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Advances in Bioresearch

ORIGINAL ARTICLE

Structure based virtual screening, molecular docking and brine shrimp bioassay of 1,3,4 oxadiazole derivatives as potent inhibitors of VEGFR.

Priyanka Patil[1,2]*, Preeti Khulbe[1], Chandrakant Magdum[3]
[1]School of Pharmacy, Suresh GyanVihar University, Jaipur, 302017, Rajasthan, India.
[2]Dr. Shivajirao Kadam College of Pharmacy, KasabeDigraj, 416305, Sangli, Maharashtra, India.
[3]Dr. BapujiSalunkhe Institute of Pharmacy, Miraj, Maharashtra, India.
Corresponding author's Email Id: papatil8001@gmail.com
Orcid Id: 0000-0002-4474-1754.

ABSTRACT
Vascular Endothelial Growth Factor (VEGF) and its receptor are key players in physiological and pathologic angiogenesis, which is associated to the progression and development of breast cancer metastases. The goals of the current study are to find a potential VEGF receptor antagonist that is essential for promoting the immunomodulatory extracellular matrix in breast cancer cells and to assess the inhibitor's efficacy using numerous in-silico methods.Using the web tools SWISS ADME, Molinspiration and AdmetSAR, in silico investigations on ADMET were conducted. The next step is to use a brine shrimp lethality test to check for cytotoxicity of compounds AM3A-3L at the dose level of 50, 100, and 150 µg/mL. As a result of a docking, the molecule AM 3D exhibits a high affinity toward the target protein. Nearly all of the compounds strongly attach to the target's active sites, with binding affinities ranging from -8.5 to -9.2 kcal/mol. Compounds AM 3C and AM 3D exhibited potent brine shrimp lethality with LC50values of 98.77 µg and 94.46 µg. These finding reveals that compounds AM 3A- AM 3L may be used as anticancer drugs in future.
Keywords. *ADMET, brine shrimp assay, cytotoxicity, molecular docking.*

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INTRODUCTION

VEGFRs are one of the most significant regulators of angiogenesis and consequently, tumour formation, as they are overexpressed in many human tumors [1]. Three subtypes of the VEGFRs family exist: VEGFR-1, VEGFR-2, and VEGFR-3 [2].The regulation of embryonic vasculogenesis by VEGFR-1 [3]. The regulation of tumour angiogenesis by VEGFR-2. On the other hand, lymphangiogenesis is caused by VEGFR-3 [4-5]. Due to this, VEGFR-2 is currently the main target for antiangiogenic therapy, and inhibiting it is acrucial strategy for the development of novel drugs for treatment of angiogenic cancers [6].

The Artemia salina mortality test is acknowledged as a cost-effective and feasible approach for the initial assessment of cytotoxicity in the design of potent and selective anticancer drugs [7-8].Lethality is one of the easiest biochemical processes to observe since there is just one possible outcome: whether in dead or surviving. Brine shrimp lethality test, established by Meyer et al.,as a simple approach, it is possible to direct the screening of compounds that are physiologically active.This bioassay may identify a variety of chemical structures and biological processes.

At a greater dose Toxicology, is essentially pharmacology, therefore if we identify harmful substances, a smaller, innocuous amount may still exert a beneficial pharmacological impact on a physiological system. However, it has been established that the cytotoxic activity test and other biological characteristics rationally correspond well with the shrimp lethality test.

In the past, brine shrimp have been used in several bioassay methods. There are numerous reports on the use of brine shrimp for environmental investigations, natural toxin screening, and ordinary bioactivities

screening. The chemical that shows promising cytotoxicity toward brine shrimp larva can also be further extended for cell-line toxicity and anticancer activities [9]. A similar approach led to the discovery of taxol, a powerful anticancer medicine used for the chemotherapy of various carcinomas [10].This study predicts the ADMET of chemicals AM3A and AM3L in order to better comprehend their molecular interactions with human VEGF.

Table 1 summerizes the structure of synthesized compounds (AM-3A to Am 3L).

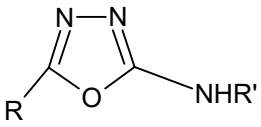
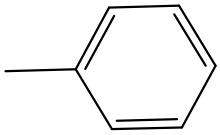
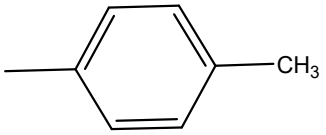
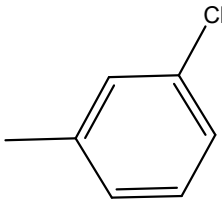
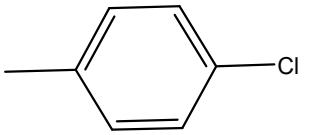
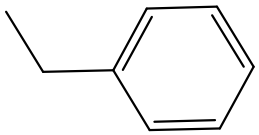
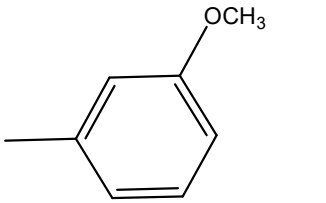
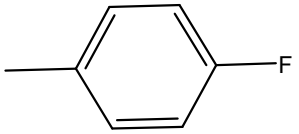
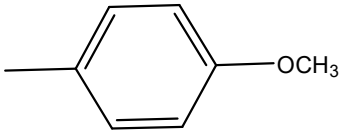
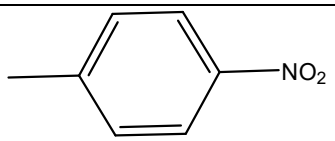
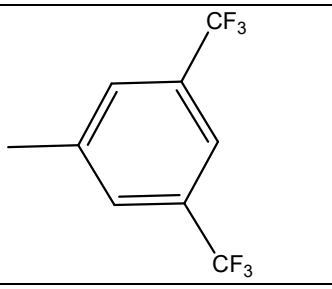


Table 1. The structure of synthesized compounds (AM 3A- AM 3L)

Compound	R'	Compound	R'
AM 3A		AM 3G	
AM 3B		AM 3H	
AM 3C		AM 3J	
AM 3D		AM 3K	
AM 3E		AM 3L	

MATERIAL AND METHODS

BIOLOGICAL EVALUATION

Brine Shrimp Lethality Assay:

As a bioassay, the brine shrimp lethality test has been applied to numerous lethal compounds. a generic bioassay that, instead of time-consuming and expensive in-vitro and in-vivo cytotoxic assays, appears to be able to identify a wide range of bioactivity, found in synthesized drugs.

Many researchers have used the brine shrimp (Artemia salina), a simplistic zoological organism, as a test subject for the test sample's lethality, and this method has proven to be beneficial for screening different chemical compounds present in various bioactivities.

After 24 hours, the number of larvae still alive was determined, and the percentage of mortality was calculated using the equation [11]:

Percent mortality = (Total no. of nauplii- No. of live nauplli)/ Total no. of nauplii × 100.

Procedure:

Preparation of seawater

The crude sea salt 25g/L dissolve in distill water and add dried Brewer's yeast 6mg/L in this solution for food of brine shrimp. It was filtered through filter paper before using.

Hatching of brine shrimp

The test organism was Artemia salina leach, which was procured from pet stores. Shrimp eggs were placed in the small tank, filled with seawater, and then sealed on one side. and a 60-100Watt bulb that was put a short distance from the jar illuminated the compartment. The shrimp was given 48 hours to hatch before being allowed to develop into nauplii. The process of hatching required a steady supply of oxygen. Since Eggshell-free nauplii were taken from the illuminated region of the tank since the freshly hatched shrimps are driven to the light. A pipette was used to gently extract the nauplii from tank, and they were then filtered to enhance visibility. Then a micropipette was used to delicately remove 10 nauplii.

Preparation of test samples

Each experiment involved adding 0.5 mL of the test material (50, 100, or 150 g/mL) to the brine solution, which was then left at room temperature for 24 hours while being lit. Surviving larvae were then measured. For each dose, sets of three tubes containing test solutions were employed. To acquire reliable results, replicas need to be kept maintained. Traditionally, a test compound's efficacy or concentration-mortality relationship is described as a (IC50) [12-13].

***IN SILICO* FORECAST OF DRUG PROPERTIES PREDICTION OF LIBRARY COMPOUNDS:**

Compound investigations in vivo are not only trick but also exceedingly expensive. Therefore, it is usual practice to simulate the interaction of a ligand with a target to anticipate its affinity using computational approaches like docking. These computational approaches can also be used to forecast pharmacokinetic characteristics. Molsoft software SWISS ADME online web tool, Molinspiration were utilized for this.

ADME prediction and drug-likeness through in-silico approach [14-16]:

To estimate the properties ADME, computational research of titled substances was conducted. Using the online web tool SWISS ADME and Molinspiration online property calculation tool set, researchers were able to compute the total polar surface area (TPSA), Log P, the number of rotatable bonds, molecular volume, and the number of hydrogen donor and acceptor atoms [16]. Drug design utilizes the qualitative idea of drug-likeness. The Lipinski Rule of Five [17],which considers molecular weight, hydrophobicity, and the number of hydrophilic groups, must be followed to determine drug-likeness. A synthetic compound's drug-likeness features were evaluated using the SWISS ADME Web tool.

Boiled EGG PLOT analysis

Besides from ADMET, effectiveness, and toxicity, weak bioavailability and pharmacokinetics are the outcomes of drug development failures. Gastrointestinal absorption and brain access are the two most crucial pharmacokinetic activities that need to be assessed at different phases of the drug development approaches. Here, the Physicochemical properties of tiny compounds, such as polarity and lipophilicity, are estimated using the Brain or IntestinaL EstimateD permeation technique (BOILEDEgg). The analysis explains that a high BBB crossing is possible when the established compound AM 3A pitching occurs beneath the yellow ellipse, or the yolk. The best virtual screened molecule carrying ID: AM 3E, on the other hand, pitches inside the white ellipse, indicating the potential for significant intestine absorption [18-19].

***In silico* Pharmacokinetic and Toxicity Prediction:**

The best-known compound's different ADMET characteristics were estimated using AdmetSAR software. The AMES toxicity test determines a substance's mutagenicity. The processed ligand designated a negative AMES toxicity test result for the established compound, indicating that the substance is not mutagenic. Additionally, the virtual screening chemical has a lower value and is not carcinogenic. In silico Pharmacokinetic prediction was done by using SWISS ADME online web tool. Here compounds GI absorption and oral bioavailability was predicted [20].

MOLECULAR DOCKING STUDY

Ligand preparation for docking

All derivatives' potential 2D and 3D structures were built using Chemdraw software, and all compounds' energies were minimised and optimised using Chem3D Pro 11.0 and Pymol, respectively. All constructed 2D and 3D structures were then translated to PDB format. When AutoDock Veena version 4.2.6 was used for ADMET screening and Docking investigation, all the ligand structures were then recorded in PDBQT file format [21-22].

Protein preparation for docking

Based on the SwissADME Target Prediction programme, the VEGFR2 target was chosenfor the docking investigation.Vascular Endothelial Growth Factor 2 (PDB ID:3VHE), a three-dimensional crystallographic structure, was obtained from the Protein Data Bank (PDB) of the Research Collaboratory for Structural Bioinformatics before the docking investigation began (RCSB).

Polar hydrogens were added to the VEGFR2 protein, which changed it and maintained it rigid during the docking process, but the Ligand module in AutoDock Tools removed all of the torsional bonds of the ligands. A protein pocket was examined using Procheck. The protein was projected in a Ramachandran plot to better understand them and dispersion of amino acid residues shown in Figure 1 [23].

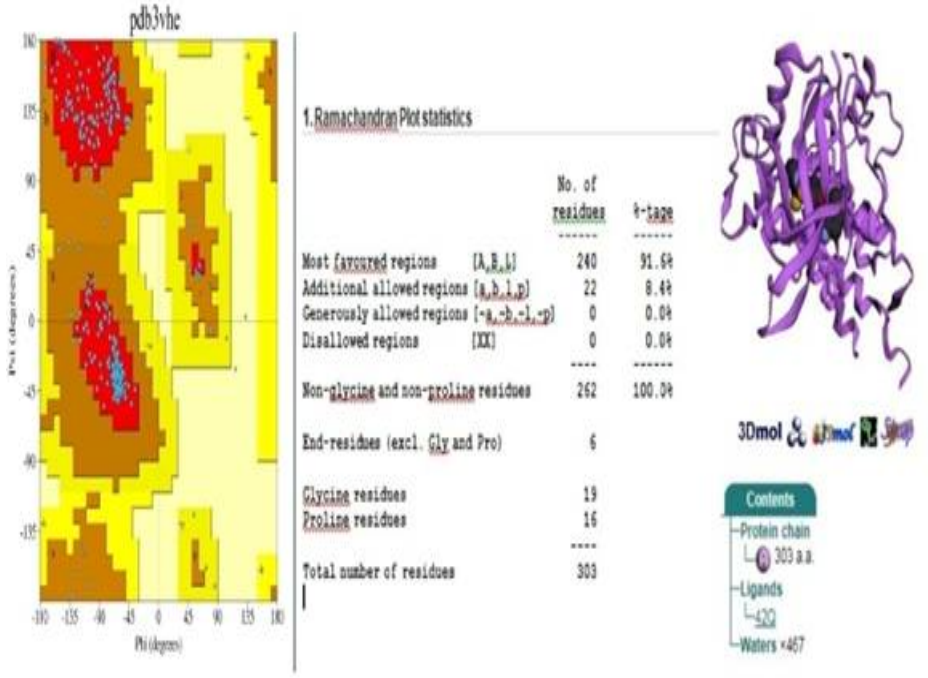


Figure 1. Ramachandran Plot of Protein Molecules (3VHE) and 3D Structure of 3VHE.

Docking simulation:

A crucial in silico method known as molecular docking predicts how a tiny ligand will interact with a target protein at a known binding site [24].The strength and degree of affinity with which a substance attaches to the pocket of a target protein are described by binding energy. As a potential drug candidate, a molecule with lower binding energy is favoured, and vice versa [25-26].

When performing docking simulations with AutoDock Vina, 9 conformations of the ligand in association with the receptor were produced. These conformations were then rated according to their binding energies [27].

Between proteins and their ligands, several bond energies, including hydrogen bonds (Hb) and electrostatic interactions, were discovered. The Discovery StudioVisualizer was utilized to analyze the final conformations [28].

RESULTS AND DISCUSSION

Brine shrimp cytotoxicity studies

The artemia salina mortalitytest is a quick, affordable, and easy method that has also shown to be practical for tracking the biological activities of synthetic compounds under study. According to the current study, hatched larvae are particular for the primary cytotoxicity screening.The brine shrimp lethality test results for the synthesized chemical and the positive control, 5-FU, are shown in Table 2 as lethal percentages and LC50 values, respectively. According to the current study, the level of lethality was proportionate to the sample's concentration in the research.

24 hours after exposure, none of the synthesised chemicals was detrimental to brine shrimp.

Table 2. Brine Shrimp lethality bioassay

Compound	Concentration of Sample µg/ml	Number of nauplii (Initial)	Number of surviving nauplii after 24 hr			Total No. of surviving nauplii	% Mortality after 24 hr	LC_{50} value (µg)
			T1	T2	T3			
AM 3A	50	30	6	3	3	12	60	91.65
	100	30	3	2	1	06	80	
	150	30	2	1	1	4	86.66	
AM 3B	50	30	0	0	0	0	100	-
	100	30	0	0	0	0	100	
	150	30	0	0	0	0	100	
AM 3C	50	30	6	3	7	16	46.66	98.77
	100	30	4	3	3	10	66.66	
	150	30	4	1	3	5	83.33	
AM 3D	50	30	6	3	7	16	46.66	94.46
	100	30	6	3	3	12	60	
	150	30	4	3	3	10	66.66	
AM 3E	50	30	6	3	3	12	60	117.55
	100	30	4	3	3	10	66.66	
	150	30	2	1	1	4	86.66	
AM 3G	50	30	4	3	3	10	66.66	94.17
	100	30	4	1	1	6	80	
	150	30	2	1	1	4	86.66	
AM 3H	50	30	4	5	4	13	56.66	94.52
	100	30	4	4	3	11	63.33	
	150	30	2	4	4	10	66.66	
AM 3J	50	30	4	1	3	8	73.33	60.99
	100	30	2	1	1	4	86.66	
	150	30	2	1	1	4	86.66	
AM 3K	50	30	0	0	0	0	0	
	100	30	0	0	0	0	0	
	150	30	0	0	0	0	0	
AM 3L	50	30	4	4	3	11	63.33	86.73
	100	30	4	1	3	5	83.33	
	150	30	2	1	1	4	86.66	

ADME and drug-likeness prediction through in silico Approach

When determining a compound's drug-likeness, the physicochemical features of the compound are closely scrutinized for conformity with filter versions like the Lipinski rule of five. Numerous characteristics are taken into account, including topological polar surface area (TPSA), molecular mass, logP, molar refractivity, rotatable bonds, hydrogen bond donors (HBD), hydrogen bond acceptors (HBA), and the number of rotatable bonds.Table3summarizes the findings that all derivatives adhere to the Lipinski Rule of Five with no violations.

Table 3. Lipinski parameters with absorption distribution metabolism elimination properties and Drug likeness properties of synthesized compounds.

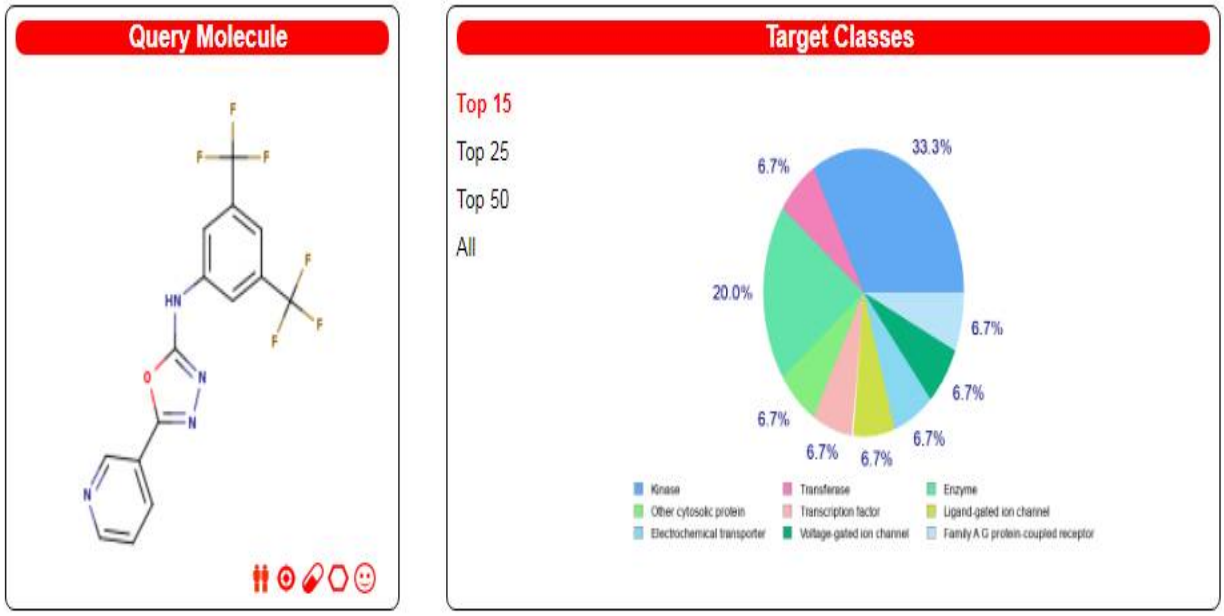
Physicochemical Properties							**Drug Likness**		
Compound	**Mol. wt**	**H-accepter**	**H-donor**	**Rotatable bond**	**Log *p***	**Total polar surface area (TPSA)**	**Lipinski violations**	**Bioavaiability Score**	**Synthetic Accessibility**
AM 3A	238.24	4	1	3	2.17	63.84	0	0.55	2.65
AM 3B	272.68	4	1	3	2.35	63.84	0	0.55	2.67
AM 3C	252.27	4	1	4	2.19	63.84	0	0.55	2.65
AM 3D	256.23	5	1	3	2.22	63.84	0	0.55	2.61
AM 3E	283.24	6	1	4	1.79	109.66	0	0.55	2.78
AM 3G	252.27	4	1	3	2.38	63.84	0	0.55	2.72
AM 3H	272.69	4	1	3	2.37	63.84	0	0.55	2.63
AM 3J	317.14	4	1	3	2.46	63.84	0	0.55	2.74
AM 3K	268.27	5	1	4	2.4	73.07	0	0.55	2.71
AM 3L	374.24	10	1	5	2.6	63.84	0	0.55	2.86

The bioactivity of synthetic substances was predicted using molecular inspiration software. The bioactivity scores of the isolated compounds are compared with standard drug on the basis of GPCR ligand (GPCRL), ion channel modulator (ICM), nuclear receptor legend (NRL), kinase inhibitor (KI), protease inhibitor (PI), enzyme inhibitor (EI).In Table 4, the bioactivity assessment is shown.

Table 4. Molinspiration Bioactivity Score.

Compound	GPCR ligand	Ion channel modulator	Kinase Inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
AM 3A	-0.22	-0.36	0.56	-0.79	-0.35	0.10
AM 3B	-0.18	-0.35	0.56	-0.73	-0.38	0.04
AM 3C	-0.26	-0.54	0.31	-0.64	-0.44	0.02
AM 3D	-0.15	-0.36	0.62	-0.66	-0.32	0.10
AM 3E	-0.25	-0.37	0.41	-0.66	-0.33	-0.00
AM 3G	-0.22	-0.44	0.51	-0.73	-0.36	0.04
AM 3H	-0.17	-0.35	0.55	-0.72	-0.34	0.07
AM 3J	-0.33	-0.45	0.56	-0.90	-0.45	-0.00
AM 3K	-0.18	-0.42	0.54	-0.63	-0.30	0.06
AM 3L	0.04	-0.17	0.57	-0.23	-0.02	0.09

This information led us to the conclusion that oxadiazole compounds had action against VEGFR inhibitors. For more precise target prediction [29], the SWISS target prediction server is also employed (Figure 2).



Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*	Known actives (3D/2D)
Vascular endothelial growth factor receptor 2	KDR	P35968	CHEMBL279	Kinase		10 / 63
Vascular endothelial growth factor receptor 1	FLT1	P17948	CHEMBL1868	Kinase		6 / 43
Glycogen synthase kinase-3 beta	GSK3B	P49841	CHEMBL262	Kinase		3 / 19
Fatty acid synthase	FASN	P49327	CHEMBL4158	Transferase		0 / 3
Gamma-secretase	PSEN2 PSENEN NCSTN APH1A PSEN1 APH1B	P49810 Q9NZ42 Q92542 Q96BI3 P49768 Q8WW43	CHEMBL2094135	Protease		12 / 0
CDC7/DBF4 (Cell division cycle 7-related protein kinase/Activator of S phase kinase)	DBF4 CDC7	Q9UBU7 O00311	CHEMBL2111377	Kinase		0 / 25
CDC7/DBF4 (Cell division cycle 7-related protein kinase/Activator of S phase kinase)	CDC7	O00311	CHEMBL5443	Kinase		0 / 21
Nuclear factor NF-kappa-B p105 subunit	NFKB1	P19838	CHEMBL3251	Other cytosolic protein		5 / 0
Activating transcription factor 1	ATF1	P18846	CHEMBL3255	Transcription factor		5 / 0
P2X purinoceptor 7	P2RX7	Q99572	CHEMBL4805	Ligand-gated ion channel		15 / 0
Glutaminyl-peptide cyclotransferase	QPCT	Q16769	CHEMBL4508	Enzyme		0 / 1

Figure 2. An example of the Swiss Target Prediction Report of Compound AM 3L.

Vascular Endothelial Growth Factor 2 (PDB ID:3VHE), a three-dimensional crystallographic structure, was obtained from the Protein Data Bank (PDB) of the Research Collaboratory for Structural Bioinformatics before the docking investigation began (RCSB).

Boiled-Egg Plot

The validity of a Boiled Egg Plot in the research and discovery of pharmaceuticals is established by its ability to predict gastrointestinal (GI) absorption and brain penetration (BBB) using a spontaneous and repeatable statistical plot. The compounds of our interest are more likely to penetrate the brain (BBB) if they are located on the yellow ellipse in the plot, which indicates a bad compound. TheGI Absorption of compounds is more if it is located in the area that is white, which denotes a compound with a high capacity for absorption. In addition to these two facts, the compounds of our interest are nonabsorptive and non-brain penetrative if they are placed on the grey region, excluding the yellow ellipse and white sections, and are also outside of the plot's range. When evaluating GI and blood-brain barrier characteristics, each of these substances was taken into account independently (BBB).The compounds AM 3A-AM3L shows good GI absorption. Figure 3display theboiled egg plot of represented compound AM 3L.

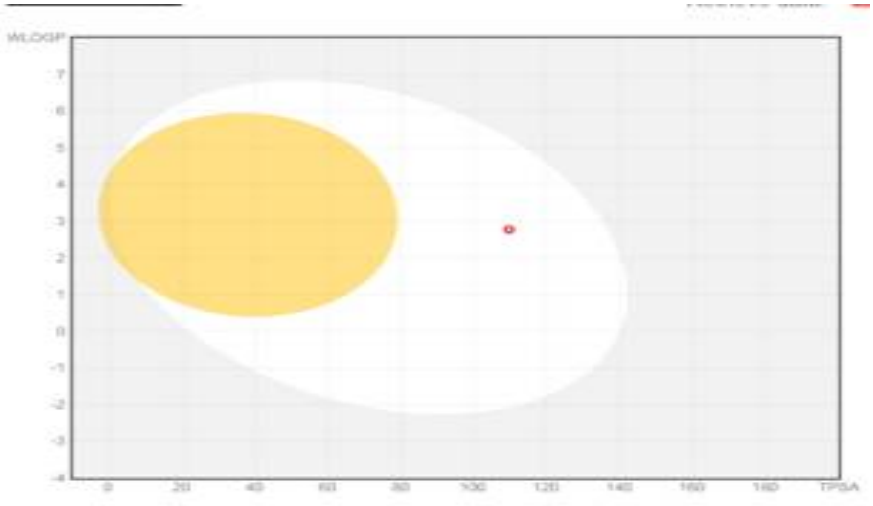


Figure 3. Reprsentation of boiled egg plot of most effective Virtual Screened and Established compound of AM 3L**.**

***In silico* Pharmacokinetic and Toxicity Prediction:**

All of the remaining oxadiazole derivatives, except AM 3L, have the maximum GI absorption, demonstrating the compounds' oral bioavailability. Additionally, all derivatives but compounds AM 3E and AM 3L exhibit blood-brain permeability. Table 5 summarizes the in silico pharmacokinetic features.

Table 5. Pharmacokinetic Prediction using SWISS ADME.

Compound	GI Absorption	Caco absorption	p-gp	CYP2C19 Inhibitor	CYP2D6 Inhibitor
AM 3A	High	Yes	No	Yes	No
AM 3B	High	Yes	No	Yes	No
AM 3C	High	Yes	Yes	Yes	Yes
AM 3D	High	Yes	No	Yes	No
AM 3E	High	Yes	No	Yes	No
AM 3G	High	Yes	No	Yes	No
AM 3H	High	Yes	No	Yes	No
AM 3J	High	Yes	No	Yes	No
AM 3K	High	Yes	Yes	Yes	Yes
AM 3L	Low	Yes	No	Yes	No

All of the substances do not inhibit P-glycoprotein, which can prevent absorption and reduce permeability whilst also.

The toxicity study was performed using the Admet SAR online server, which predicted that all derivatives were not mutagenic and neither were they carcinogenic, rendering these acceptable for biological usage. In table 6, the results of the toxicity prediction computation were compiled. All derivatives have about the same acute toxicity in rats as standard.

Table 6. Toxicity prediction by using Admet SAR online web tool.

Sr. No.	Compound	Ames Mutagenesis	Carcinogen	Acute Oral Toxicity	Acute Toxicity LD50 mol/Kg
1.	AM 3A	- 0.6500	NC 0.8143	III 0.6654	1.646
2.	AM 3B	- 0.7500	NC 0.8429	III 0.6550	1.739
3.	AM 3C	- 0.6900	NC 0.8143	III 0.6554	2.299
4.	AM 3D	- 0.5800	NC 0.8143	III 0.6977	1.998
5.	AM 3E	- 0.6900	NC 0.8857	III 0.5427	2.13
6.	AM 3G	- 0.6400	NC 0.8429	III 0.7042	2.233
7.	AM 3H	- 0.6800	NC 0.8429	III 0.6550	1.936
8.	AM 3J	- 0.6900	NC 0.8143	III 0.6875	1.859
9.	AM 3K	- 0.6700	NC 0.9143	III 0.6509	2.293
10.	AM 3L	- 0.6500	NC 0.8143	III 0.6601	2.455

Docking simulations results:

The VEGFR2 receptor was tested for a molecular docking investigation for anti-cancer potential. The dock score for the compounds with the codes (AM3a-AM3L)is summarized in the table7 and the dock score for the compound with code AM3D is the lowest which is -9.2. The ideal docking pose, where the primary interaction between the ligand and receptor can be seen, is reported. All of the proposed compounds adopt a remarkably comparable conformation at the binding pocket, exhibiting hydrogen bond interaction with the amino acids ASP1046 and GLU885 and electrostatic binding with the amino acid LYS868 as illustrated by a 2D representation diagram. superimposed image of the ligands and receptor is shown in Figure 4-7. Table7 displays the ligand-receptor residue interaction, hydrogen bond distances, and molecular docking binding energies (kcal/mol).

Table 7. Binding energy (kcal/mol) and receptor–ligand interactions from molecular docking.

Pub Chem ID	compound	Binding energy(Kcal/mol)	Residue in contact	Interaction Type	Distance (A^0)
3VHE	AM 3A	-9.0	A:ASP1046	Hydrogen	2.17516
			A: GLU885	Hydrogen	2.7844
			A:ASP1046	Hydrogen	2.66197
			A:LYS868	Electrostatic	4.71535
			A:GLU885	Electrostatic	3.83004
	AM 3B	-9.0	A:ASP1046	Hydrogen	2.59099
			A: GLU885	Hydrogen	2.39984
			A:ASP1046	Hydrogen	2.34318
			A:LYS868	Electrostatic	4.73016
	AM 3C	-8.8	A: GLU885	Hydrogen	2.30654
			A:ASP1046	Hydrogen	2.14962

			A:LYS868	Electrostatic	4.94313
			A:ASP1046	Electrostatic	3.88012
	AM 3D	-9.2	A:ASP1046	Hydrogen	1.95642
			A:ASP1046	Hydrogen	2.60672
			A:LYS868	Electrostatic	4.53548
			A:GLU885	Electrostatic	3.461
	AM 3E	-8.8	A:ARG1027	Hydrogen	2.525
			A:ARG1027	Hydrogen	2.41425
			A:ASP1046	Hydrogen	2.76987
			A:ASP814	Hydrogen	3.01659
			A:ILE1025	Hydrogen	3.04518
	AM 3G	-9.0	A:ASP1046	Hydrogen	2.68111
			A: GLU885	Hydrogen	1.96183
			A:ASP1046	Hydrogen	2.82591
			A:LYS868	Electrostatic	4.80352
	AM 3H	-8.9	A:ASP1046	Hydrogen	2.64453
			A: GLU885	Hydrogen	1.969
			A:ASP1046	Hydrogen	2.9597
			A:LYS868	Electrostatic	4.72354
	AM 3J	-9.0	A:ASP1046	Hydrogen	2.28268
			A: GLU885	Hydrogen	2.30941
			A:ASP1046	Hydrogen	2.11863
	AM 3K	-8.5	A:ASP1046	Hydrogen	2.00758
			A:ASP1046	Hydrogen	2.66489
			A:LYS868	Electrostatic	4.51325
			A:GLU885	Electrostatic	3.47935
	AM 3L	-9.2	A:ARG1027	Hydrogen	3.08887
			A:ARG1027	Hydrogen	2.8288
			A:ILE1025	Hydrogen	3.09831

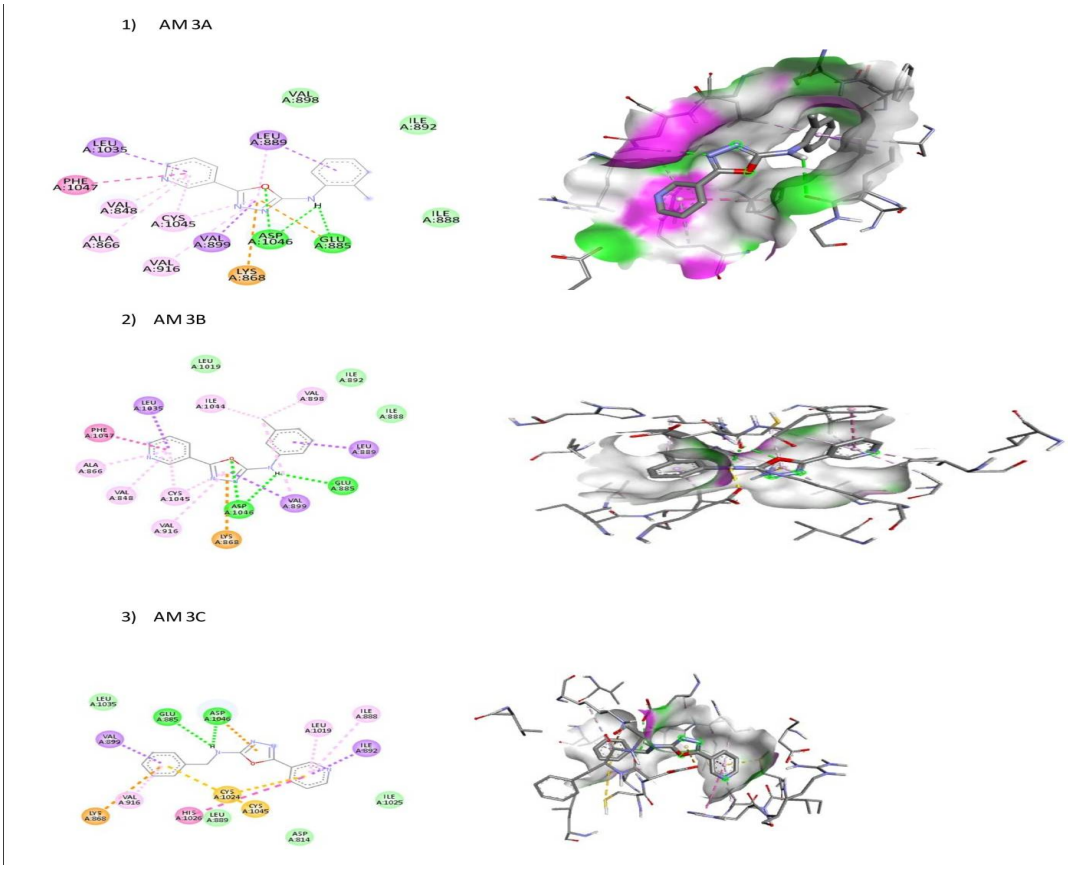


Figure 4. 2D interactions and Superimpose image representation of docking poses of compounds AM 3A, AM 3B and AM 3C.

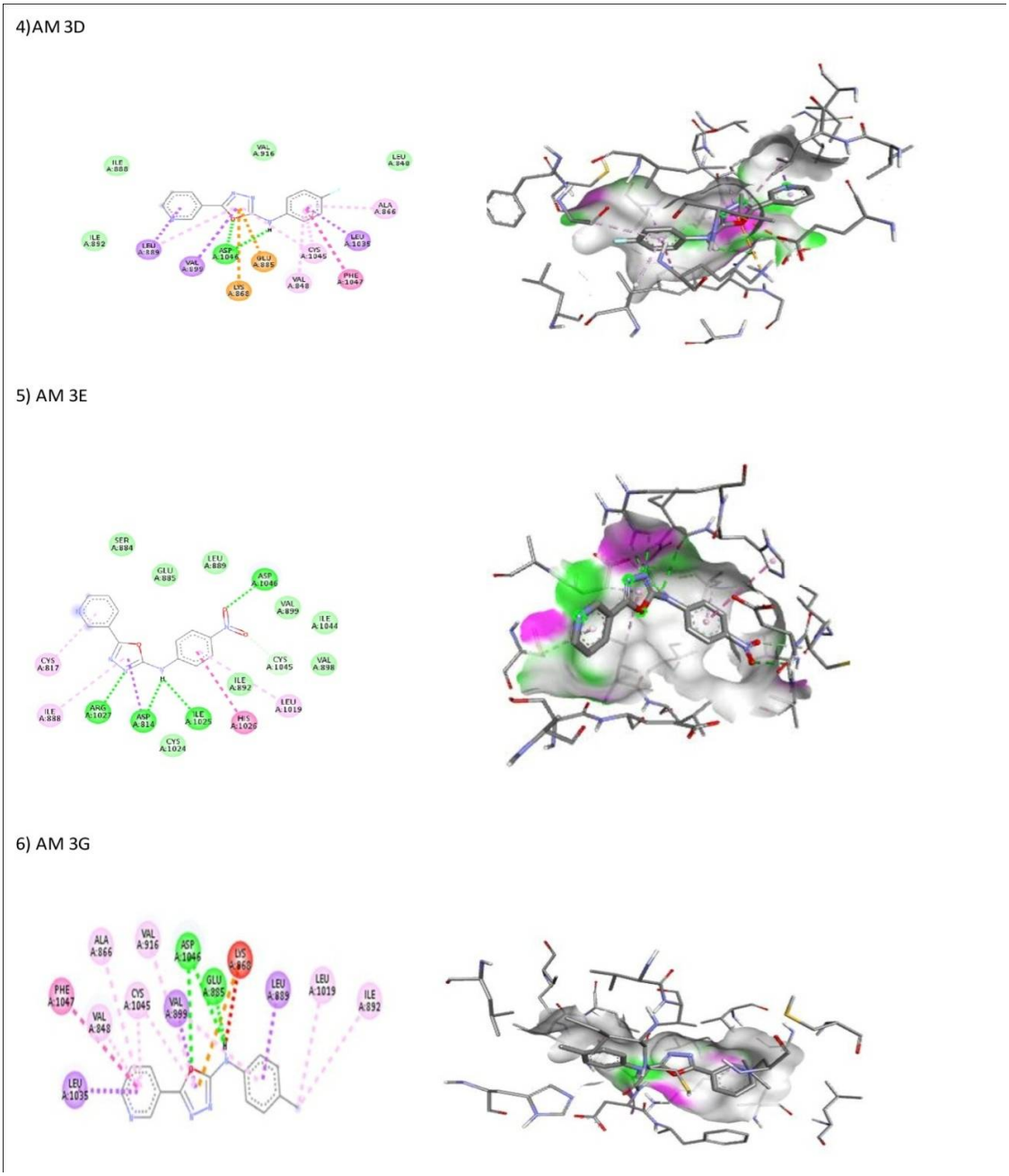


Figure 5. 2D interactions and Superimpose image representation of docking poses of compounds AM 3D, AM 3E and AM 3G.

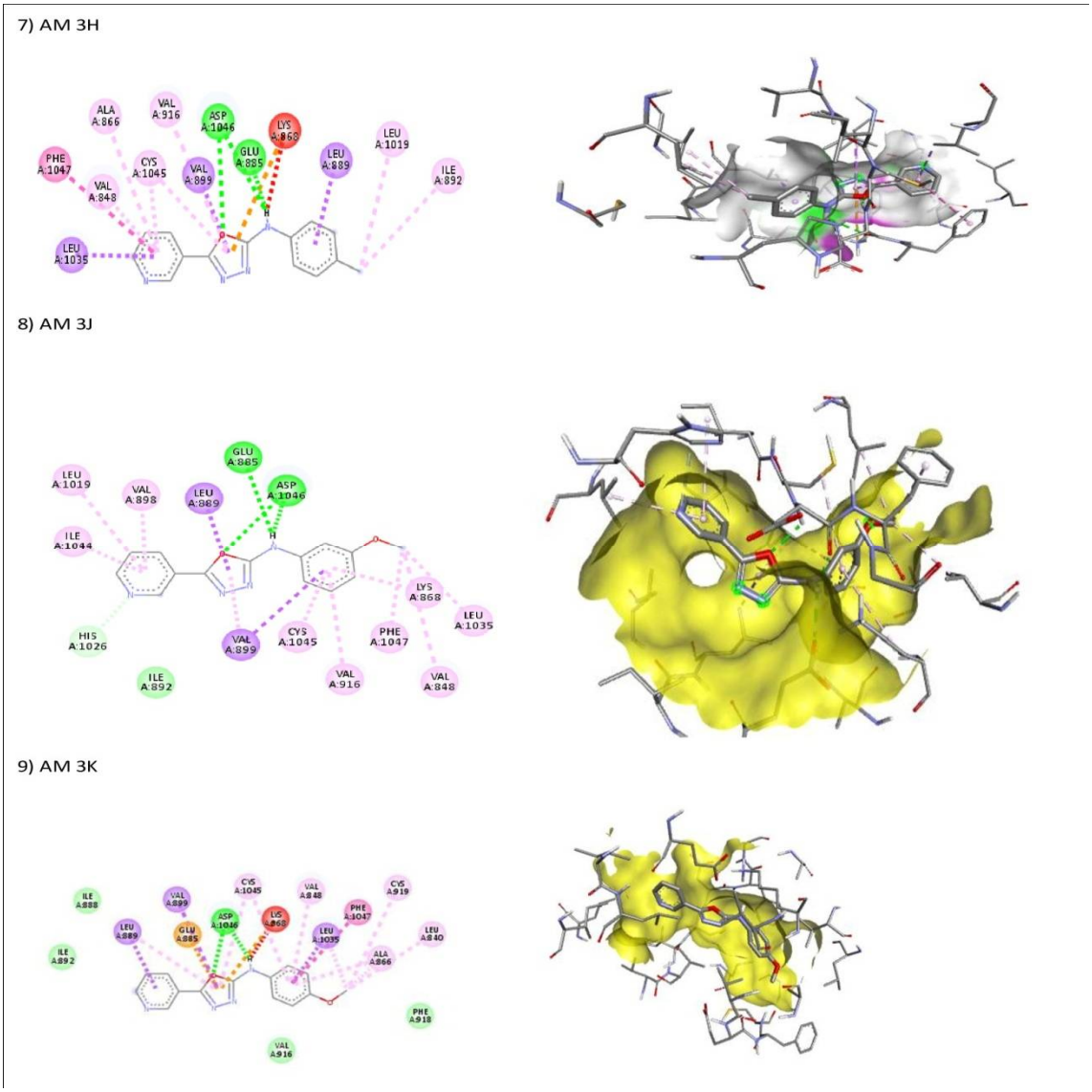


Figure 6. 2D interactions and Superimpose image representation of docking poses of compounds AM 3H, AM 3J and AM 3K.

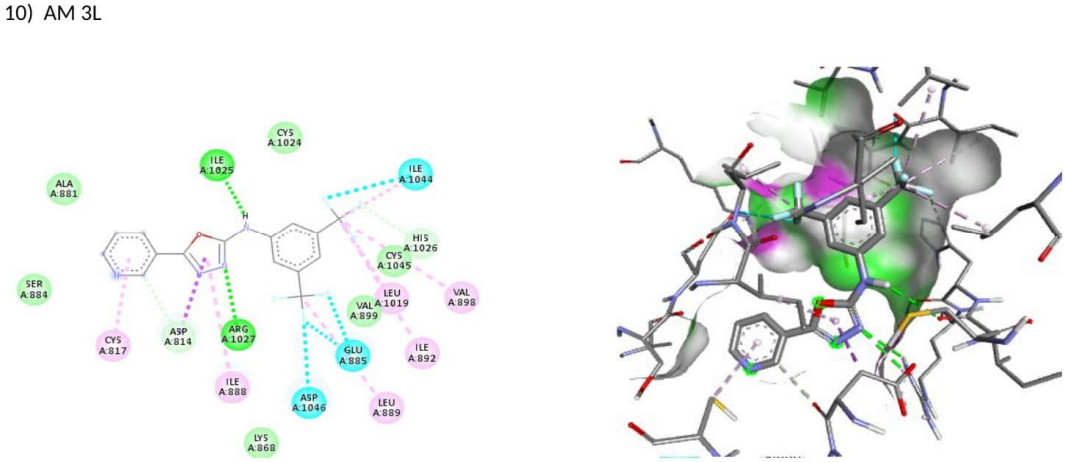


Figure 7. 2D interactions and Superimpose image representation of docking poses of compound code AM 3L. In each case, the hydrogen, pi-donor hydrogen, pi-alkyl, pi-sigma, and pi-anion bond interactions are shown as green, light blue, magenta, purple, and orange broken lines, respectively.

CONCLUSION

According to ADMET data, all of the substances are safe for oral consumption and are not mutagenic or carcinogenic. It was determined using molecular docking modelling that all the compounds had good binding energies and could function as more potential anti-cancer drugs.

On the A. salina bioassay, every compound exhibited interesting cytotoxic action. Significant cytotoxic activities were found in the tested compounds. Using tumour cell lines, we will later assess these substances' potential as anticancer medicines.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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