The adsorption of rifampicin on gold or silver surfaces mediated by 2-mercaptoethanol investigated by surface-enhanced Raman scattering spectroscopy

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ABSTRACT

In this work the adsorption of the antibiotic rifampicin (RP) on the surface of gold (AuNP) or silver nanoparticles (AgNP) was investigated using both surface-enhanced Raman scattering (SERS) and surface-enhanced resonance Raman scattering (SERRS) spectroscopies. Such spectra were obtained in the absence and presence of the surface modifier 2-mercaptoethanol (ME) using excitations by laser radiations of 532, 632.8 and 1064 nm wavelengths. The use of different conditions under the presence of ME led to changes in the spectral pattern ascribed to the influence of resonance Raman (RR) effect and distinct chemical interactions of RP with the metallic surfaces. The sensibility of the chromophoric moiety, i.e. a <pi>-conjugated orbital, to the adsorption geometries, which can be controlled by surface modifiers, impacts the RR effect. Theoretical models involving RP and metal atoms were obtained from Density Functional Theory (DFT) calculations, and used for supporting the vibrational assignment.

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1. Introduction

Gold (AuNP) or silver nanoparticles (AgNP) modified by biomolecules have been widely used for different applications as drug delivery [1], biosensors [2,3], antimicrobial actions [4] and theragnosis [5]. The study of the interactions of biomolecules with silver or gold surfaces is relevant for understanding the behavior of corresponding nanoparticles with biological systems in both *in vitro* and *in vivo* conditions [6]. In this context, the surface-enhanced Raman scattering spectroscopy (SERS) is an outstanding technique for studying the anchor site of this biomolecules adsorbed on such metallic surfaces [7]. Moreover, the chemical properties of these surfaces can be controlled by surface modifiers as polymers [8], organic ions [9–12], and mercaptans [13]. In

particular, 2-mercaptoethanol (ME) can be used to control the adsorption of organic adsorbates on silver or gold surfaces. Hong et al. [14] showed that the modification of gold surface by ME promotes an enhancement of the SERS spectra of cyclohexanol and 1,3-cyclohexanediol, which adsorbs weakly on the gold surfaces, while for benzoic acid, known for its strong interaction with the gold surface, it was not observed SERS enhancement. Tarabara et al. [15] studied the modification of citrate-reduced AgNP with ME using β-carotene as a probe molecule. The authors verified that the chemical modification of the AgNP surfaces provides favorable conditions for increasing the number of adsorption sites. Such few examples show the potential capability of ME to interfere in SERS experiments as surface modifier of silver or gold surfaces.

Rifampicin (RP) is a very important antibiotic used in the treatment of tuberculosis [16], brucellosis [17,18] and in a wide range of persistent infections. The biological activity of RP involves the inhibition of prokaryotic DNA-dependent RNA polymerases [19]. The resonance Raman (RR) spectra of RP with the corresponding excitation profiles and the surface-enhanced

resonance Raman scattering (SERRS) spectra of RP, rifamycin and rifaximin with adsorption proposal based on the vibrational assignment are reported [20,21]. The influence of pH on the adsorption mechanism of RP on AgNP was studied by UV-VIS, RR and SERRS spectroscopies [22]. The authors showed that the spectral pattern of adsorbed RP changes with protonation condition, being very similar to the RR spectrum at lower pH. The SERS spectra of RP on silver surfaces, involving interactions with lauric acid, DMSO and magnetite nanoparticles were reported [23], and the vibrational assignment allowed to infer RP adsorbs without interactions with the surface of SERS substrate.

In this work, the interactions of RP with AgNP and AuNP, modified or not by ME, were studied through SERS and SERRS experiments using exciting radiations with wavelengths of 532, 632.8 and 1064 nm. The vibrational assignments were proposed based on DFT calculations in appropriate protonation states, taking into account the pK_a values (Scheme 1). The influences of the surface modifiers ME and chloride ions on the SERS spectral patterns were investigated.

2. Experimental

2.1. Materials

The chemicals sodium borohydride ($\geq$99%), trisodium citrate dihydrate ($\geq$99%), silver nitrate ($\geq$99%), tetrachloroauric (III) acid ($\geq$99.9%), ME ($\geq$99%) and RP ($\geq$97%) were purchased from Sigma–Aldrich and used without additional purification.

Scheme 1. Optimized molecular structure of the RP, and structural formula with atomic labels.

Deionized water from a Milli-Q purification system, with resistivity of 18.2 MΩcm, was used in all aqueous solution preparations. All glass containers were cleaned, previously, using aqua regia solution, followed by copiously washing with deionized water.

2.2. Methods

The preparation of AgNP was done using borohydride as reducing agent and citrate as stabilizer of the colloidal suspension [24]. The synthesis of AuNP was based on the reduction of the metal by citrate in reflux conditions [25]. The UV-VIS-NIR of the RP, AuNP and AgNP aqueous suspensions were obtained in a Shimadzu spectrophotometer, operating in the range from 200 to 1100 nm, and using a quartz cuvette with pathlength of 0.5 cm. The SERS and Raman spectra were obtained from both a FT-Raman Bruker spectrometer, model RFS-100, equipped with a Ge detector, cooled by liquid nitrogen and a Nd/YAG laser with wavelength of 1064 nm, and a dispersive Raman spectrometer from Bruker, model Senterra, coupled with an Olympus optical microscope, equipped with a thermoelectrically cooled charge coupled device detector, laser lines with wavelengths of 532 and 632.8 nm, and using a 10$\times$ objective lens with NA = 0.25. The power of the exciting radiation in the SERS experiments were 0.2, 2 and 200 mW for the lines of 532, 632.8 and 1064 nm, respectively. The SERS spectra were obtained in AgNP and AuNP aqueous suspensions using final concentrations of RP in the range of 1.0–2.2×10^{-4} mol L^{-1}. The final concentrations of ME were in the range of 0.5–2.0×10^{-6} mol L^{-1}, and of KCl was 4.0×10^{-2} mol L^{-1}.
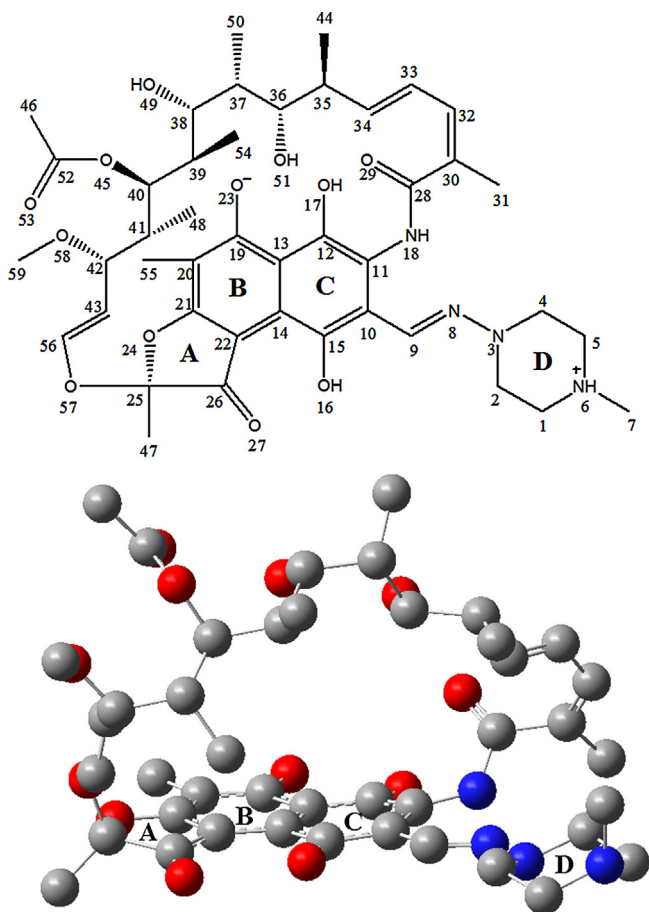
2.3. Computational details

Quantum mechanical calculations were performed to predict the structures and spectroscopic properties of RP and RP in AgNP and AuNP. The geometries were optimized in the gas phase using B3LYP DFT functional [26–28] with the 6-31G(d) basis set for all atoms, except for the Ag and Au atoms, for which the LANL2DZ [29–31] effective core potential was used. This calculation scheme is abbreviated as B3LYP/LANL2DZ/6-31G(d). The same level of theory was used for vibrational frequency calculation in order to analyze the vibrational normal modes and to characterize the structures as true minima on the potential energy surface. All calculations were performed using the Gaussian 09 program, Revision A.02 [32].

3. Results and discussions

Fig. 1 presents the analysis of RP interactions with AgNP and AuNP by UV-VIS-NIR spectroscopy. Fig. 1-A shows the spectra of RP in aqueous solutions and AgNP aqueous suspensions in the absence and presence of RP. The LSPR band from AgNP has a maximum at 390 nm with a long tail extended up to the near-infrared region that can be ascribed to a broad AgNP size distribution. Since the pH of the colloidal suspension is *ca.* 6.0, zwitterionic form of RP is the predominant species in solution [22]. The adsorption of RP on AgNP surfaces leads to the increase of the extinction between 500 and 650 nm, which can be ascribed to the formation of small AgNP clusters by changing the charge equilibrium in the metallic surface. Such clusters have plasmonic properties suitable for SERS experiments with excitation in the visible region.

Fig. 1B presents the UV-VIS-NIR spectra of the RP in aqueous solutions and AgNP aqueous suspensions in the presence of ME with and without RP. The adsorption of ME on AgNP surfaces, in submonolayer concentration, does not change significantly the spectral pattern of the LSPR band [33,34]. Nevertheless, the