

Tuning Polyol-Mediated Process towards Augmentation of Zero-Valent Copper Nanoparticles

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Polyol synthesis generally refers the reduction of metal ions towards metal nanoparticles in a polyol solvent which can act as both reducing and stabilizing agents; in some cases, an additional reducing agent can be applicable. In the present work, variation in polyol levels (ethylene glycol, propylene glycol and glycerol) provided the insights into the characteristics of zero-valent copper nanoparticles (CuNPs) and the stability of corresponding colloidal solutions. The formation of CuNPs was monitored by ultraviolet-visible spectrophotometry (UV-vis), powder X-ray diffraction (PXRD) and transmission electron microscopy (TEM), based on the tune of reaction parameters (time, temperature, initial copper concentration, molar ratio of Cu/reductant) and nature of reactants (copper precursor, reductant, solvent). Mono-disperse CuNPs were highly stable in glycerol with no sign of aggregation until 15 d, proving the feasibility of the cost-effective and eco-friendly protocol for large-scale CuNPs production and promising their biomedicine applications thanks to the use of non-toxic reagents.

1. Introduction

Nanotechnology is one of the foremost research fields in advanced materials science so far. At nanoscale, metal-based materials possess distinguished chemical and physical properties for diverse applications, fascinating numerous contributions to their synthetic strategies (Shnoudeh et al., 2019). Besides noble metals (like Au, Ag, Pd and Pt), copper nanoparticles (CuNPs) have received much attention thanks to their strong application background (catalysis, optics, electronics, antibacterial) and low-cost (Gawande et al., 2016). For centuries, copper-based compounds have been utilized as disinfectants; practically, the high surface-to-volume ratio of CuNPs yields stronger antibacterial properties (Din et al., 2017). With the diversity of microorganisms, inorganic materials-based bactericides have been continuously developed in replacement for traditional organic agents thanks to their high heat resistance, low decomposability and long-life (Anduaem et al., 2020). CuNPs are highly promising for the replacement of bactericides, widening their scope in biomedicine application.

A variety of chemical and physical procedures have been successfully reported for the synthesis of CuNPs so far (Gawande et al., 2016) with remaining drawbacks involving toxic reagents, hazardous by-products generation, and high energy consumption. In terms of biomedicine scope, there is an urgent requirement to develop simple, cost-effective, and sustainable procedures for CuNPs synthesis without using toxic chemicals. The unique physical and chemical properties of CuNPs, which are related to their applications, are often determined by their size, shape and composition, which can be rationally achieved by controlling the synthetic parameters (Umer et al., 2012). Most studies focused on the controlled synthesis to obtain well-defined CuNPs, ignoring green and sustainable criteria; on the contrary, environmentally benign processes faced difficulties in controlling the synthesis conditions.

The purpose of this study is to design a low-cost, environment-friendly, simple and well-controlled procedure for the synthesis of CuNPs, using non-toxic reagents. Unlike noble metals, copper is highly sensitive to air, and the oxide phases are thermodynamically more stable; the formation of an oxide layer on the surface of CuNPs could not be precluded (Jardón-Maximino et al., 2018). Practically, CuNPs were prepared under an inert gas atmosphere (such as nitrogen or argon); in some cases, organic solvents were also utilized to prevent the

oxidation. Besides, the synthesis of CuNPs was only possible in the presence of additional surfactants to stabilize CuNPs (El-Berry et al., 2021). In the present work, the chemical reduction of copper precursors towards CuNPs was carried out in polyol solvents, using ascorbic acid as non-toxic reducing and capping agent. The importance of polyols in immobilizing CuNPs and preventing their oxidation was also highlighted, with the aim to obtain long-term stable colloidal solution of mono-disperse CuNPs.

2. Experimental

2.1 Parameter optimization for the polyol synthesis of CuNPs

All chemicals were commercially purchased and used as received, without any further purification. Typically, a solution of copper(II) acetate ($\text{Cu}(\text{OAc})_2$) dissolved in glycerol and a solution of L-ascorbic acid (AA) dissolved in glycerol were separately prepared. Then, 20 mL of 25 mM AA solution was added to 10 mL of 2 mM $\text{Cu}(\text{OAc})_2$ solution under constant stirring at 70 °C, at ambient conditions. With the increase in time, the color of the solution gradually turned from very light blue to red and finally reddish-brown. In order to obtain CuNPs in the solid state, the solution was cooled down to room temperature and then centrifuged, washed several times with distilled water, acetone, and finally dried at room temperature.

The synthesis of CuNPs was also optimized via reaction parameters (time (up to 30 min), temperature (60–80 °C), initial copper concentration (1–5 mM) and molar ratio of copper/AA (1/20–1/40) and nature of reactants (copper precursor, reducing agent and polyol solvent). Once each factor was changed, others were kept unchanged as described above in the typical experiment.

2.2 Characterization of as-prepared CuNPs

The formation of CuNPs in the colloidal solutions was monitored by scanning their absorbance in the wavelength of 450–800 nm on ultraviolet-visible (UV-vis) spectrophotometer (Optizen Pop), using a 1 cm-path length quartz cuvette. The crystalline structure of as-prepared CuNPs in the solid state was detected on D2 Bruker powder X-ray diffractometer (PXRD), using $\text{Cu-K}\alpha$ ($\lambda = 1.5406 \text{ \AA}$) in the range 2θ of 30–80°. The size and shape of CuNPs were observed on JEOL JEM 1400 transmission electron microscope (TEM).

3. Results and discussion

3.1 Monitoring of CuNPs formation in glycerol

It has been reported that smaller size and greater concentration of synthesized CuNPs gave higher penetration power, resulting in better antibacterial activity (Din et al., 2017). The output of the present section is to control the experimental conditions, aiming at yielding CuNPs with small size, narrow distribution and high concentration as a consequence of the full reduction of copper ions.

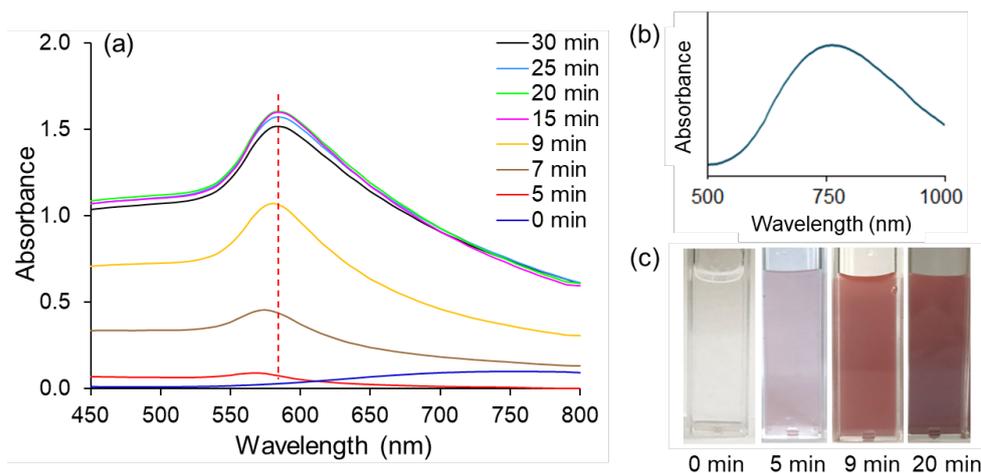


Figure 1: (a) UV-vis spectra of CuNPs solution at various intervals; (b) UV-vis spectrum of $\text{Cu}(\text{OAc})_2$ solution; (c) Photos of CuNPs solution at various intervals

In glycerol, the formation of CuNPs was attributed to the reduction of $\text{Cu}(\text{OAc})_2$ provoked by AA at 70 °C. As a critical parameter in the CuNPs synthesis, the reaction time was determined at the highest concentration of

CuNPs. The color of the solution gradually turned from very light blue (at the beginning, related to $\text{Cu}(\text{OAc})_2$ solution) to red (after 5 min) and finally reddish-brown (after 9 min and 20 min), confirming the formation of zero-valent CuNPs in the colloidal suspension (Figure 1c). In fact, the formation of CuNPs was observed starting at 5 min, as proven by the surface plasmon resonance band (SPR) at 575–585 nm (Figure 1a), in contrast to the d-d transition of $\text{Cu}(\text{II})$ at 750 nm (Figure 1b). With the increase in time, the absorption intensity uplifted due to the increase in CuNPs concentration, achieving the highest value at 20 min. Since the reduction of copper ions towards CuNPs was complete, the continued increase in time (from 20 min to 30 min) may lead to the aggregation of nanoparticles, reducing the plasmon absorption intensity. More interestingly, a red-shift absorption band (from 575 nm to 585 nm) was observed, evidencing the growth of copper nuclei to form larger particles. The reaction time determined not only the concentration of CuNPs formed, but also the particle size; in this study, the time of 20 min should be chosen due to the highest CuNPs concentration and their stability in particle size. The formation of spheres instead of anisotropic shape could be concluded with the exclusive presence of SPR band at 585 nm (Ong et al., 2015).

The effect of reaction parameters on the formation of CuNPs in glycerol after 20 min was also evaluated by UV-vis spectrophotometry, involving reaction temperature, molar ratio of copper/AA and initial copper concentration (Figure 2). At low temperature (60 °C), the chemical reduction of copper ions was incomplete; at higher temperature (80 °C), the formation of CuNPs could be maximized and the aggregation could be possible, leading to a lower quantity of CuNPs (lower absorption intensity) and larger particle size (longer absorption wavelength) (Figure 2a). Practically, the syntheses of CuNPs (Teichert et al., 2018) and other metal nanoparticles (Díaz-Álvarez et al., 2013) in various polyol solvents were reported under higher temperatures, taking advantage of the decrease in the redox potential of polyols with the increase in temperature. In this study, the use of AA as a reducing agent in glycerol permitted performing the CuNPs synthesis at low temperature (70 °C).

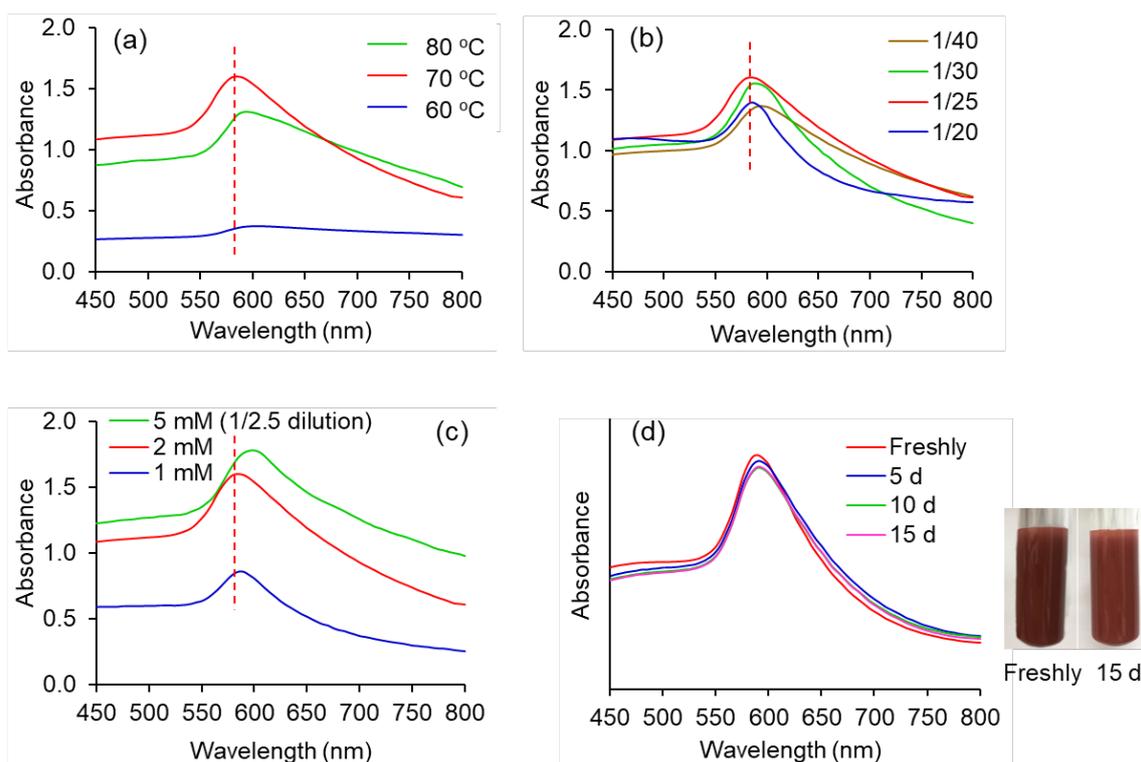


Figure 2: UV-vis spectra of CuNPs solutions synthesized at various conditions: (a) temperature; (b) molar ratio of copper/AA; (c) initial copper concentration; and (d) stability of CuNPs solution synthesized at the optimal conditions during 15 d (inset: photos of CuNPs solution)

The formation of CuNPs can be governed by the reduction rate of metal ions to generate copper nuclei and their growth (Park et al., 2007). Herein, the molar ratio of copper/AA is crucial to control the reduction rate, leading to the change in particle size. The CuNPs solution synthesized at 70 °C for 20 min was examined by UV-vis spectrophotometry, showing the highest absorption intensity with the molar ratio of 1/25 (Figure 2b). At a lower amount of AA (the molar ratio of 1/20), the chemical reduction was sluggish; when increasing the amount of

reducing agent (the molar ratio of 1/30 or 1/40), the high reduction rate speeded up the copper nuclei formation, leading to their agglomeration. With the molar ratio of 1/30 and 1/40, a red-shift and broaden absorption bands were observed, evidencing the formation of larger nanoparticles and possibly poly-disperse model.

In a similar approach, the effect of initial copper concentration on the formation of CuNPs in glycerol, using the molar ratio of copper/AA of 1/25 at 70 °C for 20 min was investigated (Figure 2c). In all cases, the chemical reductions of copper ions towards CuNPs were possibly complete. At very high precursor concentration (5 mM), a huge number of copper nuclei were formed; consequently, they were easily in contact with others and aggregated into larger particles, as proven by the increase in absorption wavelength. In brief, the optimal conditions for the synthesis of CuNPs in glycerol could be established, involving Cu(OAc)₂ concentration of 2 mM, the molar ratio of copper/AA of 1/25, reaction temperature of 70 °C and reaction time of 20 min. More importantly, the colloidal solution of CuNPs in glycerol prepared under the optimal conditions showed the excellent stability until 15 d, as evidenced by the insignificant change in both the color of the solution and corresponding recorded UV-vis spectra (Figure 2d). With no sign of sedimentation in CuNPs solution during a long-term storage, the highly stable dispersion of CuNPs in glycerol will promise its practical applications, in contrast to previous reports on unstable CuNPs in aqueous media (Yu et al., 2009). In fact, the oxidation and agglomeration of CuNPs could be possible; the use of an additional stabilizing agent (such as polyvinylpyrrolidone, sodium dodecyl sulphate, cetyltrimethylammonium bromide, etc.) was introduced (Gawande et al., 2016) and as-prepared CuNPs should be kept in the solid state. In the present work, AA acts as both reducing and stabilizing agents, and glycerol permits immobilizing CuNPs in its supramolecular network and preventing dissolving oxygen, resulting in well-dispersion and high stability of CuNPs (Kawasaki et al., 2011).

The effects of copper precursor and reducing agent on size, shape and crystallinity of CuNPs were previously reported (Shankar and Rhim, 2014); in this work, the formation of CuNPs at 70 °C was affirmed in the case of using Cu(OAc)₂ and ascorbic acid. On the other hand, the use of Cu(NO₃)₂, CuSO₄ as copper precursors and tannic acid, citric acid, D-glucose as reducing agents could not afford the red colloidal solutions, failing the formation of CuNPs, even in a longer time (up to 1 h) (Figure 3). In fact, the reduction of such copper precursors towards CuNPs could be possible using mentioned reducing agents under harsher conditions (such as higher quantity of reducing agent, higher temperature, longer time, requirement for pH adjustment, etc.) (Gawande et al., 2016). In this study, the intrinsic features of the CuNPs system have not been adjusted, facilitating its diverse applications in biomedicine fields.

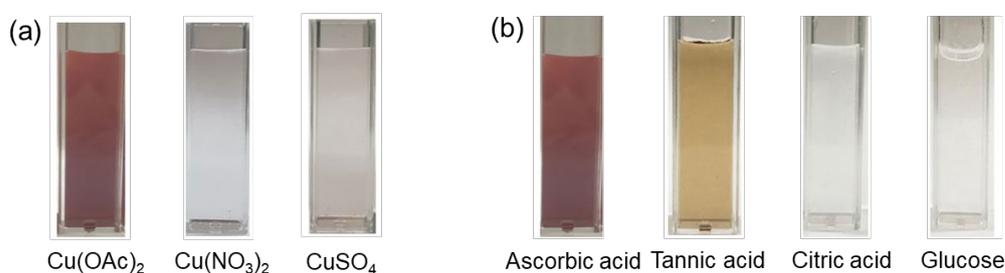


Figure 3: Photos of CuNPs solutions using various reactants: (a) various copper precursors using AA as a reducing agent; (b) various reducing agents using Cu(OAc)₂ as a copper precursor

3.2 Variation of polyols for the immobilization of CuNPs

The multifunctional roles of polyols in the synthesis of metal nanoparticles have been practically evidenced, involving solvent, mild reducing agent, stabilizing agent, etc. (Fiévet et al., 2018). In fact, the physical chemical properties of polyols can be tuned by varying their carbon chain length and hydroxyl groups, leading to the differences in size, shape and composition of obtained metal nanoparticles. In comparison with ethylene glycol (EG) and propylene glycol (PG), glycerol (GL) possesses longer carbon chain length and more hydroxyl groups, triggering more efficient supramolecular network; consequently, CuNPs can be better trapped in glycerol. The CuNPs solution in glycerol showed the highest absorption intensity and lowest absorption wavelength (Figure 4a), evidencing the efficient synthesis of CuNPs. In contrast to the long-term stability of the red colloidal solution of CuNPs in glycerol, those obtained from ethylene glycol and propylene glycol were dark colloidal, but precipitated after 24 h. In water, the precipitates were observed, instead of the colloidal suspensions as those in polyol solvents (Figure 4b). The results admitted the important role of glycerol in immobilizing CuNPs; in

water, the only use of ascorbic acid was not enough and the additional stabilizing agent (like polyvinylpyrrolidone) should be utilized.

The effect of polyol solvents on crystalline structure of as-synthesized CuNPs was investigated via PXRD patterns (Figure 5a), showing the exclusive formation of zero-valent copper bulk as face-centered cubic structure in glycerol (Cu-GL). On the other hand, the crystalline phase of cuprous oxide was detected on the samples synthesized in ethylene glycol (Cu-EG) and propylene glycol (Cu-PG), attributed to the partial reduction of Cu(II) towards Cu(I) during synthesis or the oxidation of Cu(0) on the CuNPs surface during centrifugation. Briefly, glycerol is beneficial to the formation of zero-valent CuNPs and their long-term stability.

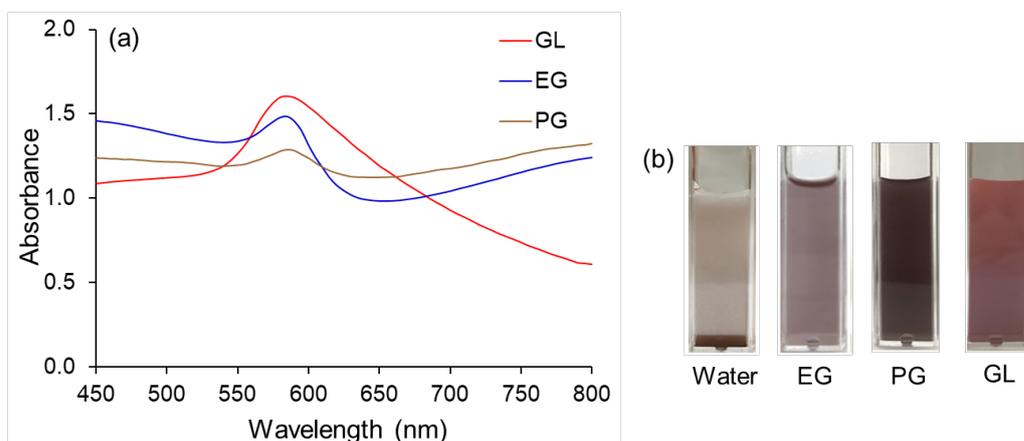


Figure 4: (a) UV-vis spectra; (b) Photos of CuNPs solutions using various polyol solvents (GL: glycerol; PG: propylene glycol; EG: ethylene glycol)

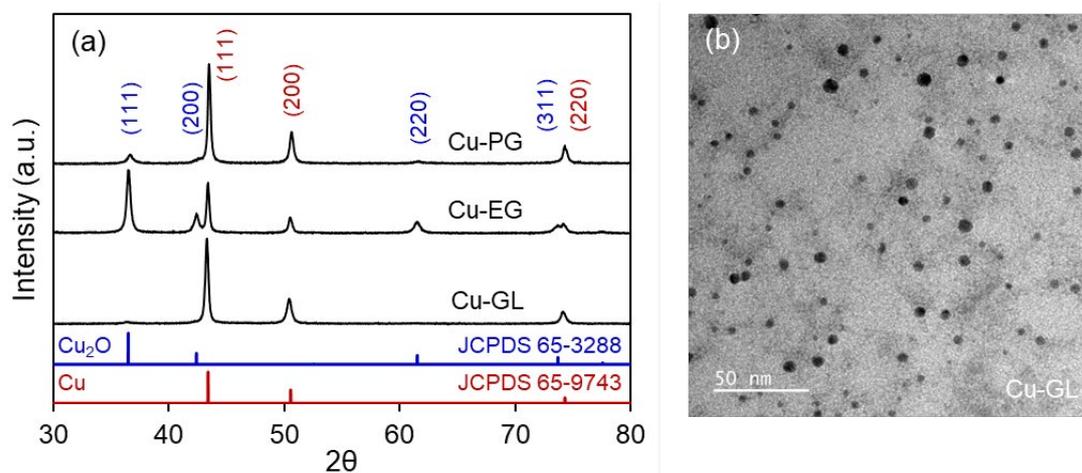


Figure 5: (a) PXRD patterns of CuNPs synthesized in various polyol solvents (GL: glycerol; PG: propylene glycol; EG: ethylene glycol); (b) TEM micrograph of CuNPs synthesized in glycerol under optimal conditions

The size and shape of CuNPs in glycerol synthesized at optimal conditions were examined by TEM analysis, showing the presence of spherical nanoparticles with small size (ca. 5 nm in mean diameter) and well-dispersion (Figure 5b). The homogeneity in particle size evidenced the formation of mono-disperse CuNPs, in agreement with above UV-vis analysis (Park et al., 2007).

4. Conclusions

Compared to traditional polyol solvents, the use of glycerol in CuNPs synthesis practically evidenced some advantages, such as its low-cost and non-toxicity, mild reducing ability, efficient supramolecular network in immobilization of metal nanoparticles and prevention of their re-oxidation. The present work proposed the

straightforward, environment-friendly and cost-effective protocol for large-scale mono-disperse zero-valent CuNPs production, in particular long-term stability, facilitating its diverse applications in biomedicine fields.

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