Supplementary Information

Table S1: Some selected known Inhibitors of alpha glucosidase obtained from literature used in screening against alpha glucosidase and their corresponding references.

Compound	IC_{50}	Unit	Reference
Acacetin	0.16	mmol/L	[1]
Kaempferol	$1.16 \pm 0.04 \times 10^{5}$	mol/L	[2]
	153.39 ± 1.79	µM	[3]
Hesperetin 5-O-glucoside	41.25 ± 1.25	µg/mL	[4]
Luteolin	82.73 ± 2.51	µM	[3]
Rutin			
	0.196	mM	[5]
	173.58 ± 1.23	µM	[3]
Plicatanoside	111.23 ± 0.65	uM	[6]
Sulochrin	8.5	mg/mL	[7]
Vitexin	0.42	mmol/L	[1]
Isoquercetrin			
	0.185	mM	[5]
	0.24	mmol/L	[1]
Rosmarinic acid	33.0 ± 4.6	µmol/L	[1]
Swertisin	0.37	mmol/L	[1]
Acteoside	1.62 ± 0.29	mmol/L	[1]
Acarbose	$2.09 \pm 0.03 \times 10^{4}$	mol/L	[1]
	0.59 ± 0.14	µM	[1]
	996	nM	[8]
Fisetin	19,600	nM	[8]
Quercetin	0.017	mM	[5]
	14.6 ± 3.72	µmol/L	[1]
Myricetin	11.63 ± 0.36	µM	[3]
	30,200	nM	[8]
4-(p-toluenesulfonamide)-3,4-dihydroxy chalcone	193,700	nM	[8]
4-Amino-4-hydroxychalcone	268,900	nM	[8]
Apigenen-7-O-rutinoside	64.29 ± 2.41	µg/mL	[9]
Miglitol	465.1	µM	[10]
Naringenin	44.65	µg/mL	[11]
Tiliroside	14.5 ± 0.1	µmol/L	[1]
verbascoside	0.5 ± 0.03	mmol/L	[1]
Leucosceptoside	0.7 ± 0.04	mmol/L	[1]
Isoacteoside	0.1 ± 0.01	mmol/L	[1]

Table S2. Binding affinities and molecular interactions between selected known inhibitors and alpha glucosidase (5nn8).

Known Inibitors compounds	**Binding Energy kJ/mol**	**Hydrogen bonding residues and bond length** Å	**Hydrophobic bonding residues**
Apigenin-7-O-Rutinoside	-38.1	Tyr^{360}(3.08) Met^{363}(3.04) His^{584}(3.11) Arg^{594}(3.07) Arg^{608}(2.84, 3.09) Ser^{864}(2.93)	Gly^{359}, Phe^{362}, Tyr^{609}, His^{717}, Leu^{865}, Glu^{866} Val^{867}, Leu^{868}, Glu^{869}
Plicatanoside	-37.7	Asp^{356}(2.85) Arg^{608}(2.70, 3.00) Glu^{869}(3.22)	Leu^{355}, Gly^{359}, Phe^{362}, His^{584}, Val^{718} His^{717}, Leu^{860}, Leu^{865}, Glu^{866}, Val^{867}, Leu^{868}, Glu^{869}
Rutin	-37.7	Trp^{360}(2.67) Leu^{355}(2.91) Asp^{356}(2.85) Met^{363}(3.22) Arg^{608}(2.89,3.10,3.10)	Pro^{361}, Phe^{362}, Gly^{359}, Val^{718} His^{717}, Leu^{860}, Leu^{865}, Glu^{866} Val^{867}, Leu^{868}
Leucosceptoside	-36.0	Asp^{365}(2.99) His^{584}(3.12) Arg^{608}(2.81) His^{717}(2.92) Ser^{864}(2.92) Val^{867}(2.99)	Try^{360}, Gly^{359}, Met^{363}, Pro^{595}, Glu^{866}, Val^{867}, Leu^{868}, Glu^{869}
Vitexin	-35.6	Tyr^{360}(2.70) Met^{363}(3.12) Arg^{608}(3.26, 3.30) Val^{867}(2.80) Leu^{868}(3.00)	Pro^{361}, Phe^{362}, His^{584}, Arg^{594}, Tyr^{609}, His^{717}, Leu^{865}, Glu^{866}, Glu^{869}
Isoacteoside	-35.1	Pro^{94}(2.93, 3.27) Asp^{95}(2.98) Arg^{275}(3.15) Arg^{331}(2.79, 2.92) Tyr^{543}(3.17) Val^{544}(2.92, 3.15)	Asp^{91}, Ile^{98}, Tyr^{110}, Gly^{123}, Gln^{124}, Pro1^{25}, Cys^{127}, Val^{321}
Verbascoside	-35.1	Asp^{356}(2.95,3.17) Arg^{608}(2.76) His^{717}(3.03) Ser^{864}(2.80) Va^{l867}(3.03)	Try^{360}, Gly^{359}, Met^{363}, His^{584}, Arg^{594}, Pro^{595}, Glu^{866}, Val^{867}, Leu^{868}, Glu^{869}
Hesperetin_5-O-glucoside	-34.3	Ile581(2.86) Arg^{608}(3.25) Ser^{864}(2.79) Leu^{868}(3.04,3.26) Glu^{869}(3.20)	Pro^{361}, Met^{363}, Phe^{362}, His^{584}, Arg^{585}, Arg^{594}, Tyr^{609}, His^{717}, Leu^{865},
Swertisin	-33.9	Arg^{594}(3.01) Ser^{864}(2.84) Glu^{866}(2.97) Leu^{868}(3.05, 3.07) Glu^{869}(2.97)	Phe^{362}, His^{584}, Arg^{585}, His^{717}, Leu^{865}, Val^{867}

Tiliroside	-33.5	Tyr[360](2.67) His[584](2.89) His[717](2.99) Arg[608](3.10) Glu[866](2.72) Leu[868](2.86) Glu[869](3.08)	Pro[361], Phe[362], Arg[594], Leu[865], Val[867]
Isoquercetrin	-33.1	Asp[91](3.17) Glu[124](2.91) Trp[273](2.70, 3.00) Arg[331](2.84, 3.60) Tyr[543](3.20, 3.21)	Ala[93], Ile[98], Tyr[110], Gly[123], Gln[124], Pro[125], Trp[126], Cys[127], Trp[274], Val[321],
Fisetin	-31.4	Tyr[360](2.17, 3.21) His[584](2.94) Val[867](3.08)	Phe362, Arg594, Arg608, His717, Ser864, Leu865, Glu866
Luteolin	-31.4	Asp[282](3.13) Asp[404](3.03) Ser[523](3.09) His[674](2.92)	Trp[376], Trp[481], Trp[516], Asp[518], Met[519], Phe[525], Asp[616], Phe[649]
Myricetin	-31.4	Tyr[360](2.90, 3.07) His[584](2.89) Arg[608](2.85) Val[867](3.16)	Phe[362], Arg[594], Pro[595], His[717], Leu[865], Glu[866]
Quercetin	-31.4	Tyr[360](2.88) His[584](3.06) Arg[608](2.91) Val[867](2.88,3.15)	Phe[362], Arg[594], Pro[595], His[717], Leu[865], Glu[866]
Sulochrin	-31.0	Met[363](2.86) His[584](3.30) Val[867](3.00)	Phe[362], Arg[594], Arg[608] His[717], Asp[860], Leu[865], Glu[866], Val[867],Leu[868]
Acacetin	-30.1	Leu[756](2.91)	Val[740], His[742], Thr[739], Gln[743], Val[755], Gln[757], Lys[760], Glu[762], Thr[764], Trp[804]
Naringenin	-30.1	Leu[756](2.91)	Val[740], His[742], Thr[739], Gln[743], Val[755], Gln[757], Lys[760], Glu[762], Thr[764], Trp[804]
Rosmaric_acid	-30.1	His[584](2.95) Arg[608](2.95,3.26) Val[867](2.85) Leu[868](2.95) Gln[869](3.24)	Phe[362], Met[363], Arg[594], Pro[595], Tyr[609], His[717], Ser[864], Leu[865], Glu[866]
Kaempferol	-29.3	Leu[756](3.01)	Thr[739], Gln[743], Val[755], Gln[757], Lys[760], Glu[762], Thr[764], Trp[804]
4'-Amino-4-hydroxychalcone	-28.03	Asp[518](2.87)	Trp[376], Asp[404], Trp[516], Arg[600], Asp[616], Phe[649], Leu[677]
Voglibose	-24.7	Met[363](2.78) His[584](3.02) Ser[864](3.04) Val[867](3.16) Leu[868](2.87)	Phe[362], Arg[594], Pro[595], His[717], Leu[865], Glu[866],
Miglitol	-23.4	Met[363](2.89, 2.96) His[717](3.01) Ser[864](2.70)	Phe[362], Arg[594], Pro[595], Leu[865], Glu[866]

		Val[867](3.17) Leu[868](3.17,3.03)	
4-(p-toluensesul fonamide)-3,4-dihydroxy chalcone	-23.4	Val[236](3.00)	Val[84], Phe[90], Phe[129], Pro1[30], Pro[131], Pro[217], Ala[237], Pro[238]

Table S3. Per – residue decomposition analysis of amino acids of the potential lead compounds.

Compound	**H-bond Residue**	**Total Energy (kJ/mol)**
Taraxasterol	Leu[677]	-0.0050
	Leu[687]	-0.0075
Syriogenin	Asp[281]	0.3686
	Asp[282]	-0.4018
	Asp[616]	-0.3891
	Leu[677]	-0.0750
Isorhamnetin-3-O-robinobioside	Asp[282]	-5.61
	Asp[404]	0.63
	Trp[481]	-24.04
	Asp[518]	19.19
	Arg[600]	9.63
	Asp[616]	-4.67
Calotoxin	Asp[282],	0.1122
	Asn[524]	0.0073
	Phe[525]	-0.0382
	Asp[616]	-0.0404
Acarbose	Asp[282]	17.0038
	Asp[404]	19.5988
	Asn[524]	0.2110
	Phe[525]	-0.3763
	Arg[600]	-8.3071
	Asp[616]	31.1002
	His[674]	-2.2183

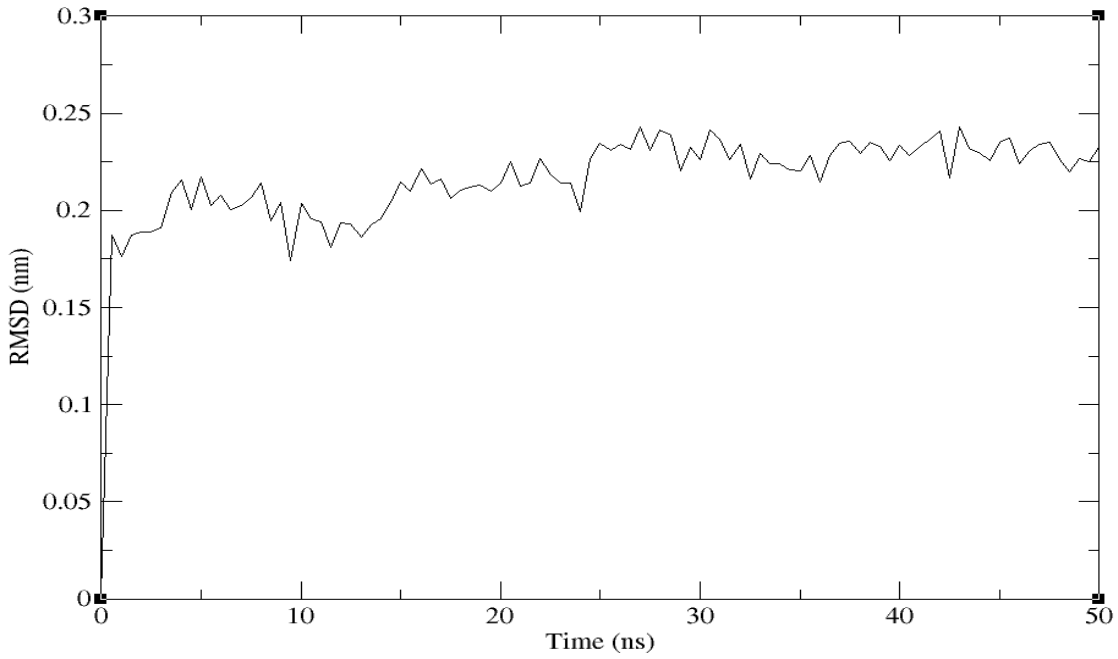

Figure S1. RMSD of 5nn8 during molecular dynamics simulations for 50ns.

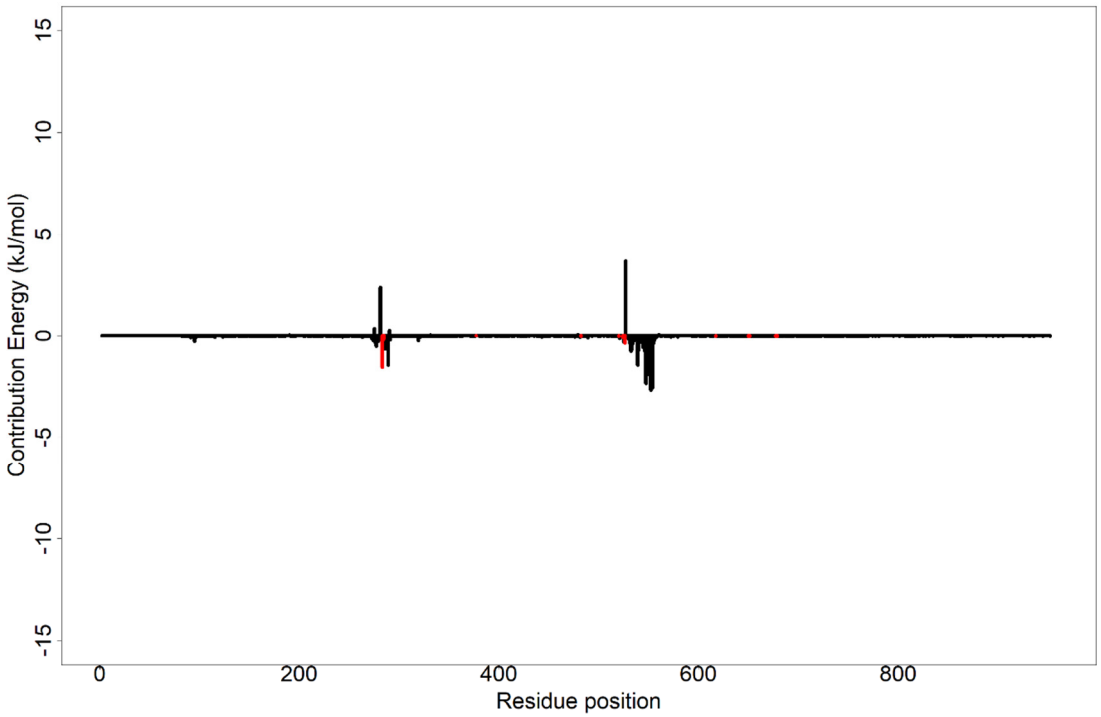

Figure S2. MM-PBSA plot of free binding energy contribution per residue decomposition of taraxasterol-alpha glucosidase complex.

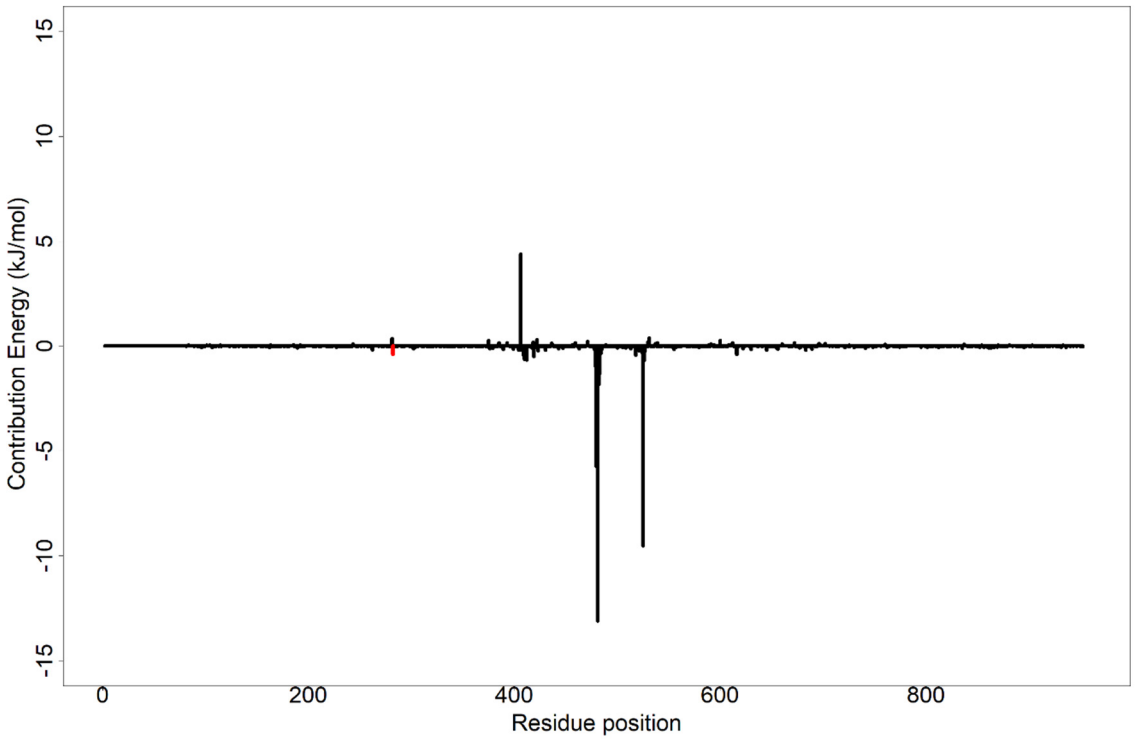

Figure S3. MM-PBSA plot of free binding energy contribution per residue decomposition of syriogenin-alpha glucosidase complex. *Hydrogen bonding residues labelled in red*

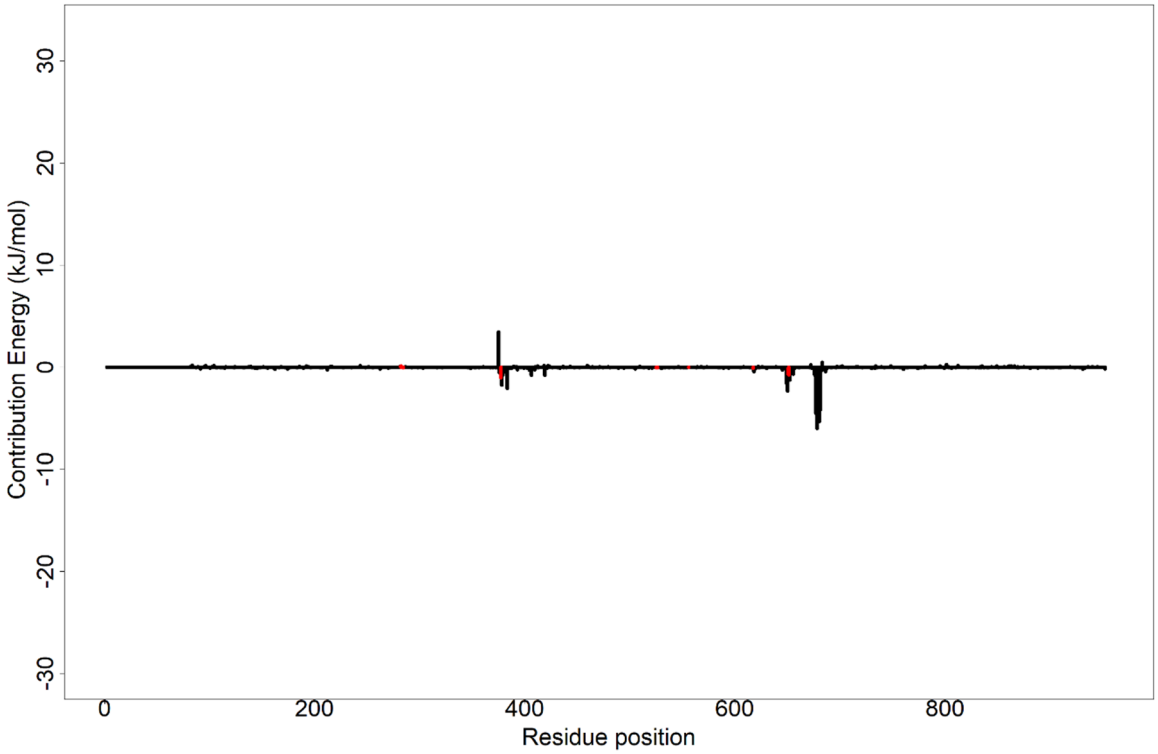

Figure S4. MM-PBSA plot of free binding energy contribution per residue of the complex of calotoxin with alpha-glucosidase. *Hydrogen bonding residues labelled in red*

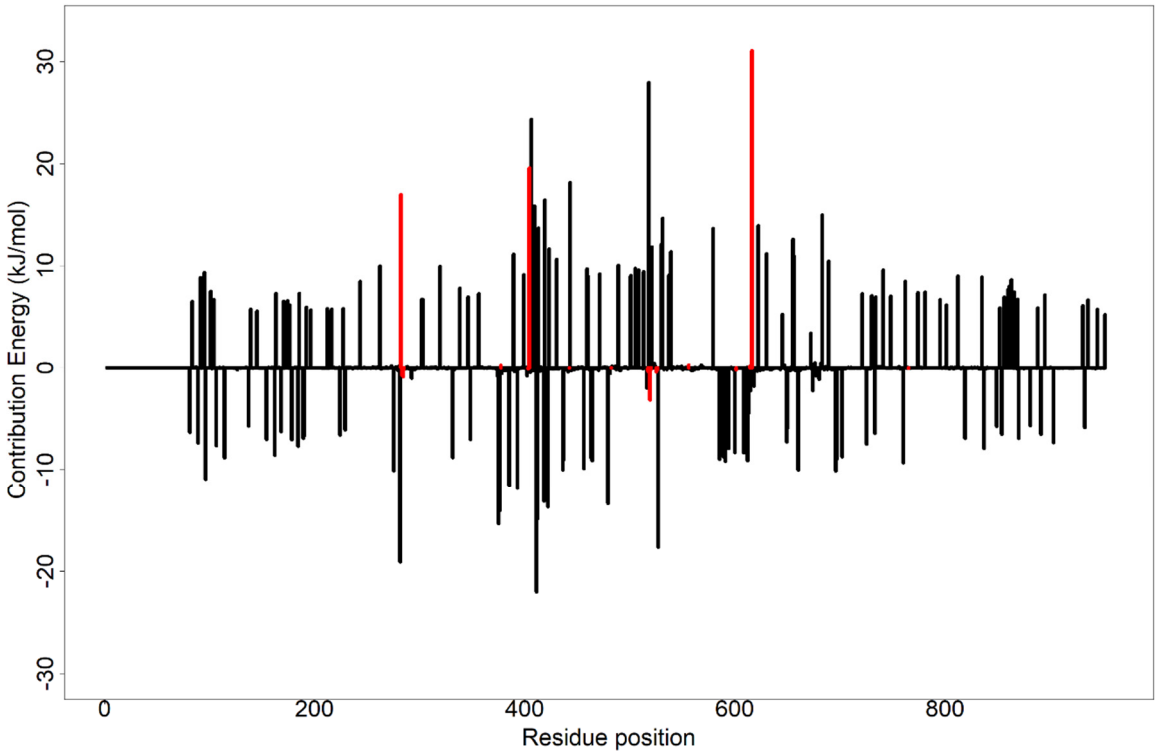

Figure S5. MM-PBSA plot of free binding energy contribution per residue of acarbose-alpha glucosidase complex. *Hydrogen bonding residues labelled in red.*

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