WHY SERS AND DFT? A COMBINATION THAT CAN CERTAINLY HELP IN ANALYZING PHARMACEUTICAL MATERIALS AND THEIR BEHAVIOR NEAR A BIOLOGICAL ARTIFICIAL MODEL

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**Abstract:** The results obtained on pharmaceutical or potentially biological active organometallic complexes provide a benchmark illustration of the value of DFT for aiding interpretation of their rich vibrational spectra attainable by using SERS, as well as furnishing detailed insight into the relation between the vibrational properties and the nature of the Ag substrate-adsorbate bonding.

Although the theories explaining SERS are not definite and still evolving, the experimental research and development in recent years has demonstrated SERS to be a potential technique for environmental and biological trace analysis, enabling the detection of even single molecules. Moreover, it can provide information about the changes of molecular identity or orientation to the metal surface with the concentration. In many cases the surface-adsorbed molecule may exist in a variety of forms related to one another by means of an acid–base reaction, complex formation, tautomerization, and the like.

But for a correct interpretation of the SERS data, it is necessary to have a reliable and complete vibrational assignment of the Raman spectra as a guideline. Therefore, the Raman and SERS spectra of well-known pharmaceuticals (1,4-dihydrazinophthalazine sulfate (DHPZ) \([1]\), caffeine \([2]\), papaverine hydrochloride, and 5-fluorouracil) or new potentially biological active organometallic complexes (nickel(II) cupferronato complexes NiL\(_2\)A\(_n\), \(L = \text{PhN}_2\text{O}_2\)-, \(n = 1, A = \text{o-phenanthroline, o,o'-bipyridine and } n = 2, A = \text{H}_2\text{O, o-NH}_2\text{Py, o-C}_6\text{H}_4(\text{NH}_2)_2 \([3, 4]\)) were discussed with the assistance of results obtained from DFT calculations (harmonic vibrational wavenumbers and Raman scattering activities, e.g. in Fig. 1A, B). One should take into account that for a number of instances the theoretical calculations have aided the interpretation of Raman spectra and many previous incomplete assignments have been analyzed and improved \([5,6]\). In addition, the geometries of the compounds, for which no crystal structure data were available, were theoretically characterized for the first time using DFT calculations \([1,3,4]\). The total electron density of the molecules (shown in Fig. 1C) and the partial charges situated on selected atoms (by the natural population analysis) were also determined theoretically in order to establish the probability of different atoms acting as an adsorptive site for the metal surface \([2]\). Moreover, the closer examination of the calculated orbitals of molecules brought further arguments about the presence or absence of the photoproducts at the Ag surface during the irradiation \([1]\) (shown in Fig. 1D).

Overall, the results provide a benchmark illustration of the virtues of DFT in aiding the interpretation of rich vibrational spectra attainable for larger polyatomic adsorbates by using SERS, as well as in furnishing detailed insight into the relation between the vibrational properties and the nature of the Ag substrate-adsorbate bonding. Therefore, we strongly believe that theoretical calculations will become a matter of rapidly growing scientific and practical interest in SERS. That is, we already try to model the adsorption of very simple molecules on an Ag substrate by the construction of a proper cluster. Regarding this aspect very few results have been reported so far and almost all have involved only a single or two metal atoms, which is clearly not a quantitative model of the metal surface \([7]\). We also try to find out the method, which could fit the experimental results the best. We used the Hartree-Fock, the Möller-Plesset (MP2), and DFT methods (SVWN, BLYP, B3LYP, BPW91, B3PW91), and the basis sets were LANL2DZ, 3-21G, 6-31G, and 6-311G.
The first calculations indicate the BPW91/LANL2DZ combination as very reliable for the noble-metal systems and less expensive, due to its accuracy and computational efficiency. In fact, almost all the DFT-based methods, particularly when allied with the LANL2DZ basis set, yielded results, which were significantly closer to the experimental values than those of the traditional Hartree-Fock and the Moller-Plesset electron correlation method. Supplementing this basis set by the addition of diffuse and/or polarization functions revealed no benefit.

Fig. 1. 
A: BPW91/6-311+G(d) determined in-phase and out-of-phase ν(CO) of caffeine.
B: Their calculated Raman scattering activities.
C: Total electron density of caffeine.
D: Calculated HOMO and LUMO of DHPZ sulfate with BPW91/6-311+G(d).

It is now clear that quantum mechanical DFT calculations represent an indispensable complement not only for the spectroscopical studies in chemistry, but they can also help for a better understanding and exploring of other young fields in physical chemistry, such as SERS.

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References: