

## **Supplementary Information**

### **Plasmon-mediated N-dealkylation instead chiral discrimination of propranolol drug adsorbed on gold nanoparticles**

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## Chemicals

To synthesize gold nanoparticles (GNPs) and modify its surface, the following reagents were used: hydrogen tetrachloroaurate trihydrate (Aurat), silver nitrate (Silver salt), tri-sodium citrate 5.5-hydrate (Vekton), sodium borohydride (Sigma-Aldrich), ascorbic acid (Sigma-Aldrich), cetyltrimethylammonium bromide (CTAB) (BLDpharm), 6-mercapto-6-deoxy- $\beta$ -cyclodextrin (SH- $\beta$ -CD) (BLDpharm), L-cysteine (J&K Scientific), sodium polystyrene sulfonate (Sigma-Aldrich) (PSS), average  $M_w \approx 70,000$  g/mol, poly-(diallyldimethylammonium chloride) (PDDA) (BLDpharm), average  $M_w \approx 250,000$  g/mol.

The studied beta-blockers (propranolol hydrochloride (PL), amlodipine (AN), and carvedilol (CL)) were purchased from Sigma-Aldrich. Sodium azide used in the immersion experiment was purchased in Dia-m.

In capillary electrophoresis experiments, the following reagents were used to prepare buffers and background electrolytes: sodium dihydrogen phosphate (Vekton), sodium hydroxide (Reakhim), hydrochloric acid (Reakhim), phosphoric acid (Reakhim), 2-hydroxypropyl- $\beta$ -cyclodextrine (HP- $\beta$ -CD) (Sigma-Aldrich),

In liquid chromatography, the following solvents were used: formic acid (Khimmed), acetonitrile (Khimmed),

All reagents were used without further purification. All aqueous solutions were prepared with deionized water with resistivity 18.2 MOhm·cm (Milli-Q Reference, Millipore).

## General laboratory equipment

During GNPs preparation, modification, centrifugation, and subsequent analysis of supernatant and pellet the following equipment was used: automatic micropipettes (Sartorius, Germany), analytical balance Shimadzu AUW (Shimadzu, Japan), magnetic stirrer C-MAG HS 7 (IKA, Germany), centrifuge 5430 (Eppendorf, Germany), high speed centrifuge 2236R (Gyrozen, South Korea), pH-meter 211 (Hanna Instruments, USA), deionizer Milli-Q Reference (Millipore, France), multi vortex V32 (Biosan, Latvia), ultrasonic bath (Kristal, Russia).

### **Instrumentation and analysis conditions**

Ultraviolet-visible (UV-Vis) absorption spectra of GNPs dispersions were recorded on a UV-1800 spectrophotometer (Shimadzu, Japan). All spectra were measured at room temperature in a quartz cell with optical pathway of 1 cm and spectral resolution of 1 nm.

Transmission electron microscopy (TEM) images were obtained with a Libra 200FE microscope (Carl Zeiss, Germany) at an accelerating voltage of 200 kV. TEM images in scanning mode were taken from at least three random domains. In order to prepare the samples for TEM measurements, 10  $\mu$ L of nanoparticles dispersion was drop casted on top of carbon films and air dried.

Zeta potentials were measured based on laser Doppler microelectrophoresis with a Zetasizer Nano ZS (Malvern Instruments Ltd., Great Britain). The refractive index value of 0.27 was used for gold in Smoluchowski equation. The viscosity of solvent was set as 0.887 cP for water and refractive index was set as 1.33.

Surface-enhanced Raman scattering SERS spectra of GNPs dispersion were recorded using a Senterra (Bruker, USA) spectrometer at the excitation with a 785 nm laser and power at a sample of 20 mW. The spectra were registered in four acquisitions and 40 s accumulation time.

A capillary electrophoresis system Capel-205 (Lumex, Russia) equipped with spectrophotometric detector (190 – 400 nm) and a water-cooling cassette ( $\pm 0.1$  °C) for the capillary was used in the electrophoretic experiments. Dimensions of bare fused-silica capillaries were 50 mm (id)  $\times$  375 mm (od). The lengths of the used capillary to the detector were 53.0 cm with a total length of 60.0 cm and 68.0 cm with a total length 75.0 cm. Processing was carried out using the Elforan-205 software (Lumex, Russia).

High performance liquid chromatography (HPLC) was performed with a chromatographic column Inspire 3  $\mu$ m Phenyl-hexyl, 150 $\times$ 2.1 mm from Dikma (China) was utilized, operating at T = 40 °C. The eluents consisted of two mobile phases: mobile phase A consisted of aqueous formic acid (100:0.1, v/v), mobile phase B consisted of acetonitrile/formic acid (100:0.1, v/v). The gradient profile was: holding for 3 min on 20% phase B, followed by 3.0 – 10.0 min from 20 to 90% of mobile phase B, then holding for 2.0 min on 90% mobile phase B for washing the column. This was succeeded by gradient back to 80% mobile phase A and 20% mobile phase B from 12.0 – 12.1 min to re-equilibrate. Total analysis run time was 16 min. The needle wash solvent consisted of 50 % 2-propanol in water. The eluents flow rate was set at 0.300 mL/min.

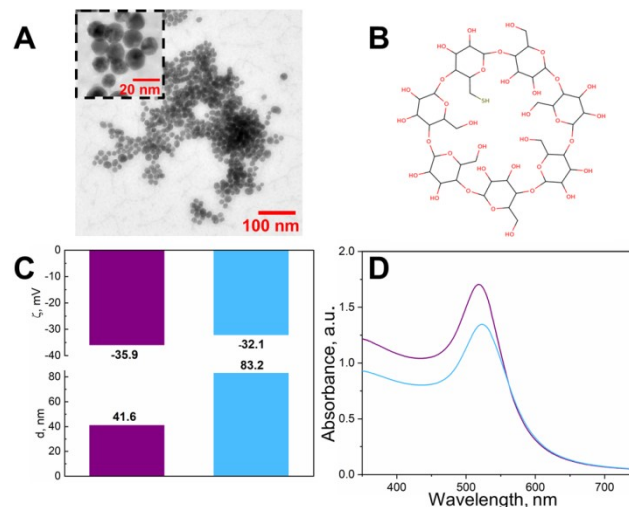
Liquid chromatography with mass spectrometric detection (LC-MS) was performed on a LCMS-9030 instrument (Shimadzu, Japan) with LC-30 AD binary pump, SPD-M20A diode array detector, SIL-30AC cooling autosampler, CTO-20A coupled thermostat. The electrospray interface source of triple quadrupole mass spectrometer was utilized in the positive ion mode and operated with a spray voltage set at 4.50 kV. The temperature of nitrogen and flow rate were set at 400 °C and 10 L/min, respectively. Identification was conducted with scanning, single ion and product ions monitoring modes. Nitrogen was used as collision gas.

Time-of-flight mass spectrometer "MaXis" (Bruker, USA) was applied for high-resolution electrospray ionization mass spectrometry (HR-ESI-MS). A sample was directly injected into mass spectrometer with electrospray ionization source in positive polarity mode. Nitrogen was used as a drying gas (180 °C) with flow of 3 L/min. Capillary voltage was 4.5 kV.

### **Gold nanoparticles synthesis and characterization**

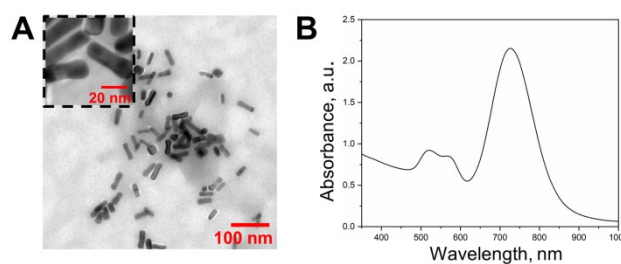
Spherical gold nanoparticles were synthesized through reduction of hydrogen tetrachloroaurate by sodium citrate according to the known procedure<sup>1</sup> adapted to the present study. 50 mL of a 1 mM hydrogen tetrachloroaurate solution were poured in a flat bottom round flask equipped with a reflux condenser and brought to a boil. Then, 5 mL of a 38.8 mM sodium citrate solution were quickly poured into the flask under vigorous stirring. The boiling was continued for 10 min then the solution was cooled to a room temperature under gentle stirring.

Size, zeta potential and UV-Vis spectra of as-prepared GNPs synthesized through gold reduction by citrate corresponded to the conventionally observed for such GNPs (**Fig. S1**). The decreasing of zeta potential and increasing of hydrodynamic radius with a slight shift in the absorption band indicated the success of the modification of GNPs. Neutral molecules of thiolated  $\beta$ -cyclodextrine partially replace citrate anions of GNP sphere that leads to a decrease in surface potential.



**Fig. S1** TEM image of bare gold nanoparticles (A); Structure of 6-mercapto-6-deoxy- $\beta$ -cyclodextrin (B); Zeta potential, hydrodynamic diameter (C) and UV-Vis spectra (D) of GNPs before (purple) and after (blue) modification.

Rod-shaped GNPs, used in the comparative experiment, were synthesized according to the seed-mediated method described elsewhere<sup>2</sup>. A seed solution was obtained by mixing 0.25 mL of 10 mM hydrogen tetrachloroaurate solution with 7.5 mL of 0.1 M CTAB, followed by addition of 0.60 mL of ice-cooled 10 mM sodium borohydride solution. This seed solution was placed in a thermostatically controlled water bath and incubated at 30 °C for at least 2 h until the next use. The growth solution was a mixture of 47.5 mL of 0.10 M CTAB solution, 2 mL of 10 mM hydrogen tetrachloroaurate solution, 0.32 mL of 0.1 M ascorbic acid and 0.4 mL of 10 mM silver nitrate. A few minutes after the addition of 0.1 mL of seed solution to the growth solution, it showed, a development of color, indicating the formation of CTAB-capped gold nanorods. The obtained dispersion of gold nanorods was purified from excess CTAB by double centrifugation. TEM image and UV-Vis spectrum of the obtained gold nanorods are represented in Fig. S2.



**Fig. S2** TEM image (A) and UV-Vis spectrum (B) of gold nanorods.

## References

- [1] K.C. Grabar, R.G. Freeman, M.B. Hommer, M.J. Natan, Preparation and characterization of Au Colloid Monolayers, *Anal. Chem.* 67 (1995) 735–743. 10.1021/ ac00100a008.
- [2] A. Yoshida, N. Uchida, N. Kometani, Synthesis and Spectroscopic Studies of Composite Gold Nanorods with a Double-Shell Structure Composed of Spacer and Cyanine Dye J-Aggregate Layers, *Langmuir*. 25(19) (2009) 11802–11807. 10.1021/ la901431r.