Journal of Molecular Structure 1302 (2024) 137521

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstr

Synthesis, molecular docking, enzyme inhibition and antioxidant potential of new 1H-benzo[*d*]imidazole-5-carboxamide derivatives

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ARTICLE INFO

Keywords:
Benzimidazole
Antioxidant
Lipoxygenase
Xanthine oxidase
Molecular docking

ABSTRACT

The therapeutic potential of benzimidazole has brought them widespread recognition as a class of heterocyclic compounds having nitrogen-containing rings. In recent years, there has been a lot of focus on synthesizing these molecules in order to reveal a broad range of biological actions. Therefore, a novel series of 1H-benzo[*d*]imidazole-5-carboxamide derivatives were designed, synthesized, and investigated for their antioxidant and enzyme inhibitory activities. The structural elucidation of synthesized compounds was accomplished by a variety of spectroscopic techniques, such as elemental analysis, ^{1}H and ^{13}C NMR, and LC-MS. Using the DPPH and FRAP techniques, the antioxidant activity of newly synthesized compounds was assessed. With IC_{50} values of 81.45, 72.14, and 77.35 μM, respectively, in the DPPH assay and 86.07, 75.02, and 81.14 μM, respectively, in the FRAP assay, the compounds 10c, 10f, and 10 g shown have significant antioxidant activity in comparisons with reference drugs ascorbic acid and Trolox. Furthermore, the inhibitory activity of xanthine oxidase (XO) and lipoxygenase (LOX) enzymes was assessed for the most potent molecules. Compounds 10c, 10f, and 10 g show superior inhibitory effects than reference drugs allopurinol and baicalein, with IC_{50} values of 19.52, 13.95, and 15.83 μM, respectively, against LOX and 26.14, 18.43, and 22.05 μM, respectively, against the XO enzyme. Moreover, studies using molecular docking were conducted to gain a deeper understanding of the interactions between the 3NM8 and 1N8Q protein and the most effective compounds, 10c, 10f, and 10 g. While compared to the reference medications, the studied compounds showed substantial docking scores and binding affinities, as indicated by docking studies. Through the use of drug-likeness and structure-activity relationships (SAR), an association between the newly synthesized compounds' biological and physicochemical properties was established.

1. Introduction

Reactive oxygen species and free radicals are produced by the human body and are advantageous to the living system. On the other hand, an increase in the production of free radicals can cause oxidative stress, which can harm cellular macromolecules including DNA, proteins, and lipids. As a result, oxidative stress contributes to disease development and ageing [1]. By providing an electron, antioxidants can safely interact with free radicals, stop the process, and change them into a harmless molecule. Numerous techniques exist for assessing antioxidant activity, which may be classified into two categories according to the reaction mechanism of radical deactivation-either electron transfer or hydrogen atom transfer. Antioxidant structure and characteristics will determine whether process predominates; both mechanisms may occur concurrently [2]. As such, it is not feasible to evaluate antioxidant activity using a single assay. Because of this, a wide range of approaches have been used to thoroughly investigate the antioxidant properties of several substances [3,4]. Even though the identification of antioxidant compounds has been extensively researched, research into novel natural or synthetic compounds that can function as free radical scavengers and

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https://doi.org/10.1016/j.molstruc.2024.137521
Received 14 December 2023; Received in revised form 1 January 2024; Accepted 7 January 2024
Available online 8 January 2024