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RESEARCH ARTICLE

Targeting the ENV spike protein of HIV with naturally occurring compounds: an *in-silico* study for drug designing

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Abstract

Human Immunodeficiency Virus (HIV) infects human by destroying the immune system. The types of HIV strains HIV-1 and HIV-2, among HIV-1 being more prevalent and considered deadly. Eventually either of the strains leads to disease Acquired Immunodeficiency Syndrome (AIDS). Traditional medicinal plants have a pivotal role in the modern pharmacological process due to their rich composition of secondary metabolites with significant biological activity. Computational tools are gaining momentum as they predict with higher accuracy, robust and provide insight in the interaction of small molecule with the disease target protein. This study was conducted for understanding the interaction mode of Phyto compounds with Env spike proteins of HIV. The compounds are studied for ADME properties and molecular docking using Schrödinger software was performed. From the results, Ethyl gallate was observed with least docking score and higher binding affinity for HIV-ENV protein (4CC8) and Cinnamyl acetate (cis/trans) with HIV-1-ENV protein (6ULC).

Keywords ENV protein · Medicinal plants · Molecular docking · ADMET properties · *In-silico* drug design

Abbreviations

HIV	Human immunodeficiency virus
AIDS	Acquired Immune deficiency syndrome
Env Protein	Envelop protein
ADMET	Absorption, distribution, metabolism, excretion and toxicity
RNA	Ribo nucleic acid
PDB	Protein data bank
CNS	Central nervous system

Introduction

From time immemorial plants or microbes with medicinal activities have been employed in the treatment of various diseases. Traditional herbal products and proper standardization of the botanical drug system with potent scientific evidence can pave the way for creating an efficient therapeutic process (Patwardhan and Mashelkar 2009). Ayurveda clearly emphasizes the importance of natural formulations from herbal for novel drug discovery (Jaiswal and Williams 2017). In Ethiopia, traditional medicine is always related to the curing of disease as well as the protection of human livelihood (Kassaye et al. 2007). Traditional medicine has always been a part of our sustainable living for ages. A rising trend is being observed with drug designing that encompasses the secondary metabolites to target molecules as a therapy for human disorders (Rollinger, Stuppner and Langer 2008).

By incorporating the molecular biology techniques the ability to produce novel natural compounds from microbes or combinational chemistry approaches which provides a platform to establish screening libraries resembling drug-like compounds (Harvey 2008). A drug is said to be a failure or ineffective when (a) they don't provide any therapeutic effect against the particular disease (b) they are not safe, in certain setting target identification and validation is the essential step (Hughes et al. 2011). Target can be referred

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to as the place where the drug molecules go attach to a specific biomolecule, it can be proteins, genes, and RNA. A compound is believed to be druggable when it meets all the standard requirements of being a drug in terms of efficacy, safety, and displaying a positive gesture in the clinical trials.

The Human Immunodeficiency Virus (HIV) a human killer attacks the immune system and thereby slowly disintegrating the whole body. Without a strong immune system, the body will be incapable of warding off the foreign particle entering inside the body. It's been three decades since HIV was identified and its effect continues to persist in a large group of people, it is a global epidemic affecting millions of people from all age groups (Piot et al. 2001). It is to be taken into note that the heterosexual mode of transmission is the dominant mode of transmission and it is liable for 85% of total HIV-1 infections. South Africa remains to be the focal point of disease and the infections continue to prevail (Hayes and Weiss 2006). The white blood cells which form the important part of the immune system will be ravaged by HIV and the class of white blood cells the CD4+ will be destroyed as a result. Complications will arise when a large amount of these blood cells are destroyed whereby putting the body on the verge of immune deficiency and eventually death. AIDS (Acquired Immunodeficiency Syndrome) is the climax stage of infection, at this point, the lives are at stake and cancers seem to occur which is not visible in a healthy person. With a strong base of antiretroviral treatment, AIDS has been demoted to chronic manageable disease from inevitable fatal disease (Simon, Ho and Abdool Karim 2006). To date a permanent cure for HIV/AIDS hasn't been identified, combination antiretroviral therapy is the only solution in practice for the effective treatment of the disease for a lifetime (Mamo et al. 2010). HIV takes around 10-12 years to transform into AIDS, competitive treatment procedures can be done during this period. With the onset of the disease, a broad range of associated diseases will be prevalent in the body, from pneumonia to tumors which will be present in a stage-wise manner in the body (Lucas 2002).

Recently a key protein structure has been visualized which acts as a mediator for HIV to enter into the human immune system and cause dysfunction. The surface protein viral in nature is termed the ENV (PDB id 4CC8). The protein is believed to be a potential target for vaccines amid the dilemma of quick mutations occurring in the ENV. An outer coating of sugar molecules protects the protein from the immune system (Bartesaghi et al. 2013). It is considered that HIV infection commences by the binding of trimeric viral envelop glycoprotein (Env) to CD4 and a co-receptor of the target T-cells (Tran et al. 2012). Another protein HIV-1 Env bound with fab of antibody PG16 (PDB id 6ULC) was also retrieved to be docked with the phytoligands. The goal of vaccine development is to mimic the closed conformation in a desired immunogen (Pan et al. 2020).

In this study, we will be employing the *in-silico* methods to provide a new therapeutical intervention for HIV/AIDS. The ultimate aim of this study will be focused on developing a drug molecule from the naturally occurring bioactive compounds using computational tools, primarily consisting of molecular docking and ADME analysis.

Materials and methods

Structure based drug designing

Structure based drug designing serves a powerful method in identifying new lead compounds when a receptor structure is available (Anderson 2003).

Databases

In this study 12 number of naturally occurring bioactive compounds from 5 plant species; *Corbichonia decumbens*, *Ocimum sanctum*, *Syzygium cumini*, *Momordica charantia*, and *Terminalia bellerica* were selected for docking studies. All the ligand molecules were retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov/). The target proteins (PDB Id: 4CC8 and 6ULC) was retrieved from the protein data bank (PDB) (https://www.rcsb.org/) (Berman et al. 2000).

Protein preparation

The proteins were prepared by removing the native auto inducer and all water molecules Hydrogen were added using the templates for the protein residues using Maestro 10.2 version. It is a very essential process as it can rectify if there's any confrontations in the protein structure like missing side chains, and updating the missing residues. The water molecules were removed from the structure and whereby increasing the entropy of the target molecule.

Ligand preparation

The ligands were converted into 3D structures using the Ligprep tool in maestro Schrodinger version 10.2. The ligand was also geometrically optimized, the 2D sdf files were converted into 3D structures using the ligprep tool.

ADMET profiling

An account of druggability is very essential while performing a docking study, the ligands were checked for Absorption, distribution, metabolism, excretion and toxicity (ADMET) test. It is a preliminary step in drug preparation. The knowledge on drugs for HIV is very scanty,

and it is very reasonable to make out more and reduce the cost of treatment as a lot of developing countries can rely on it. 12 compounds successfully scored well in all the ADMET parameters analyzed using Qikprop version 4.4. in the Schrodinger suite (Quikprop module 4.4 2012). Some important parameters like CNS, Blood-barrier coefficient, human blood absorption, Lipinski's rule of three and five were analyzed. The bioactive phyto-compounds which displayed pragmatic result were chosen for the ADME and preferable docking poses has been tabbed for the rationale of docking (Vijayakumar et al. 2018).

Molecular docking

Molecular docking outlays the ligand's preferred orientation with the target molecule while interacting with each other in forming a highly stable complex. For this purpose, we have employed Maestro v10.2 to conduct the extra precision (XP) docking for speculating the binding affinity, analyzing efficacy of the ligand, and inhibitory constant of ligand against target. In this study, the entire ligand was docked with the target molecule flexibly using the Glide Xtra precision (XP) tool. As a result of successful docking we have obtained better docking scores, poses with accurate hydrophobic contacts between target residues to ligand (Maniam et al. 2017).

Results

ADME analysis

In the initial steps of drug discovery process, physio-chemical properties of the small molecules were determined to speculate the key properties of the molecules affecting the biological functions (ADME). In this analysis some 26 key parameters were chosen like, Central Nervous System (CNS), molecular weight, dipole, Total solvent accessible surface area (SASA), total solvent accessible volume, donor and acceptor hydrogen bonds (HB), metabolic reactions, human oral absorption and it's percentage, rule of five & three, stars, amide, rotor, number of reactive functional groups (rtvFG), FOSA, FISA, PISA, QPlogPoct, QPlogPw, QPlogPo/w, QPPCaco, QPlogBB, QPlogKp, QPlogKhsa. The ADMET results related to the study has been divided into two sections and portrayed in the (Table 1). About 100 compounds selected from which, only a handful of compounds were obeying the required levels of quality controls.

Molecular docking

Molecular docking methods are currently widespread across the globe in this pandemic era, new approaches are being introduced to bring out a substantial result in the race for an effective drug. A lot of electrostatic energy and van der wall forces (inter-atomic interactions) are participating during the docking analysis. In this context two proteins concerning HIV have been analyzed (i) ENV (4CC8); (ii) HIV-1 ENV (6ULC) with the phytoligands obtained from the plants like *Corbichonia decumbens*, *Ocimum sanctum*, *Syzygium cumini*, *Momordica charantia*, and *Terminalia bellerica*.

The docking results of phytoligands with the HIV-ENV protein (4CC8) are mentioned in Table 2. The compound ethyl gallate obtained from *Terminalia bellerica* showed a very significant G. score (Glide score) of -9.37Kcal/mol than other ligands. The interacting residue are as follows; GLU-148 (Fig. 1)**.** Followed by the Glide score of -8.17Kcal/mol was p-Cyanophenyl p-(2- propoxyethoxy) benzoa (Fig. 2) from the herb *Corbichonia decumbens*. The residues were GLU-148 and ALA-9 with a bond length (Å) of 2.0 and 2.8. Coniferyl alcohol of *Syzygium cumini*, 1H-Imidazo [1,5-c] thiazole-5,7(6H,7ah)-dio, and Benzenamine, 2,5-dichloro-4-nitr of *Corbichonia decumbens* had a significant g. score of −7.7, −6.42, and −6.12Kcal/mol respectively. The residues that interacted with the ligand are GLU-148, TYR-176, GLU-148, VAL-10, and VAL-108. Kaempferol obtained from *Syzygium cumini* also showed a G. score of -5.21Kcal/mol with residues of VAL-10 and GLU-148. The last three compounds were N-acetyl-3-methoxyamphetamine Methoxyamphetamine (G. score −4.7Kcal/mol), N'-isopropylureidoacetic acid (G. score -3.98), and Cinnamyl acetate, (cis/ Trans) (G. score -4.15Kcal/mol) of the plants *Ocimum sanctum* and *Syzygium cumini*.

Similarly, the docking results of phytoligands with HIV-ENV protein (6ULC) are mentioned in Table 3. This was the second spike protein considered for the docking studies, and the results obtained were comparatively appreciable. The compound cinnamyl acetate showed a G. score of −9.67Kcal/mol (Fig. 3) with residues interacted such as TRP-69. The compound was obtained from the plant *Syzygium cumini*. The other compounds were 2, 5-dihydroxybenzyl alcohol 3 (G. score −9.32Kcal/mol) (Fig. 4) with residue TRP-69 and ethyl gallate (G. score −7.15Kcal/mol) with residue LEU-261, VAL-254, and GLU-482 from the plants *Corbichonia decumbens* and *Terminalia bellerica*. From the medicinal herb *Corbichonia decumbens*, compounds such as 2,4,6,8- Tetraazabicyclo[3.3.0] oct an-3-one (G. score –6.6Kcal/mol), residues LEU-261, LEU-261; p-Cyanophenyl p-(2- propoxyethoxy) benzoa (G. score -5.15Kcal/mol), residues ASN-262, ARG-252; 1H-Imidazo[1,5-c]thiazole-5,7(6H,7ah)- dio (G. score –5.21Kcal/mol), residues ASN-262, ASN-377 were obtained. One compound phenylalanine (G. score -6.2 Kcal/mol) residues LEU-261, LEU-261, and VAL-254 from the plant *Momordica charantia* and two compounds N-acetyl-3-methoxyamphetamine Methoxyamphetamine (G. score –4.96) residue LEU-261 and N'-isopropylureidoacetic acid

Table 1 ADMET analysis of plant compounds

Phytoligands (Pubchem ID)	CNS	mol_MW	Dipole	SASA	Volume	Donor HB	Accptor HB	#metab	Human oral absorption	Percent human oral absorption	Rule of five	Rule of three
	NEG 2–POS 2	130.0–725.0	1.0–12.5	300–1000	500-2000	0–6	2–20	1–8	1- Low, 2- Medium, 3- High	>80%high, < 25%poor	Max 4	max 3
6140	−1	165.191	6.564	372.295	600.139	3	3	4	2	46.895	0	0
13250	−2	198.175	5.594	428.816	675.002	3	4.25	3	3	65.138	0	0
21059	0	140.138	6.141	334.021	510.778	1	3.25	2	3	91.205	0	0
122282	0	198.224	5.832	407.346	677.198	0	4	0	3	86.826	0	0
541553	−2	160.172	10.247	396.896	608.708	2.25	3.25	1	2	56.175	0	0
541954	0	207.272	5.774	482.352	791.418	1	3.25	2	3	95.91	0	0
1549095	0	180.203	4.298	418.158	665.104	2	3.2	3	3	87.32	0	0
5280863	−2	286.24	5.622	501.402	840.36	3	4.5	4	3	64.746	0	0
5282110	0	176.215	3.159	457.308	715.701	0	2	1	3	100	0	0
5375053	1	188.016	6.876	347.027	530.362	1	2	0	3	100	0	0
12313091	2	325.363	3.194	531.376	956.878	1	5	6	3	100	0	0
80364733	−1	223.015	3.966	378.478	595.481	2	2	1	3	79.726	0	0

Phytoligands	#stars	#amide	#rotor	#rtvFG	FOSA	FISA	PISA	QPlogPoct	QPlogPw	QPlogPo/w	QPPCaco	QPlogBB	QPlogKp	QPlogKhsa
	0-5	0-1	0-15	0-2	0-750	7-330	0-450	8−35	4−45	neg 2−6.5	<25 poor, >500 great	Neg 3−1.2	Neg 8−1	Neg 1.5−1.5
6140	0	0	4	0	48.705	138.187	185.404	12.228	9.283	-1.135	30.618	−0.358	−5.092	−0.722
13250	0	0	5	1	140.451	202.814	85.551	13.051	10.19	0.187	118.199	−1.533	−4.476	−0.581
21059	0	0	2	0	134.366	97.257	102.398	8.129	6.106	1.579	1184.715	−0.315	−2.759	−0.616
122282	1	0	0	0	311.971	95.375	0	9.082	5.288	0.777	1234.396	−0.195	−3.277	−0.486
541553	0	1	3	0	225.056	171.84	0	12.174	9.724	0.254	35.473	−1.113	−4.398	−0.978
541954	0	1	4	0	296.541	53.353	132.459	10.911	8.388	1.919	1679.742	−0.161	−1.652	−0.338
1549095	0	0	5	0	175.359	111.757	131.042	10.442	7.355	1.336	863.202	−0.697	−2.638	−0.42
5280863	0	0	4	0	0	235.218	266.185	16.695	12.28	1.06	58.255	−1.803	−4.533	−0.196
5282110	0	0	3	1	163.801	66.979	226.528	8.089	4.124	2.659	2294.743	−0.241	−1.668	0.033
5375053	1	0	0	1	0	64.898	134.129	9.165	5.394	1.913	2401.466	0.408	−2.243	−0.312
12313091	0	0	2	1	315.27	34.48	181.626	14.523	8.416	2.667	1163.658	0.547	−3.386	0.197
80364733	0	0	3	1	0	164.782	84.078	10.037	6.605	1.576	271.189	−0.642	−3.972	−0.361

Table 2 Molecular docking analysis of phyto compounds with HIV-ENV (4CC8) protein

Name of plant	Name of compound	G. Score (Kcal/mol)	Residues interacted	Bond length	No. of bonds
Terminalia bellerica	Ethyl gallate	−9.37	GLU-148 (H–O)	2.1	1
Corbichonia decumbens	p-Cyanophenyl p-(2- propoxyethoxy)benzoa	−8.17	GLU-148 (H–O)	2	2
			ALA -9 (H–O)	2.8	
Syzygium cumini	Coniferyl alcohol	−7.7	GLU-148 (O–H)	2.1	2
			TYR 176 (H–O)	2.5	
Corbichonia decumbens	1H-Imidazo[1,5- c]thiazole-5,7(6H,7ah)- dio	−6.42	GLU 148 (H–O)	2.2	1
Corbichonia decumbens	Benzenamine, 2,5- dichloro-4-nitr	−6.12	VAL 10 (H–O)	2	2
			VAL 108 (H–O)	2	
Syzygium cumini	Kaempferol	−5.21	VAL 10 (H–O)	2	2
			GLU 148 (H–O)	2	
Ocimum sanctum	N-acetyl-3-methoxyamphetamine Methoxyamphetamine	−4.7	GLU 148 (H–O)	2	1
Syzygium cumini	Cinnamyl acetate, (cis/ trans)	−4.15	TYR 176 (O-H)	3.1	1
Ocimum sanctum	N'-isopropylureidoacetic acid	−3.98	GLY 106 (H–O)	2.3	3
			GLY 106 (H–O)	1.9	
			GLU 89 (H–O)	1.6	

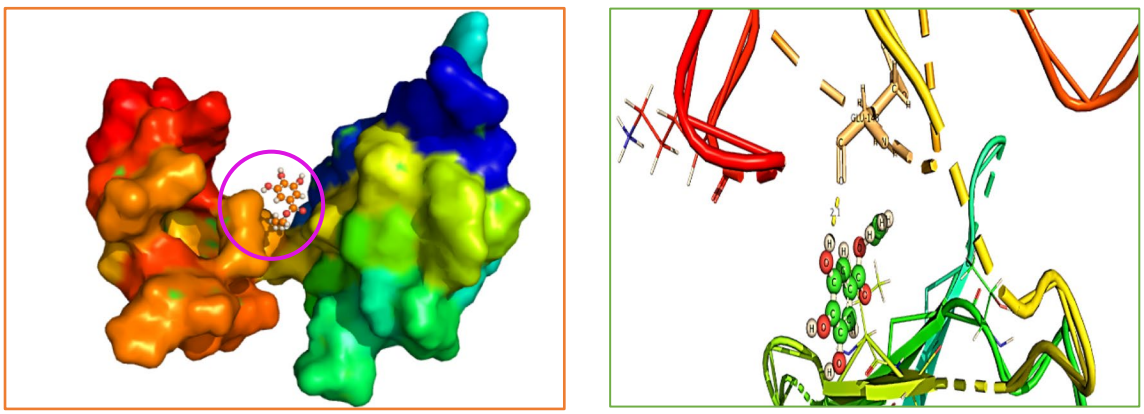

Fig. 1 Interaction of Phytoligand Ethyl gallate with the HIV-ENV (4CC8) protein having a least Glide score of -9.37Kcal/mol extracted from the plant *Terminalia bellerica* indicating a suitable drug candidate molecule

(G. score –4.08Kcal/mol) residues LEU-261, GLU-482, and GLU-482 from the plant *Ocimum sanctum* were successfully docked with the protein.

Discussion

From the beginning, the proposal of work was based on the laboratory needs, but due to the sudden unexpected pandemic we couldn't carry out the wet labs, enforcing us from a complex to a facile work. In future, these could be executed in laboratories to substantiate the existing data. Therefore, the phytoligands from the different plants are collected from the reputed unbiased journal articles.

The most important part of drug discovery and development is conducting DMPK (Drug Metabolism and Pharmacokinetics) studies, also known as ADMET studies. It is believed that ADME shows the toxicity of small molecules (Pajouhesh and Lenz 2005; Mondal et al. 2009). With the advent of drug discovery, *in-silico* works have predominantly seen an upsurge with the assessment of drug efficacy and toxicity levels. ADMET has been given utmost importance right from the beginning of drug discovery using *in-silico* techniques (Selick, Beresford, and Tarbit 2002). Molecular docking is a common method to assess the protein-ligand interaction thereby predicting an efficient binding of the ligand with the target protein molecule. Not only protein-ligand binding, but we can also carry

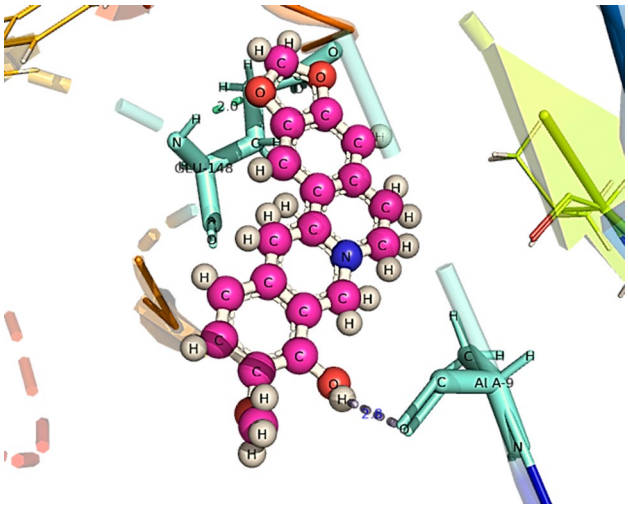

Fig. 2 Interaction of Phyto ligand p-Cyanophenyl p-(2- propoxyethoxy)benzoa with the HIV-ENV (4CC8) protein with the second least Glide score of -8.17Kcal/mol extracted from the plant *Corbichonia decumbens*

out protein-protein, DNA-protein, DNA-ligand interactions (Morris and Lim-Wilby 2008). The binding affinity of a molecule to target is reckoned upon the contributions from various factors such as entropy, de salvation, and flexibility of receptor molecule to the ligand.

Secondary metabolites are defined as a heterogeneous group of natural metabolic products that are not essential for the vegetative growth of the producing organisms. The multitude of secondary metabolite secretions is harvested by humankind to improve their health (antibiotics, enzyme inhibitors, immunomodulators, antitumor agents, and growth promotors of animals and plants), widen the pyramid of healthy nutrition (pigments and nutraceuticals), and hence impacting economics our society in a certain positive way. They are a source of antibiotics (Demain and Fang 2000). Plants are rich in a wide variety of secondary metabolites, such as tannins, terpenoids, alkaloids, and flavonoids, which have been found to have in vitro antimicrobial properties (Rodbey et al. 2000).

Bioactive compounds from medicinal plants are very well utilized for their therapeutic purpose, the preliminary docking studies form a base for these kinds of works (Srinivasan et al. 2011). Most of the compounds studied fall under the class Flavonoids, Tannins, Anthocyanins- Anthocyanidins. Flavonoids are a group of plant metabolites thought to provide health benefits through cell signaling pathways and antioxidant effects. These molecules are found in a variety of fruits and vegetables (Kim et al. 2003). The flavonoids are recognized to function essentially in the management of disorders and diseases in humans (Husain et al. 2017). One flavonoid called quercetin can help to alleviate eczema, sinusitis, asthma, and hay fever. Some studies have shown that flavonoid intake is inversely related to heart disease, with these molecules inhibiting the oxidation of low-density lipoproteins and therefore reducing the risk of atherosclerosis

Table 3 Molecular docking analysis of phyto compounds with the HIV-1-ENV (6ULC) protein

Name of plant	Name of compound	G. Score @ (Kcal/mol)	Residues interacted	Bond length	No. of bonds
Syzygium cumini	Cinnamyl acetate, (cis/ trans)	−9.67	TRP 69 (O–H)	2	1
Corbichonia decumbens	2,5-dihydroxybenzyl alcohol 3	−9.32	TRP 69 (O–H)	2	1
Terminalia bellerica	Ethyl gallate	−7.15	LEU 261 (O–H)	2	3
			VAL 254(H–O)	2.3	
			GLU 482 (H–O)	2.1	
Corbichonia decumbens	2,4,6,8- Tetraazabicyclo[3.3.0]oct an-3-one	−6.6	LEU 261 (O–H)	1.9	2
			LEU 261 (O–O)	3.3	
Momordica charantia	Phenylalanine	−6.2	LEU 261 (O–H)	2.4	3
			LEU 261 (H–O)	2.6	
			VAL 254 (O–H)	2.1	
Corbichonia decumbens	p-Cyanophenyl p-(2- propoxyethoxy)benzoa	−5.15	ASN 262 (O–H)	2.4	2
			ARG 252 (O–H)	2.5	
Corbichonia decumbens	1H-Imidazo[1,5- c]thiazole-5,7(6H,7ah)- dio	−5.21	ASN 262 (N–H)	2.6	2
			ASN 377(H–O)	1.9	
Ocimum sanctum	N-acetyl-3-methoxyamphetamine Methoxyamphetamine	−4.96	LEU 261 (O–H)	1.7	1
Ocimum sanctum	N'-isopropylureidoacetic acid	−4.08	LEU 261 (H–O)	1.7	3
			GLU 482(H–O)	2.6	
			GLU 482 (H–O)	2.1	

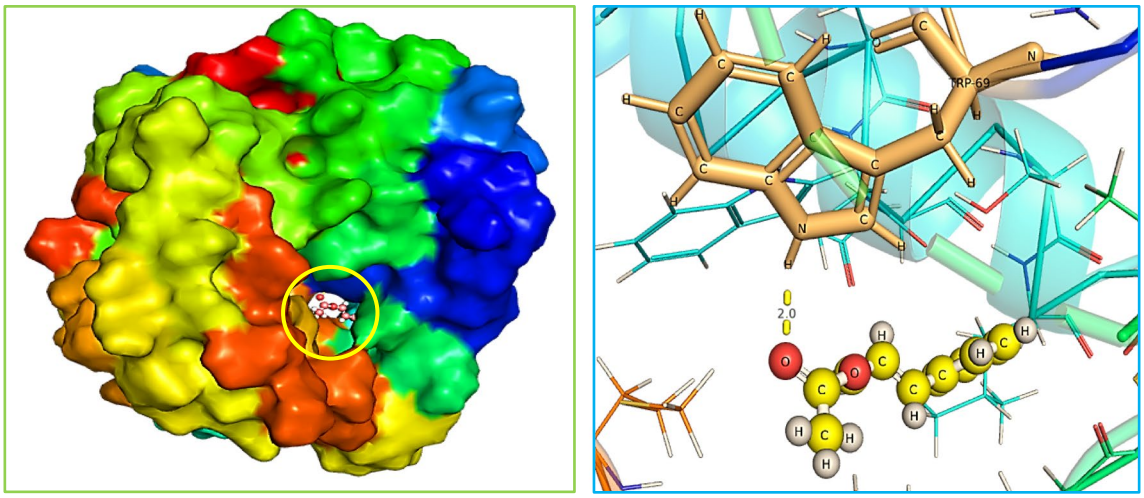

Fig. 3 Interaction of Phytoligand Cinnamyl acetate, (cis/ trans) with HIV-1-ENV protein (6ULC) extracted from plant *Syzygium cumini* with the least Glide score of -9.67Kcal/mol suggesting a new drug candidate molecule

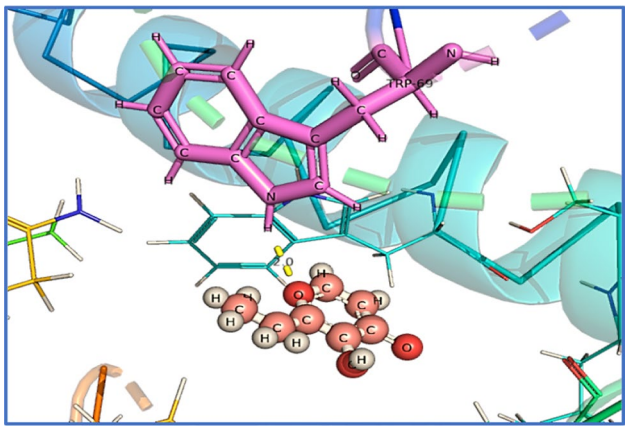

Fig. 4 Interaction of Phyto ligand 2,5-dihydroxybenzyl alcohol 3 with HIV-1-EVN protein (6ULC) with the second least Glide score of -9.32Kcal/mol extracted from *Terminalia bellerica*

developing (Pasetto, Pardi and Murata 2014)**.** Tannin, also called tannic acid**,** is a class of phenolic compounds in woody flowering plants that are important deterrents to herbivores and have several industrial applications. Because of its styptic and astringent properties, tannin has been used to treat tonsillitis, pharyngitis, hemorrhoids, and skin eruptions; it has been administered internally to check diarrhea and intestinal bleeding and as an antidote for metallic, alkaloidal, and glycosidic poisons, with which it forms insoluble precipitates (Encyclopedia Britannica 2021*).* On the other hand, plant anthocyanins have been widely studied for their medicinal values. Anthocyanins are commonly found in flowers and the fruits of many plants. Most of the red, purple, and blue-colored flowers contained anthocyanins. Red flowers are red hibiscus, red rose, red pineapple sage, red clover, and pink blossom. These red flowers are edible. Blue, red, and purple-colored pigments extracted from flowers, fruits, and vegetables are traditionally used as dye and food colorants. Besides being used as natural colorants, some of the anthocyanin-rich flowers and fruits have been traditionally used as medicine to treat various diseases Anthocyanins possess antidiabetic, anticancer, anti-inflammatory, antimicrobial, and anti-obesity effects, as well as prevention of cardiovascular diseases (CVDs) (Khoo et al. 2017).

Terminalia bellerica is a type of medicinal plant abundantly found in the Indian Subcontinent, Sri Lanka, Bangladesh, etc. There are a wide variety of constituents which serves as an antioxidant, antimicrobial, antidiarrheal, anticancer, antipyretic agent (Anindita, Sikha, and Biswajit 2016). Ethyl gallate is a food additive denoted by the E313, it is obtained by the formal condensation of gallic acid with ethanol. It is also present naturally in a variety of plant sources including walnuts, etc. It is well known for its antioxidant and anticancer properties (Mohan, Thiagarajan, and Chandrasekaran 2017). Traditionally *C. decumbens* leaves are used as an herbal alternative for healing various diseases such as to treat gonorrhea and kidney stones. Root paste can be consumed orally for treating yellow and white jaundice. Similarly, the crude extract shows antioxidant, anti-inflammatory, and antiulcer activities (Arora and Saini 2018). *Syzygium cumini* is an evergreen tropical tree, also known as Malabar plum, Java Plum, or even jambolana which has been used against dysentery, inflammation, and diabetes mellitus (Shafi et al. 2002). The plant is a rich repository of secondary metabolites such as anthocyanins, glucoside, ellagic acid, isoquercetin, kaemferol, and myricetin, and the plant as a whole is medicinally effective (Ayyanar and Subash-Babu 2012). Kaempferol is well known for its medicinal

activity, it is said to provide the body with the best antioxidant defense system against free radicals. It regulates apoptosis, angiogenesis, inflammation, and metastasis (Chen and Chen 2013). *Momordica Charantia*, commonly known as bitter gourd, karela, or balsam pear whose fruits are used for diabetic treatment, anticancer, anti-inflammation, antiviral, and has cholesterol-lowering effects. The fruits, stems, leaves, as well as roots of bitter melon aids in the treatment of ailments such as hyperlipidemia, digestive disorders, microbial infections, and menstrual problems (Baby and Jini 2013). Different parts of the Ocimum sanctum are used since traditional systems for the treatment of skin diseases, arthritis, asthma, malaria, and many more. Tulsi possesses a wide variety of therapeutic uses such as antidiabetic, antimicrobial, hepatoprotective, cardioprotective, antispasmodic, analgesic actions (Prakash and Neelu 2005).

Conclusion

The study focused on HIV/AIDS a sexually transmitted viral infection that affects the human immune system. Antiretroviral therapy is the only mode of effective treatment available even after 30 years of onset of disease. The treatments procedure currently followed are highly expensive and cannot be taken by a common man. Here, Phyto-compounds are predicted with significant interactions with target protein indicating the potency in the treatment. Ethyl gallate showed least docking score with the protein HIV-ENV (4CC8). Followed by Cinnamyl acetate (cis/trans) from *Syzygium cumini* with the target protein HIV-1-ENV (6ULC). Therefore, it is summarized that Phyto-compounds have a better drug candidate for HIV/AIDS. It is to be noted that *in-vitro* & *in-vivo* assessment will be essential and looking forward that these computational results would prove to be helpful in successful drug development.

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Declarations

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Conflict of interest S. Sreeram has no conflict of interest. R. Sathishkumar has no conflict of interest. P. S. Amritha has no conflict of interest.

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