

Anti-angiogenic potential of bioactive Phytochemicals from *Abies Webbiana* targeting VEGFR2 and related protein to fight cancer through molecular docking

Authors Name: Ms. Priyanka S. Rajge*, Mr. Nilesh V. Salunkhe, Ms. Kranti B. Jagtap, Ms. Sneha S. Yadav, Ms. Aishwarya A. Patil, Ms. Sanika P. Kale, Mr. Sushant T. Khot, Mr. Saurabh L. Kudale.

Adarsh College of Pharmacy, Vita (Affiliated to Dr. Babasaheb Ambedkar Technological University, Lonere), Maharashtra, India.

*Address for correspondence Ms. Priyanka. S. Rajge, Assistant Professor of Pharmacology, ACOP Vita. (Affiliated to Dr. Babasaheb Ambedkar Technological University, Lonere), Maharashtra, India.

Abstract

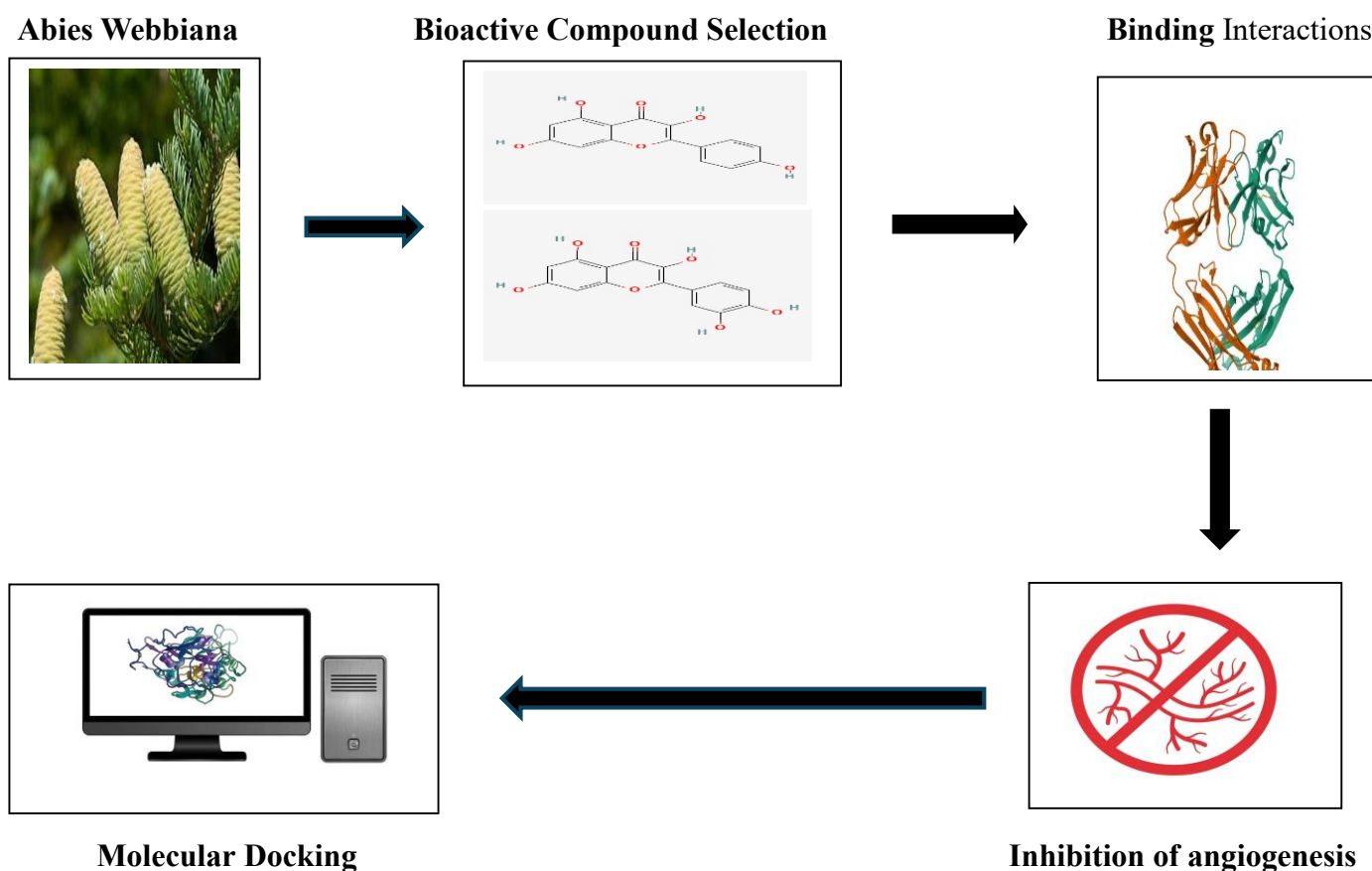
Angiogenesis is nothing but the formation of new blood vessels which is required in tumor growth, metastasis and cancer progression.¹ Cancer is one of the leading causes of death.² There is constant demand of the antiangiogenic agents for the cancer treatment.³

Natural plant derived molecules contributing significantly for providing safer alternatives for discovering novel antiangiogenic drug candidates. This research is attempted to investigate antiangiogenic potential of *Abies Webbiana* phytochemicals targeting vascular endothelial growth factor receptor two (VEGFR -2), Human epithelial growth factor receptor 2(HER2), Epidermal growth factor receptor (EGFR) and Fibroblast growth factor receptor two (FGFR2) via molecular docking.

The common name of *Abies Webbiana* is Talispatra in Bengali and Hindi, Talispatram in Sanskrit and Indian silver fir in English.⁴ This is the tall and evergreen tree and it occurs in himalayan region of India ⁵. *Abies Webbiana* is reported with significant pharmacological activities previously which contains 25 bioactive compounds mainly Kaempferol ⁶, Beta Sitosterol ⁷, Limonene⁸, Alpha pinene⁹, Bornyl acetate¹⁰, 1,8-cineol¹¹ and Quercetin¹² ⁴. Quercetin have highest binding affinity.

For the molecular docking using Protein data bank three-dimensional structure of receptor was obtained¹³ and prepared computationally before docking (<https://pubchem.ncbi.nlm.nih.gov/>)¹⁴. Ligand structures were downloaded from public chemical databases in SDF format and optimised before molecular docking studies. The PyRx¹⁵ and BIOVIA discovery studio¹⁶ are the software used in this study. This study supports the use of natural plant derived molecules in anti-angiogenic drug development. While the results of molecular docking encourage further in vivo and in vitro validation of predicted inhibitors later.

Keywords:- Angiogenesis, Abies Webbiana, Docking study, Binding affinity, Receptors, Ligand



Introduction

Angiogenesis is the mechanism which is involved in physiological functions as well as many diseased states¹⁷. Angiogenesis is the formation of new blood vessels from preexisting vasculature which is required in tumor growth, metastasis and cancer progression¹⁷.

Angiogenesis is linked to number of diseases including cancer which is one of the leading causes of death¹⁷. Tumor blood vessels have different structure compared to normal blood vessels with irregular branches and they are more heterogeneous it may prevent tumor by blocking tumor blood vessels.¹ vascular endothelial growth factor receptor two (VEGFR-2) Human epithelial growth factor receptor 2 (HER2), Epidermal growth factor receptor (EGFR) and Fibroblast growth factor receptor two (FGFR2) is responsible for angiogenesis.¹ Vascular endothelial growth factor is secreted by the over expressive tumor. Vascular endothelial growth factor binds to high affinity signalling receptors present on the endothelial cells of existing blood vessels, which provide the necessary nutrients for tumor cell survival and tumor growth¹⁸. Fibroblast growth factor receptor (FGFR2) regulate angiogenesis, as well as cell proliferation and differentiation Vascular Endothelial growth factor receptor 2 (VEGFR2), Human epithelial growth factor receptor 2 (HER2), Epidermal growth factor receptor (EGFR) and Fibroblast growth factor receptor two (FGFR2) acts as center modulator of angiogenesis hence it is targeted frequently for developing antiangiogenic agents to fight cancer.³

Medicinal plants are the rich resources of traditional medicine system which are used to treat various disorders.³ Many modern medicines are produced using medicinal plants.³ *Abies webbiana* it is one of the medicinal plants which belongs to the family Pinaceae¹⁹. The common name of *Abies Webbiana* is Talispatra in Bengali and Hindi, Talispatram in Sanskrit and Indian silver fir in English.⁴ These are the coniferous trees which found in high altitude areas. It is the tall and evergreen tree which is mainly occurring from Kashmir to Assam in Himalayan region of Indian.⁵ This plant also exist in Afghanistan, Tibet, Bhutan and Nepal at an altitude 2500-4000 m.⁵ In Ayurveda the traditional system of Indian medicine the leaves of *Abies Webbiana* have different uses.⁵ *Abies webbiana* is previously reported with significant pharmacological activities like antibacterial, antifungal, anti tumor, mast cell stabilizing, anxiolytic, antitussive female antifertility and CNS depressant actions.⁴ It contains 25 bioactive compound such as terpenoids, flavonoid, amino acids, tannins, alkaloids, lipids, steroids and glycosides. *Abies webbiana* mainly contains Kaempferol⁶, Beta sitosterol⁷, Limonene⁸, Alpha pinene⁹, Bornyl acetate¹⁰, 1,8-cineol¹¹ and Quercetin^{12,4}. Quercetin have highest binding affinity.

Various antiangiogenic products from natural resources are being used in multiple cancer because of lesser toxicity compared to currently used therapeutics. Using molecular docking it is possible to predict interaction between two structures that is Protein and ligand or between two proteins. Thus, the present study is aimed to understand the inhibition of cancer-causing protein through docking studies.

Materials and Methods

For the research we apply biological database such as PubChem. PDB (Protein Data Bank) and software like PyRx. PDB is the single global Open access archive as a 3D structural data for biological micro molecules including proteins DNA and RNA established in 1971 at Brookhaven National Laboratories (BNL) in collaboration with the Cambridge Crystallographic Data Centre (UK). They store biomolecular information as a 3D atomic coordinated mainly from X-ray crystallographic (along with NMR or cryo-EM) in standardised text format²⁰. PyRx is free virtual screening and molecular docking software that provides an easy to use graphical interface for ligand preparation and energy minimization and docking using Autodock and Autodock Vina¹⁵

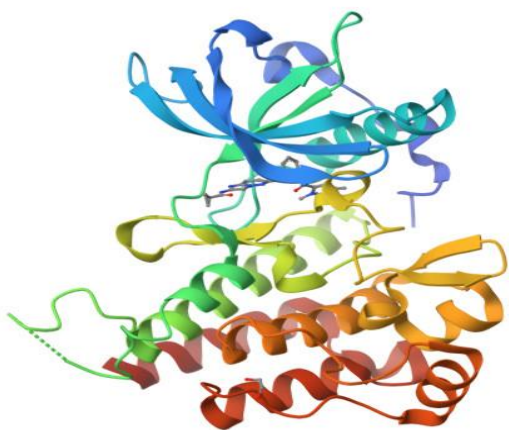
Molecular docking is an efficient method to identify targets and screen potential drug candidates. It allows virtual screening of compound databases quickly. It also predicts binding affinity and identifies strong binders.

Preparation of protein macromolecule

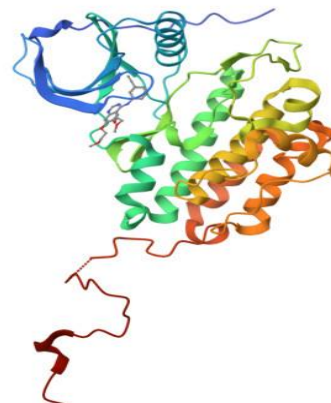
Protein data bank PDB was used to obtain the Three-dimensional crystals structure of VEGFR macromolecules. PDB is the large public repository of experimental data include the resolution of protein determined using X-ray diffraction method. Unwanted components and water molecules were removed from the PDB file using BIOVIA (Discovery studio visualized)²¹

Preparation of ligands

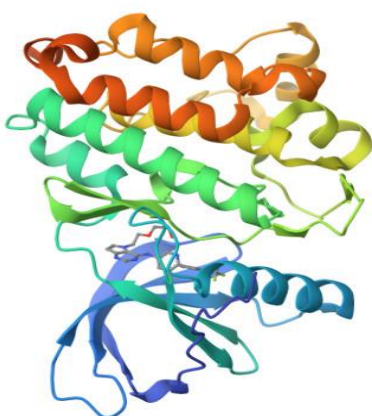
A total of 25 Bioactive phytochemicals of *Abies webbiana* were selected. The docking process involves three main steps: ligand conformational analysis, binding placement and scoring evaluation. Then take best seven Out of 25 Phytochemicals for analysis. Fill the phytochemicals confirmers were obtained in structure data format (SDF) from PubChem database (<https://pubchem.ncbi.nlm.nih.gov/>)²².



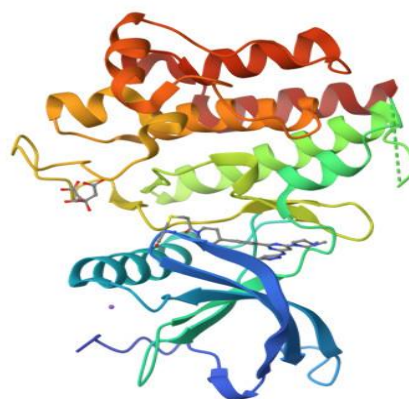
Structure of VEGFR2 receptor



Structure of EGFR receptor

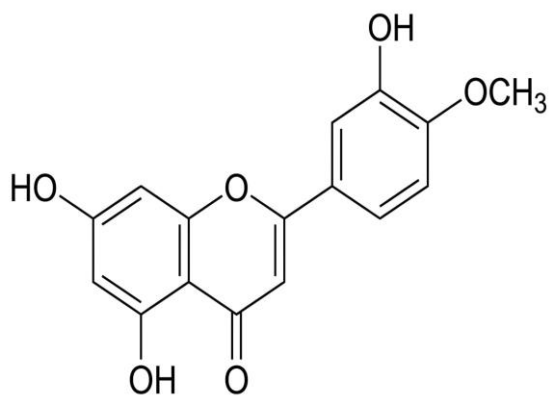


Structure of HER receptor

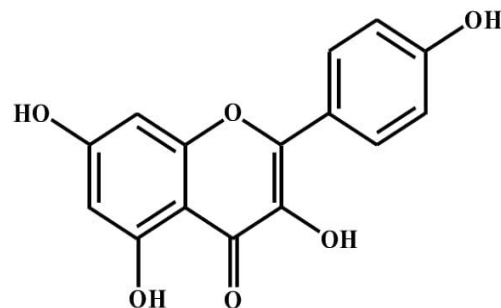


Structure of FGFR receptor

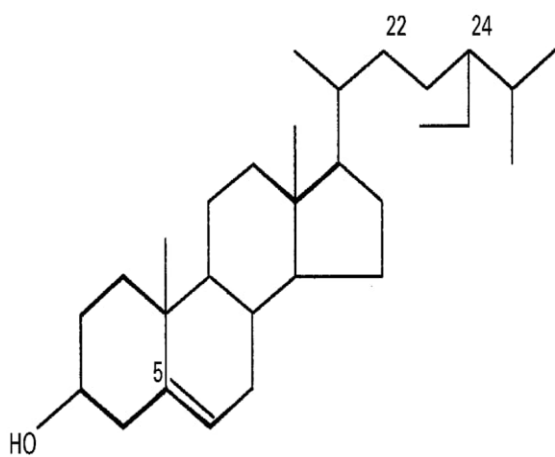
By using BINOVA discovery studio the all of the SDF file were opened that was already installed²¹. The docking analysis of Quercetin, Kaempferol, Beta sitosterol, Limonene, Alpha pinene, Bornyl acetate, 1,8-cineole and vascular endothelial growth factor receptor was performed by PyRx docking software. Docking enables virtual screening of compound database and identifies they strongest binder based on their scoring function. Discovery studio visualizer (BINOVA) was used to create 3D and 2D interaction photos²¹.



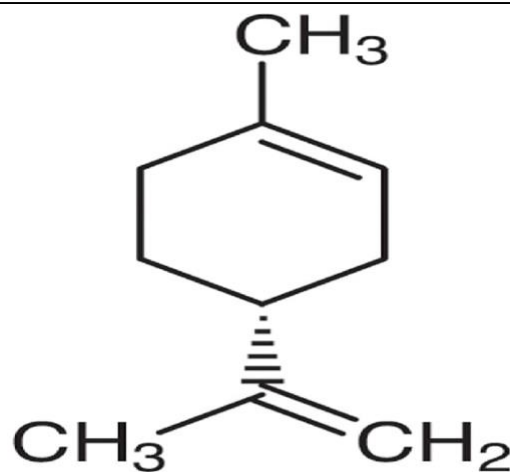
QUERCETIN



KAEMPFEROL



BETA SITOSTEROL



LIMONEN

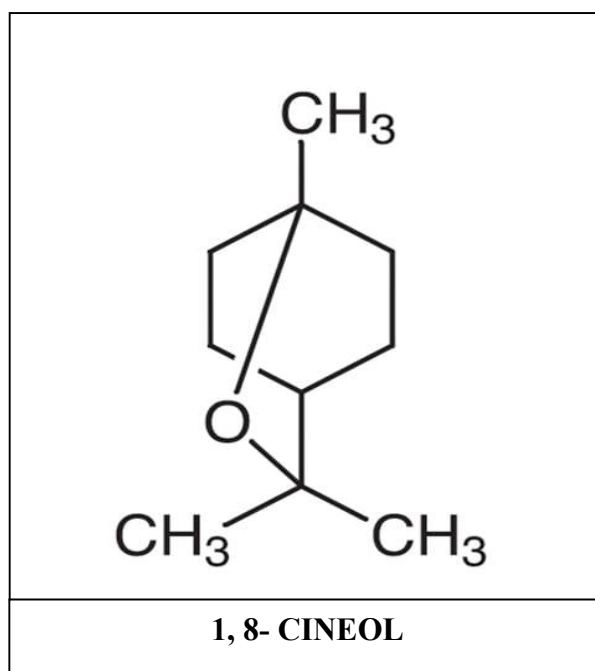
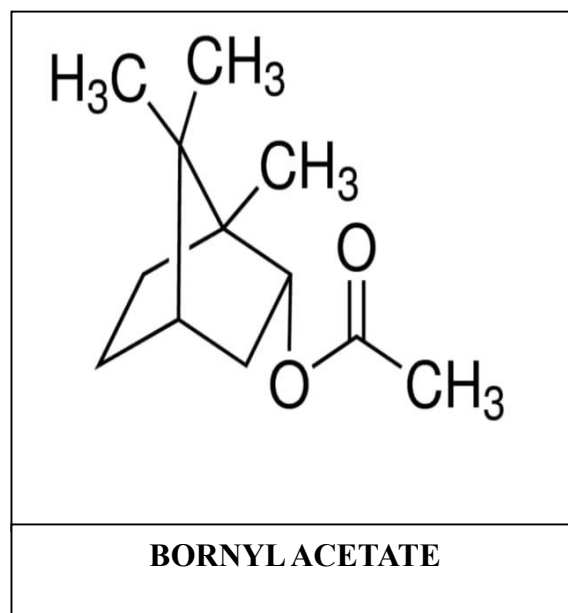
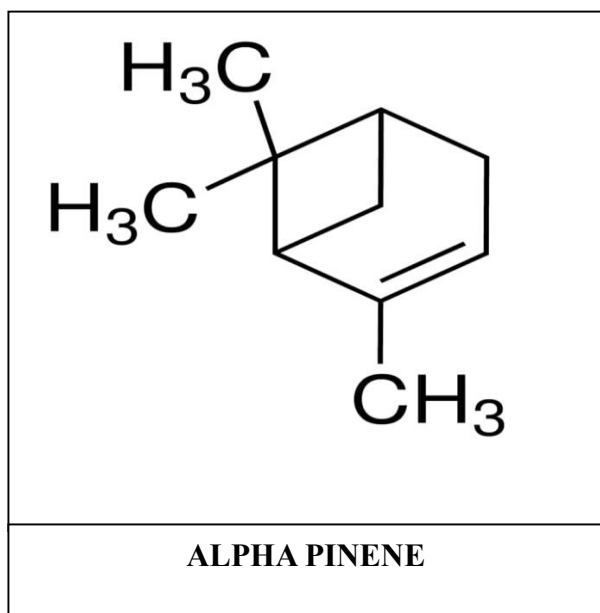


Fig 2. Structures of 7 selected ligand molecules

Protein ligand interaction using Pyrx

Pyrx is computer based molecular docking software that integrates Autodock and Autodock vina to predict protein - ligand interaction. It estimates binding energy, binding orientation and stability of ligand - protein complex. It also supports ligand optimization, energy minimization and analysis of interaction such as hydrogen bonds, bond lengths and binding conformations.

Result

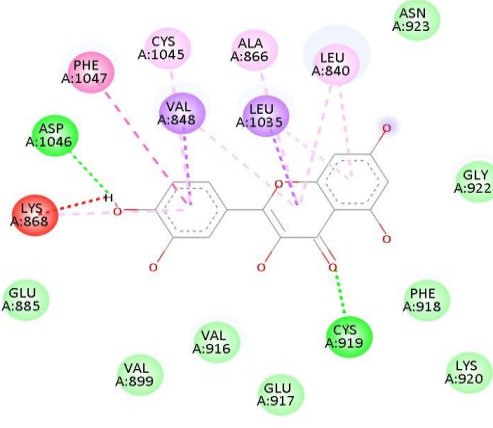
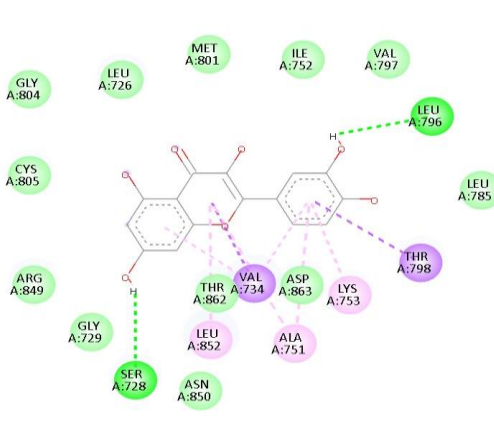
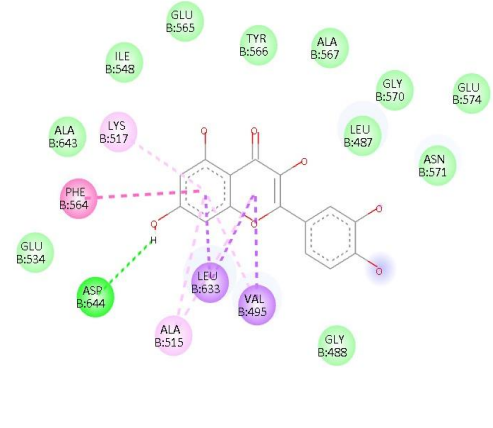
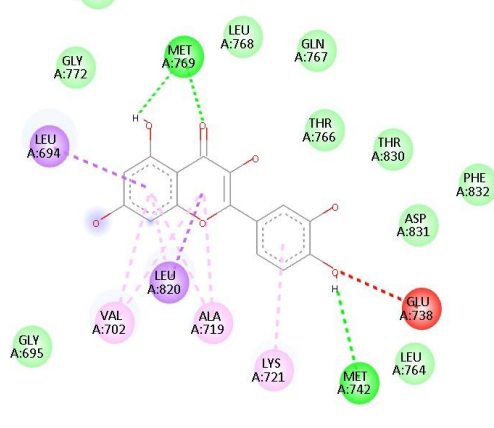
Analysis of visualization of docking study

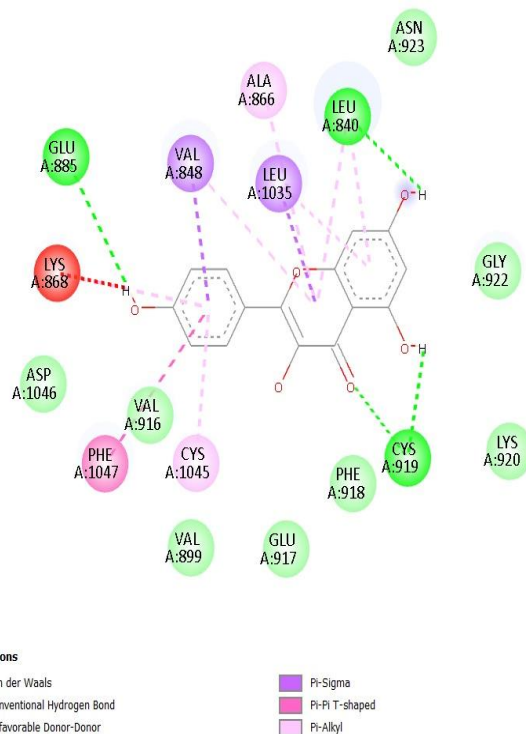
The binding energy of the protein–ligand complexes and the analysis of docking results were evaluated using molecular docking studies and Discovery Studio Visualizer v16.1.0.15350. After completion of the docking process, Quercetin exhibited a strong binding affinity of -10.2 kcal/mol with 3VO3 (VEGFR2) among all the selected receptor proteins. The binding affinities of Quercetin with 1M17 (EGFR) and 3PP0 (HER) were found to be -8.6 and -9.2 kcal/mol, respectively, calculated using Auto Dock Vina on the PyRx platform.

Kaempferol showed the highest binding affinity of -10.2 kcal/mol with 3VO3 (VEGFR2) 3PP0 (HER) protein, followed by slightly lower affinities with 1M17 (EGFR) and 7KIA (FGF), recorded as -8.8 and -8.5 kcal/mol, respectively. Limonene demonstrated its best binding affinity of -6.6 kcal/mol with 7KIA (FGF), while its affinities with 3VO3 (VEGFR2) and 7KIA were -6.3 and -6.6 kcal/mol, respectively.

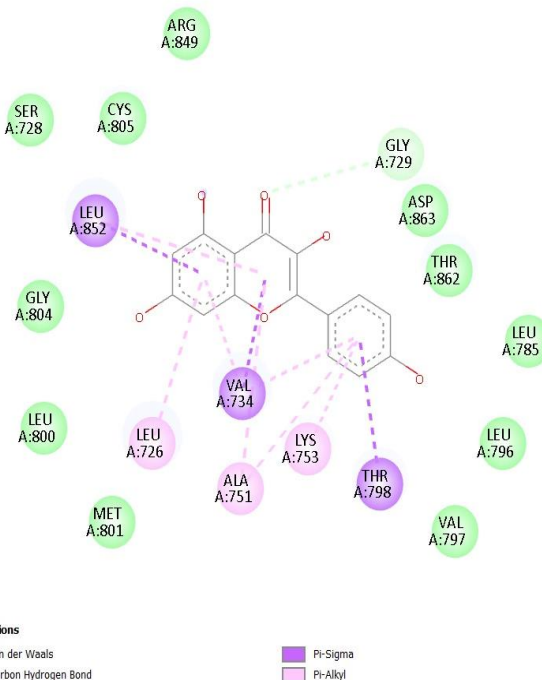
Alpha-pinene displayed its maximum binding affinity of -6.2 kcal/mol with 3PP0 (HER). Alpha pinene showed comparatively lower binding affinities with 7KIA (FGF), 3VO3 (VEGFR2), and 1M17 (EGFR), recorded as -5.6 , -5.3 , and -5.4 kcal/mol, respectively. Bornyl acetate exhibited its highest binding affinity of -5.8 kcal/mol with 7KIA (FGFR), while its interactions with 1M17 (EGFR), 3PP0 (HER), and 3VO3 (VEGFR2) were -6.0 , -5.8 , and -5.4 kcal/mol, respectively.

The compound 1,8-cineole showed binding affinities of -6.0 kcal/mol with 3PP0 (HER), -5.3 kcal/mol with 3VO3 (VEGFR), -5.2 kcal/mol with 1M17 (EGFR), and -5.1 kcal/mol with 7KIA (FGFR). Free energy plays a crucial role in determining the interaction strength between binding partners. Positive free energy values indicate non-spontaneous interactions requiring energy input, whereas negative values suggest spontaneous binding. In this study, all obtained values were negative, indicating that the ligand–protein interactions occur spontaneously.

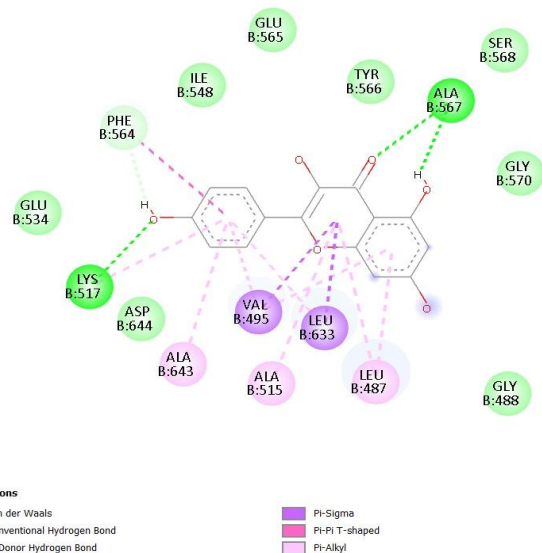
 Interactions - van der Waals - Conventional Hydrogen Bond - Unfavorable Donor-Donor - Pi-Sigma - Pi-Pi T-shaped - Pi-Alkyl	 Interactions - van der Waals - Conventional Hydrogen Bond - Pi-Sigma - Pi-Alkyl
Molecular interaction of Quercetin with 3vo3 (VEGFR2) protein	Molecular interaction of Quercetin with 3PP0 (HER) protein
 Interactions - van der Waals - Conventional Hydrogen Bond - Pi-Sigma - Pi-Pi T-shaped - Pi-Alkyl	 Interactions - van der Waals - Conventional Hydrogen Bond - Unfavorable Acceptor-Acceptor - Pi-Sigma - Pi-Alkyl
Molecular interaction of Quercetin with 7KIA (FGFR) protein	Molecular interaction of Quercetin with 1M17 (EGFR) protein



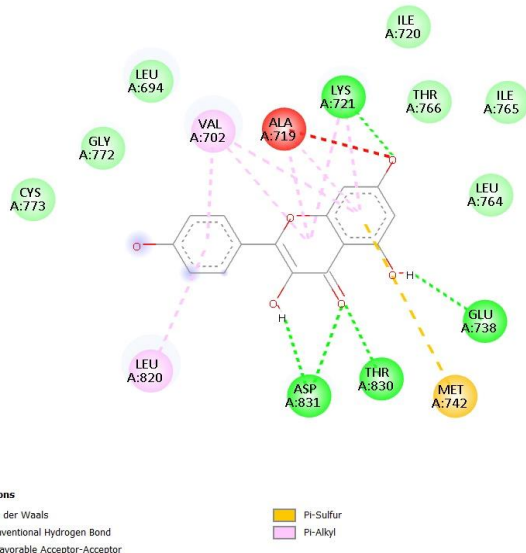
Molecular interaction of Kaempferol with 3VO3 (VEGFR2) protein



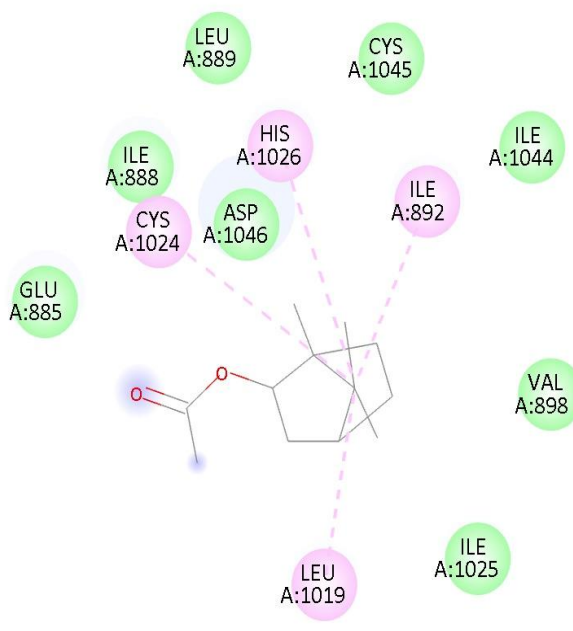
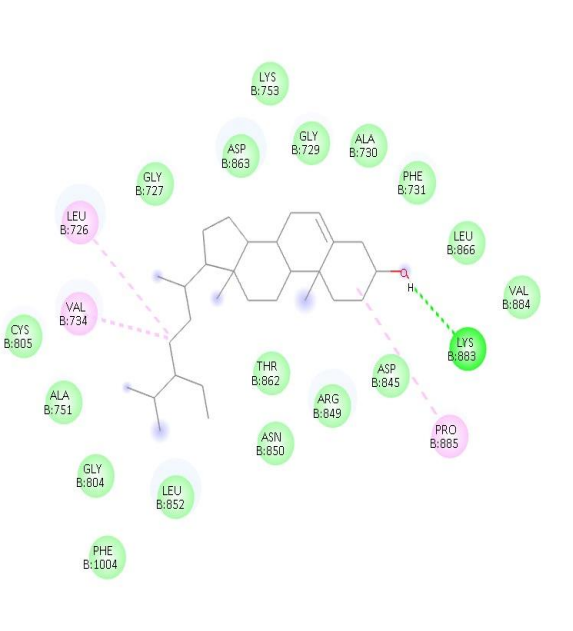
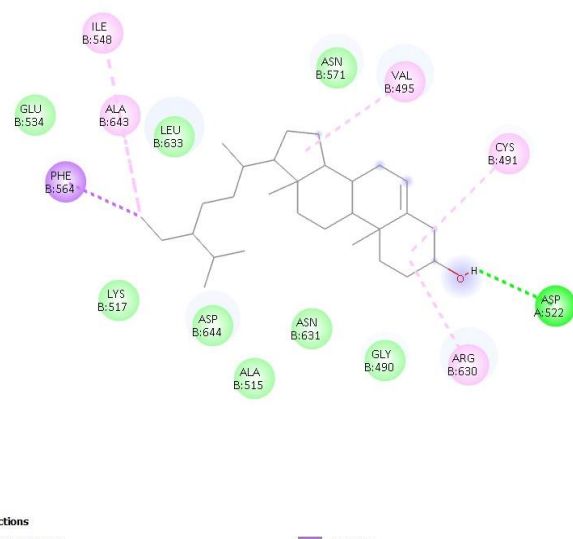
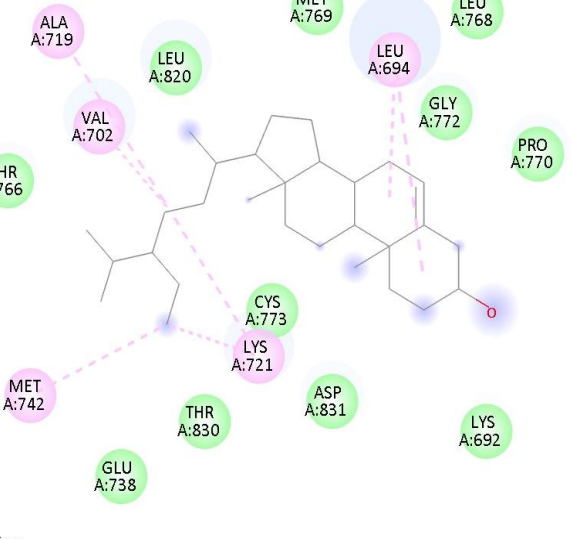
Molecular interaction of kaempferol with 3PP0 (HER) protein

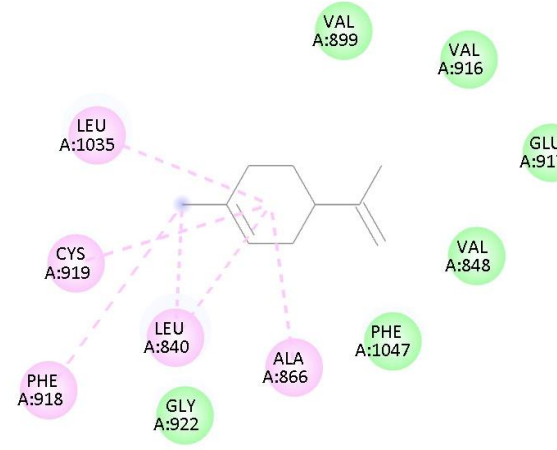
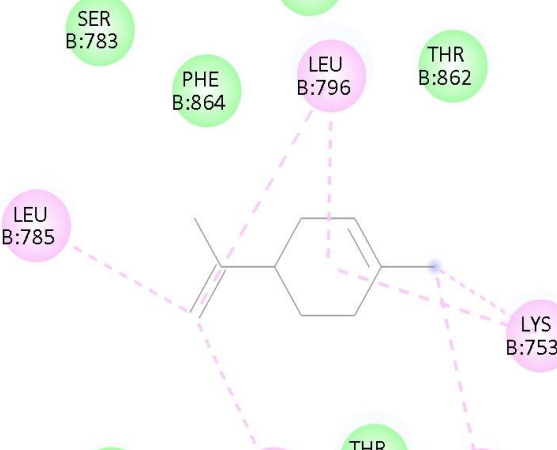
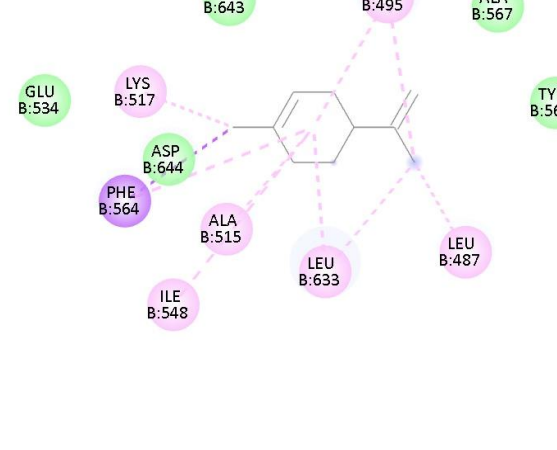
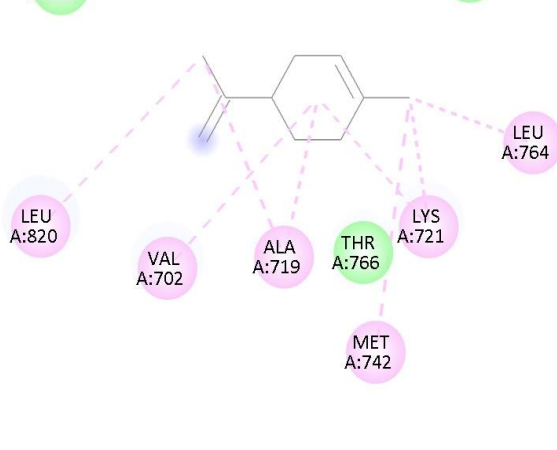


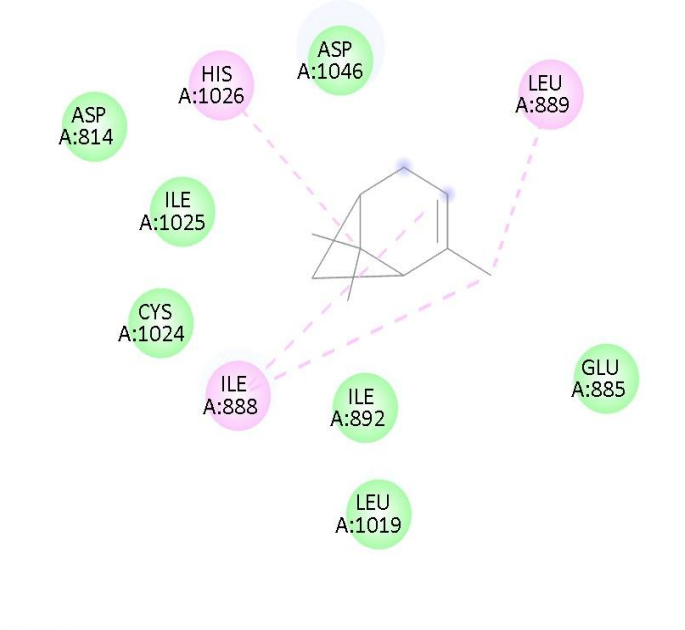
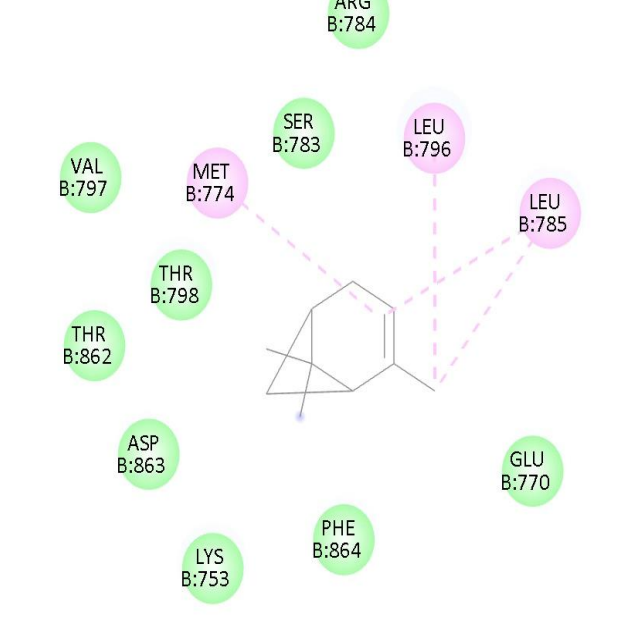
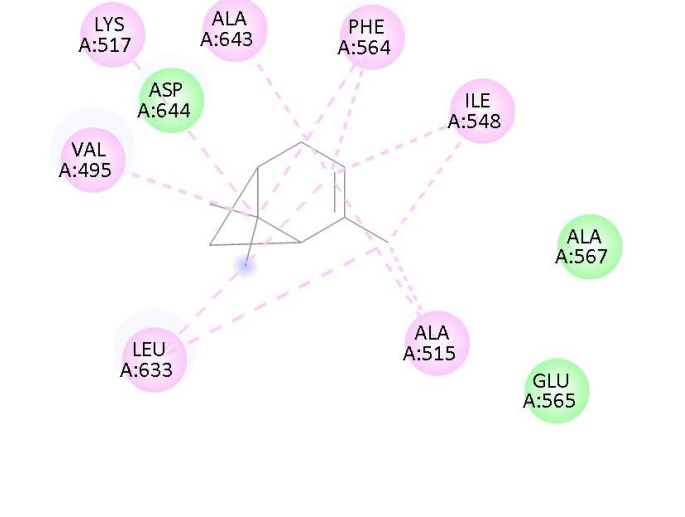
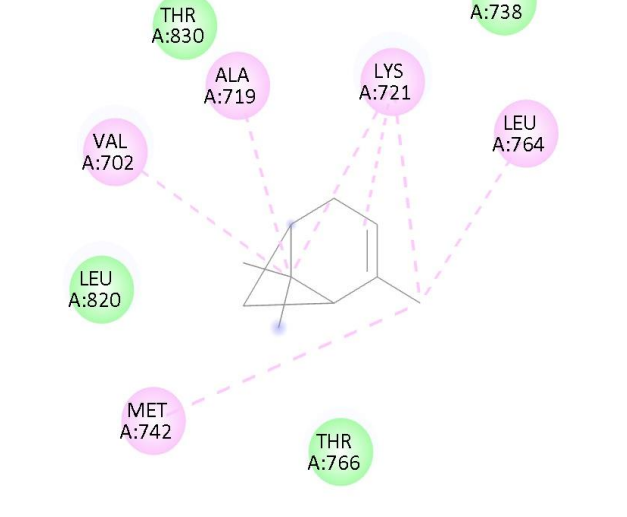
Molecular interaction of kaempferol with 7K1A (FGFR) protein

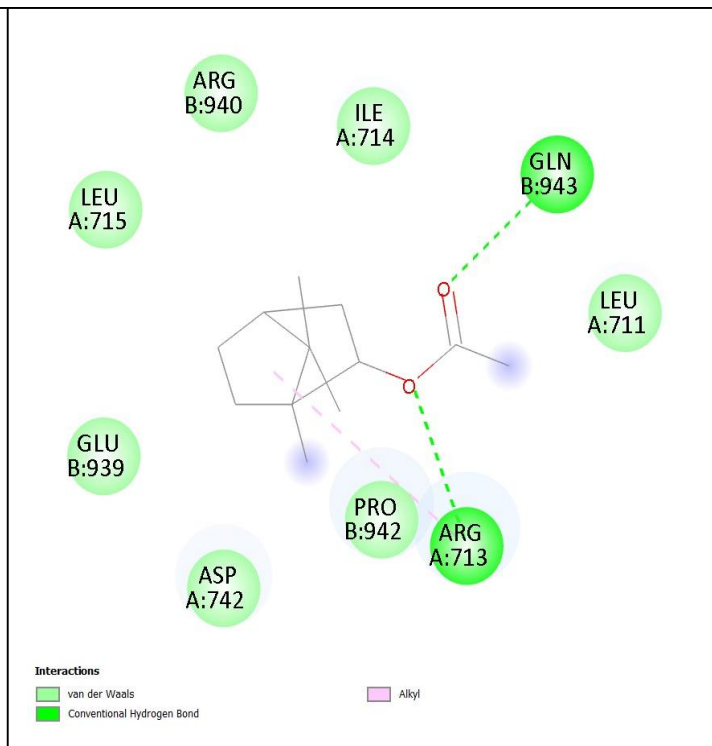
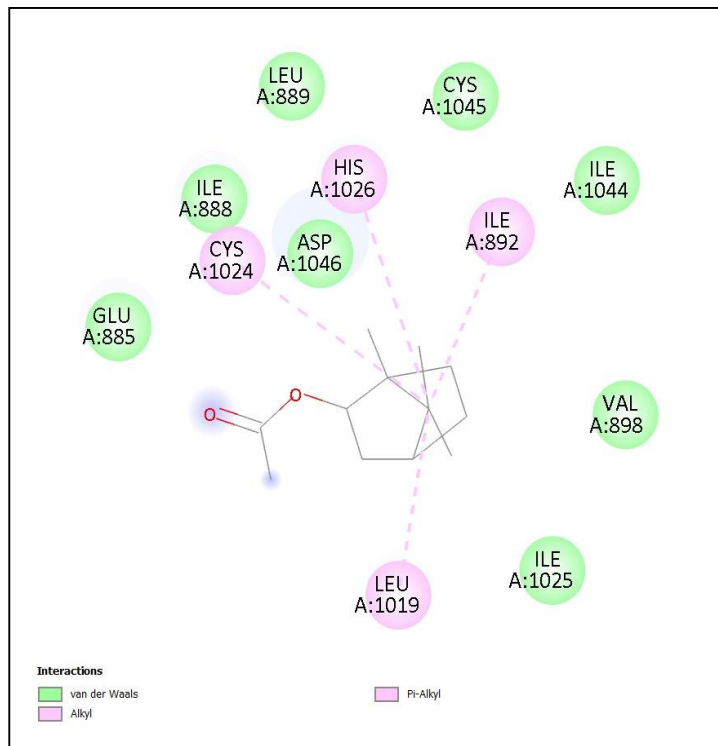


Molecular interaction of kaempferol with 1M17 (EGFR) protein

 Interactions - van der Waals - Pi-Alkyl - Alkyl	 Interactions - van der Waals - Conventional Hydrogen Bond - Alkyl
Molecular interaction of Beta sitosterol with 3VO3 (VEGFR2) protein	Molecular interaction of Beta sitosterol with 3PP0 (HER) protein
 Interactions - van der Waals - Conventional Hydrogen Bond - Pi-Sigma - Alkyl	 Interactions - van der Waals - Alkyl
Molecular interaction of Beta sitosterol with 7KIA (FGFR) protein	Molecular interaction of Beta sitosterol with 1M17 (EGFR) protein

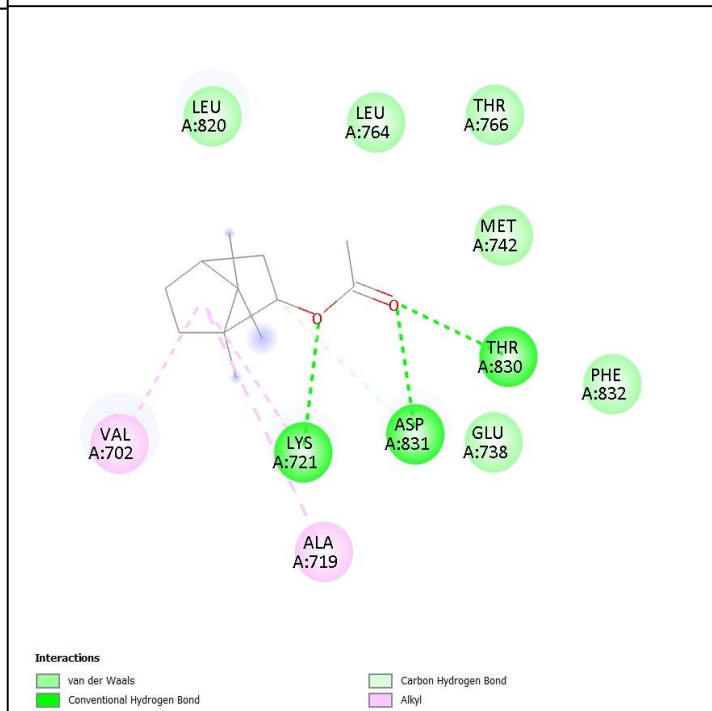
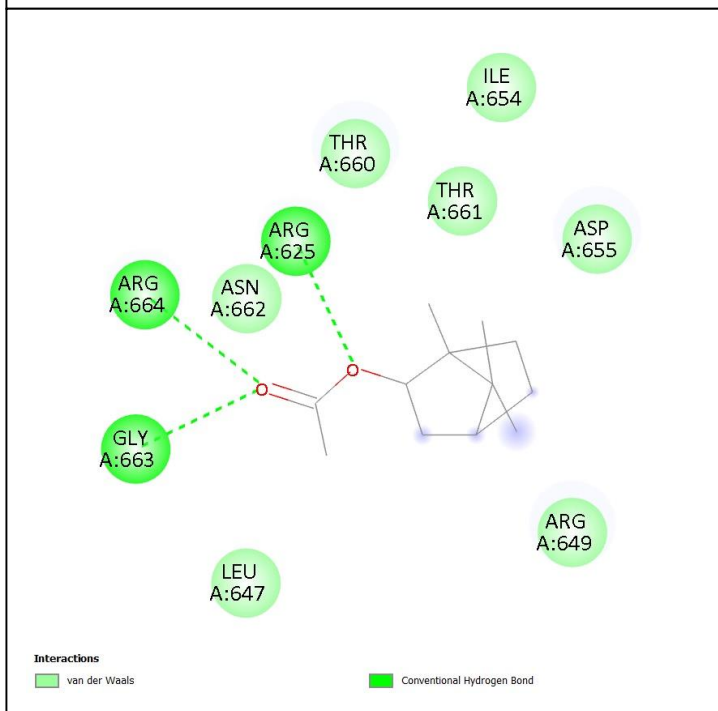
 Interactions - van der Waals - Pi-Alkyl - Alkyl	 Interactions - van der Waals - Alkyl - Pi-Alkyl
Molecular interaction of Limonene with 3VO3 (VEGFR2) protein	Molecular interaction of Limonene with 3PP0 (HER) protein
 Interactions - van der Waals - Alkyl - Pi-Sigma - Pi-Alkyl	 Interactions - van der Waals - Alkyl - Pi-Alkyl
Molecular interaction of Limonene with 7KIA (FGFR) protein	Molecular interaction of Limonene with 1M17 (EGFR) protein

 Interactions - van der Waals - Alkyl - Pi-Alkyl	 Interactions - van der Waals - Alkyl
Molecular interaction of Alpha pinene with 3VO3 (VEGFR2) protein	Molecular interaction of Alpha pinene with 3PP0 (HER) protein
 Interactions - van der Waals - Alkyl - Pi-Alkyl	 Interactions - van der Waals - Alkyl
Molecular interaction of Alpha pinene with 7KIA (FGFR) protein	Molecular interaction of Alpha pinene with 1M17 (EGFR) protein



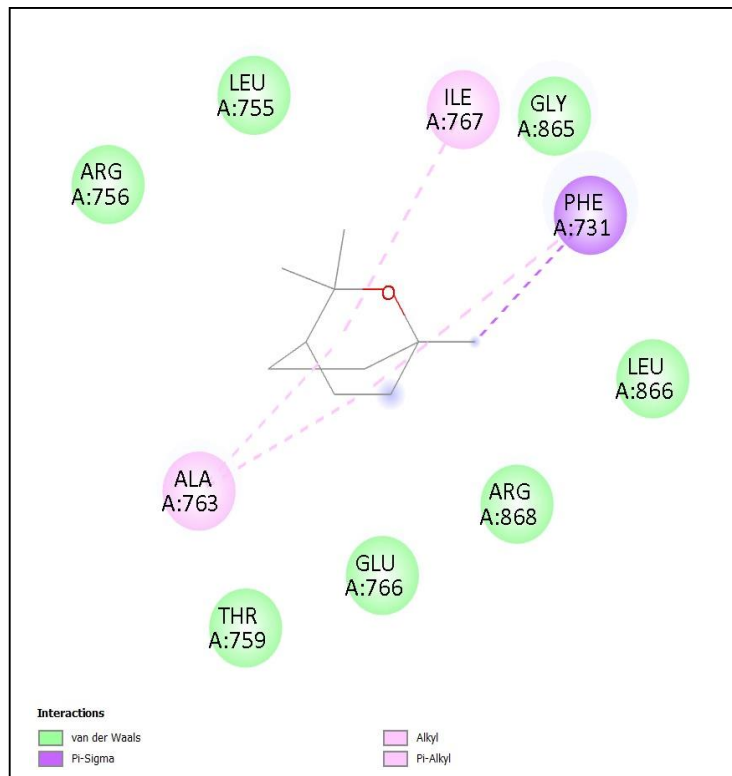
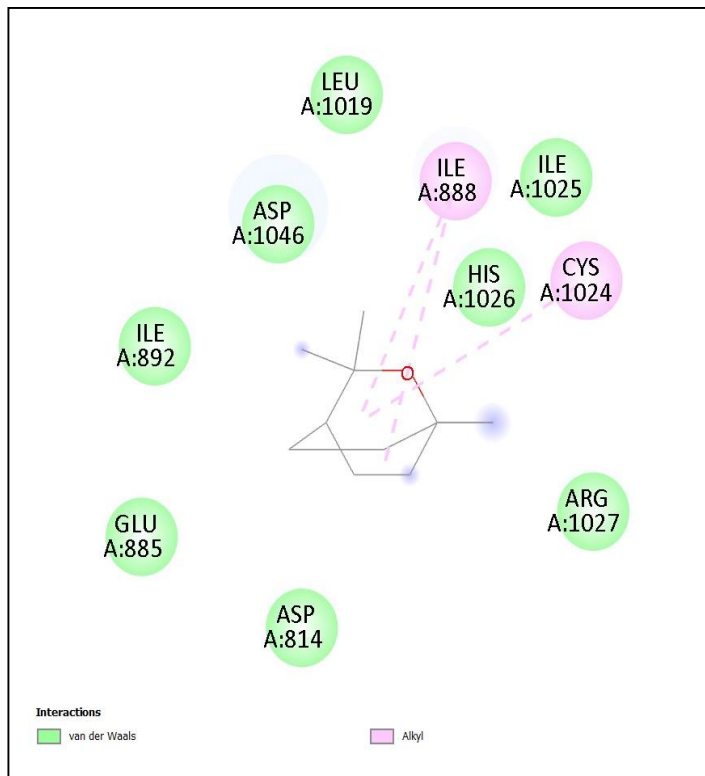
Molecular interaction of Bornyl acetate with 3VO3 (VEGFR2) protein

Molecular interaction of Bornyl acetate with 3PP0 (HER) protein



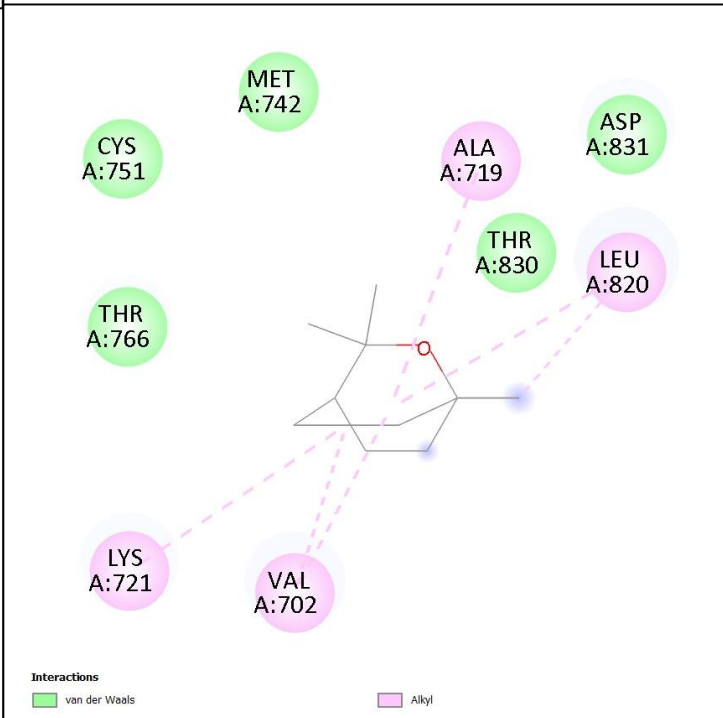
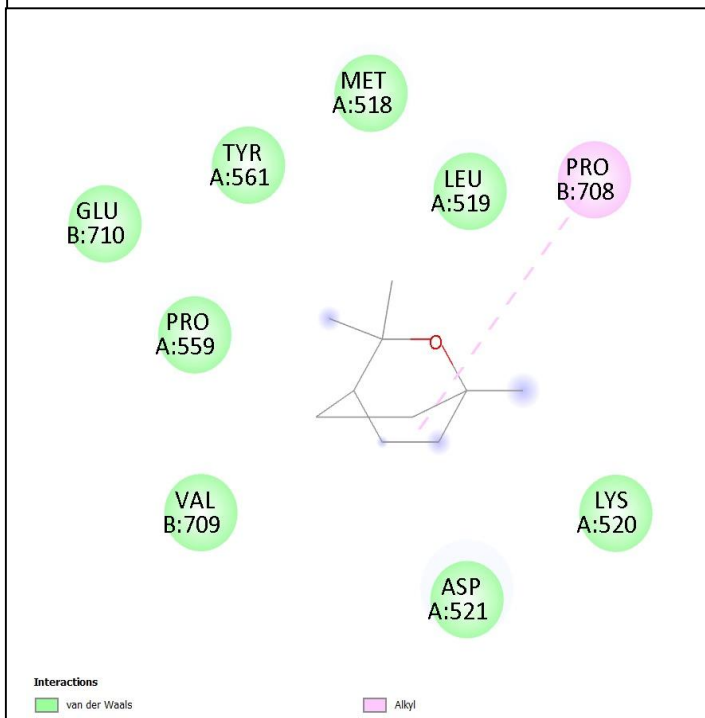
Molecular interaction of Bornyl acetate with 7KIA (FGFR) protein

Molecular interaction of Bornyl acetate with 1M17 (EGFR) protein



Molecular interaction of 1,8-cineol with 3VO3 (VEGFR2) protein

Molecular interaction of 1,8-cineol with 3PP0 (HER) protein



Molecular interaction of 1,8-cineol with 7KIA (FGFR) protein

Molecular interaction of 1,8-cineol with 1M17 (EGFR) protein

Interaction between chemical constituent of plant name: *Abies webbiana* and 3vo3

PDB DOI: <https://doi.org/10.2210/pdb3vo3/pdb>.

Drug	Docking score/binding energy (kcal/mol)	Van Der waals	H Bond	Pi -Sigma	Pi - Alkyl
Quercetin	-10.2	GLU A:885 VAL A:899 VAL A:916 GLU A:917 PHE A:918 LYS A:920 GLY A:922 ASN A:923	ASP A:1046 CYS A:919	VAL A:848 LEU A:1035	CYS A:1045 ALA A:866 LEU A:840
Kaempferol	-10.2	ASP A:1046 VAL A:916 VAL A:899 GLU A:917 PHE A:918 LYS A:920 GLY A:922 ASN A:923	GLU A:855 LEU A:804 CYS A:919	VAL A:848 LEU A:1035	CYS A:1045 ALA A:866
Beta sitosterol	-8.1	GLU A:885 ILE A:888 LEU A:889 CYS A:1045 ASP A:1046 ILE A:1044 VAL A:898 ILE A:1025			CYS A:1024 HIS A:1026 ILE A:892 LEU A:1019
Limonene	-5.2	GLY A:922 VAL A:899 VAL A:916 VAL A:848 PHE A:1047 GLU A:917			LEU A:1035 LEU A:840 ALA A:866 CYS A:919 PHE A:918
Alpha pinene	-5.3	ASP A:814 ASP A:1046 ILE A:1025 ILE A:892 LEU A:1019 CYS A:1024 GLU A:885			ILE A:888 HIS A:1026 LEU A:889
Bornyl acetate	-5.6	GLU A:885 INU A:888 LEU A:889 ASP A:1046 CYS A:1045 ILE A:1044 ILE A:1025 VAL A:898			CYS A:1024 HIS A:1026 INE A:892 LEU A:1019
1, 8-cineole	-5	LEU A:1019 ASP A:1046			ILE A:888 CYS A:1024

		ILE A:892 ILE A:1025 HIS A:102 ARG A:1027 ASP A:814 GLU A:885			
--	--	--	--	--	--

Interaction between chemical constituent of plant name: *Abies webbiana* and 3pp0

PDB DOI: <https://doi.org/10.2210/pdb3pp0/pdb>.

Drug	Docking score/binding energy (kcal/mol)	Van Der waals	H Bond	Pi – sigma	Pi - alkyl
Quercetin	-9.2	GLY A:729 ARG A:849 CYS A:805 GLY A:804 LEU A:726 MET A:801 ILE A:752 BAL A:797 LEU A:785 ASP A:863 THR A:862 ASN A:850	SER A:728 LEU A:796	VAL A:734 THR A:798	LEU A:852 ALA A:751 LYS A:753
Kaempferol	-8.8	MET A:801 LEU A:800 GLY A:804 SER A:728 CYS A:805 ARG A:849 ASP A:863 THR A:862 LEU A:785 ILU A:796 VAL A:797		LEU A:852 VAL A:734 THR A:798	LEU A:726 ALA A:751 LUS A:753
Beta sitosterol	-8.4	ASP B:845 ARG B:849 THR B:862 ASN B:850 LEU B:852 PHE B:1004 GLY B:804 ALA B:751 CYS B:805 GLY B:727 ASP B:863 LYS B:753 GLY B:729 ALA B:730 PHE B:731 LEU B:866	LYS B:883		PRO B:885 VAL B:734 LEU B:726

		VAL B:884			
limonene	-6.5	THR B:798 THR B:862 GLU B:770 ASP B:863 PHE B:864 SER B:783			LEU B:785 LEU B:796 LYS B:753 VAL B:734 MET B:774
Alpha pinene	-6.2	GLU B:770 PHE B:864 LYS B:753 ASP B:863 THR B:862 THR B:798 VAL B:797 SER B:783 ARG B:784			MET B:774 LEU B:796 LEU B:785
Bornyl acetate	-5.5	PRO B:942 ASP A:742 GLU B:939 LEU A:715 ARG B:940 ILE A:714 LEU A:711	ARG A:713 GLN B:943		
1,8-cineole	-6	ARG A:756 LEU A:755 GLY A:865 LEU A:866 ARG A:868 GLU A:766 THR A:759		PHE A:731	ALA A:763 ILE A:767

Interaction between chemical constituent plant name: *Abies webbiana* and 7KIA

PDB DOI: <https://doi.org/10.2210/pdb7KIA/pdb>

Drug	Docking score/binding energy (kcal/mol)	Van Der waals	H Bond	Pi -sigma	Pi- alkyl
Quercetin	-8.5	GLU B:534 ALA B:643 ILE B:548 GLU B:565 TYR B:566 ALA B:567 GLY B:570 LEU B:487 GLU B:574 ASN B:571 GLY B:488	ASP B:644	LEU B:633 VAL B:495	LYS B:517 ALA B:515
kaempferol	-8.5	GLU B:534	LYS B:517	VAL B:495	ALA B:643

		PHE B:564 ILE B:548 GLU B:565 TYR B:566 SER B:568 GLY B:570 GLY B:488	ALA B:567	LEU B:633	ALA B:515 LEU B:487
Beta sitosterol	-9.4	GLY B:490 ASN B:631 ALA B:515 ASP B:644 LYS B:517 GLY B:534 ASN B:571	ASP A:522	PHE B:564	ILE B:548 ALA B:643 VAL B:485 CYS B:495 CYS B:491 ARG B:630
Limonene	-6.6	GLU B:534 ASP B:644 ALA B:643 TYR B:566		PHE B:564	LYS B:517 VAL B:495 LEU B:487 LEU B:633 ALA B:515 ILE B:548
Alpha pinene	-5.6	ALA A:567 GLU A:565 ASP A:644			ALA A:515 ILE A:548 PHE A:564 ALA A:643 LYS A:517 VAL A:495 LEU A:633
Bornyl acetate	-5.8	ASN A:662 LEU A:647 ARG A:649 ASP A:655 THR A:661 THR A:660 ILE A:654	ARG A:625 ARG A:664 GLY A:663		
1,8-cineole	-5.1	ASP A:521 LYS A:520 VAL B:709 PRO A:559 GLU B:710 TYR A:561 MET A:518 LEU A:519			PRO B:708

Interaction between chemical constituent plant name: *Abies webbiana* and 1M17

PDB DOI: <https://doi.org/10.2210/pdb1M17/pdb>

Drug	Docking score/binding energy (kcal/mol)	Van Der waals	H Bond	Pi-sigma	Pi -alkyl
Quercetin	-8.6	GLY A:695 LEU A:764	MET A:769 MET A:742	LEU A:820 LEU A:694	ALA A:719 VAL A:702

		ASP A:831 PHE A:832 THR A:830 THR A:766 GLN A:767 LEU A:768 GLY A:772 PRO A:770			LYS A:721
Kaempferol	-8.2	CYS A:773 GLY A:772 LEU A:694 ILE A:720 THR A:766 ILE A:765 LEU A:764	LYS A:721 ASP A:831 THR A:830		VAL A:702 LEU A:820
Beta sitosterol	-8.4	THR A:766 LEU A:820 PHE A:699 MET A:769 GLY A:772 PRO A:770 LEU A:768 CYS A:773 ASP A:831 LYS A:692 THR A:830 GLU A:738			ALA A:719 VAL A:702 LYS A:721 MET A:742 LEU A:694
Limonene	-5.4	MET A:769 THR A:830 THR A:766			LEU A:820 VAL A:702 ALA A:719 MET A:742 LYS A:721 LEU A:764
Alpha pinene	-5.4	GLU A:738 ASP A:831 THR A:830 LEU A:820 THR A:766			MET A:742 VAL A:702 ALA A:719 LYS A:721 LEU A:764
Bornyl acetate	-6.0	LEU A:820 LEU A:764 THR A:766 MET A:742 PHE A:832 GLU A:738	LYS A:721 ASP A:831 THR A:830		ALA A:719 VAL A:702
1,8-cineole	-5.2	ASP A:831 THR A:830 MET A:742 CYS A:751 THR A:766			ALA A:719 LEU A:820 VAL A:702 LYS A:721

Discussion

The present investigation focused on evaluating the anti-angiogenic potential of phytochemicals obtained from *Abies webbiana* through molecular docking studies against key proteins involved in angiogenesis. Since angiogenesis is a fundamental process in tumor development and metastasis, targeting this pathway offers a promising strategy for cancer management. The computational analysis provided valuable insights into the binding behaviour of selected bioactive compounds with receptor proteins associated with angiogenic signalling.

Among the evaluated compounds, flavonoids such as quercetin and kaempferol exhibited strong binding affinity toward the selected targets. This may be attributed to their structural features, particularly the presence of hydroxyl groups that facilitate hydrogen bond formation and enhance interaction stability within the active site of proteins. These compounds have been widely reported for their antioxidant and anticancer activities, which further supports their possible role in inhibiting angiogenesis.

In addition to flavonoids, beta-sitosterol also demonstrated considerable interaction with the receptor proteins, suggesting its involvement in disrupting angiogenic pathways. Furthermore, volatile constituents including 1,8-cineole, alpha-pinene, and bornyl acetate showed moderate yet meaningful binding interactions. These molecules are likely to contribute through hydrophobic interactions and van der Waals forces, aiding in the stabilization of ligand–protein complexes.

The observed negative binding energy values indicate that the interaction between ligands and target proteins is energetically favourable and occurs spontaneously. Such interactions may interfere with signalling pathways regulated by angiogenic receptors, thereby reducing endothelial cell proliferation and new blood vessel formation, which are critical for tumor growth.

Overall, the results align with previously reported studies that emphasize the therapeutic importance of plant-derived phytochemicals, especially flavonoids and terpenoids, in cancer prevention and treatment. However, it is important to acknowledge that the present findings are based solely on *in silico* methods. Therefore, further experimental validation through *in*

vitro and in vivo studies is necessary to confirm the biological activity, safety, and pharmacokinetic profile of these compounds.

Conclusion

In this study, the molecular docking simulation found that Quercetin, Kaempferol, Beta sitosterol, Limonene, Alpha pinene, Bornyl Acetate and 1,8 cineol are potential anti-angiogenic compounds against VEGFR and other angiogenic receptors. These are potential anti-angiogenic compounds with high binding affinities and good molecular interactions, suggesting that they have potential uses in the treatment of cancer by inhibiting pathological angiogenesis. These findings are significant in supporting the discovery of anti-angiogenic compounds for the treatment of cancer using natural resources. These findings also support the advantages of using phytochemicals in drug discovery. Although the use of molecular docking is good in selecting potential drug candidates, it is also important to note that experimental studies are also significant. These anti-angiogenic compounds need to be tested in vitro to evaluate their potential to inhibit endothelial cell proliferation, migration, and tube formation. These anti-angiogenic compounds also need to be tested in vivo to evaluate their pharmacokinetic, bioavailability, and toxicity profile. If successful in preclinical studies, these types of agents have the potential to be a foundation for new, and less toxic, anti-angiogenic treatments for cancer patients. In conclusion, overall, the present research demonstrates the enormous potential of natural agents in contemporary medicine and underlines the value of a hybrid approach, combining both computational and experimental methods, in drug discovery research. With the pharmacological potential of plant compounds, researchers are likely to lay the foundation for more targeted and less toxic cancer treatments.

Reference

1. Ean Jeong Seo OK. Targeting Angiogenesis By Phytochemicals. *Med Aromat Plants (Los Angel)*. 2012;02(05). doi:10.4172/2167-0412.1000134
2. Haruna Isiyaku Umar Isaac Olatunde Awonyemi-Segun Micheal Abegunde Festus O. Igbe². Bushra Siraj. In Silico Molecular Docking of Bioactive Molecules Isolated from *Raphia taedigera* Seed Oil as Potential Anti-cancer Agents Targeting Vascular Endothelial Growth Factor Receptor-2. 2020;(5 nov):1-14.

3. Dr. Pradnya Jagtap MNJMrSKMSJadhav. Anti-angiogenic potential of bioactive phytochemicals from caraway (Caramel carvi) targeting protein to fight cancer through Molecular Docking. 2025;10(4 april 2025):1-13.
4. Yadav DK, Ali M, Ghosh AK, Kumar B. Isolation of flavonoid from *Abies webbiana* leaves and its activity. *Pharmacognosy Journal*. 2016;8(4):341-345. doi:10.5530/pj.2016.4.6
5. Timothy CN, Nandhini JST, Varghese SS, Rajeshkumar S. *Abies webbiana* Ethanolic Extract Based Mouthwash and Its Antimicrobial and Cytotoxic Effect. *J Pharm Res Int*. Published online December 29, 2021:371-385. doi:10.9734/jpri/2021/v33i62B35625
6. Jeong H, Phan AiNH, Choi JW. Anti-cancer effects of polyphenolic compounds in epidermal growth factor receptor tyrosine kinase inhibitor-resistant non-small cell lung cancer. *Pharmacogn Mag*. 2017;13(52):595. doi:10.4103/pm.pm_535_16
7. Awad AB, Downie AC, Fink CS. Inhibition of growth and stimulation of apoptosis by beta-sitosterol treatment of MDA-MB-231 human breast cancer cells in culture. *Int J Mol Med*. Published online May 1, 2000. doi:10.3892/ijmm.5.5.541
8. Shahnaz Sultana^{1 2}, Mohammed Ali^{1 *} and Showkat Rasool Mir¹. CHEMICAL CONSTITUENTS OF THE LEAVES OF *CAYRATIA TRIFOLIA* (L.) DOMIN AND *ABIES WEBBIANA* (WALL EX D. DON) LINDL. 2023;12(8 /2023):1-14.
9. Hou J, Zhang Y, Zhu Y, et al. α -Pinene Induces Apoptotic Cell Death via Caspase Activation in Human Ovarian Cancer Cells. *Medical Science Monitor*. 2019;25:6631-6638. doi:10.12659/MSM.916419
10. Wu J, Ren J, Wang L, et al. The active constituent of pine needle oil, bornyl acetate, suppresses NSCLC progression by inhibiting the PI3K/AKT/ABCB1 signaling axis. *Front Pharmacol*. 2025;16. doi:10.3389/fphar.2025.1653461

11. MURATA S, SHIRAGAMI R, KOSUGI C, et al. Antitumor effect of 1, 8-cineole against colon cancer. *Oncol Rep.* 2013;30(6):2647-2652. doi:10.3892/or.2013.2763
12. Hashemzaei M, Far AD, Yari A, et al. Anticancer and apoptosis-inducing effects of quercetin in vitro and in vivo. *Oncol Rep.* 2017;38(2):819-828. doi:10.3892/or.2017.5766
13. Johannes Kirchmair †, ‡ Patrick Markt, † Simona Distinto, †, § Daniela Schuster, † Gudrun M. Spitzer, | Klaus R. Liedl, | Thierry Langer, ⊥ and Gerhard Wolber*, †, ‡. The Protein Data Bank (PDB), Its Related Services and Software Tools as Key Components for In Silico Guided Drug Discovery. 2008;51(11/1/2008):1-20.
14. Kim S, Chen J, Cheng T, et al. PubChem 2025 update. *Nucleic Acids Res.* 2025;53(D1):D1516-D1525. doi:10.1093/nar/gkae1059
15. Ayodele PF, Bamigbade A, Bamigbade OO, et al. Illustrated Procedure to Perform Molecular Docking Using PyRx and Biovia Discovery Studio Visualizer: A Case Study of 10kt With Atropine. *Progress in Drug Discovery & Biomedical Science.* 2023;6(1). doi:10.36877/pddbs.a0000424
16. Jayanti DAPIS, Abimanyu IGA, Azzamudin H. Spirulina platensis's phycocyanobilin as an antiangiogenesis by inhibiting VEGFR2-VEGFA pathway in breast cancer: in silico study. *JSMARTech.* 2021;2(3):87-91. doi:10.21776/ub.jsmartech.2021.002.03.87
17. Tayal N, Srivastava P, Srivastava N. Anti Angiogenic Activity of Carica papaya Leaf Extract. *J Pure Appl Microbiol.* 2019;13(1):567-571. doi:10.22207/JPAM.13.1.64
18. Rachana R. Desai' DHBVTJHAP and RMR. Molecular Docking of Vascular Endothelial Growth Factor with Phytochemicals for Anti-Angiogenesis. 2012;3(dec 2012):1-5.
19. Sheetal Ramachandran and Darsan Balakrishnan Menon. A novel protein fraction isolated from the leaves of Abies webbiana Lindl. Induces apoptosis in lung cancer cells via the intrinsic pathway. 2016;(6/9/2016):1-8.

20. Zardecki C, Dutta S, Goodsell DS, Voigt M, Burley SK. RCSB Protein Data Bank: A Resource for Chemical, Biochemical, and Structural Explorations of Large and Small Biomolecules. *J Chem Educ*. 2016;93(3):569-575. doi:10.1021/acs.jchemed.5b00404
21. Baroroh SSi, MBiotek, U, Muscifa ZS, Destiarani W, Rohmatullah FG, Yusuf M. Molecular interaction analysis and visualization of protein-ligand docking using Biovia Discovery Studio Visualizer. *Indonesian Journal of Computational Biology (IJCB)*. 2023;2(1):22. doi:10.24198/ijcb.v2i1.46322
22. Cheng T, Pan Y, Hao M, Wang Y, Bryant SH. PubChem applications in drug discovery: a bibliometric analysis. *Drug Discov Today*. 2014;19(11):1751-1756. doi:10.1016/j.drudis.2014.08.008

Copyright & License:

© Authors retain the copyright of this article. This work is published under the Creative Commons Attribution 4.0 International License (CC BY 4.0), permitting unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.