JOURNAL OF BIOMOLECULAR STRUCTURE AND DYNAMICS
https://doi.org/10.1080/07391102.2023.2276879

Exploring the potential of biologically active phenolic acids from marine natural products as anticancer agents targeting the epidermal growth factor receptor

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Communicated by Ramaswamy H. Sarma

ABSTRACT

The epidermal growth factor receptor (EGFR) dimerizes upon ligand bindings to the extracellular domain that initiates the downstream signaling cascades and activates intracellular kinase domain. Thus, activation of autophosphorylation through kinase domain results in metastasis, cell proliferation, and angiogenesis. The main objective of this research is to discover more promising anti-cancer lead compound against EGRF from the phenolic acids of marine natural products using in-silico approaches. Phenolic compounds reported from marine sources are reviewed from previous literatures. Furthermore, molecular docking was carried out using the online tool CB-Dock. The molecules with good docking and binding energies scores were subjected to ADME, toxicity and drug-likeness analysis. Subsequently, molecules from the docking experiments were also evaluated using the acute toxicity and MD simulation studies. Fourteen phenolic compounds from the reported literatures were reviewed based on the findings, isolation, characterized and applications. Molecular docking studies proved that the phenolic acids have good binding fitting by forming hydrogen bonds with amino acid residues at the binding site of EGFR. Chlorogenic acid, Chicoric acid and Rosmarinic acid showed the best binding energies score and forming hydrogen bonds with amino acid residues compare to the reference drug Erlotinib. Among these compounds, Rosmarinic acid showed the good pharmacokinetics profiles as well as acute toxicity profile. The MD simulation study further revealed that the lead complex is stable and could be future drug to treat the cancer disease. Furthermore, in a wet lab environment, both in-vitro and in-vivo testing will be employed to validate the existing computational results.

ARTICLE HISTORY
Received 26 June 2023
Accepted 22 October 2023

KEYWORDS
Phenolic compounds; marine natural products; in-silico; anti-cancer; EGFR

1. Introduction

In the production of medicines, nutraceuticals, and food ingredients, plant secondary metabolites have a crucial economic role (Siahsar et al., 2011). This group includes substances like phenolic acids, which have several therapeutic benefits. To prevent severe diseases and improve health, phenolic compounds have been proposed as significant bioactive molecules (Huang et al., 2008). A surge in interest in herbal replacements for synthetic goods in the nutraceutical and pharmaceutical industries is being driven by consumer demographics and health concerns on a global scale. Phenolic compounds may be found in a wide range of amounts in a wide range of terrestrial plants, including fruits, vegetables, and many medicinal plants, where they play several important functions (Alamgir, 2018; Greenwell & Rahman, 2015). Since the identification of novel sources of phenolic compounds has attracted scientific and economic attention, marine ecosystems have a lot of potential in this field.

The surface of the planet is covered more than 70% by the marine oceans, seas, rivers, and lakes, which are rich sources of microorganisms and consequently of bioactive secondary metabolites. These compounds play a vital role in the ecological relationships of organisms with their hosts (Abd-Ellatif et al., 2019). Marine macroalgae, seaweeds, or seagrasses are rich sources of numerous substances with numerous biological impacts, including antioxidant (Ramah et al., 2014), antibacterial (Chandrasekaran et al., 2014), anti-cancer (Pradhan et al., 2020), anti-inflammatory (Dahms & Dobretsov, 2017), anti-viral (Besednova et al., 2021), anti-influenza (Besednova et al., 2021), and anti-COVID-19 (Rahman et al., 2022) activities. Marine organisms are the source of hundreds of novel compounds discovered every year. According to Hu et al. (2015), more than 1000 novel compounds have been found since 2008. Since the maritime environment is different, marine bioactive substances often have distinctive chemical structures and significant biological activity (Hamidi et al., 2019). The biological actions of these substances are intriguing to the drug development

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