



International Journal of Biology Sciences

ISSN Print: 2664-9926
 ISSN Online: 2664-9934
 NAAS Rating (2026): 4.82
 IJBS 2026; 8(6): 211-216
www.biologyjournal.net
 Received: 24-03-2026
 Accepted: 26-04-2026

All authors' names and
 affiliations are given below,
 after the references.

***In silico* investigation of phytochemicals present in leaves of *Pongamia pinnata* as potential VEGFR-2 inhibitors: Integrated ADMET and molecular docking analysis of anti-angiogenesis based anticancer activity**

Monoshree Sarma, Diptirani Rath, Sandesh Kumar Pattanaik, Ritu Gupta, Abhishek Kumar, Safeeda Sultana Begum, Mokhtar Hussain, M Bindu Pushpa, Shabnam Akhtar, Farida Rahman, Khumtya Debbarma and Mrinmoyee Sarma

DOI: <https://www.doi.org/10.33545/26649926.2026.v8.i6c.889>

Abstract

There is over expression of VEGFRs and their specific agonist in multitudes of human tumours like gliomas and carcinomas. Hence, VEGFRs are regarded as one of the pivotal regulators of angiogenesis and tumour growth. *Pongamia pinnata* belonging to the family Leguminosae and subfamily 'Papilionaceae' is widely distributed in Asia and Australia. This plant is reported to possess antioxidant, anticancer, cytotoxic, antidiabetic, anti-inflammatory, antiparasitic, antimicrobial, anticonvulsant, antihyperammonaemia, anthelmintic, insecticidal, analgesic and anti-inflammatory properties. The leaves of *P. pinnata* possess many flavones and chalcone derivatives such as Pongagallone A, Pongagallone B, Pongone, Galbone and Pongalabol. This research work was taken to study the anti-angiogenic and anticancer potential of Pongagallone A, Pongagallone B and Pongone by molecular docking against VEGFR-2 pathways. These compounds demonstrated favourable ADME parameters along with acceptable toxicity profile. Pongone exhibited the highest binding affinity of -10.1 kcal/mol, outperforming the co-crystallized ligand Axitinib (-9.2 kcal/mol). The Pongone-VEGFR-2 complex formed three hydrogen bonds with key active site residues ASP1044, CYS917, PHE916, along with additional hydrophobic interactions with other residues. Overall, the insights of binding energies obtained from molecular docking studies are suggestive of tumour related antiangiogenic properties of these ligands that acts via inhibition of VEGFR-2 pathway

Keywords: *Pongamia Pinnata*, Pongone, anti-angiogenic, anticancer, molecular docking

1. Introduction

Cancer has been declared as the second leading cause of death as per the reports of World Health Organization (Bray *et al.*, 2018) [6]. It is predicted that cancer deaths would reach thirteen million worldwide by 2030 (Barbosa *et al.*, 2015) [5].

Angiogenesis is imperative for growth and regeneration of tissues that plays a pivotal role in preventing ischaemic necrosis and survival of the damaged tissues (Chu and Wang, 2012). Angiogenesis is regulated by a plethora of protein kinases such as EGFRs, FGFRs, and VEGFRs (Ghith *et al.*, 2017) [10].

There are overexpression of VEGFRs and their specific agonist in multitudes of human tumours like gliomas and carcinomas (Hamerlik *et al.*, 2012) [13]. Hence, VEGFRs are regarded as one of the pivotal regulators of angiogenesis and tumour growth (Guo *et al.*, 2010) [12]. VEGFR-1, VEGFR-2, and VEGFR-3 constitutes the VEGFRs family, where VEGFR-1 regulates embryonic vasculogenesis and VEGFR-2 is responsible for both tumour angiogenesis as well as embryonic vasculogenesis (Takahashi, 2011) [24]. Hence, inhibition of VEGFR-2 can be useful in management of angiogenesis-dependent malignancies (Holmes, 2007) [14]. Profound suppression of progression of tumour has been demonstrated by VEGFR-2 blockers, whose primary target is the ATP binding site (Modi and Kulkarni, 2019; Alanazi *et al.*, 2021) [17, 2].

Corresponding Author:
Ritu Gupta
 Assistant Professor, Institute
 of Veterinary Science and
 Animal Husbandry, Siksha 'O'
 Anusandhan, Deemed to be
 University, Odisha, India

Although cancer diagnosis and treatment is advancing rapidly, yet, the patient's survival stands unsatisfactory owing to mammoth adverse effects associated with anti cancer agents (El Newahie *et al.*, 2016) ^[9]. Hence, it is the need of the hour to explore for novel, selective, less toxic and high efficacious anti cancer agents (Nam and Parang, 2003) ^[18].

Pongamia pinnata belonging to the family Leguminosae and subfamily 'Papilionaceae' is widely distributed in Asia and Australia. This plant also flourishes in the US, Africa and many other countries. In India this plant can be seen along rivers and streams as well as in coastal forests. In Tamil it is called as 'Ponga', 'Pongam,' 'Dalkaramacha' and 'Punku' While in Hindi and Bengal, it is referred to as 'Karanj', 'Kanji' or 'Papar'. In English, it is called as 'Karum Tree' or the 'Poonga Oil Tree' (Tanaka *et al.*, 1992) ^[25]. Folklore use of this plant has prompted scientists to investigate its pharmacological profile. This plant is reported to possess antioxidant, anticancer, cytotoxic, antidiabetic, antiparasitic, antimicrobial, anticonvulsant, antihyperammonaemia, anthelmintic, insecticidal (Rangaswami and Seshadri, 1942) ^[21], analgesic and anti-inflammatory properties (Rahman *et al.*, 2025) ^[20]. The leaves of *P. pinnata* possess many flavones and chalcone derivatives such as Pongagallone A, Pongagallone B, Pongone, Galbone and Pongalabol. This research work was taken to study the anti angiogenic and anti cancer potential of Pongagallone A, Pongagallone B and Pongone by molecular docking against VEGFR-2 pathways.

2. Materials and Methods:

2.1. Retrieval of chemical structure and target protein

Pongagallone A (CID: 14483495), Pongagallone B (CID: 14483496) and Pongone (CID: 44257567) were obtained in SDF format from the database PubChem available at <https://pubchem.ncbi.nlm.nih.gov/> (Kim *et al.*, 2023). The 2-D structures of the ligands were derived from the database PubChem (Figure 1). The crystal structure of VEGFR-2 (PDB ID: 2OH4) was retrieved from the database RCSB PDB available at <https://www.rcsb.org/>.

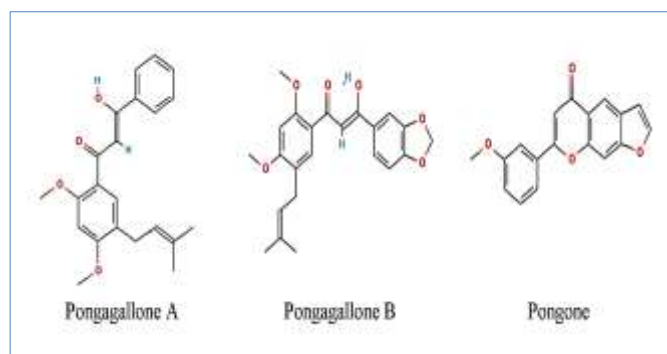


Fig 1: Two dimensional chemical structures of the phytochemicals

2.2. Prediction of Toxicity and ADME

The ADME characteristics were predicted with Swiss ADME server available at <https://www.swissadme.ch/>. The toxicity and LD₅₀ (median lethal dose) values of the phytoconstituents were predicted with ProTox-3.0 server (<https://tox.charite.de/protox3/>) (Banerjee *et al.*, 2024) ^[4].

2.3. Molecular Docking

In this study, molecular docking was carried out in order to

assess the binding affinities of the selected phytochemicals with VEGFR-2 (PDB ID: 2OH4). For this, three dimensional structure of the protein was retrieved from RCSB Protein Data Bank. Selection of ligand candidates were done based on published literature reporting the phytochemical profile of the plant under investigation. The 3-D structures of the ligands were retrieved from the PubChem database. The protein preparation prior to docking involved removal of native ligands and co-crystallized water molecules, along with addition of atoms of polar hydrogen using Discovery Studio Visualizer (DSV), which were then converted to PDBQT from PDB format within the PyRx environment (Abdisa *et al.*, 2026) ^[1]. Ligands were prepared by minimizing energy using Open Babel and then converted to PDBQT to facilitate its compatibility with PyRx integrated AutoDock Vina (Ghose *et al.*, 2025) ^[11]. The coordinates of docking grid were decided on the basis of position of bound co-crystallized ligands or inhibitors with the centroid coordinates assigned for VEGF-2, i.e., x = 1.396, y = 32.317, z = 15.938. In order to validate the docking protocol, re-docking of co-crystallized ligand or inhibitor with the respective binding pocket, and the binding affinity obtained was compared to the original crystal conformation to ensure reproducibility and reliability of the parameters of docking. Subsequently, the binding affinities of the selected phytochemicals were assessed by comparing with reference co-crystallized ligand and compound-protein complexes were selected for further interaction analysis using Discovery Studio Visualizer (Pattanaik *et al.*, 2026) ^[19].

3. Results

3.1. Prediction of Toxicity and ADME

A comprehensive assessment of pharmacokinetic and toxicity parameters was done to ensure the candidature of the phytochemicals as potential VEGFR-2 inhibitors. The drug-likeness of the selected ligands were determined as per the Lipinski's Rule of Five (RO5), that considers vital physicochemical parameters (molecular weight, partition coefficient, hydrogen bond donor, hydrogen bond acceptor and topological polar surface area) influencing oral bioavailability. All the ligands fulfil the requirements of Lipinski's Rule of Five without any violation. As per the prediction of LD₅₀ values using ProTox 3.0 server, all the ligands belong to class 5, which is indicative of low toxicity of the selected phyto-compounds. Among all the ligands, Pongone have the safest toxicity profile with LD₅₀ values of 4000 mg/kg (Table 1). Moreover, the ADME prediction and radar images reveal that all parameters lie within acceptable range (Fig. 2). Pongagallone A and Pongone were predicted to penetrate the blood brain barrier and thus expanding its pharmacological role in treating cancer of central nervous system (Table 1 and Fig. 3). These outcomes enhance their candidature as drugs for further experimental validation as inhibitors of VEGFR-2

Table 1: Toxicity assessment and ADME properties of selected compounds

S. N.	Ligand	BBB Penetration	Toxicity	
			Class	LD ₅₀ (mg/kg)
1.	Pongagallone A	Yes	5	3000
2.	Pongagallone B	No	5	3800
3.	Pongone	Yes	5	4000

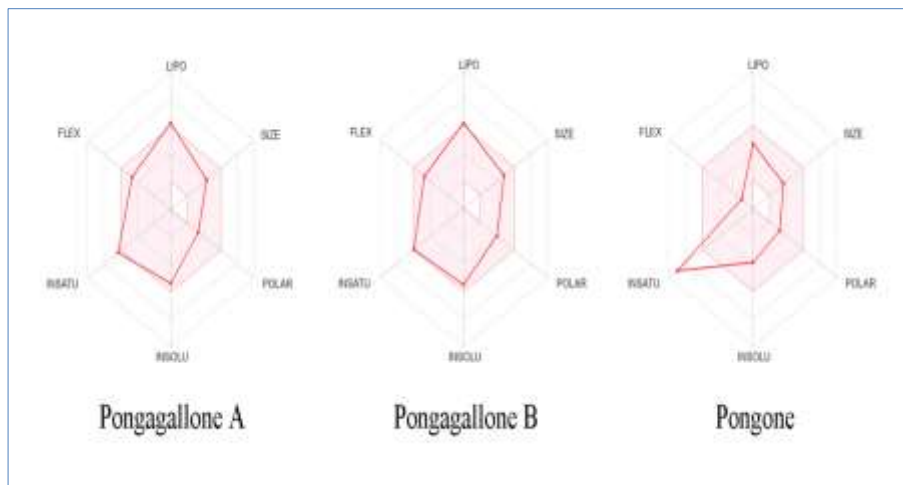


Fig 2: Radar chart of the physicochemical properties of the selected ligands

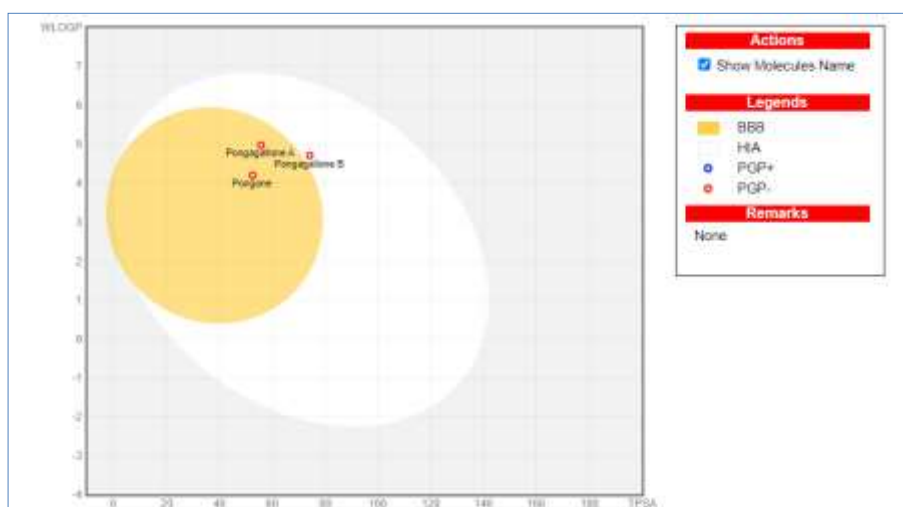


Fig. 3: BOILED-Egg Analysis

3.2. Molecular Docking

Molecular docking has surfaced out as a useful tool to assess protein-ligand binding, adding new scope to drug designing (Kashaw *et al.*, 2019). Molecular docking was carried out to investigate binding affinities involving selected 3 phyto-compounds and VEGFR-2 protein (PDB ID: 2OH4) (Figure 3). Pongone exhibited the highest binding affinity of -10.1 kcal/mol, outperforming the co-crystallized ligand Axitinib (-9.2 kcal/mol). The Pongone-VEGFR-2 complex formed three hydrogen bonds with key active site residues ASP1044, CYS917, PHE916, along with additional

hydrophobic interactions with LEU1033, VAL846, VAL914, LYS866, ALA864, LEU838, PHE1045 (Table 2). Also, the binding energies of Pongagallone A and B are -7.6 and -8.4 kcal/mol. The binding affinity of Pongagallone B is only slightly less than co-crystallized ligand Axitinib. The binding energies and interactions of the top docked ligands i.e., Pongone and Pongagallone B with the amino acids of the active site makes them preferable candidates as lead scaffolds in discovery of anti-cancer drugs (Kashaw *et al.*, 2019) ^[15]

Table 2: Binding affinity and intermolecular interaction between *P. pinnata* compounds and the target protein VEGFR-2

Target Protein	Compound Name	Binding affinity (Kcal/mol)	No. of H-bonds	H-bond interaction	Other Interaction
VEGFR-2 (2OH4)	Pongagallone B	-8.4	1	CYS917	VAL846, ALA864, LYS866, VAL914, LEU1033, CYS1043, PHE1045
	Pongagallone A	-7.6	-	-	LEU838, VAL846, ALA864, LYS866, VAL897, VAL914, PHE916, CYS917, LEU1033
	Pongone	-10.1	3	ASP1044, CYS917, PHE916	LEU1033, VAL846, VAL914, LYS866, ALA864, LEU838, PHE1045
	Axitinib*	-9.2	4	SO 4302, LEU 838, GLU 915, ASP 1044	CYS 917, ALA 864, LEU 1033, ARG 1049, VAL 846, VAL 914, LYS 866

* Co-crystallized ligand

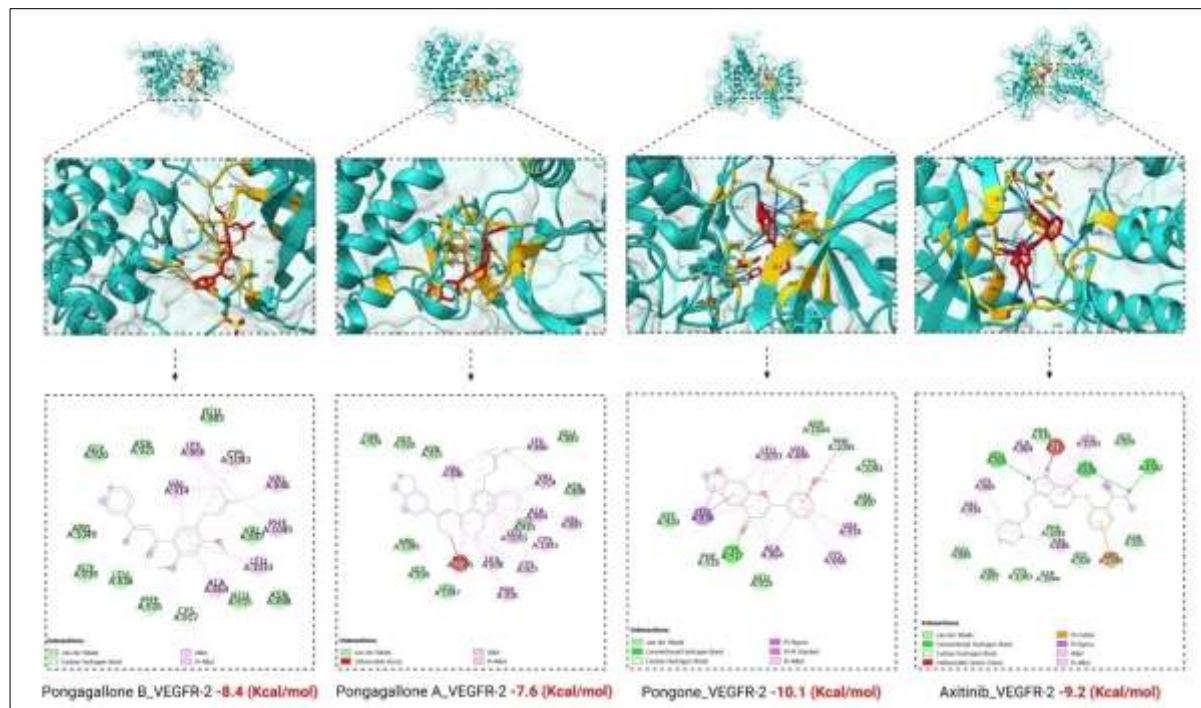


Fig. 3: Three-dimensional (3D) and two-dimensional (2D) molecular interaction of phytoconstituents from *Pongamia pinnata* with VEGFR-2.

4. Discussion:

Molecular docking is a widely used computation tool that investigates how properly and with how much affinity a ligand binds with the active site of the targeted protein. It reduces the time required by conventional chemical synthesis and biological experimentation. By simulation of protein ligand interaction occurring at molecular level, *In silico* studies facilitate identification of promising drug candidates, thereby accelerating the drug development process. Computational and simulation studies have become an integral part of Research and Development in Pharmaceutical Industries accounting for almost 10% of total expenditure (Van De Waterbeemd, and Gifford, 2003) [26].

Multitudes of receptor tyrosine kinases, such as VEGFR2, Flt1/VEGFR1, VEGFR3, or PDGFR, play pivotal role in tumour angiogenesis. Upon activation these receptors orchestrate various signal pathways leading to neoangiogenesis. VEGFR-2 plays a critical role in survival of endothelial cell, migration as well as in proliferation of blood vessels (Baeriswyl and Christofori, 2009) [3]. As per the tumour linked angiogenesis model of canonical, VEGF is expressed by tumour cells that bind to VEGFR-2 receptor of endothelial cells (Carmeliet, 2000) [7], and thereby signalling blood vessel formation around tumour. This transition from prevascular hyperplasia to highly vascularized tumors has been referred to as the angiogenic switch (Baeriswyl and Christofori, 2009) [3]. Hence, VEGFR-2 has emerged as an important drug target pertaining to cancer therapy.

Screening of phytobiotics using molecular docking against VEGFR-2 exhibited a set of potential drug candidates, with Pongone standing out. Furthermore, these compounds demonstrated favourable ADME parameters along with acceptable toxicity profile. Also, Pongone was predicted to penetrate the blood brain barrier and thus may inhibit neoangiogenesis associated with brain tumour. Overall, the insights of binding energies obtained from molecular

docking studies are suggestive of tumour related antiangiogenic properties of these ligands that acts via inhibition of VEGFR-2 pathway.

5. Conclusion

Phytochemicals in leaves of *Pongamia pinnata*, more particularly Pongone can inhibit VEGFR-2 pathway that is responsible for 'angiogenic switch' leading to tumour angiogenesis. By this mechanism, it can emerge as a potential chemotherapeutic agent, which has acceptable toxicity profile. For further validation, in vitro and in vivo studies should be conducted.

6. Acknowledgment

The authors acknowledges Siksha 'O' Anusandhan, Deemed to be University for providing research facilities.

References

1. Abdisa G, Bizualem H, Ketema B, Chaluma E, Girma S, Ahmed U, *et al.* In vivo and molecular docking studies of *Micromeria imbricata* var. *imbricata* extract reveal alleviation of the DSS-induced IBD phenotype via interaction with key inflammatory mediators. *J Ethnopharmacol.* 2026;121843.
2. Alanazi MM, Eissa IH, Alsaif NA, Obaidullah AJ, Alanazi WA, Alasmari AF, *et al.* Design, synthesis, docking, ADMET studies, and anticancer evaluation of new 3-methylquinoxaline derivatives as VEGFR-2 inhibitors and apoptosis inducers. *J Enzyme Inhib Med Chem.* 2021;36(1):1760-1782.
3. Baeriswyl V, Christofori G. The angiogenic switch in carcinogenesis. *Semin Cancer Biol.* 2009;19(5):329-337.
4. Banerjee P, Kemmler E, Dunkel M, Preissner R. ProTox 3.0: a webserver for the prediction of toxicity of chemicals. *Nucleic Acids Res.* 2024;52(W1):W513-W520.

5. Barbosa IR, Souza DLB, Bernal MM, Costa ICC. Cancer mortality in Brazil: temporal trends and predictions for the year 2030. *Medicine (Baltimore)*. 2015;94:e746.
6. Bray F, Ferlay J, Soerjomataram I, *et al*. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68:394-424.
7. Carmeliet P. Mechanisms of angiogenesis and arteriogenesis. *Nat Med*. 2000;6(4):389-395.
8. Chu H, Wang Y. Therapeutic angiogenesis: controlled delivery of angiogenic factors. *Ther Deliv*. 2012;3:693-714.
9. El Newahie AM, Ismail NS, Abou El Ella DA, Abouzid KA. Quinoxaline-based scaffolds targeting tyrosine kinases and their potential anticancer activity. *Arch Pharm*. 2016;349:309-326.
10. Ghith A, Ismail NS, Youssef K, Abouzid KA. Medicinal attributes of thienopyrimidine based scaffold targeting tyrosine kinases and their potential anticancer activities. *Arch Pharm*. 2017;350:1700242.
11. Ghose S, Bhattacharya K, Baruah S, Singh NK, Kumar S, Prasad SK, *et al*. Bioactive catechins from *Potentilla fulgens* Wall. ex Sims roots ameliorate oral carcinogenesis through modulation of oxidative stress, inflammatory, and apoptotic pathways. *J Ethnopharmacol*. 2025;120446.
12. Guo S, Colbert LS, Fuller M, *et al*. Vascular endothelial growth factor receptor-2 in breast cancer. *Biochim Biophys Acta Rev Cancer*. 2010;1806:108-121.
13. Hamerlik P, Lathia JD, Rasmussen R, *et al*. Autocrine VEGF-VEGFR2-Neuropilin-1 signaling promotes glioma stem-like cell viability and tumor growth. *J Exp Med*. 2012;209:507-520.
14. Holmes K, Roberts OL, Thomas AM, Cross MJ. Vascular endothelial growth factor receptor-2: structure, function, intracellular signalling and therapeutic inhibition. *Cell Signal*. 2007;19:2003-2012.
15. Kashaw SK, Agarwal S, Mishra M, Sau S, Iyer AK. Molecular docking analysis of Caspase-3 activators as potential anticancer agents. *Curr Comput Aided Drug Des*. 2019;15:55-66.
16. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, *et al*. PubChem 2023 update. *Nucleic Acids Res*. 2023;51(D1):D1373-D1380.
17. Modi SJ, Kulkarni VM. Vascular endothelial growth factor receptor (VEGFR-2)/KDR inhibitors: medicinal chemistry perspective. *Med Drug Discov*. 2019;2:100009.
18. Nam NH, Parang K. Current targets for anticancer drug discovery. *Curr Drug Targets*. 2003;4:159-179.
19. Pattanaik SK, Mohanty D, Ray A, Jena S, Pattanaik S, Rath D. Phytotherapy for ageing-related multimorbidity: systems-level insights into *Centella asiatica* in diabetes and Alzheimer's disease. *Phytomedicine*. 2026;158026.
20. Rahman F, Mohan P, Sarma J, Baruah H, Nath R, Begum SA, *et al*. Analgesic and anti-inflammatory property of *Pongamia pinnata* plant. *Int J Adv Biochem Res*. 2025;9(4S):428-434.
21. Rangaswami S, Seshadri TR. Chemistry of pongamol. Part I. *Proc Indian Acad Sci Sect A Phys Sci*. 1942;15(6):417-423.
22. Shibuya M. Vascular endothelial growth factor receptor-1 (VEGFR-1/Flt-1): a dual regulator for angiogenesis. *Angiogenesis*. 2006;9:225-230.
23. Stuttfeld E, Ballmer-Hofer K. Structure and function of VEGF receptors. *IUBMB Life*. 2009;61:915-922.
24. Takahashi S. Vascular endothelial growth factor (VEGF), VEGF receptors and their inhibitors for antiangiogenic tumor therapy. *Biol Pharm Bull*. 2011;34:1785-1788.
25. Tanaka T, Iinuma M, Yuki K, Fujii Y, Mizuno M. Flavonoids in root bark of *Pongamia pinnata*. *Phytochemistry*. 1992;31(3):993-998.
26. Van De Waterbeemd H, Gifford E. ADMET *In silico* modelling: towards prediction paradise? *Nat Rev Drug Discov*. 2003;2:192-204.

Authors Names

Monoshree Sarma

Assistant Professor, Institute of Veterinary Science and Animal Husbandry, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India

Diptirani Rath

Assistant Professor, Department of Pharmacology, School of Pharmaceutical Science, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India

Sandesh Kumar Pattanaik

Research Scholar, Department of Pharmacology, School of Pharmaceutical Science, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India

Ritu Gupta

Assistant Professor, Institute of Veterinary Science and Animal Husbandry, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India

Abhishek Kumar

Research Scholar, College of Veterinary Science and Animal Husbandry, Orissa University of Agriculture and Technology, Odisha, India

Safeeda Sultana Begum

Assistant Professor, Department of Veterinary Medicine, College of Veterinary and Animal Sciences, BASU, Bihar, India

Mokhtar Hussain

Senior Scientist (AR&G), ICAR-National Research Centre on Yak, Arunachal Pradesh, India

M Bindu Pushpa

Assistant Professor, Institute of Veterinary Science and Animal Husbandry, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India

Shabnam Akhtar

Assistant Professor, Institute of Veterinary Science and Animal Husbandry, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India

Farida Rahman

Research Scholar, Department of Veterinary

Pharmacology and Toxicology, College of Veterinary Science, Assam, India

Khumtya Debbarma

Research Scholar, Department of Veterinary Pharmacology and Toxicology, College of Veterinary Science, Assam, India

Mrinmoyee Sarma

Assistant Professor, Institute of Veterinary Science and Animal Husbandry, Siksha 'O' Anusandhan, Deemed to be University, Odisha, India