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Discovery of Amaranthin as a Promising Drug Target for Vascular Endothelial Growth Factor (VEGF) Therapy †

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Abstract: Background: Angiogenesis plays a major role in the process of tumour genesis through its capacity to acquire sustenance in the form of nutrients and oxygen. Hence, defining as one of the hallmarks of cancer. Vascular endothelial growth factor (VEGF) is a major regulator of angiogenesis both under normal conditions and in disease state, numerous studies has been shown that targeting VEGF has become the most prominent approach to stop tumour growth. Recently, amaranth has become an area of increasing scientific. This is due to its valuable biological properties, and wide pharmacological activity. Therefore it is of interest to study the molecular docking analysis of VEGF with amaranthin compounds as drug target discovery. **Material and methods:** A molecular docking study were conclude using autodock vina briefly the VEGF 3D structure was retrieve from protein data bank under the code of 2PVF, Amaranthin was retrieve from PUBCHEM (CID 6325284) both the protein and ligand were prepare using MGLTools then dock using autodick vina (V. 4.0). **Results:** the molecular docking results were visualizate using pymol software, our results shown that the binding affinity was −6.8 kcal/mol. Analysis of the docking results showed that selected compound interact with VEGF protein via H bond interactions. **Conclusions:** Natural products provide a promising opportunity to discover new compounds that can utilize as drugs given their chemical structure diversity. Of note Amaranthin shown an interesting drug target for targeting VEGF need further studies.

Keywords: angiogenesis; VEGF; amaranthin; molecular docking

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1. Introduction

Cancer in the last decades was defined as a disease of altered signaling and metabolism, causing uncontrolled division and survival of transformed cells [1]. Recently a new definition of cancer has emerged as a disease of uncontrolled proliferation by transformed cells subject to evolution by natural selection [2]. Beyond the concept of cancer, the most unique characteristic of cancer is its highly vascularized nature, enabling the tumors to grow and invade the surrounding tissues [3,4]. Through angiogenesis process which is tightly regulated by a balance of numerous positive and negative angiogenic factors within the vascular microenvironment. Among them vascular endothelial growth factor (VEGF) and its receptor (VEGFR) have been shown to play crucial roles not only in physiological but also in most pathological angiogenesis, such as cancer. VEGF/VEGFRs interaction has been regarded as a key regulator and attractive target for the development of anti-angiogenic drugs [5]. In the light of the complications and the side effect of most anticancer drugs, which Emerged as threats to human health that require a massive concerted effort in search of both preventive and treatment strategies. The focus of drugs target have been switch to natural compounds that may offer an alternative and promising drug target due to their special features in comparison with conventional synthetic molecules [6]. Hence *Amaranthus caudatus* L. has gained the focus of attention in recent years due to the

nutritional profile of its seeds additionaly to numerous bioactivities responsible for the therapeutic potential of this species [7]. Of note Amaranthin have a dual role in food and medicine [8]. Which make it a promising target of drug target. Therefore in this study we focus on the evaluation of the molecular docking analysis between VEGF receptor and Amaranthin compounds for potential drug discovery.

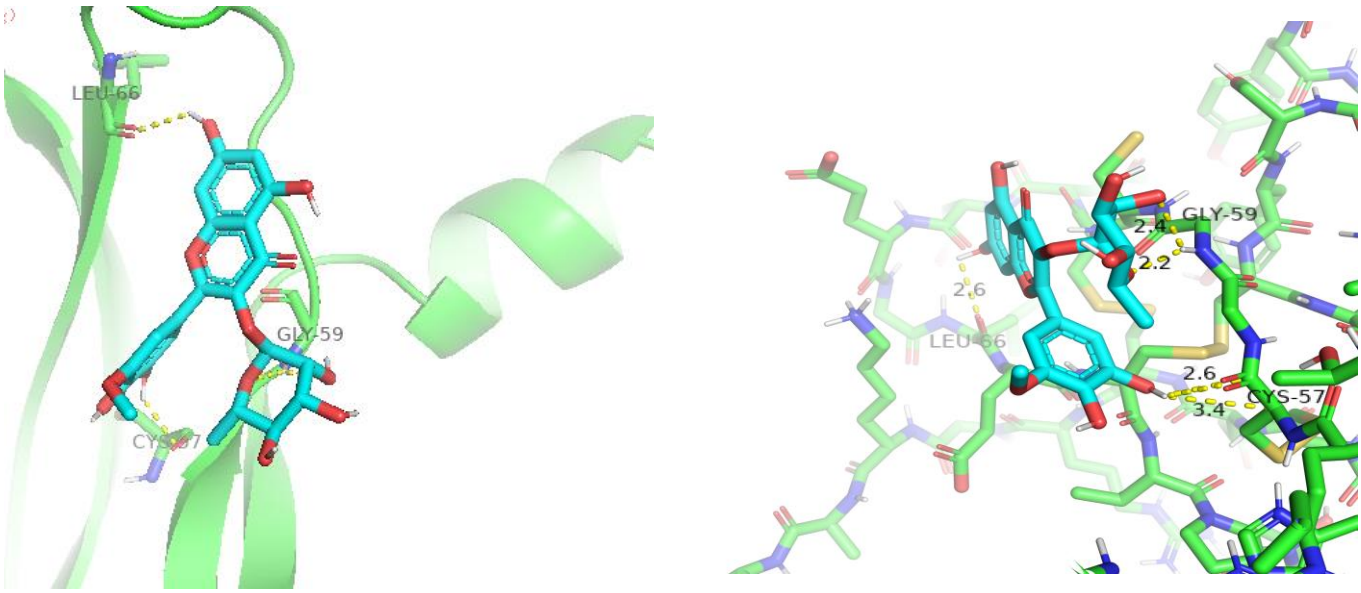
2. Materials and Methods

Protein/ligand Preparation

The The X-ray crystal structure of VEGF was retrieve from protein data bank (www.rcsb.org/pdb). Under the code of 2PVF, Amaranthin was retrieve from PUBCHEM (CID 6325284). The protein and ligand were subjected to simple preparation using MGLtools before dock using auto dock vina. Our output file was visualizated using PYMOL program.

3. Results and Discussion

In order to shield the light on the capacity of Amaranthin to interaction with the active VEGF site, the compound has been subjected to molecular docking simulation studies performed using autodock vina. The molecular docking of bioactive compound at the VEGF binding site was carried out on VEGF (PDB code: 2PVF). By using pymol the output file was then visualizated. The complex structures and the highest suitable binding modes were shown in Figure 1. The binding energy and H-bond information have been shown in Table 1.



(**A**) (**B**)

Figure 1. (**A**) Represent the docked pose of the VEGF interactions shown in ribbon representation. (**B**) The hot-spot residues shown in sticks representation and their appropriate distances.

Table 1. Interactions between VEGF (PDB: 2PVF)/ Amaranthin and the selected hot-spot residues, after docking.

Compound	Binding Energy Kcal/mol	H-Bond Interaction	Distance A^0
Amaranthin	−6.8 kcal/mol	CYS-57	2.6
		CYS-57	3.4
		GLY-59	2.2
		GLY-59	2.4

LEU-66	2.6

The binding affinity of VEGF interaction with Amaranthin was −6.8 kcal/mol. Additionally the Amaranthin show a strong hydrogen bonding interactions through amino acid residues CYS-57, GLY-59 and LEU-66. Analysis of the docking results showed that selected compounds interact with VEGF protein via H bond interactions with distance below $3A^0$. Which showed a strong interaction with active site residues. The presence of the H-bond interactions lay in their important role played by them that enabled the complex to attain the specified configuration of the complex structure. Based on Krishnan et al. study that was conducted on the compound of tomatos with VEGF [9] and our data we can suggest that Amaranthin compound may have anti-angiogenic activity.

4. Conclusions

Computational approaches have emerged as useful tools to guide experiments to expedite the drug design process. Molecular docking is one of the Basic CADD workflow in drug discovery. Our study showed the possibility of the interaction between Amaranthin and the active site of VEGF. Finally, the present study should open the way to further investigations.

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