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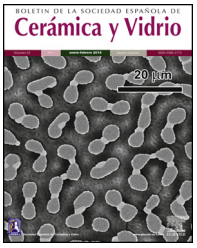

Synthesis of mesoporous silica nanoparticles by sol–gel as nanocontainer for future drug delivery applications

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ABSTRACT

Development of mesoporous silica nanoparticles as carriers for drug delivery systems has increased exponentially during the last decade. The present work is focused on the synthesis of silica carriers by sol–gel from tetraethyl orthosilicate (TEOS) as precursor of silica and cetyltrimethylammonium bromide (CTAB) as pore generating agent. The synthesis conditions were modified varying the molar ratio of water/TEOS, NH_3/TEOS and amount of CTAB. The silica particles were characterized by scan electron microscopy techniques (FESEM), high resolution transmission electron microscopy (HR-TEM), N_2 adsorption–desorption isotherms, Zeta-potential and Dynamic Light Scattering (DLS). The results show that the specific surface area and the porosity of silica particles were strongly affected by the addition of CTAB and the amount of H_2O. The dispersion and stability of silica mesoporous particles is achieved in spite of the high surface reactivity. The synthesis formulation affects considerably to the particle morphology, which changes from spheres to rods when the molar ratio of H_2O increases. A maximum specific surface area of 1480 m^2/g was obtained with pore sizes ranging 2.5–2.8 nm.

Síntesis de nanopartículas mesoporosas de sílice como futuros sistemas de liberación controlada de medicamentos

Palabras clave:
Sol-gel
Nanopartículas de sílice
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RESUMEN

El interés por el uso de partículas mesoporosas de sílice como vehículos para sistemas de liberación de fármacos ha aumentado exponencialmente en la última década. Este trabajo se centra en la síntesis de portadores de sílice por sol-gel usando tetraetilortosilicato (TEOS) como precursor de sílice y bromuro de cetiltrimetilamonio (CTAB) como agente generador de poros. Se ha analizado el efecto en las propiedades morfológicas de los cargos de sílice de la modificación de algunas condiciones de síntesis como las relaciones molares agua/TEOS

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y amoniaco/TEOS, o la cantidad de CTAB. Las partículas obtenidas se han caracterizado mediante microscopia electrónica de barrido y de emisión de campo, por microscopia electrónica de transmisión, adsorción/desorción de N_2, potencial zeta y dispersión dinámica de luz (DLS). Los resultados muestran que la superficie específica y la porosidad de las partículas de sílice se ven especialmente afectadas por la cantidad de CTAB, alcanzándose superficies específicas de 1.480 m^2/g con una porosidad media de 2,5-2,8 nm. Las partículas mesoporosas de sílice permanecen dispersas y estables a pesar de su elevada reactividad superficial. La formulación de la disolución precursora cambia considerablemente la morfología de las partículas, que pasan de ser esféricas a adoptar una morfología de varillas cuando aumenta la cantidad de H_2O adicionada.

Introduction

In the last decades, drug delivery technologies have been changed substantially. In general, the human body is a complex system which depends on the disease to be treated, and hence, the procedure to introduce each drug in the tissue is different. Moreover, the secondary effect of drugs is that can affect to other parts of the body, so drugs must only interact with the target and, at the same time, its release should be controlled to avoid the secondary effects. Amount carriers, mesoporous materials have been emerged as novel tools in biomedical applications [1,2]. Mesoporous structures are characterized by having a large specific surface area and pores with diameters between 2 and 50 nm. Among inorganic structures, silica (SiO_2) materials have been intensely studied as potential applications in catalysis, biological, biomedicine, etc., due to its outstanding characteristics including availability for mass production and simple synthesis method [3,4]. Mesoporous silica nanoparticles (MSNs) can be used as host materials for transporting therapeutics medicaments or encapsulation of molecules [5,6]. Good biocompatibility, high loading capacity, the possibility of attachment target ligands for specific cellular recognition or the design of well-defined and tunable porosity, make MSNs suitable for drug delivery [7,8]. But for all applications, the morphology of the material is one of the most important aspects. One common synthesis route to obtain MSNs is based on the use of templating agents, typically a surfactant which neutral or charged and that acts as structure-directing agent [9]. In fact, first mesoporous silica particles were produced via modification of the Stöber process by using soft template strategy [10]. In general, MSNs are synthesized by using a silica precursor (tetraethylorthosilicate or sodium silicate) in an alcoholic solution under basic conditions and incorporating a surfactant [11,12]. Some authors have reported the mechanism to obtain silica nanospheres and nanorods changing the surfactant concentration [13,14] and sol dilution [15]. The interaction between the surfactant with the Si–O–Si species was studied, and the pore sizes, shapes and order, as well as MSNs morphology, were related with the characteristics of the surfactant (size, length, etc.) and the formation of the micelles [16,17]. The final morphology of the particles affect to the capacity of absorption of drug and their subsequent release [18].

On the other hand, synthesis of mesoporous silica particles in non-alcoholic medium were described in the literature [14,15] but the formation of spherical particles is limited by the amount of the surfactant (<0.8–1 wt.%). The specific surface area of the mesoporous silica particles reported is 1030–1070 m^2/g with a pore volume of 0.81–0.85 cm^3/g. Wang et al. [13] considered the use of EtOH but change the amount of water for a fixed amount of CTAB (4.1 wt.%), obtaining spherical and rod-like particles with an ordered mesoporous structure. Silica particles reached a specific surface area of 1500 m^2/g and a pore volume of 0.86 cm^2/g. the dilution of the sol changes the specific surface area and transforms the morphology of the particles form spherical to rod-like, evidencing that both the evolution of the mesoporosity and the morphology of silica particles depend on the micelles formation and ordering.

The aim of the work is to study the particle size morphology and dispersion of mesoporous silica nanoparticles prepared by sol–gel by changing simultaneously the water content and amount of surfactant (CTAB). The silica nanoparticles were characterized by field-emission scanning (FESEM) electron microscopy, high resolution transmission electron microscopy (HR-TEM), zeta-potential measurements and Dynamic Light Scattering, and N_2 adsorption–desorption measurements. Difference morphologies, spherical and rod-like, have been obtained and compared considering all of synthesis parameters.

Experimental

Alkoxides precursor used was tetraethyl orthosilicate, purchased in ABCR (TEOS, 99%) and cetyltrimethylammonium bromide (CTAB, 99%) as surfactant, from Aldrich. The rest of precursors used were analytical grade reactant from Aldrich. Silica sol was prepared by mixing EtOH, H_2O and ammonia solution (NH_4OH). Afterwards, CTAB was added to the first solution and maintained under stirring for 15 min. Then, TEOS was added drop by drop under continuous stirring for 2 h at room temperature. The solution turned opaque almost immediately, indicating that the reaction has started. The white powder precipitated was filtrated and washed with deionized water. The particles were dried at room temperature overnight. Then, the particles were calcined at 550 °C for 3 h to remove the surfactant. The final molar ratio of TEOS/EtOH was fixed to 1/20 and the molar ratios of $H_2O/NH_3{\cdot}H_2O$/CTAB were varied, Table 1.