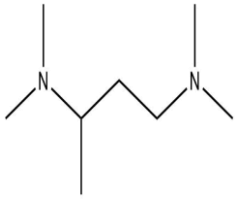
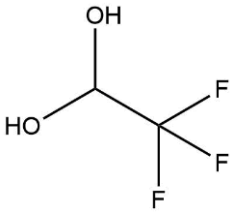
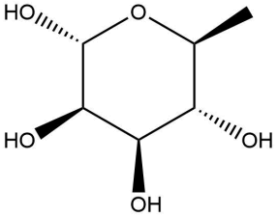
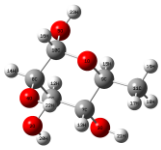
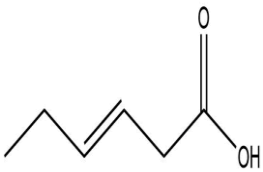
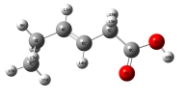
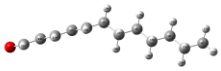
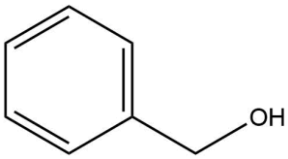
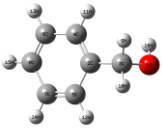
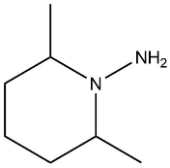
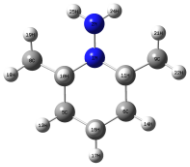
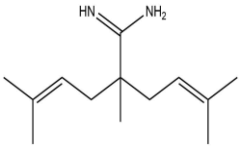
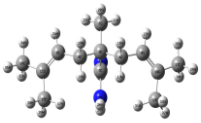
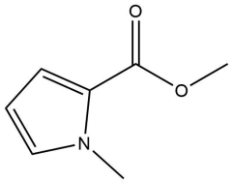
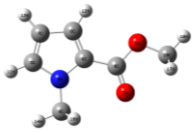
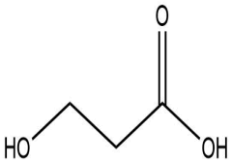
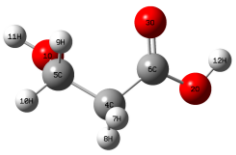
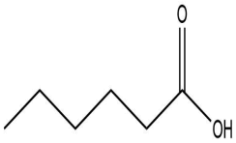
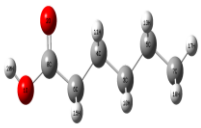
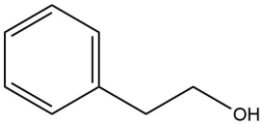
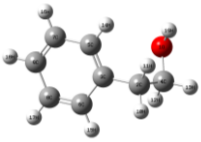
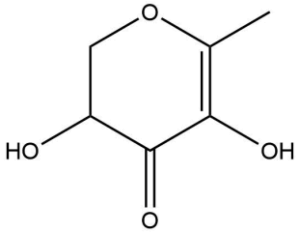
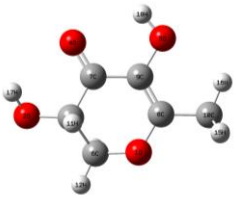
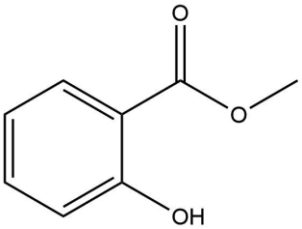
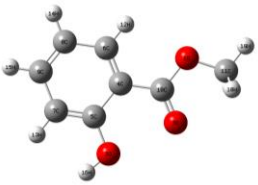
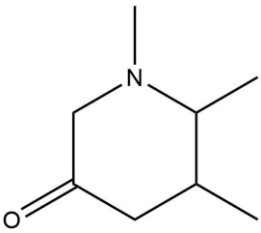
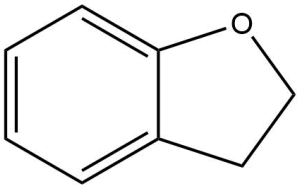
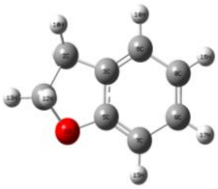
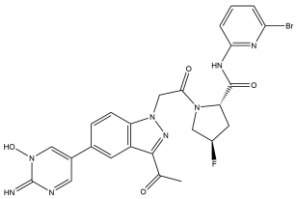
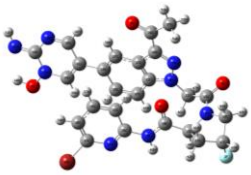
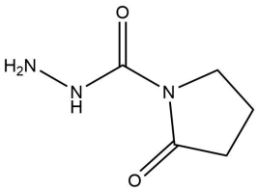
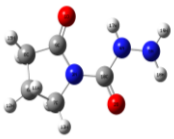
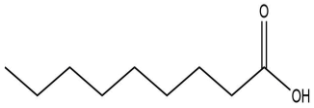
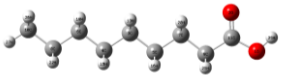
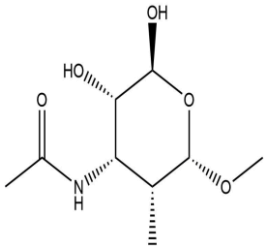
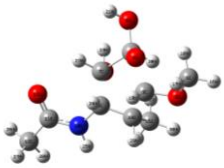
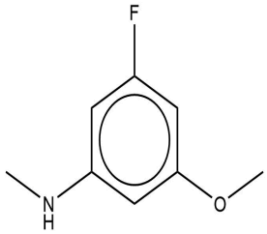
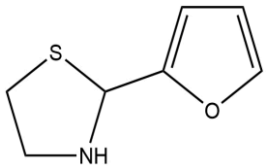
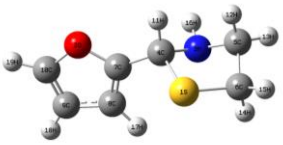
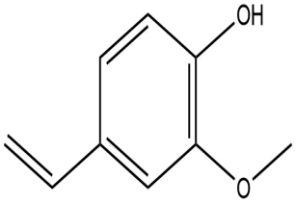
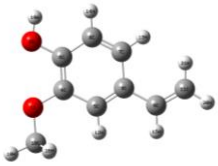
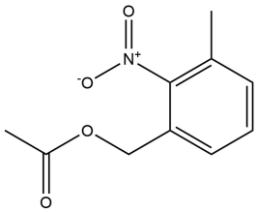
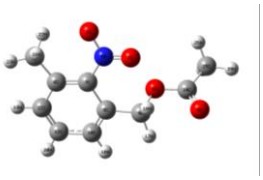
Supplementary in silico data

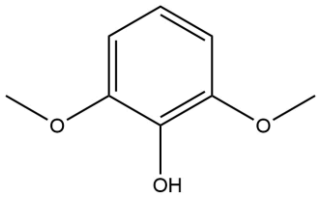
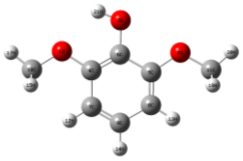
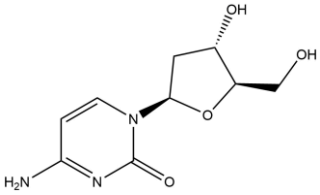
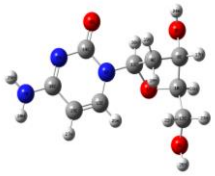
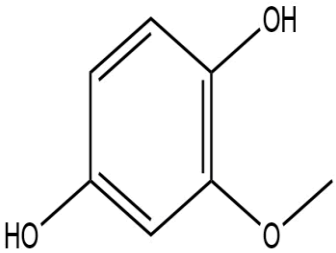
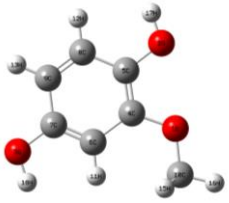
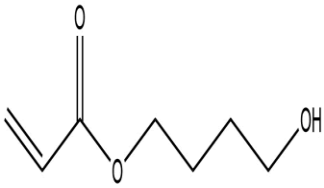
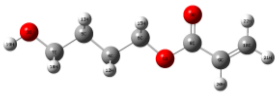
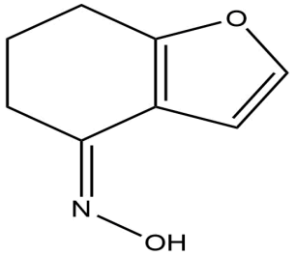
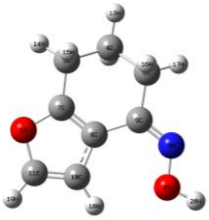
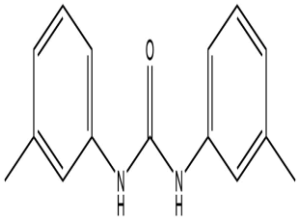
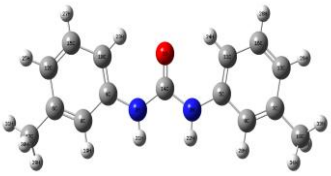
Table ST13: General information of the ligand library for the computational analysis.

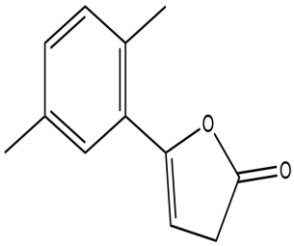
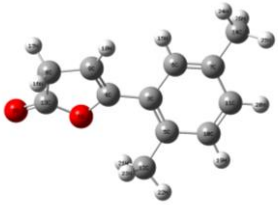
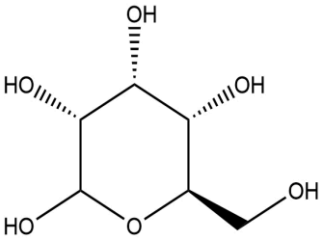
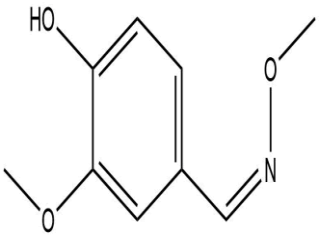
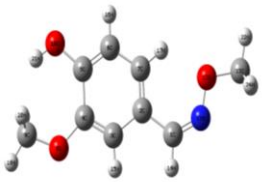
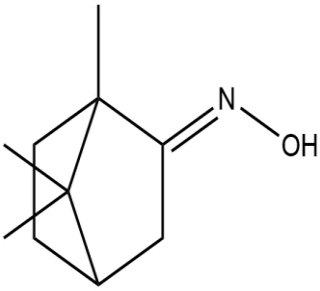
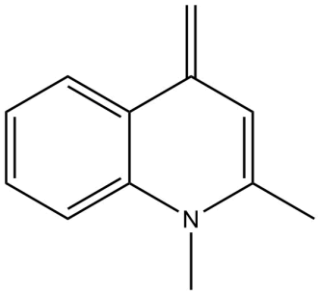
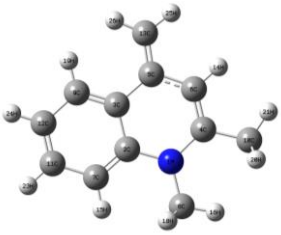
Compound	Name	PubChem CID	2D Structure	Optimized 3D structure
1	1,3-Butanediamine, N,N,N',N'-tetramethyl-	7350	 CC(CCN(C)C)N(C)C	
2	Trifluoroacetaldehyde hydrate	67901	 C(C(F)(F)F)(O)O	
3	Alpha-l-rhamnopyranose	439710	 C[C@H]1[C@@H]([C@H]([C@H]([C@@H](O1)O)O)O)O	
4	3-Hexenoic acid, (E)-	5282708	 CC/C=C/CC(=O)O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

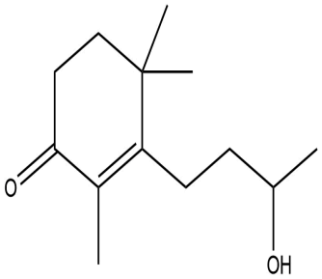
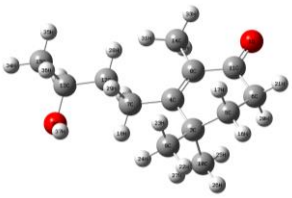
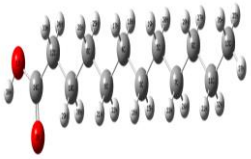
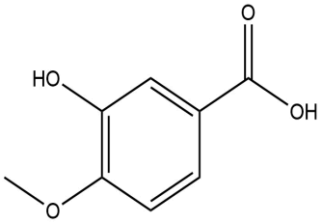
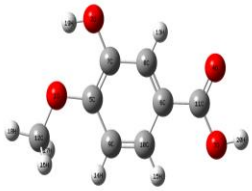
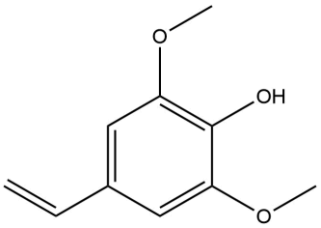
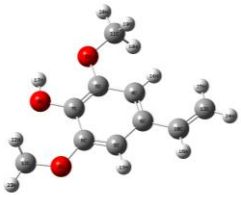
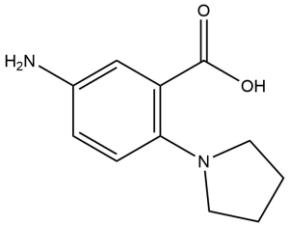
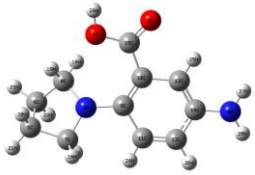
6	Benzyl alcohol	244	 C1=CC=C(C=C1)CO	
7	1-Amino-2,6-dimethylpiperidine	123482	 CC1CCCC(N1N)C	
8	2,6-Dimethylhex-4-enamidine, 2-(3-methylbut-2-enyl)-	586884	 CC(=CCC(C)(CC=C(C)C)C(=N)N)C	
9	Methyl 1-methylpyrrole-2-carboxylate	142178	 CN1C=CC=C1C(=O)OC	
10	3-Hydroxypropionic acid	68152	 C(CO)C(=O)O	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

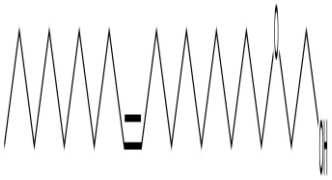
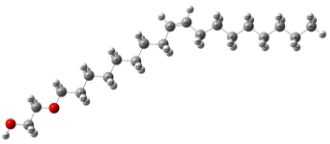
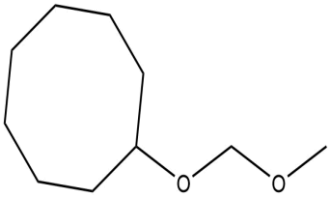
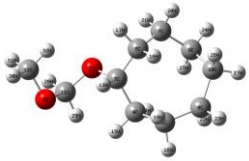
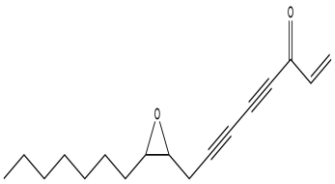
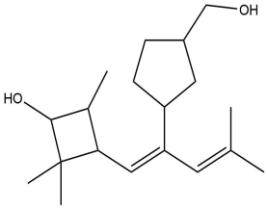
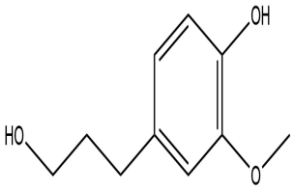
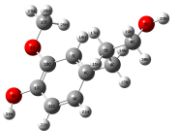
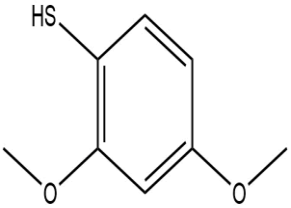
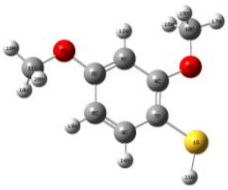
13	4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	119838	 CC1=C(C(=O)C(CO1)O)O	
14	Methyl salicylate	4133	 COC(=O)C1=CC=CC=C1O	
15	Azacyclohexan-3-one, 1,5,6-trimethyl-	566749	 CC1CC(=O)CN(C1C)C	
16	Benzofuran, 2,3-dihydro-	10329	 C1COC2=CC=CC=C21	
17	2-Aminopyrimidine-1-oxide	126623006	 CC(=O)C1=NN(C2=C1C=C(C=C2)C3=CN(C(=N)N=C3)O)CC(=O)N4C[C@@H](C[C@H]4C(=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

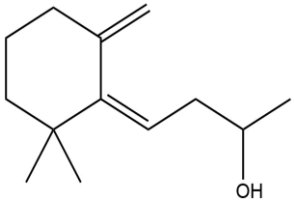
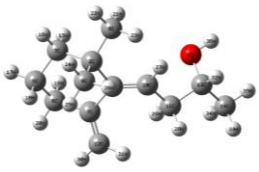
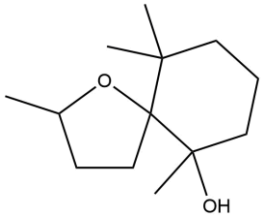
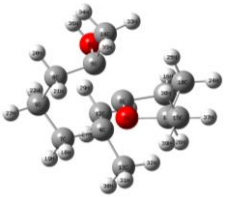
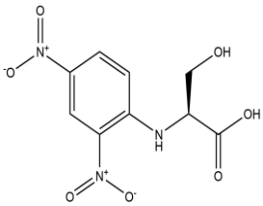
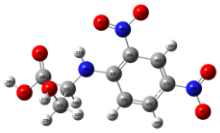
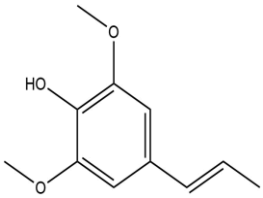
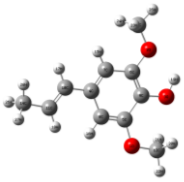
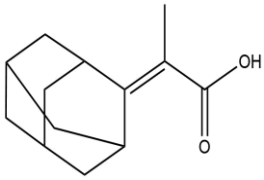
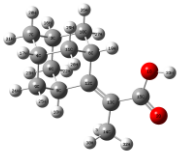
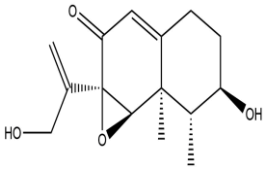
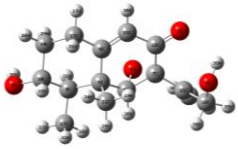
			C1CC(=O)N(C1)C(=O)NN	
19	Nonanoic acid	8158	 CCCCCCCCC(=O)O	
20	Talopyranoside, methyl 4-acetamido-4,6-dideoxy-, a-D-	N/A	 CO[C@H]1O[C@@H]([C@H]([C@H]([C@H]1C)NC(C)=O)O)O	
21	3-Amino-4-fluorophenol, N,O-dimethyl-	N/A	 COc1cc(F)cc(NC)c1	
22	Thiazolidine, 2-(2-furyl)-	593153	 C1CSC(N1)C2=CC=CO2	
23	2-Methoxy-4-vinylphenol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

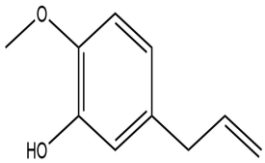
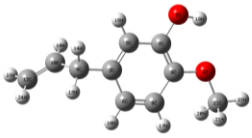
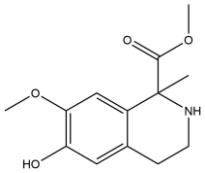
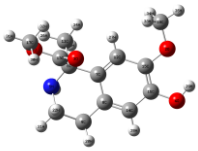
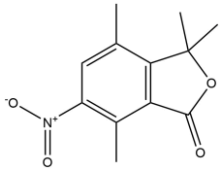
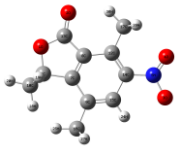
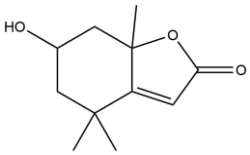
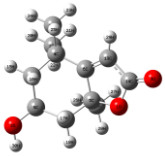
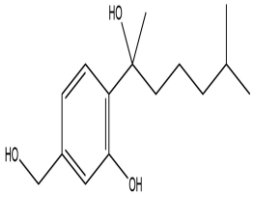
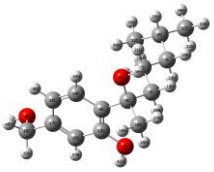
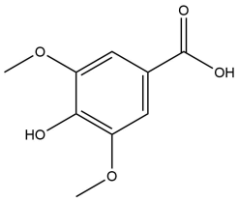
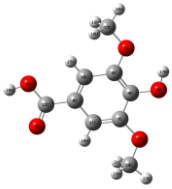
25	Phenol, 2,6-dimethoxy-	7041	 COC1=C(C(=CC=C1)OC)O	
26	Deoxycytidine	13711	 C1[C@@H]([C@H](O[C@H]1N2C=CC(=NC2=O)N)CO)O	
27	1,4-Benzenediol, 2-methoxy-	69988	 COC1=C(C=CC(=C1)O)O	
28	4-Hydroxybutyl acrylate	75588	 C=CC(=O)OCCCCO	
29	Benzofuran-4(5H)-one, 6,7-dihydro-, oxime	6537039	 C1CC2=C(C=CO2)/C(=N\O)/C1	
30	Urea, N,N'-bis(3-methylphenyl)-	136428	 CC1=CC(=CC=C1)NC(=O)NC2=CC=CC(=C2)C	

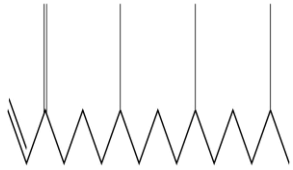
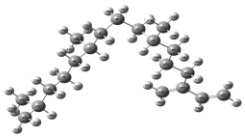
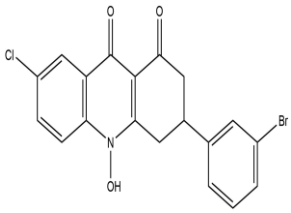
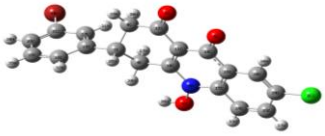
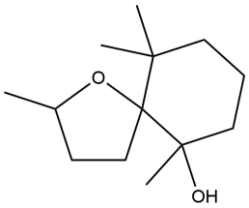
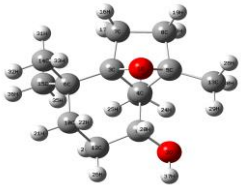
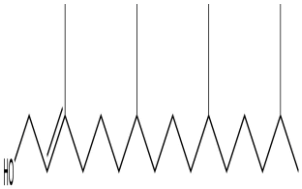
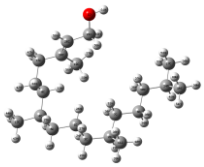
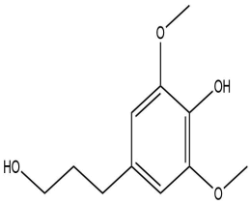
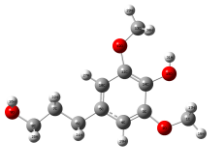
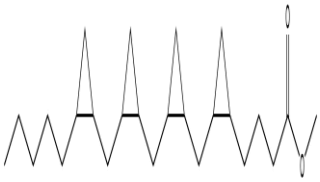
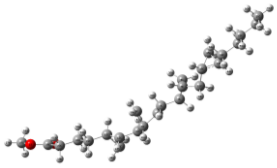
31	2(3H)-Furanone, 5-(2,5-dimethylphenyl)-	604728	 CC1=CC(=C(C=C1)C)C2=CCC(=O)O2	
32	D-Allose	439507	 C([C@@H]1[C@H]([C@H]([C@H](C(O1)O)O)O)O)O	
33	(Z)-4-hydroxy-3-methoxybenzaldehyde O-methyl oxime		 COC1=CC(/C=N\OC)=CC=C1O	
34	Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-, oxime, (1R)-	5908504	 CC1(C2CCC1(/C(=N/O)/C2)C)C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

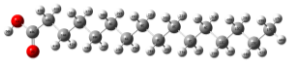
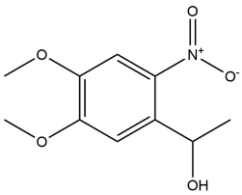
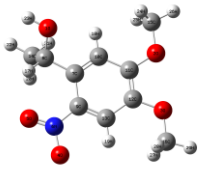
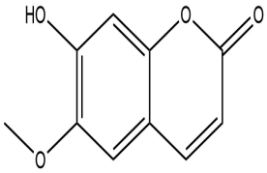
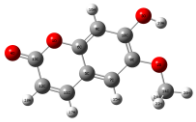
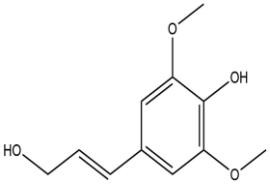
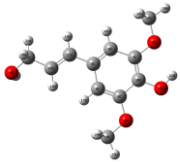
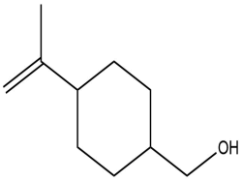
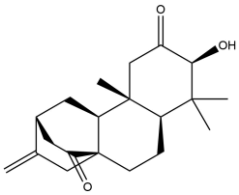
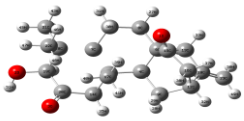
36	2-Cyclohexen-1-one, 3-(3-hydroxybutyl)-2,4,4-trimethyl-	520295	 CC1=C(C(CCC1=O)(C)C)CCC(C)O	
37	Dodecanoic acid	3893	CCCCCCCCCCCC(=O)O	
38	3-Hydroxy-4-methoxybenzoic acid	12575	 COC1=C(C=C(C=C1)C(=O)O)O	
39	Phenol, 4-ethenyl-2,6-dimethoxy-	35960	 COC1=CC(=CC(=C1O)OC)C=C	
40	Benzoic acid, 3-amino-6-(1-pyrrolidinyl)-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

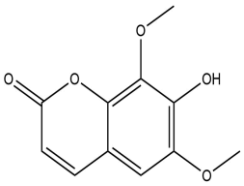
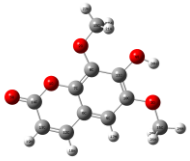
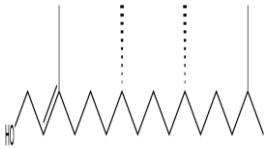
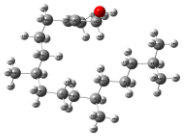
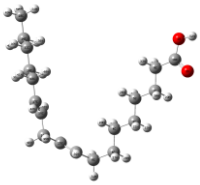
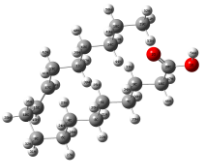
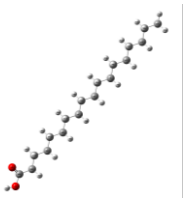
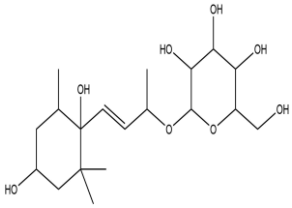
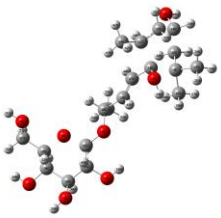
41	Ethanol, 2-(9-octadecenyloxy)-, (Z)-	5364713	 CCCCCCCC/C=C\CCCCCCCCOCCO	
42	Cyclooctane, (methoxymethoxy)-	542175	 COCOC1CCCCCCC1	
43	Ginsenoyne E	5320336	 CCCCCCCC1C(O1)CC#CC#CC(=O)C=C	
44	(E)-3-(2-(3-(hydroxymethyl)cyclopentyl)-4-methylpenta-1,3-dien-1-yl)-2,2,4-trimethylcyclobutan-1-ol	N/A	 C/C(C)=C\C(C1CCC(C1)CO)=C\C2C(C(C2(C)C)O)C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

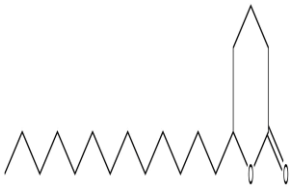
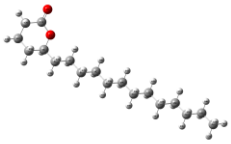
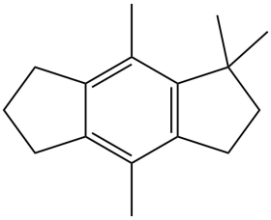
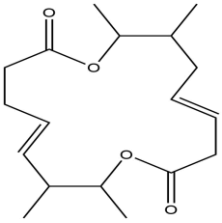
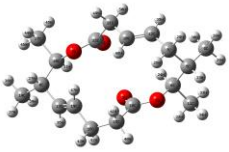
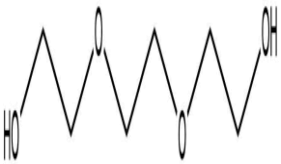
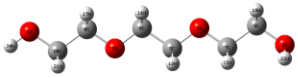
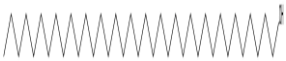
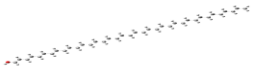
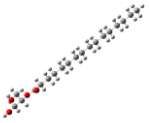
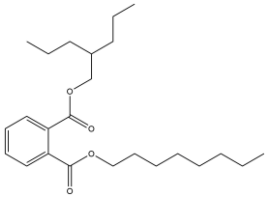
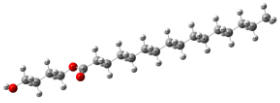
47	2-Butanol, 4-(2,2-dimethyl-6-methylenecyclohexylidene)-	5372134		
			CC(C/C=C/1\C(=C)CCCC1(C)C)O	
48	2,6,10,10-Tetramethyl-1-oxaspiro[4.5]decan-6-ol	65428		
			CC1CCC2(O1)C(CCCC2(C)O)(C)C	
49	Dnp-L-serine	96800		
			C1=CC(=C(C=C1[N+](=O)[O-])[N+](=O)[O-])N[C@@H](CO)C(=O)O	
50	(E)-2,6-Dimethoxy-4-(prop-1-en-1-yl)phenol	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	

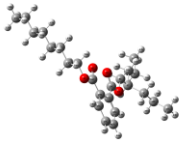
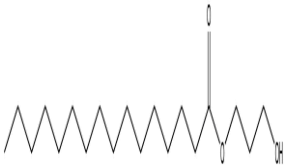
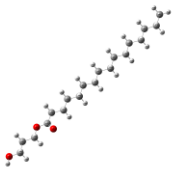
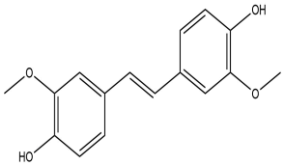
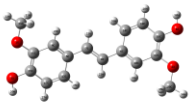
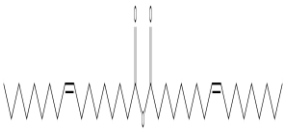
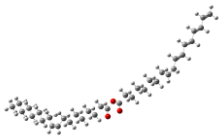
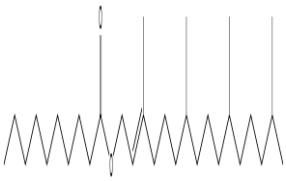
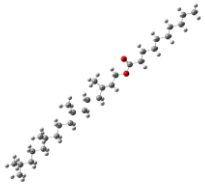
53	3-Allyl-6-methoxyphenol	596375	 COC1=C(C=C(C=C1)CC=C)O	
54	Tetradecanoic acid	11005	CCCCCCCCCCCCCC(=O)O	
55	(+)-1,2,3,4-Tetrahydroisoquinolin-6-ol-1-carboxylic acid, 7-methoxy-1-methyl-, methyl(ester)	606044	 CC1(C2=CC(=C(C=C2CCN1)O)OC)C(=O)OC	
56	1,3-2H-Isobenzofuranone, 3,3,4,7-tetramethyl-6-nitro-	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		
			CCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCCO	
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		
			CCCCCCCCCCCCCCCCCC(OCC(C(CCCC(C)C)C)C)=O	

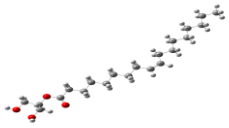
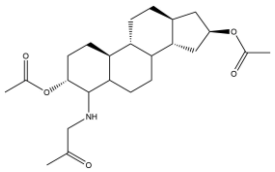
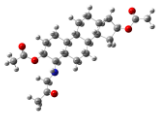
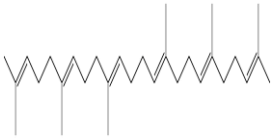
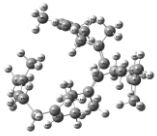
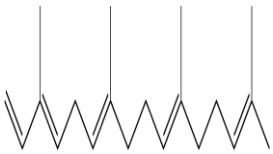
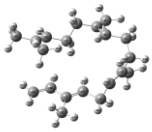
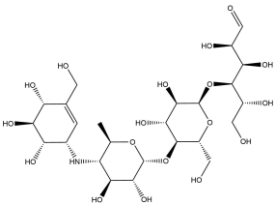
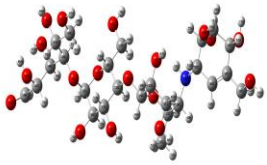
93	1,3-dihydroxypropan-2-yl (Z)-octadec-9-enoate	5319879		
			CCCCCCCC/C=C\\CCCCCCCC(=O)OC(CO)CO	
94	(5ß)Pregnane-3,20ß-diol, 14a,18a-[4-methyl-3-oxo-(1-oxa-4-azabutane-1,4-diyl)]-, diacetate			
			CC(O[C@@H]1CC[C@H]2[C@@H]3CC[C@H]4C[C@H](C[C@@H]4C3CCC2C1NCC(C)=O)OC(C)=O)=O	
95	Squalene	638072		
			CC(=CCC/C(=C/CC/C(=C/CC/C=C(/CC/C=C(/CCC=C(C)C)\C)\C)/C)/C)C	
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 all GC-MS-identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL) against both target proteins.

Compound	Docking score (kcal/mol) in α amylase	Docking score (kcal/mol) in α glucosidase
1.	−4	−4.4
2.	−4.5	−4.8
3.	−5.6	−5.7
4.	−4.6	−5
5.	−4.9	−5.4
6.	−5	−5.3
7.	−4.8	−5.2
8.	−6.2	−6
9.	−4.6	−4.6
10.	−4	−4.4
11.	−4.4	−4.9
12.	−5.5	−5.6
13.	−5.1	−5.2
14.	−5.4	−5.7
15.	−4.8	−5
16.	−5.1	−6
17.	−10.4	−10.5
18.	−5.5	−5.7
19.	−5	−5.6
20.	−6	−6.4
21.	−5.3	−5.2
22.	−4.7	−5.5
23.	−5.6	−5.4
24.	−6	−6.4
25.	−4.9	−5.8
26.	−6.7	−7.2
27.	−5	−5.2
28.	−4.5	−5.1
29.	−6.4	−6.1
30.	−8.9	−7.9
31.	−6.9	−6.9
32.	−5.4	−5.7
33.	−5.8	−5.8
34.	−6.9	−6.4
35.	−6.3	−6.5
36.	−6.3	−6.4
37.	−5.1	−5.7
38.	−5.5	−6.1
39.	−5.1	−5.5
40.	−6.9	−6.5
41.	−5.1	−5.8
42.	−5.4	−5.6

43.	−6.5	−5.8
44.	−7.1	−7.7
45.	−6.1	−5.9
46.	−4.6	−4.6
47.	−6.8	−6.4
48.	−7	−6.6
49.	−6.8	−7.2
50.	−5.4	−5.7
51.	−7.1	−7.2
52.	−7.2	−7.6
53.	−5.8	−6.2
54.	−5.5	−5.7
55.	−6.5	−6.6
56.	−7.1	−6.9
57.	−6.7	−6.8
58.	−6.8	−7.2
59.	−5.5	−6.1
60.	−5.8	−6.8
61.	−9.9	−9.4
62.	−6.5	−7.3
63.	−5.9	−6.8
64.	−5.7	−5.9
65.	−6.6	−7.3
66.	−5.7	−6
67.	−5.2	−6
68.	−5.8	−5.9
69.	−6.4	−7.1
70.	−5.9	−6.3
71.	−6.1	−6
72.	−9	−9
73.	−6.2	−6.6
74.	−6.3	−6.8
75.	−5.9	−6.2
76.	−5.4	−6.2
77.	−4.8	−6.2
78.	−7.7	−8.8
79.	−5.8	−6.1
80.	−7.8	−7.7
81.	−8.6	−8.5
82.	−4	−4.6
83.	−5.4	−5.8
84.	−5.3	−5.9
85.	−5	−6.4
86.	−6.5	−6.3
87.	−5	−6
88.	−7.8	−7.5

89.	−5.8	−6.3
90.	−5.1	−6.1
91.	−5.8	−7.1
92.	−5.4	−6.2
93.	−5.5	−6.7
94.	−8.3	−9.3
95.	−7.2	−8.5
96.	−6.4	−8
97.	−8.1	−3.7
Control	−7.8	−8

Table ST16: 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	18

Table ST17: 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 (Fluorine)
		ALA106	2.81	Hydrogen Bond;Halogen	
		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 ST18: 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 ST19: 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 ST20: 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
	Gamma−secretase	PSEN2 PSENEN NCSTN APH1A PSEN1 APH1B	Protease	0.09
	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	Sodium/glucose cotransporter 2	SLC5A2	Electrochemical transporter	0.11
	Adenosine A1 receptor (by homology)	ADORA1	Family A G protein−coupled receptor	0.11
	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 catalytic subunit	PPP1CC	Phosphatase	0.11
	Serine/threonine protein phosphatase 2A, 56 kDa regulatory subunit, alpha isoform	PPP2R5A	Phosphatase	0.11
	Adenosine deaminase	ADA	Hydrolase	0.11
	Sodium/glucose cotransporter 1	SLC5A1	Electrochemical transporter	0.11
	Adenosine A2a receptor (by homology)	ADORA2A	Family A G protein−coupled receptor	0.11
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

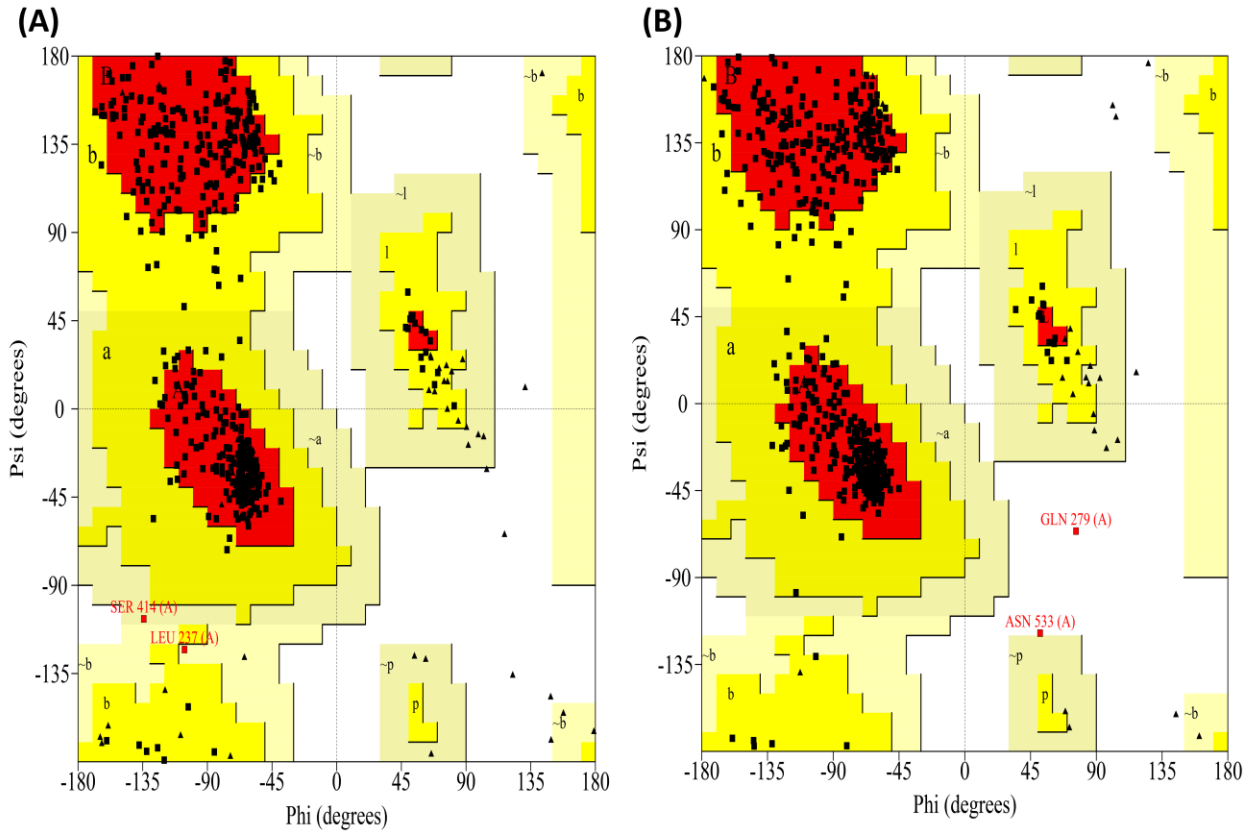


Figure SF4: PROCHECK Ramachandran plots of (A) α amylase, (B) α glucosidase.

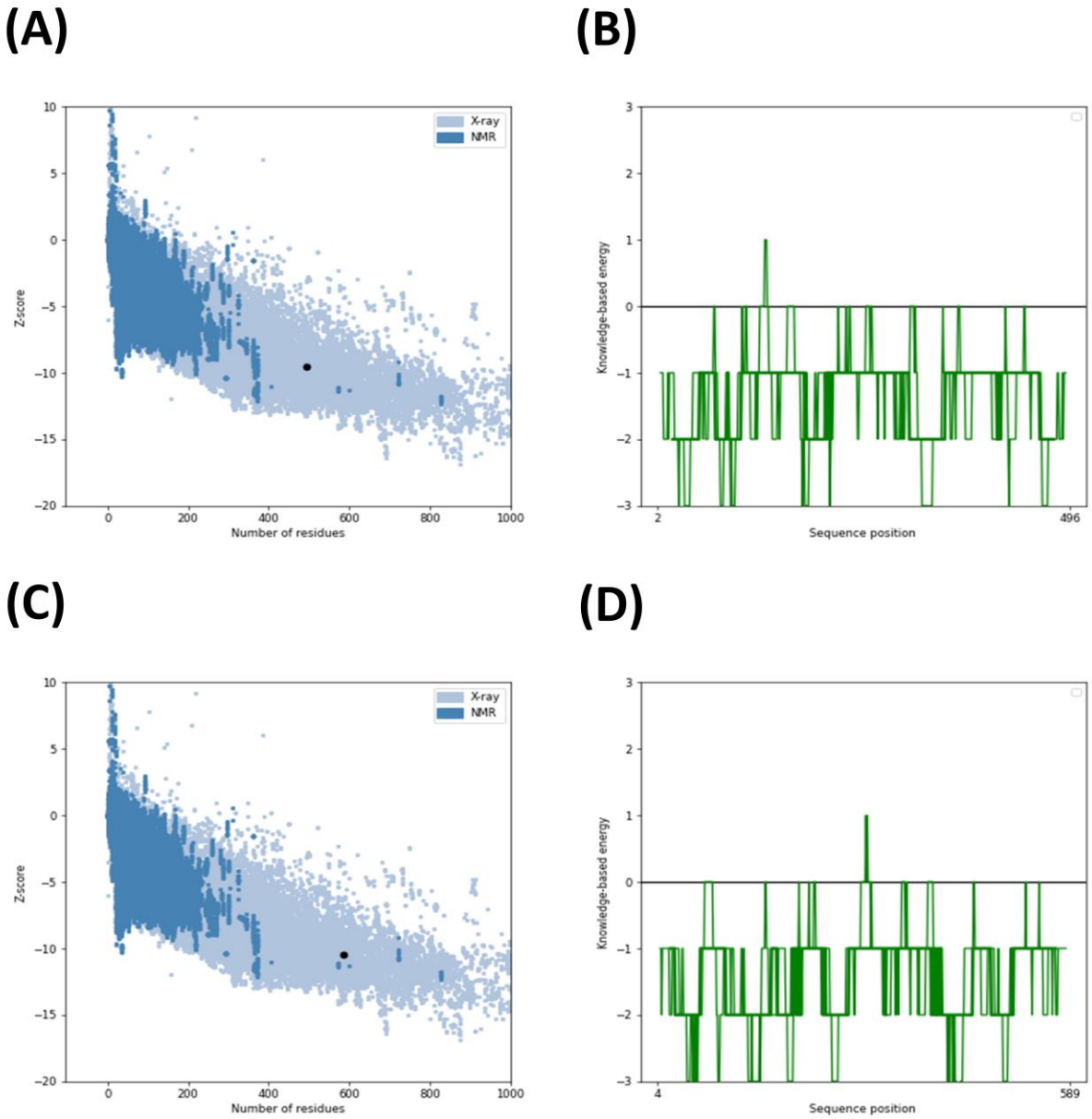


Figure SF5: ProSA-Web validation parameters of the target proteins. (A, B) Z scores of α amylase and α glucosidase within the range of experimentally determined NMR structures; (C, D) residue wise energy profiles of α amylase and α glucosidase, respectively.

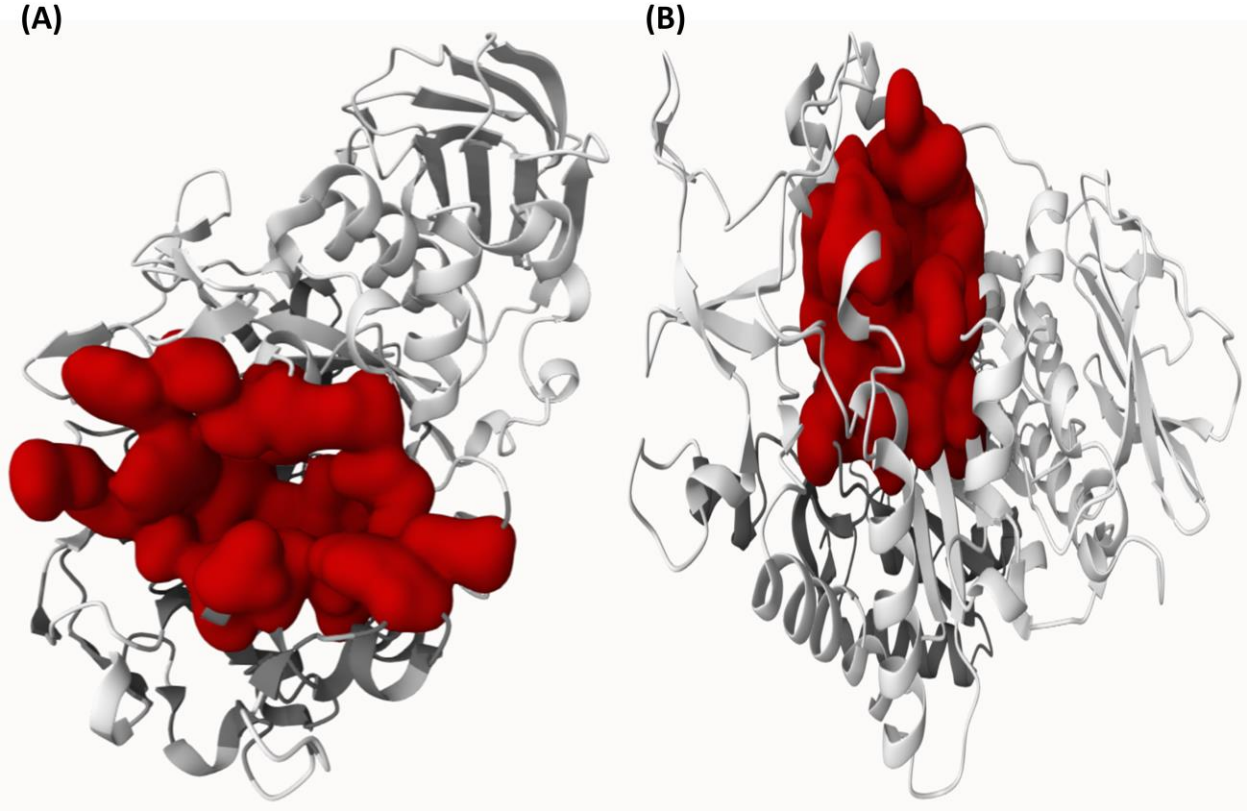


Figure SF6: PrankWeb predicted active site of (A) α amylase, (B) α glucosidase.

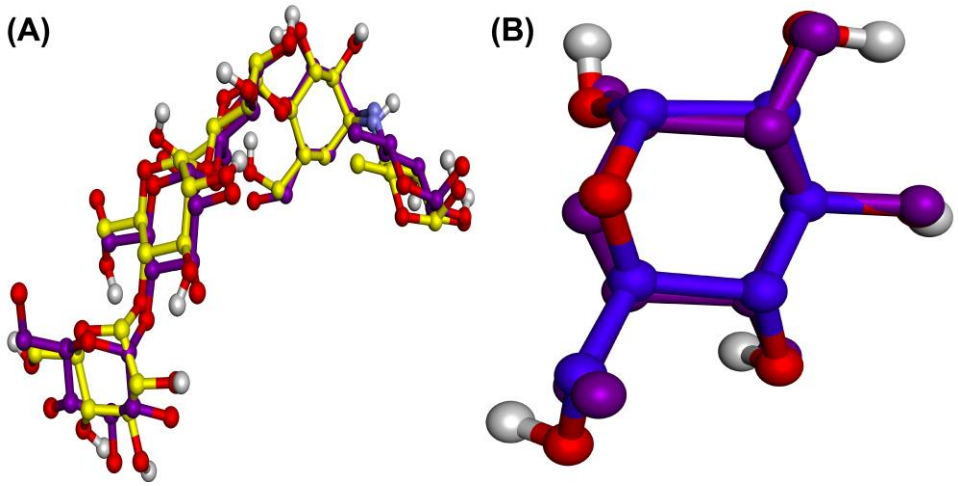


Figure SF7: Validation of the molecular docking protocol by superimposition of the redocked ligands onto the corresponding co-crystallized ligands. Superimposition of the redocked and co-crystallized ligands for (A) α-amylase (PDB ID: 2QV4; RMSD = 0.89 Å) and (B) α-glucosidase (PDB ID: 3A4A; RMSD = 0.72 Å). Here, purple indicates the color of the co-crystalized ligand.

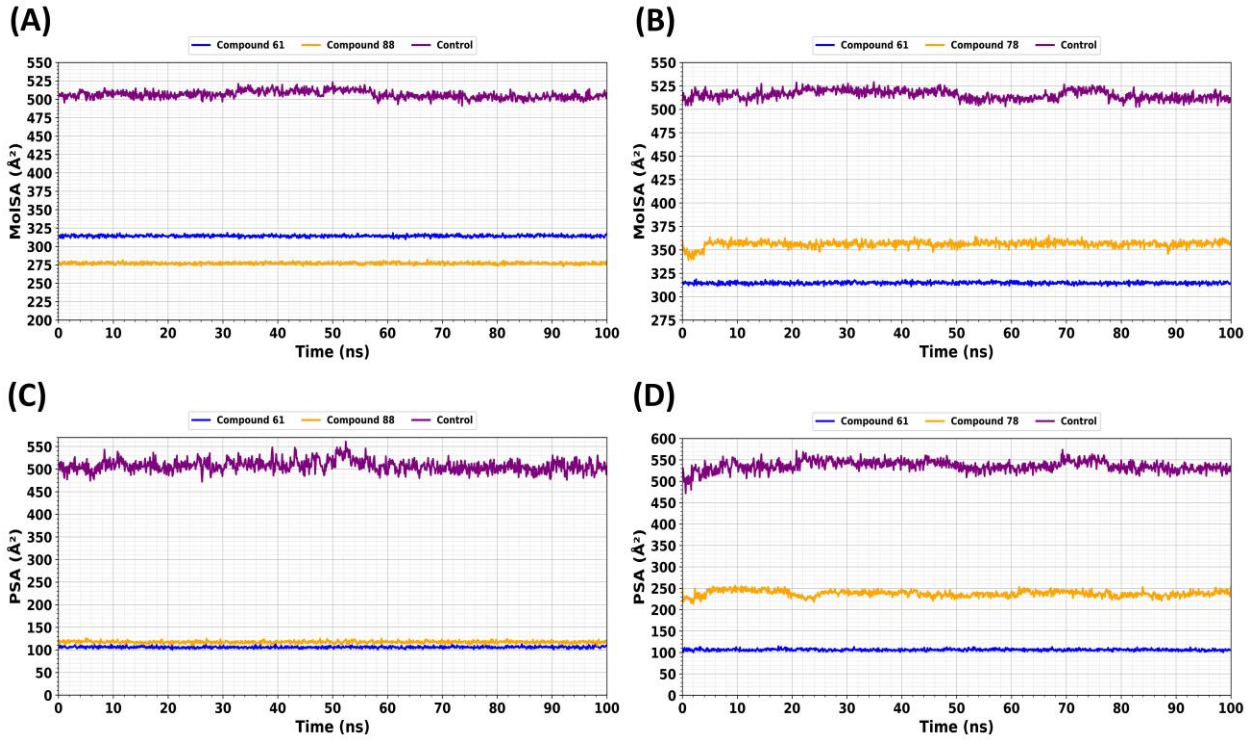


Figure SF8: Molecular surface area (MolSA) and polar surface area (PSA) profiles of selected GC–MS identified compounds from the methanolic extract of *H. fomes* leaves (MEHFL). (A, B) MolSA in α amylase and α glucosidase, respectively; (C, D) PSA in α amylase and α glucosidase, respectively.