In Silico Study of Phytochemicals of *Andrographis Paniculata* against Oral Cancer Potential

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Abstract

Novel treatment agents are needed since oral cancer continues to be a major worldwide health burden. The potential anti-cancer activities of phytochemicals derived from medicinal plants have garnered significant attention. The traditional medicinal herb Andrographis paniculata is well-known for its wide range of pharmacological properties, including anticancer properties. The purpose of this in silico study is to investigate the phytochemicals from Andrographis paniculata *that may be able to prevent oral cancer. We investigated and found compounds in* Andrographis paniculata *that may have anticancer effects against oral cancer using computational techniques. Using molecular docking experiments, the interactions between these phytochemicals and known molecular targets such as signaling proteins and receptors involved in oral cancer pathways were examined. Furthermore, the stability and binding affinities of the protein-ligand complexes were evaluated using molecular dynamics simulations. According to preliminary findings, a number of phytochemicals from* Andrographis paniculata *show interesting interactions with important targets that are involved in the advancement of oral cancer. Particularly, substances such as andrographolide and neoandrographolide showed a high propensity for binding and consistent interactions with important biomolecules connected to pathways related to oral cancer. To sum up, this in silico analysis offers insightful information on the phytochemicals found in* Andrographis paniculata *that may be useful for additional experimental validation and development as oral cancer treatment agents. These results stimulate more investigation in to the clinical uses of natural chemicals and add to the increasing body of data in favor of their usage in cancer treatment.*

Keywords: *Oral cancer, Molecular Docking, Molecular Dynamics, Phytochemicals,* Andrographis paniculata.

INTRODUCTION

The lining of the lips, mouth, or upper throat can develop cancer, which is referred to as oral cancer, mouth cancer, or oral cavity cancer. It typically begins in the mouth as a painless red or white area that develops, becomes ulcerated, and keeps spreading. When it appears on the lips, it typically resembles a chronic, slowly-growing crusting ulcer that does not heal. Oral cancer accounts for 48% of head and neck cancer occurrences, making it the sixth most frequent cancer in humans. Histologically, oral squamous cell carcinomas (OSCCs) account for 90% of instances of oral cancer(figure-1)[1]. Approximately 400,000 new instances of oral cancer are projected to be detected worldwide each year, with two-thirds of those occurrences occurring in Asian nations like Bangladesh, Pakistan, India, Indonesia, and Sri Lanka[2].

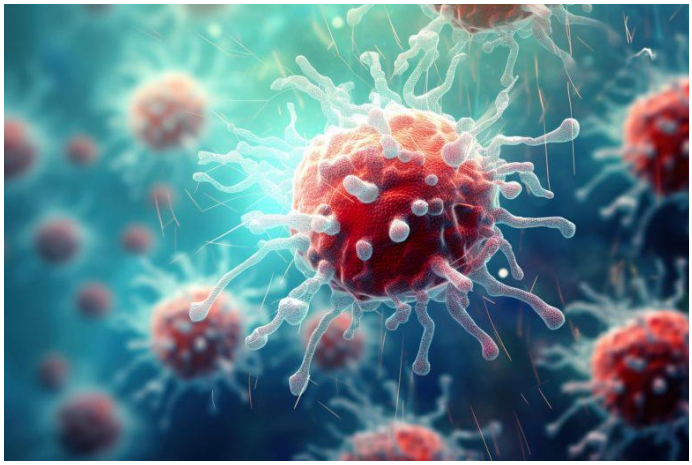


Figure-1. Cancer

Oral cancer is one of the many malignancies for which protein kinase B (Akt) is extremely important. Nevertheless, it exists in three isoforms (Akt1, Akt2, and Akt3), each of which has a unique function and even a different involvement in a certain malignancy. Evaluating Akt's isoform-specific function in oral cancer is therefore crucial. The current work aims to clarify the role of Akt, which is isoform-specific, in oral cancer. Oral cancer tissues subjected to immune histochemistry examination revealed upregulation of Akt1 and 2 isoforms, but not Akt3 [3].

It is believed that almost two-thirds of people in many poor nations primarily rely on traditional healers and medicinal plants to cover their basic healthcare needs[4]. Researchers are now revaluing many plant species based on species variety and their chemical principles for therapeutic purposes as a result of the many issues with conventional medicationsA plant species that was utilized in traditional oriental and ayurvedic medicine is *Andrographis paniculata* (*A. paniculata*). Within the Acanthaceae family, the genus *Andrographis*includes approximately forty species. Just a select few are widely used in folk medicine to treat a range of ailments. (figure-2). The most significant of these few is A. paniculata. Known by many as the King of Bitters or Kalmegh, *A. paniculata* is an annual that grows upright and branches [5].

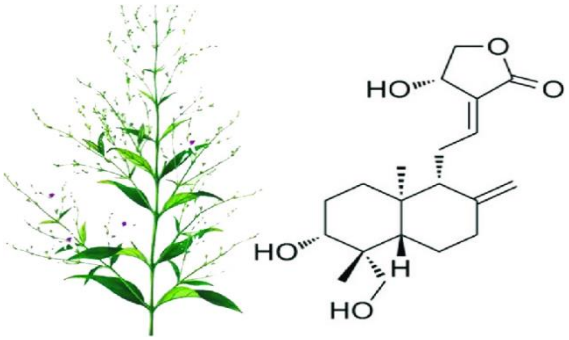


Figure-2. *Andrographis paniculata* and Chemical structure of andrographolide

Asia has long practiced traditional medicine using the aerial parts, roots, and entire plant of *A. paniculata* to treat a wide range of illnesses. Traditional medical professionals have used it to treat pyrexia, stomachaches, inflammation, and sporadic fevers [6]. The process of determining a medicinal compound's potential fate within the body is known as pharmacokinetics, and it is crucial information to have when developing new medications. Traditionally, the linked effects have been analyzed using individual indicators known as the Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) factors. Chemicalize and the online SwissADME software was used in this study to estimate a few ADMET parameters [7].

METHODOLOGY

2.1. To perform the physiochemical properties and pharmacokinetic activity-

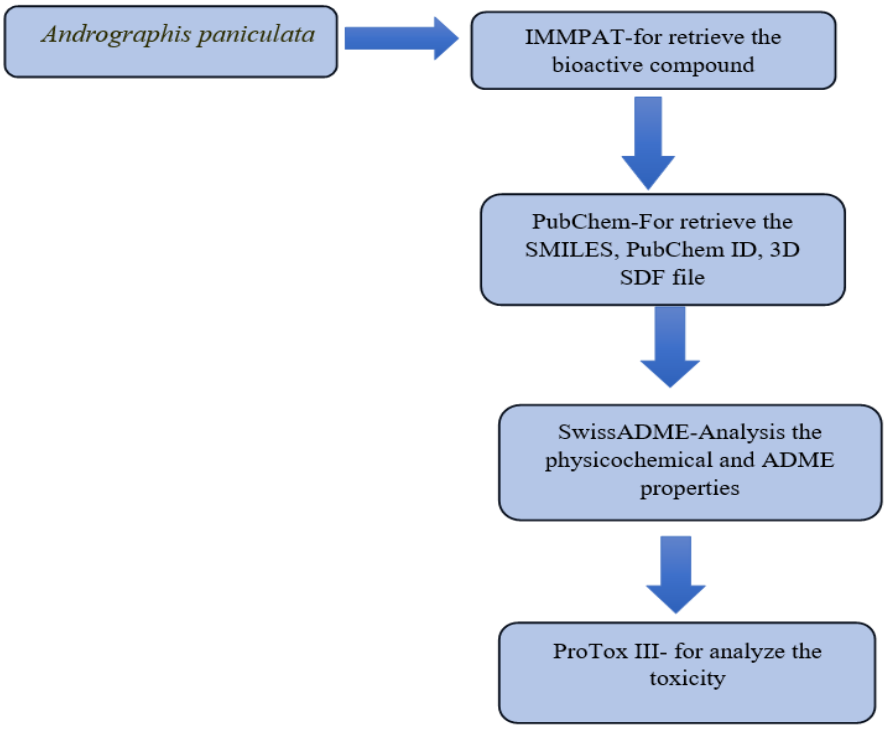
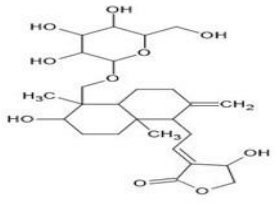


Figure-3. Schematic representation of physiochemical properties and pharmacokinetic activity

2.2. Molecular structure-



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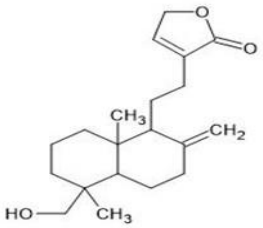

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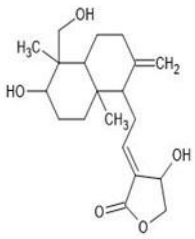

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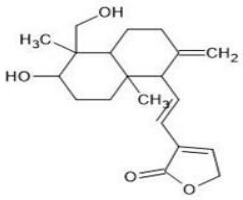

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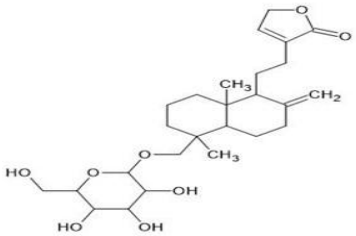

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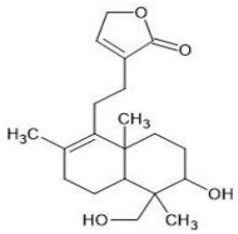

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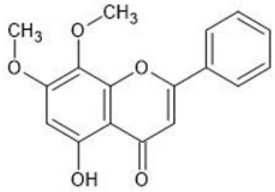

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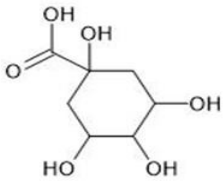

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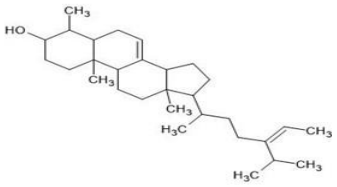

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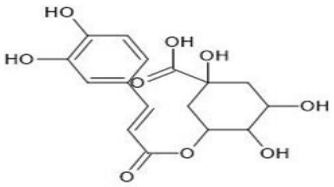

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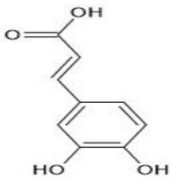

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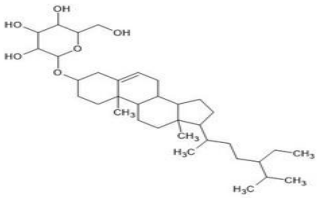

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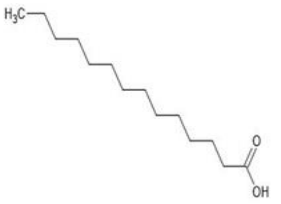

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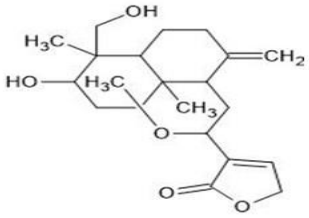

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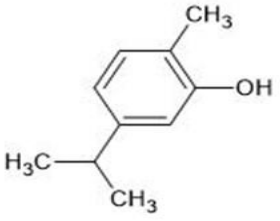

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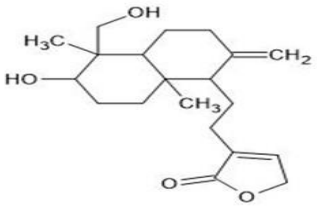

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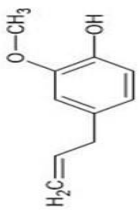

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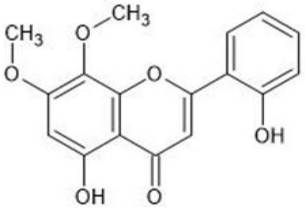

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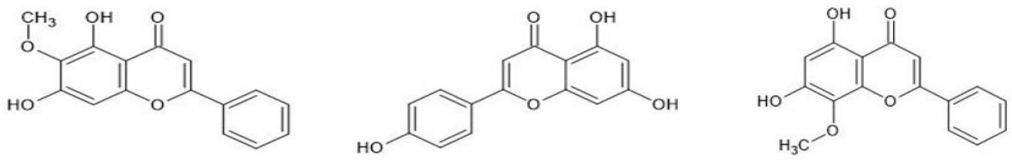


19. 20. 21.

Figure.4- The 2D structure of bioative constituents:1=Andrographiside, 2=Andrograpanin, 3=Andrographolide, 4=14-Deoxy-11,12-didehydroandrographolide, 5=Neoandrographolide, 6=Deoxyandrographolide, 7=5-Hydroxy-7,8-dimethoxyflavone, 8=Quinic acid, 9=alpha1-Sitosterol, 10=Chlorogenic acid, 11=Caffeic acid, 12=Daucosterol, 13=Myristic Acid, 14=14-Deoxy-12-methoxyandrographolide, 15=Carvacrol, 16=14-Deoxyandrographolide, 17= Eugenol, 18=Skullcapflavone I, 19=Oroxylin A, 20=Apigenin, 21=Wogonin.

2.3. To prepare protein-

Here we retrieved 3D PDB targeted protein AKT1 (5wbl) of humans by using theRCSB Protein data bank in PDB format [8]. After the preparation of protein, we processed it for the next step by using the AutoDock toolsv4.26.

2.4. To prepare ligand-

For the preparation of ligand, we need to retrieve the 3D SDF files with the help of the PubChem database [9]. Then we converted 3D SDF files into 3D PDB files and then opened AutoDock tool 1.5.7. after this task, the ligand will be shown on the screen, with one fragment looking red in color and the aromatic carbons appearing green.

2.5. To prepare the grid-

In this process, first we click on the grid button, then click on macromolecule to choose protein molecule (5 wbl), then type as protein pdbqt files. Likewise, click on set map type, then choose ligand, and then select the ligand as pdbqt files. After this step, we have to click on the grid box and then cover the ligand portion by changing the size of the grid the grid box in the in the x, y, and z- directions directions and the grid box cover range should not be greater than 100 A^0[11]. In the final the final step, we have to click on the output the output button and save the ligand as gpf files.

2.6. To prepare docking parameters-

In this step of molecular docking, we have done the docking procedure by using AutoDock Tools 4.2.6. [12]. After that autogrid and autodock are ready to run the next process. These autogrids and autodocks take a take a little more time to complete the process, and then we get a dlg file.

2.7. To analyze protein-ligand interaction-

Here, an examination of interactions is done the ligand and protein, including hydrophobic interactions, and hydrogen bonds. The PyMOL software is used to perform visualization and analysis of protein-ligand complexes PLIP (Protein-Ligand Interaction Profiler) is used to perform protein-ligand interactions [13].

RESULTS AND DISCUSSION

3.1 Analysis of the physicochemical properties of phytoconstituents-

Christopher Lipinski states that the molecular mass (g/mol) of the ligand molecules, the calculated octanol/water partition coefficient (cLogP) of ≤ 5, the number of hydrogen bond donors (NoHNH) of ≤ 5, and the number of hydrogen bond acceptors (nON) of ≤ 10 should all fall within this range.In this study, all of the phytocnstituents listed in Table 3.1 follow Lipinski's rule of five except Daucosterol.Deoxyandrographolide, 14-Deoxyandrographolide (334.45 g/mol), and Oroxylin A, Wogonin (284.26 g/mol) molecules are predicted to have similar molecular weights and to show similarities in TPSA and % absorption (Table 3.1). While molecules with a TPSA of 60 $Å^2$ would be efficiently absorbed (> 90% fractional absorption), those with a TPSA of 140 $Å^2$ and beyond would be poorly absorbed (<10% fractional absorption).An analysis of the %Abs indicates that eugenol has the greatest percent absorption (98.8%). Lipinski's Rule of 5, have a LogP value <5, ideally between 1.35 and 1.8 for optimal intestinal and oral absorption.

Table-1. The physicochemical Properties and drug-likeness of phytochemical

S NO.	Bioative compound	Molecular Weight (g/mol)	No. of rotable bond	No. of H-bond acceptor	No. of H-bond donor	TPSA (Å²)	Log Po/w (iLOGP)	% Absorption
1	Andrograpanin	318.45	4	3	1	46.53	3.34	92.9
2	Andrographolide	350.45	3	5	3	86.99	2.45	78.9
3	14-Deoxy-11,12-didehydroandrographolide	332.43	3	4	2	66.76	2.85	85.9
4	Neoandrographolide	480.59	7	8	4	125.68	3.27	65.6
5	Deoxyandrographolide	334.45	4	4	2	66.76	3.03	85.9
6	5-Hydroxy-7,8-dimethoxyflavone	298.29	3	5	1	68.90	2.99	85.2
7	Quinic acid	192.17	1	6	5	118.22	-0.12	68.2
8	alpha1-Sitosterol	426.72	5	1	1	20.23	5.18	102
9	Chlorogenic acid	354.31	5	9	6	164.75	0.96	52.1
10	Caffeic acid	180.16	2	4	3	77.76	0.97	82.1
11	Daucosterol	576.85	9	6	4	99.38	4.98	74.7
12	Myristic Acid	228.37	12	2	1	37.30	3.32	96.1
13	14-Deoxy-12-methoxyandrographolide	364.48	5	5	2	75.99	3.34	82.7
14	Carvacrol	150.22	1	1	1	20.23	2.24	102
15	14-Deoxyandrographolid	334.45	4	4	2	66.76	2.91	85.9

	e							
16	Eugenol	164.20	3	2	1	29.46	2.37	98.8
17	Skullcapflavone I	314.29	3	6	2	89.13	2.83	78.2
18	Oroxylin A	284.26	2	5	2	79.90	2.61	81.4
19	Apigenin	270.24	1	5	3	90.90	1.89	77.6
20	Wogonin	284.26	2	5	2	79.90	2.55	81.4

3.2 Predicting drug-likeness and ADME-

The rate and extent of a pharmacological product's absorption are referred to as its bioavailability. All of the phytconstituents have high GI absorption except Quinic acid, alpha1-Sitosterol, Chlorogenic acid, Daucosterol (Table 2). The use of the SwissADME webtool, we estimated that Andrograpanin,14-Deoxy-11,12-didehydroandrographolide.

Deoxyandrographolide,5-Hydroxy-7,8dimethoxyflavone,MyristicAcid,14-Deoxy-12-methoxyandrographolide,Carvacrol,14-Deoxyandrographolide,Eugenol can permeate BBB,and rest of compound cannot permeate BBB (Table 2). Andrograpanin and 5-Hydroxy-7, 8-dimethoxyflavone can act as CYP2C19 inhibitor. Andrograpanin, 14-Deoxy-11,12-didehydroandrographolide,5-Hydroxy-7,8-dimethoxyflavone,Skullcapflavone I, Oroxylin A,Wogonin can act as CYP2C9 inhibitor and the rest of the phytoconstituents cannot act as CYP2C9 inhibitors. 5-Hydroxy-7,8-dimethoxyflavone, Skullcapflavone I, Oroxylin A,Wogonin are predicted as CYP2D6 inhibitors. It has been found that as molecular size increases, log Kp lowers (becomes less negative).All of the phytoconstituents had skin permeability (Kp) values ranging from -9.15 to -2.49 cm/s.

Table - 2 The prediction of Pharmacokinetics properties of phytochemical compound

S. No.	Bioactive compounds	GI Absorption	BBB permeant	P-gp substrate	CYP1A2 inhibitoer	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	LogKp (cm/s)
1	Andrograpanin	High	Yes	No	No	Yes	Yes	No	No	-5.25
2	Andrographolide	High	No	Yes	No	No	No	No	No	-6.90
3	14-Deoxy-11,12-didehydroandrographolide	High	Yes	Yes	No	No	Yes	No	Yes	-6.03
4	Neoandrographolide	High	No	Yes	No	No	No	No	Yes	-7.36

5	Deoxyandrographolide	High	Yes	Yes	No	No	No	No	No	-6.28
6	5-Hydroxy-7,8-dimethoxyflavone	High	Yes	No	Yes	Yes	Yes	Yes	Yes	-5.76
7	Quinic acid	Low	No	Yes	No	No	No	No	No	-9.15
8	alpha1-Sitosterol	Low	No	No	No	No	No	No	No	-2.49
9	Chlorogenic acid	Low	No	No	No	No	No	No	No	-8.76
10	Caffeic acid	High	No	No	No	No	No	No	No	-6.58
11	Daucosterol	Low	No	No	No	No	No	No	No	-4.32
12	Myristic Acid	High	Yes	No	Yes	No	No	No	No	-3.35
13	14-Deoxy-12-methoxyandrographolide	High	Yes	Yes	No	No	No	No	Yes	-6.63
14	Carvacrol	High	Yes	No	Yes	No	No	No	No	-4.74
15	14-Deoxyandrographolide	High	Yes	Yes	No	No	No	No	No	-5.90
16	Eugenol	High	Yes	No	Yes	No	No	No	No	-5.69
17	Skullcapflavone I	High	No	No	Yes	No	Yes	Yes	Yes	-6.12
18	Oroxylin A	High	No	No	Yes	No	Yes	Yes	Yes	-5.56
19	Apigenin	High	No	No	Yes	No	No	Yes	Yes	-5.80
20	Wogonin	High	No	No	Yes	No	Yes	Yes	Yes	-5.56

GI-Gastro-intestinal, BBB-Blood brain barrier, P-gp- p-Glycoprotein, logKp (skin permeation)

3.3 Toxicity profile-

The toxicological endpoints (hepatotoxicity, neurotoxicity, nephrotoxicity, respiratory toxicity, cardiotoxicity, carcinogenicity, immunotoxicity, mutational toxicity, cytotoxicity, ecotoxicity, clinical toxicity, and nutritional toxicity) and the level of toxicity (LD50, mg/kg) and toxicity class of the twenty phytoconstituent derivatives were predicted in the current study. Table 3. The results showed that all of the phytoconstituents are not active for cardiotoxicity except Andrographolide, 14-Deoxy-11, 12-didehydroandrographolide, Neoandrographolide, Deoxyandrographolide, Daucosterol, 14-Deoxy-12-methoxyandrographolide, 14-Deoxyandrographolide, Oroxylin A, and Wogonin.

The results showed that all of the phytoconstituents are not active for mutagenicity. The results demonstrate that all of the phytoconstituents are inactive except neoandrographolide in Cytotoxicity. The results found that all of the phytoconstituents are not ecotoxic except 5-Hydroxy-7, 8-dimethoxyflavone, alpha-1-Sitosterol, Myristic Acid, Caracol. Andrographolide, 14-Deoxy-11, 12-didehydroandrographolide, Neoandrographolide, Deoxyandrographolide, Quinic acid, alpha1-Sitosterol, Chlorogenic acid, Caffeic acid, 14-Deoxy-12-methoxyandrographolide, and 14-Deoxyandrographolide are active for clinical toxicity, and the rest of the phytoconstituents are inactive for clinical toxicity.Quinic acid, chlorogenic acid, caffeic acid, myristic acid, carvacrol, eugenol, and apigenin are not active for nutritional toxicity, and the rest of the phytoconstituents are active for nutritional toxicity.

The findings indicated that the median lethal dose (LD50) ranged from 5 to 9800 mg/kg. As per the globally harmonized system of classification of labeling of chemicals (as described in Pro Tox III), Neoandrographolide are fatal (Class I), Andrograpanin, 14-Deoxy-12-methoxyandrographolide, 14-Deoxyandrographolide are fatal (Class II), Andrographolide, Deoxyandrographolide, alpha1-Sitosterol, Myristic Acid, Carvacrol, Eugenol harmful (Class IV), 5-Hydroxy-7,8-dimethoxyflavone, Chlorogenic acid, Caffeic acid, Skullcapflavone I, Oroxylin A, Wogonin "may be harmful" (Class V), and 14-Deoxy-11,12-didehydroandrographolide, Quinic acid, and Daucosterol are nontoxic (Class VI) toxicity classes. The results indicated that the majority of drug-like substances tend to exhibit more nephrotoxicity and respiratory toxicitythan any toxicological endpoints.

Table-3. ProTox III predicted organ toxicity, toxicological endpoints, and acute toxicity

S. No.	Phytoconstituents	Hepatotoxicity	Neurotoxicity	Nephrotoxicity	Respiratory	Cardiotoxicity	Carcinogenicity	Immunotoxicity	Mutagenicity	Cytotoxicity	Ecotoxicity	Clinical Toxicity	Nutritional Toxc.	LD 50 (mg/kg)	Toxicity Class
1	Andrograpanin	Inactive	Inactive	Inactive	Active	Inactive	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Active	34	2
2	Andrographolide	Inactive	Inactive	Inactive	Active	Active	Inactive	Active	Inactive	Inactive	Inactive	Active	Active	1890	4
3	14-Deoxy-11,12-didehydroandrographolide	Inactive	Inactive	Active	Active	Active	Inactive	Active	Inactive	Inactive	Inactive	Active	Active	6060	6
4	Neoandrographolide	Inactive	Inactive	Active	Inactive	Active	Inactive	Active	Inactive	Active	Inactive	Active	Active	5	1
5	Deoxyandrographolide	Inactive	Inactive	Active	Active	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Active	Active	5000	4
6	5-Hydroxy-7,8-dimethoxyflavone	Inactive	Inactive	Active	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Active	Inactive	Active	3919	5
7	Quinic acid	Inactive	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Active	Inactive	9800	6
8	alpha1-Sitosterol	Inactive	Active	Inactive	Active	Inactive	Inactive	Active	Inactive	Inactive	Active	Active	Active	2000	4
9	Chlorogenic acid	Inactive	Inactive	Active	Active	Inactive	Inactive	Active	Inactive	Inactive	Inactive	Active	Inactive	5000	5

10	Caffeic acid	Inactive	Inactive	Active	Inactive	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Active	Inactive	2980	5
11	Daucosterol	Inactive	Inactive	Active	Inactive	Active	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Active	8000	6
12	Myristic Acid	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Active	Inactive	Inactive	900	4
13	14-Deoxy-12-methoxyandrographolide	Inactive	Inactive	Active	Active	Active	Inactive	Active	Inactive	Inactive	Inactive	Active	Active	35	2
14	Carvacrol	Inactive	Active	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Active	Inactive	Inactive	810	4
15	14-Deoxyandrographolide	Inactive	Inactive	Active	Active	Active	Inactive	Active	Inactive	Inactive	Inactive	Active	Active	34	2
16	Eugenol	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	1930	4
17	Skullcapflavone I	Inactive	Inactive	Active	Active	Inactive	Inactive	Active	Inactive	Inactive	Inactive	Inactive	Active	4000	5
18	Oroxylin A	Inactive	Inactive	Active	Active	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Active	4000	5
19	Apigenin	Inactive	Inactive	Active	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Active	Inactive	Inactive	2500	5
20	Wogonin	Inactive	Inactive	Active	Active	Active	Inactive	Inactive	Inactive	Inactive	Inactive	Inactive	Active	3919	5

3.4 Analysis of molecular docking-

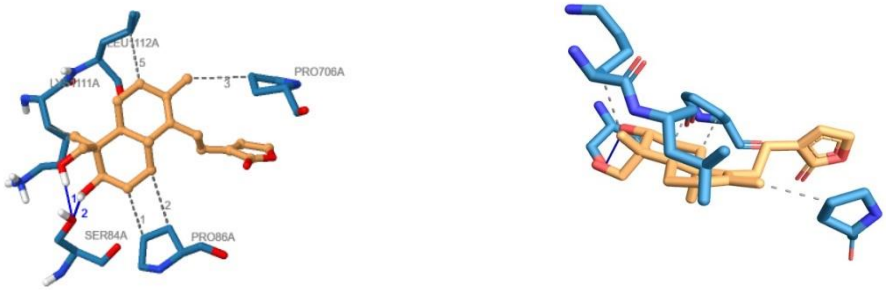
The objective of molecular docking is to precisely measure the strength of binding and forecast the configuration of a ligand inside the boundaries of a receptor binding site. The binding affinities, binding types, and active amino acid residues of the drugs under research in the target enzyme have been determined using a molecular docking analysis. The analysis of the docking experiment focused on the ligand's binding affinity with the target AKT1. Table 4 presents the statistical data for the highest-ranked ligand that was obtained during docking. According to a docking experiment analysis of the ligands, phytochemical binding affinities range from -9.17 kcal/mol to -4.87 kcal/mol (Table- 4). The top five phytoconstituents with low binding energies were andrograpanin, 14-deoxyandrographolide, deoxyandrographolide, alpha-1-sitosterol, 14-deoxy-11, 12-didehydroandrographolide.

3.5 Analysis of Ligand-Protein Interaction-

After completion of the docking experiment for all twenty phytochemicals by using AutoDock, a vast range of ligand poses were generated. The best binding affinity ligand pose was analyzed in the investigation.Overall, the *in-silico* docking analysis indicated thatalpha1-Sitosterol interact with one hydrogen bonding(GLU -1157A) and seven hydrophobic and other interacting residues(PRO-610A,LEU-611A,PRO-650A,GLN-651A,TRP-969A,HIS-973A,GLU-1157A), 14-deoxyandrographolide forms hydrogen bond interactions with three amino acid residues(LEU-707A,SER-848A,ARG -850A) and Deoxyandrographolide formed hydrogen bond interactions with one amino acid residues(SER-84A) and four hydrophobic and other interacting residue(PRO-86A, PRO-706A,LYS-111A,LEU-1112A). Andrograpanin interact with three hydrogen bonding (SER-84A,LEU-87A,LEU-707A) four hydrophobic and other interacting residues (PRO-86A,PRO-706A,ARG-850A,ILE-851A). The 3D structure of the ligand-protein interactions and its amino acid residue include salt bridges, hydrophobic bonds, and hydrogen bond.

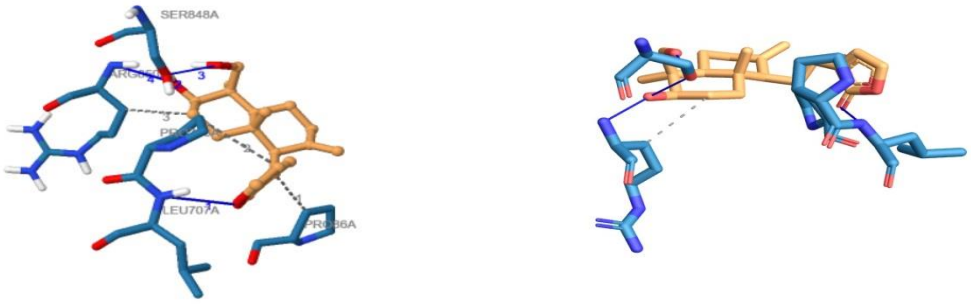
Table- 5 Molecular docking interaction of AKT1 with phytoconstituents by using PLIP

Sr.No.	Phytoconstituents	Binding energy	Hydrogen bond interaction	Hydrophobic and other interaction
1	5-Hydroxy-7,8-dimethoxyflavone	-6.23	LEU-87A, SER -848A	ARG-77A,PRO-706A,LEU-707A
2	14-Deoxy-11,12-didehydroandrographolide	-8.44	SER-84A,LEU-707A	PRO-86A,PRO-706A,ILE-851A,LYS-1111A
3	14-Deoxy-12-methoxyandrographolide	-6.23	LYS-97A,LYS-460A,SER-501A	PRO-461A,TRP-494A,LEU-498A
4	14-deoxyandrographolide	-8.83	LEU-707A,SER-848A,ARG -850A	PRO-86A,PRO-706A,ARG-850A
5	alpha1-Sitosterol	-8.58	GLU -1157A	PRO-610A,LEU-611A,PRO-650A,GLN-651A,TRP-969A,HIS-973A,GLU-1157A
6	Andrograpanin	-9.17	SER-84A,LEU-87A,LEU-707A	PRO-86A,PRO-706A,ARG-850A,ILE-851A
7	Andrographolide	-7.61	SER-81A, SER-848A,ARG -850A	PRO-86A,LYS-1111A
8	Apigenin	-7.92	ASP -79A,SER-84A,SER-705A,LEU-707A	PRO-86A,PRO-706A,LEU-707A
9	Carvacrol	-5.02	VAL-1113A,THR -1114A	ARG-77A,PRO-86A,LEU-87A,LEU-707A
10	Daucosterol	-7.23	ASN -517A,GLU -518A,GLN -521A,ILE-522A	ASP-490A,MET-491A,ILE-522A, PHE-525A
11	Deoxyandrographolide	-8.68	SER-84A	PRO-86A, PRO-706A,LYS-1111A,LEU-1112A
12	Eugenol	-4.87	LEU-87A	ARG-77A,LEU-87A, PRO-706A,LEU-707A
13	Neoandrographolide	-7.27	SER -81A,SER -84A,LEU -707A, LYS-1111A	PRO-706A, LYS-1111A
14	Wogonin	-7.11	ASP -79A, SER-84A, LEU-87A	PRO-86A,PRO-706A,LEU-707A



1) Deoxyandrographolide

2) Alpha1-Sitosterol



3) 14-deoxyandrographolide

4) Andrograpanin

Figure-5. The 2D and 3D view of the ligand-protein interactions and its amino acid residue include salt bridges, hydrophobic bonds, and hydrogen bond- The no. (1 to 4) stand for 1: Deoxyandrographolide, 2: alpha1-Sitosterol, 3: 14-deoxyandrographolide, 4: Andrograpanin.

CONCLUSION

In conclusion, study was done on the pharmacokinetics, drug-likeness, and toxicity profiles of twenty phytoconstituents. The twenty phytoconstituents found in the *Andrographis Paniculata* were expected to have inhibitory effects on oral cancer using in silico approaches.For oral availability, all twenty adhere to Lipinski's rule of five except Daucosterol which is typical for natural goods. The results showed that Andrograpanin, 14-Deoxyandrographolide, Deoxyandrographolide, alpha1-Sitosterol, and 14-Deoxy-11,12-didehydroandrographolide have lower binding energies, indicating that they may fit neatly in the human AKT1 binding pocket and form a stable inhibitor-protein complex. The compounds with the best binding energy that showed good ADME properties. According to a research that analyzes toxicological endpoints, the range of the median fatal dosage (LD50) is 48–23000 mg/kg.Overall result concludes that Alpha1-Sitosterol, 14-Deoxyandrographolide, Deoxyandrographolide, and Andrograpanin are potential agent for oral cancer.

FUTURE PROSPECTIVE

Alpha1-Sitosterol, 14-Deoxyandrographolide, Deoxyandrographolide, and Andrograpanin are identified as potential agents for the synthesis of oral cancer compounds for further in vitro and in vivo research based on the outcomes of the molecular docking, pharmacokinetic properties, and predicted drug-likeness.

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Conflict of interest

All the authors’ promuglate that there is no conflict of interest.

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