GREEN SYNTHESIS OF GOLD NANOPARTICLE COLLOIDAL SOLUTIONS AND USED AS A NEW X-RAY CONSTRAST AGENT

Nguyen Thi Phuong Phong, Ngo Hoang Minh*, Huynh Chi Quoc, Vo Quoc Khuong.

Faculty of Chemistry, University of Sciences, VNU HCM City

***Faculty of Chemistry, Lac Hong University Email: ntpphong@hcmus.edu.vn**

ABTRACT

Gold colloidal solutions have been rapidly synthesized in green conditions by using microwave irradiation or by conditional heating. Acid cloroauric $HAuCl_4$ was reduced by trisodiumcitrat (TSC) and DI water. Trisodiumcitrat was used as stabilizer. The particle size and morphology of gold nanoparticles can be controlled by altering several factors such as the time, the power of microwave exposure, the ratio of Au^{3+} and TCS, and so on. The synthesized gold colloidal solutions were characterized by UV–Vis and by TEM. The AuNPs showed a biocompatibility and without toxicity in the mice. Primary, colloidal AuNPs show a blood-pool agent for x-ray CT imaging.

Keywords: gold nanoparticle; AuNPs; x-ray imaging; contrast agent

1. INTRODUCTION

Nanoparticles based on gold chemistry have recently attracted significant research and practical attention. They are versatile agents with a variety of biomedical applications including the use in highly sensitive diagnostic assays [1], thermal ablation and radiotherapy enhancement [2], as well as drug and gene delivery [3]. For instance, antibody-modified gold nanoparticles used for detection of prostate specific antigen, had an almost a million-fold higher sensitivity compared to conventional ELISA-based assay [4]. Near-infrared radiation absorbing gold-silica nanoshells have been prepared and evaluated for thermal ablation of tumors after systemic administration [5]. Microwave (MW) dielectric heating is a new potential technique for the preparation of size-controlled metallic nano-structures due to its rapid heating and penetration.

A medical contrast medium (or contrast agent) is a substance used to enhance the contrast of structures or fluids within the body in medical imaging. It is commonly used to enhance the visibility of blood vessels and the gastrointestinal tract [6].

In this paper, the colloidal nanoparticles of gold in different sizes were prepared by chemical reduction with tricitrat sodium or with DI water media in traditional heating or microwave irradiation method with trisodiumcitrat as stabilizer. The change in advantage altering several factors such as the time, the power of microwave exposure, the ratio of Au^{3+} and trisodiumcitrat and

so on were investigated. The synthezed colloidal AuNPs used as a contrast agent for X-ray CT imaging.

2. EXPERIMENTAL

2.1. Materials

Acid chloroauric, $HAuCl_4.3H_2O$ 99.99%, Merck; Trisodium citrat (TSC) $C_6H_5Na_3O_7$ 99.0% Prolabo; Milipore Water (Water for chromatography) Merck

2.2. Experimental process

A 100-ml glass flask was placed in an MW oven and connected to a condenser. 500µl of 10.3 mmol $HAuCl_4.3H_2O$ solution in DI water (50ml) containing trisodium citrate 5% (250, 500, and 1000 µl) was heated by routine heating method or was irradiated by MW in a CW mode (Shikoku Keisoku: 800 W). TSC acts as a stabilizer of small gold nanostructures. All the reactions were carried out in a microwave oven operating in a cycling mode (on for 2 minute, off for 1minute) to prevent the intense boiling of solvents as well as the agglomeration of metals. The particle size and morphology of these solutions can be controlled by altering several factors like the time, the power of microwave exposure, and the ratio of $HAuCl_4$ and TSC.

Animals: healthy mice of either sex not previously used for testing, weighing 18-22g are maintained in normal husbandry conditions. The female mice are not pregnant or breast-feeding.

Procedure: administer 0.5 ml gold nanoparticles (1000ppm) to each of five mice by intravenous. Inject regularly into vein of the tail over a period of 15-30 seconds.

2.3. Characterization

The synthesized gold colloidal solutions were characterized by several analytical techniques like UV–Vis (CARI100, Varian-Autralia), TEM (JEM-1400). Finally, we used the synthesized silver colloidal solutions can be used as x-ray contrast agents.

2.4. Toxicity test

The test for abnormal toxicity of a test substance is determined by observing the death of mice within a period of 24 hours after the animals received a dose of test substance by injection or other route of administration.

Interpretation of result: The sample complies the test if none of the mice dies. If one of the animals dies, repeat the test using another 10 mice, each weighing 19 ± 1g. The sample complies the test if none of the second group of mice dies within 48 hours [7].

2.5. X-ray

The x-ray machine permise the x-ray imaging determination on the mice after inject the contrast agent. We used the x-ray machine at the Hanh Phuc laboratory. A Lorad Medical Systems

mammography unit (Hologic, Inc., Danbury, CT; model XDA101827) was used with 8 mAs exposures (0.4 s at 22 kVp). Kodak Min-R2000 mammography film, 18 cm x 24 cm (Eastman Kodak, Rochester, NY) was used.

3. RESULTS AND DISCUSSION

3.1. UV-vis absorbance spectra

The results from UV-Vis of the samples are illustrated in the Fig. 1 and Fig.2. Fig. 1 shows the UV-Vis absorption spectra of AuNPs synthesized with microwave method (Microwave powder 160W, time: 8min). Fig. 2 show the UV-Vis absorption spectra of AuNPs synthesized with traditional heating method (time of 120mins). The wavelength in Fig. 1 (527nm) is different from that obtain from Fig. 2 (532nm). The result may be probably the size of AuNPs synthesized by MW, which is smaller than the size of AuNPs synthesized by traditional heating.

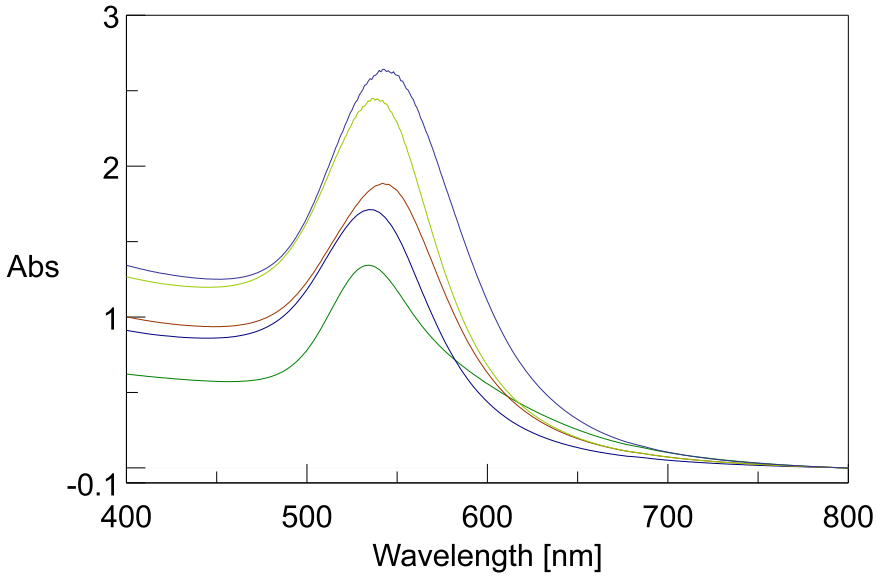


Fig.1. UV-Vis Absorption spectra of synthesized AuNPs by MW method

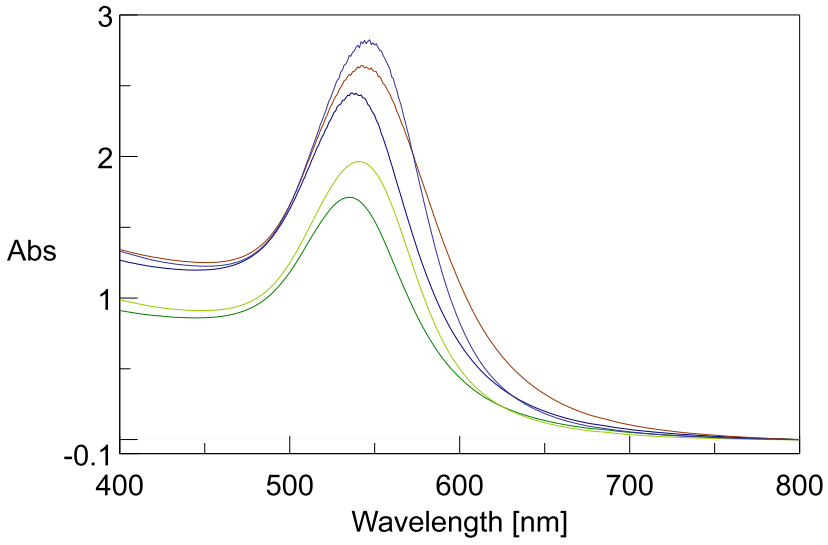


Fig.2. UV-Vis Absorption spectra of synthesized AuNPs by traditional heating method

3.2. TEM images

TEM as a powerful tool has been extensively used to investigate the morphologies and size distribution of synthesized AuNPs. In the case of synthesis AuNPs by MW method, TEM images and histogram of size distribution of AuNPs presented in Fig. 3 and Fig.4. It can be observed in Fig. 3, the distribution is centered on 4-6nm, resulting in an average diameter of 7,26nm. Note also that all nanoparticles tend to be well separated from each other and they not form aggregates. As a result of the above reduction process, nucleation and growth processes of gold yield a mixture of spherical and close-to-spherical nanoparticles. These nanoparticles were well-dispersed because of the presence of trisodium citrat that could chemically adsorb onto the surfaces of gold solid probably through an interaction between three O–C=O group and Au. The surface energies of large particles are lower than those of smaller ones. Therefore, it is expected that some small nanoparticles are grown to larger ones via an Ostwald-ripening process. The TSC adsorbed on specific crystalline surfaces could significantly decrease their growth rates and lead to a highly anisotropic growth.

In the case of routine heating method, it can be observed, the distribution is centered on 16-24nm, and resulting in an average diameter of 19,6nm.

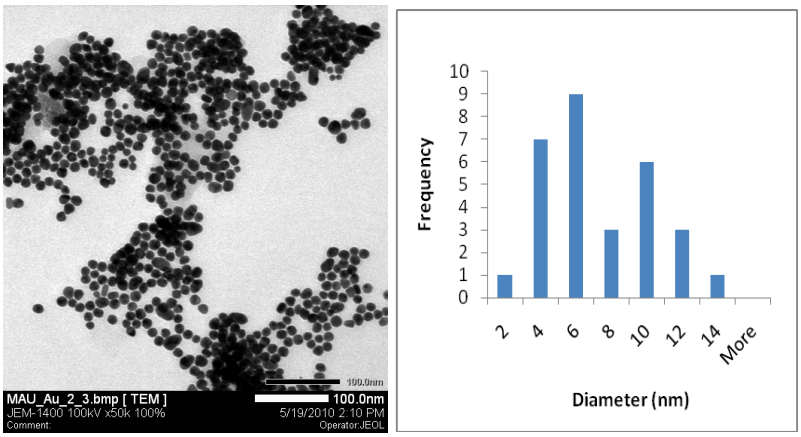


Fig 3. TEM images of synthesize by MW irradiation for 8 mins at 160W with $HAuCl_4$:TSC=1:68

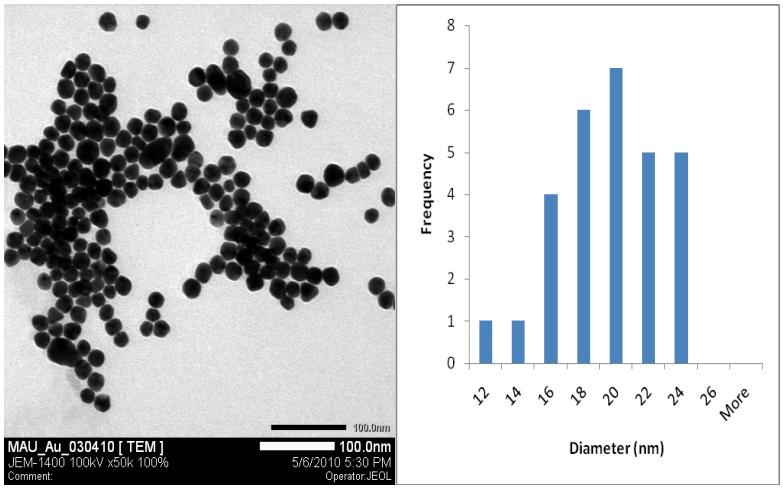
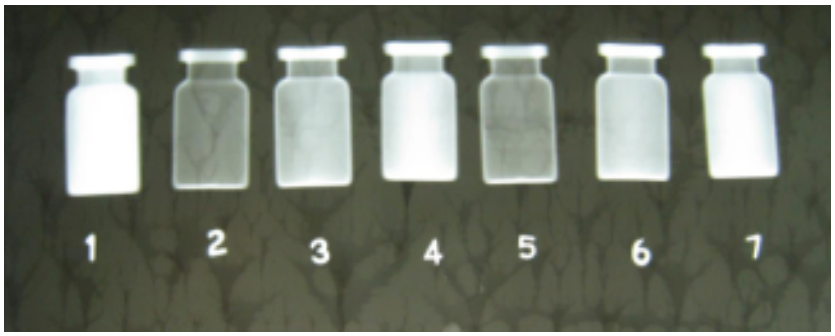


Fig 4. TEM images of synthesized AuNPs by traditional heating $HAuCl_4$:TSC=1:68

3.3.Toxicity test

With all animals were weighed and observed regular for in vivo, mice were intravenously injected with AuNPs at 0.5ml (1000 ppm), survived longer than 24 hours. No dead mouse was found. So, AuNPs complies the toxicity test by British Pharmacopoeia 2007.

3.4.X-ray imaging



1:Control sample (Iodin)
2:AuNPs1(MicroWave)
3: AuNPs1:Iodin (2:1)
4: AuNPs1:Iodin (1:1)
5: AuNPs 2 (Traditional Heating)
6: AuNPs2:Iodin (2:1)
7: AuNPs2:Iodin (1:1)

Fig.5. X-Ray CT Images of the different samples

The X-Ray images of the different samples were shown in Fig.5. Thus, a part of gold nanoparticle solution which can be replace with the Iodin contrast agent, have no influence on the image quality of X-Ray images.

4. CONCLUTION

Gold colloidal solutions have been rapidly synthesized in green conditions (DI water and Trisodium citrat) by using microwave irradiation or by conditional heating. The synthesized gold colloidal solutions were characterized by UV–Vis, TEM. The AuNPs showed a biocompatibility and without toxicity in the mice. Primary, colloidal AuNPs show a blood-pool agent for x-ray CT imaging.

.

REFERENCES

1. Cailin Fan, Wei Li, Shiju, et al., Materials Letters 62 (2008) 3518-3520
2. Angshuman Pal, Sunil Shah, Surekha Devi, A: Physicochem.Eng.Aspects 302 (2007) 51-57.
3. T.García, E.Casero, et al., Biosensor and bioelectronics 24(2008)184-190
4. Wan-Seob Cho, Minjung Cho, et al., Toxicology and Applied Pharmacology xxx (2009)
5. Partha Ghosh, Gang Han, et al., Advanced Drug Delivery Reviews 60 (2008) 1307-1315.
6. J.F.Hainfeld, D.N.Slatin, et al, The Bristish Journal of Radiology, 79(2006)248-253
7. British Pharmacopoeia 2007