SYNTHESIS AND CHARACTERIZATION OF NANOPARTICLES USING MICROFLUIDICS

Aliye Hazal KOYUNCU, Ondřej KAŠPAR, Pavel ULBRICH, Viola TOKÁROVÁ

University of Chemistry and Technology Prague (UCT Prague), Prague, Czech Republic, EU,
tokarovv@vscht.cz

Abstract

In recent years, nanoparticles have high importance in various areas such as biomedical, environmental or pharmaceutical applications due to their chemical and physical properties. In all these applications, maintaining control over the particle size and shape is of high significance due to their size and shape-dependent properties. The most abundant method of synthesis of nanoparticles is a batch process because of its fast and easy reaction setup. However, many types of nanoparticles are very sensitive to reaction parameters which directly affect the size and shape of the final particles and the process is hardly reproducible.

In this work, we present nanoparticle synthesis using microfluidic devices. Compared to a batch process, microfluidics offers a high control over the reaction process by easy control of the system parameters (e.g. mixing and flow rates of reactants and reaction time) with the ability to make an operative change of parameters during the synthesis. Specifically, the synthesis of silica and silver nanoparticles using a droplet generation microfluidic device will be presented. The size and morphology of final nanoparticles will be analyzed and compared to a traditional batch method.

Keywords: Nanoparticles, microfluidics, silver, flow-focusing

1. INTRODUCTION

Nanoparticles have high importance in various areas such as bio-pharmaceutical, tissue-engineering, gene, and drug delivery, biomedicine and environmental technology due to their unique structural, chemical and physical properties [1,2]. Especially, biomedical applications like cancer treatment or bactericidal applications of nanoparticles have been used extensively [2,3]. For all these applications, controlling the particle size and producing a unique size and shape of particles are significant due to their size and shape-depended properties. Traditionally batch synthesis methods are the most preferred method for particles production [4,5]. However, in the batch methods, it is often hard to control bulk shearing forces, affecting the nucleation and consequently size and shape of the final particles. Besides, traditional methods are not flexible or efficient, and obtained particle size distributions are usually wide [6]. Therefore, there is an increasing demand for better synthesis methods to produce particles with a monodispersed size and defined morphology suitable for high-end applications [7].

Microfluidics is nowadays more than ever employed as a promising method for nanoparticle synthesis overcoming limits of batch-wise synthesis [8]. Firstly, large surface area to volume ratio of microchannels helps to increase mass and heat transfer in the system. It increases the efficiency of the reaction in a smaller volume compared to a high-volume batch method. Secondly, microchips are more suitable to work in harsh conditions in comparison to the batch reactors in regards to rapid temperature or pressure changes while using toxic and/or explosive materials [9]. Moreover, very fast reactions need to be effectively controlled in the batch, by mixing conditions or immediate parameter changes in the system. In those cases, microfluidic devices allow to control the parameters and to screen the system more flexible than batch reactor [6],[8] and it can provide higher reproducibility of final products [9].

In this paper, the synthesis of silver nanoparticles using the microfluidic device is discussed. The structure of the paper follows the experimental description of silver nanoparticle production by both microfluidic and

batch methods, evaluation of the results obtained by characterization techniques, critical discussion of the suitability of both methods for efficient production of nanoparticles, and finally a conclusion.

2. MATERIALS AND METHODS

2.1. Chemicals

The following chemicals were used: silver nitrate ($AgNO_3$, Sigma, purity > 99 %), trisodium citrate dihydrate ($C_6H_5Na_3O_7.2H_2O$, Penta, purity > 99 %), tannic acid ($C_{76}H_{52}O_{46}$, Sigma Aldrich), Rhodamine B (Aldrich), polydimethylsiloxane (PDMS, Sylgard 184, Dow Corning), silicone elastomer (Sylgard 184, Dow Corning), mineral oil (Sigma), diethyl ether ($C_4H_{10}O$, Penta). Demineralized water (Aqual 25, conductivity ~ 0.07 µS/cm) was used for all reactions and treatment processes where noted.

3. EXPERIMENTAL PART

3.1. Batch process

The synthesis of silver nanoparticles in the batch was done by the precipitation of silver nitrate as the silver source according to Ranoszek-Soliwoda et al. [10]. An aqueous solution of silver nitrate (0.9625 mM, 95 mL), trisodium citrate dihydrate (0.07 M, 4.03 mL) and tannic acid (0.0015 M, 0.60 mL) were prepared using demineralized water. The molar ratio of the silver nitrate, trisodium citrate dihydrate, tannic acid was calculated to be 1.0:3.1:0.1. Silver nitrate solution was placed in a 250 ml glass round bottom flask, and the mixture of silver nitrate solution with the tannic acid solution was added dropwise into the flask at room temperature under continuous stirring at 500 rpm. When the addition was completed, stirring was kept for 15 more minutes. Samples were collected every minute for the first 5 minutes and every 5 minutes for the rest of the synthesis process. The samples were analysed by a dynamic light scattering (DLS, Malvern Zetasizer NanoZS) and spectrophotometer (Tecan Infinite 200 PRO Series). Additionally, nanoparticles were visually characterized by transmission electron microscopy (TEM, Jeol JEM-1010).

3.2. Microfluidic chip design

The microchip (**Figure 1A**) was designed to have three inputs, i.e. two for the disperse phases (1) and (2) and one for the continuous phase (3), the flow-focusing junction (4), where the droplet generation occurs, and one output (5). The basic principle using the microfluidic setup for nanoparticle preparation is based on a droplet formation where all reactants are mixed. The two immiscible fluids meet at the flow focusing point (**Figure 1B**) to generate droplets (aqueous solution) surrounded by the continuous phase (mineral oil). Each input was connected by a polytetrafluoroethylene (PTFE) capillary to a syringe (Hamilton) containing a reagent. A computer controlled linear pump (neMESYS) was used to precisely control the flow rates of the reagents and the continuous phase.

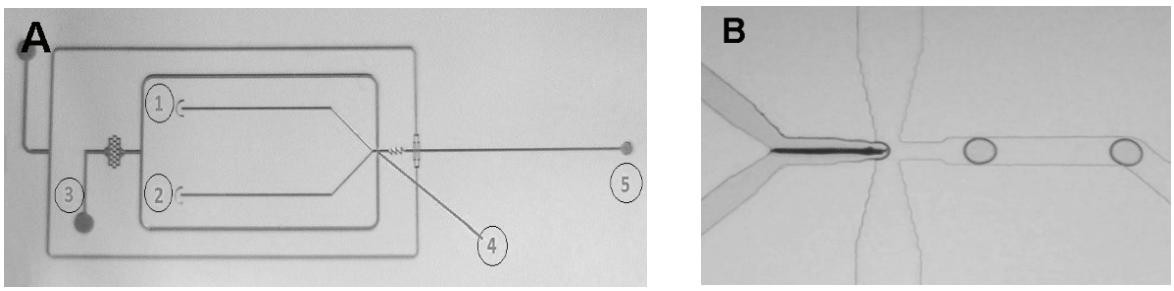

Figure 1 Microfluidic chip: A) silicon wafer with the chip design; B) the detailed image of the flow focusing part for droplet generation

3.3. Fabrication of PDMS microfluidic chips

The microchips were prepared using a soft lithography method using polydimethylsiloxane (PDMS) and a silicon wafer serving as a master mould. The PDMS was prepared by mixing the curing agent and the silicone elastomer (1:5 w:w) and poured over the silicon wafer placed in a Petri dish. The polymer mixture was degassed and heat-treated at 75 °C for 22 minutes. The crosslinked PDMS was peeled off from the wafer and holes were punched for the channel inlets and outlets. The bottom part of the chip was prepared using a PDMS mixture of 1:14 w:w ratio (curing agent to silicone elastomer) poured inside an empty Petri dish and put in the oven at 75 °C for 22 minutes. The surface of the PDMS layer remained sticky, and the upper part of the chip with channels was placed on top of it. The resulting chip made of the two combined parts was left in the oven at 75°C overnight to ensure strong bonding. The width of the nozzle orifice and outlet microchannel was 46 μm and 70 μm, respectively with a uniform height of 20 μm.

3.4. Microfluidic process

Silver nanoparticles were synthesized by the reduction reaction of silver nitrate using trisodium citrate dihydrate solution as a reduction agent. Briefly, silver nitrate (SN, $AgNO_3$) solution (1 mL and 0.92 mM), trisodium citrate dihydrate (SC, $C_6H_5Na_3O_7.2H_2O$) solution (1 mL and 5.72 mM) and tannic acid (TA, $C_{76}H_{52}O_{46}$) solution (1 mL and 0.185 mM) were prepared with demineralized water. The molar ratio of all reactants (1.0:3.1:0.1) was kept the same as in the batch process. 1 ml of TA solution was added into 1 ml SC solution as a stabilizing agent. They were mixed, and 1 ml of the mixture solution was taken as one of the dispersed phases. The both disperse phases - silver nitrate and trisodium citrate dihydrate with tannic acid solutions were pre-filtered before use. 1 ml SN solution was transferred into a 1 ml volume glass syringe. Then, 1 ml of SC and TA solution was transferred to the other glass syringe (Hamilton) of 1 ml volume. Finally, 2 ml of a mineral oil (as continuous phase) was transferred into a 2.5 ml volume glass syringe, and they were all connected to the microchip via PTFE (Adtech, 4 mm diameter) tubings. The flow rates were set for each phase and experimental setup individually by the linear pump software. The final product was collected into sample tubes pre-filled with 0.5 mL demineralized water to quench the reaction and particles growth. Then the W/O emulsion was separated by centrifugation for 3 minutes at 13.4 rpm (Eppendorf, MiniSpin) to oil and aqueous phases. After discarding of the oil phase, samples were further cleaned by the extraction with diethyl ether to remove remaining traces of the oil. **Table 1** summarizes studied experimental conditions for all samples.

Table 1 Experimental compositions and conditions of all studied samples of silver nanoparticle synthesis

				Flow Rate 1	Flow Rate 2	Total Flow Rate	Flow Rate 3
Sample	C_{SN}	C_{SC}	C_{TA}	Q_{SN}	$Q_{SC\ and\ TA\ mixture}$	$Q_{SC\ TA}+Q_{SN}$	$Q_{mineral\ oil}$
	[mM]	[mM]	[mM]	[μl/h]	[μl/h]	[μl/h]	[μl/h]
1	0.92	5.72	0.185	8	8	16	60
2	0.92	5.72	0.185	8	8	16	80
3	0.92	5.72	0.185	16	16	32	60
4	0.92	5.72	0.185	16	16	32	80

4. RESULTS

4.1. Comparison of batch and microfluidic methods of silver nanoparticles production

Two different methods were used to produce silver nanoparticles using a consistent molar ratio of reagents (1.0:3.1:0.1) in the systems as described in the Experimental Section. The dynamic behaviour of the batch synthesis was examined using dynamic light scattering (DLS) and opposite to the expectations a linear growth of particles in time was not observed. Additionally, the samples were relatively polydisperse. On the other

hand, in microfluidic production process, DLS measurements of the final product show less polydisperse populations than in the case of batch production (**Figure 2A**), except for one case, the product which was produced at 16 µl/h flow rates for both dispersed phases and 60 µl/h flow rate of the continuous phase (sample 3 from **Table 1**). The polydispersity in the final product is probably caused by the presence of many particle nuclei in some samples as it will be shown in section 4.3. All DLS data are shown in the result **Table 2**.

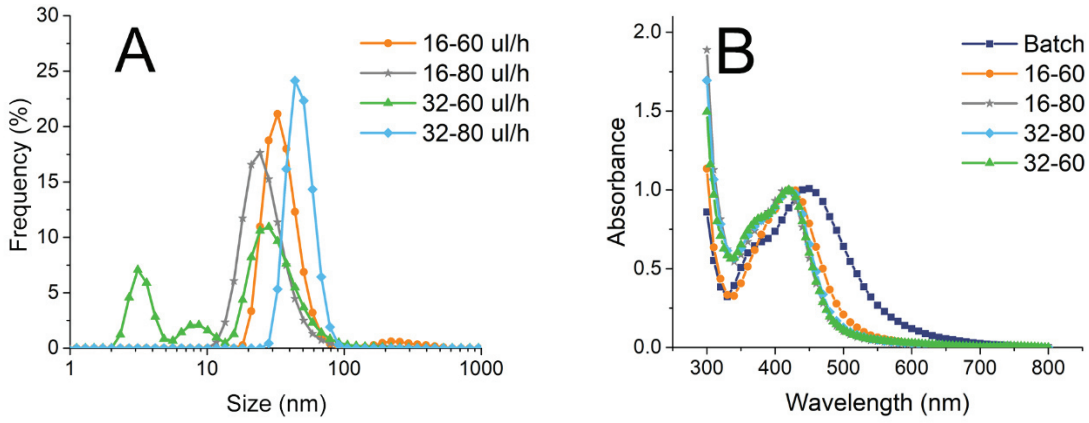

Figure 2 (A) Volume size distribution graphs of Ag nanoparticle samples produced by microfluidics with various flow rates; (B) UV-Vis spectra of Ag NPs prepared by both methods.

Figure 2B shows UV-Vis spectra for all prepared samples. The batch sample showed relatively constant spectra after the first 5 minutes with the maximal intensity at 440 nm. The higher wavelength of the maxima and broader peak are both indicators of larger particles and the presence of agglomerates. In contrast, results from microfluidic preparation show a much narrower spectra with a sharp peak with the absorbance maxima at 420 nm.

4.2. Image analysis of particles from TEM images

The transmission electron microscope (TEM) was used to observe particle structure, morphology, and size. The results show that at the end of the microfluidic process, the final particles are obtained mostly spherical and relatively monodisperse. Additionally, it also proves that there is no agglomeration in the final product. The batch product shows more polydisperse and larger particles having more irregular shape compared to microfluidic products.

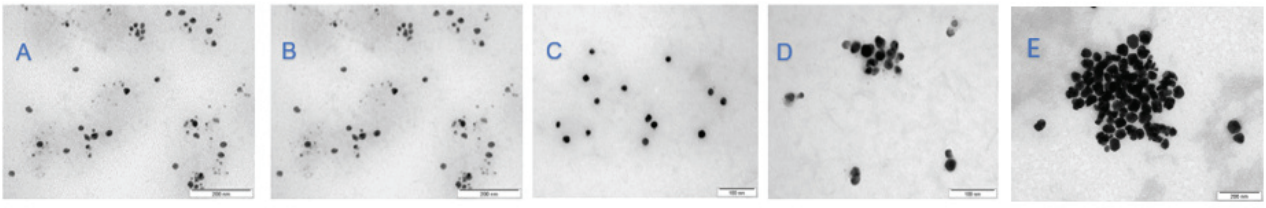

Figure 3 TEM pictures of final silver nanoparticles from microfluidic (A-D) and batch (E) proces: A) sample 1 B) sample 2, C) sample 3, D) sample 4 (all microfluidic samples correspond with the designation in **Table 10**), E) sample of the batch process collected at 15 min.

4.3. Effect of flow rate on particle size

The average sizes and their standard deviations for particles prepared using different flow rates of dispersed and continuous phases are shown in **Table 2**. The results of DLS are defined based on the volumetric size

distributions. The results show that increased flow rate of the dispersed phase and fixed continuous phase lead to increased values of the final particle size measured by both DLS and image analysis of TEM images. By increasing the flow rate of the dispersed phase from 16 to 32 µl/h, the size of the particles increased from 27.7 nm to 46.1 nm. The results of the batch process shows the biggest size values of the silver nanoparticles.

Table 2 Influence of the flow rates of dispersed and continuous phases on particle size distribution for microfluidic experiments and comparison with the batch process.

Experiment No	$Q_{disperse}$ [µl/h]	$Q_{continuous}$ [µl/h]	Particle Size DLS (nm)	Particle Size TEM (nm)
1	16	60	32.8 ± 7.9	16.3 ± 9.0
2	16	80	27.7 ± 8.3	12.8 ± 9.9
3	32	60	35.7 ± 5.6	20.7 ± 14.4
4	32	80	46.1 ± 9.1	22.3 ± 8.2
Batch		-	65.2 ± 26.5	42.4 ± 29.1

5. CONCLUSION

In this work, silver nanoparticle synthesis is carried out by two different methods, batch and microfluidic. The nanoparticles are prepared using trisodium citrate dihydrate as a reducing agent, tannic acid as a stabilizer and finally silver nitrate as a metal reductant. The experimental results presents that both methods were successful in nanoparticle production. However, the microfluidic method provides better control over the system parameters via internal settings. In comparison to batch process, microfluidic process results in narrower particle size distribution and more spherical morphology. Additionally, silver solution changes colour to yellow-brown during the synthesis. Thus, due to the susceptibility of silver nanoparticles to light absorption, the particle size and shape could be measured during the process and their final properties could be controlled. Finally, both methods were compared successfully and the important parameters of the syntheses in relation to the resulting particle qualities were identified.

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