

Original Research Paper

Synthesis, Ant Proliferative Activity and Docking Study of New Quercetin Derivatives against MDA-MB231 Breast Cancer Cell Lines

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Abstract: MDA-MB231 is a very aggressive and invasive triple negative breast cancer, which present with limited treatment options. Unlike other breast cancer types, it is characterized by absence of hormonal receptors of estrogen, progesterone as well as human epidermal growth factor receptor 2, rendering it unsuitable for hormonal therapy and a perfect candidate for chemotherapy. Quercetin is a common natural flavonoid present in many food items, which have a wide range of biological activities, likes anticancer, antiviral, antibacterial and antioxidant. This study involves the synthesis of new Quercetin derivatives and the investigation their effects against MDA-MB231 cell lines. The structures of the derivatives were established using UV, IR, ¹HNMR, CHNS, EIMS and ESIMS techniques. Their antiproliferative activities were investigated in vitro using Microculture Tetrazolium (MTT) assay. The percentage cell viability following exposure to Quercetin and its derivatives (Compounds 1-5) were measured. Both compounds 1 and 4 show a significant decrease in percentage cell viability from 100% to 43.7% and 38.1% respectively. IC₅₀ value was calculated for compound 1 and 4 and found to be 2.042 and 1.838 μM respectively, indicating that they have a potential anticancer activity against the triple negative breast cancer type. The antiproliferative activity was supported and evidenced by molecular docking study.

Keywords: Quercetin, MDA-MB231, Molecular Docking, MTT Assay

Introduction

Triple Negative Breast Cancer (TNBC) is a cancer type that is devoid of the three typical types of receptors known to stimulate most breast cancer growth; estrogen, progesterone and human Epidermal Growth Factor Receptor 2 (EGFR2). Due to the absence of necessary receptors, common hormonal therapy and drugs that target these receptors are ineffective. However, TNBC is considered perfect candidate for chemotherapy as stated by (Chavez *et al.*, 2010). Although Triple negative breast cancer accounts for only 15% of other breast cancer subtypes, it shows high rate of recurrence and develops resistance to chemotherapy as previously reported by (Rakha *et al.*, 2008). In addition, patients have shown poor prognosis due to the lack of specific targeted therapy (Nguyen *et al.*, 2017). Therefore, it is vital to look for new therapeutic agents that are

effective, less toxic and can prevent relapse emergence. Quercetin is 3, 3', 4', 5, 7-pentahydroxyflavone (Fig. 1) which is a natural poly phenolic compound that belongs to the flavanol class of flavonoids and present within various concentrations in different vegetables and fruits such as onion, broccoli, apple, garlic and tomatoes (Al-Jabban *et al.*, 2015; Hertog *et al.*, 1992). Quercetin characterize by powerful antioxidant activity and wide pharmacological applications including various antiproliferative activities against colon, pancreatic, prostate, brain, bone, gastric and breast cancer (Rauf *et al.*, 2018), in addition to its antimicrobial, anti-inflammatory, antidiabetic, neuroprotective, anti-obesity and the prevention of cardiovascular disease activities (Amic *et al.*, 2007; D'Andrea, 2015; Dajas, 2012; Massi *et al.*, 2017; Moalin *et al.*, 2011; Pietta, 2000; Procházková *et al.*, 2011; Ramos *et al.*, 2006; Wang *et al.*, 2006).