Preparation and Characterization of Natural Degradable Microcapsules

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Abstract

In this work, multilayer microcapsules of size 350 nm were prepared by layer-by-layer (L-b-L) assembly of oppositely charged chitosan and dextran sulphate on silica template, followed by removal of silica using Hydrofluoric acid. Particular emphasis is given on synthesis of monodisperse silica particles (310nm) with fine spherical shape. The hollow microcapsules obtained by the removal of the colloidal template with hydrofluoric acid solution were characterized by Scanning Electron Microcopy (SEM) and Energy Dispersive X- ray Analysis (EDX). The size distribution of silica particle was analyzed by Dynamic Light Scattering (DLS) method. Scanning electron microscopy (SEM) and Energy dispersive X-ray spectroscopy (EDX) measurements proved the purity of the hollow capsules. These microcapsules can be used for drug encapsulation and release in pharmaceutical applications.

Keywords: Biodegradable polymers, Chitosan, Dextran sulphate, L-b-L technique, Polyelectrolytes.

1. Introduction

Drug delivery is becoming a whole interdisciplinary field of research gaining much attention in pharmaceutical industry. Controlled release technologies are more popular in modern medicine and pharmaceuticals. Various drug delivery systems have been formulated using different types of materials such as micelles [1], lipid vesicles [2], micro particles [3, 4] and hydrogels [5]. Capsules were fabricated using wide variety of polymers such as synthetic polyelectrolytes, polysaccharides, polynucleotides etc. The layer-by-layer (L-b-L) self-assembly technique is a useful technology to fabricate multilayer thin films of nanometer precision [6]. L-b-L technology takes advantage of the charge-charge interaction between substrate and polyelectrolytes to create multilayers by electrostatic interactions. The main attractions of L-b-L method include the process is simple, inexpensive, fine tuning of layer thickness and independent of shape and geometry of template. Capsules in the nanometer to micrometer range are important for a range of different applications, including the encapsulation and controlled release of substances. The permeability of capsule wall and release of encapsulated drug depend on the thickness and composition of the shell.

During last few years much attention have been given to polysaccharides such as carboxy methyl cellulose [7], chitosan sulphate [8], chitosan [9] and dextran sulphate [10] for capsule preparation due to their excellent properties like biodegradation, biocompatibility, non-toxicity, and adsorption. The applications of Chitosan in pharmaceutical industry showed a great potential as a drug carrier system [11-21]. Chitosan is a non-toxic, biocompatible polymer that has found a number of applications in controlled drug delivery. Predominantly, polystyrene (PS), melamine Formaldehyde (MF), $CaCO_3$, $MnCO_3$ etc. has been employed as templates for the L-b-L preparation of capsules. Each of these sacrificial cores has certain limitations associated with their application. The main attraction of silica particles is it can be used in the presence of biological materials without significantly affecting bioactivity. The biodegradable and biocompatible nature of dextran sulphate has been used for the controlled release of basic drugs. The negatively charged sulphate groups of dextran sulphate binds with positively charged amino groups of chitosan to form polyelectrolyte complexes [22]. Biodegradability is one of the most important requirements in biomedical applications. In this paper, fabrication of microcapsules by layer-by-layer technique using chitosan and dextran sulphate was presented. These microcapsules can be used for drug encapsulation and release in pharmaceutical applications.

2. Materials and Methods

2.1 Materials

Chitosan (Mw 650000Da, degree of deacetylation >75%) and Dextran sulphate (Mw 500000Da), were obtained from Sigma Aldrich, Bangalore, India. Monodisperse colloidal silica particles of size 310 nm was synthesised in our laboratory. TEOS (tetra ethyl ortho silicate), NH_4OH, C_2H_5OH, NaCl, HCl and HF were obtained from Merck, India. Millipore water (18.2MΩ resistivity) was used in all experiments.

2.2 Methods

2.2.1 Silica template preparation

The synthesis of monodisperse silica particles were carried out based on Stober's protocol [23]. The mean diameter and particle size distribution of silica particles were measured by Dynamic Light Scattering (DLS) method using a Brookhaven B1 9000AT analyzer (Brookhaven Instruments Corporation, USA).

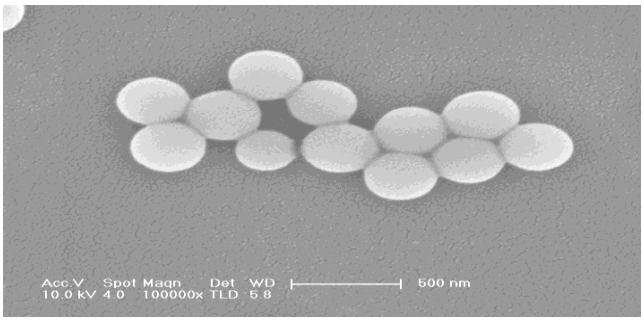

Figure 1. Scanning Electron Micrograph of Silica Particles

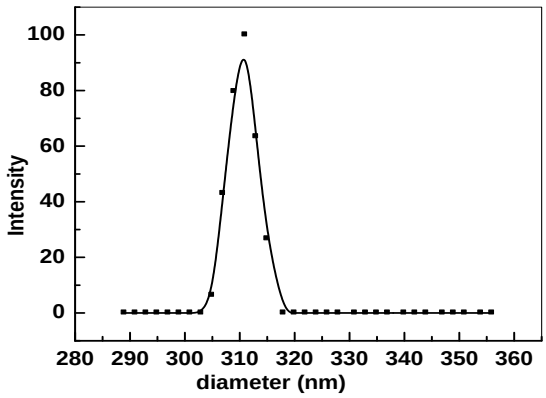

Fig. 2. Size distribution of Silica Particles

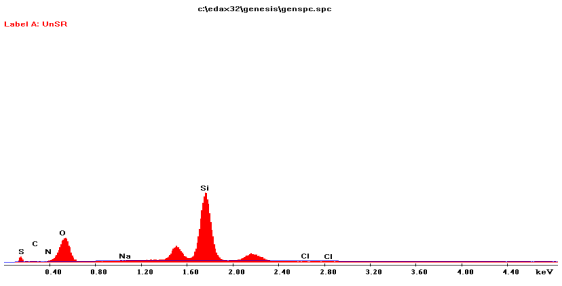

Fig.3. EDX Spectra of Silica Particles

2.2.2. Preparation of capsules

Capsules were prepared by the L-b-L technique [24, 25] with chitosan as the first layer. The adsorption of polyelectrolytes (1mg/ml) was conducted in 1M NaCl solution for 15 minutes followed by three washings in water. Then the respective oppositely charged polyelectrolytes were adsorbed. After the desired number of layers was deposited, the coated particles were treated with 1M HF to remove silica core. The resulting hollow capsules were washed with pure water and centrifuged 5 times to remove traces of HF. The capsules were characterised by SEM (FEI- Sirion, Eindhoren, The

Netherlands) at an operating voltage of 3kV. Samples were prepared by placing a drop of capsule suspension on a pre-cleaned silicon wafer, dried under a nitrogen stream followed by gold sputtering.

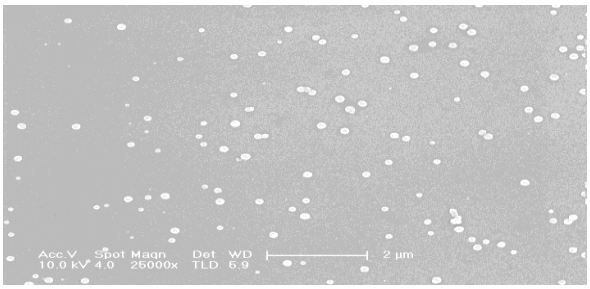

Fig.4. Chitosan - Dextran sulphate hollow capsules

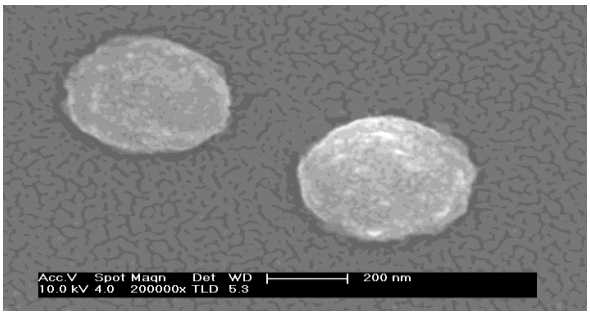

Fig.5. Chitosan - Dextran sulphate hollow capsules at high magnification

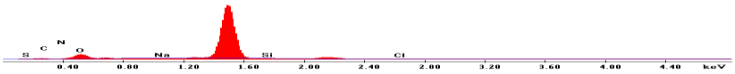

Fig.6. EDX Spectra of Chitosan - Dextran sulphate hollow capsules

3. Results and Discussion

Silica particles were synthesized by the Stober's protocol. The Scanning Electron Micrograph as shown in Fig.1 illustrates that the particles are spherical, well dispersed and of uniform size. Particle size analysis in Fig.2 showed a narrow size distribution with an average size of 310nm. Figure 3 shows the EDX spectra of silica particles. All analyses were repeated six times and the results were averaged. DLS measurements were done with a laser wavelength of 658.0 nm and at 27^0C. Eight layers of polyelectrolytes were deposited followed by core dissolution. The capsules were rinsed 3 times with water before use. Fig.4 and Fig.5 shows the micrograph of hollow capsules. The capsules showed good integrity and high yield with diameter around 350 nm. The capsule wall appears thick due to the high molecular weight of the polyelectrolytes used. EDX spectra in Fig.6 reveal that the silica cores have been completely removed from the capsules. No aggregation of the capsules was observed which is critical from application point of view. L-b-L self-assembly has the advantages of accurate control over size, composition, and the thickness of the multilayer shell make these capsules very promising for a number of applications in materials and biomedical science.

4. Conclusion

In this study, chitosan- dextran sulphate hollow capsules of about 350 nm were prepared by the layer-by-layer technique using silica as template. The employability of silica particles as template proves the successful fabrication of capsules. The surface texture of the particle surface determines the morphology of the derived capsules as well as the capsule wall thickness. The obtained capsules are of special interest in pharmaceutical applications due to their desirable wall thickness,

surface texture and high surface area. The layer-by-layer (L-b-L) templating technique has attracted significant interest as a simple, highly versatile approach that has been widely used to prepare nanostructured materials with tailored properties.

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