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Docking study of HIV-1 reverse transcriptase with phytochemicals

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Received August 29, 2010; Accepted October 22, 2010; Published February 15, 2011

Abstract:
Natural products are important sources of drug discovery. In this context groups of different set of phytochemicals were taken and docked into the different cavities of the Reverse transcriptase (PDB ID: 1REV) of Human immunodeficiency virus (HIV) and results were discussed. Natural compounds such as Curcumin, Geranin, Gallotannin, Tiliroside, Kaempferol-3-o-glucoside and Trachelogenin were found to very effective according to its binding energy and ligand efficiency score. Those compounds also were found to have no adverse effect as carcinogenicity and mutagenicity and favorable drug likeness score. Hence, considering the facts those compounds could use effectively for HIV-1 drug discovery.

Background:
Human immunodeficiency virus (HIV) is a lentivirus (a member of the retrovirus family) that causes *acquired immunodeficiency syndrome* (AIDS), **[1-2]** a condition in humans in which the immune system begins to fail, leading to life-threatening opportunistic infections. Once HIV enters the human body, its primary target is a subset of immune cells that contain a molecule called CD4. In particular, the virus attaches itself to CD4+T cells and, to a lesser extent, to macrophages. Reverse Transcriptase (RT) converts the single-stranded HIV RNA genome to a double-stranded DNA copy by catalyzing both DNA-dependent and RNA-dependent DNA polymerization as well as RNase H cleavage activity to remove the RNA template once the DNA has been synthesized. Because of its unique catalytic properties, RT has been the target enzyme for many antiviral therapeutic agents used in the treatment of AIDS, including nucleoside and nonnucleoside analogues **[3-6]**.

The aim of molecular docking is to evaluate the feasible binding geometries of a putative ligand with a target whose target site is known. The binding geometries is often known as binding poses, includes, in principle, both the position of the ligand relative to the receptor and conformational state of the ligand and the receptor. There are three basic tasks any docking procedure must accomplish: (1) characterization of the binding site; (2) positioning of the ligand into the binding site (orienting); and (3) evaluating the strength of interaction for a specific ligand-receptor complex ("scoring"). The first challenge for computer-aided design is to identify one or more lead compounds that show activity in an appropriate assay. Until recently most drugs in the market come from the lead compounds discovered by screening of natural products or exploring the analogues of known structures.

There are many small molecule databases in public domain such as ZINC, Pubchem, ChemDB, ChemSpider, KEGG ligand database and DrugBank for virtual screening. The procedure of structure based virtual screening through docking has become crucial when it is necessary to test a database of thousands of compounds against one or more protein targets in a feasible time.

An increasing number of patients with HIV infection cannot use the currently approved anti-HIV drugs, including the reverse transcriptase and protease inhibitors, due to the adverse effects and the emergence of drug resistance, the search for new effective and safe as well as affordable anti-HIV agents is not merely an academic curiosity but rather a necessity **[7]**. It is important to note that a number of promising anti-HIV natural products have made it to the clinical level and are anticipated to be available to patients very soon **[7]**. The following natural products can be cited as promising anti-HIV agents of plant origin: baicalin (a flavonoid) **[8]**, calanolides (coumarins) **[9]**, betulinic acid (a triterpene) **[10-11]**, polycitone A (an alkaloid) **[12]**, lithospermic acid, sulphated polysaccharides, cyanovirin-N **[13]**, pokeweed antiviral protein [**14**] and alpha-trichobitacin (proteins). In this context six different set of phytochemicals were taken and docked into the cavities of the Reverse transcriptase and results were discussed.

Methodology:
The three dimensional structure of target HIV reverse transcriptase (PDBID: 1REV) was retrieved from protein data bank at 2.6 Å RMSD resolution. Phytochemicals with anti-HIV activity such as Curcumin, Geranin, Gallotannin, Tiliroside, Kaempferol-3-o-glucoside and Trachelogenin were obtained from Dr. Duke database (http://www.ars-grin.gov/duke/), which were searched against pubchem and chemspider database for the 2D structures and then with the help of open babel [http://openbabel.org/wiki/Main_Page] these 2D structures are converted to 3D structures. The 3D structures which are obtained are minimized using Hyperchem's MM+ force field. Molegro Virtual Docker **[15]** was used to detect the active sites and docking was performed by moldock function, which is an implementation of evolutionary algorithms (EAs), focused on molecular docking simulations. Docking was performed with all the potential active sites detected on HIV reverse transcriptase enzyme. During Docking at first the molecules were prepared and bonds, bond orders, explicit hydrogens, charges, flexible torsions, were assigned if they were missing by the MVD program to both the protein and ligands. From the docking wizard ligands were selected and the scoring function used is Moldock score. The Ignore distant atoms option is used to ignore atoms far away from the binding site. It reduces overall computing time. The Enforce hydrogen bond directionality option is used to check if bonding between potential hydrogen bond donors and acceptors can occur. If hydrogen bonding is possible, the hydrogen bond energy contribution to the docking score is assigned a penalty based on the deviations from the ideal bonding

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angle. Using this option can significantly reduce the number of unlikely hydrogen bonds reported also internal electrostatic interaction, internal hydrogen bond sp2-sp2 torsions are calculated from the pose by enabling the ligand evaluation terms. The search algorithm is taken as Moldock SE and numbers of runs are taken 10 and max iterations were 2000 with population size 50 and with an energy threshold of 100 also at each step least 'min' torsions/translations/rotations are tested and the one giving lowest energy is chosen. If the energy is positive (i.e. because of a clash or an unfavorable electrostatic interaction) then additional 'max' positions will be tested. Pose clustering was done by tabu based clustering method, using this clustering technique each found solution is added to a 'tabu list': during the docking simulation the poses are compared to the ligands in this 'tabu list'. If the pose being docked is closer to one of the ligands in the list than specified by the RMSD threshold, an extra penalty term (the Energy penalty) is added to the scoring function. This ensures a greater diversity of the returned solutions since the docking engine will focus its search on poses different from earlier poses found. The energy penalty was set to 100, RMSD threshold was 2.00 and RMSD calculation by atom ID (fast) were set.

After the docking simulation is over the poses which were generated were sorted by rerank score. The Rerank Score uses a weighted combination of the terms used by the MolDock score mixed with a few addition terms (the Rerank Score includes the Steric (by LJ12-6) terms which are Lennard-Jones approximations to the steric energy – the MolDock score uses a piecewise linear potential to approximate the steric energy) **[15]**. The reranking score function is computationally more expensive than the scoring function used during the docking simulation but it is generally better than the docking score function at determining the best pose among several poses originating from the same ligand **[15]**. Ligand efficiency is most commonly defined as the ratio of the free energy of binding over the number of heavy atoms in a molecule **[18]**. Binding affinities were calculated using Molegro data modeler and MVD used to find Ligand Efficiency 1(LE 1) as Moldock score divided by Heavy Atoms count, ligand efficiency 2(LE2) as a result of binding Affinity divided by Heavy Atoms count and Ligand Efficiency 3 (LE 3) as rerank Score divided by Heavy Atoms count.

The coefficients for the binding affinity terms were derived using multiple linear regression. The model was calibrated using a data set of more than 200 structurally diverse complexes from the PDBbind database with known binding affinities (expressed in kJ/mol) **[16]**. The Pearson correlation coefficient was 0.60 when doing 10-fold cross validation. It is important to note that this particular model was trained only on strongly interacting ligands in their optimal conformation known from the PDB complexes. Since the binding affinity measure was trained using known binding modes only, it might sometimes assign too strong binding affinities to weakly or non-binding molecules (false positives). Therefore recommend ranking the results of a virtual screening run using the rerank score. The binding affinity measure may then be used subsequently to get a rough estimate of the highest ranked poses.
The scoring function used by MolDock is derived from the piecewise linear potential (PLP) scoring functions **[17]**. The scoring function used by MolDock further improves these scoring functions with a new hydrogen bonding term and new charge schemes **[15]**. Based on evolutionary agorithms (EAs) classification moldock algorithm may be classified as an Evolutionary simulator (ES), since it employs direct ranking of the solutions and the crossover operators. MolDock showed better overall performance in docking simulations when compared with other software.

ADMET (Absorption, Distribution, Metabolism, Excretion and Toxicity) properties were predicted using PreADMET server (http://preadmet.bmdrc.org/) to know whether the phytochemicals has the potential of adverse effect in human.

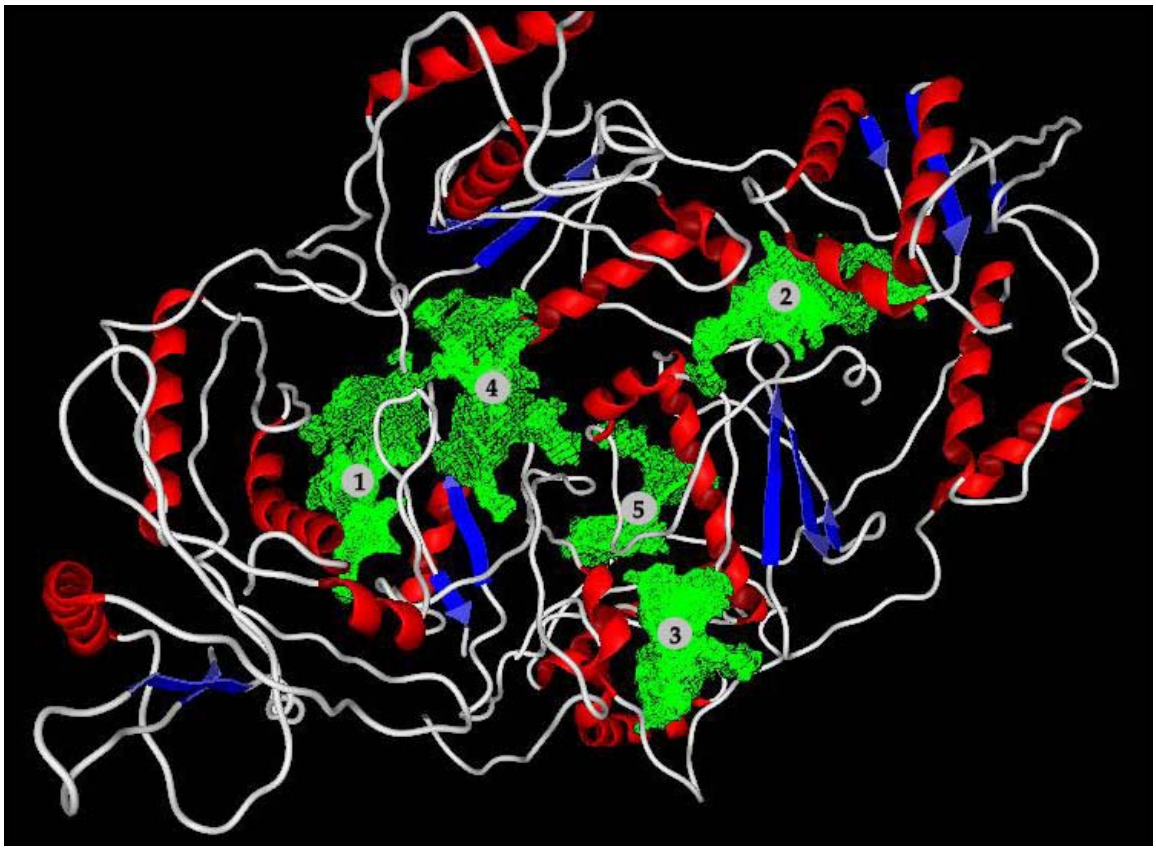

Figure 1: Five cavities detected in reverse transcriptase enzyme (PDB ID: 1REV)

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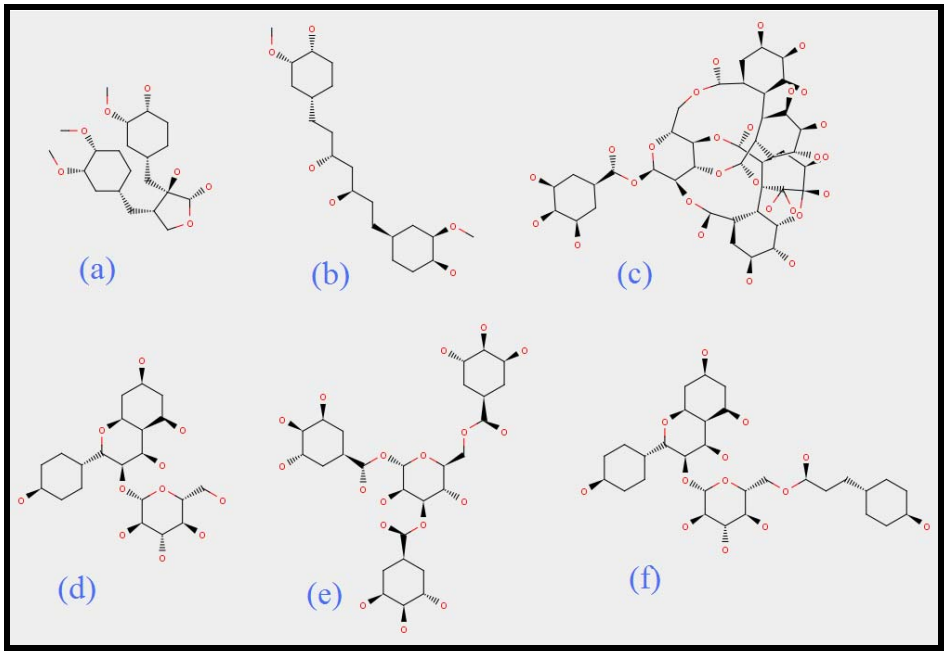

Figure 2: Structure of compounds used for docking study. (a) Trachelogenin (b) Curcumin (c) Geraniin (d) Kaempferol-3-O-Glucoside (e) Gallotannin (f) Tiliroside

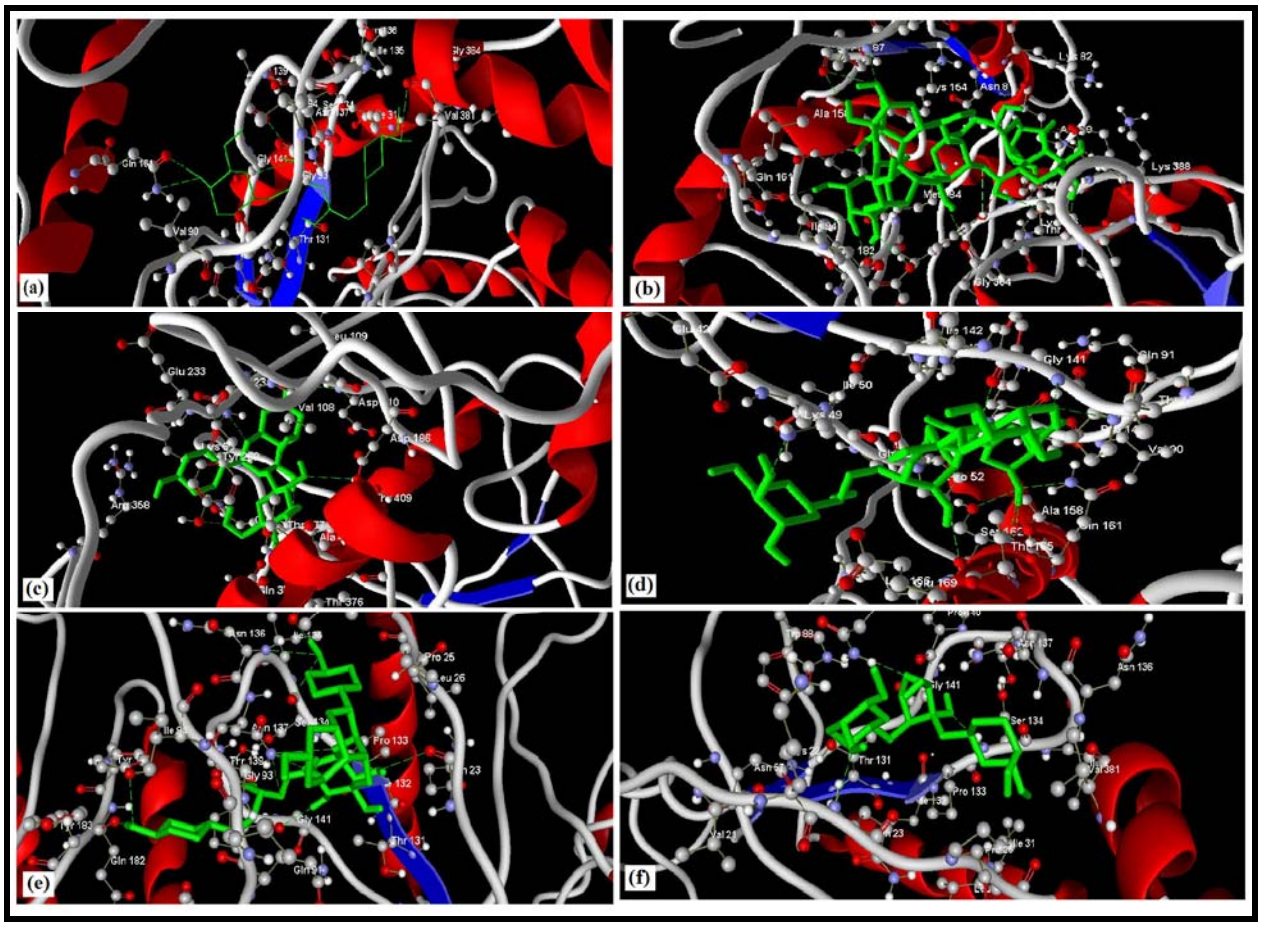

Figure 3: Different ligands at highly bound cavity. (a) cucurmin in cavity 1, (b) geranin in cavity 2, (c)kaempferol-3-o-glucoside in cavity 5, (d) gallotannin in cavity 3, (e) tiliroside in cavity 1, (f) trachelogenin in cavity 1

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Results and Discussion:
A total of five cavities **(Figure 1)** were able to detected in reverse transcriptase enzyme (PDB ID: 1REV) by using Molegro Virtual Docker and were named cav1, cav2, cav3, cav4 and cav5, the volume and surface area details were given as **Table 1(see Supplementary material).** Details of five cavities are given in **Table 4(see Supplementary material)**.

Reverse Transcriptase has, there are two p66 domains and one p51 domain. p66 and p51 share a common amino terminus; p66 is 560 amino acids in length, p51 is 440 amino acids long. The larger subunit of the RT heterodimer, p66, contains the active sites for both of the enzymatic activities of RT (polymerase and RNase H); the smaller subunit plays a structural role. p66 is composed of two spatially distinct domains, polymerase and RNase H. The polymerase domain is composed of four subdomains: fingers (residues 1–85 and 118–155), palm (residues 86–117 and 156–236), thumb (237–318), and connection (319–426). The nucleic-acid binding cleft is formed primarily by the p66 fingers, palm, thumb, connection, and RNase H subdomains of p66. The polymerase active site is composed of three catalytic carboxylates in the palm subdomain of p66 (D110, D185, and D186) that bind two divalent ions **[19]**. The cavity 5 has such residues in them and the residue shows their contributions to their inhibitors.

Curcumin is mainly found in *Curcuma longa, Curcuma xanthorrhiza, Curcuma zedoaria, Costus speciosus* and *Zingiber officinale*. Geranin is found in *Phyllanthus amaru*, *Erythroxylum coca var. coca*, *Geranium thunbergii*, *Spondias pinnata* and *Terminalia catappa.* Gallotannin is found in following plants *Camellia sinensis, Salvia officinalis, Arctostaphylos uva-ursi, Juniperus communis, Rosmarinus officinalis, Vaccinium myrtillus, Ginkgo biloba, Prunus cerasus, Psidium guajava, Thymus vulgaris, Plantago major, Urtica dioica, Achillea millefolium, Equisetum arvense, Fragaria spp, Terminalia catappa, Cynara cardunculus subsp. Cardunculus* and *Glechoma hederacea.* The compound tiliroside is found in *Althaea officinalis, Helianthemum glomeratum, Pteridium aquilinum, Rosa spp, Tilia sp*. Trachelogenin found in *Arctium lappa* and *Cnicus benedictus.* The compound kaempferol-3-o-glucoside found in *Vitis vinifera, Urtica dioica and Echinacea spp.* Structures of each compound is displayed in **Figure 2**.

All the phytochemicals were used as ligand at mentioned 5 cavities of reverse transcriptase enzyme (PDB ID: 1REV) and the results of the top ligands whose rerank score > -100 were selected and which were given in **Table 2(a-e) (see Supplementary material)** of the context along with the hydrogen bond interaction values, the hydrogen bond number and other electrostatic interaction values. Binding pose of each ligand at their highly bound cavity is showed in **figure 3**. Selected phytochemicals were studied with potential Anti HIV compound 4,5,6,7-tetrahydroimidazo[4,5,1-jk][1,4]benzodiazepin-2(1H)-thione (TIBO) **[20]** and rerank score and moldock score were found to be good than (TIBO) **(Table 5 see Supplementary material)**. A study also conducted by using similar structural analogue of ligands in all the cavities and phytochemicals showed higher binding score than structural analogue **(Table 6 see Supplementary material)**.

The molecules were searched for Lipinski rule of 5, lead like rule, CMC like rule, MDDR like rule, WDI like rule, Reactive functional group for drug likeness. Typical ADME prediction methods involves Caco-2cell permeability, Madin-Darby Canine Kidney Cell Permeability (MDCK), Human Intestinal Absorption (HIA), Skin Permeability, Blood-Brain Barrier (BBB) penetration were also calculated for the molecules along with the mutagenicity and carcinogenicity test based on Ames Test using PreADMET online webserver (http://preadmet.bmdrc.org/). The results of ADMET and drug-likeness are given as **Table 3 (see Supplementary material)**. All the phytochemicals were bound to its target with rerank scores ranging from -100.56 to -136.23 at multiple binding sites on the enzyme. ADMET prediction resulted any carcinogenic effects in selected compounds. Trachelogenin found to be mutagenic by Ames test model of preADMET **(Table 3 see Supplementary material)**. These results will probably become a lead phytochemical for further drug discovery process.

References:
[1] RA Weiss, *Science* (1993) **260:** 5112 [PMID 8493571]
[2] DC Douek *et al. Annu Rev Med.* (2009) **60**: 471 **[**PMID 18947296]
[3] E De Clercq, *Biochem Pharmacol.* (1994) **47**: 155 [PMID: 7508227]
[4] E De Clercq, *Clin Microbiol Rev*. (1997) **10**: 674 [PMID: 9336668]
[5] SP Goff, *J Acquired Immune Defic Syndr.* (1990) **3**: 817 [PMID: 1694894]
[6] H Mitsuya *et al. Science* (1990) **249**: 4976 [PMID: 1699273]
[7] K Asres *et al. Phytother Res*. (2005) **19**: 557 [PMID: 16161055]
[8] K Kitamura *et al. Antivir Res.* (1998) **37**: 131 [PMID: 9588845]
[9] P Zhou *et al. Phytochemistry* (2000) **53**: 689 [PMID: 10746882]
[10] RH Cichewicz & SA Kouzi, *MedRes Rev.* (2004) **24**: 94 [PMID: 14595673]
[11] SL Holz-Smith *et al. Antimicrob Agents Chemother*. (2001) **45**: 60 [PMID: 11120945]
[12] S Loya *et al. Biochem J.* (1999) **344**: 85 [PMID: 10548537]
[13] B Dey *et al. J Virol*. (2000) **74**: 4562 [PMID: 10775592]
[14] FM Uckun *et al. Antimicrob Agents Chemother.* (1998) **42**: 383 [PMID: 9527790]
[15] R Thomsen & MH Christensen, *J Med Chem.* (2006) **49**: 3315 [PMID: 16722650]
[16] R Wang *et al. J Med Chem.* (2004) **47**: 2977 [PMID: 15163179].
[17] JM Yang & CC Chen, *Proteins* (2004) **55**: 288 [PMID: 15048822]
[18] C Abad-Zapatero & JT Metz, *Drug Discov Today.* (2005) **10**: 464 [PMID: 15809192]
[19] SG Sarafianos *et al. J Mol Biol.* (2009) **385**: 693 [PMID: 19022262]
[20] R Pauwels *et al. Nature* (1990) **343**: 6257 [PMID: 1689015]

Edited by A Cherkasov
Citation: Seal *et al.* Bioinformation 5(10): 430-439 (2011)
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Supplementary material:

Table 1: Cavity information of enzyme (1REV.pdb)

Cavity Name	Volume(Å^3)	Surface Area(Å^2)
Cav1	497.664	1689.6
Cav2	425.984	1276.16
Cav3	387.584	1290.24
Cav4	365.568	1058.56
Cav5	342.016	912.64

Table 2(a): Docking result at Cavity one

Ligand name	Molecular formula	MolDock Score	Rerank Score	No of H Bond	HBond Energy	Binding Affinity	Ligand efficiency			Interacting_Residues
							LE1	LE2	LE3	
Curcumin	$C_{21}H_{20}O_6$	-144.75	-110.84	7	-5.87	-11.22	-5.36	-0.41	-4.10	Gln 161, Gln 161, Pro 140, Thr 139, Ser 134, Ser 134, Val 381
Geraniin	$C_{41}H_{28}O_{27}$	-121.93	-110.14	11	-14.14	5.14	-1.79	0.08	-1.62	Gln 23, Gln 23, Gln 23, Gln 23, Pro 25, Ile 94, Asn 137, Gly 93, Pro 140, Gly 91, Lys 22
Gallotannin	$C_{27}H_{24}O_{18}$	-150.38	-111.14	15	-16.01	1.82	-3.34	0.04	-2.47	Gln 91, Pro140,Thr 139, Asn 137, Ser134, Gln 23 , Val 21, Asn 57
Tiliroside	$C_{30}H_{26}O_{13}$	-183.39	-134.95	14	-15.23	-8.27	-4.26	-0.19	-3.14	Tyr 181, Val 381, Ile 132, Pro 140 ,Gln 23, Asn 137, Ser 134, Asn 136, Thr 139, Gln 182
Kaempferol-3-o-glucoside	$C_{21}H_{20}O_{11}$	-153.02	-110.3	12	-10.40	-11.47	-4.78	-0.36	-3.45	Asn 137 ,Ile132,Pro 140 ,Gln23, Leu26, Ser 134,Thr 139
Trachelogenin	$C_{21}H_{24}O_7$	-128.58	-107.07	3	-6.82	-19.37	-4.59	-0.69	-3.82	Ser 134, Gln 23, Gln 91

Table 2(b). Docking result at Cavity two

Ligand name	Molecular formula	MolDock Score	Rerank Score	No of H Bond	H Bond	Binding Affinity	Ligand efficiency			Interacting Residues
							LE1	LE2	LE3	
Geraniin	$C_{41}H_{28}O_{27}$	-217.3	-136.23	19	-18.44	-8.37	-3.20	-0.12	-2.00	Phe 87, Phe 87, Phe 87, Gly 384, Thr 386, Thr 386, Glu 413, Glu 413, Glu 413, Tyr 183, Tyr 183, Tyr 181, Ile 411, Ile 411, Gln 182, Gln 182, Gln 182, Lys 154, Glu 413
Gallotannin	$C_{27}H_{24}O_{18}$	-166.53	-123.11	5	-18.80	-2.87	-3.70	-0.06	-2.74	Tyr 181, Asn 81, Lys 154, Gln 182
Tiliroside	$C_{30}H_{26}O_{13}$	-168.47	-111.34	10	-9.75	-4.73	-3.92	-0.11	-2.59	Gln 161, Ala 158, Phe 87, Pro 95, Ile 94,Tyr 181, Gln 182,Met 184

Table 2(c) Docking result at Cavity three

Ligand name	Molecular formula	MolDock Score	Rerank Score	No of H Bond	H Bond	Binding Affinity	Ligand efficiency			Interacting Residues
							LE1	LE2	LE3	
Gallotannin	$C_{27}H_{24}O_{18}$	-155.14	-128.16	4	-17.61	1.60	-3.45	0.04	-2.85	Arg 172, Gly 141, Arg 143, Gln 161
Trachelogenin	$C_{21}H_{24}O_7$	-136.75	-104.60	11	-10.46	-19.38	-4.88	-0.69	-3.74	Glu 169, Lys 173, Glu 89, Gly 141, Pro 140, Thr 39, Glu 42, Tyr 144, Ile 50

Table 2(d): Docking result at Cavity four

Ligand name	Molecular formula	MolDock Score	Rerank Score	No of H Bond	H Bond	Binding Affinity	Ligand efficiency			Interacting_Residues
							LE1	LE2	LE3	
Gallotannin	$C_{27}H_{24}O_{18}$	-132.75	-109.48	7	-22.01	-0.78	-2.95	-0.02	-2.43	Gln 507, Glu 404, Trp 406, Lys 431, Tyr 532

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Tiliroside	$C_{30}H_{26}O_{13}$	-182.88	-127.85	16	-11.83	-9.18	-4.25	-0.21	-2.97	Gln 500, Gly 504, Arg 354, His 361, Lys 366,Trp 406,Gly 504,Glu 404, Gln 507, Asn 418, Thr 419,Pro 420
Kaempferol-3-o-glucoside	$C_{21}H_{20}O_{11}$	-140.62	-100.56	9	-10.87	-10.63	-4.39	-0.33	-3.14	Glu 430, Leu 533, Tyr 532, Gln 509, Gln 507, Lys 431,Glu 404

Table 2(e): Docking result at Cavity five

Ligand name	Molecular formula	MolDock Score	Rerank Score	No of H Bond	H Bond	Binding Affinity	Ligand efficiency			Interacting_Residues
							LE1	LE2	LE3	
Kaempferol-3-o-glucoside	$C_{21}H_{20}O_{11}$	-168.548	-118.36	8	-5.709	-6.038	-5.26	-0.18	-3.69	Trp 410, Asp 186, Gln 407, Tyr 232, Tyr 354, Glu 370
Gallotannin	$C_{27}H_{24}O_{18}$	-167.67	-127.30	11	-13.12	-1.66	-3.72	-0.04	-2.83	Gln 373, Gly 231,Tyr 232 , Glu 233, Arg 358,Tyr 405, Gln 407, Lys 366, Glu 404
Tiliroside	$C_{30}H_{26}O_{13}$	-196.749	-133.33	5	-3.39	-3.61	-4.58	-0.08	-3.1	Glu 370,Tyr 232, Gly 231, Gln 407
Trachelogenin	$C_{21}H_{24}O_7$	-119.203	-102.71	3	-4.07	-18.29	-4.26	-0.65	-3.67	Glu 233, Gln 407,Tyr 232

Table 3. Toxicity and Drug-likeness report of the molecule

Ligand	Formula	CMC like rule	Lead like rule	MDDR Rule	Rule of 5	WDI Rule	HIA%	C2C Permeability (nm/sec)	MDCK (nm/sec)	Logkp cm/hr	PPB (%)	BBB c.brain/ c.blood	AMES test
Curcumin	$C_{21}H_{20}O_6$	Q	violated	MS	Suitable	out of 90% cutoff	76.07	19.18	25.52	-3.85	70.35	0.2612	NM
Geraniin	$C_{41}H_{28}O_{27}$	NQ	violated	MS	violated	out of 90% cutoff	0	16.51	0.0434	-4.76	4.3979	0.027001	NM
Kaempferol-3-o-glucoside	$C_{21}H_{20}O_{11}$	NQ	violated	MS	violated	out of 90% cutoff	6.46	11.51	0.468	-5.141	30.74	0.029	NM
Gallotannin	$C_{27}H_{24}O_{18}$	NQ	violated	MS	violated	out of 90% cutoff	0	8.95	13.73	-5.005	7.37	0.02718	NM
Tiliroside	$C_{30}H_{26}O_{13}$	NQ	violated	MS	violated	out of 90% cutoff	6.182	15.92	0.396	-4.99	36.84	0.03101	NM
Trachelogenin	$C_{21}H_{24}O_7$	Q	violated	MS	Suitable	In 90% cutoff	83.26	24.63	1.989	-4.403	47.399	0.08727	M

Carcinogenity (Mouse), Carcinogenity (Rat) result of all the compound found as negative. NQ = Not qualified, Q = Qualified, MS = Mid-Structure, NM = Non-Mutagen, M = Mutagen, HIA = Human Intestinal Absorption, PPB = Plasma Protein Binding, BBB = Blood Brain Barrier, C2C = CaCo 2 Cell, MDCK = Madin-Darby canine kidney cell, WDI = World Drug Index

Table 4:

(a) Cavity 1:			(b) Cavity 2:		
Secondary strucure	Target Atoms:Molecule	Residue ID	Secondary strucure	Target Atoms:Molecule	ResidueID
C	1REV [B]	Val 21	H	1REV [B]	Phe77
C	1REV [B]	Lys22	H	1REV [B]	Arg78
C	1REV [B]	Gln23	H	1REV [B]	Glu79
C	1REV [B]	Trp24	H	1REV [B]	Asn81
C	1REV [B]	Pro25	H	1REV [B]	Lys82
H	1REV [B]	Leu26	C	1REV [B]	Gln85
H	1REV [B]	Ile31	C	1REV [B]	Asp86
C	1REV [B]	Asn57	C	1REV [B]	Phe87
C	1REV [A]	Trp88	C	1REV [B]	Trp88
C	1REV [A]	Glu89	C	1REV [B]	Leu92
C	1REV [A]	Val90	C	1REV [B]	Ile94
C	1REV [A]	Gln91	C	1REV [B]	Pro95
C	1REV [A]	Leu92	C	1REV [B]	His96
C	1REV [A]	Gly93	H	1REV [B]	Lys154
C	1REV [A]	Ile94	H	1REV [B]	Gly155
C	1REV [A]	Pro95	H	1REV [B]	Pro157
C	1REV [A]	His96	H	1REV [B]	Ala158
E	1REV [B]	Thr131	H	1REV [B]	Ile159
E	1REV [B]	Ile132	H	1REV [B]	Gln161

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C	1REV [B]	Pro133	H	1REV [B]	Ser162
T	1REV [B]	Ser134	C	1REV [B]	Tyr181
T	1REV [B]	Ile135	C	1REV [B]	Gln182
C	1REV [B]	Asn136	T	1REV [B]	Tyr183
T	1REV [B]	Asn137	C	1REV [B]	Met184
T	1REV [B]	Thr139	C	1REV [B]	Tyr319
C	1REV [B]	Pro140	C	1REV [B]	Trp383
C	1REV [B]	Gly141	C	1REV [B]	Gly384
H	1REV [A]	Gln161	C	1REV [B]	Lys385
C	1REV [A]	Tyr181	C	1REV [B]	Thr386
C	1REV [A]	Gln182	C	1REV [B]	Pro387
T	1REV [A]	Tyr183	E	1REV [B]	Lys388
C	1REV [A]	Tyr232	C	1REV [B]	Ile411
E	1REV [A]	Lys350	C	1REV [B]	Pro412
H	1REV [A]	Thr377	C	1REV [B]	Glu413
H	1REV [A]	Glu378			
H	1REV [A]	Ile380			
H	1REV [A]	Val381			
H	1REV [A]	Ile382			
H	1REV [A]	Gly384			

(c) Cavity 3:

Secondary structure	Target Atoms:Molecule	ResidueID
C	1REV [B]	Val21
C	1REV [B]	Lys22
C	1REV [B]	Gln23
C	1REV [B]	Trp24
C	1REV [B]	Pro25
C	1REV [B]	Leu26
H	1REV [B]	Ile31
H	1REV [B]	Glu42
B	1REV [B]	Ser48
C	1REV [B]	Lys49
C	1REV [B]	Ile50
T	1REV [B]	Gly51
C	1REV [B]	Pro52
C	1REV [B]	Asn57
C	1REV [A]	Trp88
C	1REV [A]	Glu89
C	1REV [A]	Val90
C	1REV [A]	Gln91
E	1REV [B]	Thr131
E	1REV [B]	Ile132
C	1REV [B]	Pro133
C	1REV [B]	Ser134
C	1REV [B]	Ile135
C	1REV [B]	Asn136
T	1REV [B]	Asn137
C	1REV [B]	Thr139
C	1REV [B]	Pro140
C	1REV [B]	Gly141
B	1REV [B]	Ile142
C	1REV [B]	Arg143
H	1REV [A]	Ala158
H	1REV [A]	Gln161
H	1REV [A]	Ser162
H	1REV [A]	Thr165
H	1REV [A]	Lys166
H	1REV [A]	Glu169
H	1REV [A]	Arg172
H	1REV [A]	Ile380
H	1REV [A]	Val381
H	1REV [A]	Ile382

(d) Cavity 4:

Secondary structure	Target Atoms:Molecule	ResidueID
C	1REV [A]	Arg358
C	1REV [A]	Gly359
C	1REV [A]	Ala360
C	1REV [A]	His361
C	1REV [A]	Thr362
H	1REV [A]	Asn363
H	1REV [A]	Lys366
H	1REV [A]	Trp401
H	1REV [A]	Glu404
H	1REV [A]	Tyr405
C	1REV [A]	Trp406
C	1REV [B]	Asn418
C	1REV [B]	Thr419
C	1REV [B]	Pro420
C	1REV [B]	Pro421
C	1REV [B]	Leu425
C	1REV [A]	Gln428
C	1REV [A]	Leu429
C	1REV [A]	Glu430
C	1REV [A]	Lys431
C	1REV [A]	Glu432
H	1REV [A]	Gln500
H	1REV [A]	Tyr501
H	1REV [A]	Leu503
H	1REV [A]	Gly504
H	1REV [A]	Ile505
H	1REV [A]	Ile506
H	1REV [A]	Gln507
H	1REV [A]	Ala508
T	1REV [A]	Gln509
C	1REV [A]	Pro510
C	1REV [A]	Val531
B	1REV [A]	Tyr532
C	1REV [A]	Leu533
C	1REV [A]	Ala534

(e) Cavity 5:

Secondary structure	Target Atoms:Molecule	ResidueID
C	1REV [B]	Ile63
C	1REV [B]	Lys64
T	1REV [B]	Lys65
C	1REV [B]	Lys66
C	1REV [B]	Arg72
C	1REV [B]	Val108
B	1REV [B]	Leu109
T	1REV [B]	Asp110
T	1REV [B]	Asp186
C	1REV [B]	Tyr188
C	1REV [B]	Gly231
C	1REV [B]	Tyr232
C	1REV [B]	Glu233
C	1REV [B]	Tyr354
C	1REV [B]	Met357
C	1REV [B]	Arg358
H	1REV [B]	Lys366
H	1REV [B]	Thr369
H	1REV [B]	Glu370
H	1REV [B]	Ala371
H	1REV [B]	Gln373
H	1REV [B]	Lys374
H	1REV [B]	Thr377
T	1REV [B]	Glu404
T	1REV [B]	Tyr405
T	1REV [B]	Trp406
C	1REV [B]	Gln407
C	1REV [B]	Ala408
C	1REV [B]	Thr409
C	1REV [B]	Trp410

C= Coil T = turn , H= alpha Helix E beta sheet B = beta bridge

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Table 5: Rerank score of TIBO and phytochemicals, Rerank score better than TIBO showed as bold.

Name of ligands	Cavity 1	Cavity 2	Cavity 3	Cavity 4	Cavity 5
TIBO	-88.0895	-78.1128	-101.874	-96.8846	-92.4498
CURCUMIN	**-110.836**	**-85.8405**	-99.9434	**-98.7942**	-72.57
GERANIIN	**-110.141**	**-136.227**	-56.3255	-87.5479	-63.0893
KAEMPFEROL-3-O-GLUCOSIDE	**-110.3**	**-86.413**	-97.4775	**-100.557**	-118.36
GALLOTANNIN	**-111.141**	**-123.105**	**-128.155**	**-109.482**	**-127.304**
TILIROSIDE	**-134.951**	**-111.342**	-98.9275	**-127.852**	**-133.33**
TRACHELOGENIN	**-107.071**	**-87.4864**	**-104.603**	**-99.9473**	**-102.709**

Table 6: (a) Curcumin and its derivatives at cavity 1

Sl. No	Ligand Name	SMILES	Rerank score
1	Curcumin	OC(C1)(c(o)o)CC(O)C(O)C1OC(O)CCC(C2)CCC(O)C2O	-110.836
2	4-[5-(aminomethyl)-7-(4-chloro-3-methylcyclohex-3-en-1-yl)-3-methylheptyl]-2-methylcyclohex-1-en-1-ol	ClC(=C(C)C1)CCC1CCC(C[NH3+])CC(C)CCC(C2)CCC(O)=C2C	-96.3325
3	4-chloro-6-[3-(hydroxymethyl)cyclohex-3-en-1-yl]-2-{2-[4-(hydroxymethyl)cyclohex-3-en-1-yl]ethyl}hexan-1-ol	ClC(CCC1CC(CO)=CCC1)CC(CO)CCC(CC=2)CCC=2CO	-99.7003
4	1-[4-chloro-3-(hydroxymethyl)cyclohex-3-en-1-yl]-7-[4-(hydroxymethyl)cyclohex-3-en-1-yl]heptane-3,5-diol	ClC(=C(C1)CO)CCC1CCC(O)CC(O)CCC(CC=2)CCC=2CO	-105.156
5	4-[7-(3-amino-4-methylphenylidene)heptyl]-2-chloroaniline	Clc([cH]1)c(N)[cH][cH]c1CCCCC[CH]C=c([cH]2)[cH][cH]c(C)c2N	-100.938
6	(1S,2S,5S)-2-chloro-5-[(3R,5R)-3,5-diamino-7-[4-(hydroxymethyl)cyclohexyl]heptyl]cyclohexan-1-ol	ClC(C(O)C1)CCC1CCC(N)CC(N)CCC2CCC(CO)CC2	-102.884

Table 6: (b) Geraniin and its derivatives at cavity 2.

Sl. No	Ligand Name	SMILES	Rerank Score
1	Geraniin	OC(O1)(C2(O)O)C(O)CC(C(O)OC43)C2C5C1C(O)C(O)CC5C(O)OC6C3OC(O)C7CC(O)C(O)C(O)C7C8C(O)C(O)C(O)CC8C(O)OCC4OC6OC(O)C(C9)CC(O)C(O)C9O	-136.227
2	(1S,38S)-28-[hydroxy(3,4,5-trihydroxy-2-methylphenyl)methoxy]-2,20-dimethyl-6,9,27,30,40- pentaoxa-24-azaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 17(22),18,20,32,34,36-hexaen-5,15,18,19,34,35,39,39-octol	OC1(O)C2c3c(CO4)[cH]c(O)c(O)c3OC1C(C)CC2C(O)OC5C(O6)CNCc7[cH]c(C)c(O)c(O)c7C8C(O)CCCC8COC5C4C6OC(O)c9[cH]c(O)c(O)c(O)c9C	-130.206
3	(1S,8S,29R,38S)-2-[(S)-amino(methyl)hydroxysulfanyl]-1,35-dichloro-28- [chloro(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 14,17,19-trien-10,13,14,15,18,19,20,23,31,39,39- undecol	ClC(O1)(C2(O)O)C(S(C)(N)O)CC(COC43)C2C5C1C(Cl)CCC5C(O)OC6C3OC(O)C7CC(O)C(O)=C(O)C7C8=C(O)C(O)=C(O)CC8C(O)OCC4OC6OC(Cl)C9CC(O)=C(O)CC9	-123.149
4	(1R,8S,29R,38S)-31-chloro-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-1,35-diethyl-2- methanesulfonyl-39-methoxy-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 14,18,35-trien-10,13,14,15,18,19,20,23-octol	ClC(O1)C2CCC(CC)=C(O3)C2C4C(OC)C3(CC)C(S(C)(=O)=O)CC4COC5C(O6)COC(O)C7CC(O)C(O)=C(O)C7C8C(O)=C(O)C(O)CC8C(O)OC5C1C6OCC9CC(O)=C(O)CC9	-127.869
5	(1S,2E,8S,38S)-34-chloro-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-1-ethyl-39- methoxy-35-(methylamino)-2-(methylimino)- 6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 14,18,32,34,36-pentaen-10,13,14,15,18,19,20,23- octol	Clc([cH]1)c(NC)c2OC(C3OC)(CC)C(=[NH]C)CC(COC54)C3c2c1COC6C4OC(O)C7CC(O)C(O)=C(O)C7C8C(O)=C(O)C(O)CC8C(O)OCC5OC6OCC9CC(O)=C(O)CC9	-121.035
6	(1R,2E,8S,38R)-5,34-dibromo-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-2-	BrC(OC21)C3CC(=[NH]C)C(O4)CC3C5C4=C(CCC)C(Br)CC5COC6C1OC(O)C7CCC(O)=C(O)C7C8C(O)C(O)=C(O)CC8COCC2OC6O	-134.6

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	(methylimino)-35-propyl-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 14,19,35-triene-10,14,15,18,19,20-hexol	CC9CC(O)=C(O)CC9

Table 6: (c) Kaempferol-3-o-glucoside and derivatives at cavity 5

Sl.No	Ligand Name	SMILES	Rerank Score
1	Kaempferol-3-o-glucoside	OC(C(CO)O1)C(O)C(O)C1OC2C(O)C3C(O)CC(O)CC3OC2C4CCC(O)CC4	-118.36
2	2-{[4,5-bis(hydroxymethyl)-7-methyl-2-(2-methyl-4-propylcyclohexyl)-5,6,7,8-tetrahydrochromen-3-yl]oxy}-6-(hydroxymethyl)-3-methylpyridin-4-ol	ClC(C1)CCC(C2)C1N(C)C(=C3CCC(C)CC3)C2Oc(n4)c(C)[cH]c(Cl)c4CC	-116.759
3	7-chloro-3-[(5-chloro-6-ethyl-3-methylpyridin-2-yl)oxy]-1-methyl-2-(4-methylcyclohexylidene)-decahydroquinoline	ClC(C1)CCC(C2)C1N(C)C(=C3CCC(C)CC3)C2Oc(n4)c(C)[cH]c(Cl)c4CC	-110.413
4	(4S)-2-(4-bromocyclohexyl)-3-{[6-(2-bromoethyl)-4- methoxy-2,3,4,5-tetrahydro-1$l^{4}-pyridin-2- yl]oxy}-4-(hydroxymethyl)-5-methyl-4-propyl-octahydro-2H-1-benzopyran-7-ol	BrC(CC1)CCC1C2OC3CC(O)CC(C)C3C(CO)(CCC)C2OC([NH]=4)CC(OC)CC=4CCBr	-111.262
5	{3-[(4-chloro-3,6-dimethylpyridin-2-yl)oxy]-5-(hydroxymethyl)-7-methyl-2-(2-methyl-4-propylcyclohexyl)-5,6,7,8-tetrahydrochromen-4-yl}methanol	Clc(c1(C))[cH]c(C)nc1Oc2c(CO)c3C(CO)CC(C)Cc3oc2C(CC4)C(C)CC4CCC	-97.1581
6	2-{[4,5-bis(chloromethyl)-7-methyl-2-(2-methyl-4-propylcyclohexyl)-5,6,7,8-tetrahydrochromen-3-yl]oxy}-4,6-dichloro-3-methylpyridine	ClCc1c2C(CCl)CC(C)Cc2oc(C3CCC(CCC)CC3(C))c1Oc4nc(Cl)[cH]c(Cl)c4C	-113.533

Table 6: (d) Gallotannin and its derivatives at cavity 3

Sl. No	Ligand Name	SMILES	Rerank Score
1	Gallotannin	OC1C(OC(C2CC(C(C(C2)O)O)O)O)C(O)C(OC(C3CC(C(C(C3)O)O)O)O)OC1COC(O)C(C4)CC(O)C(O)C4O	-128.55
2	(1R,2Z,8S,38S)-3-amino-2-[(3-aminopropyl)(ethyl)imino]-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-34-imino-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta-15,19,32(37)-triene-10,14,15,18,19,20-hexol	OC(OC21)C3CCC(O)C(O)=C3C4C(O)C(O)=C(O)CC4COCC(O5)C2OCC6C(N)C(=N(CCCN)CC)C(O7)CC6C=8C7CC(=[NH2])CC=8COC1C5OCC9CC(O)=C(O)CC9	-81.4704
3	(1R,8S,38R)-5,34-dibromo-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-2-[ethyl(methyl)amino]-35-propyl-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta-15,19,33,35-tetraene-10,14,15,18,19,20-hexol	BrC(OC21)C3CC(N(C)CC)C(O4)CC3C5C4=C(CCC)C(Br)=CC5COC6C1OC(O)C7CCC(O)C(O)=C7C8C(O)C(O)=C(O)CC8COCC2OC6OCC9CC(O)=C(O)CC9	-99.9452
4	(1R,2Z,8S,38R)-2-[(3-aminopropyl)(ethyl)imino]-5,34-dibromo-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 15,19-diene-10,14,15,18,19,20-hexol	BrC(OC21)C3CC(=N(CCCN)CC)C(O4)CC3C5C4CC(Br)CC5COC6C1OC(O)C7CCC(O)C(O)=C7C8C(O)C(O)=C(O)CC8COCC2OC6OCC9CC(O)=C(O)CC9	-98.8631
5	(1S,8S,38S)-5,34-dibromo-35-(diethylamino)-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta-15,19,32,34,36-pentaene-10,14,15,18,19,20-hexol	BrC(OC21)C3CCC(O4)CC3c5c4c(N(CC)CC)c(Br)[cH]c5COC6C1OC(O)C7CCC(O)C(O)=C7C8C(O)C(O)=C(O)CC8COCC2OC6OCC9CC(O)=C(O)CC9	-108.013

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6	(1R,8S,38R)-2-[(3-aminopropyl)(ethyl)amino]-28-[(3,4-dihydroxycyclohex-3-en-1-yl)methoxy]-34-imino-6,9,24,27,30,40-hexaoxaoctacyclo[34.3.1.0^{4,38}.0^{7,26}.0^{8,29}.0^{11,16}.0^{17,22}.0^{32,37}]tetraconta- 3,15,19-triene-3,10,14,15,18,19,20-heptol	OC(OC21)C3CCC(O)C(O)=C3C4C(O)C(O)=C(O)CC4COCC(O5)C2OCC6=C(O)C(N(CCCN)CC)C(O7)CC6C8C7CC(=[NH2])CC8COC1C5OCC9CC(O)=C(O)CC9	-99.8931

Table 6: (e) Tiliroside and its derivatives at cavity 1

Sl. No	Ligand Name	SMILES	Rerank Score
1	Tiliroside	OC(C(COC(CCC2CCC(CC2)O)O)O1)C(O)C(O)C1OC3C(O)C4C(O)CC(O)CC4OC3C5CCC(O)CC5	-134.951
2	4-(3-{[6-({5-amino-2-[4-(ethylimino)cyclohexyl]-4,7-dihydroxy-5,6,7,8-tetrahydrochromen-3-yl}methyl)-4-chloro-3,5-dihydroxypyran-2-yl]methoxy}-3-hydroxypropyl)cyclohexane-1-carboxylic acid	Clc(c1O)c(O)c(COC(CCC2CCC(CC2)=c(o)o)O)oc1Oc3c(O)c4C(=[NH2])CC(O)Cc4oc3C(CC5)CCC5=N(C)CC	-86.8885
3	4-[3-({4-amino-6-[(5-amino-2-{4-[ethyl(methyl)amino]cyclohexyl}-4,7-dihydroxy-5,6,7,8-tetrahydrochromen-3-yl)oxy]-5-chloro-3-hydroxypyran-2-yl}methoxy)-3-hydroxypropyl]cyclohexane-1-carboxylic acid	Clc1c(=[NH2])c(O)c(COC(CCC2CCC(CC2)=c(o)o)O)oc1Oc3c(O)c4C(=[NH2])CC(O)Cc4oc3C(CC5)CCC5=N(C)CC	-128.952
4	4-(3-{[4-amino-6-({5-amino-4-fluoro-7-hydroxy-2-[4-(hydroxymethyl)cyclohexyl]-5,6,7,8-tetrahydrochromen-3-yl}amino)-3,5-difluoropyran-2-yl]methoxy}-3-hydroxypropyl)cyclohexane-1-carboxylic acid	Fc(c(COC(CCC2CCC(CC2)=c(o)o)O)o1)c(=[NH2])c(F)c1=[NH]c3c(F)c4C(=[NH2])CC(O)Cc4oc3C(CC5)CCC5CO	-112.242
5	5-amino-3-[(6-{[3-(4-aminocyclohexyl)-1-hydroxypropoxy]methyl}-4,5-dichloro-3-hydroxypyran-2- yl)(methyl)-$l^{3}-chloranyl]-2-{4-[ethyl(methyl)amino]cyclohexyl}-5,6,7,8-tetrahydrochromene-4,7-diol	Clc(c(COC(CCC2CCC(CC2)=[NH2])O)o1)c(Cl)c(O)c1Clc3c(O)c4C(=[NH2])CC(O)Cc4oc3C(CC5)CCC5=N(C)CC	-128.181
6	5-amino-3-[(6-{[3-(3-aminocyclohexyl)-1-hydroxypropoxy]methyl}-4,5-dichloro-3-hydroxypyran-2-yl)oxy]-2-[4-(3-hydroxycyclohexyl)cyclohexyl]-5,6,7,8-tetrahydrochromene-4,7-diol	Clc(c(COC(CCC2CC(=[NH2])CCC2)O)o1)c(Cl)c(O)c1Oc3c(O)c4C(=[NH2])CC(O)Cc4oc3C(CC5)CCC5C(C6)CCCC6O	-105.166

Table 6: (f) Trachelogenin and its derivatives at cavity 1

Sl. No	Ligand Name	SMILES	Rerank Score
1	Trachelogenin	OC1(CC2CC(C(CC2)O)OC)C(O)OCC1CC(C3)CCC(OC)C3OC	-107.071
2	(3R)-2-amino-3-[(4-hydroxy-3-methoxycyclohexyl)methyl]-4-{[3-(2-hydroxyethyl)-4-(4-methylcyclohexyl)cyclohex-3-en-1-yl]methyl}oxolan-3-ol	OC1(CC2CC(C(CC2)O)OC)C(=[NH2])OCC1CC(CC=3CCO)CCC=3C4CCC(C)CC4	-87.7697
3	4-{[(3R)-2-amino-3-hydroxy-4-({3-[(hydroxymethyl)amino]-4-(4-methylcyclohexyl)cyclohexyl}methyl)pyrrolidin-3-yl]methyl}cyclohex-1-ene-1,2-diol	OC1(CC2CC(=C(CC2)O)O)C(=[NH2])NCC1CC(CC3=[NH]CO)CCC3C4CCC(C)CC4	-90.1273
4	4-{[(3R)-2-amino-4-({3-[ethyl(methyl)amino]-4-(4-methylcyclohexyl)cyclohexyl}methyl)-3-hydroxypyrrolidin-3-yl]methyl}cyclohex-1-ene-1,2-diol	OC1(CC2CC(=C(CC2)O)O)C(=[NH2])NCC1CC(CC3N(C)CC)CCC3C4CCC(C)CC4	-87.7609
5	4-{[(3R)-2-amino-4-{[4-(3,4-dichlorocyclohex-3-en-1-yl)-3-[ethyl(methyl)amino]cyclohexyl]methyl}-3-hydroxypyrrolidin-3-yl]methyl}cyclohex-1-ene-1,2-diol	ClC(=C(Cl)C1)CCC1C(C(N(C)CC)C2)CCC2CC3CNC(=[NH2])C3(O)CC(C4)CCC(O)=C4O	-89.5052
6	4-{[(3S)-2-amino-4-{[4-(3,4-dichlorocyclohex-3-en-1-yl)-3-[ethyl(methyl)amino]cyclohexyl]methyl}-3-propylpyrrolidin-3-yl]methyl}cyclohex-1-ene-1,2-diol	ClC(=C(Cl)C1)CCC1C(C(N(C)CC)C2)CCC2CC3CNC(=[NH2])C3(CCC)CC(C4)CCC(O)=C4O	-82.9021

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