Synthesis and Characterisation of Monodisperse Silica Templates for Pharmaceutical Applications

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Abstract

The aim of the study was to synthesize stable mono disperse silica particles of size around 380 nm by seeded growth process using Ethanol, Tetra Ethyl Ortho Silicate (TEOS) and Ammonia solution. The synthesized micro particles have been characterized by DLS (Dynamic Light Scattering), SEM (Scanning Electron Microscope), Zeta Potential measurement, XRD (X-ray Diffraction) and FTIR (Fourier Transform Infrared Spectroscopy). These particles were successfully employed as template for coating oppositely charged chitosan and dextran sulphate by Layer - by - layer method for the preparation of natural degradable capsules.

Keywords : chitosan, electrostatic attraction; Layer-by- Layer; micro particles; polyelectrolytes; template

1. Introduction

Nano and micro particle carriers have received great deal of attention in the area of biotechnology, pharmaceuticals, controlled drug delivery, and environmental engineering due to its potential functional properties .The preparation of silica particles of irregular shape have been investigated extensively, but synthesis of silica particles of uniform size and shape is not common [1-6]. Silica particles have been extensively used as templates in the fabrication of polymeric capsules due to its mono disperse nature, highly porous surface structure and easy removal of templates. It is very important to control the size, shape and surface morphology of the particles. Silica particles of size ranges from nanometre to micron were synthesized by different routes [7].The structure of colloidal particles may vary from isolated spherical particles to agglomerates of complex structure [8]. Common issues associated with silica particle synthesis are poly dispersity and meso porous orientation [9-12]. Colloidal particles with uniform size, shape and composition finds wider applications in industry [13-17]. Mono dispersity is one of the major requirements of template synthesis for the capsule preparation.

This study deals with the development of mono disperse silica particles of uniform size by seeded growth technique by the continuous addition of TEOS to improve mono dispersity, size and shape of the particles in sustained drug delivery applications.

2. Materials and Methods

Materials

TEOS (Tetra Ethyl Ortho Silicate), NH_4OH, C_2H_5OH and HCl and NaCl are obtained from Merck, India. Chitosan (Mw 650 kDa, degree of deacetylation >75%) and Dextran sulphate (Mw 500 kDa), are purchased from Sigma Aldrich, Bangalore, India. Millipore water (18.2MΩ resistivity) was used in all experiments.

2.1 Synthesis of micro particles

Colloidal silica particles were prepared by mixing 0.4 ml of Tetra Ethyl Ortho silicate (TEOS), 50 ml ethanol and 10 ml of aqueous ammonia under rapid stirring conditions for 6 hours. After stirring the mixture, 7 ml of TEOS was added drop wise and the SiO_2 particles were separated from the solution by centrifugation at 5000 rpm and washed at least twice with pure ethanol. The base catalyzed reaction, using ammonia, ethanol,

water and Tetra Ethyl Ortho Silicate (TEOS), can be controlled to yield spherical SiO_2 particles with low poly dispersity. The synthesized silica particle suspension was dried at 340 K overnight. The proper amount of water relative to other reactants during a second step is a prerequisite for the formation of a uniform and regular ordered shell structure surrounding the core particle. The overall reaction in the synthesis of silica particles is

$$Si(OR)_4 + 2H_2O \text{ ---------- } > SiO_2 + ROH$$

3. Results and Discussion

3.1 Synthesis of silica Particles

Monodisperse silica particles of 380 nm size were prepared by seeded growth method. The SEM micrograph of the particles shows the particles are well dispersed without any aggregation and spherical in shape with size around 380 nm having a solid core. The SEM micrograph of the particles is shown in Figure 1. The size of particles was analyzed by Dynamic Light Scattering method as shown in Figure 2. A single peak shows particles are of uniform size with a diameter around 380 nm. Morphological attributes of silica were measured using Scanning Electron Microscope (FEI-Sirion, Eindhoren, The Netherlands) at an accelerating voltage of 10 keV. The silica particles are spherical in shape with a smooth surface morphology. The high magnification SEM images in Figure 1 shows well separated mono disperse spherical silica particles are more or less uniform in size and shape. These results indicate that the seeded growth technique using continuous drop addition of TEOS can not only improve mono dispersity and spherical shape but also increase the size of silica particles.

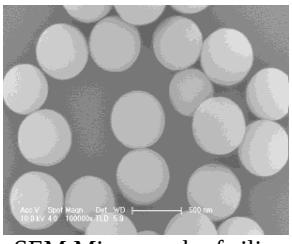

Figure 1: SEM Micrograph of silica particles

3.2 DLS measurement

The size of the particles is measured by passing monochromatic laser beam onto a solution of synthesized spherical silica particles in Brownian motion which causes Doppler shift, thereby changing the wavelength of the incoming light. This change is related to the size of the particles. The particle size distribution is shown in Figure 2.

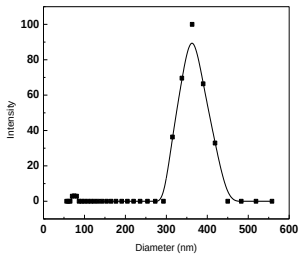

Figure 2: Size distribution of silica particles using DLS

3.3 Zeta Potential Measurement

Zeta potential measurement was carried out using a zeta probe potentiometric series. The graph of pH versus zeta potential is shown in Figure. 3. It is seen that the iso electric point of the particles are obtained at pH 4.02. At this point the surface charge of the particles is neutral. The effect of variation of pH with conductivity is shown in Figure 4.

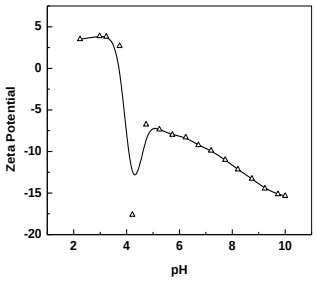

Figure 3: Variation Zeta potential with pH

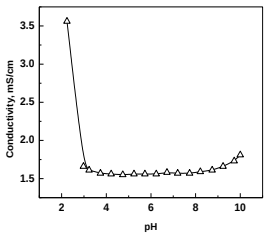

Figure 4: Variation of conductivity with pH

3.3 XRD analysis

The phase identification of crystalline silica particle is measured analytically by X-ray powder diffraction method. The particles are finely ground and

homogenized for average bulk composition. The intensity of diffracted X-rays is continuously recorded as the sample and detector rotate through their respective angles. The powder XRD patterns exhibited a strong diffraction peak at an angle of $2\theta = 25^0$ as shown in Figure 5.

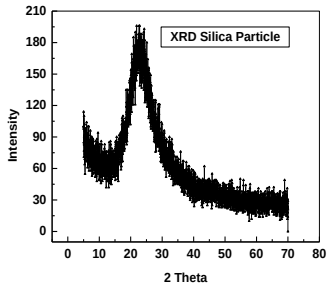

Figure 5: X- ray diffraction pattern of Silica Particles

3.5 FTIR measurement

To identify the presence of certain functional groups present in silica particles is performed using FTIR measurement. Also, one can use the unique collection of absorption bands to confirm the identity of a pure compound or to detect the presence of specific impurities. All spectra were collected at a resolution of 4 cm^{-1} and for 128 scans using a Nicolet Magna 750 FTIR spectrometer. The FTIR spectra of silica particle are presented in figure 6.

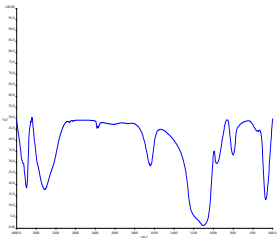

Figure 6: FTIR Spectra of Silica Particles

3.6 Coating of chitosan and dextran sulphate

The synthesized silica particles are coated with oppositely charged chitosan and dextran sulphate by layer-by-layer method. The surface morphology of the coated particle was analyzed by scanning Electron microscopy and the image is shown in figure 8.

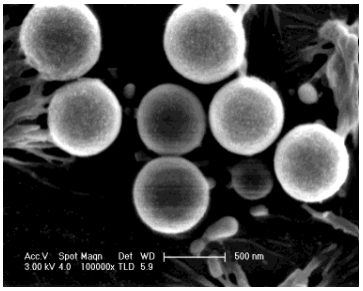

Figure 8: SEM of Coated Particles

3.5 EDX measurement

The elemental analysis of the silica particle is performed by exciting high energy electrons around the atoms present in the silica particles, causing them to jump to higher energy shells. When the electrons fall back to the lower energy shells, they emit electromagnetic radiation in the form of X-rays. The wavelengths, and hence energies, of the X- rays are characteristic of the electron shell energies, and the spectrum of X-rays can be used to identify different elements present in the silica powder. The SEM EDX measurement of coated particles is shown in figure 7.

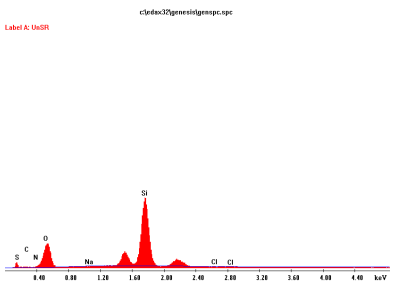

Figure 7: EDX spectra of chitosan Dextran sulphate Coated Particles

Conclusion:

In this work, mono disperse spherical silica particles of size around 380 nm were successfully synthesized by seeded growth technique. These silica particles were demonstrated to be promising template for fabrication of polyelectrolyte capsules by L-b-L method. These particles are successfully employed as templates for coating oppositely charged chitosan and dextran sulphate for capsule preparation. The use of silica template is a way of fabrication of biodegradable capsules. This method allows for easy synthesis of mono disperse silica particles with higher reproducibility. Further investigation is now under way

to regulate the mesopore orientation on different curved or planar substrates, which will make the mesoporous materials more applicable to practical, academic and industrial demands.

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