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Research Article

COMPUTATIONAL RESEARCH USING PHYTOCHEMICALS FROM THE *ACACIA CAVEN* PLANT TO COMBAT THE VP40-FUNCTIONALIZED EBOLA VIRUS ILLNESS

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ABSTRACT

Objectives: The Ebola virus is an extraordinarily deadly illness that affects both humans and wild animals. Key elements in viral proliferation include viral adhesion to cell membranes and viral penetration into the host organism. The viral protein present in the Ebola virus is the matrix protein Viral Protein-40 (VP-40) which is required for the development and integration of the nucleocapsid. Limiting VP40 activity prevents the viral infection from spreading.

Methods: Ten phytochemicals from *Acacia caven* were examined for their physicochemical properties, drug-likeness, and their potential to impede VP40 to assess their potential as anti-Ebola virus therapeutics.

Results: Considering the pharmacological uses, ten bioactive chemicals were chosen for this investigation. Predicated on their docking score and binding interactions, Pimara-8(14), 15-diene, Heptacosane, and Geranylacetone were recognized as VP-40 inhibitors.

Conclusion: Developing medicines that can inhibit VP40 could be a potential anti-Ebola virus treatment solution as VP40 is a fundamental protein for the assemblage of virion. Using the ligands Geranylacetone, Heptacosane, and Pimara-8(14), 15-diene, anti-Ebola virus therapeutics can be developed that specifically target the VP40 suppression which aids in the management of Ebola Virus disease.

Keywords: Ebola Virus, *Acacia caven,* VP40 protein, Phytochemicals, Drug-likeness.

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INTRODUCTION

Ebola virus disease (EVD) is a deadly disease with occasional outbreaks that occur mostly on the African continent. EVD most commonly affects people and nonhuman primates (such as monkeys, gorillas, and chimpanzees). It is caused by an infection with a group of viruses within the genus *Ebolavirus* [1]. Two successive outbreaks of deadly hemorrhagic fever in various regions of Central Africa led to the discovery of EVD. The Ebola River, which gave the virus its name, is located close to where the initial epidemic happened in the Democratic Republic of the Congo (formerly Zaire). The second epidemic happened 850 kilometers distant, in what is now South Sudan [2].

Public health experts first believed that both outbreaks were a single incident linked to a carrier who traveled between the two places. The Sudan ebolavirus and the Zaire ebolavirus, however, were eventually found to be the viruses responsible for the two epidemics. Following this observation, researchers concluded that the virus originated from two distinct origins and was transmitted to humans in each of the impacted locations independently [2-4].

The viral protein present in the Ebola virus is VP-40 (Viral Protein-40). This protein is found in the matrix of the virus, that is, in the space between the envelope and nucleocapsid. It plays three different roles in three different configurations in the virus [5]. As a cyclic octamer, it bonds to RNA and is involved in viral replication. As a dimer, it transports the elements from the nucleocapsid to the host cell membrane. On the arrival of this dimer, it reconfigures itself into a hexamer that forms a filamentous matrix necessary for assembling the new copies of the virus [5,6].

Herbal medicine is a therapeutic approach that is constructed from the active ingredients of plant parts or products such as roots, flowers, seeds, and fruits. However, when modern medicine proves ineffectual in treating an illness, such as advanced cancer, and in the face of emerging infectious diseases, the use of traditional medicines, that is, herbal medicines rises [7]. Herbal remedies are primarily used for chronic, rather than life-threatening, diseases and health promotion. Here active ingredients of the tree *Acacia caven* (Fig. 1) are used for the study of the inhibitors which can be used for the viral protein present in EVD. Phytocompounds retrieved from the plant were investigated for the possibility to be developed as anti-Ebola therapeutics that can specifically target the matrix protein VP-40.

The data for the proteins and ligands were initially retrieved and the Lipinski rules were employed to screen phytocompounds. The ligands that satisfied the rules were subjected to further analysis. The interaction of the phytocompounds with the protein was assessed and visualized to conclude the possible mechanisms through which the ligands can suppress the activity of VP-40.

MATERIALS AND METHODS

Protein retrieval and purification

The PDB databases (https://www.rcsb.org/) [8] were used to obtain the crystal structure of viral protein 40 (VP40; PDB ID-4LDD). The structure was downloaded with a resolution of 3.50 Å and was isolated through the X-ray diffraction method. The water molecule's free energy does not coincide with the crystallographic structure. Since water molecules might affect docking scores, they were eliminated before docking. To allow binding with the ligands chosen for the study faster, the prebound ligands are removed from the crystal structures. Additional chains were removed from the protein structures to reduce their intricacy while preserving chain A for examination. Polar hydrogen atoms are added to purified structures to optimize them.

Fig. 1: *Acacia caven* tree

Ligand retrieval
For the ligand-protein docking research, phytochemicals such as Octanal, 2-Undecanol, Geranylacetone, Heptacosane, Octadecane, 2-Decanol, Benzyl Alcohol, Methyl salicylate, Pimara-8(14), 15-diene, and 4-Methoxybenzaldehyde were chosen based on their medicinal and therapeutic applications. These ten ligands were chosen from the *A. caven* plant from the IMPPAT server (https://cb.imsc.res.in/imppat/basicsearch/phytochemical) [9]; however, only three were chosen after screening. PubChem Database (https://pubchem.ncbi.nlm.nih.gov/) [8] was used to retrieve the.sdf (Structure Data Format) files of these ligands.

Pharmacological studies
The tool SWISS-ADME (http://www.swissadme.ch/index.php) [10] was used to perform an ADME (absorption, distribution, metabolism, and excretion) analysis. It is a technique for finding new drugs that assess drug similarity, aggregation qualities, physicochemical characteristics, and, the Lipinski rule of 5. The other tool used for the ADMET properties which help in screening is ADMET LAB 2.0 (https://admetmesh.scbdd.com/service/screening/index) [11]. By taking into account five crucial factors, including molecular mass, hydrogen bond donors and acceptors, lipophilicity, and molar refractivity, the Lipinski rule of five aids in the screening of phytocompounds that can be considered as leads in the screening. Toxicity prediction was made using the online tool ProTox-II (https://tox-new.charite.de/protox_II/index.php?site=compound_input) [12]. The BOILED EGG model was retrieved from the SWISS-ADME tool. Aggregation analysis of these ligands was done using the tool ChemAgg (https://admet.scbdd.com/ChemAGG/index/) [13].

Protein structure analysis
Ramachandran plot for the protein, that is, VP-40 was obtained using the tool PDBSUM (http://www.ebi.ac.uk/thornton-srv/databases/pdbsum/Generate.html) [14]. Ramachandra plot statistics, the secondary structure of the protein, and motifs of the protein were also retrieved from the same tool. Protein statistics were retrieved from EMBOSS PepStats Tool (https://www.ebi.ac.uk/Tools/seqstats/emboss_pepstats/) [15] using the FASTA sequence of the VP-40 protein. A hydropathy plot was obtained using the EMBOSS PepWindow tool (https://www.ebi.ac.uk/Tools/seqstats/emboss_pepwindow/) [10].

Molecular docking studies
Molecular docking is an essential tool in computer-assisted drug design and structural molecular biology. Finding the protein-ligand interaction, pinpointing the possible interaction location, and computing binding affinity scores are all significant. The protein was purified using a pre-docking technique with the Biovia Discovery Studio 2021 tool [16]. Water molecules and hetero atoms were removed from the protein. Polar hydrogen atoms were added to the protein. Using the PyRx tool [17], more analysis was carried out. PyRx Tool consists of embedded versions of Auto dock, Vina wizard, and Open Babel.

Initially, the purified protein is loaded into the PyRx software and recognized as a macromolecule, and converted to pdbqt format. The ligands are loaded and docked to the protein using the vina wizard tool in PyRx by applying the universal force field the energy of the ligands was minimized. There will be salt moieties in the SDF files and hence they have been removed from the macromolecule before docking. Following this, the ligands are prepared to AutoDock ligand. pdbqt format. Grid dimension is set to X: 38.6029 Y: 20.6859 Z: 32.3133. By default, parameters, the PyRx software assumes the macromolecules as rigid and the ligands as flexible. The flexible ligand undergoes nine different conformational changes to attain the best optimal fit with the macromolecule. The interaction of the ligand with the macromolecule is evaluated on grounds of ligand binding affinity. The binding affinities corresponding to the least negative values represent the best binding interactions. The binding energies were obtained and the output was saved as a CSV file. Out of the examined phytocompounds, the top three are chosen whose negative binding affinity score was highest and saved in PDB format. The saved PDB files were analyzed in Biovia Tool and the interactions between the selected ligand and the protein were studied. Hydrophobic properties were visualized and 2D structures were also obtained.

RESULTS

Ligand preparation
Ten phytocompounds from *A. caven* were selected from the IMPPAT server and their 3D structure was obtained from the PubChem database. The structure was viewed using Biovia, as shown in Fig. 2.

Protein purification
The viral protein VP-40 is downloaded in PDB format and is purified using Biovia Discovery Studio 2021 tool. Water molecules, hetero atoms, and other protein chains are removed from the protein and only one protein chain is kept for further analysis. This process is protein purification. Here, Fig. 3a is a non-purified protein and Fig. 3b is a purified protein.

Analysis of ligands
Using ADME analysis, the phytocompounds having drug-like properties were identified,

Ligand retrieval
Ten phytocompounds were retrieved from the IMPPAT server. Canonical smiles of these phytocompounds were retrieved from the PubChem Database (Table 1).

Physicochemical properties of ligand
The standard parameters for physicochemical properties in the Swiss ADME are shown in Table 3 and the physicochemical properties of the selected phytocompounds are documented in Table 2. The compounds are screened based on their properties. The ligands highlighted in red do not fulfill the optimal ranges for the physicochemical properties.

Lipinski filter analysis
The Lipinski Rule of Five is useful for identifying drug-like compounds and those that are not. Due to the similarity of the molecules to drugs and their compliance with two or more of the following rules, it forecasts a high probability of success or failure (Table 4).

Criteria for Lipinski rule: Molecular mass <500, lipophilicity <4.15, hydrogen bond donors <5, hydrogen bond acceptors <10, and molar refractivity should be between 40 and 130.

Aggregation analysis
The above Table 5 is obtained from the ChemAgg tool which gives the aggregation analysis results, that is, the Aggregator class is given for the

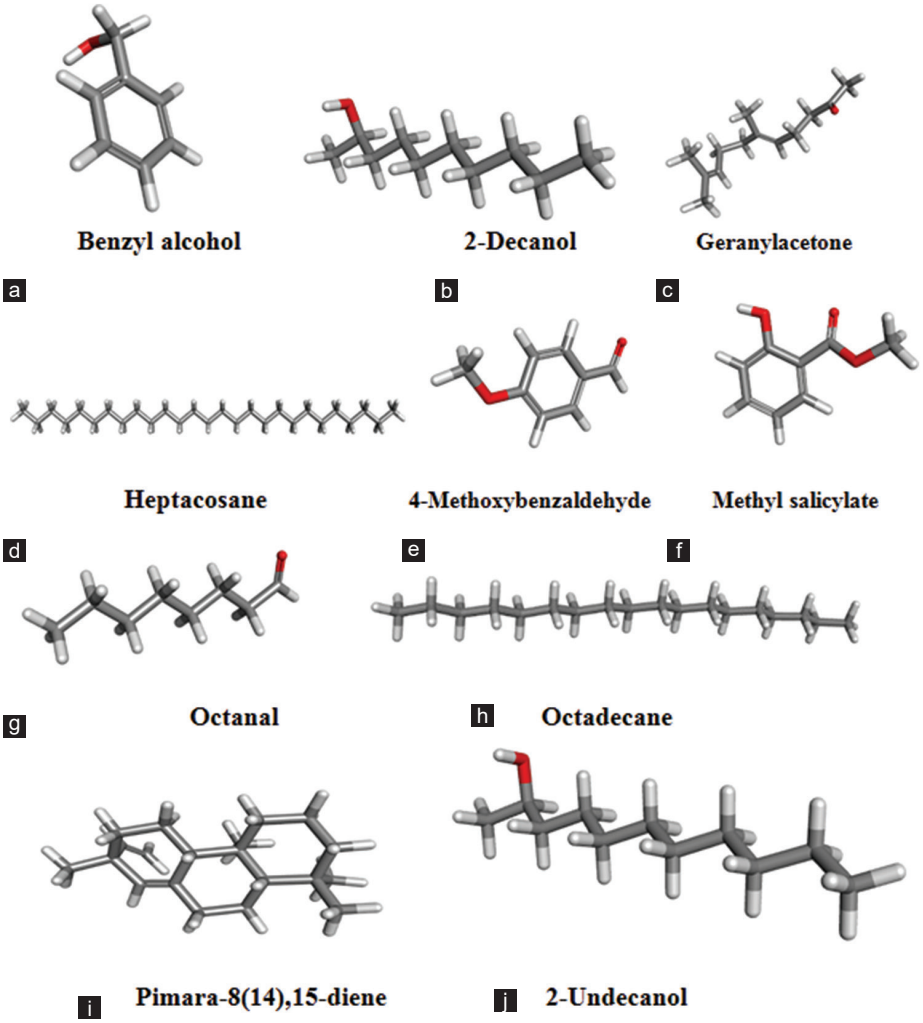

Fig. 2: (a-j) 3D structures of all selected phytocompounds from the plant *Acacia caven*

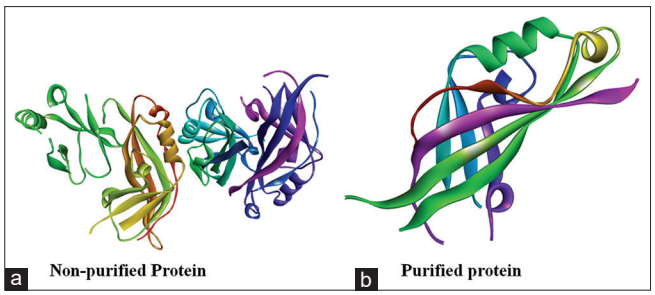

Fig. 3: (a and b) Crystal structure of the viral protein VP-40

given Phytocompounds. Aggregator class 0 represents non-aggregators and aggregator Class 1 represents aggregators.

ADMET analysis

ADMET analysis is done using SWISS-ADMET and ADMET LAB 2.0 tools. The results are given for the selected phytocompounds. Values such as blood-brain barrier value, gastrointestinal absorption value, and the permeability of glycoprotein value are given (Table 6).

Toxicity prediction

Toxicity prediction is done using the ProTox-II tool. The prediction gives the result in classes ranging from 1 to 6. Class 1 is very toxic and fatal if swallowed and class 6 is non-toxic.

The compounds highlighted in green indicate that the compounds are comparatively safe but can be dangerous if ingested in higher doses. These compounds have the potential to be developed as drugs (Table 7).

Brain Or IntestinaL EstimateD Permeation Method (BOILED EGG)

Brain Or IntestinaL EstimateD Permeation technique (Boiled-Egg) is a precise prediction model that analyses the polarity and lipophilicity of tiny compounds. The white region corresponds to a high probability of passive absorption of the gastrointestinal tract. The yellow region corresponds to a high probability of brain penetration. White and yellow regions are not mutually exclusive. If the points are colored in blue, they are actively effluxed by PGP+ and if it is red, they are non-substrate of Pgp and it is PGP–. Octadecane is out of range; hence, octadecane is predicted as not absorbed and not brain penetrant (Fig. 4).

Analysis of protein

Ramachandran plot

The main chain N-C and C-alpha links in a polypeptide are comparatively free to spin. The torsion angles phi and psi, respectively, stand in for these rotations. To identify stable conformations, GN Ramachandran utilized computer simulations of tiny polypeptides to repeatedly change phi and psi. The structure was analyzed for atom-atom interactions in each configuration. White regions denote conformations in which polypeptide atoms are closer together than the total of their van der Waals radii. The alpha-helical and beta-sheet conformations are the permissible zones,

Table 1: Ligand retrieval

Compound	PUBCHEM CID	Canonical Smiles
Octanal	454	CCCCCCCC=O
2-Undecanol	15448	CCCCCCCCCC(C)O
Geranylacetone	1549778	CC(=CCCC(=CCCC(=O)C)C)C
Heptacosane	11636	CCCCCCCCCCCCCCCCCCCCCCCCCCC
Octadecane	11635	CCCCCCCCCCCCCCCCCC
2-Decanol	14254	CCCCCCCCC(C)O
Benzyl Alcohol	244	C1=CC=C(C=C1)CO
Methyl salicylate	4133	COC(=O)C1=CC=CC=C1O
Pimara-8 (14),15-diene	440909	CC1(CCCC2(C1CCC3=CC(CCC32)(C)C=C)C)C
4-Methoxybenzaldehyde	31244	COC1=CC=C(C=C1)C=O

Table 2: Physicochemical properties

Ligand	Molecular weight	Molecular formula	Fraction Csp3	Rotatable bonds	TPSA	Lipophilicity
Octanal	128.21	C8H16O	0.88	6	17.07	2.72
2-Undecanol	172.31	C11H24O	1	8	20.23	4.52
Geranyl acetone	194.31	C13H22O	0.62	6	27.07	3.7
Heptacosane	380.73	C27H56	1	24	0	14.24
Octadecane	254.49	C18H38	1	15	0	9.37
2-Decanol	158.28	C10H22O	1	7	20.23	3.98
Benzyl Alcohol	108.14	C7H8O	0.14	1	20.23	1.1
Methyl salicylate	152.15	C8H8O3	0.12	2	46.53	2.55
Pimara-8 (14),15-diene	272.47	C20H32	0.8	1	20	7.03
4-Methoxybenzaldehyde	136.15	C8H8O2	0.12	2	26.3	1.76

Table 3: Parameters for physicochemical properties

Properties		Optimal range
Lipophilicity	xLogP	−0.7–+5.0
Size	MW	150–500 g/mol
Polarity	TPSA	20–130
Saturation	Sp3 hybridization	Not <0.25
Flexibility	Rotatable bonds	Not more than 9

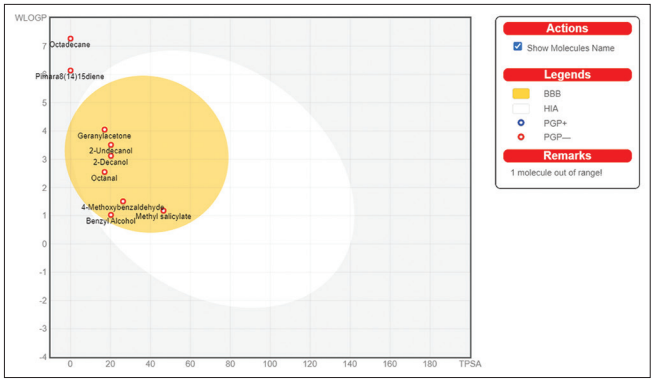

Fig. 4: Boiled egg

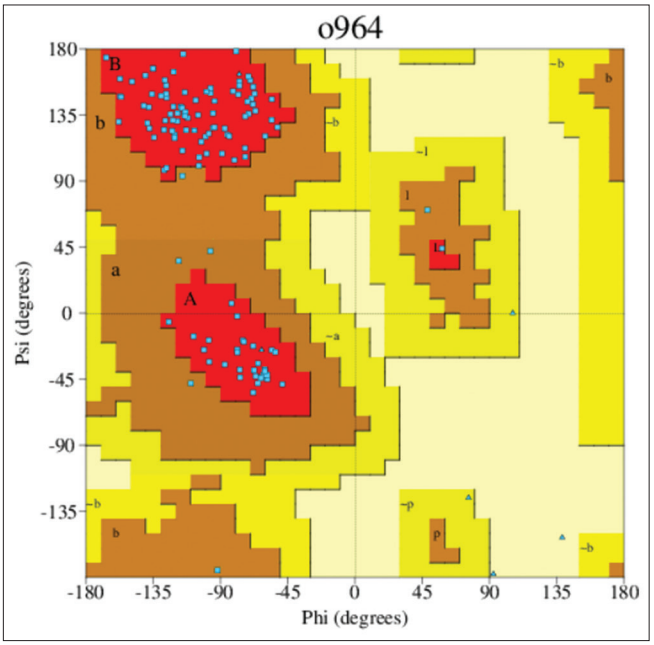

Fig. 5: Ramachandran plot purified protein VP-40

and the red regions correspond to conformations in which there are no steric collisions. If the computation uses slightly shorter Van der Waals radii, or if the atoms are permitted to get a bit closer together, the yellow regions represent the permitted zones (Fig. 5).

Secondary structure of protein and motifs

The secondary structure pf the protein VP-40 contains 5 sheets, 1 beta alpha unit, 3 beta hairpins, 1 psi loop, 3 beta bulges, 17 strands, 19 helices, 21 helix-helix interacs, 29 beta turns, and 3 gamma turns (Fig. 6).

Protein statistics

The frequency of each amino acid residue in the protein sequence under a specific attribute is shown in the protein statistics. EMBOSS PeptStats was employed to compile statistical data on the amino acids under various conditions, including size, charge, pH, etc. Table 8 shows that the protein has a large number of tiny, non-polar residues while having fewer aromatic and basic residues.

Hydropathy plot

The hydrophobicity or hydrophilicity of the amino acids in a protein is quantitatively analyzed using a hydrophilicity plot. It is used to describe or pinpoint a protein's potential structure or domains. The plot's X-axis represents the amino acid sequence of a protein, while the Y-axis represents the degree of hydrophobicity and hydrophilicity. The degree of interaction between certain amino acids and polar solvents like water may be determined using a variety of techniques (Fig. 7).

Table 4: Lipinski filter analysis

Ligand	Molecular weight	MLogP	H donors	H acceptors	Molar Refractivity
Octanal	128.21	2.07	0	1	40.77
2-Undecanol	172.31	3.13	1	1	56.15
Geranylacetone	194.31	3.34	0	1	63.86
Heptacosane	380.73	8.86	0	0	131.9
Octadecane	254.49	6.92	0	0	88.64
2-Decanol	158.28	2.84	1	1	51.35
Benzyl Alcohol	108.14	1.54	1	1	32.57
Methyl salicylate	152.15	1.32	1	3	39.74
Pimara-8(14),15-diene	272.47	4.82	0	0	90.18
4-Methoxybenzaldehyde	136.15	1.12	0	2	38.32

Table 5: Aggregation analysis

Compound	Canonical smiles	Probability score	Aggregator class
Octanal	CCCCCCCC=O	0.032	0
2-Undecanol	CCCCCCCCCC(C)O	0.014	0
Geranylacetone	CC(=CCCC(=CCCC(=O)C)C)C	0.032	0
Heptacosane	CCCCCCCCCCCCCCCCCCCCCCCCCCC	0.024	0
Octadecane	CCCCCCCCCCCCCCCCCC	0.024	0
2-Decanol	CCCCCCCCC(C)O	0.014	0
Benzyl Alcohol	C1=CC=C(C=C1)CO	0.021	0
Methyl salicylate	COC(=O)C1=CC=CC=C1O	0.156	0
Pimara-8 (14),15-diene	CC1(CCCC2(C1CCC3=CC(CCC32)(C)C=C)C)C	0.009	0
4-Methoxybenzaldehyde	COC1=CC=C(C=C1)C=O	0.169	0

Table 6: ADMET analysis

Ligands	BBB Barrier	GI Absorption	PGP substrate	Solubility (LOGSw-SILICOS IT)	PAINS	Bioavailability	SA SCORE
Octanal	0.994 (yes)	0.003 (high)	0.002 (No)	−2.6 (soluble)	0	0.55	1.43
2-Undecanol	0.87 (yes)	0.004 (high)	0.187 (No)	−3.36 (soluble)	0	0.55	2.2
Geranyl acetone	0.684 (yes)	0.007 (high)	0.007 (No)	−3.18 (soluble)	0	0.55	3
Heptacosane	0.005 (no)	0.003 (low)	0 (Yes)	−10.71 (insoluble)	0	0.55	3.56
Octadecane	0.065 (no)	0.002 (low)	0 (No)	−7.13 (poorly soluble)	0	0.55	2.49
2-Decanol	0.919 (yes)	0.004 (high)	0.207 (No)	−2.95 (soluble)	0	0.55	2.1
Benzyl Alcohol	0.886 (yes)	0.008 (high)	0.003 (No)	−2.16 (soluble)	0	0.55	1
Methyl salicylate	0.793 (yes)	0.006 (high)	0.001 (No)	−1.88 (soluble)	0	0.55	1.11
Pimara-8 (14),15-diene	0.147 (no)	0.006 (low)	0 (No)	−5.02 (moderately soluble)	0	0.55	4.92
4-Methoxybenzaldehyde	0.988 (yes)	0.009 (high)	0.005 (No)	−2.44 (soluble)	0	0.55	1

Table 7: Toxicity prediction

Compound	Canonical smiles	Predicted LD 50 (mg/kg)	Predicted toxicity class
Octanal	CCCCCCCC=O	5000	5
2-Undecanol	CCCCCCCCCC(C)O	1000	4
Geranyl acetone	CC(=CCCC(=CCCC(=O)C)C)C	1190	4
Heptacosane	CCCCCCCCCCCCCCCCCCCCCCCCCCC	750	3
Octadecane	CCCCCCCCCCCCCCCCCC	750	3
2-Decanol	CCCCCCCCC(C)O	1000	4
Benzyl alcohol	C1=CC=C(C=C1)CO	1230	4
Methyl salicylate	COC(=O)C1=CC=CC=C1O	887	4
Pimara-8 (14),15-diene	CC1(CCCC2(C1CCC3=CC(CCC32)(C)C=C)C)C	5000	5
4-Methoxybenzaldehyde	COC1=CC=C(C=C1)C=O	1510	4

Molecular docking analysis

Docking score

The Docking score is a computational result that is specific for a particular program and energy function, and that in an ideal case allows you to predict binding free energy and binding affinity, or to at least rank different complexes according to those parameters.

The ligands highlighted in orange, that is, Pimara-8(14),15-diene, Heptacosane and Geranylacetone had a higher binding affinity of −6.5, −5.5, and −5.1, respectively, with VP-40 and hence the interaction of ligands was studied based on their binding affinity (Table 9).

Pimara-8(14),15-diene

The interaction of the ligand Pimara-8(14),15-diene with that of the protein VP40 is documented in the following Table 10 and the molecular interactions as visualized is illustrated in Fig 8.

Heptacosane

The interaction of the ligand Heptacosane with that of the protein VP40 is documented in the following Table 11 and the interactions are given in Fig 9.

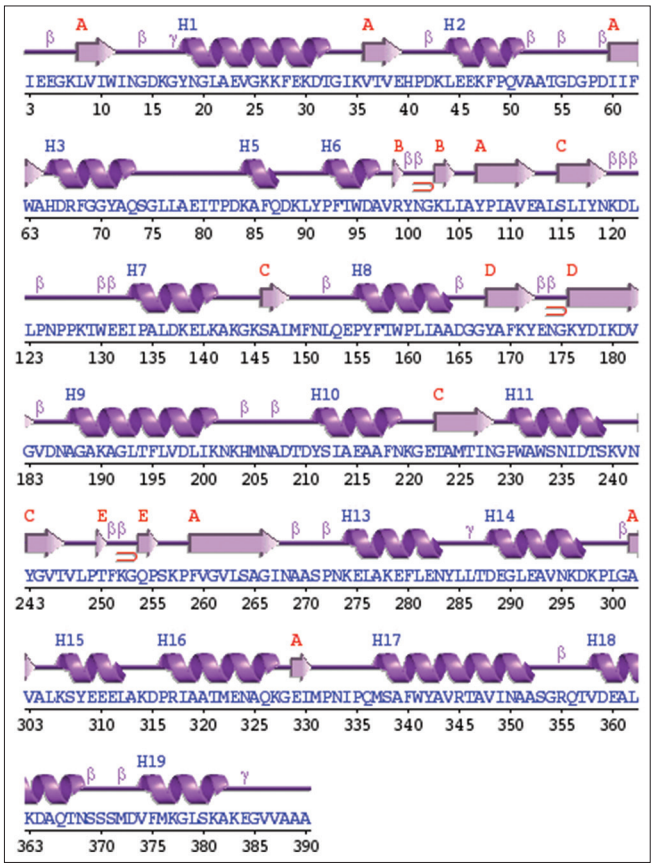

Fig. 6: Secondary structure of protein VP-40

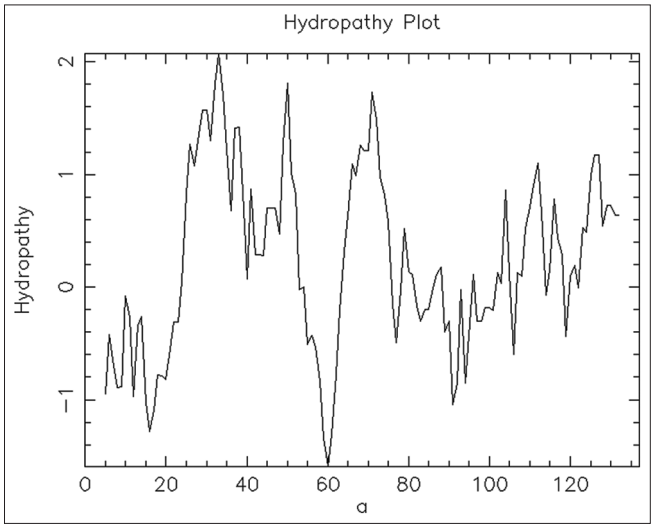

Fig. 7: Hydropathy plot for the purified protein VP-40

Geranyl acetone

The interaction of the ligand Geranyl acetone with that of the protein VP40 is documented in the following Table 12 and interactions are depicted in Fig 10.

DISCUSSION

In northwest Argentina, the usage of herbal beverages has long been a component of the local cuisine and medicine traditions. Many local communities use the liquids from the flowers of *A. caven* as an infusion or as a decoction of the native Argentine species *A. caven* as anti-inflammatory and anti-rheumatic treatments. The floral drinks of all the plant species under research showed significant levels of phenolic compounds with comparable chromatographic patterns in both infusions and decoctions, and the primary components of these compounds have been identified [18].

Despite their many medical applications, drugs only serve to improve anti-inflammatory and anti-rheumatic therapies [19]. FDA-approved

Table 8: Protein statistics

Property	Residues	Number	Mole %
Tiny	(A+C+G+S+T)	38	27.737
Small	(A+B+C+O+G+N+P+S+T+V)	74	54.015
Aliphatic	(A+I+L+V)	47	34.307
Aromatic	(F+H+L+Y)	15	10.949
Non-polar	(A+C+F+G+I+l+M+P+V+W+Y)	84	61.314
Polar	(O+E+H+K+N+Q+R+S+T+Z)	53	38.686
Charged	(B+O+E+H+K+R+Z)	22	16.058
Basic	(H+K+R)	12	8.759
Acidic	(B+O+E+Z)	10	7.299

Table 9: Docking score

Ligand	Ligand name	Binding Affinity
pu_4ldd_440909_uff_E=338.66	Pimara-8 (14),15-diene	-6.5
pu_4ldd_11636_uff_E=85.38	Heptacosane	-5.5
pu_4ldd_1549778_uff_E=108.04	Geranyl acetone	-5.1
pu_4ldd_4133_uff_E=86.76	Methyl salicylate	-4.9
pu_4ldd_11635_uff_E=56.94	Octadecane	-4.8
pu_4ldd_14254_uff_E=50.80	2-Decanol	-4.6
pu_4ldd_15448_uff_E=54.73	2-Undecanol	-4.6
pu_4ldd_244_uff_E=68.48	Benzyl Alcohol	-4.5
pu_4ldd_31244_uff_E=74.15	4-Methoxybenzaldehyde	-4.5
pu_4ldd_454_uff_E=27.41	Octanal	-4.2

Table 10: Interaction data of VP-40- Pimara-8 (14),15-diene interaction

Name	Distance	Category	Types
Valine	4.8828	Hydrophobic	Alkyl
Methionine	5.08824	Hydrophobic	Alkyl
Methionine	5.10083	Hydrophobic	Alkyl
Methionine	4.84956	Hydrophobic	Alkyl
Isoleucine	4.61121	Hydrophobic	Alkyl
Leucine	5.20228	Hydrophobic	Alkyl
Proline	4.38555	Hydrophobic	Alkyl
Proline	5.13777	Hydrophobic	Alkyl
Unknown	4.90749	Hydrophobic	Alkyl
Phenylalanine	5.36939	Hydrophobic	Pi -Alkyl

Table 11: Interaction data of VP-40-Heptacosane interaction

Name	Distance	Category	Types
Valine	3.76467	Hydrophobic	Alkyl sky
Methionine	5.11324	Hydrophobic	Alkyl
Isoleucine	4.11234	Hydrophobic	Alkyl
Proline	4.77416	Hydrophobic	Alkyl
Proline	4.67314	Hydrophobic	Alkyl
Leucine	4.50776	Hydrophobic	Alkyl
Leucine	5.09247	Hydrophobic	Alkyl
Proline	4.19359	Hydrophobic	Alkyl
Leucine	5.21346	Hydrophobic	Alkyl
Proline	5.43297	Hydrophobic	Alkyl
Histidine	4.67123	Hydrophobic	Pi-Alkyl
Phenylalanine	5.44896	Hydrophobic	Pi-Alkyl

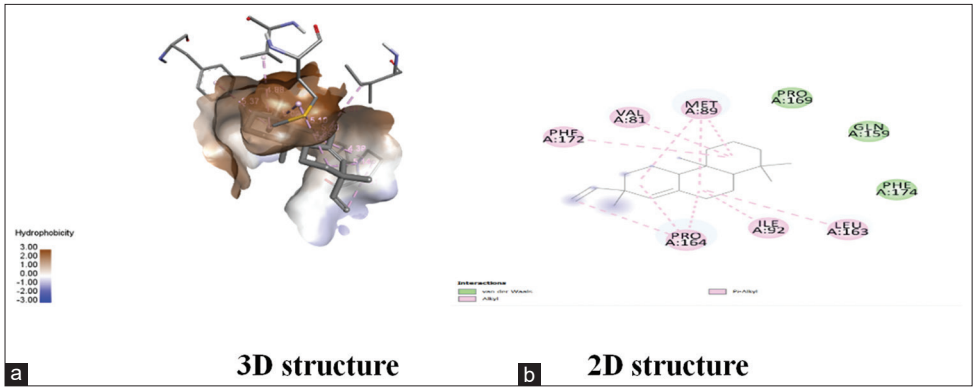

Fig. 8: (a and b) Protein-ligand interaction of VP40 and Pimara-8(14),15-diene interaction

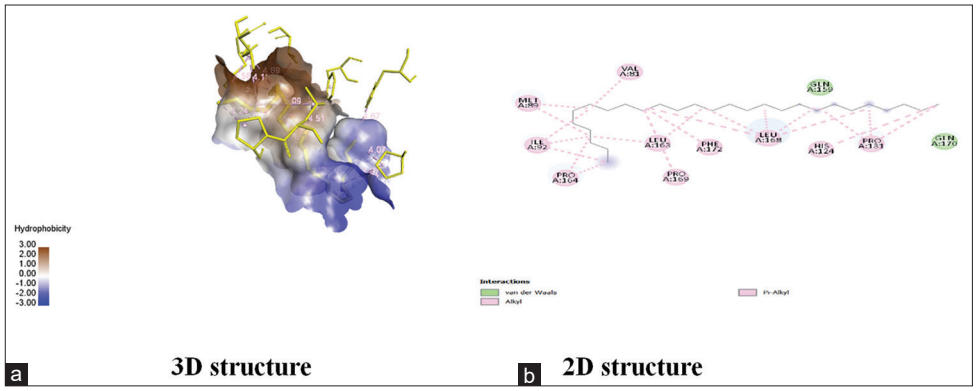

Fig. 9: (a and b) Protein-ligand interaction of VP40 and Heptacosane

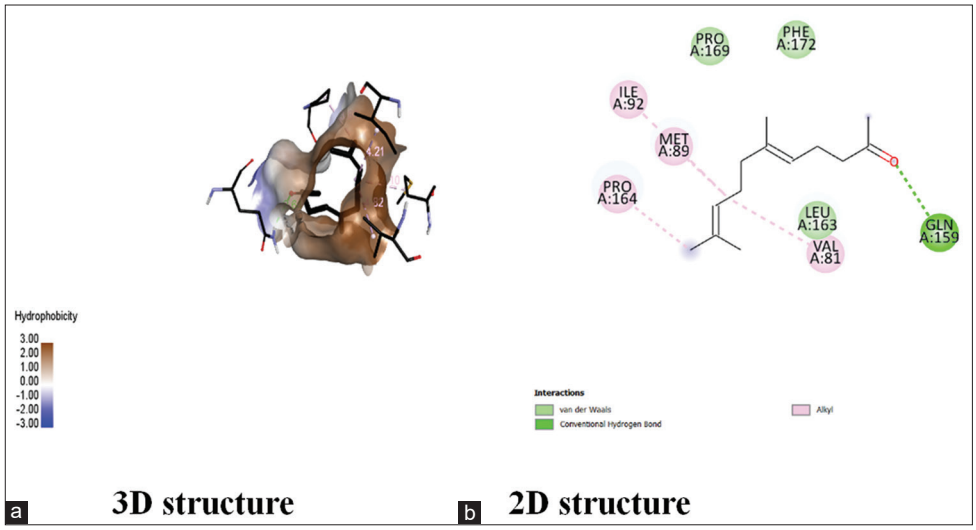

Fig. 10: (a and b) Protein-Ligand interaction of VP40 and Geranyl acetone

Table 12: Interaction data of VP-40-Geranylacetone interaction

Name	Distance	Category	Types
Glutamine	2.6421	Hydrogen Bond	Conventional Hydrogen bond
Valine	4.81753	Hydrophobic	Alkyl
Methionine	4.10001	Hydrophobic	Alkyl
Isoleucine	4.2074	Hydrophobic	Alkyl
Unknown	3.8683	Hydrophobic	Alkyl

A. caven medications are not available to treat EVD. There is thus the potential for research into and a market for medicine development using this herb [18,19].

Geranyl acetone, also known by its chemical name 3,7-dimethyl-2,6-octadienyl acetone, is a type of natural perfume with a Magnolia fragrance. Due to its light and airy floral scent and slightly sweet rose aroma, it is frequently used in food perfume fixatives, edible essence, and daily chemical flavor enhancers. In addition, geranyl acetone is employed as a pharmaceutical intermediary and a synthetic vitamin in medicine due to its significant biological activity and antioxidant properties [20]. Pimara-8(14),15-diene which comes under diterpenoids has various medicinal uses. The naturally occurring antispasmodic phytochemicals have drawn a lot of attention as a possible treatment for cardiovascular

disorders. Diterpenes are organic compounds with a wide range of biological actions, such as anti-inflammatory, antibacterial, and antispasmodic properties [21]. Heptacosane which is a straight-chain alkane is also found in this herb. It has a lengthy chain of hydrocarbon but it cannot be used for biological purposes. It is mainly used in the production of detergents or proteins [22].

The African continent's native Ebola virus is spreading to several other nations through those who have the disease. The virus spread when infected individuals from nations like Guinea, Liberia, and Sierra Leone immigrated to other nations. Many nations strictly forbade the immigration of residents of West African countries. However, since non-Africans have already contracted the illness, the scrutiny has increased. The airports of every country bordering Africa are being examined. An examination of the travelers from Africa is performed. Therefore, it is impossible to recognize the individual, even if he is affected as the virus takes approximately 21 days to incubate, [23].

A. caven has more than 70 bioactive compounds which are available from the IMPPAT server [9]. Based on their pharmacological uses, ten bioactive chemicals were chosen for this research. Octanal, 2-Undecanol, Geranyl acetone, Heptacosane, Octadecane, 2-Decanol, Benzyl Alcohol, Methyl salicylate, Pimara-8(14),15-diene, and 4-Methoxybenzaldehyde were the ten phytocompounds. After the screening ligands such as Pimara-8(14),15-diene, Heptacosane, and Geranylacetone had a higher binding affinity of -6.5, -5.5, and -5.1, respectively, with VP-40 and hence these 3 were selected. Biovia Discovery Studio was used to visualize these interactions. From their 2D structure, it was seen that several amino acids such as VAL, MET, PHE, PRO, and GLN which are involved in hydrogen bonds, electrostatic interactions, and hydrophobic interactions were studied. The final phytocompounds were good drugs for the creation of a medicine that could prevent EVD by acting on the viral protein VP-40.

Some significant amino acids, including VAL, MET, PHE, PRO, GLN, LEU, and ILE, are shown to be involved in the binding of Pimara-8(14),15-diene, and VP-40 in the 2D diagram. All these amino acids except PRO, GLN, and PHE are bounded by hydrophobic bonds.

The involvement of certain significant amino acids, including VAL, MET, PHE, PRO, GLN, LEU, HIS, and ILE, is shown in the 2D figure for the binding of heptacosane and VP-40. All these amino acids except GLN are bounded by hydrophobic bonds.

Some significant amino acids, including VAL, MET, PHE, PRO, GLN, LEU, and ILE, are involved in the binding of geranyl acetone and VP-40, as shown in the 2D binding diagram. Here, the amino acid GLN is bounded by hydrogen bonding. Amino acids such as VAL, MET, ILE, and PRO are bounded by hydrophobic bonds. Amino acids such as PRO, PHE, and LEU are not bounded.

Although these two compounds have benefited from in silico research, they may potentially have significant shortcomings that overshadow their potential as a therapeutic option. Geranyl acetone and heptacosane are irritants that cause skin-related issues, whereas Pimara-8(14),15-diene which is a diterpenoid is known to cause local skin reactions such as erythema, flaking/scaling, and crusting. The fact that *in vitro* and *in silico* research might provide diverse results must always be kept in mind.

CONCLUSION

A. caven is rich in more than 70 bioactive compounds which are available from the IMPPAT server. In this study, ten bioactive compounds were selected based on their pharmacological applications. The ligands Pimara-8(14),15-diene, Heptacosane, and Geranylacetone were selected for VP-40 which is based on their docking score and binding interactions. These interactions were visualized using Biovia Discovery Studio 2021 tool. These three ligands are found in flowers of *A. caven* and can be used as the medication for EVD. The viral protein causing EVD has some receptor sites where ligands bind to can be used to inhibit the viral protein. Phytocompounds from various medicinal plants can be studied for the development of medications for these diseases. There are more possibilities to find an even more potent drug that can inhibit this viral protein, that is, VP-40 in various other plants.

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CONFLICTS OF INTEREST

The author declares no conflict of interest.

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