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Synthesis, Anticancer Activity, and Computational Studies of New Pyrazole Derivatives

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Abstract—new pyrazole derivatives were synthesized through a cyclization reaction of chalcones derivatives with hydrazine hydrate under acidic catalysis and characterization by different techniques. The MTT assay was used to examine the cytotoxic activity of the produced compounds against the tumor cell lines MCF-7 and MDA-MB-231. Morphological screening images by using the IC_{50} values of 2-[3-(3,4-dimethoxyphenyl)-4,5-dihydro-1*H*-pyrazol-5-yl]quinoline at various concentrations to the cancer cell lines MCF-7 and MDA-MB-231 were done. Molecular docking for the most active compound inside the active sites of the (PDB: 1M17) was done. The geometry optimization and reactivity descriptors, such as energy band gap (ΔE), chemical potential (μ), electronegativity (χ), chemical hardness (η), chemical softness (S), electrophilicity (ω), and least unoccupied molecular orbital (LUMO), were also analyzed using the DFT calculation performed using DFT/B3LYP/6-311+G(d,p). Additionally, a thorough in silico prediction of the compounds physicochemical ADME profile was completed.

Keywords: anticancer activity, chalcones, DFT calculations, docking, hydrazine hydrate, pyrazole

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INTRODUCTION

Chalcone derivatives that come from natural or synthetic sources demonstrate a wide range of pharmacological actions [1–4]. It is not surprising, then, that various synthetic techniques for generating heterocycles from chalcone precursors that have been evaluated for anticancer activity have been established heterocyclic compounds account for more than half of all known chemical compounds, and most novel medications [5–9]. Heterocyclic compounds with pyrazole moieties take center stage in this study due to their diverse and essential applications in biology, pharmacology, industry, and other fields [10]. Several pyrazole-containing drugs have been successfully commercialized to date, including celecoxib, rimonabant, sulfaphenazole, and penthiopyrad [11]. These scaffolds are categorized as alkaloids; however, they are extremely rare in nature. Noe et al. [12] identified the first natural pyrazole, 1-pyrazolylalanine, from the seeds of watermelons in 1959. Many other works have recently been published and have been utilized by many research teams to prepare the substituted pyrazole cycle [13–15]. All interest in these substances has returned because of their sample and rapid process of synthesis that can be tailored to the demands of the customer [16–18]. Considering these discoveries, this work created, synthesized and evaluated novel pyrazole compounds for cytotoxicity against MCF-7 and MDA-MB-231 cells. The DFT computational method is especially helpful for handling electronic aspects and comprehending the molecular/electronic structure and behavior of various substances [19, 20] because of its speed and adaptability for recovering dynamic electron correlations and computational research. The DFT computations were successful in finding relationships between the electrical and geometrical features of the molecule, as evidenced by a comparison of the study data with the real results [21]. To create chalcone derivatives, we continued our research using the most feasible method yet discovered: the Claisen–Schmidt condensation of equimolar quantities of aryl aldehydes and substituted acetophenone in the presence of alcoholic alkali. Moreover, the interaction of chalcones with hydrazine hydrate in the presence of hydrochloric acid resulted in the production of pyrazole compounds. It was investigated how effective they were against the cancer cell lines MCF-7 and