The Vibrational Spectral Analysis of Amprenavir molecules using Infrared and Raman Spectroscopy and Quantum chemical Computations

P S Sindhu,*Department of Physics, Aquinas College, Edacochin, Kerala, India*

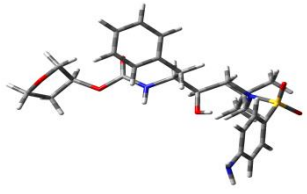
The inhibition of HIV-1 and HIV-2 protease plays a crucial role in the drug design for treatment of HIV infection. The present work report overview of HIV inhibition and structural features of amprenavir, a clinical HIV protease inhibitor, responsible for binding, using FT IR and FT Raman spectral investigation, aided by density functional theoretical computations.

The title compound has been subjected to FT IR and FT Raman spectral recording. The geometry, IR spectrum and Raman spectrum have been computed using DFT, using Gaussian '09 program package [1]. The analysis of PED of vibrational modes and natural bond orbital (NBO) analysis have been conducted. The compound has been docked with HIV-1 and HIV-2 protease using Autodock tool [2].

The possible intermolecular interaction of OH group is found to generate broad profile in the stretching region, with the red shift in band position and asymmetric NH_2 and NH stretches are found to create strong shoulders on the higher and lower wavenumber sides of the profile centre. The carbonyl stretching is found to be red shifted due to the conjugation with neighbor CN bond, making CN bond stronger which in turn causes the blue shift of CN stretch. The changes in structural parameters due to carbonyl conjugation have been studied in detail, using optimized geometry and natural bond orbital (NBO) analysis.

The nucleophilic sites of amprenavir have been identified using Molecular Electrostatic Potential (MEP) mapping and the possible binding moieties for intermolecular interactions have been determined. The title compound amprenavir has been docked with HIV-1 and HIV-2 and the binding constants have been computed as 8.34 kcal/mol and 7.38 kcal/mol respectively. In HIV-1, binding occurs through amino group of Aspartic acid 30 through site 1 and in HIV-2, interaction takes place through Aspartic acid 30 through site 4 of ligand. The short contacts and features such as charge, shape complementarity features and the proximity of nucleophilic site of ligand with binding residue, responsible for binding, have been analyzed.

Vibrational analysis shows that the carbonyl group is conjugated and OH forms intermolecular interaction with neighbour molecule. The amprenavir is found to bind with HIV-1 and HIV-2 through intermolecular N-H···O interaction of amino group of Aspartic acid 30 with the nucleophilic site of ligand. The short contacts, features such as charge, shape complementarity features and the proximity of nucleophilic site of ligand with binding residue have been found to play crucial role in binding process.



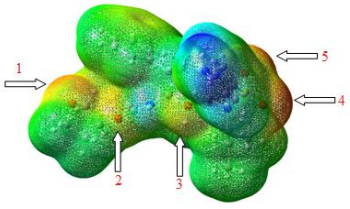


Fig 1. Geometry of Amprenavir . Fig 2. ESP mapping of amprenavir showing nucleophilic sites.

REFERENCES

[1] M.J. Frisch et.al. Gaussian 09, Revision A.02, Gaussian, Inc., Wallingford, CT, 2009.
[2] G.M. Morris, R. Huey, W. Lindstrom, M.F. Sanner, R.K. Belew, D.S. Goodsell, A.J. Olson, *J. Comput. Chem.* 2009; **16:** 2785–2791.