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Exploring *Oroxylum indicum* Phytochemicals as VEGFR-2 Inhibitors: A Molecular Docking Approach for Cancer Management

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Abstract

Cancer is still a major health problem around the world and is one of the top causes of death. A protein called VEGFR-2 (vascular endothelial growth factor receptor 2) is important because it helps blood vessels grow by supporting the survival, movement, and growth of certain cells. This process is essential for tumors to grow and spread to other parts of the body. This study focused on evaluating the binding energy of phytochemicals from Oroxylum indicum with VEGFR-2 using computational techniques. Molecular docking was conducted via PyRx, a virtual screening tool, to analyze ligand-protein interactions. The data and molecular structures of the plant-based compounds and target proteins were obtained from databases like IMPPAT (Indian Medicinal Plants, Phytochemistry and Therapeutics) and PubChem. Protein structure validation was performed using tools, such as Protein Data Bank (PDB) Sum and BIOVIA Discovery Studio. The pharmacological properties of the ligands were assessed using ADME filters to determine their drug-like characteristics and therapeutic viability. Docking results identified Apigenin 7,4'-dimethyl ether, Biochanin A, Chrysin, Flavone (5,7-dihydroxy-6-methoxy), Hispidulin, Oroxylin A, and Prunetin, as ligands with the lowest binding energies to VEGFR-2. These plant-based compounds show promise as effective blockers of growth factor receptors, which are known to play a key role in the development and spread of cancer. While these findings suggest their suitability as candidates for cancer treatment and suppression, further in vitro investigations are essential to confirm their efficacy.

Keywords: VEGFR-2 inhibition, Oroxylum indicum, phytochemicals, molecular docking, tumor angiogenesis, cancer therapeutics

INTRODUCTION

Cancer is a condition characterized by disrupted cell signalling and unregulated cell division. It is among the most severe diseases affecting humans, resulting in millions of deaths annually across the world [1]. Cancer is a major global health challenge, ranking among the top causes of death and posing a significant obstacle to increased life expectancy. In 2019, the World Health Organization reported that cancer was the leading or second leading cause of death in individuals under 70 in 112 out of 183 countries [2]. Carcinogenesis is a complex process influenced by endogenous, exogenous, and environmental factors. Lifestyle factors, as part of the exogenous components, interact with endogenous elements, like genetic variations, metabolic imbalances, and hormonal changes, along with environmental factors, such as radiation, stress, infections, and toxins. This interplay disrupts cellular processes, ultimately leading to cancer [3].

Angiogenesis, the formation of new blood vessels from the existing vascular network, is essential for vascular system development and growth.

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Moreover, it is a precisely controlled process involved in embryonic development, tissue repair, wound healing, organ growth, and the menstrual cycle [4]. However, disequilibrium in angiogenesis regulators can result in inadequate blood vessel formation, contributing to conditions, such as ischemia, ulcers, infertility, and hair loss. Conversely, excessive angiogenesis has been linked to tumor growth, metastasis, and various other diseases, including age-related macular degeneration, which is associated with increased VEGF levels [5].

Tumor growth and metastasis are heavily dependent on tumor angiogenesis, which is controlled by both pro-angiogenic and anti-angiogenic factors produced by tumor and host cells [6]. Among several key growth factors, including VEGFs, PDGFs, FGFs, and cytokines, VEGFs and their receptor, VEGFR-2 (KDR), have a profound effect on angiogenesis. Upon activation, VEGFR-2 undergoes autophosphorylation, promoting endothelial cell proliferation, tumor angiogenesis, and metastasis. VEGFR-2 is found to be overexpressed in various cancers, such as breast, cervical, non-small cell lung, hepatocellular carcinoma, and renal carcinoma. In recent years, several VEGFR-2 inhibitors have been developed, with angiogenesis inhibition through VEGFR-2 blockade emerging as a promising strategy for creating targeted anticancer therapies [7].

The human VEGFR-2 gene, also called the kinase insert domain-containing receptor (KDR), is situated on chromosome 4q11-12 and encodes a receptor composed of 1,356 amino acids. The fully matured VEGFR-2 is a transmembrane glycoprotein with a molecular weight of 230 kD. Additionally, it has two other forms: a non-glycosylated version weighing 150 kD and an intermediate variant of 200 kD. Among these, only the mature glycosylated form facilitates intracellular signal transduction. In mice, VEGFR-2 is known as fetal liver kinase 1 (Flk-1), consisting of 1,367 amino acids and exhibiting 83% sequence similarity with human KDR [8].

VEGFR-2 exhibits a high affinity for VEGF-A and VEGF-E and a lower affinity for VEGF-C and VEGF-D. While primarily expressed in endothelial cells of blood and lymphatic vessels, VEGFR-2 is also weakly present in other cells, such as hematopoietic cells, neurons, retinal progenitors, osteoblasts, pancreatic ductal cells, and certain tumor cells. During embryonic development, VEGFR-2 plays a pivotal role in vasculogenesis. It is expressed early, around day 7.5 of gestation, on mesodermal hemangioblasts, guiding their migration, differentiation into endothelial cells, and the formation of vascular structures in the yolk sac. The absence of VEGFR-2 in animal models leads to embryonic death due to a lack of vascular development [9].

Upon VEGF binding, VEGFR-2 undergoes autophosphorylation at distinct sites, initiating intracellular signalling. Unlike VEGFR-1, which has limited tyrosine kinase activity, VEGFR-2 is highly active. Its activation triggers a cascade of signalling molecules, including VRASP, PLCγ, ScK, Cdc42, Src, and PI3K, which regulate key cellular processes, such as migration, proliferation, survival, and permeability. These signals are transmitted through downstream pathways like ERK, p38MAPK, and Akt/PKB. VEGFR-2 is central to physiological and pathological angiogenesis, driving VEGF-induced endothelial cell responses [10].

Dysregulated VEGFR-2 expression and signalling, observed in most cancer types, are strongly associated with poor prognosis. This suggests that targeting VEGFR-2 overexpression in endothelial or malignant cells could serve as a promising therapeutic approach for various cancers [11].

Oroxylum indicum, commonly referred to as the Indian trumpet flower, is native to tropical regions including India, Japan, China, Sri Lanka, and Malaysia. with its rich ethnomedicinal history, has been used in Ayurveda and traditional medicine, where its roots, bark, seeds, and leaves treat various ailments, such as asthma, bronchitis, skin disorders, rheumatoid arthritis, cancer, diarrhoea, fever, ulcers, and jaundice. The plant is recognized for its wide range of therapeutic properties, including anti-inflammatory, antiulcer, hepatoprotective, anticancer, antioxidant, photo cytotoxic, antiproliferative, antiarthritic, antimicrobial, antimutagenic, and immunostimulant effects [12–14]. It has been

demonstrated that extracts of *Oroxylum indicum* have potential as sources of anticancer compounds [13].

In addition to its broad pharmacological activities, *Oroxylum indicum* has shown promising anti-cancer potential. Its bioactive compounds, such as oroxylin A, chrysin, and baicalein, have demonstrated the ability to induce apoptosis, inhibit tumor progression, and modulate cancer-related signalling pathways like NF-κB and p53. These properties highlight its potential as a valuable resource for developing novel anticancer therapies while underscoring its importance in both traditional and modern medicine [14].

This study focuses on 33 phytochemicals derived from *Oroxylum indicum* to evaluate their therapeutic potential against VEGFR-2, a critical factor in cancer pathogenesis. Their efficacy was assessed using molecular docking and pharmacological property analysis.

METHODS

Retrieval of Ligands

Phytochemicals from *Oroxylum indicum* were sourced from the IMPPAT database (https://cb.imsc.res.in/imppat/), and their canonical SMILES, PubChem CID, and 2D SDF models were subsequently retrieved from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/).

Physicochemical Analysis of Ligands

To assess the pharmacokinetic and physicochemical properties of the selected phytochemicals, ADME (Absorption, Distribution, Metabolism, and Excretion) analysis was conducted using the SwissADME tool (http://www.swissadme.ch/). The evaluation focused on molecular weight, bioavailability, gastrointestinal absorption, hydrogen bond acceptors, Lipinski's rule compliance, and PAINS and Brenk alerts. Based on these criteria, 11 phytochemicals were identified as potential candidates for docking studies with VEGFR-2 [15].

Retrieval of Protein and its purification

The VEGFR-2 protein structures with PDB IDs: 1VR2 and 1Y6A were obtained from the PDB database. Using Biovia Discovery Studio, the protein structures were refined by removing ligands, water molecules, and other heteroatoms. The purified proteins were then saved as separate PDB files for subsequent docking studies.

In PyRx, the purified proteins were loaded and converted into macromolecules. The Vina Wizard in PyRx was used to prepare the protein structure files, converting them from PDB to PDBQT format. The grid box centre and dimensions were adjusted to define the docking region accurately [16].

Validation of Protein Structure

Ramachandran plots are used to evaluate the distribution of the (ϕ, ψ) torsion angles of a protein's backbone [17]. This method is highly effective and convenient as it allows the assessment of three-dimensional protein structures using just two variables: the φ and ψ angles. These angles are represented on a two-dimensional graph known as the Ramachandran plot. This plot serves as a key tool for verifying the stereochemical quality of protein structures by analyzing the distribution of (φ, ψ) angle pairs [18]. A hydrophilicity plot measures the hydrophobicity or hydrophilicity of amino acids in a protein. The purified protein files were used to generate the Ramachandran plot and determine the secondary structure of the protein using PDBsum Generate (https://www.ebi.ac.uk/thornton-srv/databases/pdbsum/). The hydrophilicity chart was then obtained using ProtScale (https://web.expasy.org/protscale/) to analyze the distribution of hydrophilic and hydrophobic regions within the protein [19].

Molecular Docking

This research utilized Molecular Docking to evaluate potential therapeutic interactions. PyRx, a computational drug discovery platform, was used to screen 11 selected phytochemicals against two

VEGFR-2 target proteins with PDB IDs 1vr2 and 1y6a. Prior to docking, the purified proteins were loaded into the PyRx environment and converted into a macromolecule. Subsequently, the phytochemicals were prepared as ligands by undergoing energy minimization and conversion to the PDBQT format. For each target protein, specific grid parameters were defined: VEGFR-2 (1vr2): Centre: X: 38.9641, Y: 25.0873, Z: 13.4357; Dimensions (Angstrom): X: 46.0348, Y: 60.0396, Z: 48.2460 and VEGFR2 (1y6a): Centre: X: 5.9987, Y: 38.8482, Z: 23.0917; Dimensions (Angstrom): X: 46.8630, Y: 47.5170, Z: 62.4940. The docking simulations were then executed, allowing each ligand to explore nine distinct conformational changes within the defined grid. The binding affinity of each conformation was rigorously assessed, and the top five conformations exhibiting the lowest binding affinity, which corresponded to zero RMSD, were identified as the most promising binding complexes. Finally, the docked ligand structures were extracted in PDB format and visualized to gain insights into the specific protein-ligand interactions.

Visualization

The docked structures generated by PyRx were further analyzed using the Biovia Discovery Studio. The top 5 best combinations for each protein, exhibiting the least binding energies, were extracted in PDB format and visualized within the Biovia Discovery Studio. A comprehensive analysis was conducted, encompassing the investigation of non-bonded interactions and the generation of three-dimensional interaction models [20].

RESULTS

Purification and Structural Analysis of Protein

Two VEGFR-2 protein structures, identified by PDB IDs 1VR2 and 1Y6A, were retrieved from the Protein Data Bank (PDB) and refined by removing ligands, water molecules, and heteroatoms using Biovia Discovery Studio. The resulting, purified protein structures were saved as individual PDB files for use in subsequent docking analyzes.

Secondary Structure

Figure 1 of VEGFR-2 (PDB ID: 1VR2), comprising 275 residues, is characterized by two distinct structural domains. The first domain (CATH 3.30.200.20) falls under the Alpha-Beta class with a 2-layer sandwich architecture, while the second domain (CATH 1.10.510.10) belongs to the Mainly Alpha class with an orthogonal bundle design. Additionally, the structure features two beta sheets, eight strands, five beta hairpins, and five beta bulges. It also includes 13 helices with 16 helix–helix interactions, 20 beta turns, and two gamma turns, showcasing its intricate and well-organized configuration.

Figure 2 of VEGFR-2 (PDB ID: 1Y6A), composed of 261 residues, consists of two domains. The first domain (CATH 3.30.200.20) falls under the Alpha–Beta class, exhibiting a 2-layer sandwich architecture, while the second domain (CATH 1.10.510.10) is classified as mainly Alpha, featuring an orthogonal bundle design. The structure includes 2 beta sheets, 7 strands, 4 beta hairpins, 4 beta bulges, 14 helices with 13 helix–helix interactions, 12 beta turns, and 2 gamma turns.

Ramachandran Plot

The Ramachandran Plot statistics for VEGFR-2 (PDB ID: 1VR2) reveals that out of 275 residues, 87.3% fall within the most favored regions, 12.2% are in additional allowed regions, and 0.4% are in generously allowed regions. Importantly, no residues are found in disallowed regions. Of the 237 non-glycine and non-proline residues, 6 are end residues (excluding glycine and proline), while the structure includes 18 glycine and 14 proline residues.

The Ramachandran Plot statistics for VEGFR-2 (PDB ID: 1Y6A) shows that 92.8% of the residues are in the most favored regions, 6.7% are in additional allowed regions, and 0.4% are in generously allowed regions, with no residues in disallowed regions. The structure contains 223 non-glycine and non-proline residues, including 9 end residues, 15 glycine residues, and 14 proline residues, totalling 261 residues [21].

The secondary structure and Ramachandran plot of the protein were derived from PDBsum Generate (https://www.ebi.ac.uk/thornton-srv/databases/pdbsum/).

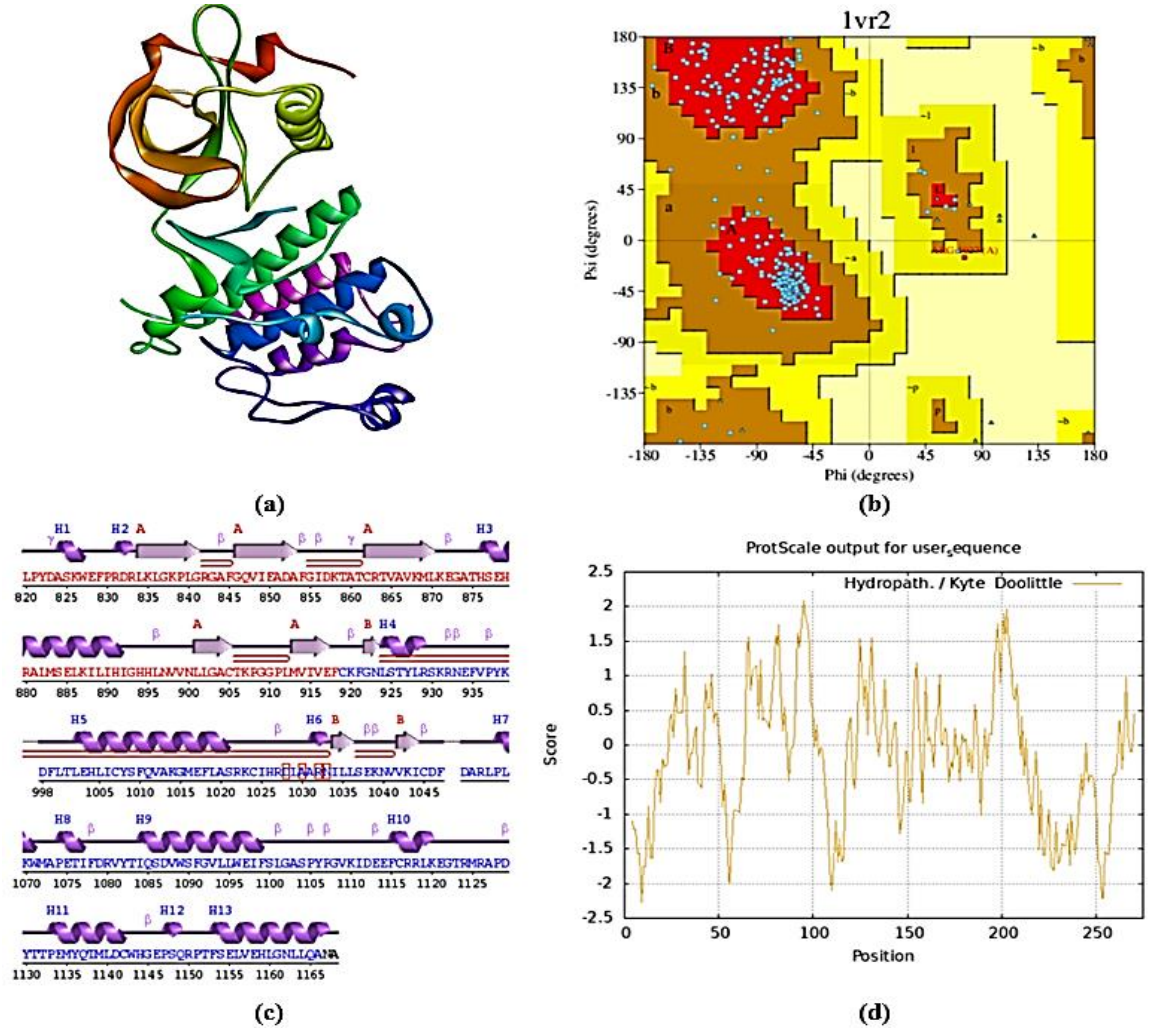

Figure 1. Structural characterization of VEGFR-2 (1VR2) protein (a) 3D structure of the purified protein, (b) The Ramachandra plot, (c) Secondary protein structure, and (d) The hydrophobicity plot.

Pharmacological Studies

The canonical SMILES and PubChem CIDs of 33 phytochemicals belonging to the plant *Oroxylum indicum* was obtained from the IMPPAT database and subjected to ADME (Absorption, Distribution, Metabolism, and Excretion) analysis using the SwissADME tool (Table 1).

Table 1. Name, PubChem ID, and the canonical smiles of the top ligands chosen.

S.N.	Phytochemical Name	PubChem CID	Smiles
1	Apigenin 7,4'-dimethyl ether	5281601	COC1=CC=C(C=C1)C2=CC(=O)C3=CC(C=C(C=C3O2)OC)O
2	Biochanin A	5280373	COC1=CC=C(C=C1)C2=COC3=CC(=CC(=C3C2=O)O)O
3	Chrysin	5281607	C1=CC=C(C=C1)C2=CC(=O)C3=CC(C=C(C=C3O2)O)O
4	Flavanone, 5,7-dihydroxy-6-methoxy-	177032	COC1=C(C2=C(C=C1O)C@@HC3=CC=CC=C3)O
5	Hispidulin	5281628	COC1=C(C2=C(C=C1O)OC(=CC2=O)C3=CC=C(C=C3)O)O
6	Oroxylin A	5320315	COC1=C(C2=C(C=C1O)OC(=CC2=O)C3=CC=CC=C3)O
7	Prunetin	5281804	COC1=CC(=C2C(C=1)OC=C(C2=O)C3=CC=C(C=C3)O)O

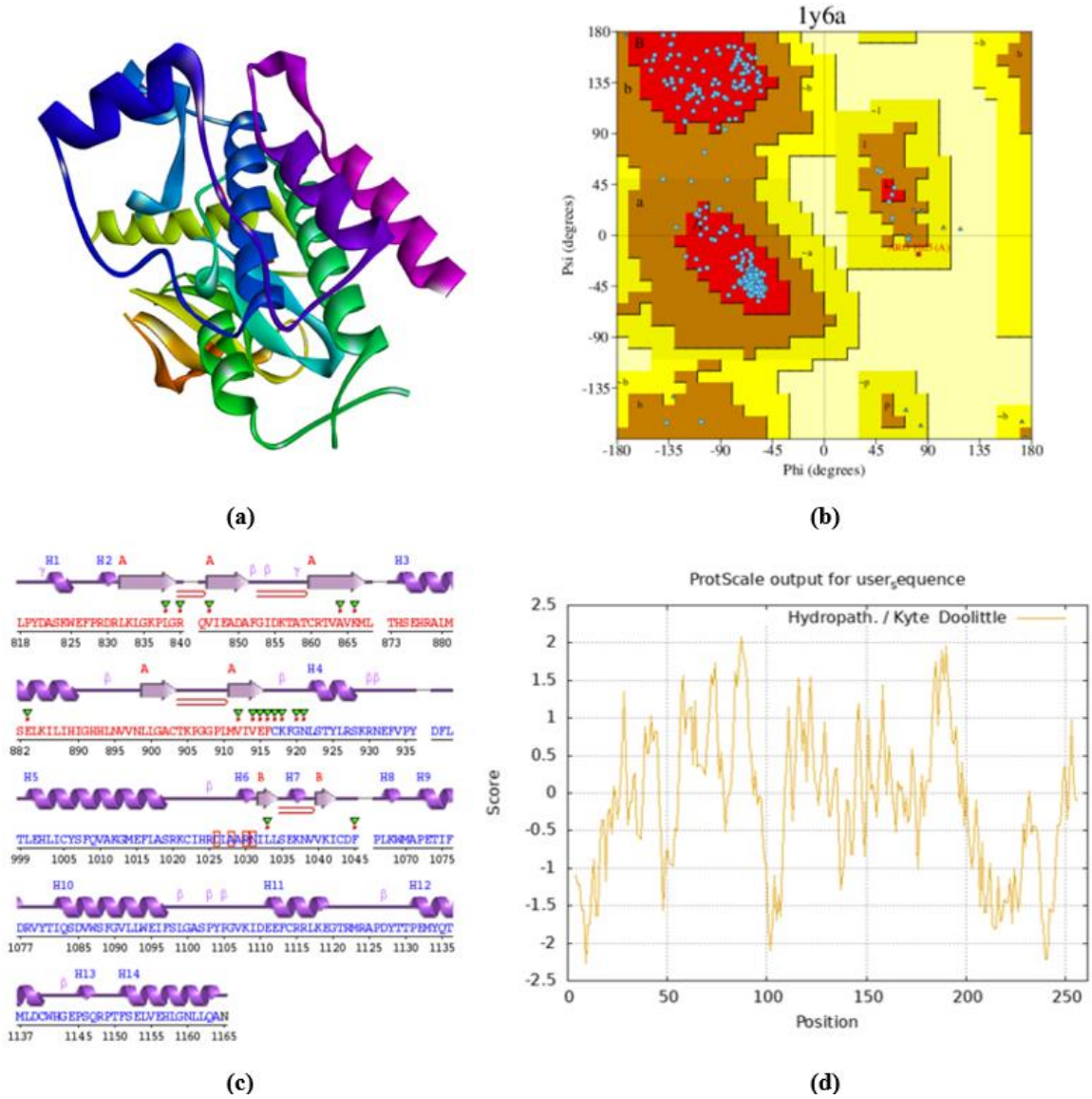

Figure 2. Structural characterization of VEGFR-2 (1Y6A) protein (a) 3D structure of the purified protein, (b) The Ramachandra plot, (c) Secondary protein structure, and (d) The hydrophobicity plot.

Key parameters, such as molecular weight, drug-likeness (Lipinski's Rule of Five), gastrointestinal absorption, and bioavailability score were evaluated. Based on these parameters, 11 ligands were shortlisted for molecular docking studies. The 2D SDF format of these ligands was retrieved from the PubChem database.

Table 2. Physicochemical properties of the top ligands chosen.

Ligand	MW	H-bond acceptors	H-bond donors	GI absorption	Lipinski violations	Bioavailability Score	PAINS alerts	Brenk alerts
5281601	298.29	5	1	High	0	0.55	0	0
5280373	284.26	5	2	High	0	0.55	0	0
5281607	254.24	4	2	High	0	0.55	0	0
177032	286.28	5	2	High	0	0.55	0	0
5281628	300.26	6	3	High	0	0.55	0	0
5320315	284.26	5	2	High	0	0.55	0	0
5281804	284.26	5	2	High	0	0.55	0	0

Molecular docking simulations were carried out using PyRx, a virtual screening tool designed for efficient docking analysis. Binding energies and RMSD values were recorded for all docking results. Among the nine docking conformations generated, those with RMSD values of 0 were prioritized. From these, the five ligands with the lowest binding energies for each target protein were selected for further analysis (Table 2).

For VEGFR2, the top five ligands with the lowest binding energies were identified as Apigenin 7,4'-dimethyl ether, Flavanone, 5,7-dihydroxy-6-methoxy-, Hispidulin, Prunetin, and Oroxylin A for PDB ID: 1VR2, and Flavanone, 5,7-dihydroxy-6-methoxy-, Biochanin A, Chrysin, Prunetin, and Oroxylin A for PDB ID: 1Y6A (Tables 3 and 4).

Table 3. Binding affinity of top 5 ligands towards VEGFR2 (PDB ID: 1vr2).

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
Apigenin 7,4'-dimethl ether	-7.2	0	0
Flavanone, 5, 7-dihydroxy-6methoxy-	-7.3	0	0
Hispidulin	-7.3	0	0
Prunetin	-7.4	0	0
Oroxylin A	-7.2	0	0

Table 4. Binding affinity of top 5 ligands towards VEGFR2 (PDB ID: 1y6a).

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
Flavanone, 5,7-dihydroxy-6-methoxy-	-8.3	0	0
Biochanin A	-8.4	0	0
Oroxylin A	-8.4	0	0
Chrysin	-8.7	0	0
Prunetin	-8.6	0	0

This systematic approach adheres to widely accepted computational protocols for ligand screening, ADME profiling, and docking simulations [22, 23].

Molecular Docking Analysis

Molecular docking was carried out to investigate the interactions between selected ligands and the VEGFR-2 protein targets. In this study, 11 ligands were docked against two VEGFR-2 protein structures: PDB IDs 1VR2 and 1Y6A. The docking simulations were performed using PyRx software. The protein structures were retrieved from the Protein Data Bank (PDB), while the ligands were downloaded from the PubChem database in SDF format. Prior to docking, the ligand structures were energy-minimized and converted into PDBQT format, and the protein structures were prepared as macromolecules.

For the docking setup in PyRx, a grid box was defined with specific coordinates and dimensions to encompass the binding site of the proteins. The docking results, including binding affinities, RMSD/ub, and RMSD/lb values, were generated, and the conformations with the lowest binding affinities and RMSD values were selected as the best docking poses.

Among the 11 ligands screened, the five ligands with the lowest binding affinities for each VEGFR-2 protein structure were selected for further analysis. These included:

- *For VEGFR-2 (PDB ID: 1VR2):* Apigenin 7,4'-dimethyl ether, Flavanone, 5,7-dihydroxy-6-methoxy-, Hispidulin, Prunetin, and Oroxylin A.
- *For VEGFR-2 (PDB ID: 1Y6A):* Flavanone, 5,7-dihydroxy-6-methoxy-, Chrysin, Biochanin A, Prunetin, and Oroxylin A.

Visualization

The selected ligands were further analyzed. Visualization included generating three-dimensional (3D) interaction diagrams to understand key interactions, such as hydrogen bonds, hydrophobic interactions, and van der Waals forces. Bond distances and the amino acid residues involved in these interactions were also analyzed to provide deeper insights into the binding mechanisms (Figure 3).

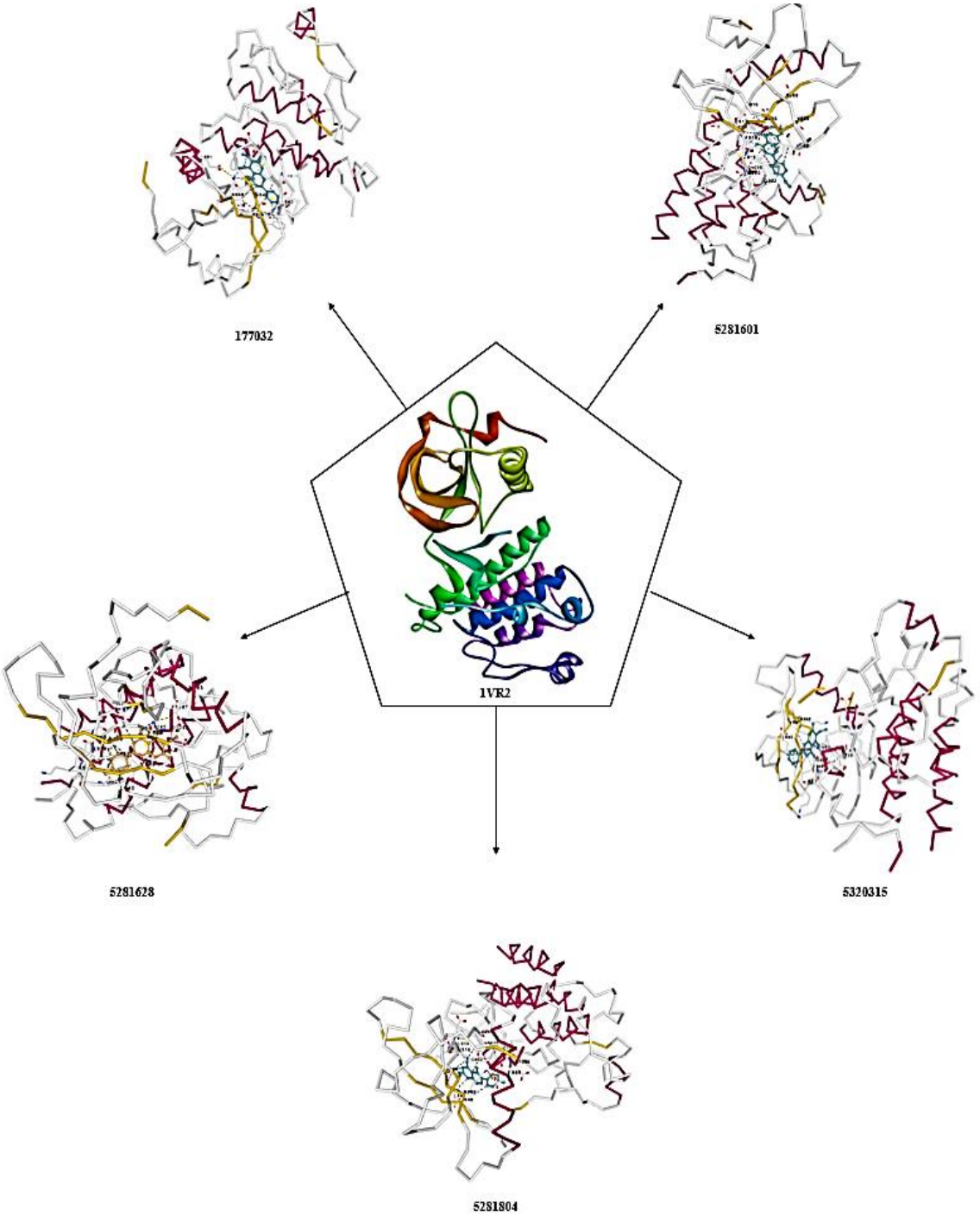

Figure 3. 3D interactions of top ligands with VEGFR2 (PDB ID: 1VR2).

This comprehensive docking and visualization study enabled the identification of potential ligands with strong binding affinities for VEGFR-2, laying the groundwork for further experimental validation and development (Figure 4) [24].

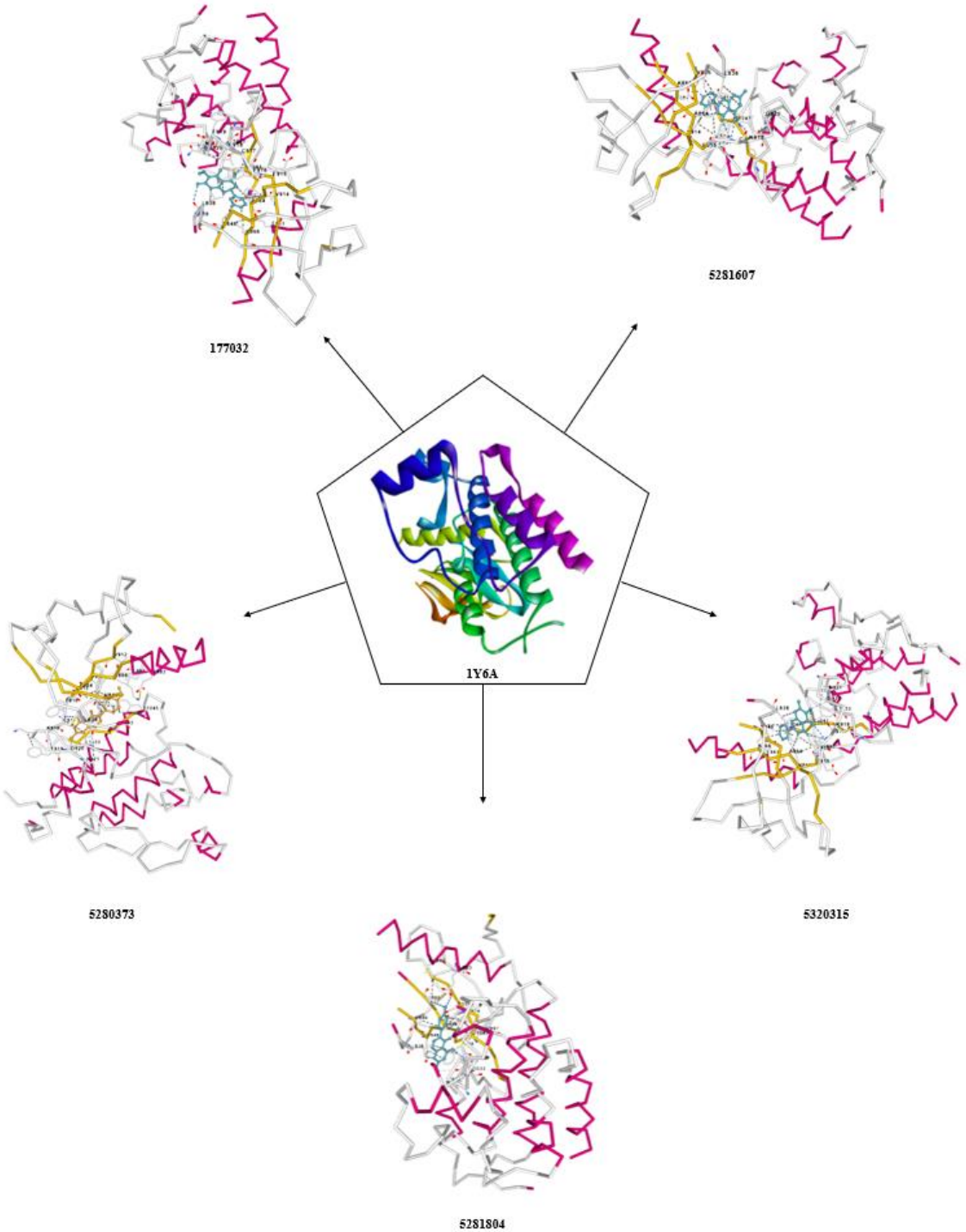

Figure 4. 3D interactions of top ligands with VEGFR2 (PDB ID: 1Y6A).

DISCUSSION

Neovascularization, a key process in tumor growth and metastasis, is largely driven by vascular endothelial growth factor (VEGF), a critical factor in stimulating angiogenesis. While various growth factors and cytokines contribute to angiogenesis, VEGF plays a central role in promoting the formation of new blood vessels. Overexpression of VEGF is commonly observed in many solid tumors. VEGF activates VEGFR2, triggering downstream signalling pathways that enhance vascular permeability and stimulate endothelial cell proliferation, migration, and survival, playing a role in both normal and abnormal angiogenesis.

VEGFR2 is expressed in cells from various solid tumors, such as breast, gastrointestinal, prostate, melanoma, and non-small cell lung cancer (NSCLC). Targeting VEGF-VEGFR2 signalling in the treatment of these cancers may inhibit tumor angiogenesis and simultaneously reduce tumor cell proliferation, invasion, and survival [25].

Oroxylum indicum has been traditionally utilized in various medicinal applications across Southeast and South Asian countries, as documented in numerous ethnobotanical texts. Phytochemical studies on different parts of the plant have led to the identification of around 111 compounds, with flavonoids, naphthalenoids, and cyclohexylethanoids being the most prominent groups. The crude extracts and their isolated compounds demonstrate a broad range of pharmacological activities, both in vitro and in vivo, including antimicrobial, anti-inflammatory, anti-arthritic, anticancer, anti-ulcer, hepatoprotective, antidiabetic, antidiarrheal, and antioxidant properties [26].

Extensive phytochemical studies on *Oroxylum indicum* have highlighted its richness in natural flavonoids, including baicalein, chrysin, and oroxylin A. The plant and its flavonoid components have been widely recognized for their diverse biological and pharmacological activities. In recent years, *O. indicum* has garnered increasing attention for its potential in treating various cancer types, particularly by targeting cell division and inhibiting proliferation [27].

A total of 11 ligands were identified based on their compliance with key drug-likeness parameters, including a molecular weight of less than 500, fewer than 10 hydrogen bond acceptors, fewer than 5 hydrogen bond donors, high gastrointestinal (GI) absorption, and a bioavailability score of 0.55 or higher. Additionally, all selected ligands showed zero Lipinski violations and no Brenk alerts, ensuring their suitability for further analysis.

These 11 ligands were docked with vascular endothelial growth factor receptor 2 (VEGFR2), using the crystal structures 1VR2 and 1Y6A. Based on the docking results, the top five ligands exhibiting the least binding energies for each protein structure were selected:

- *For VEGFR-2 (PDB ID: 1VR2):* Apigenin 7,4'-dimethyl ether, Flavanone, 5,7-dihydroxy-6-methoxy-, Hispidulin, Prunetin, and Oroxylin A
- *For VEGFR-2 (PDB ID: 1Y6A):* Flavanone, 5,7-dihydroxy-6-methoxy-, Chrysin, Biochanin A, Prunetin, and Oroxylin A.

These ligands demonstrated the strongest binding affinities with VEGFR-2, as indicated by their low binding energies. This highlights their potential as promising inhibitors of VEGFR-2, a critical target in angiogenesis-related studies, including cancer therapeutics.

FUTURE PROSPECTS

Future research can prioritize optimizing the therapeutic efficacy of *Oroxylum indicum* phytochemicals through advanced drug delivery strategies, such as nanotechnology-based formulations, to improve bioavailability, stability, and targeted action. Rigorous comparative studies with existing VEGFR-2 inhibitors may provide insights into their relative efficacy and potential for combination therapies. Furthermore, comprehensive clinical evaluations assessing long-term safety, pharmacokinetics, and effectiveness across multiple cancer types will be essential for their successful integration into VEGFR-2-targeted treatments [28].

CONCLUSIONS

The findings of this study highlight the potential of *Oroxylum indicum* phytochemicals as effective inhibitors of VEGFR-2, a critical target in cancer therapy. By adhering to stringent drug-likeness criteria, 11 ligands were identified and subjected to molecular docking with VEGFR-2 crystal structures 1VR2 and 1Y6A. Among these, the top ligands for each protein, including Apigenin 7,4'-dimethyl ether, Flavanone, 5,7-dihydroxy-6-methoxy-, Chrysin, Hispidulin, Prunetin, Biochanin A, and Oroxylin A,

demonstrated the strongest binding affinities. These results underscore the potential of these phytochemicals in disrupting VEGFR-2-mediated angiogenesis, which is crucial for tumor growth and metastasis. Further in vitro and in vivo studies are essential to validate these findings and explore their therapeutic applicability in cancer management.

Acknowledgment

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Abbreviations

ADME	Absorption, Distribution, Metabolism, Excretion
Akt/PKB	Protein kinase B
Cdc42	Cell division cycle 42
ERK	Extracellular signal-regulated kinase
FGFs	Fibroblast growth factors
IMPPAT	Indian Medicinal Plants, Phytochemistry and Therapeutics
NF-κB	Nuclear factor kappa B
PAINS	Pan Assay Interference Compounds
PDB	Protein Data Bank
PDGFs	Platelet-derived growth factors
PI3K	Phosphoinositide 3-kinase
PLCγ	Phospholipase C gamma
p38MAPK	p38 Mitogen-activated protein kinase
ScK	Src kinase
Src	Proto-oncogene tyrosine-protein kinase Src
VEGFs	Vascular endothelial growth factors
VEGFR-2	Vascular endothelial growth factor receptor 2
VRASP	VEGF receptor-associated protein

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