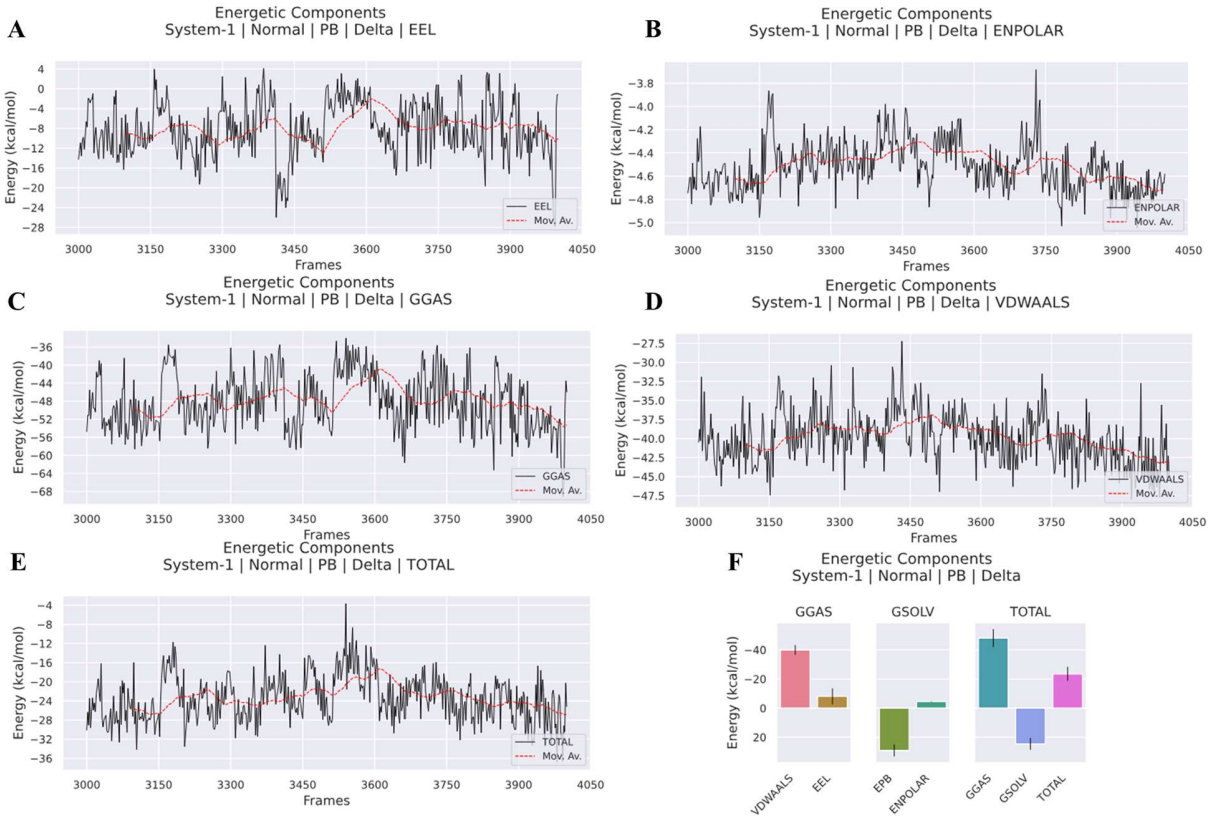
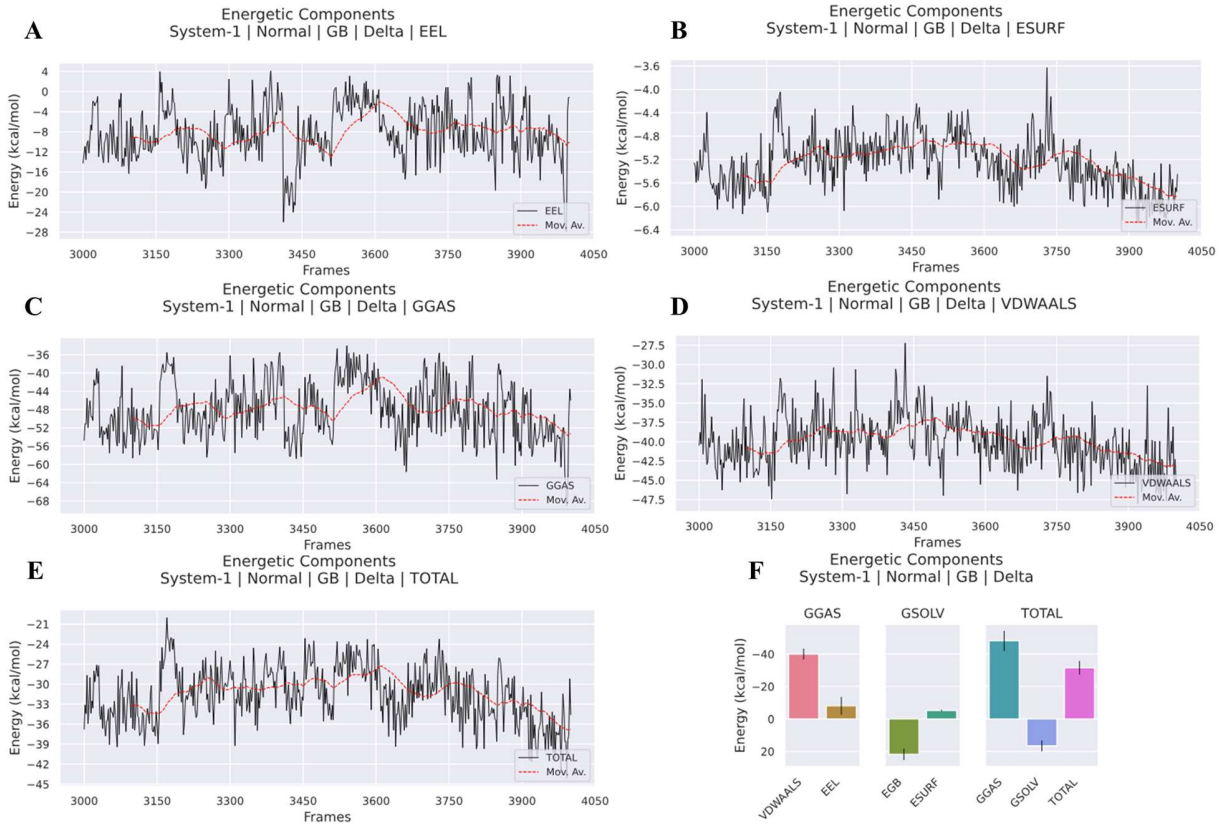
Supplementary material

Supplementary Table 1. The pharmacokinetic properties of the selected compounds and Acarbose drug.

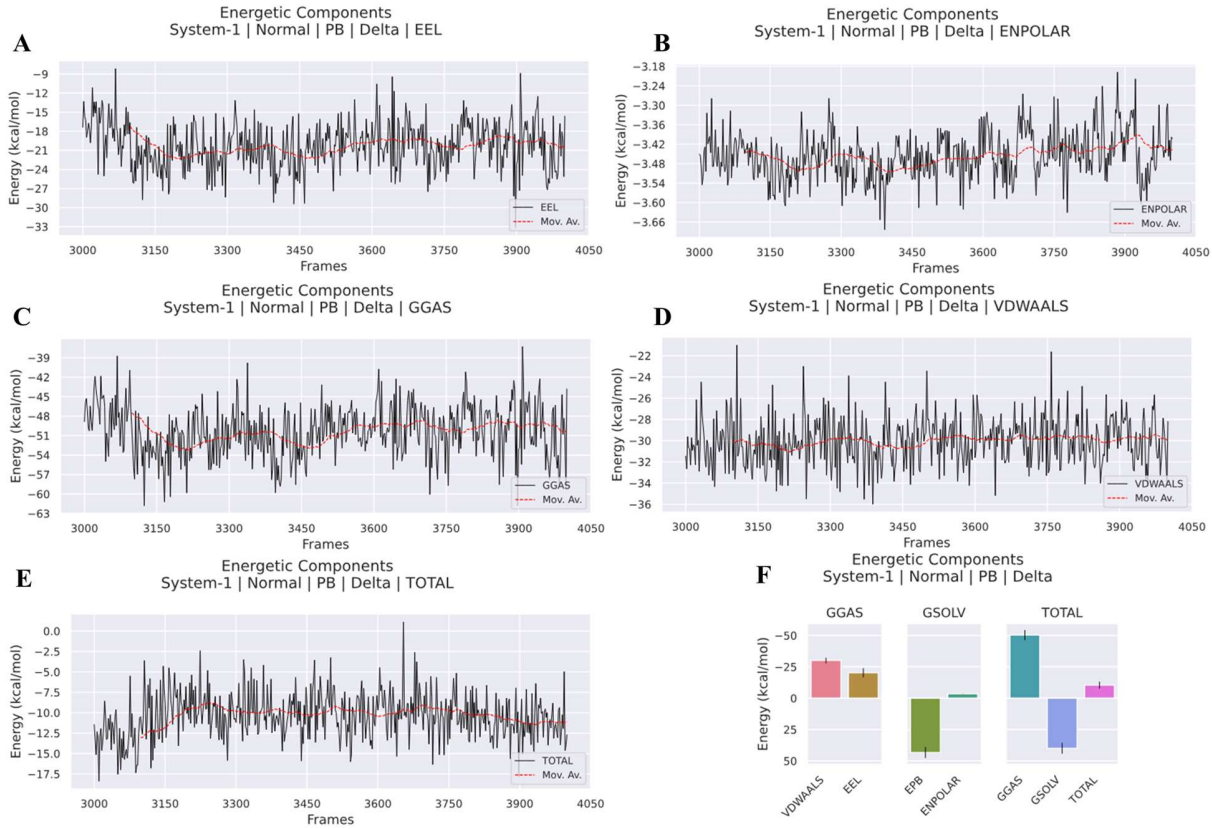
Compounds	GI absorption	BBB Permeation	Caco-2 permeability	P-glycoprotein substrate	P-glycoprotein inhibitor	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP3A4 inhibitor
Stigmasterol	94.97 %	0.771	1.213	Yes	Yes	No	No	No	Yes
Quercetin	77.207 %	-1.098	-0.229	Yes	No	Yes	No	No	No
Luteoline	81.13 %	-0.907	0.096	Yes	No	Yes	Yes	No	No
Acarbose	4.172 %	-1.717	-0.481	Yes	No	No	No	No	No



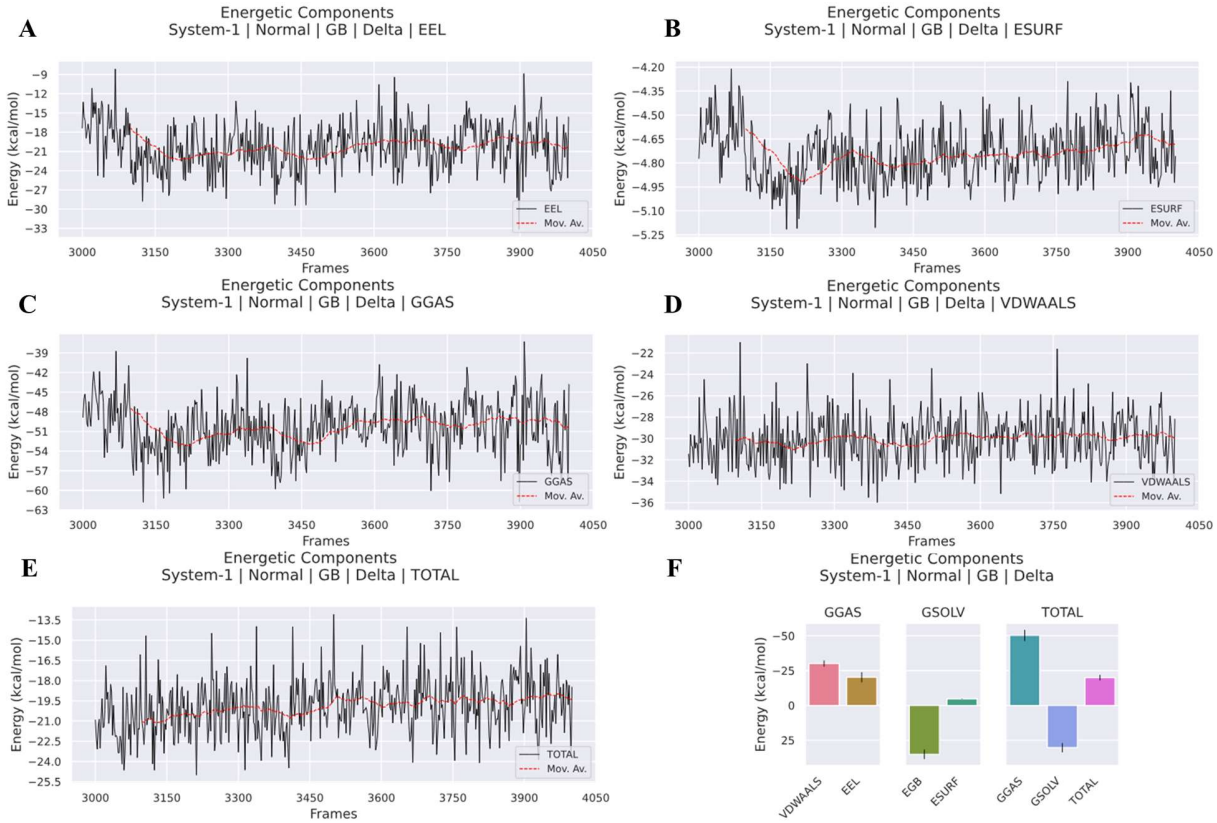
Supplementary Figure 1. The Binding free energy calculations of the 8AV1_Stigmasteol cmplex following the MD simulation using MM-PBSA. The total binding free energy was negative and indicated favorable binding energy.



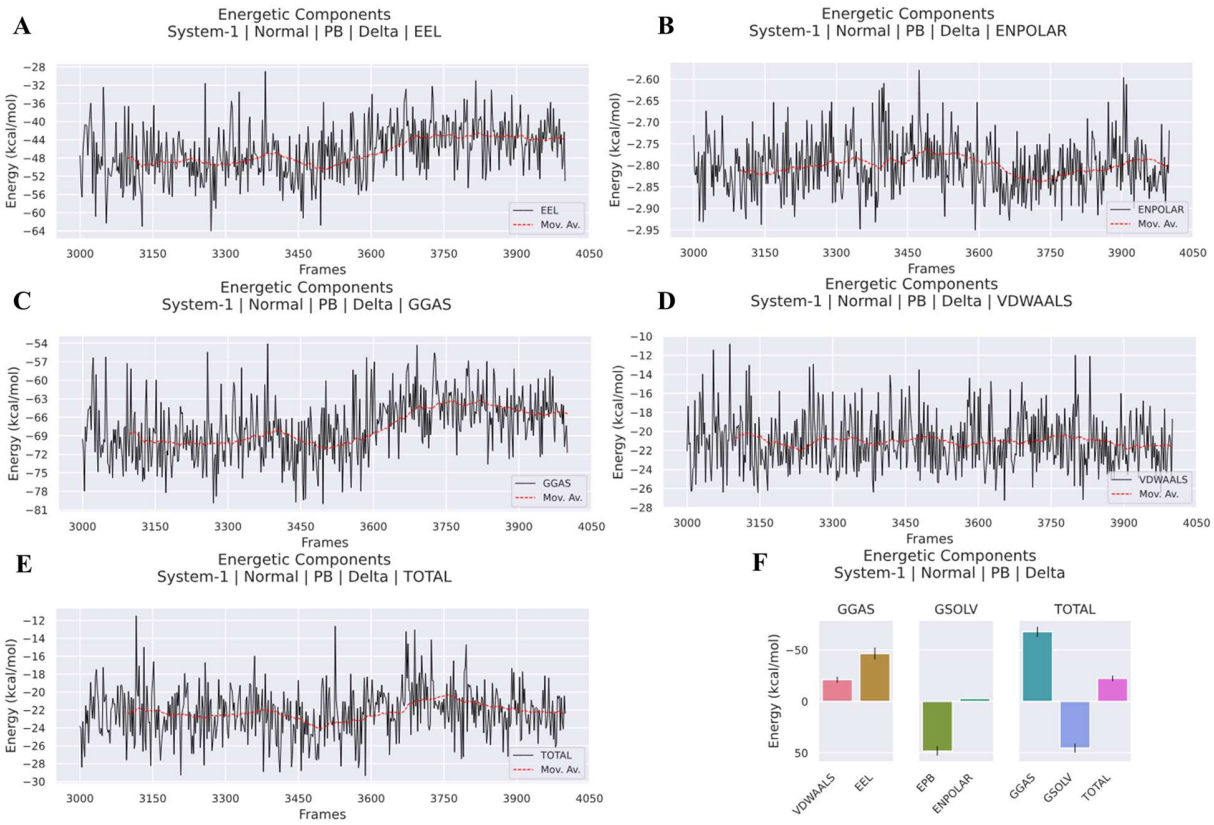
Supplementary Figure 2. The Binding free energy calculations of the 8AV1_Stigmasteol complex following the MD simulation using MM-GBSA. The total binding free energy was negative and indicated favorable binding energy.



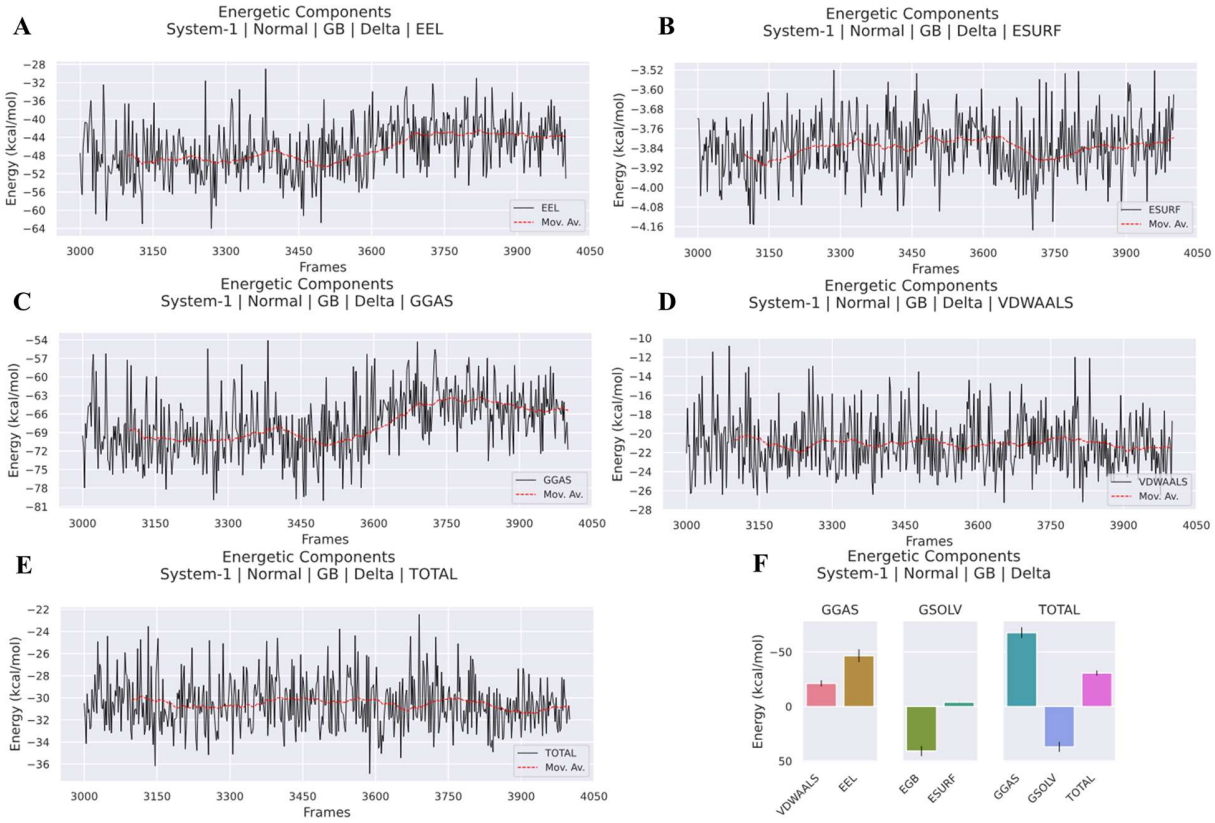
Supplementary Figure 3. The Binding free energy calculations following of the 4PH9_Luteolin complex the MD simulation using MM-PBSA. The total binding free energy was negative and indicated favorable binding energy.



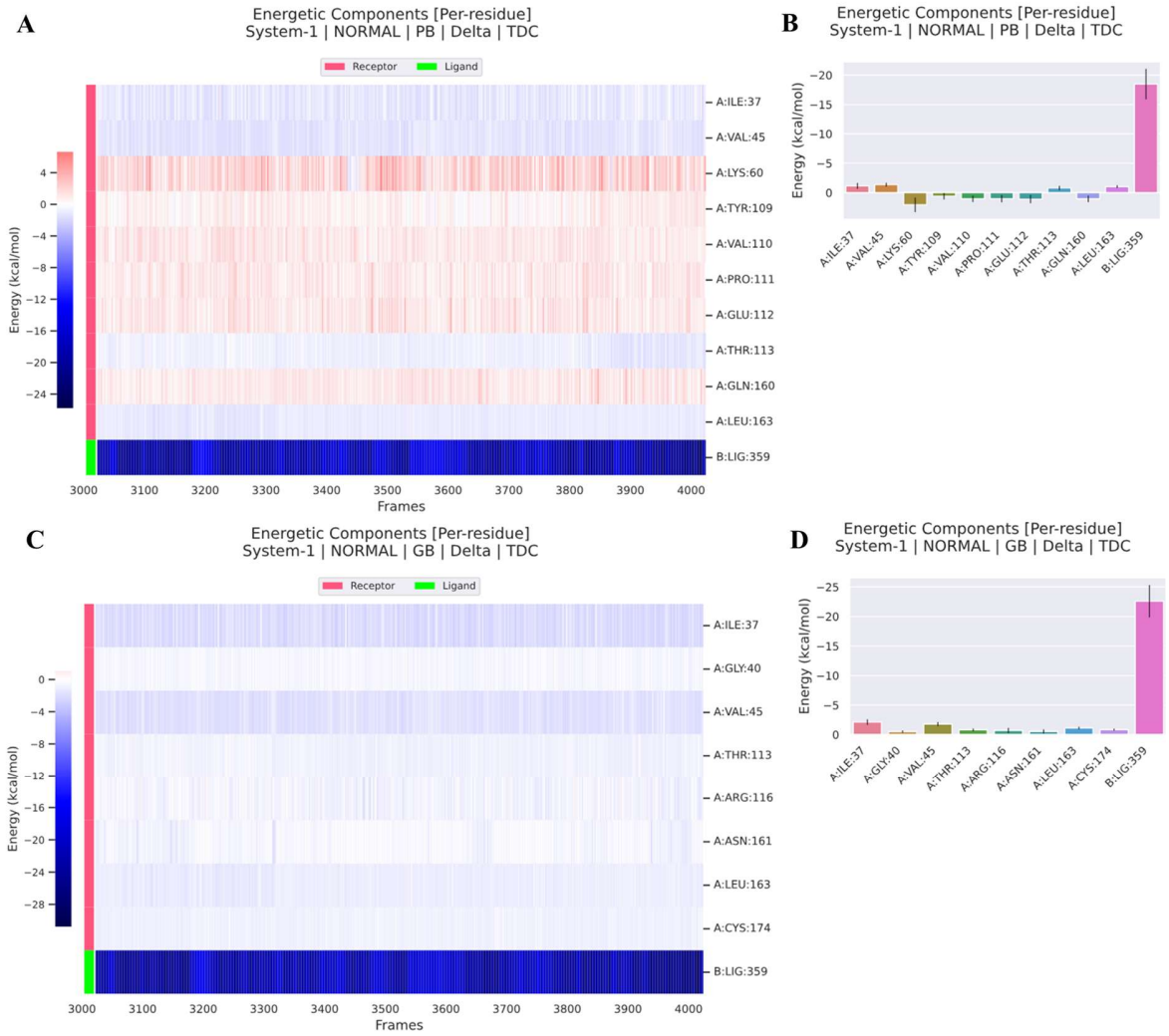
Supplementary Figure 4. The Binding free energy calculations of the 4PH9_Luteolin complex following the MD simulation using MM-GBSA. The total binding free energy was negative and indicated favorable binding energy.



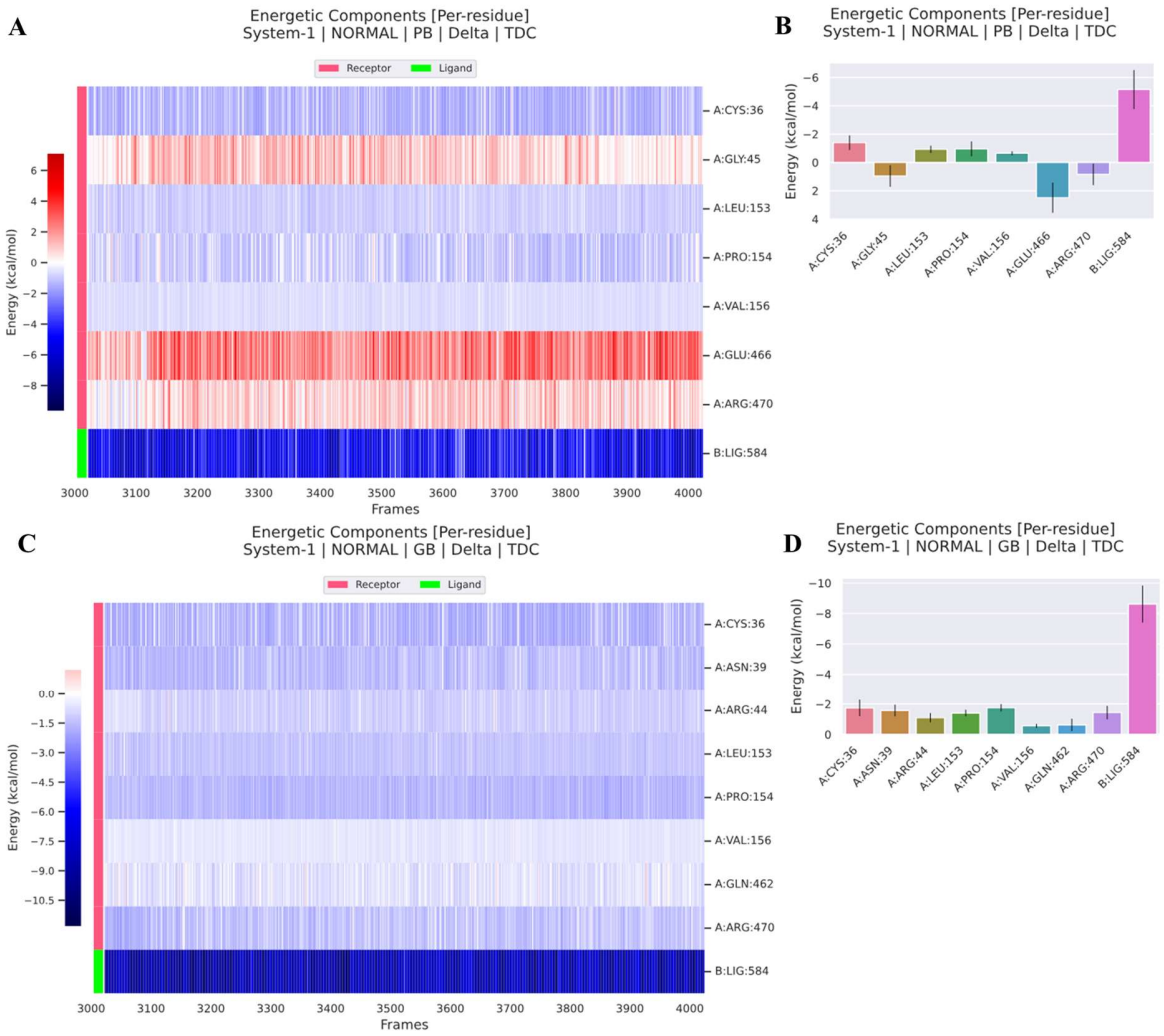
Supplementary Figure 5. The Binding free energy calculations of the 3FXI_Quercetin complex following the MD simulation using MM-PBSA. The total binding free energy was negative and indicated favorable binding energy.



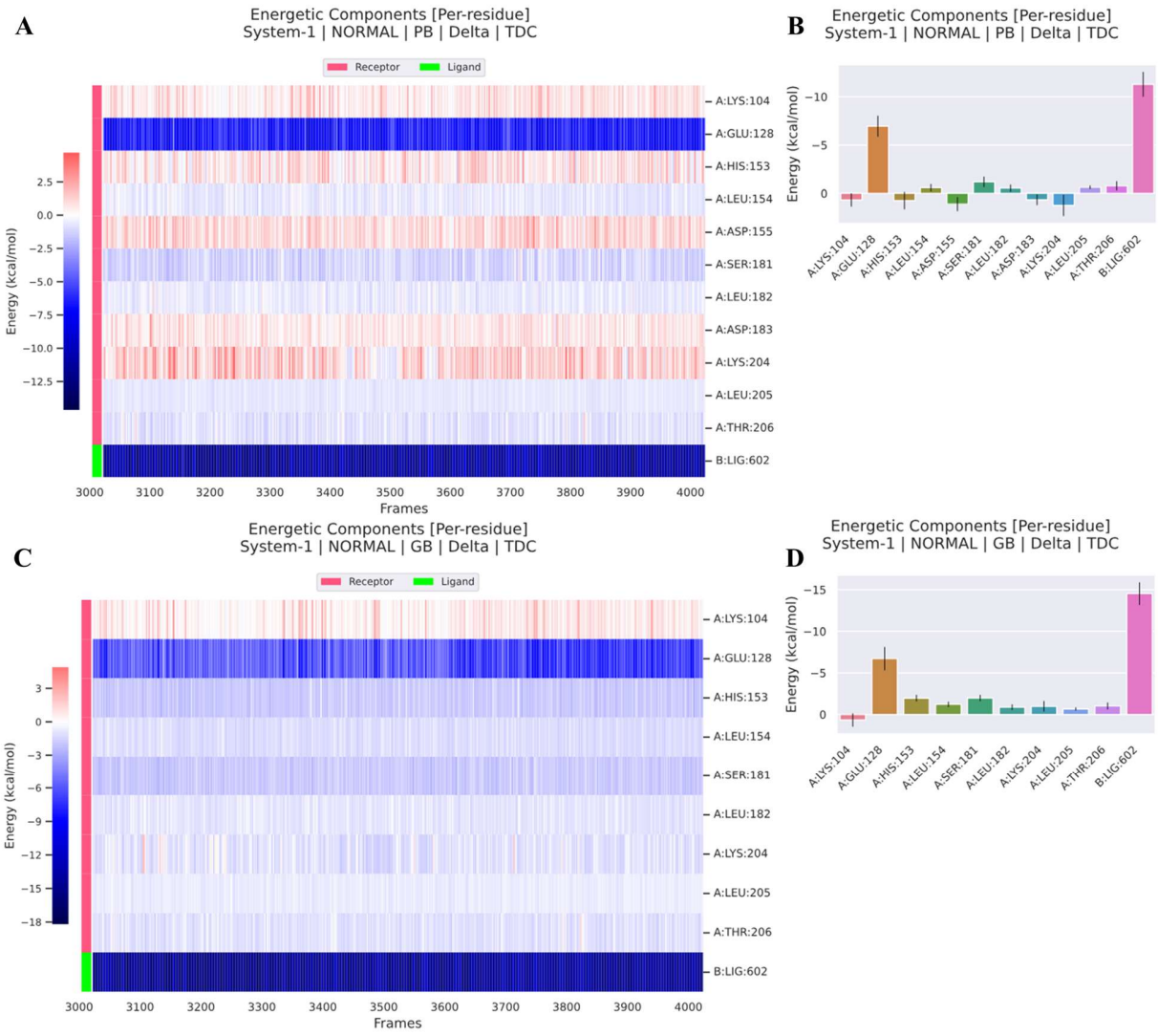
Supplementary Figure 6. The Binding free energy calculations of the 3FXI_Quercetin complex following the MD simulation using MM-GBSA. The total binding free energy was negative and indicated favorable binding energy.



Supplementary Figure 7. The per-residue decomposition studies were performed to assess the contribution of the individual amino acid in the ligand-protein complex using both MM-PBSA and GBSA parameter. VAL45 and ILE37 showed highest contributing energy in the 8AV1_Stigmasterol complex using MM-PBSA and MM-GBSA parameter, respectively.



Supplementary Figure 8. The per-residue decomposition studies were performed to assess the contribution of the individual amino acid in the ligand-protein complex using both MM-PBSA and GBSA parameter. CYS36 and PRO154 showed highest contributing energy in the 4PH9_Luteolin complex using MM-PBSA and MM-GBSA parameter, respectively.



Supplementary Figure 9. The per-residue decomposition studies were performed to assess the contribution of the individual amino acid in the ligand-protein complex using both MM-PBSA and GBSA parameter. GLU128 showed highest contributing energy in the 3FXI_Quercetin complex using MM-PBSA and MM-GBSA parameter, respectively.

Statistic Data

1. Aldose crude

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.299	6	.216	683.325	<.001
Within Groups	.004	14	.000		
Total	1.303	20			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval	
			Lower	Upper
Inhibition	Eta-squared	.997	.987	.997
	Epsilon-squared	.995	.982	.996
	Omega-squared Fixed-effect	.995	.981	.996
	Omega-squared Random-effect	.970	.896	.976

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Robust Tests of Equality of Means

Inhibition

	Statistic[a]	df1	df2	Sig.
Welch	11190.772	6	5.338	<.001
Brown-Forsythe	683.325	6	3.385	<.001

a. Asymptotically F distributed.

2. Ethylacetata

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.075	6	.179	363.363	<.001
Within Groups	.007	14	.000		
Total	1.082	20			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval	
			Lower	Upper
Inhibition	Eta-squared	.994	.976	.995
	Epsilon-squared	.991	.966	.993
	Omega-squared Fixed-effect	.990	.964	.992
	Omega-squared Random-effect	.945	.819	.956

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Robust Tests of Equality of Means

Inhibition

	Statistic[a]	df1	df2	Sig.
Welch	60996.740	6	5.355	<.001
Brown-Forsythe	363.363	6	2.718	<.001

a. Asymptotically F distributed.

3. Aqueous

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.943	6	.157	585.284	<.001
Within Groups	.004	14	.000		
Total	.947	20			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.996	.985	.997
	Epsilon-squared	.994	.979	.995
	Omega-squared Fixed-effect	.994	.978	.995
	Omega-squared Random-effect	.965	.880	.972

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Robust Tests of Equality of Means

Inhibition

	Statistic[a]	df1	df2	Sig.
Welch	6334.777	6	5.337	<.001
Brown-Forsythe	585.284	6	5.960	<.001

a. Asymptotically F distributed.

4. Hexane

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.708	6	.118	548.909	<.001
Within Groups	.003	14	.000		
Total	.711	20			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval	
			Lower	Upper
Inhibition	Eta-squared	.996	.984	.997
	Epsilon-squared	.994	.977	.995
	Omega-squared Fixed-effect	.994	.976	.995
	Omega-squared Random-effect	.963	.873	.970

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Robust Tests of Equality of Means

Inhibition

	Statistic[a]	df1	df2	Sig.
Welch	12684.985	6	5.341	<.001
Brown-Forsythe	548.909	6	4.433	<.001

a. Asymptotically F distributed.

5. Quercetein

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.442	6	.240	756.305	<.001
Within Groups	.004	14	.000		
Total	1.446	20			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.997	.989	.998
	Epsilon-squared	.996	.984	.996
	Omega-squared Fixed-effect	.995	.983	.996
	Omega-squared Random-effect	.973	.905	.978

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Robust Tests of Equality of Means

Inhibition

	Statistic[a]	df1	df2	Sig.
Welch	94870.261	6	5.361	<.001
Brown-Forsythe	756.305	6	3.351	<.001

a. Asymptotically F distributed.

6. Amylase crude

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	7.340	9	20	<.001
	Based on Median	1.376	9	20	.263
	Based on Median and with adjusted df	1.376	9	3.899	.408
	Based on trimmed mean	6.571	9	20	<.001

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.860	9	.096	909.795	<.001
Within Groups	.002	20	.000		
Total	.862	29			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.998	.992	.998
	Epsilon-squared	.996	.989	.997
	Omega-squared Fixed-effect	.996	.989	.997
	Omega-squared Random-effect	.968	.906	.972

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model

Amylase_Aquous

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	7.340	9	20	<.001
	Based on Median	1.376	9	20	.263
	Based on Median and with adjusted df	1.376	9	3.899	.408
	Based on trimmed mean	6.571	9	20	<.001

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.860	9	.096	909.795	<.001
Within Groups	.002	20	.000		
Total	.862	29			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.998	.992	.998
	Epsilon-squared	.996	.989	.997
	Omega-squared Fixed-effect	.996	.989	.997
	Omega-squared Random-effect	.968	.906	.972

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect

Amylase_ethyleacetate

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	4.300	9	20	.003
	Based on Median	1.421	9	20	.244
	Based on Median and with adjusted df	1.421	9	7.829	.318
	Based on trimmed mean	4.041	9	20	.004

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.755	9	.084	597.760	<.001
Within Groups	.003	20	.000		
Total	.758	29			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.996	.988	.997
	Epsilon-squared	.995	.983	.995
	Omega-squared Fixed-effect	.994	.983	.995
	Omega-squared Random-effect	.952	.863	.958

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model

Amylase_hexane

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	9.052	9	20	<.001
	Based on Median	.956	9	20	.502
	Based on Median and with adjusted df	.956	9	4.791	.554
	Based on trimmed mean	7.606	9	20	<.001

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.701	9	.078	542.549	<.001
Within Groups	.003	20	.000		
Total	.703	29			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.996	.987	.996
	Epsilon-squared	.994	.982	.995
	Omega-squared Fixed-effect	.994	.981	.995
	Omega-squared Random-effect	.948	.851	.954

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model

Amylase_Acarbose

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	4.127	9	20	.004
	Based on Median	.686	9	20	.713
	Based on Median and with adjusted df	.686	9	9.405	.709
	Based on trimmed mean	3.669	9	20	.007

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	.994	9	.110	1542.869	<.001
Within Groups	.001	20	.000		
Total	.995	29			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.999	.996	.999
	Epsilon-squared	.998	.993	.998
	Omega-squared Fixed-effect	.998	.993	.998
	Omega-squared Random-effect	.981	.942	.983

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model

Glucosidase_crude

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	12.444	10	22	<.001
	Based on Median	1.326	10	22	.277
	Based on Median and with adjusted df	1.326	10	2.064	.501
	Based on trimmed mean	10.497	10	22	<.001

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.376	10	.138	715.053	<.001
Within Groups	.004	22	.000		
Total	1.380	32			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.997	.991	.997
	Epsilon-squared	.996	.987	.996
	Omega-squared Fixed-effect	.995	.986	.996
	Omega-squared Random-effect	.956	.877	.960

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect

Glucosidase_ethylacetate

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	7.914	10	22	<.001
	Based on Median	1.467	10	22	.217
	Based on Median and with adjusted df	1.467	10	3.803	.386
	Based on trimmed mean	7.076	10	22	<.001

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.237	10	.124	1322.566	<.001
Within Groups	.002	22	.000		
Total	1.239	32			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval	
			Lower	Upper
Inhibition	Eta-squared	.998	.995	.999
	Epsilon-squared	.998	.993	.998
	Omega-squared Fixed-effect	.998	.993	.998
	Omega-squared Random-effect	.976	.930	.978

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Gluco_Aquous

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	6.683	10	22	<.001
	Based on Median	.901	10	22	.548
	Based on Median and with adjusted df	.901	10	7.044	.574
	Based on trimmed mean	5.796	10	22	<.001

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.083	10	.108	1153.042	<.001
Within Groups	.002	22	.000		
Total	1.085	32			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval	
			Lower	Upper
Inhibition	Eta-squared	.998	.994	.998
	Epsilon-squared	.997	.992	.998
	Omega-squared Fixed-effect	.997	.991	.997
	Omega-squared Random-effect	.972	.920	.975

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.

Gluco_hexane

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	2.761	10	22	.023
	Based on Median	.305	10	22	.972
	Based on Median and with adjusted df	.305	10	9.743	.962
	Based on trimmed mean	2.382	10	22	.043

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.037	10	.104	949.398	<.001
Within Groups	.002	22	.000		
Total	1.039	32			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval	
			Lower	Upper
Inhibition	Eta-squared	.998	.993	.998
	Epsilon-squared	.997	.990	.997
	Omega-squared Fixed-effect	.997	.990	.997
	Omega-squared Random-effect	.966	.905	.970

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect

Gluco_acarbose

Tests of Homogeneity of Variances

		Levene Statistic	df1	df2	Sig.
Inhibition	Based on Mean	2.680	10	22	.026
	Based on Median	1.149	10	22	.373
	Based on Median and with adjusted df	1.149	10	8.825	.424
	Based on trimmed mean	2.565	10	22	.031

ANOVA

Inhibition

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.340	10	.134	366.473	<.001
Within Groups	.008	22	.000		
Total	1.348	32			

ANOVA Effect Sizes[a]

		Point Estimate	95% Confidence Interval Lower	Upper
Inhibition	Eta-squared	.994	.982	.995
	Epsilon-squared	.991	.974	.992
	Omega-squared Fixed-effect	.991	.973	.992
	Omega-squared Random-effect	.917	.784	.925

a. Eta-squared and Epsilon-squared are estimated based on the fixed-effect model.