres coated with magnetite presented average size of 25 μm, while the average size of magnetite crystallites deposited on the silica surface was estimated at 50 nm. In the latter case, the heat generation was estimated to be 41 W/g, under 300 Oe and 100 kHz, showing that the silica/magnetite microsphere system is a promising one for hyperthermic treatment of cancer.

There is a possibility of a second application for this system. The controlled drug delivery could be triggered by thermomagnetic action, adjusting the magnetic field and frequency.



(a) (b) (c)

Fig. 7. (a) Induction Field schema for magnetic material in an AC coil. (b) and (c) Relaxational losses leading to heating in an alternating field (H): (b) Néel mode; (c)Brownian mode.

Considering these points, Hu and coworkers studied magnetic-sensitive silica nanospheres for ibuprofen release by controlled bursting to a therapeutically effective concentration by a high-frequency magnetic field (HFMF) (Hu et al., 2008). The acceleration of the rotation of magnetic nanoparticles deposited on the silica matrix generates heat energy; the HFMF enlarges the nanostructure of the silica matrix, producing porous channels that cause the drug to be released easily. Thus, nanospheres showed a marked ibuprofen release profile, with 180-190 min of release, when the system was triggered for 10 min in a high-frequency magnetic field (HFMF). This profile was compared with a control group of silica nanospheres without magnetic iron incorporation. The cumulative release of ibuprofen from silica nanospheres (Si:Fe = 1:1) was measured, both with and without magnetic stimulation of 50 kHz applied at the four specific times, and showed that after the magnetic stimulation, a significant increase in the amount of drug released was observed at each time interval.

A small number of studies have been conducted with mesoporous silica/magnetic particles systems for hyperthermia applications. Recently, we reported the synthesis of nanocomposite-based SBA-15 and magnetite nanoparticles by the wet impregnation method of an iron precursor (Fe3(SO4)3) into a silica framework (Souza et al., 2010). Iron oxide was formed inside the porous structure, thus producing the magnetic device.

The spontaneous magnetization of the nanocomposite is 10.31 $Am^2\ kg^{-1}$, which is lower than that of magnetite (83.98 ± 2.2 $Am^2\ kg^{-1}$), because the nanoscale particles form a single magnetic domain. The magnetic properties obtained by ^{57}Fe Mössbauer spectroscopy (figure not given) showed that the nanocrystals present superparamagnetic characteristics.

Tests of magnetic hyperthermia were performed. For this, AC magnetic-field-induced heating was measured both in the solid material and in an aqueous solution under different applied magnetic fields: 105 Oe (8.36 kA m^{-1}) and 168 Oe (13.37 kA m^{-1}).

Figure 8 shows the time-dependent temperature curves of the dry nanocomposite for 198 kHz and magnetic fields of 105 and 168 Oe AC. When the sample was exposed to an AC magnetic field for 30 min, its temperature ranged from 23 to 32.87 °C in the 168 Oe AC magnetic field and from 23 to 25.16 °C in the 105 Oe, showing its dependence on the magnetic field. This figure shows a relatively sharp increase in temperature in the beginning of heating. Moreover, a nearly steady state regime is established after 10 min under 168 Oe, reaching a temperature range of ΔT_{max} = 9.87 °C.

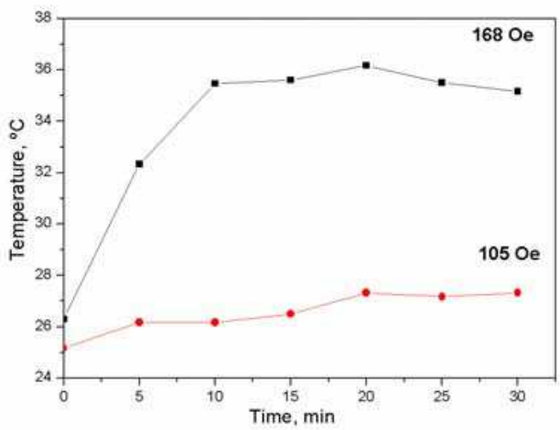


Fig. 8. Time-dependent temperature curves of the nanocomposite under 198 kHz and magnetic fields of 168 Oe (13.37 kA.m^{-1}) and 105 Oe (8.36 kA.m^{-1}).

When dispersed in water, the difference in the temperature of the nanoparticles between the starting ambient temperature and after 30 min of exposure to the magnetic field was 21 ºC under 168 Oe and 3 ºC under 105 Oe. Considering the results obtained for the dry nanoparticles and those dispersed in water in the 168 Oe magnetic field, Figures 9a and 9b, we notice a small increase in temperature for the former, resulting in ΔT_{max} = 9.87 ºC, and 21 ºC for the latter. This behavior can be explained based on the total surface area of the magnetic nanoparticles and their ability to generate heat. If the magnetic nanoparticles are well dispersed in water, their specific surface area increases, as does the convective heat transfer rate to the fluid.

The amount of heat generated by pure water in 168 Oe AC magnetic fields was measured to investigate more precisely the effect of water on the increase in the temperature of the dispersed nanoparticles. According to Figure 9b, although pure water contributes to a slight rise in temperature, from 23 to 29 ºC, heat generation is affected by the sample medium. This property of the nanoparticles dispersed in water was in fact measured after sonicating the solution for 30 min. The measured temperatures of the nanoparticle suspension after sonication and under 168 Oe AC magnetic field increased to 47.5 ºC after 30 min of assay, presenting a ΔT_{max} of 24.5 ºC.

The principle of hyperthermia is to heat a body region affected by cancer to temperatures between 43 and 45 ºC. At these temperatures, the growth of cancerous cells can be halted. Thus, a temperature variation of ΔT_{max} = 9.87 ºC would be sufficient, based on a body temperature of 37 ºC. Considering all the measurement conditions used in this work, heat generation can be controlled in selected magnetic particles by adjusting the magnetic field and choosing an appropriate medium.

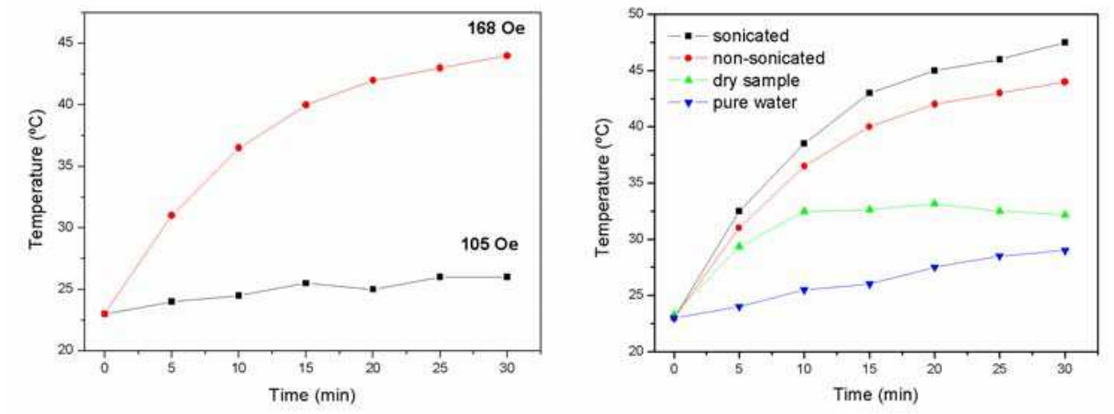


Fig. 9. (a) time-dependent temperature curves of the nanocomposite under 198 kHz and magnetic fields of 168 Oe and 105 Oe; (b) heating-induced by magnetic field of nanocomposite in different situations to 168 Oe compared with pure water, used as a control.

4. Functional hybrid mesoporous silica/poly(n-isopropylacrilamide) useful for drug delivery systems

The second category of multifunctional materials deals with organic-inorganic hybrids systems based on mesoporous materials and stimuli-responsive polymers. Recent studies

have made fundamental proposals for development of hybrids materials based on polymer and mesoporous silica. Many different polymers have been encapsulated into the pores structure of the mesoporous materials, and different procedures were used for encapsulation. Recently, strategies for development of hybrids based on ordered mesoporous silica and stimuli-responsive polymers have been reported in the literature (Tian & Yang, 2009; Fu et al., 2007; Liu et al., 2009; Gao et al., 2009; Sousa et al. 2010).These stimuli-responsive polymers show abrupt changes in their swelling behavior in response to small changes in environmental parameters such as temperature, pH, solvent composition, electric fields, etc. They have received much attention due to their potential applications in numerous fields. Among these stimuli-responsive polymers, the most important systems from a biomedical point of view are those sensitive to pH and/or temperature, because variables such as low pH and elevated temperatures are found in the body (Qui & Park, 2001).

One of the most studied temperature-responsive polymers is poly(*N*-isopropylacrylamide) [P(*N*-iPAAm)], which swells to a large extent in water, at a low temperature, and shrinks as the temperature is increased, showing a first-order phase transition around 33 ^{o}C, behaving as a polymer solution with a lower critical solution temperature (LCST) (Freitas & Cussler, 1987). Figure 10 shows this phase behavior schematically. This interesting phase behavior of a dramatic dependence of the swelling volume on temperature and a discontinuous transition has attracted the interest of many researchers all over the world in past years. Studies on the thermodynamic behavior of this system (Marchetti et al., 1990; Sousa, 1993; Sousa, 1995; Nakamoto, et al., 1996), different potential applications (Wu et al., 1996; Jin, et al., 1995), and permeability to small solutes (Palasis & Gehrke, 1992; Mukae, et al., 1993) have been reported.

The thermodynamics of polymer gels describes the swelling equilibrium as a result of two opposite contributions: the change in the free energy of mixing as the gel is in contact with a solvent and the change in the elastic free energy due to the elongation of the network as the gel swells, absorbing solvent (Ogata, 1995). The understanding of the gels' elastic structure is, therefore, fundamental. This structure is directly related to the crosslinking density and polymer-polymer interactions.

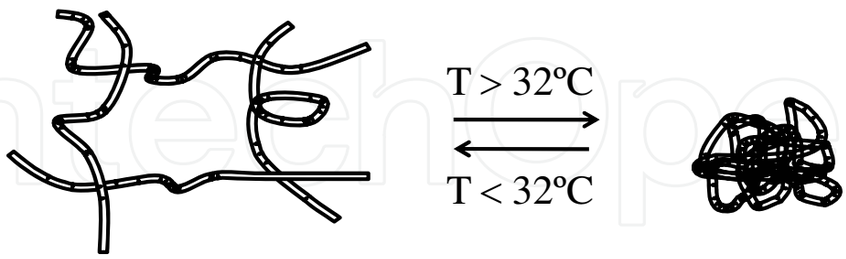


Fig. 10. Schematic representation of the phase behavior of P(*N*-iPAAm).

By utilizing this interesting phase behavior, P(*N*-iPAAm) can be used in biomedical applications such as DDS (Hoffman, 1987; Peppas & Langer, 2003). Furthermore, the interest in the use of P(*N*-iPAAm) in biomedical applications originates from a number of advantages that this presents for use as a biomaterial, such as biocompatibility, specific diffusive properties, elastomeric consistency, and low interfacial tension, among others.

Hybrid functional nanosystems based on silica- P(*N*-iPAAm) have attracted much attention for control of molecular transport, including drug release, because a self-regulated delivery

allows a drug to be released when it is needed. Thus the encapsulation of P(*N*-iPAAm) in ordered mesoporous silica has been of particular interest in the drug delivery area, since that combine the advantages of the mesoporous silica (thermal and mechanical stability, biocompatibility and textural properties) with the P*(N*-iPAAm) ability to swell or shrink in temperatures close to physiological temperature. Compared to the sustained-release system, the thermo-responsive controlled release system can realize a controlled release pattern, which can improve the therapeutic efficacy. However, studies on ordered mesoporous silica-thermoresponsive P(*N*-iPAAm) hybrids for use as DDS are few. To the best of our knowledge, only a small number of papers concerning a responsive-carrier-system-based mesoporous silica and P(*N*-iPAAm) for use in the drug delivery area has been reported up to the present (Zhou et al. 2007; Yang et al., 2008; You et al., 2008; Liu et al., 2009; Zhu, et al., 2009; Sousa et al., 2010).

Chang and co-authors (Chang et al., 2004) report the systematic application of the ordered mesoporous materials to smart controlled drug release using the thermoresponsive P(*N*-iPAAm) hybrid mesoporous structures. The P(*N*-iPAAm) hybridized mesoporous materials were prepared by the radical-initiated polymerization with *N*-iPAAm monomers on modified mesoporous silica surface with different pore sizes (10, 17, 30 nm). Indomethacin was used to study the thermosensitive drug release from hybrid. The drug release from hybrid materials was investigated during stepwise temperature changes between 25 and 40 ^{o}C and measurement of the concentration in a UV-Vis spectrophotometer at different time intervals. The release profile showed a sustained positive thermoresponsive drug release. When the temperature was increased and maintained at 40 ^{o}C, a nearly constant release pattern was observed and a rapidly decreased release was observed on the temperature change to 25 ^{o}C. According to the nanodiffusion mechanism proposed by the authors at a low temperature, the drug is trapped in the polymer and in the porous structures, and the polymers swell to prevent the drug from being significantly released into the media. When the temperature is increased above the LCST of P*(N*-iPAAm), the polymers shrink to squeeze the drug into the porous channels, and open the pore structure. Although a large amount of drug may be squeezed out of the polymer above the LCST, the amount released into the media did not show a peak, because diffusion of the drug through the porous channels is the limiting mechanism to control the drug release, rather than the phase behavior of the P(*N*-iPAAm).

In this same sense, Zhou et al. investigated a system based on stimulus-responsive P(*N*-iPAAm) inside a mesostructured cellular foam (MCF-PNIPA) as a device for drug delivery (Zhou et al., 2007). Ibuprofen (IBU) was loaded in MCF-PNIPA samples at 45 ^{o}C during 48 h. Drug release studies were performed by soaking samples in a solution with pH maintained at 7.4 and stepwise changing the temperature between 10 and 60 ^{o}C. The release process was followed spectroscopically. Loading and release data suggested that the multilayer polymers inside the pores of the MCF apparently formed an internal cavity for drug molecules increasing the IBU storage capacity, in addition to responding to changes in external temperature. A possible mechanism of the drug storage and release profile from the system was developed by the authors, and according to this mechanism, at a low temperature, the drugs are confined in the pores owing to expansion of the P*(N*-iPAAm) molecular chains and the formation of hydrogen bonding between P*(N*-iPAAm) and IBU. With an increasing temperature, the polymer chains are hydrophobic and swell within the pore network, resulting in the collapse of hydrogen bonds and pushing the drug molecules from the pores. Figure 11 shows this dependence of IBU amount released on temperature.

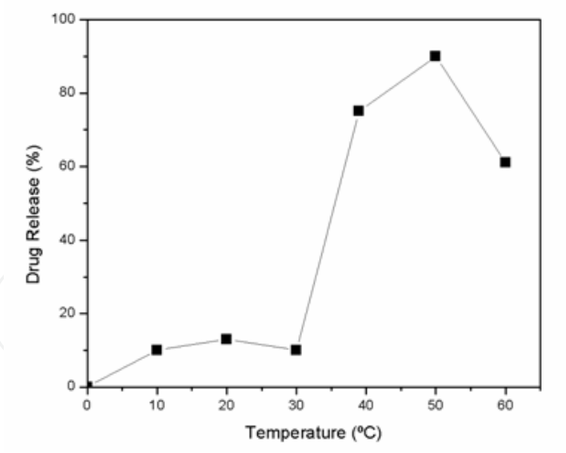


Fig. 11. The dependence of release amounts of IBU on temperature. Data obtained from (Zhou et al., 2007).

Furthermore, in 2007, a novel synthesis of a multi-functional delivery system based on ordered mesoporous silica SBA-15 with magnetic particles formed in situ and thermo-sensitive P(*N*-iPAAm) - m-SBA–PNIPA was reported. They employed hydrophilic $FeCl_2$ as an additional precursor to fabricate magnetic particles inside SBA-15 via surfactant template sol–gel process, and the polymerization of *N*-iPAAm was implemented inside the pores of SBA-15 with a magnetic particle system. Ibuprofen also was encapsulated inside the sample m-SBA–PNIPA and the in vitro delivery assays were performed according to the procedure previously described by Zhou et al., stepwise changing the temperature between 9 and 45 ºC. The system exhibited a pronounced transition at approximately 17 ºC, and when the temperature was between 7 and 11 ºC, a drug release of 40.5% from the m-SBA–PNIPA was observed. As the temperature rose to 17 ºC, the polymer shrank, leading to the progressive increase of the release rate. Similar results were found for the systems previously reported for Chang and Zhou et al., where a positive thermosensitive release profile was observed. However, this delivery system did not show characteristic bulk behavior with respect to their LCST, and as mentioned by the authors, this system is not suitable for in vivo application but could probably be used in many others fields.

Another kind of magnetic mesoporous silica/P(*N*-iPAAm) nanocomposite was also prepared recently by Liu et al. (Liu et al., 2009), who reported a strategy to prepare core/shell-structured magnetic mesoporous silica microspheres combining three advantages into one single entity. This strategy involves a Fe_3O_4 magnetic nanoparticle as the core, mesoporous silica as a sandwiched layer, and cross-linked thermosensitive poly(*N*-isopropylacrylamide/*N*-hydroxymethyl acrylamide) - P(NIPAM-co-NHMA) copolymer as an outer shell. Zn(II) phthalocyanine tetrasulfonic acid (ZnPcS4), a photodynamic therapy (PDT) drug, was used as a model drug to assess the drug loading and controlled release behavior of the core/shell composite microspheres. Drug release studies were performed by soaking loaded microsphere hybrids in a solution with pH maintained at 7.4 and measuring the cumulative release amount of ZnPcS4 after 24 h at different temperatures. These composite microspheres with different amounts of the hydrophilic co-monomer exhibited a temperature-dependent drug release behavior (Figure 12) where the cumulative release amount after 24 h at 39 ºC was almost three times higher than that at 37 ºC for two samples prepared with different monomer ratios. According to the authors, the significant difference

in cumulative release amount at different temperatures indicated a potential application in the therapy of malignant tumors. For instance, the M-MSN/P(NIPAM-co-NHMA) composite microspheres with superparamagnetic cores and temperature-sensitive shells could be guided by an external magnetic field to the target site, undergo a swelling–shrinking transition, and release the loaded drug rapidly because of the temperature difference between malignant tumor tissue and normal tissue, or because of the temperature difference caused by the magnetocaloric effect in the alternating-current magnetic field.

Yang et al. (2008) synthesized a potential material for applications in intercellular imaging, as biomarkers and biosensors. This material is based on mesoporous silica nanoparticles (MSNs) coated with poly(*N*-isopropylacrylamide) - MSN@PNIPAM. The MSN@PNIPAM was synthesized by atom transfer radical polymerization (ATRP) on the surface of MSN through the ''grafting-from'' method. The thermoresponsive properties of the MSN@PNIPAM were studied by turbidimetry and dynamic light scattering (DLS) measurements and the measured LCST of MSN@PNIPAM material was about 32ºC, consistent with pure PNIPAM in water. A fluorescent dye (FITC) was used as a model guest molecule to test the encapsulation and release ability of the MSN@PNIPAM particles. FITC was entrapped by the stretched polymer chains below LCST, and locked inside the MSNs above LCST. Additionally, the authors took MCF-7 cells to investigate the behavior of FITC MSN@PNIPAM in cells. The confocal laser scanning microscopy images showed that some particles had been internalized into the cells and localized in the cell cytoplasm. FITC was locked inside the MSN particles during the cell endocytosis process because the cell culture temperature was higher than LCST. The cytotoxicity of MSN@PNIPAM was also investigated and the results suggested that MSN@PNIPAM particles had negligible influence upon the growth of cells showing very low cytotoxicity.

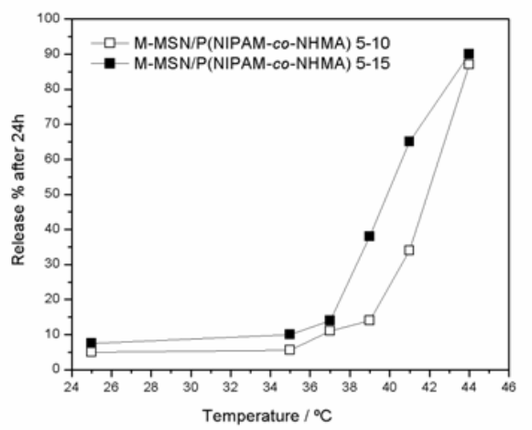
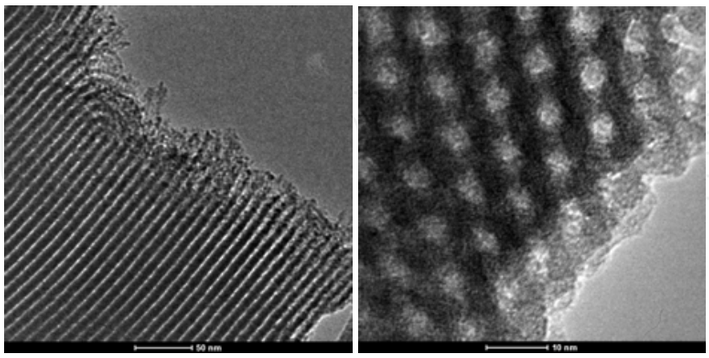


Fig. 12. Cumulative drug release of drug-loaded systems in PBS solution as a function of temperature. Data obtained from (Liu et al., 2009).

We recently reported the control of drug release in response to temperature in a system based on a temperature-responsive hydrogel, poly(*N*-isopropylacrylamide) [P(*N*-iPAAm)], inside a mesoporous silica SBA-15 (Sousa et al., 2010). The incorporation of polymer phase in the mesoporous silica led to a significant change in the structural properties of this system. However, the polymerization and pore filling did not destroy the ordered hexagonal structure of SBA-15, as shown by TEM images (Figure 13), but the surface area,

pore size, and pore volume of the hybrid decreased due to the introduction of the polymer. The primary mesopore volume and total pore volume of [SBA-15/P(*N*-iPAAm)] (0.42 and 0.48 cm^3 g^{-1}) were lower than the SBA-15 values (0.83 and 0.96 cm^3 g-1), respectively. The pore diameter decreased from 5.70 to 3.76 nm (~34%).



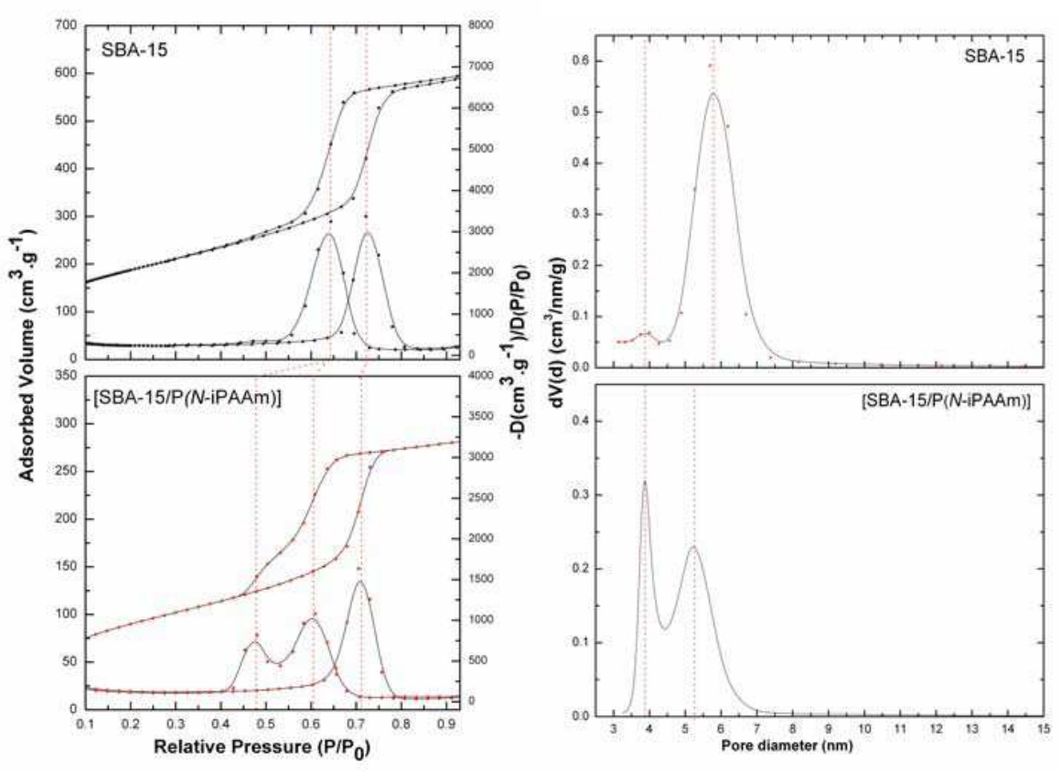
(a) (b)

Fig. 13. TEM images of [SBA-15/P(*N*-iPAAm)] (a) viewed along the pore axis and (b) viewed perpendicular to the pore axis.

Figure 14 shows the nitrogen adsorption isotherms and the pore size distribution for pure SBA-15 and for the [SBA-15/P(*N*-iPAAm)] hybrid. The analysis of the isotherms and the respective adsorption and desorption-derived curves reveal a reduction in symmetry and the occurrence of a stepwise desorption phenomenon in the hybrid sample, suggesting bimodal porosity. This behavior is often referred to as a pore blocking phenomenon and is attributed to the formation of porous plugs in the ordered channels of SBA-15. After polymerization, the shape of the hysteresis loop in the N_2-sorption isotherm displays a broadening suggestive of a reduction in pore size uniformity. Indeed, the desorption branch shifted towards lower relative pressure P/P_0 with a concurrent decrease in the pore diameters. Such a decrease can be verified by analyzing the inflection points of the desorption isotherms and the pore size distribution graphs. The desorption isotherm of mesoporous silica presented an inflection point of 0.64 at $P/_{P0}$. On the other hand, the hybrid sample presented two inflection points of 0.60 and 0.47 around P/P_0; this means that the presence of an organic phase in the silica matrix provoked a shift to a smaller relative pressure related to a decrease in pore size.

Atenolol was used to study thermosensitive drug release by hybrid sample. A continued flow was employed to assay the atenolol release profile of this system. Release studies were conducted at four different temperatures: 10, 25, 30, 35, and 40 ^oC in a simulating body fluid (SBF). A control experiment was conducted in a similar manner for SBA-15. Drug loading was determined through UV–Vis analysis in SBF solution by measuring the absorbance of atenolol at 274 nm. The cumulative drug release profiles (Figure 15) showed clear differences between the studied materials as a function of the temperature. In this figure, the discontinuity in the release profile of the hybrid system as a function of temperature is clearly observed (indicated by arrows above the respective curves). This response in the hybrid system is strongly indicative of the polymer phase behavior. A quasilinear behavior in the release profile of SBA-15 as a function of temperature is also displayed in Fig. 15b. As expected, the release of atenolol from pure SBA-15 is temperature dependent (Fig. 15a). This behavior can be explained considering that the overall drug delivery into the medium is

controlled by diffusion through the porous channels. However, as shown by the release profile, delivery seems to be less effective at temperatures as low as 10 °C, since this system presents a comparatively lower delivery rate at this temperature. In this case, the drug was trapped in the porous structures of the silica network. This may be explained by two simultaneous behaviors: the diffusion rate in the mesoporous material, which is severely affected at this temperature, and the drug interaction with the mesoporous silica through hydrogen bonds due to the affinity of the functional groups amine, amide, and hydroxyl of the atenolol molecules and the silanol groups present in the mesoporous silica, which is ascribed to the relatively polar hydrophilic character of the drug. At this temperature (10 °C), the thermodynamic conditions are not enough to destabilize the hydrogen interactions between the hydrophilic groups of the drug and the silanol groups of silica. The atenolol, then, has a tendency to remain in the silica nanostructure. When the temperature was raised to 25 °C, the interactions between the drug molecules and the silica surface were affected, causing its rupture and a major release of atenolol into the medium. At 40 °C, this phenomenon persists and is more evident, as demonstrated by the release profile in Fig. 15a.

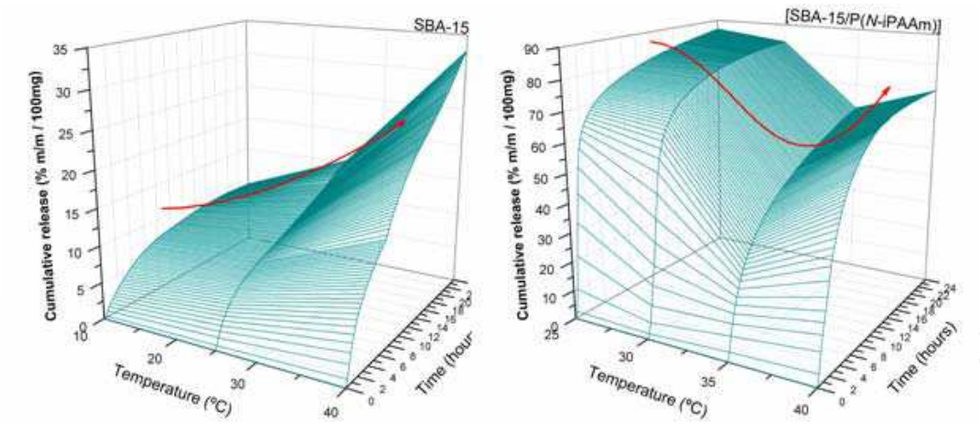


(a) (b)

Fig. 14. (a) N_2 adsorption-desorption isotherms and (b) Pore size distribution of SBA-15 and [SBA-15/P(*N*-iPAAm)].

The analysis of the performance of the hybrid system as a drug delivery device (Fig. 15b) shows that the release profiles of [SBA-15/P(*N*-iPAAm)]vary with temperature, as compared to that of pure SBA-15. At 25 °C, the release rate was high, followed by a sustained release rate; a similar behavior was observed at 10 °C. However, when the temperature was increased to and maintained at 40 °C, a slower and sustained release rate

was observed. Nevertheless, it rapidly decreased when the temperature was reduced to 35 ºC. This behavior suggests that factors other than temperature affect drug release. These observations lead us to suggest that the drug release response of hybrid systems depends on temperature and the polymer phase behavior. The LCST of P(*N*-iPAAm) is around 35 ºC; when the temperature was lower than the LCST, the polymer swelled and drug release was faster. When the temperature was above the LCST, the polymer collapsed, acting as a diffusion barrier, and the drug release from the pores was significantly blocked. With the increase in temperature, an increase in drug diffusion would be expected; however, the increase in temperature provokes a contraction of the polymer network in the hybrid nanostructure. This contraction creates a physical barrier to the drug diffusion, thus decreasing its release to the medium. This temperature-dependent behavior becomes critical upon the complete collapse of the polymer chains at around 35 ºC, when the structure barrier to diffusion is the largest. This fact explains the great reduction in the release rate of atenolol from the hybrid system from 25 and 30 to 35 ºC. Above the LCST, the polymer does not present phase change anymore, remaining contracted without structural variation. The effect of temperature is illustrated in Fig. 15b, when it varies from 35 to 40 ºC, presenting a larger release of atenolol. Even though the release rate is high at this temperature, it is lower than at 25 and 30 ºC, as the polymer expanded and consequently presented a lesser barrier to the diffusion of atenolol. Therefore, below the LCST, the contraction phenomenon of the polymeric framework in the silica exerts a more significant influence than the temperature on the release of atenolol to the medium. Above the LCST, the conformational aspect of the polymer does not affect the process and the temperature becomes the dominant variable in the release process.



(a) (b)

Fig. 15. Cumulative release profile of atenolol plotted against time and temperature for (a) SBA-15 and (b) [(SBA-15)/P(*N*-iPAAm)].

A mechanism to explain the thermosensitive release profile was developed by the authors (Figure 16). Below the LCST, the polymer swelled and drug release was faster (situations a and b). With the increase in temperature, a decrease in release was observed. It was speculated that the suppression of the release is a result of the contraction of the hydrogel network with heating, which creates a physical barrier to the drug diffusion. This temperature-dependent behavior becomes critical upon the complete collapse of the polymer chains at around 33 ºC, when the structure barrier to diffusion is the largest

(situation c). Above the LCST (situation d), the polymer does not present phase change anymore, remaining contracted without structural variation, and the temperature becomes the dominant variable in the release process, increasing the release of atenolol.

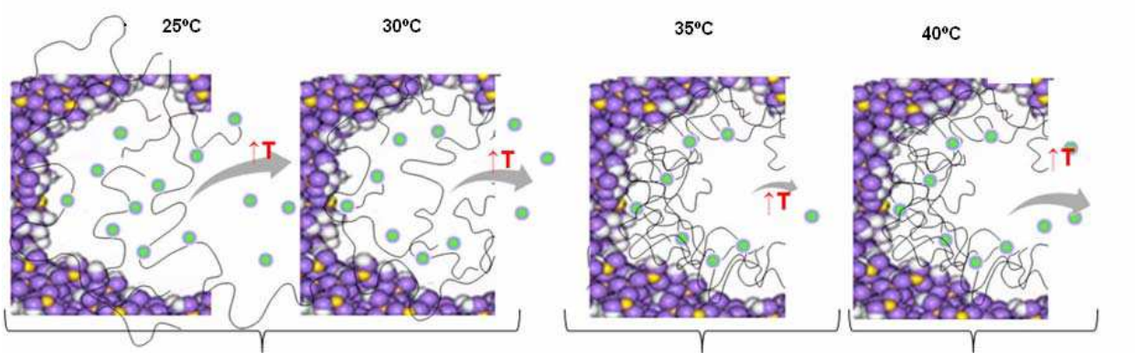


Fig. 16. Schematic representation of the proposed mechanism to explain the thermosensitive release profile.

It is important to note that this release mechanism is clearly different from those previously reported (Zhou et al., 2007; Zhu et al., 2007), since the major release rate was observed below the LCST, rather than above it (a negative thermosensitive release profile was observed). However, similar results were presented by You et al. (You et al., 2008), who studied the release of fluorescein as a function of the temperature from micro to mesoporous silica nanoparticle (MSN)/P(*N*-iPAAm) composites and obtained a greater release rate at 25 ºC, below LCST (Figure 17).

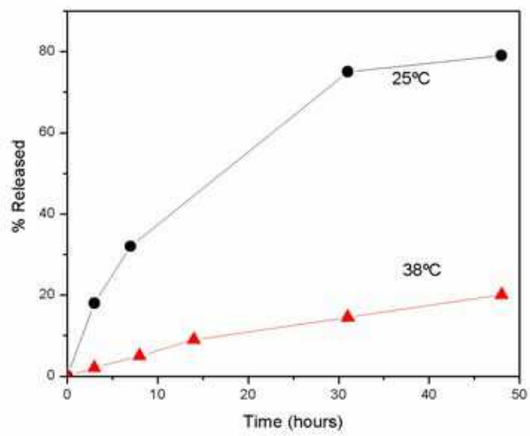


Fig. 17. Release studies conducted at 20 and 38 ºC in PBS. Data obtained from (You et al., 2008).

5. Conclusion

This review summarized the recent developments in the methods to synthesize polymer/mesoporous silica and iron nanoparticle/mesoporous silica nanocomposites. We developed an easy and direct synthesis route to obtain nanocomposites and hybrid functional nanosystems based on mesoporous silica. The applicability of this system as a

matrix for controlled drug delivery and also in magnetic hyperthermia was studied. The results indicate that different combinations of the ordered mesoporous silica have a potential to encapsulate bioactive molecules to use in biomedicine. The above results show that the composition and morphology of carrier materials and the external agents are important factors in influencing the drug delivery performance. However, a direct comparison of these results with those described by other research groups cannot be performed, since the systems were prepared from mesoporous matrices and by different procedures, including hybrid systems and with magnetic particles. Furthermore, the release assays were conducted differently, using drugs with distinct properties.

In spite of this, we have shown that mesoporous silica-coated magnetite nanoparticles with these structural and magnetic characteristics, unobstructed pores and easy functionalization of the silica surface, seem to be promising material for hosting and further delivery, under appropriate conditions, of a variety of molecules of pharmaceutical interest. Hyperthermia tests indicated that the nanocomposite can be used as a matrix for localized hyperthermia treatment of cancers. Heat generation depended on the intensity of the AC magnetic field and the nanoparticle medium.

On the other hand, even though there have been significant advances, studies involving the potential use of responsive hybrids in the area of controlled release of drugs are still incipient, and many properties of these materials are in the process of analysis, and synthesis procedures are being modified in order to gain greater control over these morphological and structural materials. Even though the pure mesoporous materials are potentially suitable for biomedical applications because they are biocompatible and resistant to biodegradation in cell media, the study of the biological response of responsive hybrids based on mesoporous materials is incipient, as in vivo assays depend heavily on parameters which are not well established, such as structural and morphological properties and their dosage forms.

A substantial effort has been made recently to develop hybrids based on mesoporous silica nanospheres combined with iron nanoparticles as well responsive polymers that can be directly targeted at the cells, releasing a given active principle in response to variations in some external stimulus. A more in depth study considering our systems with regard to morphological parameters and biological behavior is planned in the future.

6. Acknowledgments

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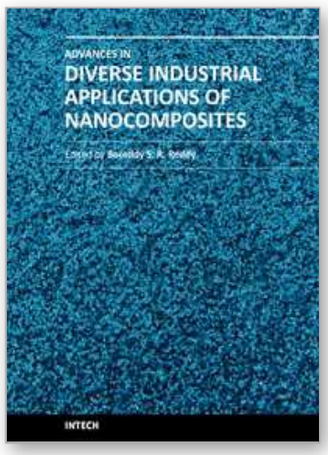

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Nanocomposites are attractive to researchers both from practical and theoretical point of view because of combination of special properties. Many efforts have been made in the last two decades using novel nanotechnology and nanoscience knowledge in order to get nanomaterials with determined functionality. This book focuses on polymer nanocomposites and their possible divergent applications. There has been enormous interest in the commercialization of nanocomposites for a variety of applications, and a number of these applications can already be found in industry. This book comprehensively deals with the divergent applications of nanocomposites comprising of 22 chapters.

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