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RESEARCH PAPER

DISCOVERY OF NOVEL 4-AMINOPTERIDINE DERIVATIVES AS EGFR INHIBITORS: AN *IN SILICO* APPROACH

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The epidermal growth factor receptor (EGFR) is a member of the ErbB family of the receptor tyrosine kinase that plays crucial role in many different cells signaling pathways. EGFR overexpression leads to the growth of cancerous cells. As a result, EGFR is considered as one of the key targets for cancer therapy. In this study, ten novel 4-amino pteridine derivatives were designed and *in silico* studies were performed to find out novel hits as EGFR inhibitors. The *in silico* methods includes molecular docking studies, druglikeness screening, *in silico* toxicity screening and bioactivity prediction. All the designed compounds had druglikeness properties and showed no violations as per the Lipinski rule. In docking studies, three compounds QZ7, QZ8 and QZ10 were found which had higher binding affinity as compared to standard drug, lapatinib. Bioactivity prediction of designed compounds suggested that all the compounds may act through kinase inhibition. Out of the ten compounds, three compounds QZ7, QZ8 and QZ10 were found with good potential to be explored as EGFR inhibitors.

Key words: EGFR inhibitor, 4-Aminopteridine derivative, Cancer, *In silico* study, Docking.

INTRODUCTION

In multicellular organisms, a balance between intercellular and intracellular communication is crucial for normal and healthy living. The passage of information between cells *via* a number of signaling pathways is crucial for different biological activities. This signaling pathways includes One of the key signaling pathways involved in numerous cellular processes such cell growth, multiplication, and death are receptor tyrosine kinases (RTKs) [1, 2]. The importance of RTKs in cancer was made clear by recent developments in the field of oncology. The development of molecular biology makes it easier to pinpoint the precise mechanism of RTK-mediated oncogenic activation [3, 4]. RTKs contain cytoplasmic domain receptors in addition to cell surface receptors. Normal cellular tyrosine kinase phosphorylation levels are strictly regulated. Multiple mechanisms exist in cancer that activate RTKs in an oncogenic manner. These aberrant actions improved signal generation, RTK oncogene fusions, gene amplifications, and oncogenic mutations. RTKs can become oncogenic activated by overexpressing ligands or adaptor proteins, and by mutating signaling pathways [5, 6].

RTKs are divided into several subfamilies, including the insulin-like growth factor receptor, fibroblast growth factor receptor, vascular endothelial growth factor receptor, and epidermal growth factor receptor. RTKs from different subfamilies are explored as cancer therapeutic targets [7]. The epidermal growth