Intermolecular interactions between cyclodextrins and pharmacetical compounds: a SERS study

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The investigation of pharmaceutical compounds by means of Raman spectroscopy has attracted much interest in the last years. The method allows getting information about structural properties of different molecules based on their specific vibrational structure. Nowadays Raman spectroscopy is gaining popularity in different areas of the pharmaceutical industry mainly due to its ability to provide information on the fundamental vibrational bands (the fingerprint region), offering a high degree of specificity in analysis. It also forms an ideal complement for existing methods of analysis such as nuclear magnetic resonance, mass spectrometry and elemental analysis.

On the other hand chiral recognition and differentiation in living organisms represents one of the most intriguing natural phenomena, which assures in the organism a high fidelity transfer of the molecular information. This phenomenon has a significant role in the pharmaceutical industry, since chirality plays a key role in the development of target drug candidates, being a structural variable parameter that needs elucidation. In this context, the subject of chiral purity gained a particular importance in the pharmaceutical industry.

In this presentation we will show that by taking advantage of the unique plasmonic properties of silver nanoparticles, the chiral separation of propranolol enantiomers was successfully studied and proved by Surface-Enhanced Raman Spectroscopy (SERS). The quantum chemistry calculations of native cyclodextrin - propranolol enantiomers complexes have been used as a further proof of the proposed interaction mechanism. We have observed (experimentally and theoretically) that β-cyclodextrin (compared with the other two classes of native cyclodextrins α and γ) had the best chiral recognition ability for propranolol enantiomers, hence producing the largest difference in the SERS spectra of propranolol enantiomers - native cyclodextrin complexes. The crucial role of this new chiral separation method is played by the colloidal silver nanoparticles. More precisely, the chiral recognition mechanism is based on the formation of different classes of inclusion complexes of propranolol and cyclodextrin and their selective attachment onto the silver nanoparticles. The plasmonic properties of the nanoparticles allowed the acquisition of specific SERS signals for the two propranolol enetiomers. In the specific case of R and S propranolol enantiomers, the naphthalene ring of R-propranolol fits better into the β-cyclodextrin cavity whereas in the case of the other two classes of native cyclodextrins γ-cyclodextrin gives only a partial enantiomeric separation whereas α -cyclodextrin shows no enantioselectivity. Computational chemistry based on DFT served as a tool for elucidating the underlying mechanism of molecular interactions responsible for chiral discrimination by giving important clues related to the evolution of the Raman peaks. The influence of several factors (nature and concentration of chiral auxiliary, selector/selectand, ratio, pH, interaction time, etc.) over the obtained SERS spectra was also successfully assessed.