

Synthesis of MUA-protected gold nanoparticles in microfluidic devices with in situ UV-vis characterization

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Abstract

Conventional synthetic methods for nanoparticles are limited by the complexity of controlling their size distribution and crystalline properties, which makes achieving a good reproducibility very difficult. Few microfluidic devices, based on the most common materials employed for miniaturization (glass, silicon or polymers), have been proposed to overcome these difficulties. Herein, we propose simple and economical microfluidic devices based on the Low-Temperature Co-fired Ceramics technology (LTCC) to synthesize and stabilize gold nanoparticles, which show an average size of 3 nm and remain stable for months. This technology, based on green tapes, shows some very interesting advantages compared to the employment of other materials, hence being an alternative technology. For instance, ceramic tapes have become an excellent material to many approaches. Owing to its versatility and chemical resistivity, the technology enables the construction of multilayered systems without the need of sophisticated facilities, which can integrate other mechanic, electronic and fluidic components in a single device, and a rapid prototyping reduces significantly the cost and production time.

Keywords: Nanoparticles synthesis, Gold nanoparticles, Microfluidic device, LTCC technology.

Introduction

Within the last years, many researchers have focused their investigations on nanomaterials and nanoscale science due to their great number of applications in electronics and physical, chemical, biological and biomedical fields [1]. Metallic nanoparticles (MNPs) are one of the most interesting nanomaterials. Moreover, gold nanoparticles (GNPs) have a broad Surface Plasmon Resonance (SPR) band in the visible region of the electromagnetic spectrum, which is suitable for designing new (bio)sensing devices, using both electrochemical and optochemical transduction principles. However, these properties directly depend on the dimensions and size distribution of the NPs and so, a strict control of the synthesis parameters is required to obtain well-defined nanomaterials [2].

Nanoparticles are usually prepared by means of batch processes, which have limited reproducibility due to the difficult control of some steps such as the addition of reagents, injection volume, rate of stirring, local temperature and concentration fluctuations, being difficult to obtain a colloidal suspension with the same characteristics in different batches. Automated and miniaturized continuous-flow methods have

been proposed as an alternative to overcome these limitations. These methodologies allow varying in a rapid, controlled and precise way most of the required experimental variables. Moreover, microfluidics reduces the consumption of reagents and, with automated in chain microsystems, it is possible to obtain nanoparticles with the same characteristics on demand.

Few microfluidic devices have been proposed with this aim, which are based on the most common employed materials for miniaturization (glass, silicon or polymers) [3-5]. However, glass and silicon not only involve special working conditions, such as clean rooms, but also require a postfabrication sealing of the microchannels that can produce leaks at the joints. Moreover, polymers show poor chemical and thermal inertness.

The LTCC technology allows a multilayer approach, being feasible the design and fabrication of 3D structures, where mechanic, electronic and fluidic components can be integrated in a single device. Thus, a careful and accurate control of the NPs synthesis can be performed by the introduction of static mixers or by the monolithic integration of temperature control systems based on resistor/thermistor couples [6]. Moreover, post fabrication steps are

avoided and the technology does not require the use of special facilities such as clean rooms. This permits a rapid prototyping, significantly reducing the cost and the production time. ,

In this paper, we report a simple microfluidic device for the synthesis and stabilization of 11-mercaptoundecanoic acid protected gold NPs (MUA Au NPs) based on ceramic tapes and the LTCC (Low Temperature Co-fired Ceramics) technology. The innovation of the present work arises from the advantages offered by the ceramic tapes as a substrate material and its associated microfabrication technologies regarding to other materials and microfabrication technologies.

Experimental Section

Ceramic Device Construction. Different designs generated in a CAD program were transferred on ceramic layers (low-temperature co-fired ceramics 951 AX tapes with a thickness of 254 μm supplied by DuPont) with a Laser (Protolaser 200) taking into account that ceramic layers shrink a $\sim 15\%$ in each axis during the sintering process. Then, the different layers were overlapped followed by a lamination step consisting of a thermo-compression process by the application of approx. 3000 psi for 30 s at 100 $^{\circ}\text{C}$. Finally, they were sintered in air atmosphere in a programmable box furnace (Carbolite CBCWF11/23P16, Afora, Spain) by applying a temperature profile. An initial increasing temperature ramp of 2 $^{\circ}\text{C min}^{-1}$ is applied until 350 $^{\circ}\text{C}$, and after 30 min of temperature stabilization, a second increasing ramp at the same rate is applied until 850 $^{\circ}\text{C}$. This temperature is maintained for 30 min and then cooling to 25 $^{\circ}\text{C}$ is performed.

Microsystem set-up. The microfluidic device was connected to 1-10 mL syringes (Hamilton series GASTIGHT 1000 TLL) with PTFE tubes (i.d. 0.9 mm) that were pumped by syringe pumps (540060 TSE systems). These pumps are controlled by a computer and allow driving reagents through the microreactor, providing microlitre per second flow rates, in a quick, simple and controlled way. Three-way isolation valves (NResearch incorporates $^{\circ}$), connected between syringes and the microfluidic device, make the automatic fill in of the syringes feasible, thus allowing a continuous dispensing of reagents. The linkage between PTFE tubes and ceramic devices was carried out through a specially designed homemade connection aluminum piece with conic PTFE connectors (Cones 1.6 mm Omnifit). These allow avoiding collateral reactions with the constituent elements of the commonly employed metallic connectors. O-rings were used to secure the holding back of

the system. A diagram of the whole set-up is showed in Figure 1.

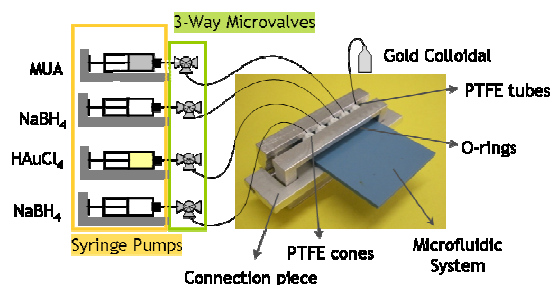


Figure 1. Diagram of the flow microsystem set-up for the synthesis of MUA protected gold nanoparticles.

Reagents and Apparatus. All solutions were prepared in double distilled water. Sodium borohydride was provided by Panreac with a 98% of purity and Gold (III) chloride hydrate by Fluka (p.a. ACS, $\geq 49\%$ Au); 11-mercaptoundecanoic acid (MUA), were obtained from Sigma-Aldrich with a purity of 99%.

A Shimadzu UV-310PC UV-Vis-NIR double-beam scanning spectrophotometer (Kyoto, Japan) was used to record spectra between 800 and 200 nm.

The shape and dimensions of the particle core were measured by Transmission Electron Microscopy JEOL 2011 and JEOL 1400 (Tokyo, Japan). The samples were prepared by dipping a copper grid, which was coated with a thin carbon film, in the gold nanoparticles suspension.

The purification of the colloidal obtained was performed by centrifugal filtration in 4 ml centrifugal filter devices (CENTRIPLUS YM30, MICROCON, MWCO 30000) at 3000 rpm for 35 min, and lyophilization was carried out in a LyoQuest freeze dryer (Telstar).

Results and discussion

Gold colloidal can be synthesized by many synthetic methods, including chemical reduction, photolysis, ultrasonic reductions or radiolysis of metal salts. In the present work, Au NPs have been synthesized by a simple one-phase reaction in which gold (III) chloride is reduced by sodium borohydride, and stabilized with MUA, taking place the following reaction in the aqueous phase: $\text{HAuCl}_4 + 4 \text{NaBH}_4 + 12 \text{H}_2\text{O} \rightleftharpoons \text{Au} + 4 \text{B(OH)}_3 + 4 \text{NaCl} + 29 \text{H}^+$.

Previously, we had reported the optimization of the manifold configuration of the ceramic microfluidic device for the synthesis of silver nanoparticles and gold nanoparticles [7-8]. Best results, in terms of repeatability and stability for gold modified nanoparticles, were obtained with the microfluidic reactor depicted in figure 2.

The first part of the microreactor is based on the synthesis of gold nanoparticles, with a hydraulic focusing of the reagents, procuring an effective and controllable lamination of the flow, thus reducing the mixing path. The typical design for this parallel lamination micromixer consists of three inlets and a channel. The configuration of the confluence point of the inlets and flows acquired a trident shape where the middle inlet was the metal salt and the other two inlets were the reducing agent, working as the sheath flows. With this conformation, the metal is located between the reductant, and thus, a more efficient mixture is generated. Best results, in terms of stability, were obtained by forcing the diffusion of reagents with the incorporation of passive mixers. Three-dimensional serpentine mixers cause a chaotic advection that improves the mixture.

The second part of the microreactor is based on the modification and stabilization of the gold nanoparticles synthesized. For this purpose, an extra channel is added for the incorporation of MUA, followed of another three-dimensional micromixer to improve the mixture.

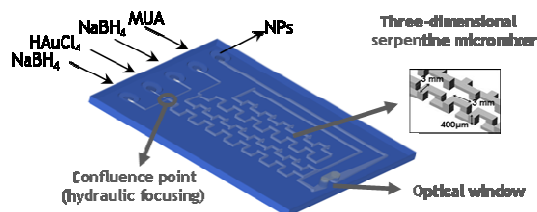


Figure 2. Microfluidic LTCC platform design for the synthesis of MUA protected gold nanoparticles consisting of the concept of hydraulic focusing and a three-dimensional serpentine micromixer for the reagent mixture.

The chemical and hydrodynamic parameters of the microreactor were optimized. Table 1a shows the effect of varying the pH of the gold nanoparticles. Their stability depends strongly on pH and hence, on the net charge of the functionalized colloid. As the pH was increased, the SPR band decreased in intensity and shifted to shorter wavelengths. At basic pH values carboxylic groups are deprotonated giving an extra stability to the NPs due to electrostatic repulsions; however the electronic density on the metal is incremented, resulting in the observed changes of the SPR spectrum.

On the other hand, the study of the flow rates of the MUA solution was also performed (Table 1b). By increasing the MUA flow rate a displacement of the band towards larger wavelengths was observed. As the amount of MUA in the reaction mixture is increased, more molecules of modifier are attached to the NPs giving larger NPs.

The optimal conditions for the first part of the reaction were a continuous pumping of a 1.5 mM NaBH₄ solution at a 1 μl s⁻¹ flow rate, and a dosage of 0.7 μl of a 1 mM H₂AuCl₄ solution sequentially dispensed every 2 s at a 2.5 μl s⁻¹ flow rate. Then, a continuous flow of 1 mM MUA solution at 1 μl s⁻¹ generated the surface modification of the nanoparticles. The flow ratio of the fluid streams was 1:6:3.3 (H₂AuCl₄:NaBH₄:MUA), being the total flow at the end of the microfluidic system of 3.3 μl s⁻¹. With these hydrodynamic parameters, the molar relationship of the reagents H₂AuCl₄, NaBH₄ and MUA is 1:10:3, and provided stable MUA protected gold nanoparticles with a SPR band located at 518 nm (Figure 3). The final concentration of the nanoparticles obtained was 5 × 10⁻⁸ M.

A		B	
Flow rate (μL min ⁻¹)	Wavelength (nm)	pH	Wavelength (nm)
10	510	9.2	517
20	510	8.3	519
30	512	6.0	521
40	513	4.8	524
50	516	3.7	527
60	516	2.7	531
70	518		
80	518		
90	520		
100	522		

Table 1. Study of the effect of pH (a) and MUA flow rate (b) on the SPR band position.

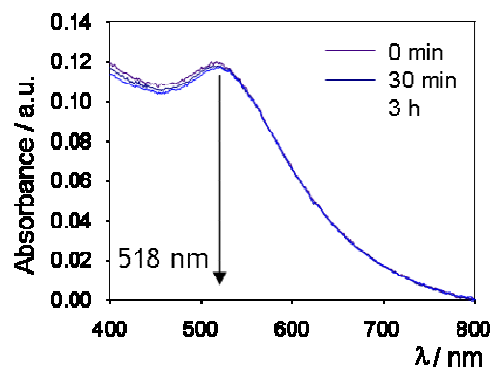


Figure 3. Study of the effect of pH and MUA flow rate on the SPR band position. (b) UV-vis spectra from the synthesized modified Au NPs using the optimized experimental conditions.

After each synthesis, and prior to the NPs characterization, the water soluble gold colloidal suspensions were purified by centrifugal filtration and finally lyophilized, obtaining a solid,

