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Research Article

In Silico, SwissADME, and DFT Studies of Newly Synthesized Oxindole Derivatives Followed by Antioxidant Studies

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The compounds were synthesized by refluxing 6-chlorooxindole with 2,3-dichlorobenzaldehyde and 2,6-dichlorobenzaldehyde in the presence of piperidine as a catalyst and characterized by spectroscopic analysis using ^{1}H NMR, ^{13}C NMR, and mass spectrometry as (E)-3-(2,3-dichlorobenzylidene)-6-chloroindolin-2-one (C-1) and (E)-3-(2,6-dichlorobenzylidene)-6-chloroindolin-2-one (C-2). Additionally, in silico ADME studies indicated that C-1 and C-2 with 1,1 rotatable bonds could have moderate water solubility and therefore could have the potential ability to cross the blood-brain barrier. Both showed high GI absorption, indicating that they are suitable for intestinal absorption while the compounds showed CYP1A2, CYP2C19, and CYP2C9 inhibition. The five drug-likeness criteria, which were Lipinski, Muegge, Ghose, Veber, and Egan, and the principles of drug-likeness are not violated by compounds C-1 and C-2. Also, the DFT computations were performed at the B3LYP level and at 6-311++G** basis set to evaluate and support the obtained results from the experiment. The FMO results revealed that C-1 could likely prefer the intramolecular interactions rather than the intermolecular interactions, and vice versa for C-2. In addition, the NBO results indicated that the resonance interaction, especially the shift of electron to empty orbitals from lone pair electrons of nitrogen, would contribute to the stabilization of both compounds greatly. In DPPH assay, the compounds showed IC_{50} values of 37.390 and 34.676 μM, respectively. Similarly, in ABTS assay, the calculated IC_{50} values for the compounds were 25.381 and 33.706 μM, respectively. In short, these results provided a solid ground for further preclinical studies in quest of new effective therapeutic agents.

1. Introduction

Oxindoles are endogenous aromatic organic compounds that are present in some plant natural products as well as in the tissues and bodily fluids of mammals. They have a bicyclic structure and are aromatic heterocyclic organic compounds. The unsubstituted oxindole nucleus is characterized as an off-white crystalline powder with a defined melting point range of 124–126°C [1, 2]. The fusion of a nitrogen-containing five-membered ring with a six-membered benzene ring results in the formation of an oxindole molecule. The structure of an oxindole is similar to that of an indoline, with the exception that one of the five members' 2-positions is occupied by a carbonyl [3]. According to the literature, oxindole has been used to treat inflammation, cancer, gastric ulcers, infections, and other medical conditions [4]. The diverse pharmacological profile of oxindole has inspired both industry and academia to create novel synthetic derivatives with a wide range of biological activities. The development of synthetic oxindole derivatives has played a crucial role in the creation of sunitinib,