Raman and SERS Investigations on Pharmaceuticals

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Today, the focus of medicine is on individualized diagnosis and treatment of patients. Although this path is still in its beginning, every small step in this direction will be a big step towards achieving this goal. To understand the behaviour of a molecule in various interactions in different environments, a complete analysis of its chemical and physical properties is required. Vibrational spectroscopic methods (Raman and FT-IR) combined with density functional theory (DFT) calculations are perfect tools for this purpose [1]. However, in some cases, weak Raman signal intensity and fluorescence interference make the use of Raman spectroscopy impossible. Surface-enhanced Raman spectroscopy (SERS) offers a possibility to overcome these drawbacks; it allows the detection of molecules at very low concentrations [2] due to the amplification of the Raman signal of species adsorbed on a metal surface. SERS spectroscopy is also used to understand the action of drugs as it is essential to identify any alteration of the adsorbed species structure relative to that of the free molecule. In these trials, the metal surface can serve as a mimic of a biological interface and, after elucidating the mechanism of adsorption of a molecule on this surface, the study can be extended to adsorption on membranes or other biological surfaces of interest for therapeutic treatments to imitate the adsorption of drugs occurring into the organism. Moreover, due to its high sensitivity and ability to detect analytes at low concentrations, SERS is an appropriate technique in therapeutic drug monitoring that could help physicians to use the optimal dose to achieve a more effective treatment tailored for each patient [3]. Taking into consideration the above-mentioned aspects we carried out in our group detailed vibrational investigations by means of FT-IR and Raman techniques coupled with DFT calculations on different pharmaceuticals such as anti-inflammatory drugs, antibiotics, tranquilizers and sedatives, chemotherapeutics, etc. to provide insights into their structure [4]. Furthermore, by analysing the SERS spectra, the adsorption behaviour *i.e.* chemisorption or physisorption, the adsorption site, the orientation of the adsorbed drug molecules on the noble metal surface, was elucidated. The influence of different factors such as pH value and concentration were investigated, and the lowest detectable concentration was also established. Despite its established sensitivity, SERS applied to quantitative analysis is still very challenging. To make the step towards clinical applications, it is necessary to obtain the same results regardless of location, equipment, or user and interlaboratory studies are currently the best way to achieve this. A recent study [5] involving 15 laboratories, including ours, was aimed to assess the reproducibility and trueness of a quantitative SERS method and to compare different methods. The study suggested that SERS is a method which can be consistently used by different laboratories if it is very well-defined. The tested methods produced a range of reproducibility results, but the best ones were reasonably reproducible, with an average standard error of performance as low as 12% and 13%. The obtained results were encouraging since different instruments were used over a wide time frame, with different setup and acquisition parameters. The next step should be the evaluation of each source of experimental uncertainty (*e.g.*, substrates, instruments, and operators) for the best performing methods. Nevertheless, it is obvious that Raman and SERS are promising tools to be used in medical applications such as therapeutic drug monitoring or personalized medicine.

References

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