

Time dependent size control of sodium hydroxide catalyzed sol-gel synthesized silica nanoparticles modified with organosilane molecules by post-grafting

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Introduction

Aminopropyl modified silica nanoparticles (SiNP), are well known delivery platforms offering many advantages in pharmaceutical industry including anchorage points and very high surface area, or better compressibility and adequate flow characteristics etc. Modified Stöber method using sodium hydroxide as a catalyst enhances the condensation reaction and NPs' formation, and is presumed to be faster compared to ammonium hydroxide catalyzed processes having reaction times of app 20h. The later also, may not provide appropriate nucleation resulting in samples with higher polydispersity, and additionally, it requires extensive post-processing to remove the ammonia from the sample. However, literature data also point to sodium ion residues adsorbed on the oxygen atoms in the silica network of the NaOH catalyzed samples resulting in thermally unstable siloxane cross-linkage. Treatment of the modified Stöber NPs with acidic solutions may contribute to the elimination of the sodium ions from the silica network and hydroxylation of the NPs' surface by coordination of hydrogen ions onto the negatively charged oxygen atoms. Replacing the conventionally used NH₄OH with NaOH which is known to have strong abrasive properties may also improve NPs surface modification, as it would increase the surface area and the number of functional groups available for grafting. In addition, particle size which is very well known to influence both, the specific surface area and the

number/concentration of silanol groups, especially sizes at the nanoscale known to affect the silica structure, also has to be considered as an important variable influencing particle properties and efficacy of grafting. However, although SiNPs, due to their highly reactive surfaces can be easily functionalized, the formation of the (3-aminopropyl)-triethoxysilane (APTES) layer on the silica surface is very complex and includes several processes which are very sensitive to reaction conditions among them protonation, physical adsorption, hydrogen-bonding and covalent attachment of silanes.

Having in mind previously said, the aim of this study was to understand the influence of the process parameters during the NaOH catalyzed synthesis of SiNPs on their physicochemical properties and to efficiently modify the NPs' surface with APTES while maintaining their stability.

Materials and methods

The solutions used to synthesize silica nanoparticles by modified Stöber method were composed of 200 µl TEOS (99.9%, Fluka), absolute ethanol (99.5%, Merck), methanol (Merck) and Mili-Q water in a ratio of 0.5:0.5:1 (20 ml), and app 50 µl sodium hydroxyde (1M solution, Merck) to adjust the initial pH of the solutions to 12. The mixtures were sonicated (amplitude 50%, power 40 W, energy 10.000 J; Ultrasonic Homogenizer, BioLogics), at 50 °C, and after different time periods (25, 35, 45, 55 min) the samples were diluted with twice the volume of Mili-Q

water and washed thoroughly with ethanol (3×; EW) or acidic solution (1% HCl, 3×; AW), centrifuged at 6000 rpm using ultrafiltration tubes (Vivaspin® 20 1000 KDa, Sartorius, Germany) to remove the excess reactants and catalyst than dried in an oven (50 °C/24h). Grafting process with APTES (3-aminopropyl)-triethoxysilane, Merck), was performed in ethanol with traces of water at 50 °C for 1h (2% APTES) followed by washing cycles using ethanol and water. Particle size and zeta potential were measured using Zetasizer Nano, Malvern, UK, FTIR spectra were recorded using Perkin Elmer 400 FTIR spectrometer (KBr pellets), and scanning electron micrographs (SEM) were performed using Jeol SEM 6400, Japan)

Results and discussion

Particles with a narrow distribution below 100 nm were produced at 25 min., below 200 nm for 35 min and between 300-1000 nm for 45 and 55 min (Figure 1). Zeta potential (pH 7.4) of SiNPs (EW) was -54.03 ± 0.05 mV, and decreased to -45.34 ± 0.10 mV for SiNP (AW) as a result of surface hydroxylation and silanol groups replenishment during the acidic washing treatment which was applied to decrease/eliminate the sodium ions from the silica network, a usual residue when NaOH is used as a catalyst.

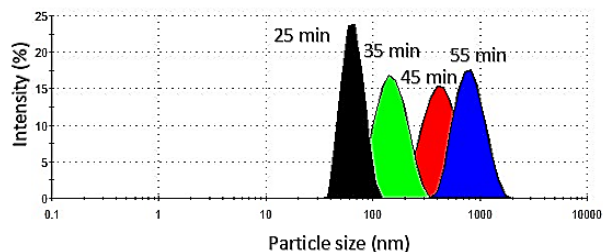


Fig. 1. Particle size distribution of prepared SiNPs

FTIR spectra of SiNPs show several characteristic bands: 3450 cm^{-1} (Si-OH stretching vibration, H-bonded), 1630 cm^{-1} (OH bending of adsorbed molecular water), 1060 cm^{-1} (Si-O-Si asymmetric stretching, AS), 955 cm^{-1} (Si-O-(H \cdots H $_2$ O bending vibration), 795 cm^{-1} (Si-O bending vibration), 552 cm^{-1} (Si-O rocking vibration). Our results point to differences in the FTIR spectra of NPs with different sizes. AS shifted towards lower wavenumbers for smaller particle sizes (Fig. 2). According to literature data this shift is due to changes in the local bonding structures of Si and oxygen atoms, i.e. Si-O-Si bond angle decrease with reduction of NPs size (Rahman et al., 2009).

FTIR spectra of APTES modified NPs contain the SiNPs and APTES peaks which confirms surface grafting. Peaks at $2800\text{-}3700 \text{ cm}^{-1}$ and peaks at 3300 and 3290 cm^{-1} belong to asymmetric and symmetric NH $_2$ stretching mode, 1582 and 1484 cm^{-1} are related to NH $_2$ deformation from

the amine group. Broad Si-O-Si band ($950\text{-}1200 \text{ cm}^{-1}$) is also present and a band at 690 cm^{-1} is ascribed as bending vibration of NH $_2$ and CH $_2$ and out of plane deformation CH. Positive zeta potential of 40.05 ± 0.90 mV at pH 2 and 13.20 ± 0.80 (pH 7.4) also confirms APTES grafting.

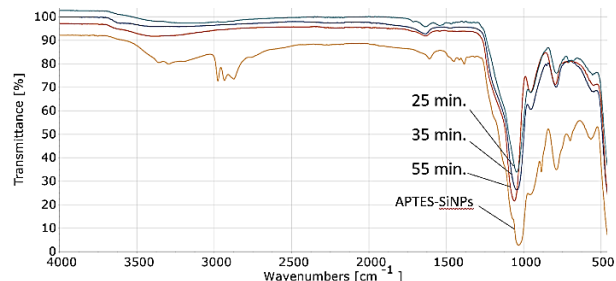


Fig. 2. FTIR spectra of SiNP produced within 25, 35 and 55 min. pointing to Si-O-Si band shift toward lower wavenumbers for smaller NPs and APTES-SiNPs.

SEM of the SiNPs produced at different time intervals (Fig. 3) confirm previous findings and the importance of understanding of the mechanism of formation and growth of the NPs in order to fine tune their properties.

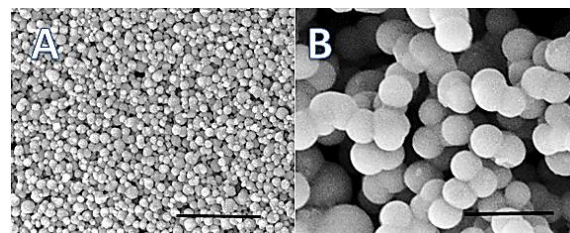


Fig. 3. SEM of SiNPs produced at different time intervals by modified Stöber method; A – 25 min process, bar=500nm; B – 45 min, bar=1μm

Conclusion

Our experiments point that modified Stöber method using NaOH as catalyst in a water: ethanol: methanol reaction system leads to quick silica particles formation with tunable size. Size dependent variabilities in physicochemical properties, like significant increase in the specific surface area and concentration of silanol groups can be observed in the FTIR spectra of the samples. Due to their highly reactive surface the produced NPs can be efficiently modified with APTES.

References

- Rahman, I.A., Vejayakumar, P., Sipaut, C.S., Chee, C.K., 2009. Size-dependent physicochemical and optical properties of silica nanoparticles, *Mater. Chem. Phys.*, 114 (1), 328-332. doi.org/10.1016/j.matchemphys.2008.09.068