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ORIGINAL RESEARCH

Microwave-assisted synthesis, molecular docking and anti-HIV activities of some drug-like quinolone derivatives

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Abstract

In targeted therapy of breast cancer, human epidermal growth factor receptor 2 HER2 (PDB ID: 3PP0) is being considered as a promising route to design novel anti-breast cancer drugs. In this work, we report two of novel *N*-substituted pyrrolidine at C-8 position of quinolone derivatives **18** and **19**, their synthesis under microwave technique, spectral methods, molecular docking study and anti-HIV activities. Docking study exhibited hydrogen bonding, polar, and Van der Waals interactions with the active site residues of HER2 target. The binding energy and hydrogen bonding interactions show that synthesized compounds are being considered to have a potential activity against breast cancer. In addition, quinolone derivatives were evaluated in vitro for antiviral activity against the replication of HIV-1 and HIV-2 in MT-4 cells. The results showed that quinolone derivatives **18** and **19** possess a potent activity against HIV-1 replication with IC_{50} values of ≥15.20 and 14.26 μM, SI ≤ 6 and >7, respectively.

Keywords Microwave synthesis · Breast cancer · HER2 (PDB ID: 3PP0) · Molecular docking · Anti-HIV activities · Quinolone derivatives

Introduction

Cancer is an incurable disease, originating from uncontrolled proliferation of cells with the potential to permeate to other organs of body (Sravanthi et al. 2019). Breast cancer is a malignant and deadly disease in the world because the current treatments are limited by the emergence of the cure-resistant cancer cells (Siegel et al. 2011; Stockler et al. 2000). Human epidermal growth factor receptor 2 HER2 (PDB ID: 3PP0) is a protooncogene, which has an important role in the regulation of cyclic cell signaling pathways involving cell proliferation and cellular replication. HER2 appears to be involved in 20% of diagnosed breast cancer. A considerable evidence indicates that HER2 (PDB ID: 3PP0) protein is expected to mutate in HER2-positive breast cancer, that leads to defective control of malignant transformation and cellular proliferation (Dent et al. 2013; Pinhel et al. 2012). Thus, targeting HER2 may be considered as a potential target for breast cancer therapy.

Quinolones are one of a common moiety in antibiotic structures such as enoxacin **1** (Vracar et al. 2018), ciprofloxacin **2** (Mitscher 2005), lomefloxacin **3** (Beberok et al. 2017), fleroxacin **4** (Zelmat et al. 2020), ofloxacin **5** (Dubar et al. 2011) and nalidixic acid **6** (Appelbaum and Hunter 2000; Bisacchi 2015; Jacoby 2005) (Fig. 1). These drugs are widely used as an effective treatment against bacterial infections, including an infectious respiratory, pneumonia, diarrhea, gonorrhea, typhoid fever and urinary tract infections (Dalhoff 2015; Naqvi et al. 2018). Due to a high intracellular penetration and good oral bioavailability of some quinolone derivatives (Anquetin et al. 2005; Baker et al. 2004), they play a vital role as an efflux pump inhibitor (Chevalier et al. 2001), antimicrobial activity (Jardosh and Patel 2013), apicoplastic (Dahl and Rosenthal 2007), anti-tuberculosis (Wohlkonig et al. 2010) and anti-leprosy (moxifloxacin **7**) (Laponogov et al. 2009; Wohlkonig et al. 2010). The compound **7** can form a reversible ternary complex via binding with two type of bacterial targets (topoisomerase IV enzymes and DNA gyrase) that leads to block the bacterial growth (Drlica et al. 2009; Drlica and

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