INTRODUCTION

Cancer is continuing to be a major health problem in developing as well as undeveloped countries. It is a leading cause of mortality worldwide accounting for most of deaths. Among all types of cancer, lung, breast, colorectal, stomach, and prostate cancers are the underlying causes for the majority of cancer deaths. In this study, we expanded the work after purified by column chromatography. In continuation and expansion of our research, here we reported the click synthesis and antiproliferative evaluation of new series of benzothiazole scaffold which could generate active pharmaceutical ingredients (API) dotted with relevant pharmacological profile for instance, antimicrobial, antimalarial, anticonvulsant, antihelmintic, analgesic, antidiabetic, and anticancer.

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MATERIAL AND METHODS

In the expansion of our CADD work, based on data generated from molecular modeling study, four molecules considered for synthesis and screening against MCF-7 cell lines in search of potential anticancer therapy. These molecules successfully synthesized (shown in figure 1) by three steps and were purified by column chromatography.

ABSTRACT

Background: Cancer is continuing to be a major health problem in developing as well as undeveloped countries. It is a leading cause of mortality worldwide accounting for most of deaths. Epidermal growth factor receptor (EGFR) is a transmembrane glycoprotein and mutations that lead to EGFR overexpression or over activity have been associated with a variety of human cancers. The purpose of this study was to investigate the antiproliferative activity of novel benzothiazole derivatives as promising epidermal growth factor receptor (EGFR) inhibitors.

Experimental work: In the present investigation, we have synthesized novel N-(3-(benzo[d]thiazol-2-yl)-4-(4-substituted benzoyl)oxy) phenyl acetamido compounds based on the data generated from molecular docking and pharmacokinetics features. After confirmation of their structures, these compounds were screened against MCF-7 cell lines. Result and Discussion: Successfully synthesized four novel N-(3-(benzo[d]thiazol-2-yl)-4-(4-substituted benzoyl)oxy) phenyl acetamido compounds and structures of these compounds were confirmed by proton NMR, IR and Mass spectroscopy. These new derivatives were tested for their cytotoxic activity toward the human breast cancer MCF-7 cell line. Conclusion: Synthesized compounds revealed good cytotoxic effect, whereas two of them, H5 and H6, were found to be more potent.

INTRODUCTION

Cancer is continuing to be a major health problem in developing as well as undeveloped countries. It is a leading cause of mortality worldwide accounting for most of deaths. Among all types of cancer, lung, breast, colorectal, stomach, and prostate cancers are the underlying causes for the majority of cancer deaths. In this study, we expanded the work after molecular docking and dynamic study on proposed benzothiazole derivatives as promising epidermal growth factor receptor (EGFR) inhibitors. The binding of a ligand to EGFR induces conformational changes within the receptor which increase its intrinsic catalytic activity of a tyrosine kinase and result in autophosphorylation, which is necessary for biological activity. Therefore, inhibitors of EGFR-inhibiting EGFR kinase activity by competing with its cognate ligands-may potentially constitute a new class of effective drugs in clinical use or cancer therapy.

Benzothiazole derivatives become a major area of emphasis for the organic chemists due to varied spectrum of pharmacological profile for instance, antimicrobial, antimalarial, anticonvulsant, antihelmintic, analgesic, antidiabetic, and anticancer.

MATERIAL AND METHODS

In the expansion of our CADD work, based on data generated from molecular modeling study, four molecules considered for synthesis and screening against MCF-7 cell lines in search of potential anticancer therapy. These molecules successfully synthesized (shown in figure 1) by three steps and were purified by column chromatography.

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Results and Discussion

Their structures were characterized by FTIR, 1H NMR and Mass spectroscopy.

Spectral data

N-(3-benzo[d]thiazol-2-yl)-4-((4-methylbenzyl)oxy)phenylacetamide (H5):

Yellow crystals, % yield: 74%, MP: 292°C, FTIR: 3048 (Ar-C), 1624 (C-O), 1596 (C=N), 1538 (C=C), 1H NMR: δ 1.98 (3H, s), 5.12 (2H, s), 6.87-6.96 (2H, 6.88 (dd, J = 8.7, 1.5 Hz), 6.93 (dd, J = 8.6, 0.4 Hz)), 7.05-7.21 (4H, 7.08 (dd, J = 8.1, 7.5, 1.8 Hz), 7.11 (dd, J = 7.6, 7.2, 1.5 Hz), 7.09 (ddd, J = 8.0, 1.1, 0.5 Hz), 7.08 (ddd, J = 8.1, 7.4, 1.1 Hz), 7.12 (1H, ddd, J = 8.1, 1.7, 0.5 Hz), 7.43-7.50 (3H, 7.44 (ddd, J = 7.5, 1.7, 0.5 Hz), 7.48 (dd, J = 1.6, 0.4 Hz), 7.45 (ddd, J = 7.3, 6.5, 1.5 Hz)), 7.89 (1H, ddd, J = 6.98 1.5, 0.5 Hz), EI-MS: m/z = 388

N-(3-benzo[d]thiazol-2-yl)-4-((2-fluorobenzyl)oxy)phenylacetamide (H6):

Pale yellow crystals, % yield: 65%, MP: 244°C, FTIR: 3062 (Ar-C), 1636 (C-O), 1584 (C=N), 1533 (C=C), 762(C=Cl), 1H NMR: δ 2.44 (3H, s), 5.12 (2H, s), 6.71-6.94 (2H, 6.83 (dd, J = 8.6, 1.5 Hz), 6.91 (dd, J = 8.5, 0.4 Hz)), 7.10-7.19 (4H, 7.11 (dd, J = 8.0, 7.4, 1.7 Hz), 7.17 (dd, J = 7.5, 7.1, 1.5 Hz), 7.08 (ddd, J = 8.2, 1.3, 0.5 Hz), 7.09 (ddd, J = 8.0, 7.4, 1.4 Hz)), 7.07 (1H, ddd, J = 8.1, 1.7, 0.5 Hz), 7.41-7.52 (3H, 7.46 (ddd, J = 7.5, 1.4, 0.5 Hz), 7.49 (dd, J = 1.5, 0.5 Hz), 7.44 (ddd, J = 7.2, 6, 1.5 Hz)), 7.46 (1H, ddd, J = 6.8, 1.5, 0.5 Hz), EI-MS: m/z = 392

3-(benzo[d]thiazol-2-yl)-4-((4-fluorobenzyloxy)aniline (H7):

Yellow brown crystals, % yield: 79%, MP: 242°C, FTIR: 3039 (Ar-C), 1648 (C-O), 1582 (C=N), 1548 (C=C), 762(C=Cl), 1H NMR: δ 2.53 (3H, s), 5.32 (2H, s), 6.77-6.88 (2H, 6.83 (dd, J = 8.6, 1.5 Hz), 6.87 (dd, J = 8.6, 0.5 Hz)), 7.08-7.18 (4H, 7.12 (dd, J = 8.2, 7.5, 1.8 Hz), 7.16 (dd, J = 7.5, 7.1, 1.5 Hz), 7.07 (ddd, J = 8.0, 1.5, 0.5 Hz)), 7.09 (ddd, J = 8.0, 1.2, 0.5 Hz), 7.08 (1H, ddd, J = 8.1, 1.7, 0.5 Hz), 7.44-7.54 (3H, 7.46 (ddd, J = 7.6, 1.5, 0.5 Hz), 7.52 (dd, J = 1.5, 0.4 Hz), 7.44 (ddd, J = 7.2, 6.8, 1.6 Hz)), 7.46 (1H, ddd, J = 6.9, 1.5, 0.5 Hz)

3-(benzo[d]thiazol-2-yl)-4-((naphthalene-1-ylmethoxy)aniline (H8):

Pale brown crystals, % yield: 62%, MP: 276°C, FTIR: 3074 (Ar-C), 1632 (C-O), 1592 (C=N), 1544 (C=C), 1H NMR: δ 2.51 (3H, s), 5.42 (2H, s), 6.74-6.88 (2H, 6.82 (dd, J = 8.6, 1.5 Hz), 6.87 (dd, J = 8.5, 0.5 Hz)), 7.07-7.14 (4H, 7.11 (dd, J = 8.2, 7.0, 1.6 Hz), 7.11 (ddd, J = 7.5, 7.2, 1.5 Hz), 7.10 (ddd, J = 8.2, 1.2, 0.5 Hz), 7.09 (ddd, J = 8.0, 7.5, 1.2 Hz)), 7.08 (1H, ddd, J = 8.0, 1.6, 0.5 Hz), 7.45-7.54 (3H, 7.45 (ddd, J = 7.5, 1.5, 0.5 Hz), 7.47 (dd, J = 1.5, 0.4 Hz), 7.46 (ddd, J = 7.2, 6.9, 1.6 Hz)), 7.49 (1H, ddd, J = 6.8, 1.5, 0.5 Hz)

Anticancer Activity

Selected synthesized benzothiazole molecules were screened for anticancer activity against MCF-7 cell lines and found to be with potential good results. The IC50 concentration MCF-7 cells were determined by MTT assay. The inhibition activity of Compound H5, H6, H7 & H8 on MCF-7 cells were plated and treated with different concentration such as 0.1, 10, 50, 100 µg/mL. The IC50 value was determined based on cell viability rates.
CONCLUSION

Based on CADD work, compounds which have shown higher selectivity and great potential have been synthesized and confirmed their structures by FTIR, Proton NMR and Mass spectroscopy. The new derivatives were tested for their cytotoxic activity toward the human breast cancer MCF-7 cell line. They revealed good cytotoxic effect, whereas two of them, H6 and H7, were found to be more potent. Therefore, it can be concluded that proposed molecules have great potential and are safer chemical agents for therapeutic application in cancer therapy.

Conflict of Interest

There is no conflict of interest.

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