

RESEARCH ARTICLE

Computational Approach to the Discovery of Phytochemical Molecules with Therapeutic Potential Targets to the PKCZ protein

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Abstract: Background: Head and neck squamous cell carcinoma (HNSCC) is one of the most common malignancies in humans and the average 5-year survival rate is one of the lowest among aggressive cancers. Protein kinase C zeta (PKCZ) is highly expressed in head and neck tumors, and the inhibition of PKCZ reduces MAPK activation in five of seven head and neck tumors cell lines. Considering the world-wide HNSCC problems, there is an urgent need to develop new drugs to treat this disease, that present low toxicity, effective results and that are relatively inexpensive.

Method: A unified approach involving homology modeling, docking and molecular dynamics simulations studies on PKCZ are presented. The *in silico* study on this enzyme was undertaken using 10 compounds from latex of *Euphorbia tirucalli* L. (aveloz).

Results: The binding free energies highlight that the main contribution in energetic terms for the compounds-PKCZ interactions is based on van der Waals. The per-residue decomposition free energy from the PKCZ revealed that the compounds binding were favorably stabilized by residues Glu300, Ileu383 and Asp394. Based on the docking, Xscore and molecular dynamics results, euphol, β -sitosterol and taraxasterol were confirmed as the promising lead compounds.

Conclusion: The present study should therefore play a guiding role in the experimental design and development of euphol, β -sitosterol and taraxasterol as anticancer agents in head and neck tumors. They are potential lead compounds, better than other ligands based on the best values of docking and MM-PBSA energy.

Keywords: HNSCC, PKCZ, molecular marker, euphorbia tirucalli, homology modeling, molecular docking, molecular dynamics.

1. INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) develops in the oral cavity and is the sixth leading cancer by

incidence worldwide. This year, globally, 600,000 new cases of head and neck cancer are likely to occur and of these, 40-50% with HNSCC will only survive for 5 years [1]. According to the World Cancer Report of 2014, adding up pharyngeal, oral and laryngeal cancers in both sexes combined, 686,000 new cases were estimated for the year of 2012 with 375,000 estimated deaths for the same year. A decline in incidence can be seen since the 1990s for some countries such as India, China, USA, and Australia. However, conversely, increasing trends in incidence are being shown in

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