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Synthesis, breast cancer activity, molecular docking and dynamic simulation of 1,4-Dihydropyridine derivatives

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ABSTRACT

Breast cancer (BC) is the most prevalent cancer diagnosed in women, accounting for more than 1 in 10 new cancer diagnoses each year. Even though chemotherapy is successful in BC treatments, resistance to spreading these medications requires a new therapy. A new 1,4-Dihydropyridine (ZL1-6) series was synthesized and characterized using spectroscopic techniques such as FT-IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectroscopy. The efficacy of these compounds against MFC7 breast cancer cells was assessed through a combination of *in vitro*, molecular docking, molecular dynamics, and MM-GBSA analyses. Notably, compound ZL4 exhibited promising activity against MFC7 cells (IC_{50} = 93.09 μg/ml), with a docking core of -6.728 kcal/mol and an MM-GBSA of -47.82 kcal/mol potentially involving the inhibition of EGFR as a mechanism of action. It is worth mentioning that these compounds were inactive against both *E. Coli* and *S. Aureus* wild strains. These findings provide a foundation for the development of innovative treatments for breast cancer.

1. Introduction

Breast cancer represents the irregular division of breast cells and represents the most common disease in women. It represents the main problem for global health if cases increase gradually [1,2]. In general, the spread of cancer cell diseases increases significantly throughout the world so that the spread of the disease is expected to reach 28 million in the coming years [3,4]. Breast cancer was the most significant percentage. The development of medicines and treatments for cancer diseases was a matter of pride [5,6]. However, it remains at the average level. It gives insight into the possibility of developing these treatments and the possibility of greening heterocyclic compounds that provide greater effectiveness and a more remarkable ability to stop the spread of cancer cells and treat them [7–9]. Nowadays, heterocyclic compounds have proven to have high effectiveness against cancer cells [10], especially compounds that contain nitrogen atoms. They were receiving increasing attention in designing treatments for cancer cells. Among these compounds that have good effectiveness are dihydropyridine derivatives, which studies have indicated have good effectiveness in the direction of these cells [11–13].

Dihydropyridine (DHP) was exposed as a derivation of important class six cyclic heterocyclic compounds [14]. it was a valuable and profitable molecule due to its extensive range of industry, biological activity, and pharmacological [15]. There were an additional 12 commercial, lawful, and clinically significant drugs on the marketplace, including nucleophilic 1,4-Dihydropyridine as Felodipine, Nifedipine, and nicardipine shown in Fig. 1, which were used to treat diseases [16, 17].

Arthur Rudolf Hantzsch was first involved in the procedure for the preparation of dihydropyridine; this includes the reaction of aldehyde derivatives with ethyl acetoacetate and the nitrogen donor [18]. The review of the literature shows that numerous new reports have described better methods to change Hantzsch conditions, whichever by using β-diketones instead of β-diketone ester or by using substituted aromatic amine for ammonia [19,20].

Some six-membered heterocyclic compounds (DHP) exhibit interesting biological activate. The DHP compounds have applications in medicinal chemistry and serve a dangerous structural module of drugs,

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