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Short Communication

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Quinoline Derivatives Containing Substituted Piperazine Moieties as Potential Anti-Breast Cancer Agents

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ABSTRACT

Quinoline derivatives have been found to be promising candidates for breast cancer treatment. In this study, we focus on synthesizing new quinolines with substituted piperazine moieties to target EGFR (Epidermal Growth Factor Receptor), an important therapeutic target in breast cancer therapy. The synthesized quinoline compounds (8a-8i) were characterized by Infrared (IR), Mass Spectrometry (MSS), and Nuclear Magnetic Resonance (NMR) spectroscopy. The molecular docking studies indicated that the syntheses have a strong binding affinity towards the EGF receptor target site, with compound 8i exhibiting the highest binding affinity. This study highlights the potential of quinoline derivatives with substituting piperazines as potential anti-breast cancer agents.

Keywords: Quinoline; EGFR; Breast cancer

DESCRIPTION

Quinoline derivatives are recognized for their medicinal properties, especially in cancer treatment. However, issues such as drug resistance and toxicity limit their therapeutic use [1]. Quinoline-containing compounds have displayed an impressive array of biological properties over the years. The study focuses on synthesizing new quinoline derivatives with substituted piperazine moieties to target EGFR (Epidermal Growth Factor Receptor), an important therapeutic target in breast cancer treatment [2-6]. EGFR inhibitors are known to play a significant role in controlling cancer cell proliferation. Quinoline is classified as a heterocyclic molecule since it has two neighboring carbon atoms fused to an arene in its double-ring structure have a wide range of pharmacological activities like anti-bacterial, anti-fungal, antimalarial, anti-leishmanial and anticancer [7,8]. In recent research, it was shown that quinoline and its derivatives can inhibit tyrosine kinase, topoisomerase and DHODH kinase. Quinoline derivatives are increasingly used as anticancer drugs in pharmaceutical chemistry. The study employs a multi-faceted approach:

Synthesis and structural elucidation

The novel quinoline derivatives (8a-8i) were synthesized and their structures confirmed using IR, MASS, and NMR spectroscopy [9].

Molecular docking

Docking studies were performed to evaluate the binding affinity of the synthesized compounds at the ATP binding site of EGFR. Compounds showed promising docking scores and MM/GBSA energy values [10]. Subsequently, the newly identified synthesized compounds (8a-8i) in this study that were biologically assessed for their inhibitory action against EGFR kinases were subjected to SP-docking using the Glide module of the Schrodinger Suite (Schrodinger Release2023-2: Glide, Schrodinger, LLC, New York, NY, 2021.

***In vitro* evaluation**

The MTT test technique evaluated the chemically produced compounds *in vitro* cytotoxicity [11]. The colorimetric MTT metabolic activity test was utilized to assess cell viability against the MCF7 breast cancer andMCF12A normal epithelial cell lines [12-14]. The anticancer activity was tested against MCF-7 breast cancer cell lines. The EGFR-TK enzyme inhibition was assessed, with compound 8i showing the highest inhibition rate at 87.5%. The response parameter was determined by calculating the IC50 values, or the concentration needed to lower cell lifespan by 50% [15,16].

***In vivo* study**

The efficacy of compound 8i was further tested in a DMBA-induced rat model, confirming its potential as an anti-breast cancer agent. They were conducted on 6 healthy female wistar rats [17]. This study's foundation was provided by acute toxicity tests, which showed the drug's great therapeutic efficacy, non-toxic makeup, capacity to offset. Different substances cause oxidative stress and inflammation in rats.

The molecular docking studies indicated that the synthesized quinoline derivatives have a strong binding affinity towards the EGFR target site, with compound 8i exhibiting the highest binding affinity [18,19]. The *in vitro* studies supported these findings, showing that compound 8i effectively inhibits the EGFR-TK enzyme, thus preventing cancer cell proliferation. *In vivo* studies reinforced the potential of compound 8i, demonstrating significant anti-breast cancer activity in the DMBA-induced rat model. The electron-donating groups in compound 8i are suggested to enhance its interaction with biological targets, contributing to its efficacy [20].

CONCLUSION

This study highlights the potential of quinoline derivatives with substituted piperazine moieties as promising candidates for breast cancer treatment. Compound 8i, in particular, shows substantial promise due to its high binding affinity, significant EGFR-TK inhibition and effective anti-breast cancer activity in both *in vitro* and *in vivo* models. Further research and clinical trials are warranted to explore its full potential and therapeutic applicability. Hence, the primary objective of this study was to synthesize substituted 5-(4-chloroquinolin-3-yl)-methylidene)-2-(piperazin-1-yl)-1,3-thiazol-4(5H)-ones, denoted as 8a-i. The chemical structures of these compounds were analyzed using IR, Mass Spectrum, and proton NMR spectroscopy. Since the EGFR pathway has been linked to the development and spread of several malignancies, including breast cancer, we used a chemical technique in DMBA-induced models of breast cancer to examine compound 8i's effects on the EGFR pathway. Overall, the research indicates the viability of using chemical 8i as a focused treatment approach for breast cancer.

IMPLICATIONS

The findings of this study provide a valuable foundation for the development of more effective quinoline-based anticancer agents. By targeting EGFR with high specificity, these compounds could offer improved treatment outcomes with reduced side effects, addressing a critical need in breast cancer therapy.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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