Quantum chemical, spectroscopic and molecular docking investigations of potential pulmonary fibrosis drug methyl 2-chloro 4-iodonicotinate

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Abstract

The potential energy surface scan was performed and the most stable molecular structure of the Methyl-2-Chloro-4-Iodopyridine-3-Carboxylate (MCIN) molecule was obtained. The molecular structure was optimized and its vibrational wavenumbers, IR intensity and Raman activity were calculated. The ultraviolet– visible spectra was calculated in both gas and liquid phase by time-dependent (TD-DFT)/B3LYP method. The NMR isotropic chemical shift values were predicted. The molecular docking analysis of the MCIN molecule was carried out.

Introduction

The pyridine derivatives have been attracted much due to their diverse applications in pharmaceutical and bio-medical fields. The pyridine derivatives have anti-cancer, anti-inflammatory, anti-diabetic, anti-microbial and anti-bacterial properties. Pulmonary fibrosis is an interstitial disease affecting the lungs. When the tissues of the lungs become damaged or scarred then pulmonary fibrosis occurs. Lung scarring is known as fibrosis. Moreover, pulmonary fibrosis is a severe lung disease leading to respiratory illness. Though the treatment of pulmonary fibrosis is limited they cannot be completely cured and are expensive with serious side effects so drug target treatment will be effective. Hence, the current study will be useful in determining novel pulmonary fibrosis drugs.

Methods

Computational details: The molecular structure of MCIN was optimized and the conformational analysis was carried out by the DFT/ B3LYP method with LANL2DZ basis set using Gaussian 09 program . The vibrational wave numbers were calculated for the optimized molecular structure on the basis of potential energy distribution (PED) calculations with the help of VEDA 4.0 program [1]. The NMR spectrum was simulated using GIAO/B3LYP method. The UV-Vis spectrum was obtained by time dependent (TD-DFT)/B3LYP method. The molecular docking calculation was performed by the AUTODOCK 4.0.1 software [2].

Results

Molecular Geometry Analysis: The potential energy surface scan was observed and the most stable conformers were obtained . The optimized molecular structure of the MCIN molecule is shown in Fig.1.

Vibrational Spectral Analysis: The vibrational wavenumbers, IR intensity and Raman activity were obtained for the most stable optimized structure of the MCIN molecule. The FT-IR and FT-Raman spectra is shown in Fig.2. From the vibrational analysis, the bands calculated at 3117 and 3088 cm^{-1} were assigned to C H stretching vibrations. The same band was observed as a medium band at 3068 cm^{-1} in FT-Raman, which was assigned to C H stretching vibration. This shows that the calculated wavenumber 3117 cm^{-1} is being blue shifted [3].

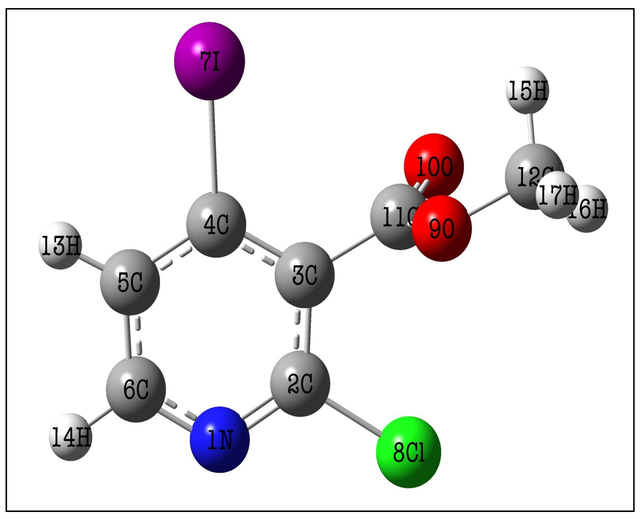

Fig.1. The Optimized molecular structure of MCIN molecule.

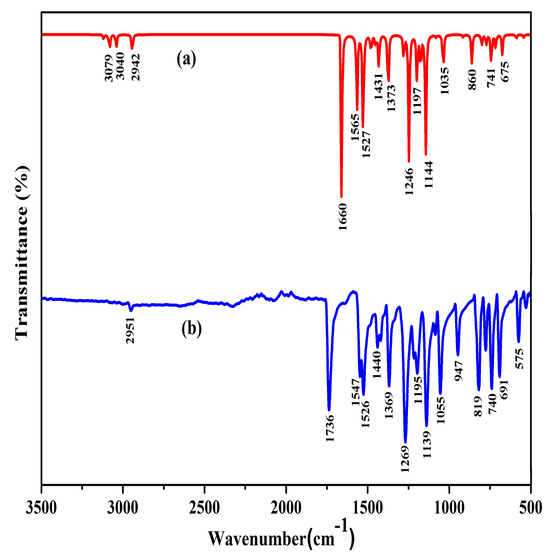

Fig.2. The FT-IR spectra of the MCIN molecule. (a) Simulated spectrum, (b) Observed spectrum.

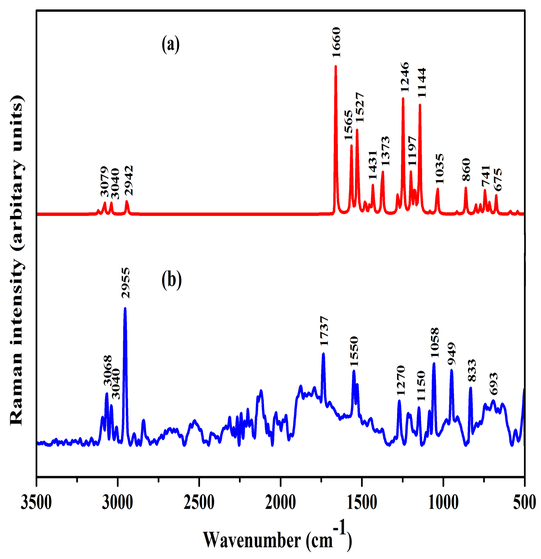

Fig.3. The FT-Raman spectra of the MCIN molecule. (a) Simulated spectrum, (b) Observed spectrum.

UV-Visible analysis: The UV-Vis spectrum was simulated and its electronic properties were studied in gas phase and liquid phase using ethanol as a solvent. The recorded absorption spectrum gives two peaks at 225& 245 nm in liquid phase and 226& 241 nm in gas phase.

NMR Spectral analysis: The downfield NMR isotropic chemical shift values were predicted for the atoms 11C (171 ppm) and 2C (151 ppm), which is due to the attachment of carbon atom with the electronegative atoms 10O and 8Cl respectively.

Molecular Docking (MD): The molecular docking analysis confirms that the title molecule acts as a good inhibitor of pulmonary fibrosis shown in Fig.3. Hence, the present investigation paves the way for designing a novel drug for the treatment of pulmonary fibrosis.

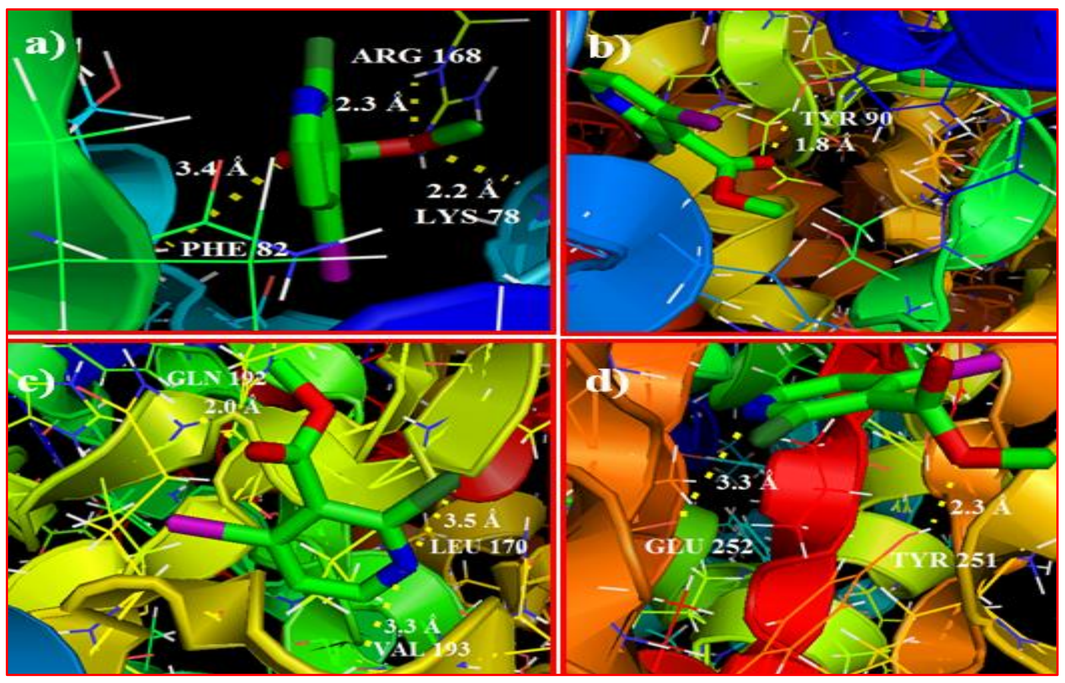

Fig.4. Lowest energy docked poses of the MCIN ligand with various protein targets such as (a) Pulmonary fibrosis, (b) Asthma, (c) MERS and (d) SARS2.

Conclusions

The optimized molecular structure of MCIN molecule was predicted by the DFT/B3LYP method with LANL2DZ basis set. The vibrational spectral analysis was performed and assigned using PED calculations. A blue shift in C-H stretching vibrational modes were observed. The NMR spectral analysis was carried out. The UV spectral analysis concludes the presence $\pi \rightarrow \pi^*$ electronic transition of the MCIN molecule. Molecular Docking reveals MCIN molecule identified as a potential inhibitor for pulmonary fibrosis.

References:

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