A RAMAN SPECTROSCOPIC STUDY OF THE DICLOFENAC SODIUM – β-CYCLODEXTRIN INTERACTION

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Abstract: In this contribution Raman and SERS techniques were applied to analyse the interaction between the guest and host molecules in the 1:1 DCFNa-βCD solid-state complex.

In the last years the inclusion of drugs in cyclodextrin became a very attractive and widely used strategy for improving their performance [1]. β-Cyclodextrin (βCD) is a cyclic oligosaccharide consisting of seven glucopyranose units. The central cavities of these molecules (host molecules) are hydrophobic and thus are able to encapsulate a wide variety of molecules (guest molecules) [2]. Diclofenac sodium (DCFNa), which consists of a phenylacetate group, a secondary amino group and a dichlorophenyl ring, is a well-known representative of non-steroidal anti-inflammatory drugs [3]. DCFNa has limited water solubility that engenders problems in its oral bioavailability and it is a drawback in terms of its formulation in controlled release devices. A possibility to overcome these limitations is the complexation of DCFNa with βCD [4]. The interaction of DCFNa with βCD has been studied both in solution and in the solid state by using different experimental techniques like NMR spectroscopy, IR absorption spectroscopy and X-ray diffraction. Depending on the aggregation state and the preparation method of the DCFNa-βCD complex different inclusion ways of the guest molecule into the βCD cavities have been found [4, 5].

In the present work the interaction between the DCFNa and βCD molecules in the solid state complex form was evidenced by means of Raman spectroscopy. The support of this study was the existence of some spectral ranges, where the Raman bands associated to atom group vibrations directly involved in interaction are not overlapped (see Fig. 1). Changes in the peak positions and the widths of the Raman bands of the complex compared with their corresponding bands of the pure DCFNa and physical mixture were observed. Raman data revealed the existence of interactions between both the dichlorophenyl ring and the phenylacetate group of the DCFNa species and the βCD molecule. Having in mind that previous studies reported about the possibility to detect inclusional complexation by cyclodextrins at the surface of a metal [6], SER spectra of the DCFNa-βCD inclusion complex were also recorded (Fig. 2) and analyzed in an attempt to elucidate the adsorption behavior of the guest-host complex on the silver surface and thus to discriminate between the possible ways of complexation. The changes evidenced in the SER spectra recorded at different pH values of the solution demonstrated that depending on the pH values different isomeric forms of the guest-host complex are preferentially adsorbed on the silver surface. Thus, at pH < 6 the isomeric form having the phenylacetate ring included in the βCD cavity is adsorbed on the metal surface, while at pH ≥ 6 the isomer with the dichlorophenyl ring included into the host molecule cavity is preferentially adsorbed on the silver surface. The adsorption of the guest molecule on the metal surface is maintained in both cases through the nonbonding electrons of the oxygen atom. The probable orientation of the adsorbed species relative to the silver surface was also indicated.

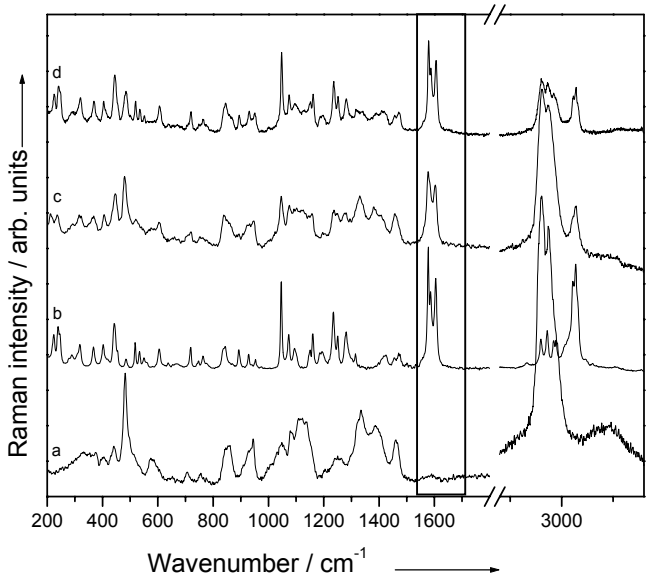

Fig. 1. FT-Raman spectra of β-cyclodextrin (a), diclofenac sodium (b), 1:1 diclofenac sodium-β-cyclodextrin (c), 1:1 diclofenac sodium-β-cyclodextrin physical mixture (d).

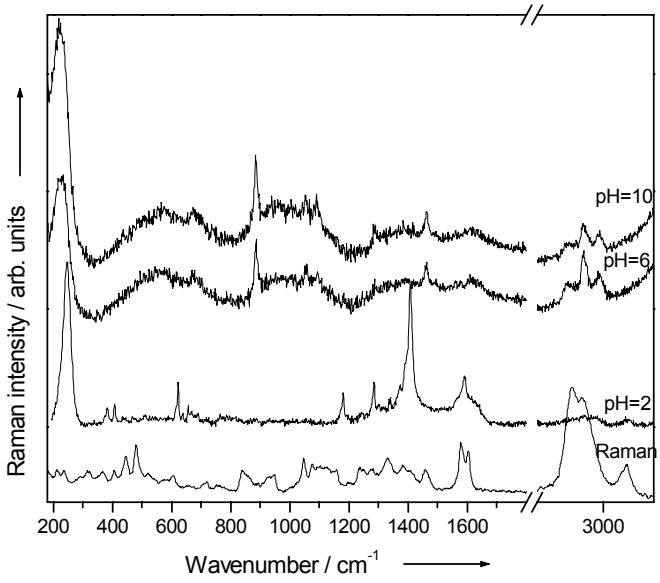

Fig. 2. FT-Raman and SER spectra of diclofenac sodium-β-cyclodextrin complex at different pH values as indicated.

References:

1. J. Szejtli, in Cyclodextrins and their inclusion complexes, Akademiai Kiado, Budapest, 1982, p. 204.
2. A.M. Amado, A.M. Moreira da Silva, P.J.A. Ribeiro-Claro and J.J.C. Teixeira-Dias, J. Raman Spectrosc. **31**, 971 (2000).
3. M. Tunçay, S. Çaliş, H.S. Kaş, M.T. Ercan, I.Peksoy and A.A. Hincal, Int. J. Pharmaeutics **195**, 179 (2000).
4. B. Pose-Vilarnovo, L. Santana-Penin, M. Echezarreta-Lopez, M.B. Perez-marco, J.L. Vila-Jato and J.J. Torres-Labandeira, S. T. P. Pharma Sciences **9**, 231 (1999).
5. B. Cwiertnia, T. Hladon and M. Stobiecki, J. Pharm. Pharmacol. **51**, 1213 (1999).
6. Y. Maeda and H. Kitano, J. Phys. Chem. **99**, 487 (1999).