Electronic Supplementary Material (ESI) for Analytical Methods

Electronic Supporting Information

Label-free SERS detection of coralyne using aptamer modified $Au@SiO_2$ core/shell nanoparticles

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Part S1 Experimental section

Preparation of SERS-active silica-Au/core-shell nanoparticles

At first，silica nanoparticles were prepared at 20℃ according to the Stober methods[1]. Briefly, ammonium solution (30 wt%) of 3 mL was mixed with 50 mL ethanol, and 1.5 mL TEOS was added. Then the solution was slowly stirred overnight. An excess of APTMS (200 μL) was added to the prepared silica nanoparticles solution (10 mL), and the solution was slowly stirred overnight. To enhance the covalent binding of APTMS with the surface of silica, the mixed solution was gently heated at 75℃ for 2h, and ethanol was added continuously to keep the total volume of solution constant. The APTMS modified silica nanoparticles were then washed using ethanol three times by centrifugation and ultrasonication and dispersed into pure ethanol (6 mL).

Next, gold seeds of 1-3 nm in diameter were prepared using the method developed by Duff et al[2]. To prepare gold seeds of 1-3 nm in diameter, 0.5 mL of 1.0 M NaOH was added to 45 mL of ultrapure water, followed by the addition of 1.0 mL THPC (50 mmol/L aqueous solution). The mixed solution was stirred for 5 min and then 36 μL of 1.0 M $HAuCl_4 3H_2O$ was added. The color of solution immediately turned to brown. After 15 min of stirring, the solution was stored at 4℃ for one week.

Then, the APTMS modified silica nanoparticles (150 μL) were added to the undiluted gold seeds solution (12 mL). The mixed solution was gently shaken by hand for 10 min and kept without interruption for 12h. The silica-gold seeds colloids were washed by ethanol and water successively and dispersed into ultrapure water (4 mL).

At last, in a reaction flask, 25 mg K_2CO_3 was added into 100 mL ultrapure water with stirring for 10 min, followed by adding 36 μL of 1.0 M $HAuCl_4 3H_2O$. The

solution turned out to be colorless in 30 min and the mixture was aged for three days before use. The colloid containing silica-gold seeds (150 μL) was injected to 10 mL of the colorless solution under vigorous stirring and 10 μL of formaldehyde was added immediately. The mixture color changed gradually from firstly purple to blue and then to green in 30 min, and the reaction of solution was finally stopped through centrifugation. The final silica-Au/core-shell nanoparticles were dispersed in ultrapure water (6 mL) for long time storage.

Immobilization of SiO_2@Au core/shell nanoparticles on quartz slides

Quartz glass was chosen as supporting substrate because of its low Raman spectral interference. Quartz slides were first submerged in a fresh prepared piranha solution (H_2SO_4:H_2O_2=3:1) for 2h at 80^{o}C, and then rinsed with dry ethanol and ultrapure water, and dried with nitrogen gas flow. Then the quartz slides were submerged in a 20 mL solution of APTMS （1 μL of APTMS per 1mL water）for 15 min, and then were removed from the APTMS solution, were rinsed with ethanol and water, and were dried with nitrogen gas flow. Afterwards, the quartz slides were submerged in an concentrated Au nanoshell suspension overnight. The SiO_2@Au core/shell nanoparticles were then distributed homogeneously on the quartz slide through self-assembly.

Fabrication of aptamer modified SERS substrate

The thiol-modified oligonucleotide was incubated in 10 mM triscarboxyethylphosphine (TCEP) in TE at pH 7.4 for 2h at room temperature, and then desalted through NAP-5 (GE healthcare) to remove excess TCEP and ionic compound. The final concentration of ssDNA was 20 μM determined by absorbance at 260 nm. The purified DNA was then heated to 90℃ for 5-10 min in water bath and then cooled in ice bath immediately. 5 μL pretreated ssDNA water solution dropped on the freshly prepared substrate under wet condition at 4℃. The samples were then kept in fridge overnight.

The ssDNA modified substrates were rinsed with pure water to remove

unbounded ssDNA and dried with flow of nitrogen gas. The substrates were then immersed in 10 nM MCH water solution for 4h, with MCH working as a spacer to remove the non-covalently attached ssDNA. Finally, the substrates were rinsed with pure water several times and dried with nitrogen gas flow.

Measurement of SERS spectra

For detection of coralyne, the ssDNA modified Au substrates were immerged in coralyne solutions with various concentrations for 8h. This step was followed by rinsing with pure water to remove nonspecifically bound coralyne. The coralyne treated substrates were dried naturally at room temperature before Raman measurements. The SERS spectra were acquired from XploRA Raman microspectrometer（Horiba Jobin Yvon）with a 785 nm laser and an Olympus 50× objective was used. The beam focus spot was within 10 μm in diameter and the laser power applied on the sample was approximately 0.2 mW. The acquisition time was 30-45 s for recording Raman spectrum of each measuring point.

Fig. S1 shows that the size of the SiO_2@Au core/shell nanoparticles can be adjusted so that the surface plasmon resonance (SPR) peak shifts from 530 nm to 750 nm. For the SiO_2@Au core/shell nanoparticles with absorption at 750 nm, optimized SERS effect can be obtained with 785 nm laser for exciation due to the electromagnetic enhancement (EM) mechanism.

Figures S1 to S5

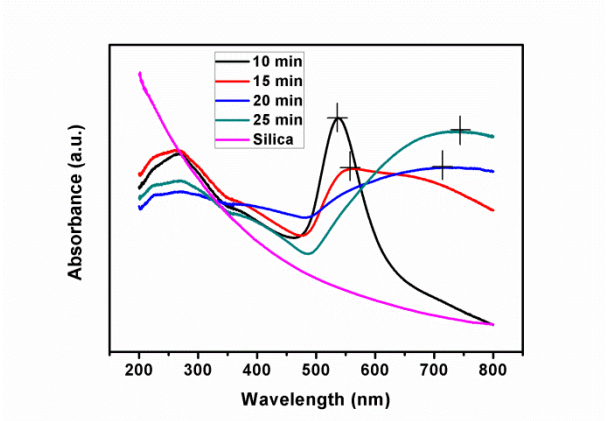

Fig. S1. UV-visible extinction spectra of different silica-Au/core-shell nanoparticles, which were obtained by controlling reaction time and molar ratio of reaction chemicals. Different curves in the figure correspond to different reaction times.

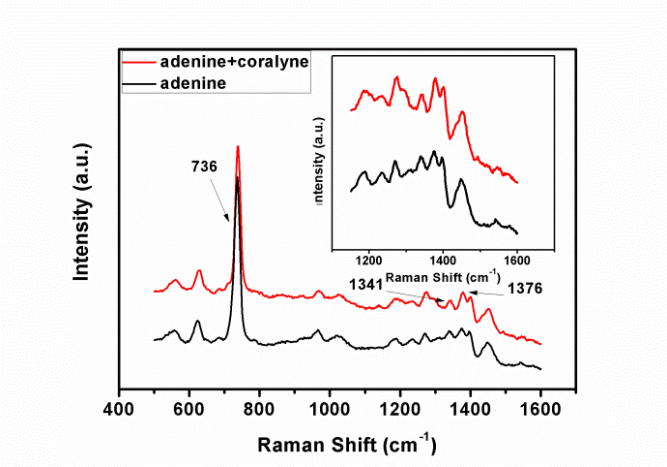

Fig. S2. SERS spectra of adenine before and after addition of coralyne.

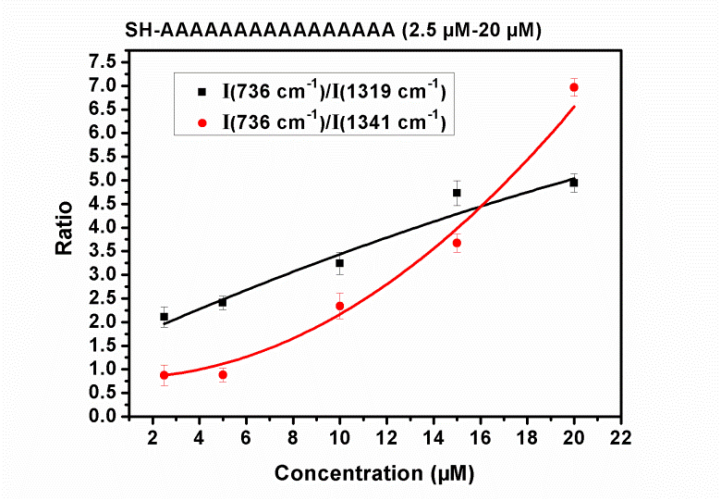

Fig. S3.The fit of the Raman intensity ratio of I(736 cm^{-1})/I(1319 cm^{-1}) changing with concentration of the ssDNA aptamer.

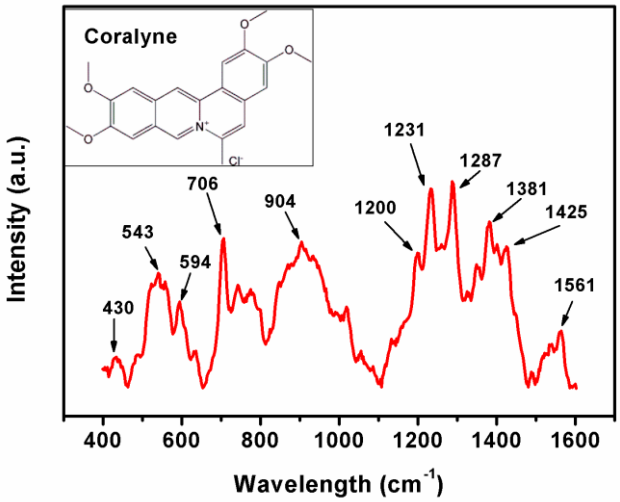

Fig. S4. The SERS spectrum of coralyne of 100 μM in aqueous solution. This spectrum is an average of ten spectra collected from different spots from the same sample.

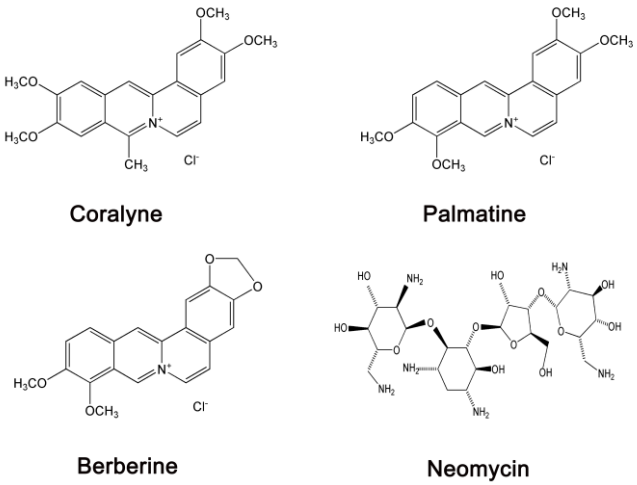

Fig. S5. The molecule structures of all the drug molecules. The molecular structures of palmatine and berberine are similar to that of coralyne, while neomycin as a DNA binder posseses the similar function as coralyne.

References

1. W. Stöber, A. Fink and E. Bohn, *J. Colloid Interface Sci.*, 1968, **26**, 62.

2. D. G. Duff and A. Baiker, *Langmuir*, 1993, **9**, 2301.