

Phase transition of captopril: a Raman scattering study

P.T.C. Freire^{1*}, D.L.M. Vasconcelos¹, C.B. Silva¹, J.G. da Silva Filho², P.F. Façanha Filho²,
A.M.R. Teixeira³, J.A. Lima Jr.¹, P.S.R. Ribeiro²

¹Departamento de Física, Universidade Federal do Ceará, C.P. 6030,60455-760, Fortaleza-CE, Brazil

²Centro de Ciências Sociais, Saúde e Tecnologia, Universidade Federal do Maranhão,65900-410, Imperatriz-MA, Brazil

³Departamento de Física, Universidade Regional do Cariri, 63020-970, Juazeiro do Norte-CE, Brazil

Keywords: high pressure, Raman spectroscopy, captopril.

*e-mail: tarso@fisica.ufc.br

Hypertension is a disease that requires the use of medicines to control it. Among various possibilities, one drug used in several countries around the world is captopril (C₉H₁₅NO₃S).

Captopril exists in two conformations, *cis* and *trans*. A previous study showed that in water solution there is a *trans:cis* ratio of 6:1. This constitutes important information due the fact the *trans* form is that bonded to enzymes [1]. The conformation, eventually, can be changed by thermodynamic effects and in this work we investigate the vibrational properties of captopril under high pressure.

Captopril crystallizes in an orthorhombic structure with $P2_12_12_1$ space group. DFT theory with the functional B3LYP and the 6-31++G(d,p) basis was utilized to perform the assignment of the normal modes as observed through Raman spectroscopy. PED calculations with contribution higher than 10% were considered.

The Raman spectra of captopril were recorded from 30 to 3200 cm⁻¹ for pressures up to about 6 GPa. From the Raman spectra one observes a series of modifications between 2 and 3 GPa. For example, the bands recorded at 1039, 1051, 1081 and 1095 cm⁻¹ change intensity above 2.1 GPa. The band observed at 602 cm⁻¹ was associated with a CCC deformation; from our study we noted that the wavenumber of the mode presents a discontinuity close to 2.7 GPa. In this last pressure values is also observed many modifications in the spectral ranges 1400 – 1600 cm⁻¹ as well as in the region 2800 – 3200 cm⁻¹. In fact, the region where one expects to observe modes associated with CH, CH₂ stretching, the spectra is mixed with bands related to the nujol, the liquid used to compress the sample.

Regarding the modes observed in the spectral range below 200 cm⁻¹, most of them can be associated with external modes. Below 160 cm⁻¹, the bands have high intensities related to the other bands of the Raman spectrum. However, increasing pressure these bands decrease intensity and above 0.9 GPa a band seems to appear from the huge band due to the quasi-elastic scattering. The main aspect, however, is the discontinuity

in several wavenumbers of the modes in the low wavenumber region that were interpreted as a phase transition undergone by captopril crystal between 2 and 3 GPa. Fig. 1 presents some spectra for pressures up to 4 GPa.

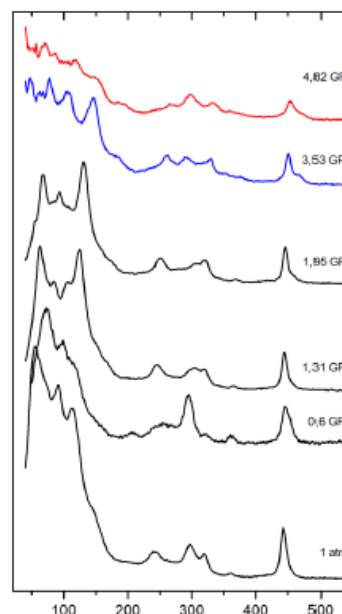


Figure 1: Raman spectra of captopril in selected pressure values in the 30 -500 cm⁻¹ wavenumber spectral range.

A final point deals with the conformation of the captopril molecules. Up to the highest pressure, we can confirm that the originally *trans* isomer remains stable during all the experiments.

Acknowledgments: This work was supported by CNPq, CAPES and FUNCAP.

[1] E.D. Thorsett et al., J. Med. Chem. 1986, **29**, 251.