Chinese Chemical Letters Vol. 16, No. 7, pp 947-950, 2005
http://www.imm.ac.cn/journal/ccl.html


# The Interaction between Propranolol and Gold Nanoparticles and its Analytical Application

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**Abstract:** The addition of propranolol induced the aggregation of gold nanoparticles, and increased Rayleigh light scattering (RLS) intensity greatly. The interaction between them was studied by RLS spectrum, UV-Vis spectrum and transmission electron microscopy (TEM). Based on these results, a novel method was proposed for propranolol assay. With the combination of solid phase microextraction (SPME), the proposed method was successfully applied to determine propranolol in urine.

**Keywords:** Propranolol, gold nanoparticles, resonance light scattering, SMPE.

In recent years, gold nanoparticles have attracted much research attention due to their unique electric, catalytic, and optical properties originating from the quantum-scale dimensions[1-3]. And gold nanoparticles have been of increasing interest in applications to biological and chemical nanosensors[4]. One aspect of the fantastic researches on gold nanoparticles is focused on the phenomena of aggregation or flocculation of gold nanoparticles in solution[5]. Particle aggregation results in further color changes of gold nanoparticle solutions due to mutually induced dipoles that depend on interparticle distance and aggregate size[6-9]. Gold nanoparticle aggregation induced by analytes has been demonstrated for DNA[9-13], several metal ions[14,15], and antibodies[16].

Propranolol is a beta-adrenergic blocking drug, which is widely used as standard therapy for the treatment of many diseases[17]. It is also used in low activity sports as doping agent[18]; therefore, it has been included in the forbidden list in stressful activities by the International Olympic Committee[19]. Herein, RLS spectrum, absorbance spectrum and TEM technique were utilized to investigate the aggregation of gold nanoparticles induced by propranolol. With the combination of solid phase microextraction (SPME), the proposed method was successfully applied to determine propranolol in urine.

## Experimental

All RLS measurements were performed using a Perkin Elmer Model LS-55 spectrometer with a quartz cuvette (1×1 cm). A Shimadzu Model UV-1601 double-beam spectrophotometer was used for recording the absorption spectra. The pH was measured with

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a Model PHS-3C meter (Shanghai Leici Equipment Factory, China). Transmission Electron Microscope (JEM-100CX II) was used for the characterization of gold nanoparticles.

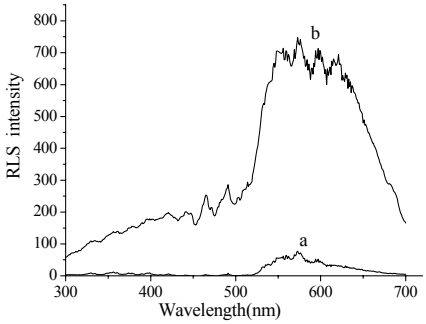
All the chemicals were in analytical grade. All the stock solutions were prepared using doubly filtered water. Propranolol was purchased from Acros. Gold nanoparticles was synthesized according to the reference[20]. The particle size and concentration of gold nanoparticles were 13.8±1.8 nm and 16.3 nmol·L$^{-1}$, respectively.

## Results and Discussion

When propranolol was added into the solution of gold nanoparticles, the color of the solution turned from red to blue, which could be explained by the aggregation of gold nanoparticles induced by propranolol. The color change was due to a combination of the absorption and scattering of light through the solution. The extent that a particle absorbs and scatters light depends on its size, shape and index of refraction to the surrounding medium[21]. **Figure 1** showed the RLS spectra of gold nanoparticles in the absence (**Figure 1a**) and presence (**Figure 1b**) of propranolol, the great enhancement of RLS signal proved the aggregation. The UV-visible spectra were shown in **Figure 2**. The solution of gold nanoparticles exhibited an absorbance band at 520 nm (**Figure 2a**), after adding propranolol, the absorbance intensity of 520 nm declined and a new absorbance band at 708 nm appeared (**Figure 2b**). Propranolol induced the aggregative state of gold nanoparticles, when more and more gold nanoparticles were in contact; the range of plasmon couple was longer and longer, which would lead to red shift of absorbance for several hundred nanometers [22].

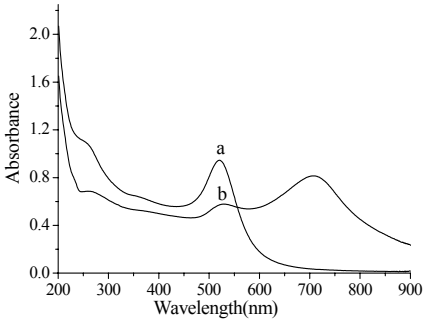
The TEM micrographs of gold nanoparticles are presented in **Figure 3**. The single separate state of gold nanoparticles and aggregative state after the addition of propranolol could be seen. The result indicated that the aggregation of gold nanoparticles was in accordance with the results of RLS and absorbance spectra.

**Figure 1** RLS spectra



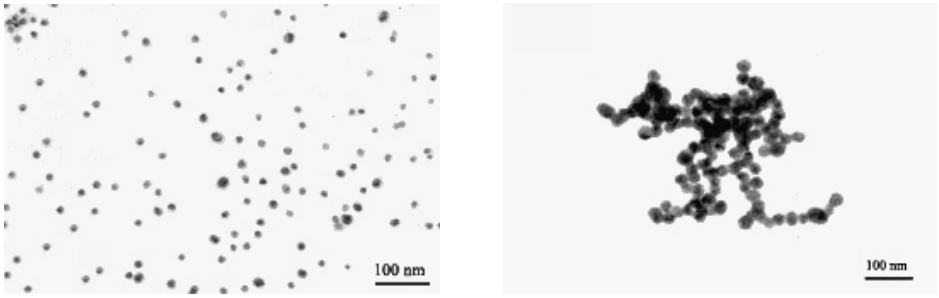

$c_{Au} = 4.9\times10^{-9}$ mol·L$^{-1}$,
$c_{propranolol} = 3.0\times10^{-6}$ mol·L$^{-1}$

**Figure 2** Absorption spectra




$c_{Au} = 4.9\times10^{-9}$ mol·L$^{-1}$,
$c_{propranolol} = 3.0\times10^{-6}$ mol·L$^{-1}$

**Figure 3** The TEM micrographs of gold nanoparticles in the absence (left) and presence (right) of propranolol, $c_{Au} = 4.9\times10^{-9}$ mol·L$^{-1}$, $c_{propranolol} = 3.0\times10^{-6}$ mol·L$^{-1}$




The effects of pH, concentration of gold nanoparticles, reaction time and addition sequence were investigated according to the enhancement of the RLS intensity ($\Delta I_{RLS}$) between sample ($I$) and blank ($I_0$) at $\lambda$ = 560 nm.. Different kinds of buffer were applied to the experiments and Hasting-Serdroy buffer was selected. The $\Delta I_{RLS}$ attained the maximum when pH was 5.9. The effect of the concentration of gold nanoparticles in the range of 1.6 ~ 14.3 nmol·L$^{-1}$ on $\Delta I_{RLS}$ was studied, and 4.9 nmol·L$^{-1}$ was chosen for further experiments. The experiments showed that the reaction was complete in 15 minutes and the RLS signals were stable for more than one hour. The addition sequence had no influence on the RLS intensity.

The interactions between gold nanoparticles and the other doping agents such as caffeine, furosemide, spironolactone, hydrochlorothiazide, methyltestosterone, testosterone, benzthiazide and acetazolamide were investigated. No color change and gold nanoparticles aggregation were observed, which elucidated that the method is selective. To the system of propranolol and gold nanoparticles, when the concentration of propranolol was higher than $1.0 \times 10^{-6}$ mol·L$^{-1}$, the color of the solution changed immediately and the RLS signals increased greatly. When the concentration was lower than $1.0 \times 10^{-6}$ mol·L$^{-1}$, it needed long time to observe the change of color and the color change was not obvious. The effects of foreign substances such as metal ions, negative ions and amino acid on the RLS intensity were studied. The result indicated that these substances had no interference.

The method was applied to determine propranolol in urine dealt with SPME. All extraction was performed with a 10 mL amber vial that contained a magnetic spin bar. A 10 μL aliquot of the standard propranolol solution (10 mg·mL$^{-1}$), 4 mL urine sample and 1.6 g NaOH were mixed, and the sample was saturated with NaCl and then was sealed into the vial with a septum-type cap. The SPME needle pierced the septum and the fiber was extended through the needle into the sample. After stirring at 90 $^0$C for 30 minutes, the fiber was withdrawn into the needle, removed from the septum, then subjected to desorption in 20 μL methanol for 30 minutes at room temperature. After evaporation of the solvent of the eluent, appropriate amount of water was added to dissolve the resulting residue. Contrast to the sample without propranolol, obvious color change could be observed, which demonstrated the applicability of the proposed method.

## Acknowledgments

The authors acknowledge the support from the National Natural Science Foundation of China (No. 20275028), 973 Program (No. 2002CB2118) and 863 Program (No. 2002AA2Z2004).

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Received 16 Augest, 2004