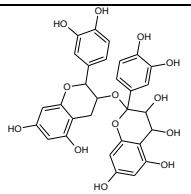
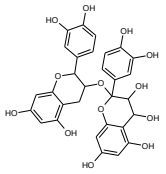
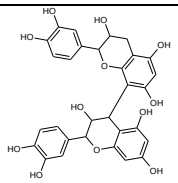
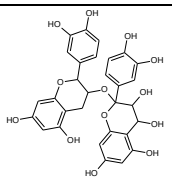
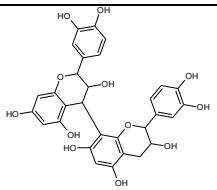
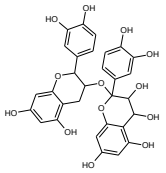
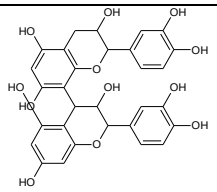
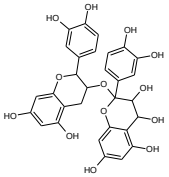
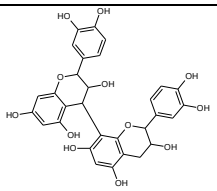
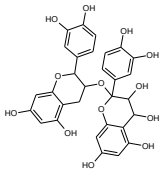
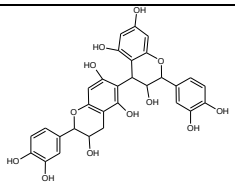
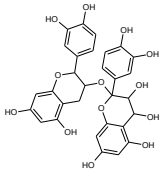
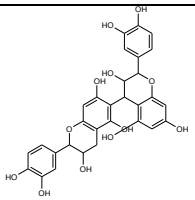
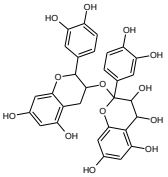
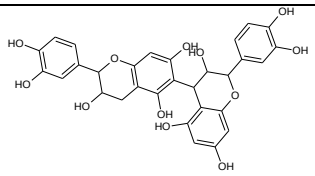
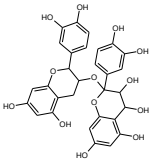
Table 1: Structure similarities among Procyanidin homologs with Procyanidin.

Homologous molecule of Procyanidin And their Pubchem CID	Structure	Parent Molecule- Procyanidin	Similarity score
Procyanidin CID 107876			1.0
Procyanidin B1 CID 11250133			0.6541096
Procyanidin B2 CID 122738			0.6541096
Procyanidin B3 CID 146798			0.6541096
Procyanidin B4 CID 147299			0.6541096
Procyanidin B5 CID 124017			0.6474576
Procyanidin B6 CID 474540			0.6474576
Procyanidin B7 CID 13990893			0.6474576

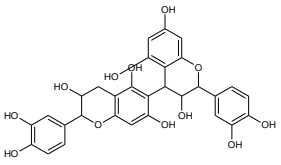
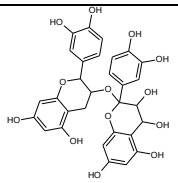
Procyanidin B8 CID 474541			0.6474576

Table 2: A) Molecular properties and Pharmacokinetics prediction of natural products filtered in for screening against T2D condition *.

Identified NPs	cLogP	Mol.wt	H-Acceptors	H-Donors	Rotatable Bonds	Total Surface Area	Polar Surface Area	Druglikeness	Human intestinal absorption	Caco-2 permeability	Blood brain barrier	CYP450 2D6 substrate
Beta-sitosterol	12.864	815.269	07	03	25	664.41	105.45	-27.511	0.884+	0.851-	0.613+	0.892-
Ellagitannin	0.0531	636.47	18	11	10	418.64	310.66	0.19723	0.758+	0.874-	0.511+	0.904-
Gallotannin	0.0531	636.47	18	11	10	418.64	310.66	0.19723	0.866+	0.874-	0.511+	0.904-
Gymnemic acid	4.2394	847.048	14	07	11	603.23	229.74	-6.9506	0.779+	0.922-	0.539+	0.898-
Hesperidin	-0.814	610.563	15	08	07	410.61	234.29	2.0396	0.816+	0.895-	0.946-	0.911-
Isoquercitrin	-0.3469	464.378	12	08	04	303.75	206.6	-3.6679	0.646+	0.939-	0.697-	0.892-
Kaempferol-3-neohesperidoside	-1.9742	740.662	19	11	08	485.32	304.21	0.68673	0.649+	0.910-	0.867-	0.894-
Mangiferin	-0.4299	422.341	11	08	02	270.83	197.37	-3.0467	0.886+	0.916-	0.647+	0.876-
Naringin	-0.744	580.537	14	08	06	388.35	225.06	0.64246	0.753+	0.918-	0.841-	0.886-
Oleanolic acid	0.055	436.412	10	07	07	305.5	177.14	-4.8731	0.402-	0.826-	0.562+	0.877-
Phlorizin	2.7421	594.523	13	10	04	393.21	229.99	0.1505	0.907+	0.878-	0.511+	0.891-
Procyanidin	-1.2573	610.519	16	10	06	397.71	265.52	1.9337	0.732+	0.917-	0.854-	0.896-
Rutin	7.603	412.699	01	01	05	335.28	20.23	1.2217	0.991+	0.795+	0.973-	0.879-
Stigmasterol	7.603	412.699	01	01	05	335.28	20.23	1.2217	0.985+	0.835+	0.776+	0.897-
Ursolic acid	6.0021	456.708	03	02	01	337.87	57.53	-3.658	0.884+	0.851-	0.613+	0.892-

***** Details of data interpretation is given in supplementary file

Table 2: B) Pharmacodynamics prediction of natural products selected for screening against T2D condition *.

Identified NPs	Mutagenic	Tumorigenic	Reproductive effective	Ocular irritancy	Aerobic biodegradibility	Ames tooxicity score	Carcinogen	Hepatotoxicity
Beta-sitosterol	NONE	NONE	NONE	0.990-	0.869-	0.804-	0.965-	0.575-
Ellagitannin	NONE	NONE	NONE	0.839-	0.835+	0.814-	0.744-	0.600+
Gallotannin	NONE	NONE	NONE	0.839-	0.833+	0.814-	0.744-	0.600+
Gymnemic acid	NONE	NONE	NONE	0.906-	0.910-	0.929-	0.686-	0.650+
Hesperidin	NONE	NONE	NONE	0.914-	0.883-	0.897-	0.699-	0.650+
Isoquercitrin	NONE	NONE	NONE	0.732-	0.625-	0.577+	0.714-	0.625+
Kaempferol-3-neohesperidoside	HIGH	NONE	NONE	0.905-	0.828-	0.581-	0.730-	0.800+
Mangiferin	HIGH	NONE	NONE	0.752-	0.781-	0.723+	0.725-	0.575+
Naringin	NONE	NONE	NONE	0.929-	0.711-	0.692-	0.702-	0.575+
Oleanolic acid	NONE	NONE	NONE	0.908-	0.962-	0.849-	0.596-	0.700-
Phlorizin	NONE	NONE	LOW	0.811-	0.933+	0.785-	0.746-	0.550+
Procyanidin	NONE	NONE	NONE	0.773-	0.926-	0.928-	0.578-	0.550-
Rutin	NONE	NONE	NONE	0.897-	0.833-	0.511-	0.671-	0.700+
Stigmasterol	NONE	NONE	NONE	0.967-	0.980-	0.913-	0.588-	0.775-
Ursolic acid	NONE	NONE	NONE	0.938-	0.962-	0.849-	0.596-	0.700-

***** Details of data interpretation is given in supplementary file

Table 2: C) Natural products structurally similar to T2D prescribed drugs, their similarity score and their interaction energy with selected cellular targets. Synthetic drug in each group is highlighted in bold letters. Values in grey cells indicate docking energy better than or equal to respective synthetic drug counterpart.

Synthetic drug and the identified NPs	Similarity score	Docking Energy (kcal/mol)
Empagliflozin		-9.3
Naringin	0.6875	-11.9
Kaempferol-3-neohesperidoside	0.6084	-11.7
Hesperidin	0.6953	-11.2
Ellagitannin	0.6582	-11.1
Gallotannin	0.6582	-11
Phlorizin	0.6258	-9.9
Procyanidin	0.7029	-9.7
Mangiferin	0.8138	-9.3
Luseogliflozin		-7.0
Isoquercitrin	0.6238	-12.4
Naringin	0.6826	-12.3
Kaempferol-3-neohesperidoside	0.6250	-11.7
Rutin	0.6126	-11.4
Hesperidin	0.6957	-11.1
Procyanidin	0.7483	-10.8
Phlorizin	0.6610	-10.1
Mangiferin	0.8782	-9.4
Prednisolone		-10.0
Ursolic acid	0.7660	-8.9
Oleanolic acid	0.7695	-9.0
Gymnemic acid	0.6193	-7.9
Beta-sitosterol	0.6716	-7.4
Stigmasterol	0.6716	-6.8

Table 2: D) Calculated MD parameters for native and ligand bound T2D drug targets obtained after the simulation along with binding energies and the contributing energy terms of prescribed drug and its most similar natural product calculated using g_mmpbsa module.

		SGLT2 RECEPTOR			SGLT2 RECEPTOR			GLUCOCORTICOID RECEPTOR		
Gromacs Modules		**Native Protein**	**Empagliflozin**	**Naringin**	**Native Protein**	**Luseogliflozin**	**Isoquercitrin**	**Native Protein**	**Prednisolone**	**Ursolic_acid**
	Potential Energy (x 10^{-6})	-1.581	-1.580	-1.580	-1.581	-1.5810	-1.585	-0.994	-1.138	-2.215
	RMSD	0.289	0.285	0.246	0.289	0.304	0.295	0.256	0.337	0.255
	RMSF	0.145	0.111	0.109	0.145	0.128	0.119	0.113	0.123	0.118
	Rg	2.334	2.333	2.341	2.334	2.326	2.324	1.865	1.876	1.880
	SASA	231.55	228.55	230.16	231.55	226.66	224.78	135.96	138.92	140.75
	Secondary Structure	797.12	797.14	800.35	797.12	790.90	784.23	375.16	371.85	375.31
	Coul-SR	-	-153.05	-112.01	-	-7.23	-69.11	-	-10.19	-6.089
	LJ-SR	-	-160.61	-184.64	-	-141.83	-97.86	-	-53.06	-77.69
MMPBSA Module	Binding Energy	-	-120.20	-127.71	-	-46.48	-151.83	-	-31.14	-79.63
	SASA Energy*	-	-23.41	-26.35	-	-17.09	-12.58	-	-7.11	-10.06
	Polar Solvation Energy*	-	206.21	213.18	-	47.93	118.10	-	48.97	38.43
	Electrostatic Energy*	-	-103.99	-69.08	-	-4.55	-44.91	-	-7.61	-7.11
	van der WAALs Energy*	-	-206.01	-238.46	-	-172.78	-112.44	-	-65.39	-100.89

* kJ/mol

Table 3: A) Molecular properties and Pharmacokinetics prediction of natural products filtered in for screening against COVID 19 condition *.

Identified NPs	cLogP	Mol.wt	H-Acceptors	H-Donors	Rotatable Bonds	Total Surface Area	Polar Surface Area	Druglikeness	Human intestinal absorption	Caco-2 permeability	Blood brain barrier	CYP2D6 substrate
12_28_Oxa_8_Hydroxy_Manzamin_A	5.2547	562.755	6	2	1	414.34	60.33	-2.227	0.696+	0.541-	0.800+	0.671-
Alstolobine_A	2.4707	398.457	7	1	6	297.41	80.86	-8.1671	0.988+	0.566-	0.896+	0.816-
Beauvericin	5.2239	783.96	12	0	9	610.8	139.83	4.3764	0.991+	0.661+	0.678+	0.825-
Beauvericin_H1	5.3247	801.95	12	0	9	617.15	139.83	3.0364	0.990+	0.599+	0.786+	0.829-
Bionectin_A	2.9631	450.542	7	3	1	282.66	139.27	5.5488	0.889+	0.508+	0.608+	0.831-
Bionectin_B	2.6488	494.595	8	4	2	311.68	159.5	5.0182	0.900-	0.525-	0.832-	0.838-
Bis(Gorgiacerol)Amine	5.4399	757.83	13	3	10	560.06	183.97	-19.005	0.965-	0.616-	0.932-	0.848-
Chaetocin	2.7962	696.852	12	4	3	409.82	246.96	5.8356	0.900+	0.626-	0.661-	0.801-
Chetracin_B	1.092	760.916	14	6	3	437.49	312.72	5.4873	0.885+	0.574-	0.816-	0.805-
Chetracin_D	0.3976	788.99	14	6	7	496.04	287.42	5.6124	0.922+	0.589-	0.869-	0.805-
Clausarin	5.9768	380.482	4	1	4	295.44	55.76	-5.9217	0.975+	0.840-	0.825+	0.867-
Cyathusal_B	0.5256	346.29	8	3	3	243.75	122.52	-4.326	0.915+	0.592+	0.767-	0.909-
Cyathuscavin_B	0.5053	376.316	9	3	4	264.22	131.75	-4.7328	0.878+	0.627+	0.775-	0.894-
Cyathuscavin_C	0.0774	362.289	9	4	3	248.31	142.75	-2.2479	0.868+	0.592+	0.767-	0.909-
Difloxacin	1.251	399.396	6	1	3	283.48	64.09	5.1997	0.985+	0.879+	0.968-	0.911-
Discorhabdin_H	-10.123	762.664	10	3	5	337.61	198.19	2.7192	0.734+	0.603-	0.903-	0.795-
Dragonamide_A	3.7111	653.905	10	2	18	539.59	125.32	-3.0172	0.969+	0.543-	0.628-	0.783-
Hexahydrodipyrrol derivative	0.2123	427.456	9	3	2	288.36	119.41	6.7335	0.946+	0.615-	0.978-	0.802-
Holstiine	1.5964	382.458	6	1	0	270.15	70.08	5.6428	0.972+	0.631+	0.567+	0.784-
Hydroxy-6-Methylpyran-2-	5.228	500.586	8	4	11	387.58	141.36	-13.889	0.984+	0.563+	0.660-	0.866-

One_Derivative												
Lamellarin_D	4.3105	499.474	9	3	4	352.71	119.09	1.8379	0.983+	0.604+	0.606+	0.448-
Lamellarin_Gamma_Acetate	5.3	573.596	10	1	8	423.68	106.84	2.3739	0.987+	0.683+	0.747+	0.628-
Luteoalbusin_A	3.1416	464.569	7	3	2	295.59	139.27	5.9847	0.890+	0.581-	0.575+	0.812-
Marineosin_A	4.6896	409.572	5	2	2	323.4	62.4	-2.232	0.986+	0.638-	0.824+	0.764-
Methaniminium derivative	-0.4649	910.463	21	10	14	679.31	329.1	6.1103	0.795+	0.647-	0.976-	0.831-
Methylstemofoline	0.9975	345.394	6	0	1	220.03	57.23	4.0559	0.922+	0.670+	0.679+	0.741-
Mollenine_A	3.3511	368.475	5	1	4	275.46	58.64	3.6919	0.980+	0.516-	0.608+	0.824-
Munroniamide	-0.4894	597.663	12	2	7	419.88	166.86	-8.9989	0.940+	0.628-	0.500+	0.808-
Oidioperazine_A	1.9865	538.647	9	3	4	357.08	167.78	6.2082	0.843+	0.510-	0.807-	0.506-
Oxyprotostemonine	1.004	431.483	8	0	2	289.89	83.53	2.3627	0.890+	0.648+	0.549+	0.803-
Phellibaumin_A	2.8483	352.297	7	4	2	248.17	120.36	0.0022	0.952+	0.828-	0.725+	0.905-
Pulvinatal	0.9535	360.317	8	2	4	259.66	111.52	-6.9354	0.919+	0.627+	0.775-	0.894-
Stemocurtisine	1.4247	347.41	6	0	1	239.64	57.23	2.9196	0.922+	0.668+	0.758+	0.744-
Symplocamide_A	0.6976	1052.03	23	11	18	763.41	359.52	1.3524	0.915+	0.634-	0.959-	0.830-
Verticillin_E	1.7482	752.872	14	4	3	439.8	281.1	4.5639	0.895+	0.536-	0.836-	0.825-

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Table 3: B) Pharmacodynamics prediction of natural products selected for screening against COVID 19 condition *.

Identified NPs	Mutagenic	Tumorigenic	Reproductive effective	Ocular irritancy	Aerobic biodegradibility	Ames tooxicity score	Carcinogen	Hepatotoxicity
12_28_Oxa_8_Hydroxy_Manzamin_A	NONE	NONE	NONE	0.946-	1.00-	0.707-	0.607-	0.525+
Alstolobine_A	NONE	HIGH	NONE	0.979-	1.00-	0.714-	0.573-	0.600+
Beauvericin	NONE	NONE	NONE	0.925-	0.912-	0.772-	0.622-	0.650+
Beauvericin_H1	NONE	NONE	NONE	0.922-	0.996-	0.776-	0.536-	0.625+
Bionectin_A	NONE	NONE	NONE	0.972-	0.986-	0.733-	0.609-	0.800+
Bionectin_B	NONE	NONE	NONE	0.965-	0.988-	0.870-	0.611-	0.875+
Bis(Gorgiacerol)Amine	NONE	NONE	HIGH	0.901-	0.623-	0.573-	0.487-	0.700+
Chaetocin	NONE	NONE	NONE	0.918-	0.994-	0.645-	0.623-	0.600+
Chetracin_B	NONE	NONE	NONE	0.911-	0.973-	0.679-	0.644-	0.575+
Chetracin_D	NONE	NONE	NONE	0.904-	0.996-	0.678-	0.627-	0.650+
Clausarin	NONE	NONE	HIGH	0.607+	0.993-	0.506-	0.472-	0.775+
Cyathusal_B	NONE	NONE	HIGH	0.561-	0.937-	0.707+	0.465-	0.850+
Cyathuscavin_B	NONE	NONE	HIGH	0.590-	0.966-	0.712+	0.515+	0.850+
Cyathuscavin_C	NONE	NONE	HIGH	0.574-	0.937-	0.707+	0.465-	0.850+
Difloxacin	NONE	NONE	NONE	0.949-	1.00-	0.885+	0.610-	0.850+
Discorhabdin_H	NONE	NONE	NONE	0.960-	1.00-	0.593-	0.532-	0.825+
Dragonamide_A	NONE	NONE	NONE	0.922-	1.00-	0.812-	0.678-	0.675+
Hexahydrodipyrrol derivative	NONE	NONE	NONE	0.927-	1.00-	0.658-	0.597-	0.575+
Holstiine	NONE	NONE	NONE	0.986-	0.951-	0.572-	0.501-	0.550-
Hydroxy-6-Methylpyran-2-One_Derivative	NONE	NONE	NONE	0.732-	0.500+	0.815-	0.723-	0.600-
Lamellarin_D	NONE	NONE	HIGH	0.833-	0.993-	0.586-	0.389-	0.800+

Lamellarin_Gamma_Acetate	NONE	NONE	HIGH	0.989-	0.995-	0.880-	0.599-	0.775+
Luteoalbusin_A	NONE	NONE	NONE	0.986-	0.987-	0.670-	0.630-	0.725+
Marineosin_A	NONE	NONE	NONE	0.972-	1.00-	0.655-	0.651-	0.700-
Methaniminium derivative	NONE	NONE	NONE	0.905-	0.962-	0.615-	0.570-	0.775+
Methylstemofoline	NONE	NONE	NONE	0.891-	1.00-	0.755-	0.470-	0.625-
Mollenine_A	NONE	NONE	NONE	0.986-	0.997-	0.572-	0.528-	0.675+
Munroniamide	LOW	HIGH	LOW	0.978-	1.00-	0.512-	0.562-	0.725+
Oidioperazine_A	NONE	NONE	NONE	0.987-	0.997-	0.670-	0.606-	0.725+
Oxyprotostemonine	NONE	NONE	NONE	0.943-	0.994-	0.681-	0.440-	0.550+
Phellibaumin_A	HIGH	NONE	HIGH	0.528-	0.911-	0.550+	0.419-	0.850+
Pulvinatal	NONE	NONE	HIGH	0.547-	0.966-	0.712+	0.515+	0.825+
Stemocurtisine	NONE	NONE	NONE	0.914-	0.995-	0.781-	0.420-	0.600-
Symplocamide_A	NONE	NONE	NONE	0.901-	0.945-	0.644-	0.594-	0.725+
Verticillin_E	NONE	NONE	HIGH	0.900-	0.986-	0.763-	0.610-	0.750+

***** Details of data interpretation is given in supplementary file

Table 3: C) Natural products structurally similar to COVID 19 prescribed synthetic drugs, their similarity score and their interaction energy with selected cellular targets**.** Synthetic drug in each group is highlighted in bold letters. Values in blue coloured cells indicates docking energy better than or equal to respective synthetic drug counterpart.

Synthetic drug and the identified NPs	Similarity score	Docking Energy (kcal/mol)
Remdesivir		-7.2
12_28_Oxa_8_Hydroxy_Manzamin_A	0.7676	-10.4
Marineosin_A	0.7558	-7.9
Bis(Gorgiacerol)Amine	0.8107	-7.8
Methylstemofoline	0.7645	-7.7
Chetracin_B	0.7877	-7.5
Oxyprotostemonine	0.7644	-7.5
Stemocurtisine	0.7569	-7.5
Munroniamide	0.7705	-6.9
Alstolobine_A	0.7598	-6.8
Discorhabdin_H	0.7665	-6.7
Arbidol		-7.1
Phellibaumin_A	0.6838	-9.4
Difloxacin	0.7363	-8.4
Lamellarin_D	0.7175	-8.4
Lamellarin_Gamma_Acetate	0.6682	-7.8
Hydroxy-6-Methylpyran-2-One_Derivative	0.6822	-7.6
Cyathuscavin_C	0.7363	-7.5
Cyathusal_B	0.7135	-7.4
Clausarin	0.6770	-7.3
Cyathuscavin_B	0.7135	-7.3
Pulvinatal	0.7010	-7.3
Lopinavir		-6.5
Hexahydrodipyrrol derivative	0.7458	-8.4
Beauvericin	0.7478	-7.2
Chaetocin	0.7615	-7.1
Mollenine_A	0.7462	-7.1
Chetracin_B	0.7877	-6.9
Beauvericin_H1	0.7549	-6.6
Dragonamide_A	0.7703	-6.3
Chetracin_D	0.7892	-6.2
Dimethyl-3-Oxodecanamide derivative	0.7569	-5.6
Symplocamide_A	0.7481	-4.6
Ritonavir		-7.7
Bionectin_B	0.7146	-8.1
Luteoalbusin_A	0.6906	-8.0
Bionectin_A	0.7122	-7.7
Oidioperazine_A	0.7153	-7.7
Holstiine	0.6876	-7.1
Chetracin_B	0.7142	-7.0
Mollenine_A	0.6796	-6.9
Methaniminium derivative	0.7274	-6.6

Verticillin_E	0.7181	-6.6
Chaetocin	0.6888	-6.4

Table 3: D) Calculated MD parameters for native and ligand bound SARS CoV2 drug targets obtained after the simulation along with binding energies and the contributing energy terms of prescribed drug and its most similar natural product calculated using g_mmpbsa module.

		HIV-1 PROTEASE I50V ISOLATE			INFLUENZA VIRUS HEMAGGLUTININ			SARS-CoV NSP12 POLYMERASE			HIV-1 PROTEASE A02 ISOLATE		
Gromacs Modules		**Native Protein**	**Lopinavir**	**Hexahydropyrrolo Derivative**	**Native Protein**	**Arbidol**	**Phellibaurin_A**	**Native Protein**	**Remdesivir**	**Hydroxy Manzamin_A**	**Native Protein**	**Ritonavir**	**Bionectin_B**
	Potential Energy (x 10^{-6})	-0.436	-0.434	-0.436	-4.605	-4.604	-4.604	-0.638	-0.638	-0.637	-0.519	-0.518	-0.518
	RMSD (nm)	0.247	0.270	0.254	0.481	0.429	0.549	0.213	0.195	0.186	0.265	0.447	0.287
	RMSF (nm)	0.130	0.141	0.130	0.176	0.216	0.231	0.105	0.055	0.099	0.140	0.144	0.139
	Rg (nm)	1.316	1.307	1.342	2.802	2.835	2.763	1.558	1.523	1.524	1.343	1.488	1.352
	SASA (nm^2)	59.57	60.05	60.92	175.24	176.47	177.43	92.95	85.00	87.13	64.83	71.84	64.44
	Secondary Structure	119.47	112.07	118.78	283.92	295.63	285.29	210.49	221.97	219.29	117.81	117.54	120.51
	Coul-SR*	-	-40.29	-30.24	-	-9.45	-65.80	-	-47.22	-3.84	-	-83.47	-66.90
	LJ-SR*	-	-113.62	-109.54	-	-109.61	-114.98	-	-92.72	-64.15	-	-326.78	-160.13
MMPBSA Module	Binding Energy*	-	-81.19	-91.66	-	-102.17	-125.49	-	-48.74	-56.19	-	-180.82	-162.08
	SASA Energy*	-	-14.04	-14.10	-	-13.52	-52.63	-	-18.86	-8.23	-	-34.72	-16.62
	Polar Solvation Energy*	-	98.18	70.62	-	43.77	129.78	-	177.89	32.97	-	176.43	74.92
	Electrostatic Energy*	-	-29.35	-15.37	-	-7.75	-13.76	-	-68.45	-4.00	-	-49.57	-34.97
	van der WAALs Energy*	-	-135.98	-132.81	-	-124.66	-62.11	-	-139.31	-76.93	-	-372.96	-185.40

* kJ/mol