ENANTIOSELECTIVE SERS DETECTION USING CHIRAL AU HELICOIDS

[1]Andrea TOSOVSKA, [1]Anastasia SKVORTSOVA, [1]Vaclav SVORCIK, [1]Oleksiy LYUTAKOV

[1]Department of Solid State Engineering, University of Chemistry and Technology, Prague, Czech Republic, EU, tosovska@vscht.cz

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Abstract

The interaction between light and matter can be significantly enhanced through the excitation of surface plasmons and related nanospace-restricted focusing of light energy. The local enhancement of light energy is especially pronounced in the case of so-called plasmonic hotspots, which have found wide application in surface-enhanced Raman spectroscopy (SERS). This work focuses on the preparation and utilization of ordered array of chiral gold nanoparticles. The nanoparticles used have unique helical shapes with chirality encoded in each individual nanoparticle. An ordered layer of Au helices with a consistent gap between nanoparticles on a plasmon-active gold grating was fabricated. The created structure was able to support the excitation and propagation of surface plasmon-polaritons and local plasmons. Chiral molecules of the analyte(s) were placed between Au helicoids (i.e., in the place of the plasmonic hot spots). The influence of the chiral dielectric „spacer“ (i.e., added chiral molecules) on the intensity of the local electric field and the SERS response of the enantiomers was investigated. A significant difference in the enhancement of SERS signal from enantiomers was observed, depending on the interplay of helicoids chirality and analytes chirality.

Keywords: Nanoparticles, gold nanoparticles, SERS, plasmon

1. INTRODUCTION

The chiral nature of molecules represents a fascinating aspect of chemistry and biochemistry, ranged from deeper understanding of molecular interactions to the potential for use in various practical applications. Considering the different impact and properties of opposite enantiomers the ability to distinguish between enantiomers is the key concept in analytical chemistry. Enantiomers can be distinguished using 3D nanostructures that interact differently with polarized light based on their shape.[1]

In this work, we used plasmon-active nanoparticles with specific shape, where chirality is encoded in each individual particle. The main advantage of such structures is their ability to support chiral plasmonic distribution in the near field, thanks to the unique shape of the particle, offering numerous benefits.[2]

Chiral plasmonic nanostructures are gradually being integrated into the field of Surface-enhanced Raman Spectroscopy (SERS).[3] In the pharmaceutical industry, SERS provide sensitive means for distinguishing between drugs and bio-active molecules, which in crucial for ensuring its efficacy and safety. In addition, enantioselective SERS discrimination offers an elegant method for rapidly obtaining structural and optical information related to molecular steric conformation, even in cases of low analytic concentrations or small sample volumes.[2]

The effort to precisely distinguish enantiomers using Raman spectroscopy has a relatively long history, beginning with the SEROA (Surface Enhanced Raman Optical Activity) technique. Recently, various strategies have been developed for the enantioselective capture of target analyte molecules on plasmon-active surface for subsequent SERS measurement and enantioselective discrimination.[3] Although these approaches are well-studied and sometimes yield satisfactory results, they have limitations mainly related to the lack of universality. In such instances, the use of chiral nanostructures capable of supporting localized plasmon should

be considered.[4] It is well known that the intensity and strength of the local plasmonic wave depend on the coupling of plasmon-active nanostructures, which is influenced by the gaps between the nanostructures and the surrounding dielectric environment. Since plasmonic nanostructures create chiral plasmonic fields, it can be supposed that local values of plasmonic energy will be directed by the chirality of the surrounding dielectric environment. In this context, improved coupling and higher values of the local electric field are expected when the plasmonic chirality aligns with the chirality of the environment. However, this phenomenon may also have another effect – an optically active dielectric environment with appropriate chirality will exhibit a higher local electric field value, thereby enhancing its SERS response.[5]

2. EXPERIMENTAL

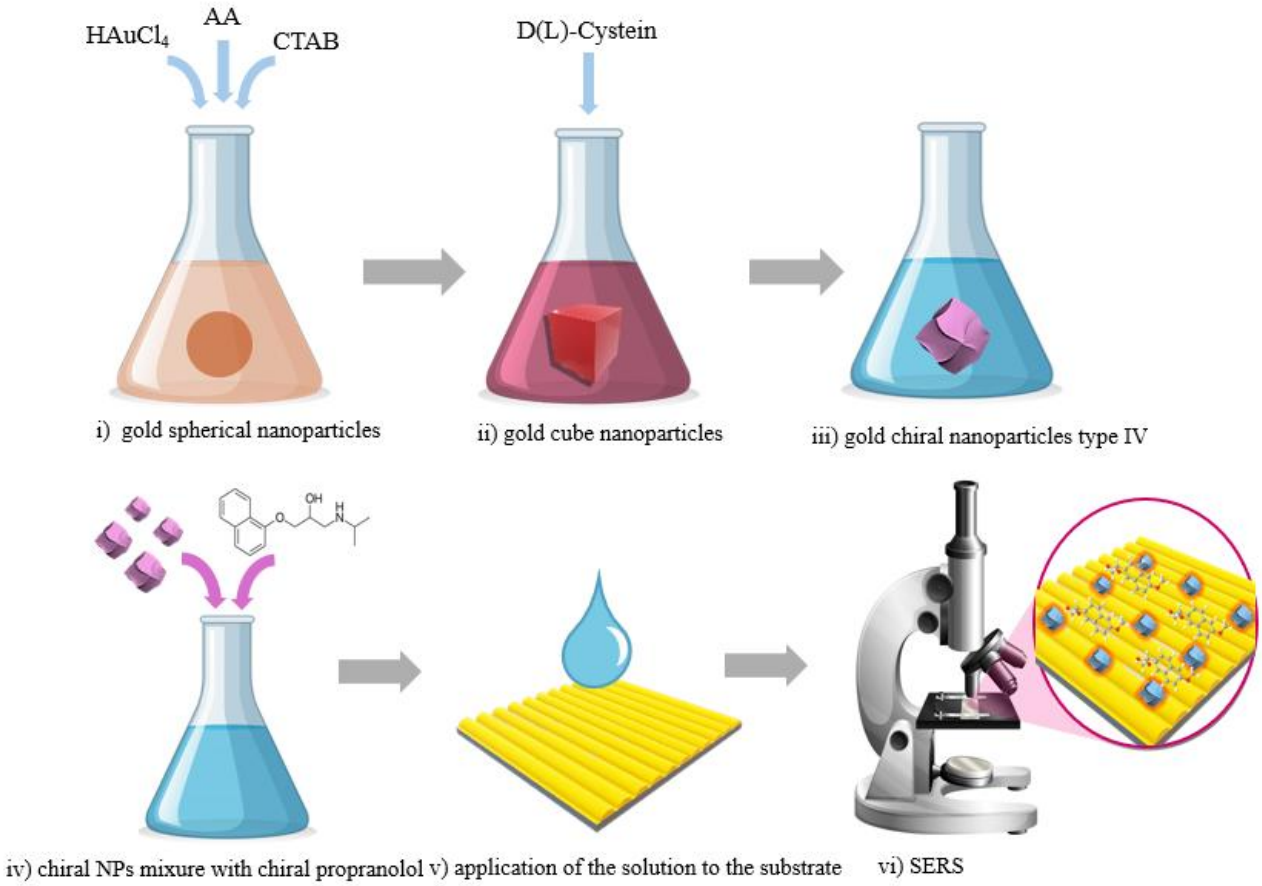

Figure 1 Schematic representation of the gold NPs synthesis and sample preparation for SERS measurement

In the initial phase of the synthesis (**Figure 1**, steps i–iii), chiral gold nanoparticles (type IV) were prepared. Step i) involved the synthesis of cubic gold nanoparticles by adding a growth solution, containing HAuCl4, ascorbic acid, and CTAB, to a solution of spherical gold nanoparticles. This step resulted in a colour change of the solution from brown to pink. Step iii) is the critical step in synthesizing chiral gold nanoparticles and forming type IV chiral structures. In this step, the growth solution along with one of the enantiomers of cysteine was added to the cubic nanoparticles. This reaction was accompanied by a colour change of the solution from pink to blue. Ascorbic acid acted as a reducing agent, converting Au3+ to Au+, while CTAB served as a stabilizer. By blocking the surface of the cubic nanoparticles, chiral cysteine facilitated the formation of chiral gold nanoparticles of type IV.

Step iv) details the preparation of the sample. The chiral analyte, specifically propranolol, was mixed with a solution containing chiral gold nanoparticles at a predetermined concentration.

Then, the solution prepared in step iv) was drop deposited on the substrate made from DVD disc (step v). Before this, the textured side of the disc was cleaned with ethanol, then coated with gold using vacuum sputtering (40 mA for 350 seconds). Once the drop had dried, the sample was ready for surface-enhanced Raman spectroscopy (SERS) measurements (step vi).

3. RESULTS AND DISCUSSION

3.1 Characterization of nanoparticles

3.1.1. Cubic nanoparticles

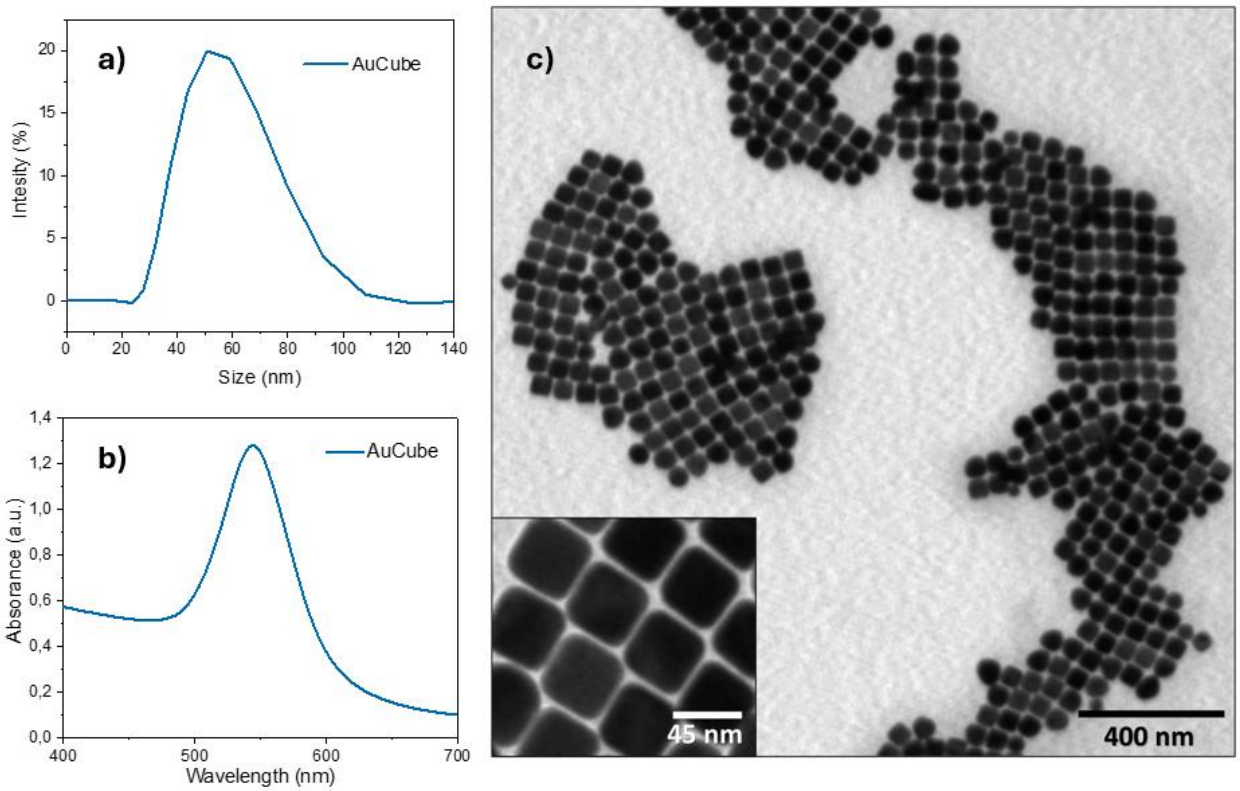

Figure 2 Characterization of cubic nanoparticles: a) DLS spectrum, b) UV-Vis spectrum, c) TEM image

Figure 2 illustrates the characterization of cubic gold nanoparticles (see **Figure 1**, step ii). The size of the cubic nanoparticles was analysed using dynamic light scattering (DLS). In **Figure 2a**, the DLS graph indicates that the predominant particle size in the solution ranges from 45 to 60 nm. **Figure 2b** presents the UV-Vis spectrum of the cubic nanoparticles, displaying an absorption maximum at 548 nm. Similar absorption maxima, such as 550 nm and 554 nm, are reported in other publications. [6]

The morphology of cubic gold nanoparticles was examined using transmission electron microscopy (TEM). **Figure 2c** displays the TEM image of the nanoparticles, revealing an approximate size of 55 nm. When comparing this to **Figure 2a**, it is evident that the sizes measured by DLS are very similar to those obtained from TEM.

3.1.2. Chiral nanoparticles type IV

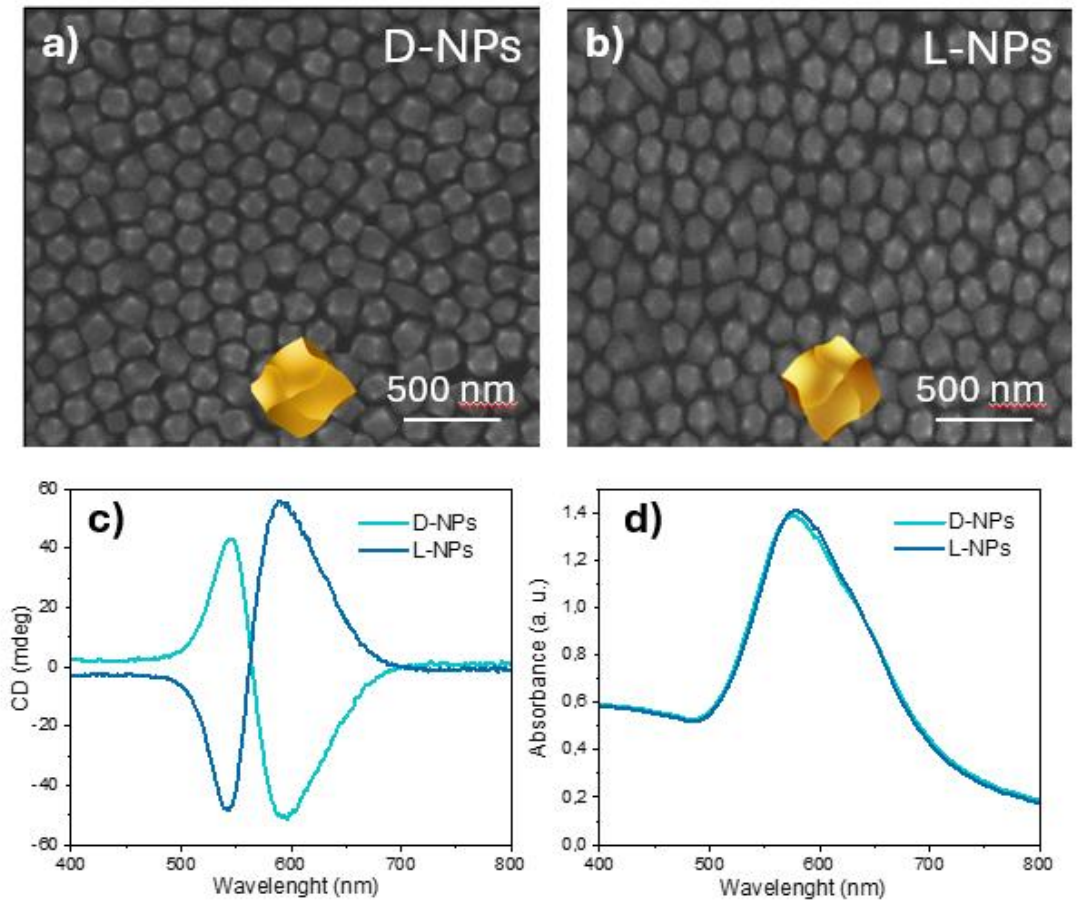

Figure 3 Characterization of chiral nanoparticles type IV: a) SEM image D-NPs, b) SEM image L-NPs, c) CD spectrum chiral NPs, d) UV-Vis spectrum chiral NPs

The characterization of chiral nanoparticles (prepared during step iii, depicted in **Figure 1**) is presented in **Figure 3**. The morphology of these nanoparticles was investigated using scanning electron microscopy (SEM). Notably, chirality is encoded in each particle due to their distinctive shapes. **Figure 3a** shows D-chiral nanoparticles, which exhibit a left-to-right twisting morphology. Conversely, **Figure 3b** illustrates L-chiral nanoparticles, characterized by a right-to-left twisting structure.

Chirality was confirmed using circular dichroism, as shown in **Figure 3c**. The signal strength for type IV chiral nanoparticles is in the range of 45-50 mdegs for both variants (D and L), indicating a high response. Furthermore, it can be observed that the graphs exhibit axial symmetry, suggesting that chiral nanoparticles efficiently absorb left or right handled light, depending on the nanoparticles shape.

Figure 3d presents the UV-Vis spectrum, showing an absorption maximum at 600 nm. In comparison to **Figure 2b**, this maximum has shifted from 548 nm to 600 nm. Similar absorption maxima can be found in other publications.[6]

3.2 SERS measure

The premise for SERS measurements was that chiral gold particles would react differently with various enantiomers. One enantiomer was expected to demonstrate a stronger response with D-NPs than with L-NPs, and vice versa.

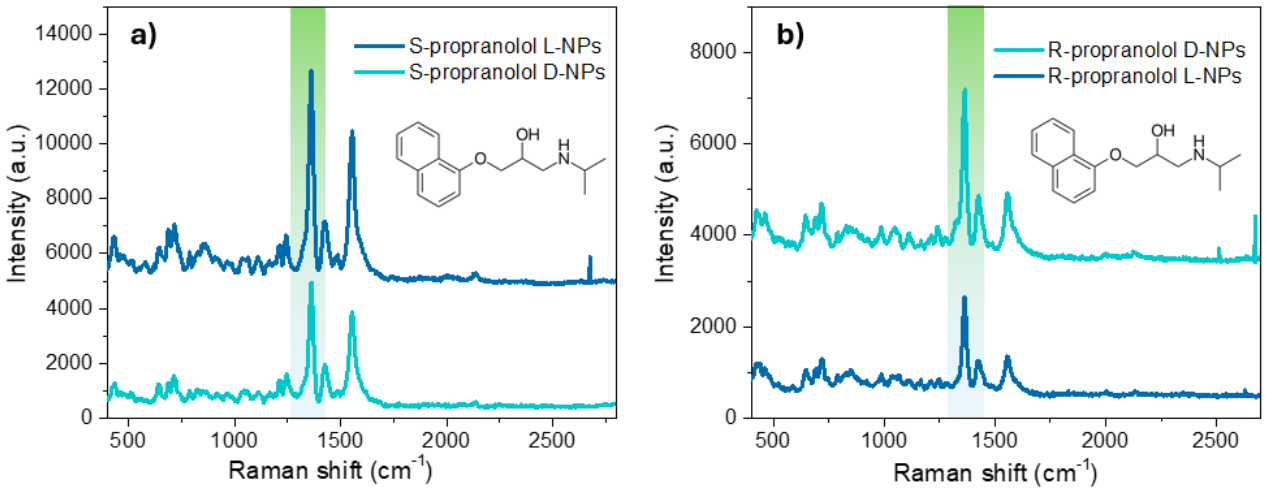

Figure 4 SERS spectrums: a) S-propranolol with chiral NPs, b) R-propranolol with chiral NPs

Figure 4a illustrates the spectra of the enantiomer (S)-(-)-propranolol combined with D and L nanoparticles. A significant signal enhancement is observed at the peak of 1350 cm^{-1}, with greater enhancement noted for the combination of L nanoparticles with (S)-(-)-propranolol. In contrast, the combination of D nanoparticles with (S)-(-)-propranolol results in a considerably lower SERS response.

Figure 4b presents the spectra of the enantiomer (R)-(+)-propranolol on substrates with L and D nanoparticles. Similarly, an increase in intensity at the same peak of 1350 cm^{-1} is observed, with more pronounced signal enhancement occurring in the combination of D nanoparticles with (R)-(+)-propranolol compared to the combination of L nanoparticles with (R)-(+)-propranolol.

Comparing the results, it is evident that the combination of (S)-(-)-propranolol with L nanoparticles and (R)-(+)-propranolol with D nanoparticles leads to higher peak intensity enhancement than the reverse combinations, allowing in this way enantioselective SERS discrimination.

4. CONCLUSION

This study investigated the use of chiral gold nanoparticles for enantioselective drug detection via surface-enhanced Raman spectroscopy (SERS). Enantioselective SERS detection was achieved by arranging chiral Au helicoids in grooves of a plasmon-active grating, ensuring homogeneous distances between the nanoparticles. The use of the plasmonic grating as a template for the self-assembly of nanoparticles also provided additional advantages from the excitation of surface plasmon polaritons (SPP) at the surface of the grating. Consequently, a significant difference in SERS signal intensities was observed for the enantiomers (S)-(-)-propranolol and (R)-(+)-propranolol using the arranged L or D gold helicoids. These differences were attributed to the varying strength of plasmonic coupling (under conditions of equal distances between the organized nanoparticles), which depends on the chirality of the dielectric gap in the plasmonic hot spot between the nanoparticles. Overall, it can be concluded that the combination of chiral nanoparticles and surface-enhanced Raman spectroscopy holds great potential for enantioselective detection and may lead to significant advancements in pharmaceutical research and other applications.

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