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Quantum chemical insight into molecular structure, NBO analysis of the hydrogen-bonded interactions, spectroscopic (FT–IR, FT–Raman), drug likeness and molecular docking of the novel anti COVID-19 molecule 2-[(4,6-diaminopyrimidin-2-yl)sulfanyl]-N-(4-fluorophenyl)acetamide - dimer

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ABSTRACT

Novel antiviral active molecule 2- [(4,6-diaminopyrimidin-2-yl)sulfanyl]-N-(4-fluoro- phenyl)acetamide has been synthesised and characterized by FT-IR and FT-Raman spectra. The equilibrium geometry, natural bond orbital calculations and vibrational assignments have been carried out using density functional B3LYP method with the 6-311G++(d,p) basis set. The complete vibrational assignments for all the vibrational modes have been supported by normal coordinate analysis, force constants and potential energy distributions. A detailed analysis of the intermolecular interactions has been performed based on the Hirshfeld surfaces. Drug likeness has been carried out based on Lipinski's rule and the absorption, distribution, metabolism, excretion and toxicity of the title molecule has been calculated. Antiviral potency of 2- [(4,6-diaminopyrimidin-2-yl)sulfanyl]-N-(4-fluoro-phenyl) acetamide has been investigated by docking against SARS-CoV-2 protein. The optimized geometry shows near-planarity between the phenyl ring and the pyrimidine ring. Differences in the geometries due to the substitution of the most electronegative fluorine atom and intermolecular contacts due to amino pyrimidine were analyzed. NBO analysis reveals the formation of two strong stable hydrogen bonded N–H···N intermolecular interactions and weak intramolecular interactions C–H···O and N–H···O. The Hirshfeld surfaces and consequently the 2D-fingerprint confirm the nature of intermolecular interactions and their quantitative contributions towards the crystal packing. The red shift in N–H stretching frequency exposed from IR substantiate the formation of N–H···N intermolecular hydrogen bond. Drug likeness and absorption, distribution, metabolism, excretion and toxicity properties analysis gives an idea about the pharmacokinetic properties of the title molecule. The binding energy −8.7 kcal/mol of the nonbonding interaction present a clear view that 2- [(4,6-diaminopyrimidin-2-yl)sulfanyl]-N-(4-fluoro- phenyl) acetamide can irreversibly interact with SARS-CoV-2 protease.

1. Introduction

Pyrimidine and its derivatives take up a key position in the field of medicinal chemistry due to its multifarious pharmacological activities. In an urge for searching new promising small therapeutic agents, we introduce 2- [(4,6-diaminopyrimidin-2-yl)sulfanyl]-N-(4-fluoro- phenyl) acetamide (DAPF). In the present study, we focus on the investigation on the molecular structure, electronic properties, vibrational spectra and molecular docking of the title compound, with the hope that the results of the present investigation may be decisive in the prognosis of its mechanism of biological activity.

Pyrimidines, the fundamental building blocks for nucleic acids, are invoking much scientific interest owing to their potential biological activities and pharmacological applications [1]. Pyrimidines are also reported to show anti-HIV, [2] antidengue [3] and anticancer [4] activities. The title compound DAPF, which has the amino substituent at the 4,6- position are found to be Troponin I-Interacting Kinase

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