ISSN 1070-3632, Russian Journal of General Chemistry, 2023, Vol. 93, No. 5, pp. 1171–1180. © Pleiades Publishing, Ltd., 2023.

Synthesis of New Pyrimidine Derivatives, Study of Anti-Cancer Activity, Structural Properties, and Molecular Docking

Z. Al Shuhaib[a], K. A. Hussein[a],*, and S. M. Ismael[a]

[a] *Department of Chemistry, College of Education for Pure Sciences, University of Basrah, Basrah, 61004 Iraq*
**e-mail: kawkab.ali@uobasrah.edu.iq*

Received March 2, 2023; revised March 29, 2023; accepted April 7, 2023

Abstract—New pyrimidine derivatives were synthesized through domino Knoevenagel–Michael cyclization reactions of aryl aldehydes, ethyl cyanoacetate, and guanidine hydrochloride or urea under a basic catalysis. Cytotoxic activity of the prepared compounds against MCF-7 and HepG2 tumor cell lines was investigated by the MTT test. Compound geometry analysis was performed using the B3LYP functional with a 6-311+G(d,p) basis set. The estimated geometries were very similar to the experimental ones.

Keywords: one-pot synthesis, 2-aminopyrimidine, heterocyclization, anticancer activity, molecular docking

DOI: 10.1134/S1070363223050183

INTRODUCTION

Multicomponent interactions have emerged as potent techniques in organic chemistry for forming several carbon–carbon or carbon–heteroatom bonds in one-pot processes [1–3]. Many approaches have been developed to produce heterocyclic compounds exhibiting important biological activity in multi-component interactions [4, 5]. Nitrogen-containing heterocyclic pyrimidine and derivatives are significant in medicinal chemistry and have been used as medicines [6]. The major pyrimidine compounds have a wide range of uses, including bactericidal [7], fungicidal [8], antioxidant [9], anti-inflammatory [10], and anticancer agents [11]. Cancer is a worldwide health concern affecting many of the human population. It is characterized by cell cycle dysregulation, which primarily results in a progressive loss of cellular differentiation and uncontrolled cellular proliferation [12]. The present situation highlights the necessity of identifying and developing slight anticancer drugs with improved tumor selectivity, effectiveness, and safety [13]. The substitute pyrimidine nucleus is a significant pharmacophore found in a variety of anticancer drugs, with some of these compounds successfully treating a variety of neoplastic disorders such as leukemia and testicular cancer [14]. Uracil and its derivatives are significant starting materials to produce a wide range of chemical compounds, pharmacological substances, and drug intermediates [15]. One of the most common approaches to developing new anticancer medications is the invention of antimetabolites based on structural similarities to naturally occurring pyrimidines and purines involved in DNA formation [16]. 1,2,3,4-Tetrahydropyrimidine is made up of a pyrimidine scaffold that resembles the architectures of nucleic acid bases present in DNA and RNA. Their role as bases in nucleic acids is extremely important in medication creation [17]. This study developed, synthesized, and tested new pyrimidine-5-carbonitrile derivatives for cytotoxicity against MCF-7, HepG2, and HdFn cells following these findings. Because it is quick and appropriate in recovering dynamic electron correlations and computational analyses, the DFT computational approach is extremely beneficial for dealing with electronic characteristics and understanding molecular/electronic structure and properties for diverse molecules. The comparison of the study data to the experimental values showed that the DFT calculations were successful in identifying connections between the compound's electronic and geometric properties [18]. As well as one of the most fundamental and significant methods used in the design and discovery of drugs has been molecular docking analysis. The medicinal properties of numerous cancer targets for the treatment of