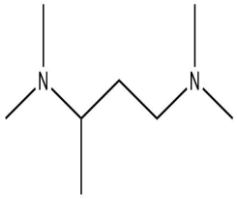
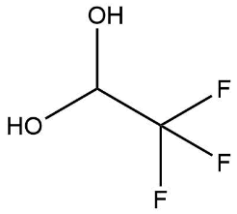
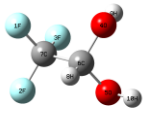
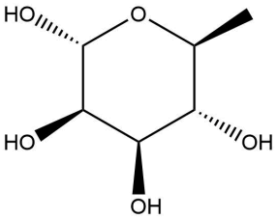
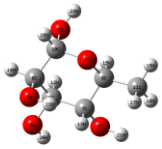
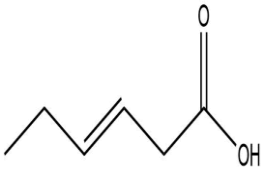
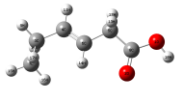
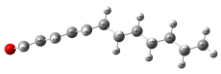
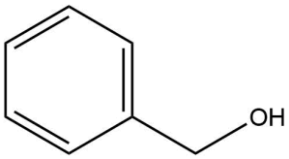
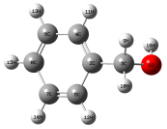
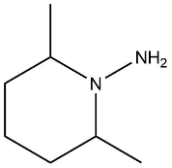
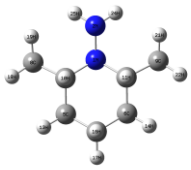
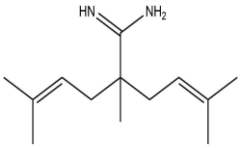
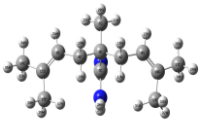
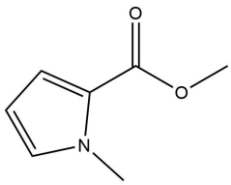
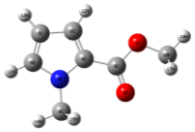
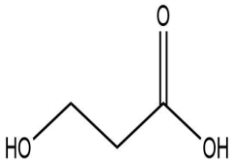
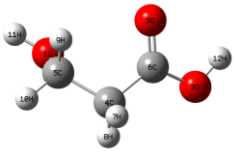
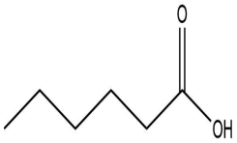
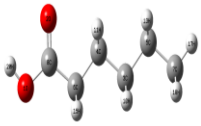
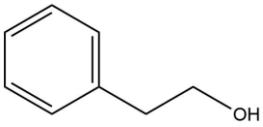
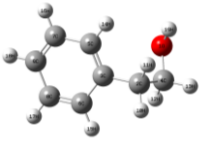
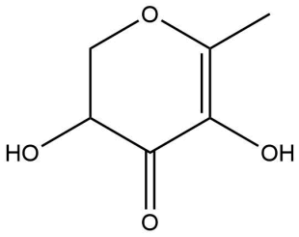
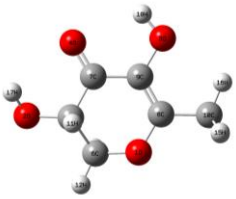
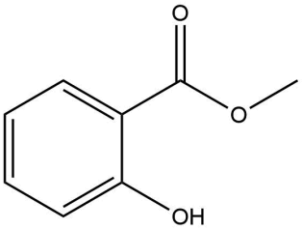
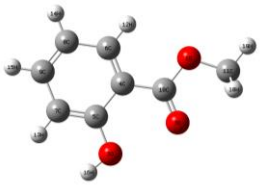
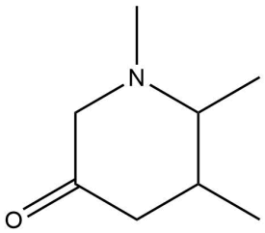
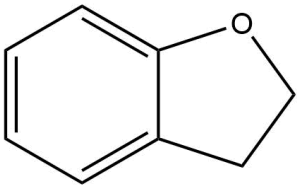
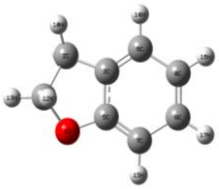
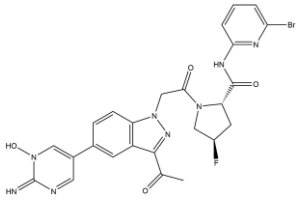
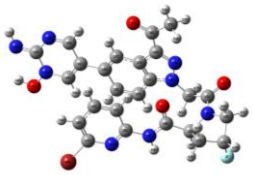
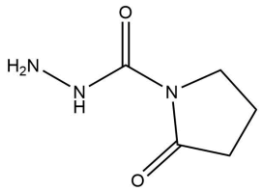
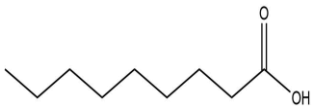
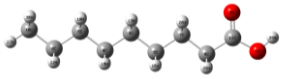
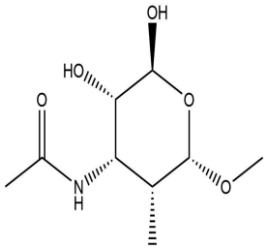
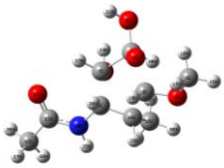
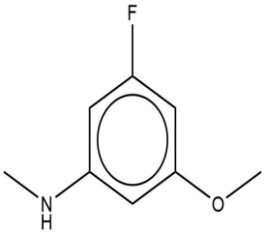
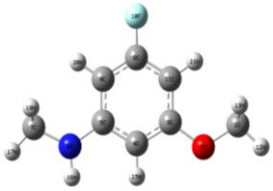
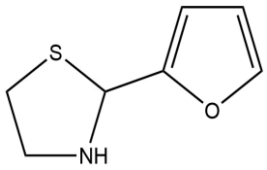
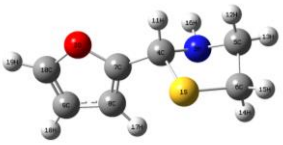
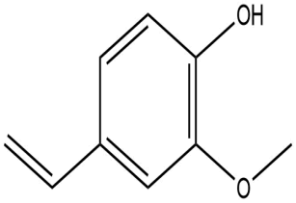
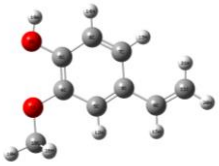
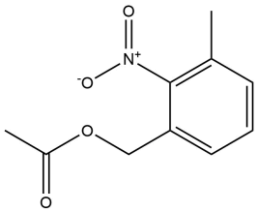
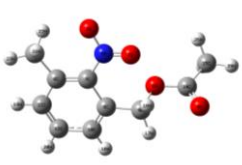
Supplementary in silico data

Table ST13: General information of the ligand library for the computational analysis.

Compound	Name	PubChem CID	2D Structure	Optimized 3D structure
1	1,3-Butanediamine, N,N,N',N'-tetramethyl-	7350		
			CC(CCN(C)C)N(C)C	
2	Trifluoroacetaldehyde hydrate	67901		
			C(C(F)(F)F)(O)O	
3	Alpha-l-rhamnopyranose	439710		
			C[C@H]1[C@@H]([C@H]([C@H]([C@@H](O1)O)O)O)O	
4	3-Hexenoic acid, (E)-	5282708		
			CC/C=C/CC(=O)O	
5	2,4-Dodecadienal, (E,E)-	5367530		
			CCCCCCC/C=C/C=C/C=O	

6	Benzyl alcohol	244	 C1=CC=C(C=C1)CO	
7	1-Amino-2,6-dimethylpiperidine	123482	 CC1CCCC(N1N)C	
8	2,6-Dimethylhex-4-enamidine, 2-(3-methylbut-2-enyl)-	586884	 CC(=CCC(C)(CC=C(C)C)C(=N)N)C	
9	Methyl 1-methylpyrrole-2-carboxylate	142178	 CN1C=CC=C1C(=O)OC	
10	3-Hydroxypropionic acid	68152	 C(CO)C(=O)O	
11	Hexanoic Acid	8892	 CCCCCC(=O)O	
12	Phenylethyl Alcohol	6054	 C1=CC=C(C=C1)CCO	

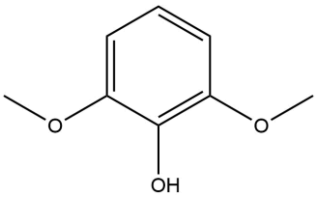
13	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	119838		
	CC1=C(C(=O)C(CO1)O)O			
14	Methyl salicylate	4133		
	COC(=O)C1=CC=CC=C1O			
15	Azacyclohexan-3-one, 1,5,6-trimethyl-	566749		
	CC1CC(=O)CN(C1C)C			
16	Benzofuran, 2,3-dihydro-	10329		
	C1COC2=CC=CC=C21			
17	2-Aminopyrimidine-1-oxide	126623006		
	CC(=O)C1=NN(C2=C1C=C(C=C2)C3=CN(C(=N)N=C3)O)CC(=O)N4C[C@@H](C[C@H]4C(=O)NC5=NC(=CC=C5)Br)F			
18	l-Pyrrolid-2-one, N-carboxyhydrazide	558364		

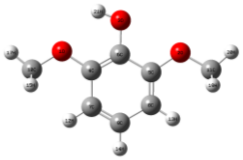
			C1CC(=O)N(C1)C(=O)NN	
19	Nonanoic acid	8158	 CCCCCCCCC(=O)O	
20	Talopyranoside, methyl 4-acetamido-4,6-dideoxy-, a-D-	N/A	 CO[C@H]1O[C@@H]([C@H]([C@H]([C@H]1C)NC(C)=O)O)O	
21	3-Amino-4-fluorophenol, N,O-dimethyl-	N/A	 COc1cc(F)cc(NC)c1	
22	Thiazolidine, 2-(2-furyl)-	593153	 C1CSC(N1)C2=CC=CO2	
23	2-Methoxy-4-vinylphenol	332	 COC1=C(C=CC(=C1)C=C)O	
24	Acetic acid, (3-methyl-2-nitrophenyl)methyl ester	91723971	 CC1=C(C(=CC=C1)COC(=O)C)[N+](=O)[O-]	

25

Phenol, 2,6-dimethoxy-

7041



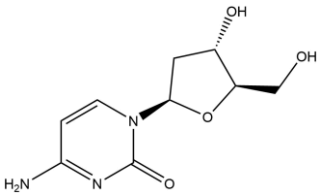


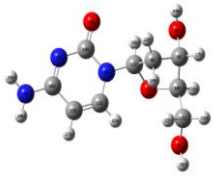
COC1=C(C(=CC=C1)OC)O

26

Deoxycytidine

13711



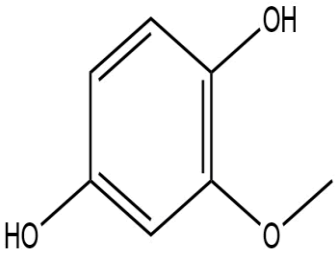


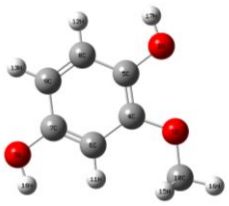
C1[C@@H]([C@H](O[C@H]1N2C=CC(=NC2=O)N)CO)O

27

1,4-Benzenediol, 2-methoxy-

69988



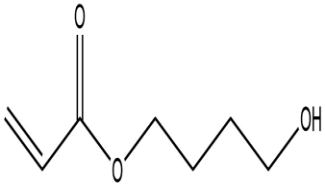


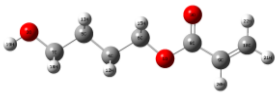
COC1=C(C=CC(=C1)O)O

28

4-Hydroxybutyl acrylate

75588



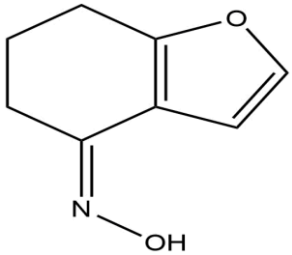


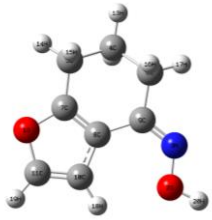
C=CC(=O)OCCCCO

29

Benzofuran-4(5H)-one, 6,7-dihydro-, oxime

6537039



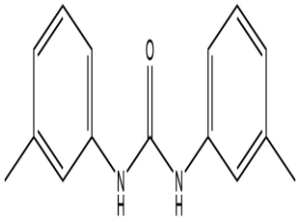


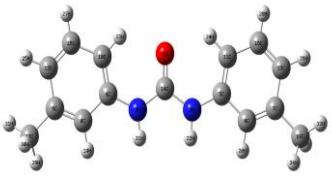
C1CC2=C(C=CO2)/C(=N\O)/C1

30

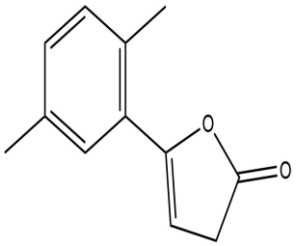
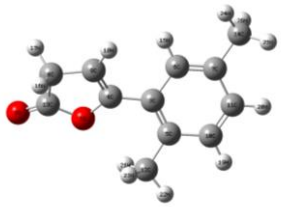
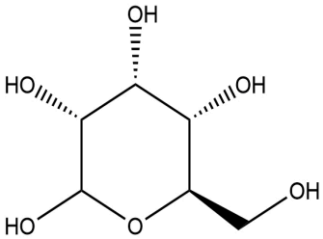
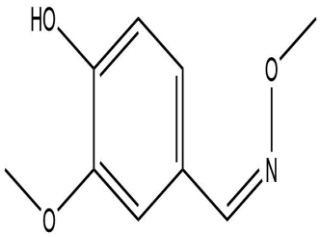
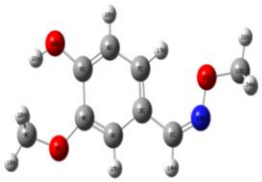
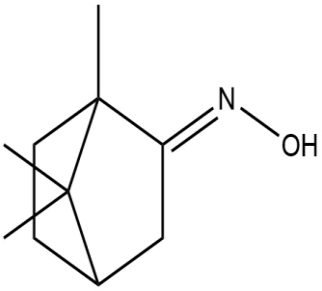
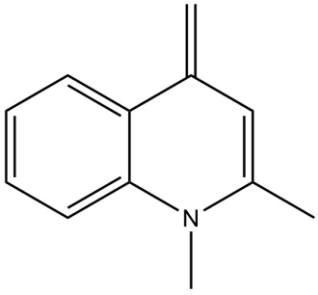
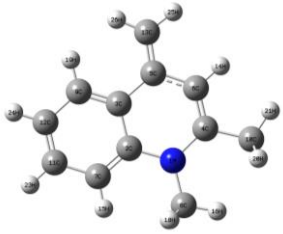
Urea, N,N'-bis(3-methylphenyl)-

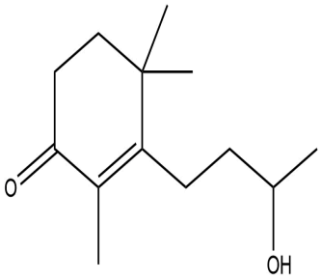
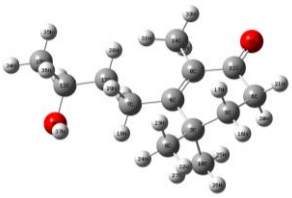
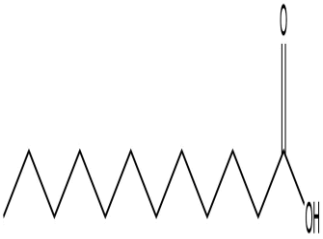
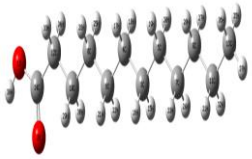
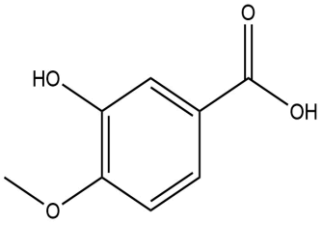
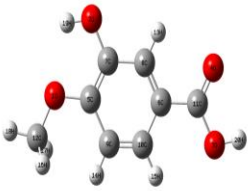
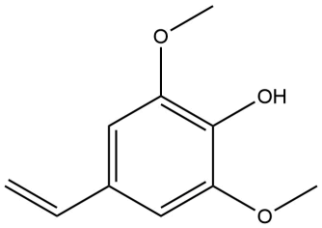
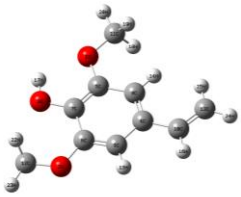
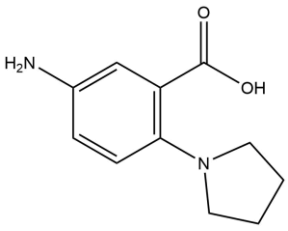
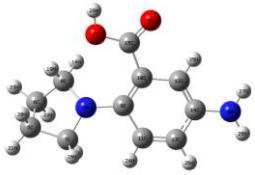
136428

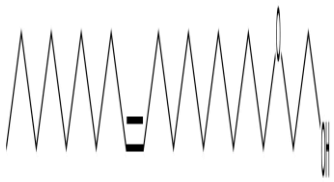
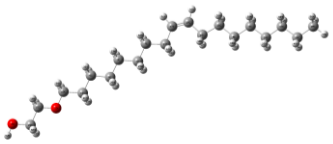
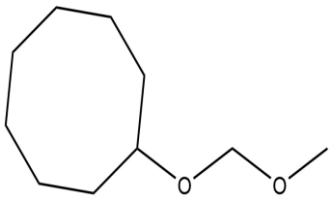
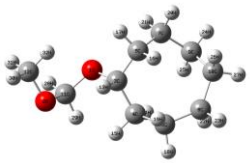
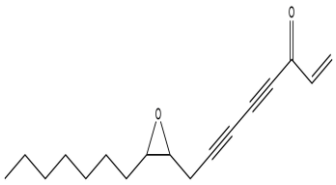
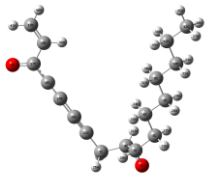
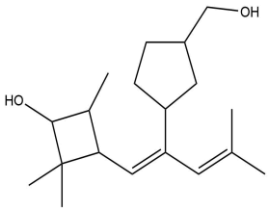
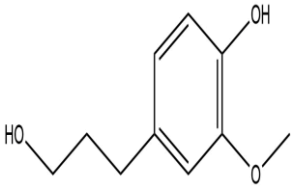
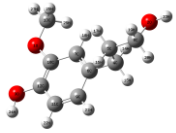
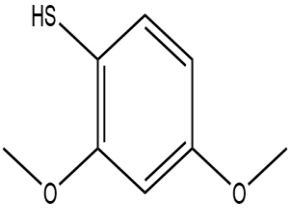
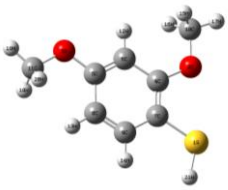




CC1=CC(=CC=C1)NC(=O)NC2=CC=CC(=C2)C

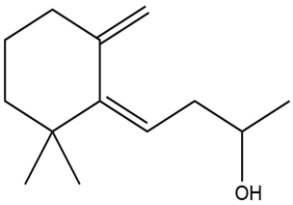
31	2(3H)-Furanone, 5-(2,5-dimethylphenyl)-	604728	 CC1=CC(=C(C=C1)C)C2=CCC(=O)O2	
32	D-Allose	439507	 C([C@@H]1[C@H]([C@H]([C@H](C(O1)O)O)O)O)O	
33	(Z)-4-hydroxy-3-methoxybenzaldehyde O-methyl oxime		 COC1=CC(/C=N\OC)=CC=C1O	
34	Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-, oxime, (1R)-	5908504	 CC1(C2CCC1(/C(=N/O)/C2)C)C	
35	1,4-Dihydro-1,2-dimethylquinolin-4-ylidenemethane	598718	 CC1(C2CCC1(/C(=N/O)/C2)C)C	

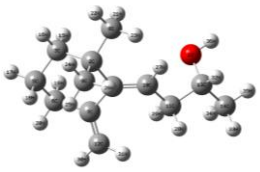
36	2-Cyclohexen-1-one, 3-(3-hydroxybutyl)-2,4,4-trimethyl-	520295	 CC1=C(C(CCC1=O)(C)C)CCC(C)O	
37	Dodecanoic acid	3893	 CCCCCCCCCCCC(=O)O	
38	3-Hydroxy-4-methoxybenzoic acid	12575	 COC1=C(C=C(C=C1)C(=O)O)O	
39	Phenol, 4-ethenyl-2,6-dimethoxy-	35960	 COC1=CC(=CC(=C1O)OC)C=C	
40	Benzoic acid, 3-amino-6-(1-pyrrolidinyl)-	609825	 C1CCN(C1)C2=C(C=C(C=C2)N)C(=O)O	

41	Ethanol, 2-(9-octadecenyloxy)-, (Z)-	5364713	 CCCCCCCC/C=C\CCCCCCCCOCCO	
42	Cyclooctane, (methoxymethoxy)-	542175	 COCOC1CCCCCCC1	
43	Ginsenoyne E	5320336	 CCCCCCCC1C(O1)CC#CC#CC(=O)C=C	
44	(E)-3-(2-(3-(hydroxymethyl)cyclopentyl)-4-methylpenta-1,3-dien-1-yl)-2,2,4-trimethylcyclobutan-1-ol	N/A	 C/C(C)=C\C(C1CCC(C1)CO)=C\C2C(C(C2(C)C)O)C	
45	Benzenepropanol, 4-hydroxy-3-methoxy-	16822	 COC1=C(C=CC(=C1)CCCO)O	
46	2,4-Dimethoxythiophenol	2758492	 COC1=CC(=C(C=C1)S)OC	

47

2-Butanol, 4-(2,2-dimethyl-6-methylenecyclohexylidene)- 5372134

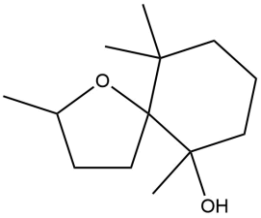


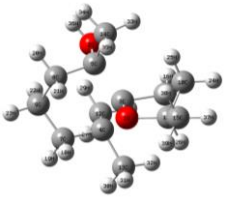


CC(C/C=C/1\C(=C)CCCC1(C)C)O

48

2,6,10,10-Tetramethyl-1-oxaspiro[4.5]decan-6-ol 65428

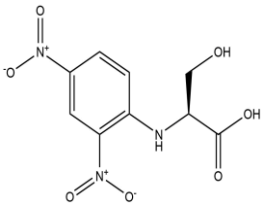


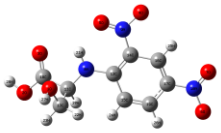


CC1CCC2(O1)C(CCCC2(C)O)(C)C

49

Dnp-L-serine 96800

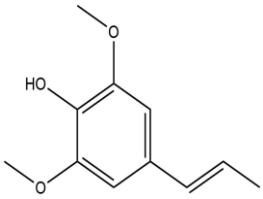


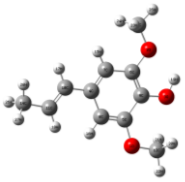


C1=CC(=C(C=C1[N+](=O)[O-])[N+](=O)[O-])N[C@@H](CO)C(=O)O

50

(E)-2,6-Dimethoxy-4-(prop-1-en-1-yl)phenol 5352905

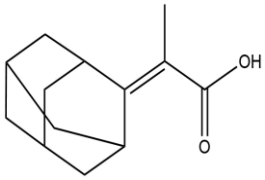


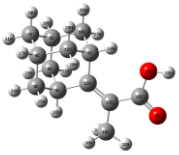


C/C=C/C1=CC(=C(C(=C1)OC)O)OC

51

Propanoic acid, 2-(tricyclo[3.3.1.13,7]dec-2-ylidene)- 609874

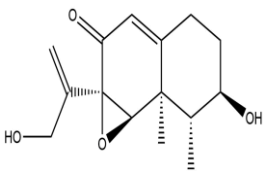


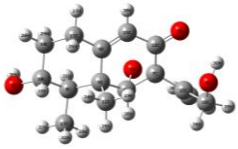


CC(=C1C2CC3CC(C2)CC1C3)C(=O)O

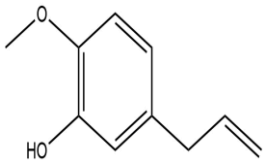
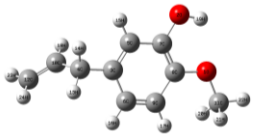
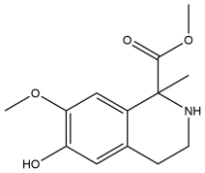
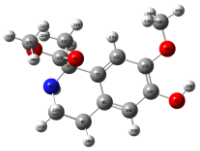
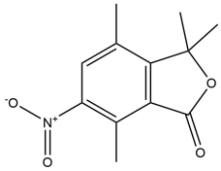
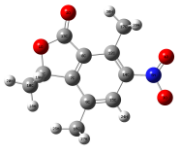
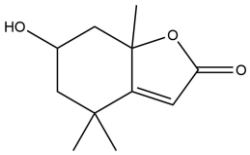
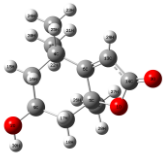
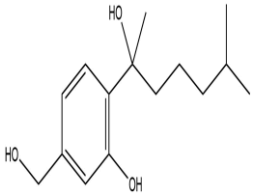
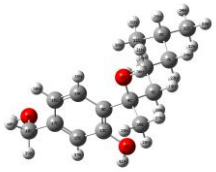
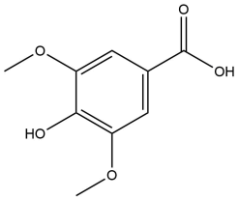
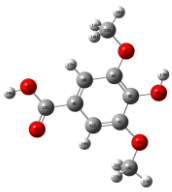
52

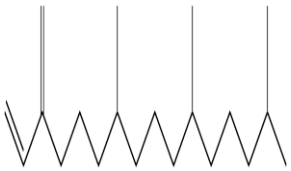
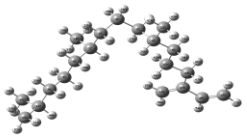
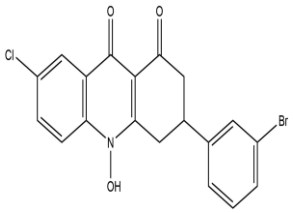
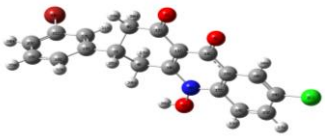
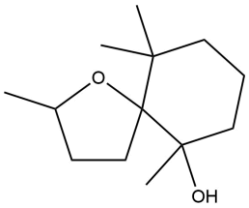
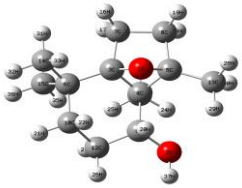
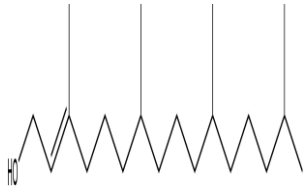
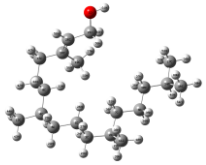
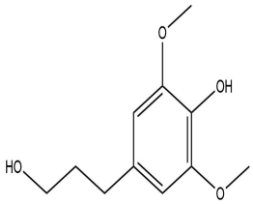
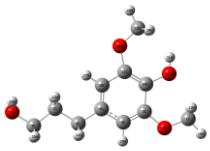
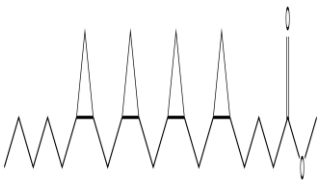
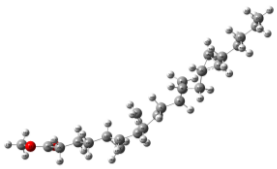
Phomenone 93306

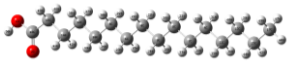
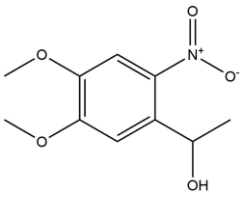
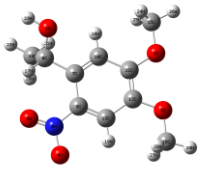
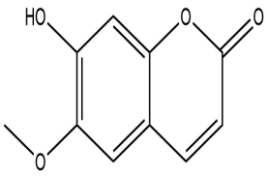
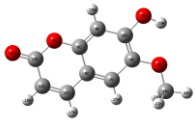
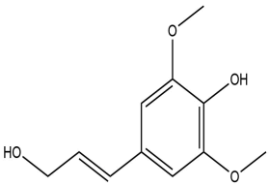
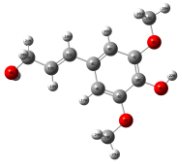
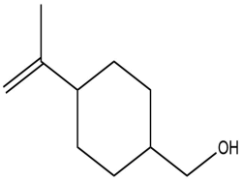
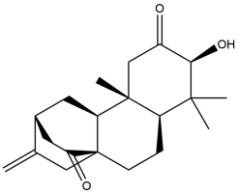
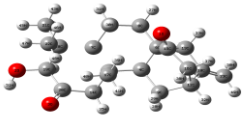


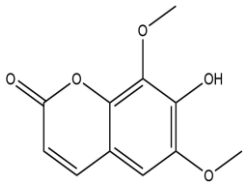
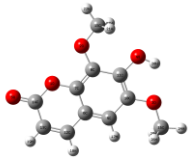
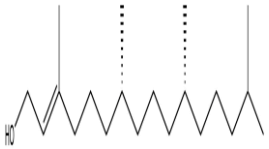
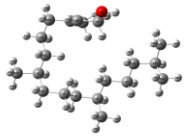
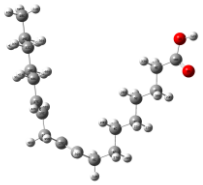
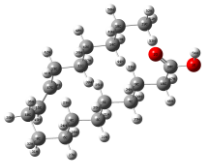
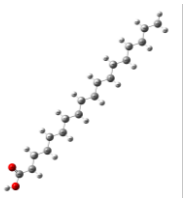
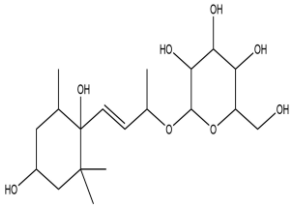
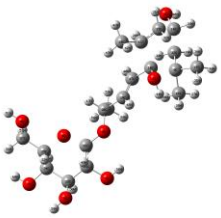


C[C@H]1[C@@H](CCC2=CC(=O)[C@]3([C@@H]([C@]12C)O3)C(=C)CO)O

53	3-Allyl-6-methoxyphenol	596375	 COC1=C(C=C(C=C1)CC=C)O	
54	Tetradecanoic acid	11005	 CCCCCCCCCCCCCC(=O)O	
55	(+)-1,2,3,4-Tetrahydroisoquinolin-6-ol-1-carboxylic acid, 7-methoxy-1-methyl-, methyl(ester)	606044	 CC1(C2=CC(=C(C=C2CCN1)O)OC)C(=O)OC	
56	1,3-2H-Isobenzofuranone, 3,3,4,7-tetramethyl-6-nitro-	613231	 CC1=CC(=C(C2=C1C(OC2=O)(C)C)C)[N+](=O)[O-]	
57	6-Hydroxy-4,4,7a-trimethyl-5,6,7,7a-tetrahydrobenzofuran-2(4H)-one	14334		
58	Sydonol	24011597	 CC(C)CCCC(C)(C1=C(C=C(C=C1)CO)O)O	
59	Benzoic acid, 4-hydroxy-3,5-dimethoxy-	10742	 COC1=CC(=CC(=C1O)OC)C(=O)O	

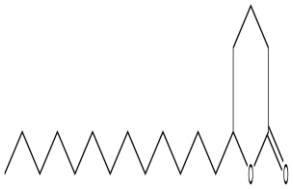
60	Neophytadiene	10446		
			CC(C)CCCC(C)CCCC(C)CCCC(=C)C=C	
61	3-[3-Bromophenyl]-7-chloro-3,4-dihydro-10-hydroxy-1,9(2H,10H)-acridinedione	536420		
			C1C(CC(=O)C2=C1N(C3=C(C2=O)C=C(C=C3)Cl)O)C4=CC(=CC=C4)Br	
62	2,2,6,7-Tetramethyl-10-oxatricyclo[4.3.1.0(1,6)]decan-5-ol	536541		
			CC1(CCC(C2(C13CCC2(O3)C)C)O)C	
63	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	5366244		
			CC(C)CCCC(C)CCCC(C)CCC/C(=C/CO)/C	
64	Dihydrosyringenin	N/A		
			COC1=CC(CCCO)=CC(OC)=C1O	
65	Cyclopropanebutanoic acid, 2-[[2-[[2-[(2-pentylcyclopropyl)methyl]cyclopropyl]methyl]cyclopropyl]methyl]-, methyl ester	554084		
			CCCCCC1CC1CC2CC2CC3CC3CC4CC4CCCC(=O)OC	

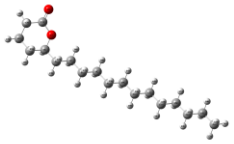
66	Pentadecanoic acid, 14-methyl-, methyl ester	21205	 CC(C)CCCCCCCCCCCCC(=O)OC	
67	n-Hexadecanoic acid	985	 CCCCCCCCCCCCCCCC(=O)O	
68	1-(4,5-dimethoxy-2-nitrophenyl)ethan-1-ol	2754046	 CC(C1=CC(=C(C=C1[N+](=O)[O-])OC)OC)O	
69	Scopoletin	5280460	 COC1=C(C=C2C(=C1)C=CC(=O)O2)O	
70	trans-Sinapyl alcohol	5280507	 COC1=CC(=CC(=C1O)OC)/C=C/CO	
71	trans-Shisool	519954	 CC(=C)C1CCC(CC1)CO	
72	Atis-16-ene, (5ß,8a,9ß,10a,12a)-	392473		

			C[C@@]12CC(=O)[C@H](C([C@H]1CC[C@]34[C@H]2C[C@H](CC3=O)C(=C)C4)(C)C)O	
73	Isofraxidin	5318565		
			COC1=C(C(=C2C(=C1)C=CC(=O)O2)OC)O	
74	Phytol	5280435		
			C[C@@H](CCC[C@@H](C)CCC/C(=C/CO)/C)CCCC(C)C	
75	Linoelaidic acid	5282457		
			CCCCC/C=C/C/C=C/CCCCCCCC(=O)O	
76	cis-Vaccenic acid	5282761		
			CCCCCC/C=C\CCCCCCCCCC(=O)O	
77	Octadecanoic acid	5281		
			CCCCCCCCCCCCCCCCCC(=O)O	
78	2-[(E)-4-(1,4-dihydroxy-2,2,6-trimethylcyclohexyl)but-3-en-2-yl]oxy-6-(hydroxymethyl)oxane-3,4,5-triol	16745401		
			CC1CC(CC(C1(/C=C/C(C)OC2C(C(C(C(O2)CO)O)O)O)O)(C)C)O	

79

2H-Pyran-2-one, tetrahydro-6-tridecyl- 518573

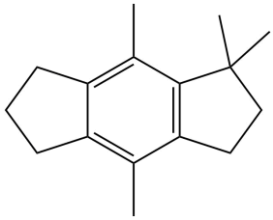




CCCCCCCCCCCCCCC1CCCC(=O)O1

80

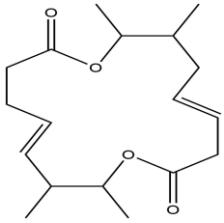
s-Indacene, 1,2,3,5,6,7-hexahydro-1,1,4,8-tetramethyl- 608083

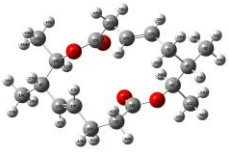


CC1=C2CCCC2=C(C3=C1CCC3(C)C)C

81

1,9-Dioxacyclohexadeca-4,13-diene-2-10-dione, 7,8,15,16-tetramethyl- 5373406

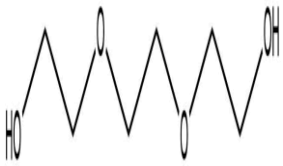


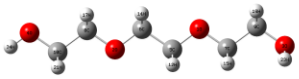


CC1C/C=C/CC(=O)OC(C(/C=C/CCC(=O)OC1C)C)C

82

Triethylene glycol 8172

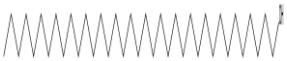


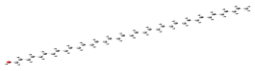


C(COCCOCCO)O

83

1-Heptatriacotanol 537071

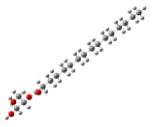




CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCO

84

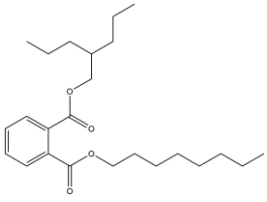
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester 123409

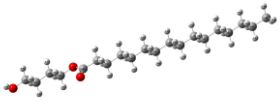


CCCCCCCCCCCCCCCC(=O)OC(CO)CO

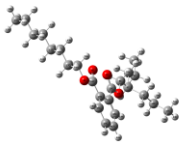
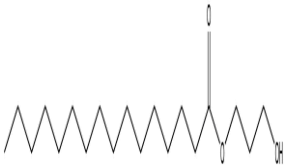
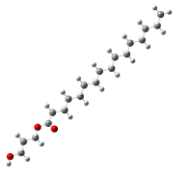
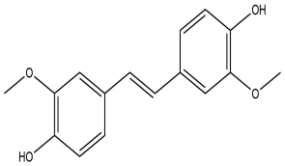
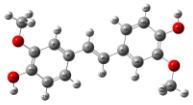
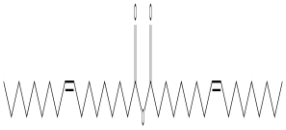
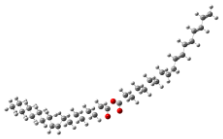
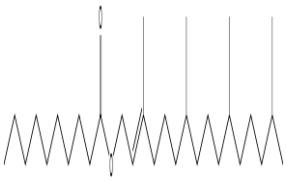
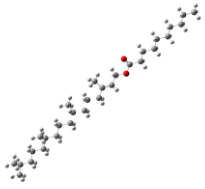
85

Phthalic acid, octyl 2-propylpentyl ester 91720176





CCCCCCCCOC(=O)C1=CC=CC=C1C(=O)OCC(CCC)CCC

86	4-Hydroxybutyl hexadecanoate	205694		
	CCCCCCCCCCCCCCCC(=O)OCCCCO			
87	3-Hydroxypropyl hexadecanoate	24802448		
	CCCCCCCCCCCCCCCC(=O)OCCCO			
88	(E)-3,3'-Dimethoxy-4,4'-dihydroxystilbene	5280698		
	COC1=C(C=CC(=C1)/C=C/C2=CC(=C(C=C2)O)OC)O			
89	Oleic anhydride	5369123		
	CCCCCCCC/C=C\CCCCCCCC(=O)OC(=O)CCCCCCC/C=C\CCCCCCCC			
90	Octadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	79075		
	CCCCCCCCCCCCCCCCCC(=O)OC(CO)CO			
91	Phytyl decanoate	91711717		
	CCCCCCCCCC(=O)OC/C=C(\C)/CCCC(C)CCCC(C)CCCC(C)C			
92	Phytyl heptadecanoate	N/A		
	CCCCCCCCCCCCCCCCC(OCC(C(CCCC(C)C)C)C)=O			

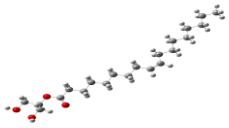
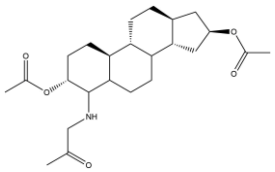
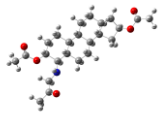
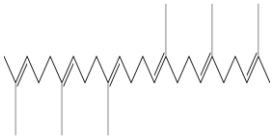
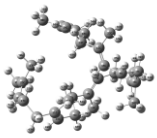
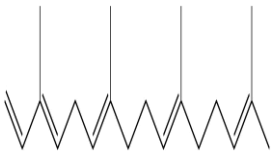
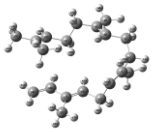
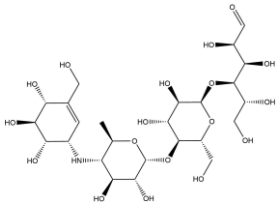
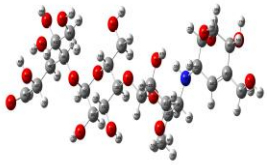
93	1,3-dihydroxypropan-2-yl (Z)-octadec-9-enoate	5319879		
	CCCCCCCC/C=C\\CCCCCCCC(=O)OC(CO)CO			
94	(5ß)Pregnane-3,20ß-diol, 14a,18a-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-, diacetate			
	CC(O[C@@H]1CC[C@H]2[C@@H]3CC[C@H]4C[C@H](C[C@@H]4C3CCC2C1NCC(C)=O)OC(C)=O)=O			
95	Squalene	638072		
	CC(=CCC/C(=C/CC/C(=C/CC/C=C(/CC/C=C(/CCC=C(C)C)\C)\C)/C)/C)C			
96	(E,E,E)-3,7,11,15-Tetramethylhexadeca-1,3,6,10,14-pentaene	5365883		
	CC(=CCC/C(=C/CC/C(=C/C/C=C(\C)/C=C)/C)/C)C			
97	Rhodopin	5365880		
	CC(=CCC/C(=C/C=C/C(=C/C=C/C(=C/C=C/C=C(\C)/C=C/C=C(\C)/C=C/C=C(\C)/CCCC(C)(C)O)/C)/C)/C)C			
Control	Acarbose	9811704		
	C[C@@H]1[C@H]([C@@H]([C@H]([C@H](O1)O[C@@H]2[C@H](O[C@@H]([C@@H]([C@H]2O)O)O[C@H]([C@@H](CO)O)[C@@H]([C@H](C=O)O)O)CO)O)O)N[C@H]3C=C([C@H]([C@@H]([C@H]3O)O)O)CO			

Table ST14: Predicted binding pockets of the target proteins identified using the PrankWeb tool.

Protein	PDB ID	Description					
α-amylase	2QV4	Rank	Score	Probability	No of Residues	Residues	Average conservation score
		1	38.70	0.95	23	51, 53, 59, 62, 63, 151, 162, 163, 165, 197, 198, 200, 201, 233, 235, 240, 299, 300, 305, 306, 307, 356, 357	1.70
		2	1.37	0.01	8	318, 322, 377, 383, 387, 388, 389, 390	0
α-glucosidase	3A4A	1	25.67	0.88	35	69, 72, 112, 156, 157, 158, 159, 160, 178, 215, 216, 240, 241, 242, 277, 279, 280, 301, 303, 307, 310, 311, 312, 313, 314, 315, 316, 350, 351, 352, 353, 411, 415, 442, 446	0.24
		2	4.84	0.22	19	8, 11, 13, 15, 16, 259, 262, 263, 271, 272, 274, 290, 292, 295, 296, 297, 298, 341, 343	0
		3	3.45	0.13	13	156, 161, 233, 235, 236, 314, 317, 415, 418, 419, 422, 423, 429	0
		4	1.98	0.04	9	95, 98, 101, 102, 103, 208, 210, 268, 270	1.22
		5	1.28	0.01	9	58, 213, 301, 303, 347, 350, 351, 352, 353	0.25

Table ST15: Results of molecular docking of shortlisted GC–MS-identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL) against both target proteins.

Protein	Compound	Docking score (kcal/mol)	Number of hydrogen bond
α amylase	17	−10.4	6
	61	−9.9	2
	72	−9	0
	30	−8.9	2
	81	−8.6	0
	94	−8.3	2
	97	−8.1	1
	80	−7.8	0
	88	−7.8	2
	Control	−7.8	8
α glucosidase	17	−10.5	8
	61	−9.4	2
	94	−9.3	2
	72	−9	1
	78	−8.8	5
	81	−8.5	1
	95	−8.5	0
	Control	−8.0	18

Table ST16: Non-bond interaction profiles of the shortlisted GC–MS-guided compounds from the methanolic extract of *H. fomes* leaves (MEHFL) with α-amylase and α glucosidase.

Protein	Compound	Residue	Distance	Category	Types
α-amylase	17				Conventional Hydrogen Bond;Halogen
		ALA106	2.81	Hydrogen Bond;Halogen	(Fluorine)
		HIS299	2.44	Hydrogen Bond	Conventional Hydrogen Bond
		ASP300	2.38	Hydrogen Bond	Conventional Hydrogen Bond
		ASP300	2.52	Hydrogen Bond	Conventional Hydrogen Bond
		ASP197	2.40	Hydrogen Bond	Conventional Hydrogen Bond
		HIS305	3.55	Hydrogen Bond	Carbon Hydrogen Bond
		GLY104	3.56	Halogen	Halogen (Fluorine)
		TRP59	4.36	Hydrophobic	Pi-Pi Stacked
		TRP59	4.01	Hydrophobic	Pi-Pi Stacked
		ALA106	4.64	Hydrophobic	Alkyl
		PRO54	4.63	Hydrophobic	Alkyl
		TRP59	5.05	Hydrophobic	Pi-Alkyl
		TRP59	5.19	Hydrophobic	Pi-Alkyl
		TRP59	4.55	Hydrophobic	Pi-Alkyl
	30	GLU233	2.71	Hydrogen Bond	Conventional Hydrogen Bond
		ASP197	2.73	Hydrogen Bond	Conventional Hydrogen Bond
		ILE235	3.58	Hydrophobic	Pi-Sigma

		TYR62	4.30	Hydrophobic	Pi-Pi Stacked
		HIS201	4.39	Hydrophobic	Pi-Pi T-shaped
		ILE235	4.85	Hydrophobic	Alkyl
		TYR151	5.06	Hydrophobic	Pi-Alkyl
		HIS201	4.98	Hydrophobic	Pi-Alkyl
		ALA198	5.32	Hydrophobic	Pi-Alkyl
		LYS200	4.77	Hydrophobic	Pi-Alkyl
	61	GLN63	2.46	Hydrogen Bond	Conventional Hydrogen Bond
		GLN63	2.21	Hydrogen Bond	Conventional Hydrogen Bond
		GLU233	3.30	Halogen	Halogen (Cl, Br, I)
		ASP300	3.89	Electrostatic	Pi-Anion
		TRP59	4.15	Hydrophobic	Pi-Pi Stacked
		TRP59	4.51	Hydrophobic	Pi-Pi Stacked
		TRP59	3.94	Hydrophobic	Pi-Pi Stacked
		TRP59	3.72	Hydrophobic	Pi-Pi Stacked
		TYR62	4.50	Hydrophobic	Pi-Pi Stacked
		ALA198	4.19	Hydrophobic	Alkyl
		TRP59	5.30	Hydrophobic	Pi-Alkyl
	88	GLN63	2.25	Hydrogen Bond	Conventional Hydrogen Bond
		ASP197	2.45	Hydrogen Bond	Conventional Hydrogen Bond
		ASP300	3.33	Electrostatic	Pi-Anion
		TRP59	4.15	Hydrophobic	Pi-Pi Stacked
		TRP59	4.13	Hydrophobic	Pi-Pi Stacked
		TYR62	4.85	Hydrophobic	Pi-Pi T-shaped
		LEU162	5.20	Hydrophobic	Alkyl
		LEU165	4.74	Hydrophobic	Alkyl
	94	GLN63	1.93	Hydrogen Bond	Conventional Hydrogen Bond
		LEU162	4.64	Hydrophobic	Alkyl
		LEU162	4.73	Hydrophobic	Alkyl
		LEU165	4.90	Hydrophobic	Alkyl
		ALA198	4.82	Hydrophobic	Alkyl
		LEU165	5.36	Hydrophobic	Alkyl
		TRP59	5.20	Hydrophobic	Pi-Alkyl
		TRP59	5.08	Hydrophobic	Pi-Alkyl
	Control	ALA106	2.10	Hydrogen Bond	Conventional Hydrogen Bond
		ASP300	2.07	Hydrogen Bond	Conventional Hydrogen Bond
		GLU233	2.49	Hydrogen Bond	Conventional Hydrogen Bond
		GLU233	2.61	Hydrogen Bond	Conventional Hydrogen Bond
		GLN63	2.37	Hydrogen Bond	Conventional Hydrogen Bond
		GLY164	3.00	Hydrogen Bond	Conventional Hydrogen Bond
		AIS305	5.33	Hydrophobic	Pi-Alkyl
α-glucosidase	17	THR310	2.71	Hydrogen Bond	Conventional Hydrogen Bond
		ASP242	2.05	Hydrogen Bond	Conventional Hydrogen Bond
		TYR158	2.37	Hydrogen Bond	Conventional Hydrogen Bond
		PRO312	2.99	Hydrogen Bond	Conventional Hydrogen Bond
		GLU411	2.68	Hydrogen Bond	Conventional Hydrogen Bond

	ASP242	3.52	Hydrogen Bond	Carbon Hydrogen Bond
	ASP307	4.71	Electrostatic	Pi-Anion
	VAL232	5.46	Hydrophobic	Alkyl
	TYR158	4.38	Hydrophobic	Pi-Alkyl
	HIS280	4.79	Hydrophobic	Pi-Alkyl
61	ARG315	2.14	Hydrogen Bond	Conventional Hydrogen Bond
	ASP307	2.46	Hydrogen Bond	Conventional Hydrogen Bond
	ASP307	3.85	Electrostatic	Pi-Anion
	TYR158	5.25	Hydrophobic	Pi-Pi T-shaped
	SER311, PRO312	4.24	Hydrophobic	Amide-Pi Stacked
	TYR158	5.12	Hydrophobic	Pi-Alkyl
	PHE159	4.60	Hydrophobic	Pi-Alkyl
	ARG315	4.45	Hydrophobic	Pi-Alkyl
	PRO312	4.18	Hydrophobic	Pi-Alkyl
78	ARG315	2.96	Hydrogen Bond	Conventional Hydrogen Bond
	ARG315	3.04	Hydrogen Bond	Conventional Hydrogen Bond
	GLN353	2.05	Hydrogen Bond	Conventional Hydrogen Bond
	LEU313	1.88	Hydrogen Bond	Conventional Hydrogen Bond
	TYR158	2.61	Hydrogen Bond	Conventional Hydrogen Bond
	TYR158	3.56	Hydrophobic	Pi-Sigma
	LYS156	5.27	Hydrophobic	Alkyl
	LYS156	3.86	Hydrophobic	Alkyl
	ARG315	4.45	Hydrophobic	Alkyl
	TYR158	5.11	Hydrophobic	Pi-Alkyl
	HIS280	4.85	Hydrophobic	Pi-Alkyl
	PHE314	5.10	Hydrophobic	Pi-Alkyl
94	ARG315	2.56	Hydrogen Bond	Conventional Hydrogen Bond
	ASP307	3.07	Hydrogen Bond	Conventional Hydrogen Bond
	TYR72	3.74	Hydrophobic	Pi-Sigma
	VAL216	5.46	Hydrophobic	Alkyl
	ARG315	4.17	Hydrophobic	Alkyl
	TYR158	5.10	Hydrophobic	Pi-Alkyl
	TYR158	5.01	Hydrophobic	Pi-Alkyl
	PHE159	5.37	Hydrophobic	Pi-Alkyl
	PHE178	5.09	Hydrophobic	Pi-Alkyl
Control	SER240	2.18	Hydrogen Bond	Conventional Hydrogen Bond
	GLN279	2.90	Hydrogen Bond	Conventional Hydrogen Bond
	ARG315	2.83	Hydrogen Bond	Conventional Hydrogen Bond
	ARG315	2.57	Hydrogen Bond	Conventional Hydrogen Bond
	ARG315	2.82	Hydrogen Bond	Conventional Hydrogen Bond
	ASP242:OD2	1.96	Hydrogen Bond	Conventional Hydrogen Bond
	ASP242:OD2	2.65	Hydrogen Bond	Conventional Hydrogen Bond
	PRO312	2.48	Hydrogen Bond	Conventional Hydrogen Bond
	HIS280	2.43	Hydrogen Bond	Conventional Hydrogen Bond

	GLU411	2.55	Hydrogen Bond	Conventional Hydrogen Bond
	GLN353	2.66	Hydrogen Bond	Conventional Hydrogen Bond
	ASP352	2.60	Hydrogen Bond	Conventional Hydrogen Bond
	GLN353	2.17	Hydrogen Bond	Conventional Hydrogen Bond
	GLU277	2.61	Hydrogen Bond	Conventional Hydrogen Bond
	ARG315	3.40	Hydrogen Bond	Carbon Hydrogen Bond

Table ST17: Comprehensive ADMET profile of shortlisted GC–MS identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL).

	Absorption						Distribution				Metabolism												Excretion				Toxicity			
Compound	HOB20%		HOB50%	HIA	PGI	PGS	BBB	FU	PPB	VDss	CYP1A2I	CYP1A2S	CYP2C19I	CYP2C19S	CYP2C9I	CYP2C9S	CYP2D6I	CYP2D6S	CYP3A4I	CYP3A4S	OATP1B1	OATP1B3	Cl	OCT2	HL	LD_{50}	TC	Hep	Car	Mut	Cyt
17	B (0.77)		B (0.66)	0.76	I	S	0.21	14.31	88.93	1.49	NI	NS	I	NS	I	S	NI	NS	NI	NS	I	NI	4.43	NI	<3	2500	5	Active	Inactive	Active	Inactive
30	B (0.85)		B (0.71)	0.98	NI	NS	0.94	2.49	96.79	0.72	I	NS	I	S	I	S	NI	NS	NI	NS	NI	NI	7.38	NI	<3	900	4	Active	Inactive	Inactive	Inactive
61	B (0.82)		B (0.68)	0.99	I	NS	0.61	0.61	99.35	0.72	I	S	I	S	I	NS	I	NS	I	S	NI	NI	1.31	NI	<3	340	4	Inactive	Inactive	Inactive	Inactive
78	B (0.76)		NB(0.18)	0.62	NI	NS	0.13	54.31	64.13	0.25	NI	NS	NI	NS	NI	NS	NI	NS	NI	NS	NI	NI	1.56	NI	≥3	2000	4	Inactive	Inactive	Inactive	Inactive
88	B (0.63)		B (0.57)	0.98	NI	NS	0.21	1.47	99.07	0.84	I	S	I	NS	NI	S	NI	NS	NI	NS	NI	NI	12.87	NI	<3	1560	4	Inactive	Inactive	Inactive	Inactive
94	B (0.72)		B (0.72)	0.98	I	NS	0.24	17.12	59.46	0.87	I	NS	NI	NS	NI	NS	NI	NS	NI	S	NI	NI	2.67	NI	<3	41	2	Inactive	Inactive	Inactive	Inactive
Control	NB(0.02)		NB(0.03)	0.0	NI	NS	0.33	61.30	18.60	0.47	NI	NS	NI	NS	NI	NS	NI	NS	NI	NS	NI	NI	0.68	NI	≥3	2000	4	Active	Inactive	Inactive	Inactive

Abbreviation: HOB20%: Human oral bioavailability 20% (Probability), HOB50%: Human oral bioavailability 50% (Probability), HIA: Human Intestinal Absorption, PGI: P−glycoprotein inhibitor, PGS: P−glycoprotein substrate, BBB: Blood−Brain barrier (Probability), FU: Fraction unbound (Human) (Percentage), PPB: Plasma protein binding (Percentage), VDss: Steady state volume of distribution (Log VDss), CYP1A2I: CYP 1A2 Inhibitor, CYP1A2S: CYP 1A2 Substrate, CYP2C19I: CYP 2C19 Inhibitor, CYP2C19S: CYP 2C19 Substrate, CYP2C9I: CYP 2C9 Inhibitor, CYP2C9S: CYP 2C9 Substrate, CYP2D6I: CYP 2D6 Inhibitor, CYP2D6S: CYP 2D6 Substrate, CYP3A4I: CYP 3A4 Inhibitor, CYP3A4S: CYP 3A4 Substrate, OATP1B1, OATP1B3, Cl: Clearance (ml/min/kg), OCT2: Organic cation transporter 2, HL: Half−life (hr), LD_{50}: LD_{50} (mg/kg), TC: Toxicity Class, Hep: Hepatotoxicity, Car: Carcinogenicity, Mut: Mutagenicity, Cyt: Cytotoxicity, B: Bioavailable, NB: Non-Bioavailable, NI: Non-Inhibitor, NS: Non-Substrate, I: Inhibitor, S: Substrate

Table ST18: Predicted passive permeability profiles of shortlisted GC–MS identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL) obtained using the PerMM web tool.

Name	Calculated parameters	Results
17	Free energy of binding (DOPC)	−2.84 kcal/mol
	Log of perm. coeff. − BLM	−9.02
	Log of perm. coeff − BBB (Po)	−6.08
	Log of perm. coeff − CACO2 (Po)	−5.79
	Log of perm. coeff − PAMPA−DS (Po)	−9.55
30	Free energy of binding (DOPC)	−5.01 kcal/mol
	Log of perm. coeff. − BLM	1.60
	Log of perm. coeff − BBB (Po)	−2.33
	Log of perm. coeff − CACO2 (Po)	−3.07
	Log of perm. coeff − PAMPA−DS (Po)	0.25
61	Free energy of binding (DOPC)	−6.19 kcal/mol
	Log of perm. coeff. − BLM	−0.40
	Log of perm. coeff − BBB (Po)	−3.03
	Log of perm. coeff − CACO2 (Po)	−3.58
	Log of perm. coeff − PAMPA−DS (Po)	−1.59
78	Free energy of binding (DOPC)	−3.60 kcal/mol
	Log of perm. coeff. − BLM	−10.02
	Log of perm. coeff − BBB (Po)	−6.43
	Log of perm. coeff − CACO2 (Po)	−6.04
	Log of perm. coeff − PAMPA−DS (Po)	−10.48
88	Free energy of binding (DOPC)	−2.39 kcal/mol
	Log of perm. coeff. − BLM	−2.87
	Log of perm. coeff − BBB (Po)	−3.91
	Log of perm. coeff − CACO2 (Po)	−4.22
	Log of perm. coeff − PAMPA−DS (Po)	−3.88
94	Free energy of binding (DOPC)	−5.12 kcal/mol
	Log of perm. coeff. − BLM	0.98
	Log of perm. coeff − BBB (Po)	−2.55
	Log of perm. coeff − CACO2 (Po)	−3.23
	Log of perm. coeff − PAMPA−DS (Po)	−0.33
Control	Free energy of binding (DOPC)	−3.33 kcal/mol
	Log of perm. coeff. − BLM	−19.93
	Log of perm. coeff − BBB (Po)	−9.93
	Log of perm. coeff − CACO2 (Po)	−8.58
	Log of perm. coeff − PAMPA−DS (Po)	−19.62

Table ST19: Predicted off targets (top 10) of the selected GC–MS identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL) from SwissTargetPrediction.

Compound	Target	Common name	Target Class	Probability
61	Matrix metalloproteinase 13	MMP13	Protease	0.09
	Matrix metalloproteinase 1	MMP1	Protease	0.09
		PSEN2 PSENEN NCSTN		0.09
	Gamma−secretase	APH1A PSEN1 APH1B	Protease	
	Histone deacetylase 8	HDAC8	Eraser	0.09
	Matrix metalloproteinase 9	MMP9	Protease	0.09
	Matrix metalloproteinase 2	MMP2	Protease	0.09
	ADAM17	ADAM17	Protease	0.09
	Nuclear receptor ROR−gamma	RORC	Nuclear receptor	0.09
	PI3−kinase p110−delta subunit	PIK3CD	Enzyme	0.09
	Protein−tyrosine phosphatase 1B	PTPN1	Phosphatase	0.09
78			Electrochemical	
	Sodium/glucose cotransporter 2	SLC5A2	transporter	0.11
			Family A G	0.11
			protein−coupled	
	Adenosine A1 receptor (by homology)	ADORA1	receptor	
	Protein−tyrosine phosphatase 1B	PTPN1	Phosphatase	0.11
	Tyrosinase	TYR	Oxidoreductase	0.11
	Protein phosphatase 2C beta	PPM1B	Phosphatase	0.11
	Serine/threonine protein phosphatase PP1−gamma			0.11
	catalytic subunit	PPP1CC	Phosphatase	
	Serine/threonine protein phosphatase 2A, 56 kDa			0.11
	regulatory subunit, alpha isoform	PPP2R5A	Phosphatase	
	Adenosine deaminase	ADA	Hydrolase	0.11
			Electrochemical	0.11
	Sodium/glucose cotransporter 1	SLC5A1	transporter	
			Family A G	0.11
			protein−coupled	
	Adenosine A2a receptor (by homology)	ADORA2A	receptor	
88	Quinone reductase 2	NQO2	Enzyme	0.26
	Cytochrome P450 1A2	CYP1A2	Cytochrome P450	0.24
	Cytochrome P450 1B1	CYP1B1	Cytochrome P450	0.23
	Cytochrome P450 1A1	CYP1A1	Cytochrome P450	0.23
	Cyclooxygenase−1	PTGS1	Oxidoreductase	0.19
	Tubulin beta−1 chain	TUBB1	Structural protein	0.19
	Estrogen receptor alpha	ESR1	Nuclear receptor	0.16
	Nuclear factor NF−kappa−B p65 subunit	RELA	Transcription factor	0.14
	Cyclooxygenase−2	PTGS2	Oxidoreductase	0.13
	Tubulin beta−3 chain	TUBB3	Structural protein	0.13

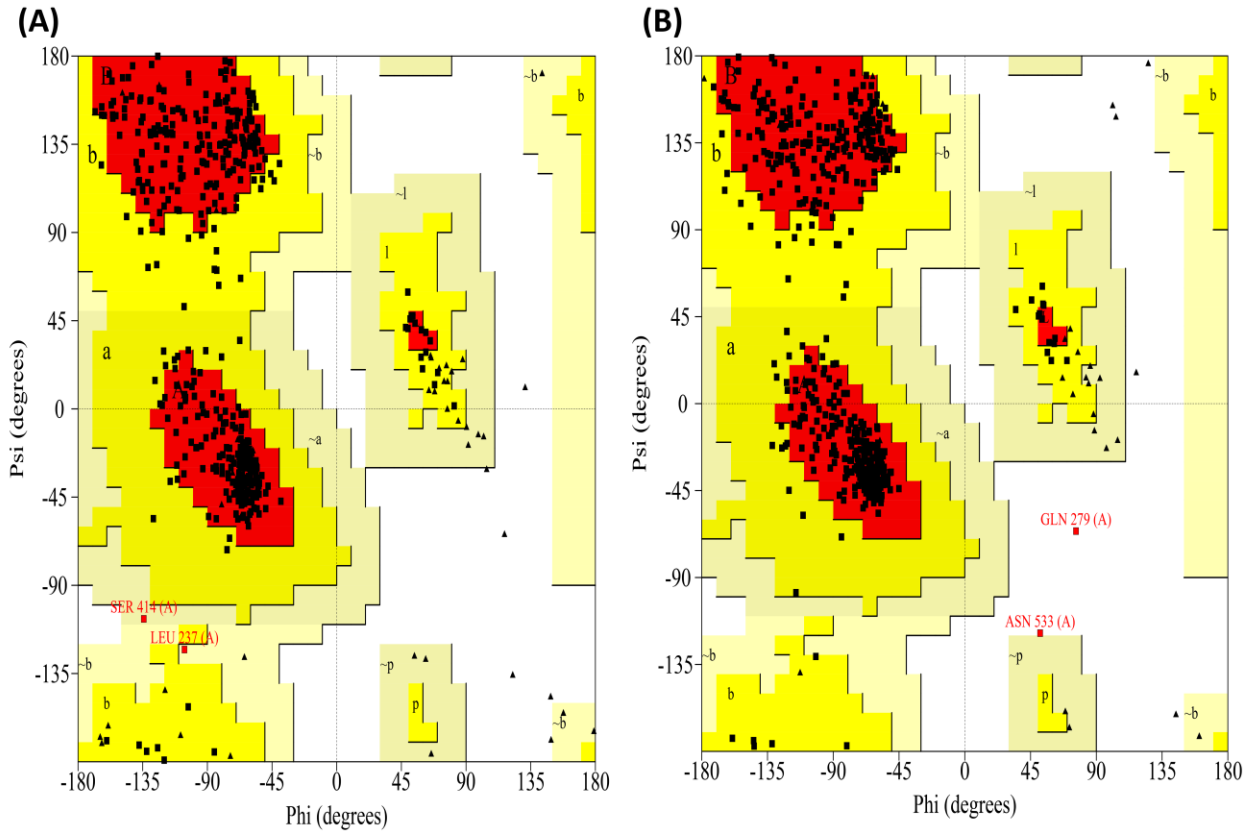


Figure SF4: PROCHECK Ramachandran plots of (A) α amylase, (B) α glucosidase.

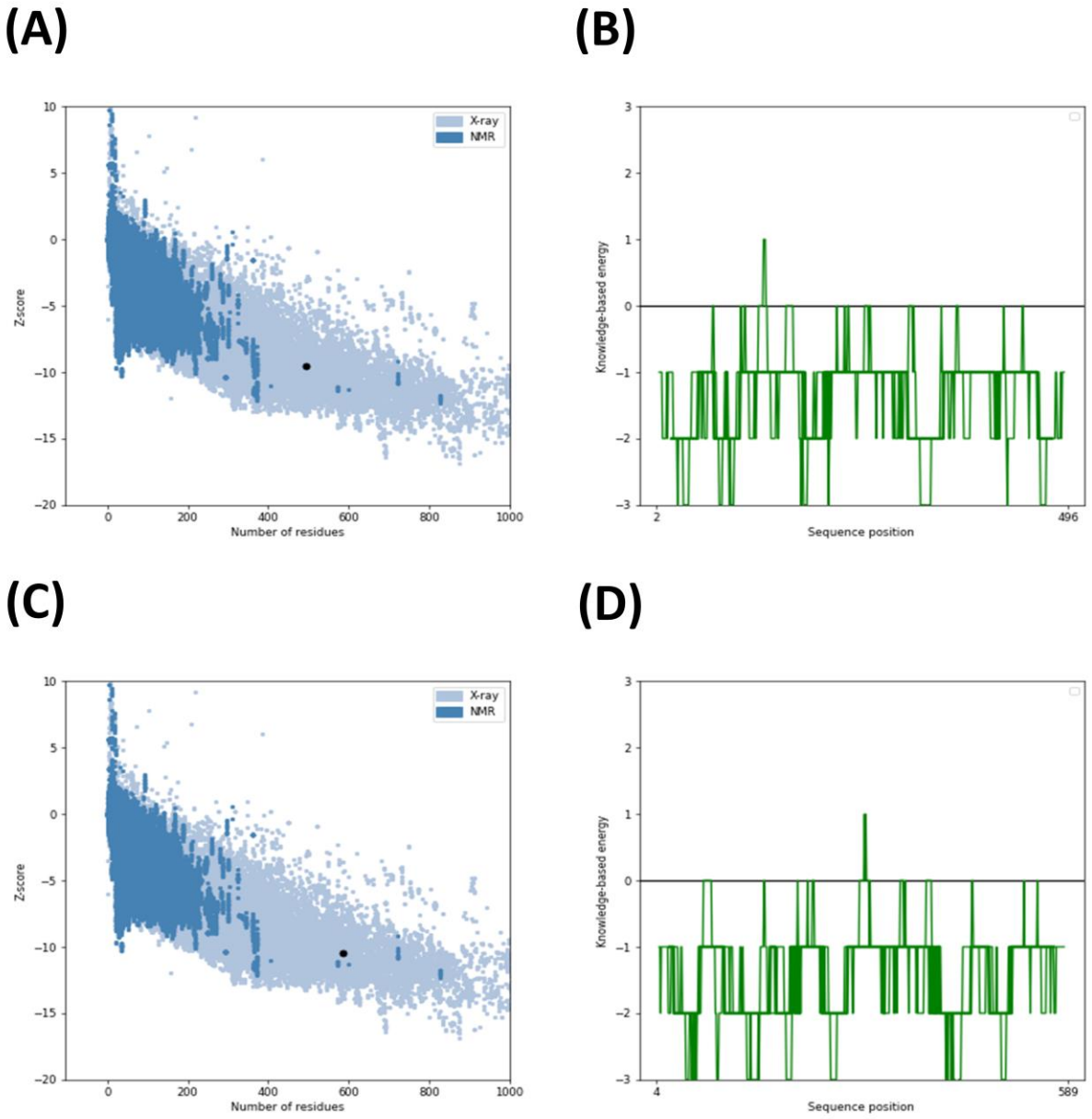


Figure SF5: ProSA-Web validation parameters of the target proteins. (A, B) Z scores of α amylase and α glucosidase within the range of experimentally determined NMR structures; (C, D) residue wise energy profiles of α amylase and α glucosidase, respectively.

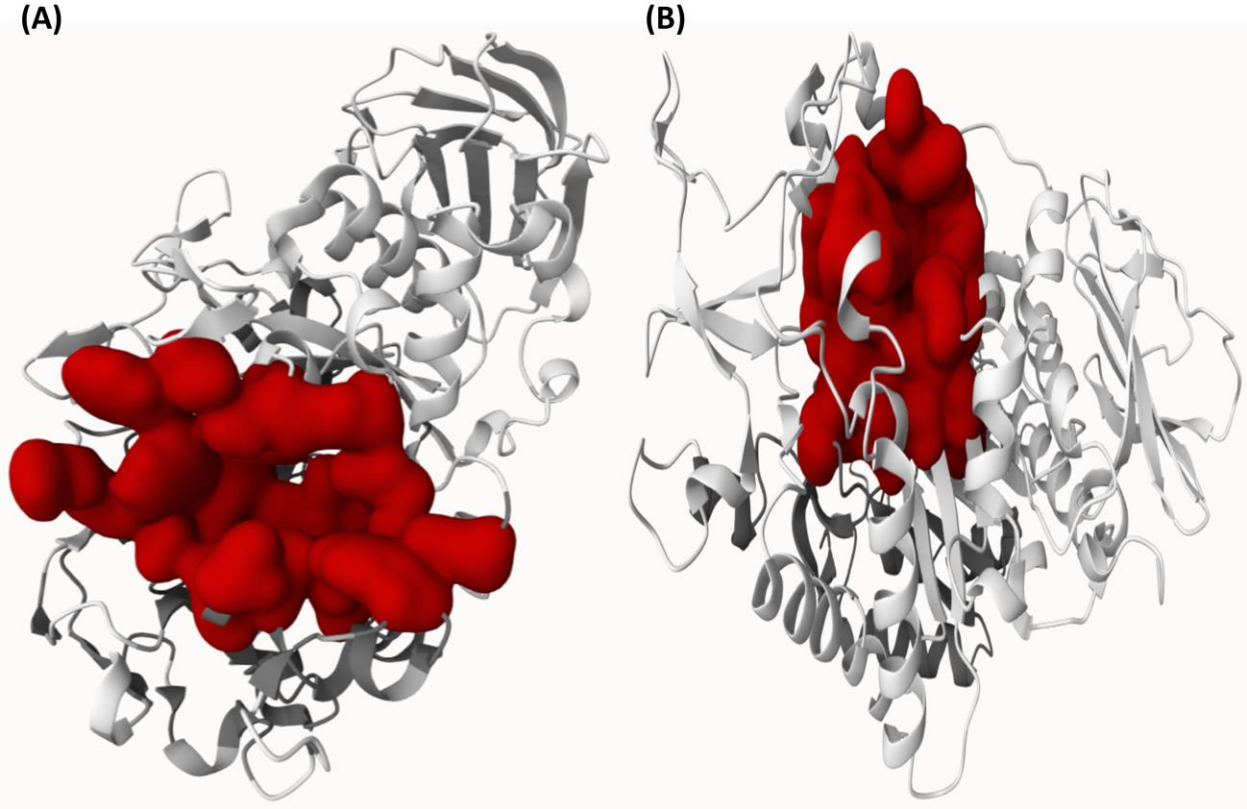


Figure SF6: PrankWeb predicted active site of (A) α amylase, (B) α glucosidase.

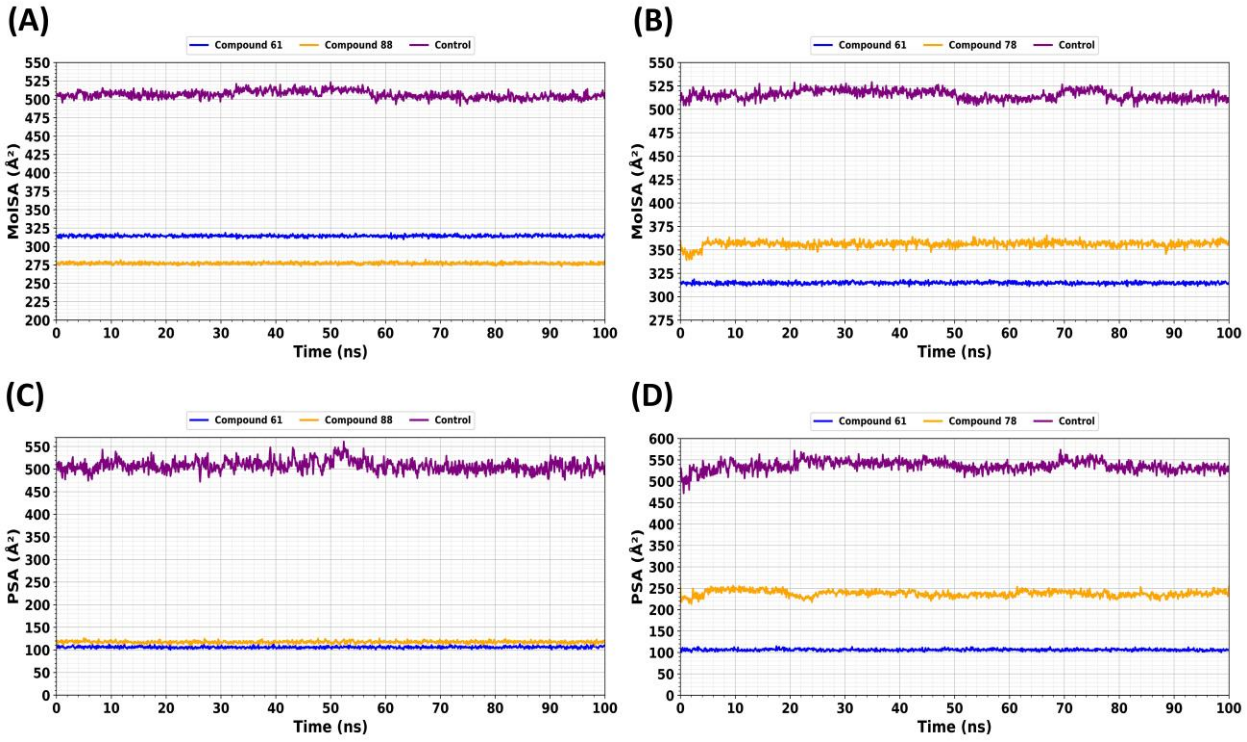


Figure SF7: Molecular surface area (MolSA) and polar surface area (PSA) profiles of selected GC–MS identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL). (A, B) MolSA in α amylase and α glucosidase, respectively; (C, D) PSA in α amylase and α glucosidase, respectively.