BIOINFORMATION

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Supplementary material:

Supplementary Figure 1: 2D structures of Tulsi phytocomounds with positive controls used for docking studies

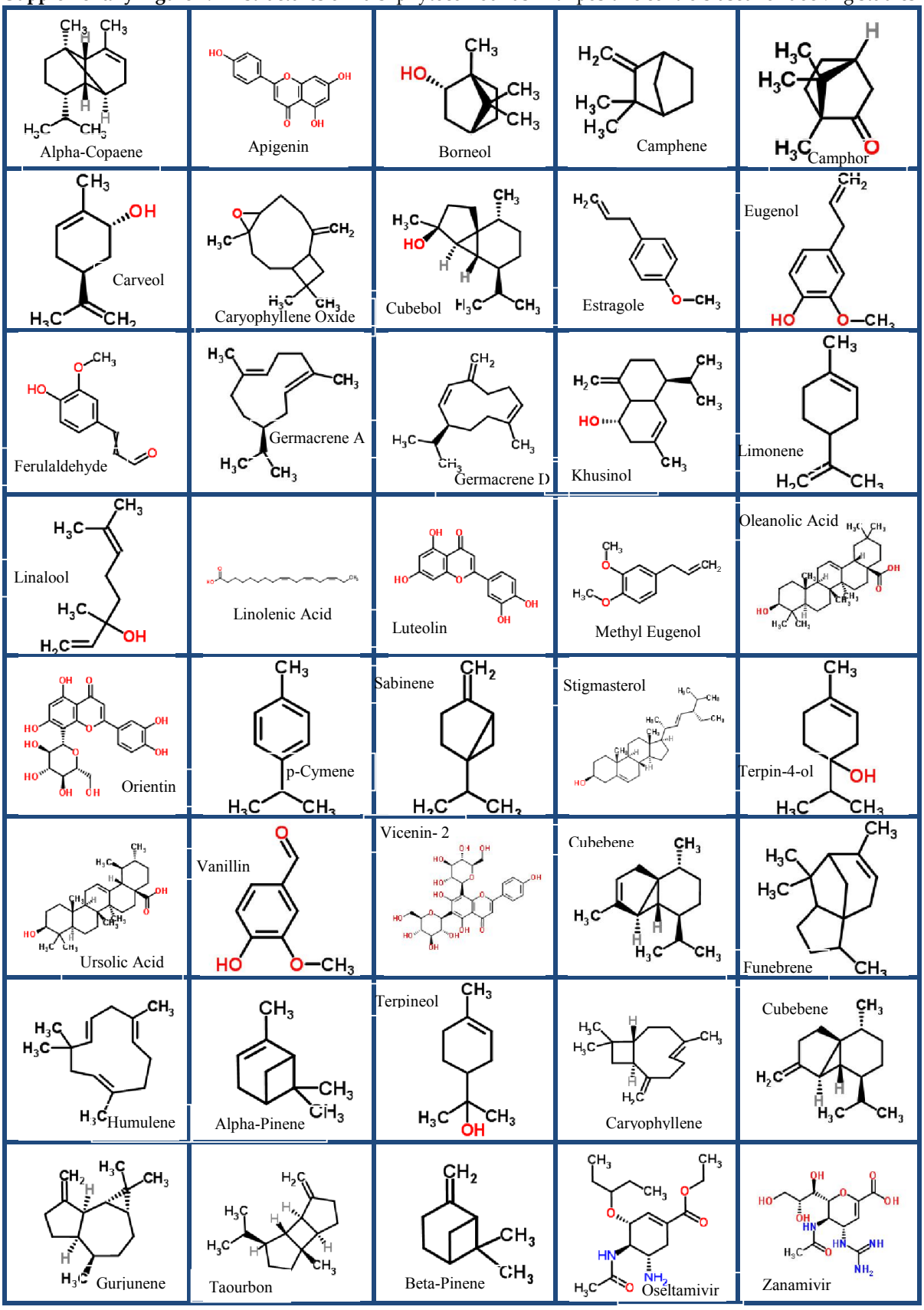

Table 1: H1N1 viral proteins used as a target in the docking study with their predicted active site

Proteins (PDB ID)	Active Binding site x, y, z, (Å)
1NCA	45.365, 40.588, 91.756
1NN2	93.068, 92.246, 64.287
2HU4	90.787, 92.589, 67.105
3CL2	-0.710, 81.087, 110.973
3B7E	-28.162, 12.483, -21.650
3CKZ	-31.559, -56.920, 7.650
3AL4	-33.295, -56.355, 8.472
3LZG	-124.334, -39.675, 27.607

Table 2: Apigenin showed the higest binding energies among all the selected phytocompounds with comparision to Oselamivir and Zanamivir control compounds while docking with Influenza viral proteins such as (PDB ID) A) 1NCA, B) 1NN2, C) 2HU4, D) 3CL2, E) 3B7E, F) 3CKZ, are Neuraminidase proteins, G) 3AL4 and H) 3LZG are Hemagglutinin proteins based on their rank (kacl/mol).

Ligands	H1N1 Viral Proteins							
	Neuraminidase Protein (Hydrolase)						Hemagglutinin Protein	
	1NCA	1NN2	2HU4	3CL2	3B7E	3CKZ	3AL4	3LZG
Apigenin	-7.7	-8.5	-8.8	-7.9	-7.8	-8.5	-8.6	-7.7
Oleanolic acid	-7.8	-8.5	-8.8	-8	-8.7	-8.5	-8.7	-8.4
Vicenin- 2	-7.6	-8.1	-8.7	-7.7	-8.1	-8.1	-8.2	-8.7
Stigmasterol	-6.9	-7.6	-8.1	-7.9	-7.7	-8	-8.2	-7.6
Ursolic Acid	-7.7	-8.6	-8.5	-7.6	-7.5	-8.5	-8.7	-7.5
Oseltamivir	-5.3	-6.3	-6.7	-6.4	-5.9	-6.6	-6.7	-6.5
Zanamivir	-5.8	-7.1	-7	-6.6	-6.5	-7.8	-7.6	-7.7

Table 3: Molinspiratin web server was used to calculate Lipinski's rule of five drug-likeness properties of potential compounds. Apigenin and Oseltamivir didn't violated Lipinski's rule of five for druglikeness properties, whereas the remain five ligands including Zanamivir was violated Lipinki's rule.

Ligands	LogP	TPSA	MW	nOH	nOHNH	Volume	nViolations
Oleanolic acid	6.725	57.527	456.711	3	2	471.139	1
Vicenin- 2	-2.102	271.187	594.522	15	11	486.357	3
Stigmasterol	7.869	20.228	412.702	1	1	450.33	1
Ursolic Acid	6.789	57.527	456.711	3	2	471.489	1
Apigenin	2.463	90.895	270.24	5	3	224.049	0
Oseltamivir	0.852	90.66	312.41	6	3	309.599	0
Zanamivir	-3.642	200.725	332.313	11	9	283.974	3

Abbreviations: LogP, lipophilic efficiency; TPSA, topological polar surface area; MW, molecular weight; n ON, hydrogen bond acceptor; n OHNH, number of hydrogen bond donor; Volume, 3D molecular geometry of ligand; and n violations, number of Lipinski's rule of five violations.

Table 4: ADMET properties of Apigenin, Oseltamivir, and Zanamivir predicted from admetSAR and Toxtree software. Apigenin showed better BBB, HIA and Caco-2 permeability as compared to Oseltamivir and Zanamivir. Whereas the remaining parameters, Apigenin showed almost similar to Oselamivir and Zanamivir.

ADMET	Apigenin	Oseltamivir	Zanamivir
BBB	+	-	-
HIA	+	+	-
Caco-2 permeable	+	-	-

Aqueous solubility	-2.77	-2.99	-2
P-gp Substrate	-	+	+
P-gp Inhibitor	-	-	-
CYP450 2C9	-	-	-
CYP450 2D6	-	-	-
CYP450 3A4	-	+	-
CYP450 1A2	+	-	-
CYP450 2C9	+	-	-
CYP450 2D6	-	-	-
CYP450 2C19	+	-	-
CYP450 3A4	+	-	-
ROCT	-	-	-
HERG-I	Weak	Weak	Weak
HERG-II	-	-	-
Ames Toxicity	-	-	-
Negative for genotoxic carcinogenity	yes	yes	yes
Negative for nongenotoxic carcinogenity	yes	yes	yes
Potential S.Typhiurium TA 100 mutagen based on QSAR	No	No	No
Potential carcinogen based on QSAR	No	No	No

Abbreviations: ADMET, absorption, distribution, metabolism, and excretion-toxicity; BBB, blood–brain barrier penetration; HIA , human intestinal absorption; Caco-2, Caco-2 permeability; CYP, cytochrome P; ROCT, renal organic cation transportation; HERG , human ether-a-go-go-related genes inhibition; P-gp, permeability glycoprotein; +, present; -, not present.