Research Article

Treating Oral Cancer by Targeting Human Epidermal Growth Factor 2

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ABSTRACT

The aim of the present study is to describe the role of HEGF pathway in oral cancer with special focus on its role during the carcinogenesis process. The study paves way for the therapeutic role of HEGF in oral cancer. The research aims at analysing the use of human epidermal growth factor 2 in treating oral cancer and its beneficial aspects. HEGF acts a potent mitogenic factor that plays an important role in the growth, proliferation and differentiation of numerous cell types by binding to its receptor HEGF. This protein acts by binding with high affinity to the cell surface receptor, epidermal growth factor on the cell surface. HEGF plays an important role in the pathogenesis of oral carcinoma. As EGFR is associated with cell proliferation, growth and differentiation, this research aims at throwing light on the use of HEGF and its benefits in treating oral cancer. Docking studies of the herbal compounds showed that, this Doxorubicin ligand is good molecule which docks well with the human epidermal growth factor and treated oral cancer.

Keywords: HEGF pathway, oral cancer, Doxorubicin ligand, Docking studies.

INTRODUCTION

Oral cancer is a serious problem growing in incidence in many parts of the world; it is considered the sixth most common cancer and despite sophisticated surgical and radio therapeutic modalities, oral squamous cell carcinoma, which represents 90% of oral cancers, is characterized by poor prognosis and a low survival rate.[4] The human epidermal growth factor 2 family of receptors plays a central role in the pathogenesis of several human cancers. They regulate cell growth, survival, and differentiation via multiple signal transduction pathways and participate in cellular proliferation and differentiation.[2] HER2 is expressed in many tissues and its major role in these tissues is to facilitate excessive/uncontrolled cell growth and tumorigenesis[3] EGF acts by binding with high affinity to epidermal growth factor receptor (EGFR) on the cell surface. This stimulates ligand-induced dimerization, activating the intrinsic protein-tyrosine kinase activity of the receptor). The tyrosine kinase activity, in turn, initiates a signal transduction cascade that results in a variety of biochemical changes within the cell – a rise in intracellular calcium levels, increased glycolysis and protein synthesis, and increases in the expression of certain genes including the gene for EGFR – that ultimately lead to DNA synthesis and cell proliferation. With increased understanding of HER biology, it has now been recognized that HER2 over expression also occurs in other forms of cancers also such as stomach, ovaries lung, uterine cervix, head and neck, and esophagus .Apart from its role in development of various cancers, it has also been intensely evaluated as a major therapeutic target.

MATERIALS AND METHODS

Herbal compounds

A literature study was made on the herbal compounds with antibacterial activity. The crystallographic structure of molecular target protein was downloaded from the RCSB protein Data Bank. The chemical structure of vinblastine, vincristine, vindesine, topothecan, irinothecan, doxorubicin, daunorubicin, epirubicin, idarubicin was obtained from PubChem compound database. It was prepared by using Biovia discovery studio 2016 and SDF format of this ligand was converted to PDBQT file using PyMol version 1.7.4.5 tool to generate atomic coordinates

Docking

Docking is a process in which we can find the best fit position or conformation of a ligand in the active site or a binding site of a protein. The active sites are the coordinates of the ligand in the original target protein grids, and these active binding sites of target protein were analyzed using the Bravio Discovery Studio version 2016. A computational ligand-target docking approach was used to analyze structural complexes of the protein (target) with vinblastine, vincristine, vindesine, topothecan, irinothecan, doxorubicin, daunorubicin, epirubicin, idarubicin in order to understand the structural basis of this protein target specificity. Docking was carried out by iGemdoc option based on scoring functions as listed in Figure 1 and Figure 3. The energy of interaction of herbal components with the adhesion protein is assigned.

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RESULTS AND DISCUSSION

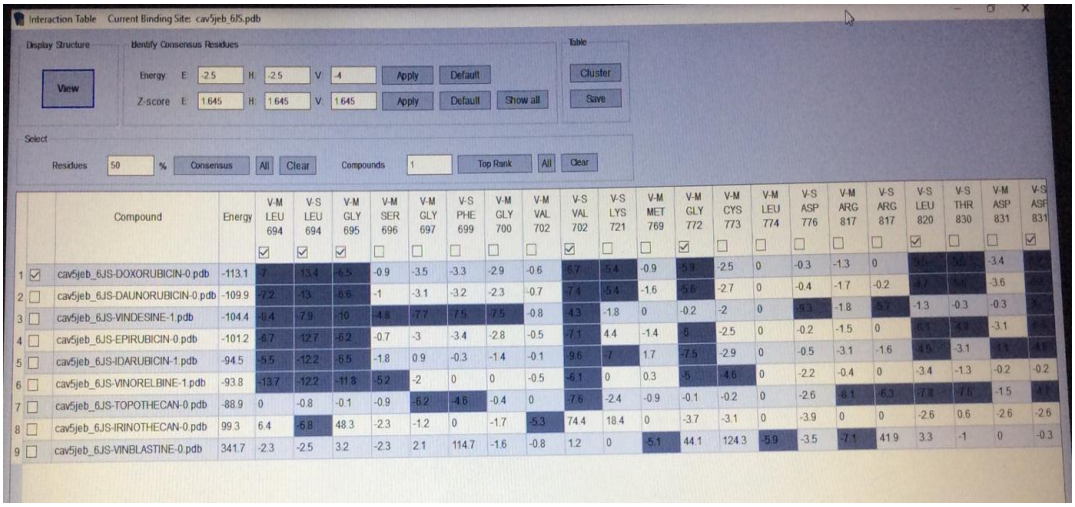

Figure 1: Table showing different herbal compounds along with their scoring

The binding energy indicates that affinity of the Human epidermal growth factor docked with herbal components.

Among the five compounds, Doxorubicin showed, lower negative value which indicates active binding to the target site and also showed the best interaction with target proteins based on the VDW values as compared to standard.

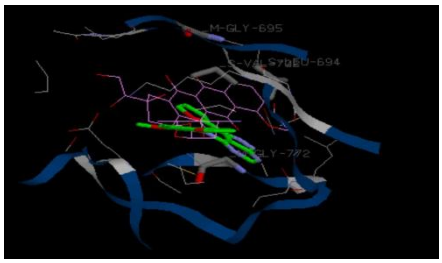

Figure 2: Molecular Graphic Structure of Doxorubicin with Target

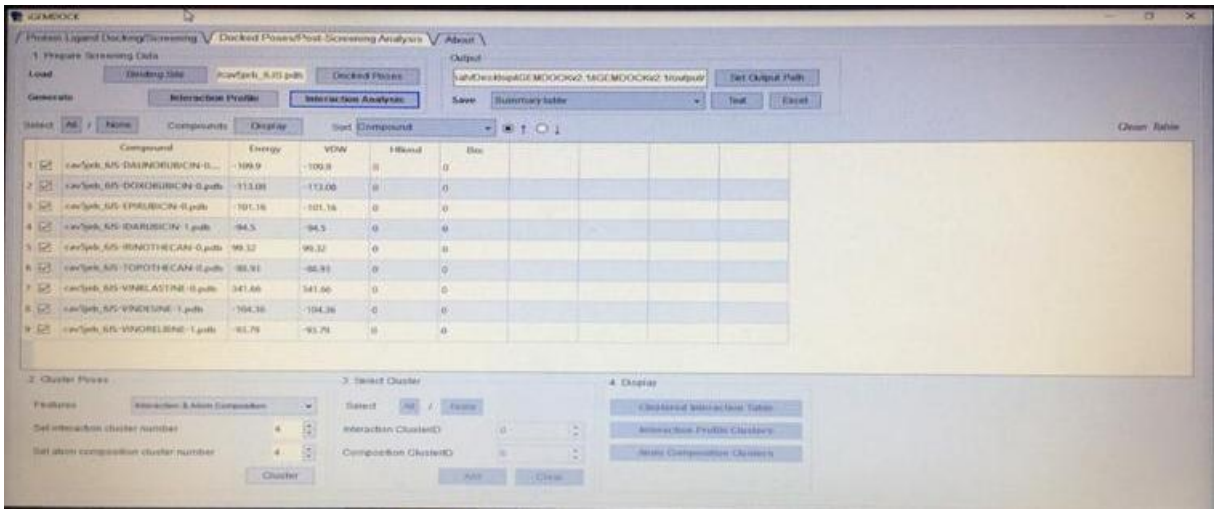

Figure 3: Table showing different compounds with their VDW

CONCLUSION

Molecular Docking helps to reduce time, effort and money required for a wet lab research in finding the best inhibitor in a group of compounds.

Docking studies of the herbal compounds showed that Doxorubicin ligand is a good molecule which docks well with Human epidermal growth factor 2.

Therefore Doxorubicin molecule plays an important role in the EGFR pathway, by inhibiting the pathogenesis of oral carcinoma.

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