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7 Chapter: Publications

7.1 Research papers:

Kojja V, Kumar D, Kalavagunta PK, Bhukya B, Tangutur AD, Nayak PK. 2-(Diarylalkyl) aminobenzothiazole derivatives induce autophagy and apoptotic death through SIRT inhibition and P53 activation In MCF7 breast cancer cells. Computational Biology and Chemistry. 2025 Jun 1; 116:108395.

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7.2 Co-author papers:

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7.3 Book Chapters:

Ramakrishna K, Viswanadh MK, Dumala N, Chakravarth G, **Venkateswarlu K,** Gutti G, Yadagiri G, Duguluri S, Rai SN. Advanced Biomaterials in Neuroprotection: Innovations and Clinical Applications. InBiomaterials and Neurodegenerative Disorders 2025 Jan 23 (pp. 69-92). Singapore: Springer Nature Singapore.

Chapter 8: Appendix

Table S1: Autodock4 Docking results displaying binding energy of ligands against SIRT1-3 receptor.

No.	Name of Compounds	SIRT1		SIRT2		SIRT3	
		Binding energy (kcal/mol)	Ligand efficiency	Binding energy (kcal/mol)	Ligand efficiency	Binding energy (kcal/mol)	Ligand efficiency
1	Apigenin	-8.97	-0.5	-8.56	-0.43	-8.92	-0.45
2	Coumestrol	-10.9	-0.5	-9.95	-0.43	-9.85	-0.44
3	Cyanidine	-9.5	-0.51	-8.43	-0.4	-8.5	-0.44
4	Enterolactone	-9.7	-0.48	-9.12	-0.41	-8.9	-0.46
5	Epicatchin	-9.5	-0.49	-8.69	-0.41	-8.91	-0.42
6	Genestine	-9.0	-0.55	-8.92	-0.45	-9.11	-0.46
7	Kaemferol	-9.26	-0.52	-8.85	-0.42	-9.06	-0.44
8	Naringenin	-8.9	-0.54	-9.04	-0.45	-9.16	-0.46
9	Resveratrol	-9.31	-0.55	-8.48	-0.5	-8.62	-0.51
10	Xanthohumol	-9.1	-0.49	-9.2	-0.4	-9.4	-0.41
11	EX527	-10.26	-0.57	-	-	-	-
12	NPD11033	-	-	-11.19	-0.3	-	-
13	EX-A3489	-	-	-	-	-10.73	-0.4

Table S2: Schrodinger Docking results displaying binding energy of ligands against SIRT1-3 receptor.

No.	Name of Compounds	SIRT1 G-Score (kcal/mol)	SIRT2 G-Score (kcal/mol)	SIRT3 G-Score (kcal/mol)
1	Apigenin	-6.416	-9.026	-7.514
2	Coumestrol	-7.912	-9.463	-8.991
3	Cyanidine	-7.182	-8.154	-7.665
4	Enterolactone	-7.202	-9.14	-7.297
5	Epicatchin	-7.187	-9.367	-8.374

6	Genestine	-7.315	-7.561	-7.373
7	Kaemferol	-7.569	-8.866	-8.221
8	Naringenin	-6.861	-8.87	-7.583
9	Resveratrol	-5.946	-8.317	-7.764
10	Xanthohumol	-7.651	-8.962	-7.924
11	EX527	-9.256	-	-
12	NPD11033	-	-9.563	-
13	EX-A3489	-	-	-8.90

Table S4: Physicochemical parameters of Coumestrol:

S.No	Physicochemical properties	Coumestrol
1	Molecular formula	$C_{15}H_8O_5$
2	Molecular weight	268.22 g/mol
3	Log P (o/w)	2.46
4	H-bond acceptors	5
5	H-bond donors	2
6	Heavy atoms	20
7	Rotatable bonds	0

Table S5: Pharmacokinetic parameters of Coumestrol

S.No	ADME parameters	Coumestrol
1	BBB penetration	0.756056
2	CYP3A4 inhibition	Inhibitor
3	CYP3A4 substrate	0.047334
4	CYP2C19 inhibition	Inhibitor
5	P-glycoprotein inhibition	Substrate
6	In-vitro plasma protein binding (%)	100

Table S6: Toxicity parameters of Coumestrol.

S.No	Toxicity parameters	Coumestrol
1	Acute fish toxicity minnow	0.00379246
2	Acute fish toxicity medaka	0.007014
3	Acute algae toxicity	0.047334
4	HERG-invitro inhibition	Medium risk
5	Carcinogenicity to mouse	Negative
6	Carcinogenicity to Rat	Negative

Table S7: binding interactions of phytoestrogens with Sirtuin proteins.

Compound	Sirt 1	Sirt 2	Sirt 3
Apigenin	A:ILE347, A:ILE347(Pi-Sigma) A:PHE273, A:PHE297, A:PHE297 (Pi-Pi T-shaped) A:ASP348 (H bond)	A:ASP170, A:PHE131(Conventional Hydrogen Bond) A:PHE190 (Pi-Pi T-shaped Pi-Pi Stacked) A:LEU134, ALA135 (Amide-Pi Stacked) A:ALA135, A:LEU134 (Pi-Alkyl)	A:PHE157 (Conventional Hydrogen Bond) A:ASP156 (Carbon Hydrogen Bond) A:ILE230 (Pi-Sigma) A:PHE157, A:PHE180, A:HIS248 ((Pi-Pi Stacked)
Coumestrol	A:ASP348, A:VAL412(Conventional Hydrogen Bond) A:ILE347 (Pi-Sigma) A:PHE273, A:PHE297 (Pi-Pi T-shaped) A:ILE316, A:ALA262, A:ILE347, A:ILE411 (Pi-Alkyl)	A:ASP170, A:PHE131 (Conventional Hydrogen Bond) A:ALA135 (Pi-Sigma) A:PHE131, A:PHE190 (Pi-Pi T-shaped) A:LEU134, ALA135 (Amide-Pi Stacked) A:ALA135, A:LEU138, A:PRO140, A:LEU134(Pi-Alkyl)	A:PHE157, A:ILE230 (Conventional Hydrogen Bond) A:SER149, A:ASP156, A:ASN229 (Carbon Hydrogen Bond) A:ALA146(Pi-Sigma) A:PHE157(Pi-Pi Stacked)
Cyadine	A:ILE347(Pi-Donor Hydrogen Bond) A:PHE273, A:PHE297 (Pi-Pi T-shaped) A:ILE347, A:ILE270, A:ILE316 (Pi-Alkyl)	A:VAL233, A:ASN168 (Conventional Hydrogen Bond) A:ASN168(Pi-Sigma) A:PHE119, A:HIS187(Pi-Pi T-shaped) A:ARG97, A:ILE169, A:ALA85(Pi-Alkyl)	A:ASP231 (Conventional Hydrogen Bond) A:ALA146(Pi-Sigma) A:PHE157(Pi-Pi Stacked) A:ILE230, A:ILE154(Pi-Alkyl)
Enterolactone	A:TYR317 (Conventional Hydrogen Bond) A:PHE273, A:PHE297 (Pi-Pi T-shaped) A:ILE270, A:ILE316, A:ILE411, A:ILE347(Pi-Alkyl)	A:PHE96(Pi-Pi Stacked) A:ILE93(Pi-Alkyl) A:ILE169, A:LEU138(Conventional Hydrogen Bond)	A:ALA146, A:ILE154, A:ILE230(Pi-Sigma) A:PHE157 (Pi-Pi Stacked) A:PHE180 (Pi-Pi T-shaped) A:ASN229 (Carbon Hydrogen Bond)
Epicatchin	A:ILE270, A:ILE316, A:ASN346 (Pi-Sigma) A:PHE273 (Pi-Pi T-shaped) A:ALA262, A:ILE347(Alkyl)	A:PHE96, A:ARG97, A:ILE169 (Conventional Hydrogen Bond) A:ALA85 (Pi-Sigma) A:PHE119 (Pi-Pi T-shaped)	A:ASP231(Conventional Hydrogen Bond) A:ILE230(Pi-Donor Hydrogen Bond) A:HIS248(Pi-Pi Stacked) A:ILE230(Alkyl)

		A:PHE96, ARG97 (Amide-Pi Stacked) A:ALA85, A:ILE169 (Alkyl)	A:PHE157, A:HIS248 (Pi Alkyl)
genistein	A:ASN346 (Carbon Hydrogen Bond) A:ILE347(Pi-Donor Hydrogen Bond) A:ILE347(Pi-Sigma) A:PHE273(Pi-Pi T-shaped) A:ALA262(Alkyl)	A:HIS187(Carbon Hydrogen Bond) A:PHE235(Pi-Pi T-shaped) A:ARG97(Alkyl) A:HIS187(Pi-Alkyl)	A:TYR165 (Conventional Hydrogen Bond) A:PHE180 (Pi-Pi Stacked) A:PHE180 (Pi-Alkyl)
kaempferol	A:ASN346 (Carbon Hydrogen Bond) A:ILE347 (Pi-Donor Hydrogen Bond) A:ILE316, A:ILE347, A:ILE411(Pi-Alkyl)	A:PHE190 (Pi-Pi Stacked) A:ALA135, A:LEU134 (Conventional Hydrogen Bond) A:LEU138(Pi-Alkyl)	A:ASN229(Carbon Hydrogen Bond) A:PHE157, A:PHE180 (P Pi Stacked) A:ALA146, A:ILE230(Pi Alkyl)
Narigenin	A:ILE347(Pi-Sigma) A:PHE297(Pi-Pi T-shaped) A:ILE411, A:ALA262, A:ILE270, A:ILE347 (Pi-Alkyl)	A:PHE190(Pi-Pi Stacked) A:LEU134, A:ALA135, A:LEU206(Pi-Alkyl)	A:PHE180(Pi-Pi Stacked) A:ILE230, A:ALA146, A:ILE230(Pi-Alkyl) A:TYR165(Conventional Hydrogen Bond)
Resvestrol	A:PHE273(Pi-Pi Stacked) A:PHE273, A:PHE297(Pi-Pi T-shaped) A:ILE316, A:ILE347, A:ILE411(Pi-Alkyl)	A:ARG97, A:HIS187(Carbon Hydrogen Bond) A:ALA85, A:ILE93(Pi-Sigma) A:ALA85, A:ARG97(Pi-Alkyl)	A:ALA146, A:ILE154, A:ASN229(Pi-Sigma) A:ALA146, A:ILE230(Pi-Alkyl)
Xanthohumol	A:ILE270, A:PHE297(Pi-Sigma) A:PHE273(Pi-Pi T-shaped) A:ALA262(Alkyl) A:HIS363, A:ILE347 (Pi-Alkyl)	A:ILE169(Pi-Donor Hydrogen Bond) A:ALA135(Alkyl) A:PHE119, A:PHE131, A:PHE143, A:PHE190 (Pi-Alkyl) A:ASN168, A:ALA135(Conventional Hydrogen Bond)	A:ALA146(Pi-Sigma), A:PHE157, A:PHE180(Pi Pi Stacked) A:HIS248, A:PHE157, A:HIS248, A:PHE294, A:PHE294(Pi-Alkyl)

Table S8: Binding interactions of **7**ab and **7**ba with Sirtuin proteins:

Compound	SIRT1	SIRT2	SIRT3
RN7-AB	A:ASP348, A:ILE347(Conventional hydrogen bond) A:ILE270 Pi-Sigma bond, A:PHE273 Pi-Sulfur bond, A:ILE316, A:PHE321,A:ILE279(Pi-Alkyl bond)A:ALA262, A:PHE413(Pi-Pi T shaped)	A:PHE96, A:ARG97(Conventional hydrogen bond) A:ILE93, A:ALA85(Halogen) A:PHE235,A:PHE119(PI-Pi stacked,PI-Pi T shaped) A:ILE169,A:LEU134,A:LEU138, A:LEU103, A:ALA 135,A:PHE131(Alkyl and PI-Alkyl bond)	A:GLN228(Conventional hydrogen bond) A:PHE294, A:PHE157(Pi-Sigma, Pi-Pi stacked, Pi-Pi T sigma) A:ALA146, A:ILE154, A:TYR165(Alkyl, Pi-Alkyl) A:ARG168(Halogen)
RN7-BA	A:ILE347,A:ILE270(Pi-sigma) A:PHE273(Pi-Sulfur)A:PHE297(Pi-Pi T shaped) A:ILE316, A:ILE411, A:PHE321, A:VAL412, A:HIS363, A:ALA262 (Alkyl, Pi- Alkyl)	A:PHE96(Conventional hydrogen bond)A:PHE235, A:PHE119(Pi-Satcked, Pi-Pi T shaped) A:ALA85, A:ILE93(Halogen)A:SER96(Carbon hydrogen) A:ILE232, A:ILE169, A:ALA135, A:LEU134, PHE131(Alkyl, Pi-Alkyl)	A:THR320(Carbon hydrogen bond) A:VAL292(Halogen) A:ARG158(Pi-Cation) A:HIS248, A:PHE157(Pi-Pi stacked) A:ALA146(Pi-Sigma) A:PHE180, A:ILE291, A:ILE230(Alkyl, Pi-Alkyl)

Table S9: Docking results displaying binding energy of ligands against SIRT1-3 receptor:

Sl.No	Name of Compounds	SIRT1		SIRT2		SIRT3	
		Binding energy (kcal/mol)	Ligand efficiency	Binding energy (kcal/mol)	Ligand efficiency	Binding energy (kcal/mol)	Ligand efficiency
1	RN-7AB	-12.44	0.43	-12.08	0.42	-12.03	0.42
2	RN-7BA	-12.07	0.4	-12.91	0.43	-11.86	0.4
3	Ex-527	-10.26	0.36				
4	NPD11033			-11.19	0.39		

5	EX-A3489					-10.73	0.4

Table S10: Physicochemical parameters of **7**ab and **7**ba:

S.No	Physicochemical properties	RN7ab	RN7ba
1	Molecular formula	C24H15Cl3N2OS	C24H16BrClN2OS
2	Molecular weight	485.81 g/mol	495.82 g/mol
3	Log P (o/w)	4.24	4.16
4	H-bond acceptors	2	2
5	H-bond donors	2	2
6	Heavy atoms	31	30
7	Rotatable bonds	4	4

Table S11: ADME parameters of **7**ab and **7**ba:

S.No	ADME parameters	RN7ab	RN7ba
1	BBB penetration	No	No
2	CYP3A4 inhibition	No	No
3	CYP2C19 inhibitor	Yes	Yes
4	CYP2D6 inhibitor	No	No
5	P-gp substrate	No	Yes

Table S12: Toxicity parameters of **7**ab and **7**ba:

S.No	Toxicity parameters	RN7ab	RN7ba
1	Acute fish toxicity minnow	1.45406e-006	4.30574e-006
2	Acute fish toxicity medaka	2.72876e-007	7.88181e-007
3	Acute algae toxicity	0.000451153	0.000814179
4	HERG-invitro inhibition	Medium risk	Medium risk
5	Carcinogenicity to mouse	Negative	Negative
6	Carcinogenicity to Rat	Negative	Positive

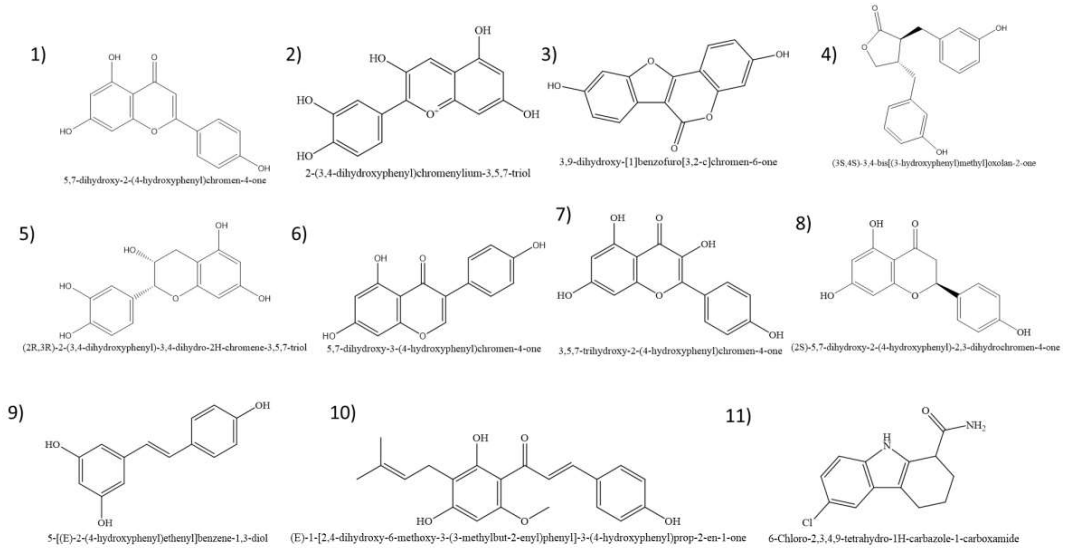

Figure S1: list of selected phytoestrogen compounds molecular structures.

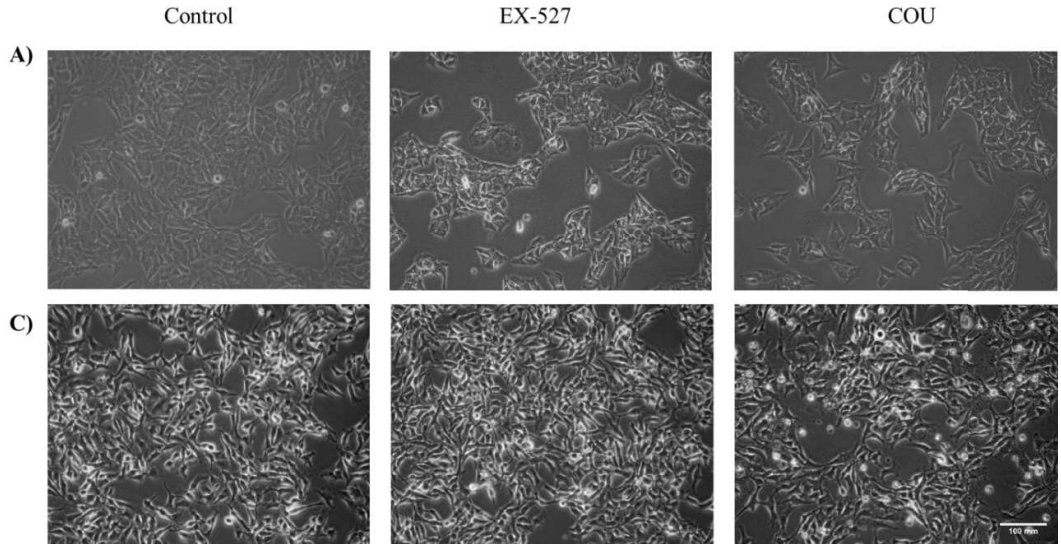

Figure S2: COU effects the cellular morphology of MCF-7 and MDAMB-231 cell line. A, cell morphology of MCF-7 cells treated with or without COU (46μM) and EX-527 (50 μM), B, cell morphology of MDAMB-231 cells treated with or without COU (46μM) and EX-527 (50 μM).

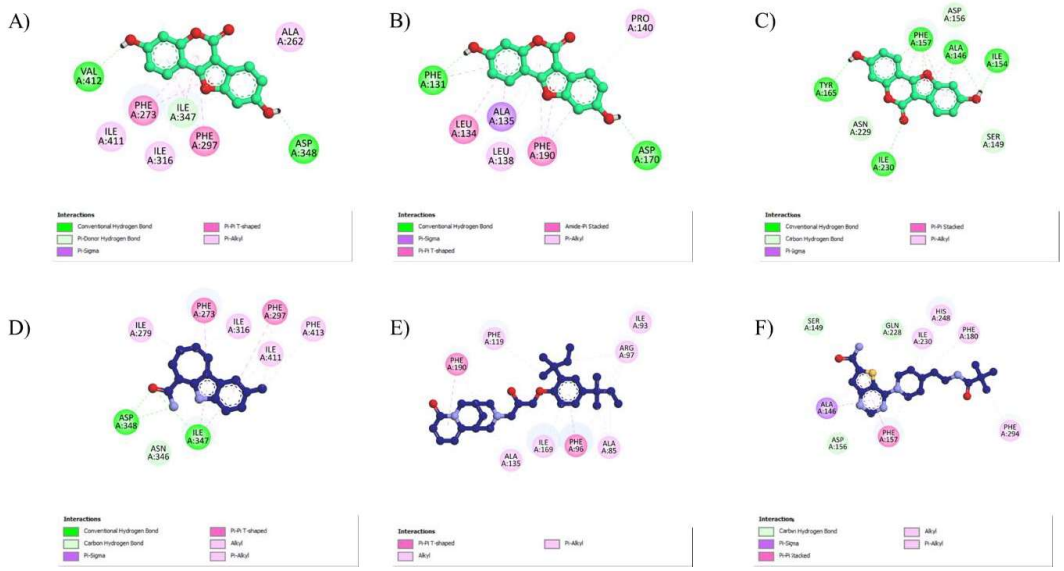

Figure S4: Binding interaction of COU and standards at SIRT1-3 active sites. A) and D) were interaction of SIRT1 with COU and EX527, B and E were interaction of SIRT2 with COU and NPD11033, and C) and F) were interactions of SIRT3 with COU and EX-A3489. (COU: Coumestrol; SIRT: Sirtuins)

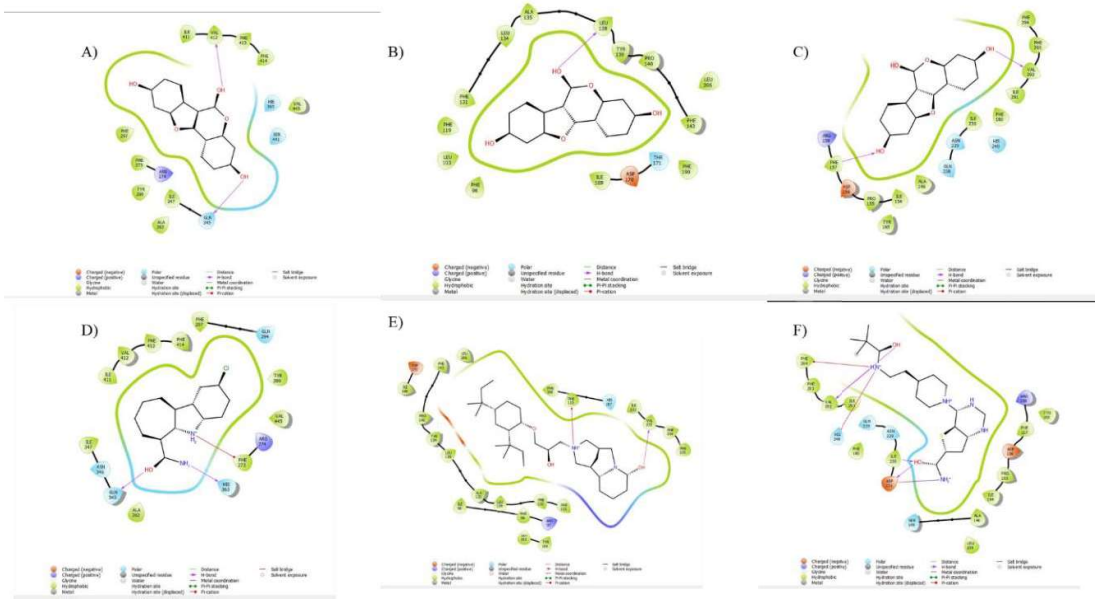

Figure S4: Binding interaction of COU and standards at SIRT1-3 active sites. A) and D) were interaction of SIRT1 with COU and EX527, B and E were interaction of SIRT2 with COU and NPD11033, and C) and F) were interactions of SIRT3 with COU and EX-A3489. (COU: Coumestrol; SIRT: Sirtuins)

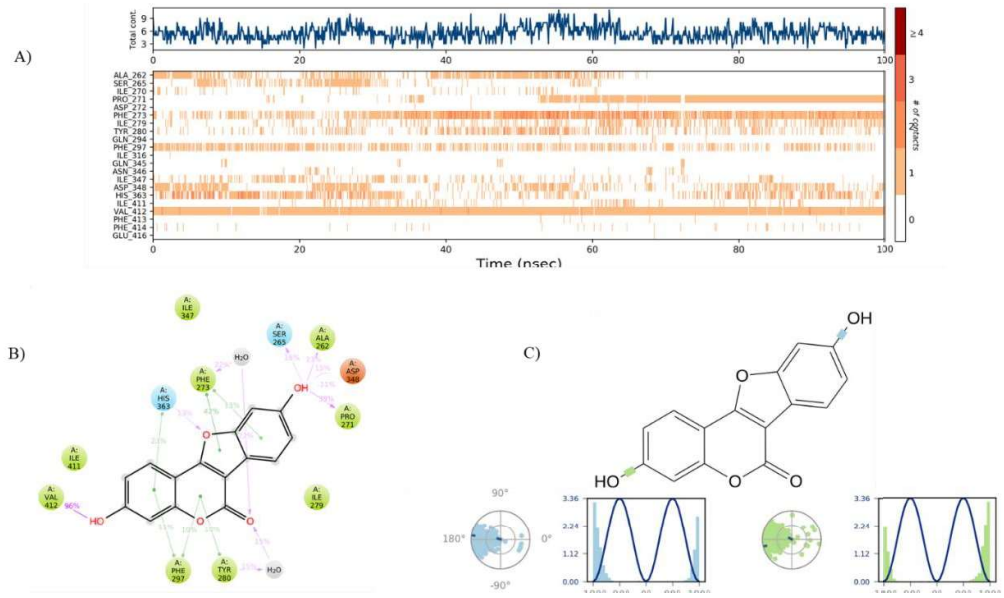

Figure S5: Coumestrol interactions with SIRT-1 protein A), Timeline of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges). B), Ligand protein interactions C), Ligand Torsions plot (0.00 through 100.00 sec).

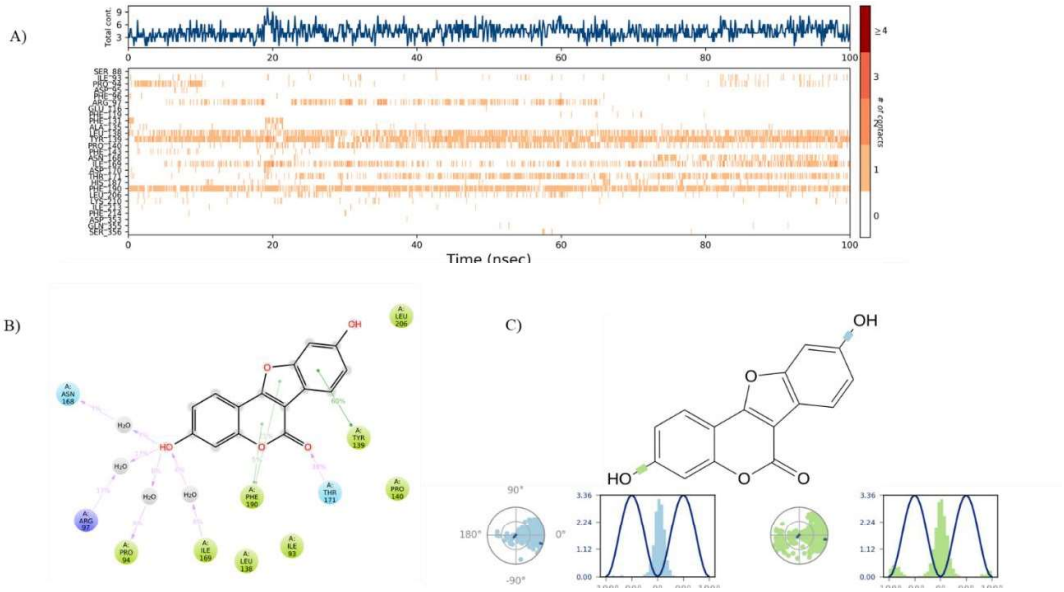

Figure S6: Coumestrol interactions with SIRT-2 protein A), Timeline of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges). B), Schematic of detailed ligand atom interactions with the protein residues. C), Ligand torsions plot (0.00 through 100.00 sec).

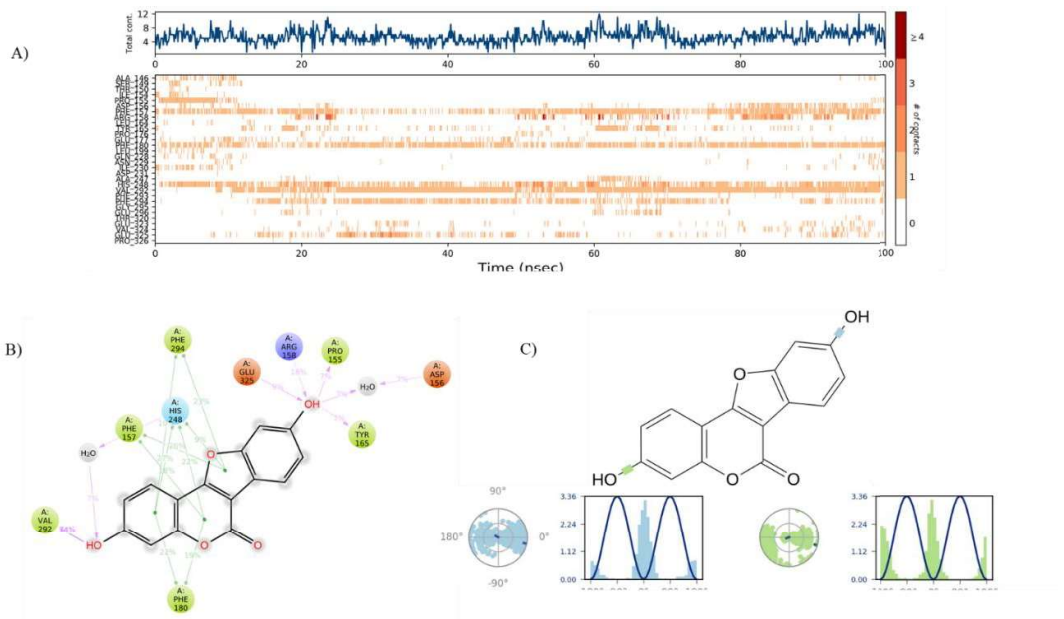

Figure S7: Coumestrol interactions with SIRT-3 protein A), Timeline of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges). B), Schematic protein ligand interactions. C, Ligand torsions plot (0.00 through 100.00 sec).

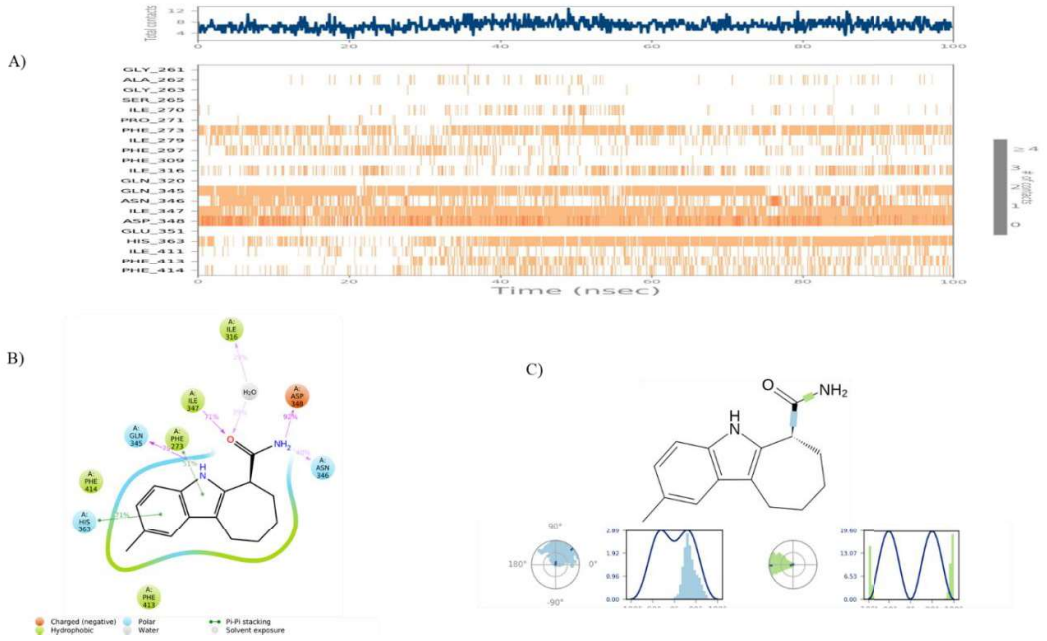

Figure S8: EX527 interactions with SIRT-1 protein A), Timeline of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges). B), Ligand protein interactions C), Ligand Torsions plot (0.00 through 100.00 sec).

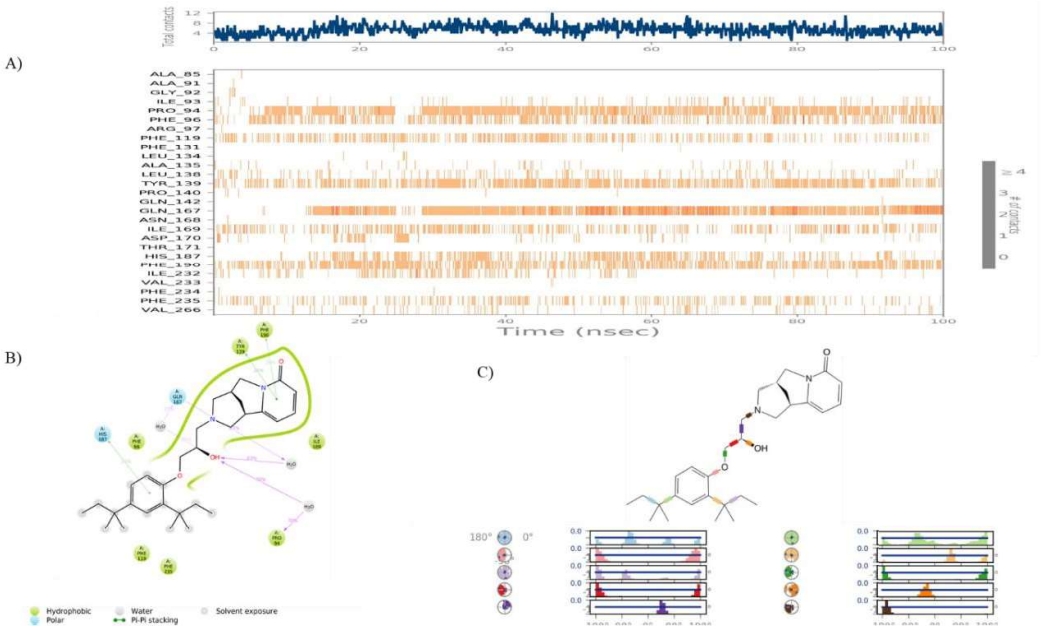

Figure S9: NPD11033 interactions with SIRT-2 protein A), Timeline of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges). B), Ligand protein interactions C), Ligand Torsions plot (0.00 through 100.00 sec).

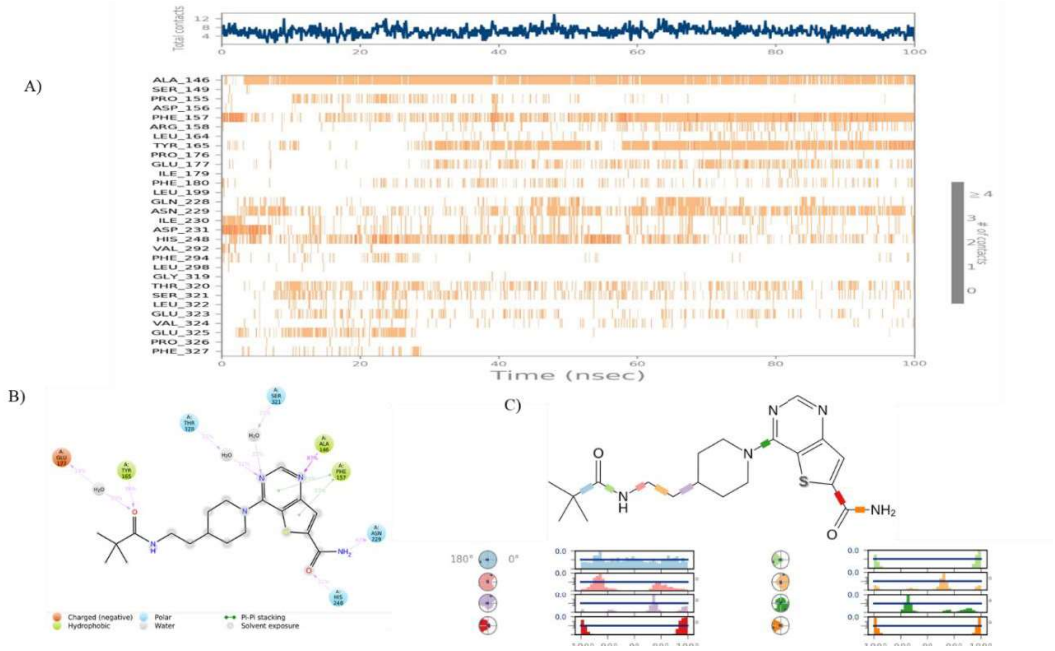

Figure S10: EX-A3489 interactions with SIRT-3 protein A), Timeline of the interactions and contacts (H-bonds, Hydrophobic, Ionic, Water bridges). B), Ligand protein interactions C), Ligand Torsions plot (0.00 through 100.00 sec).

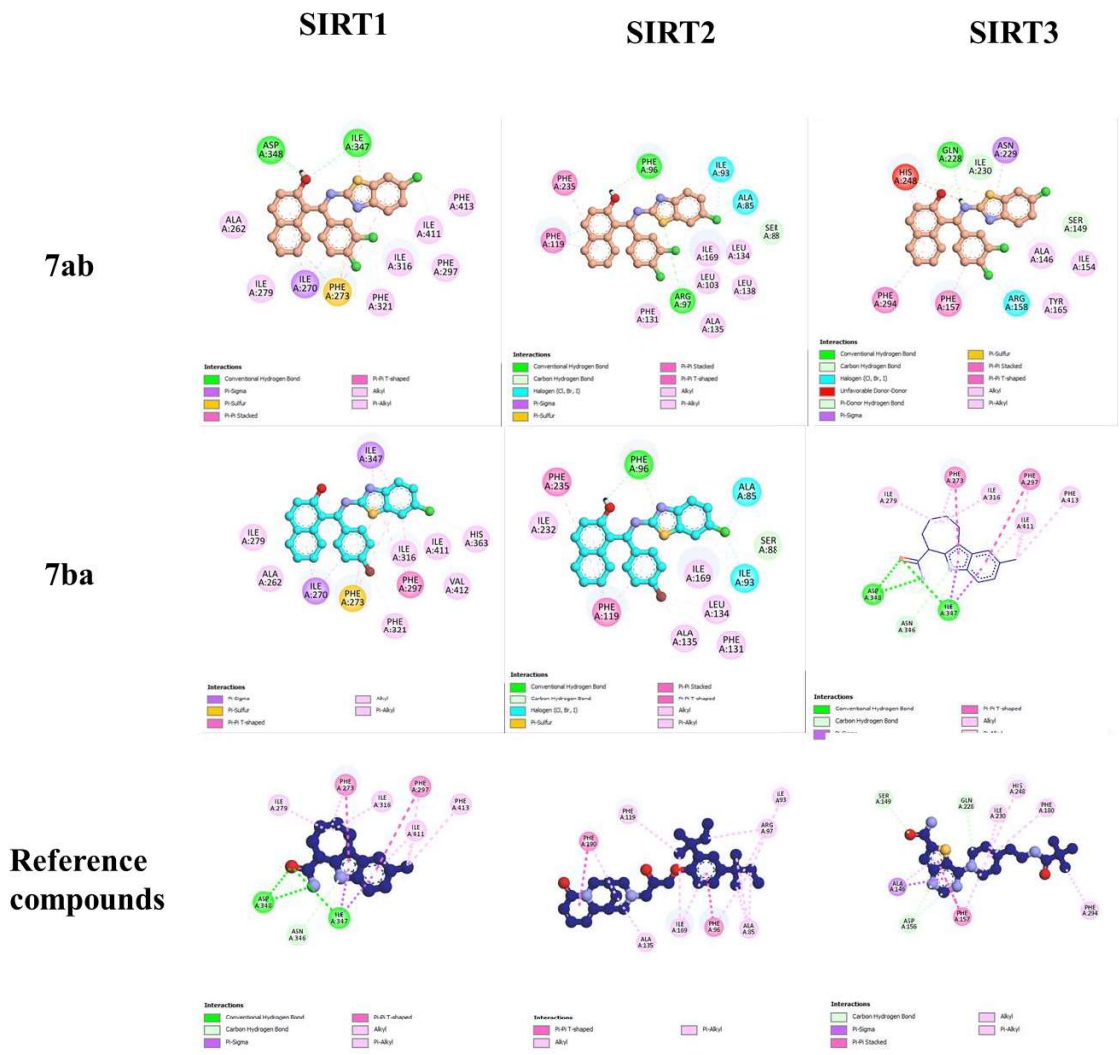

Figure S11: Binding interaction of 7ab and 7ba and reference compounds at SIRT1-3 active sites. Reference compounds were EX527 for SIRT1, NPD11033 for SIRT2 and EX-A3489 For SIRT3.

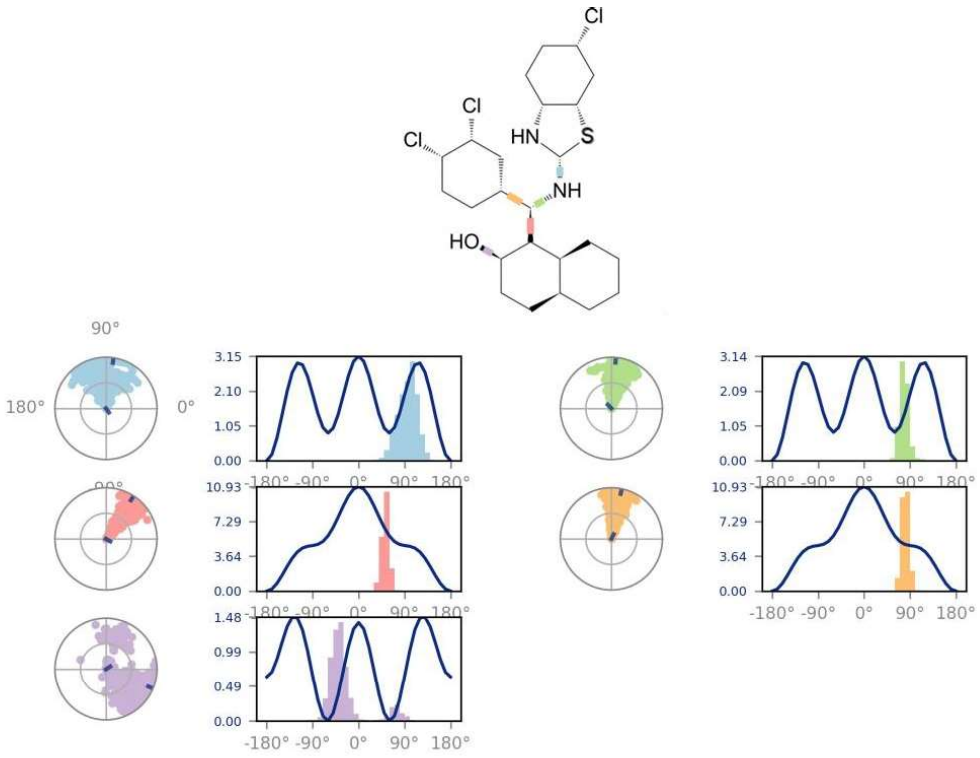

Figure S12: The ligand torsions plot of **7**ab with SIRT1 summarizes the conformational evolution of every rotatable bond (RB) in the ligand throughout the simulation trajectory (0.00 through 100.00 nsec).

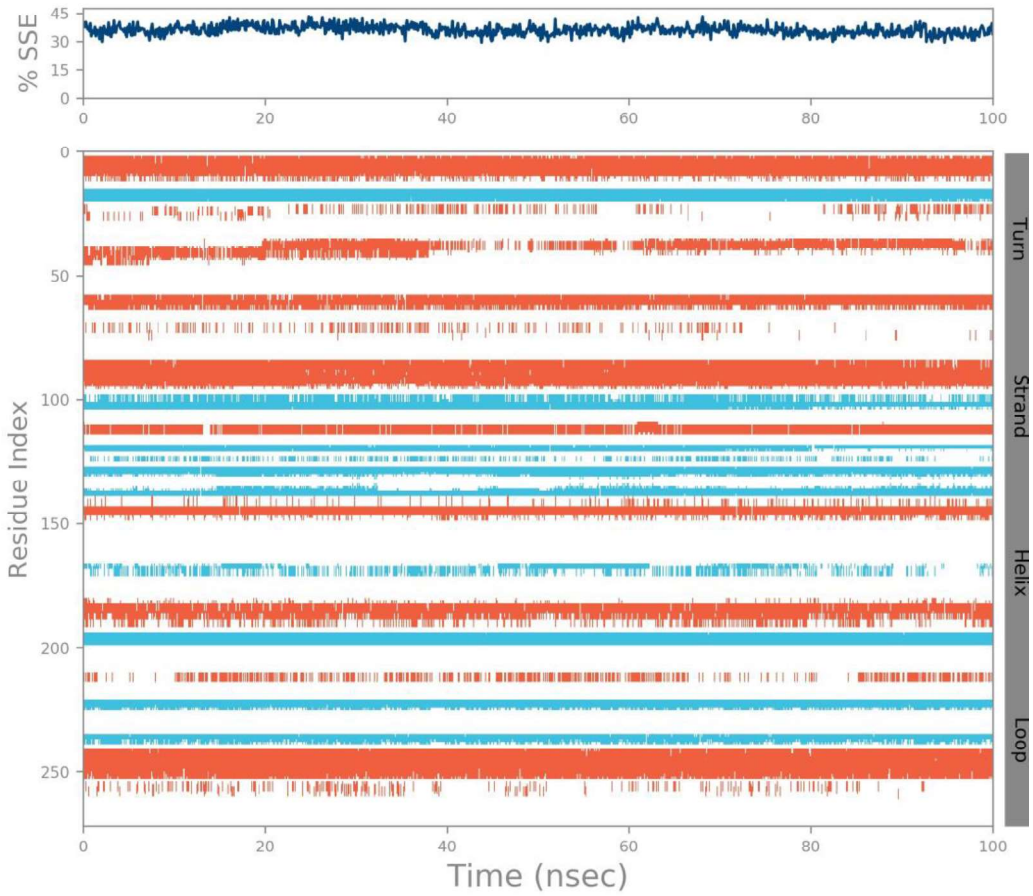

Figure S13: Protein secondary structure elements of **7**ab with SIRT1 (SSE) like alpha-helices and beta-strands are monitored throughout the simulation.

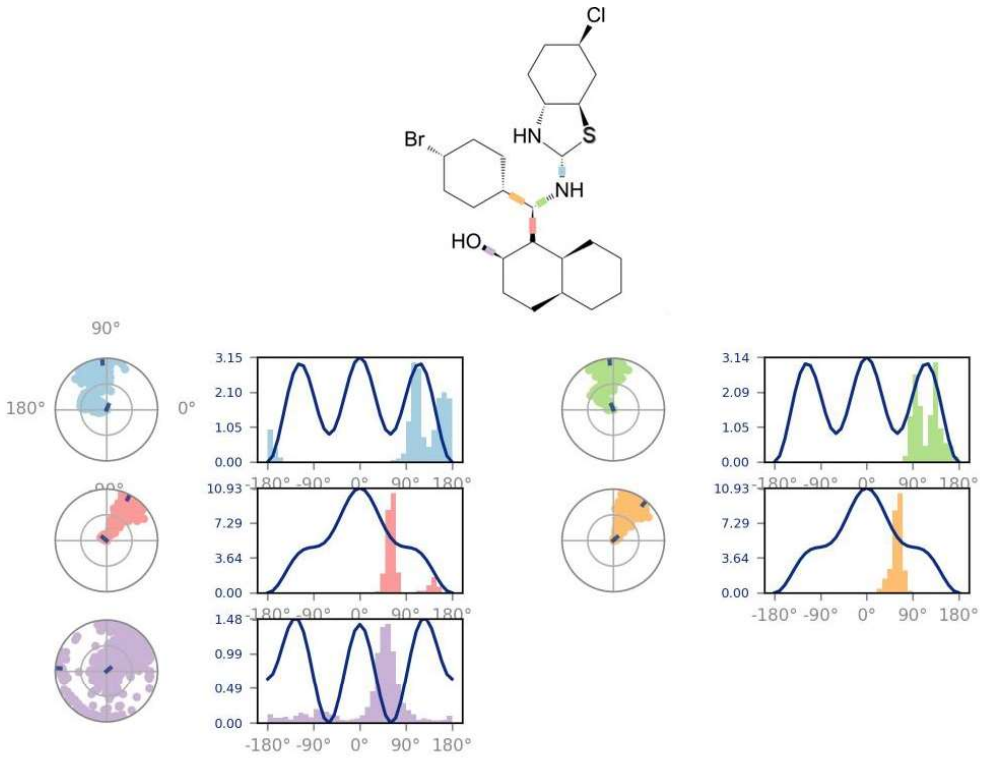

Figure S14: The ligand torsions plot of **7**ba with SIRT1 summarizes the conformational evolution of every rotatable bond (RB) in the ligand throughout the simulation trajectory (0.00 through 100.00 nsec).

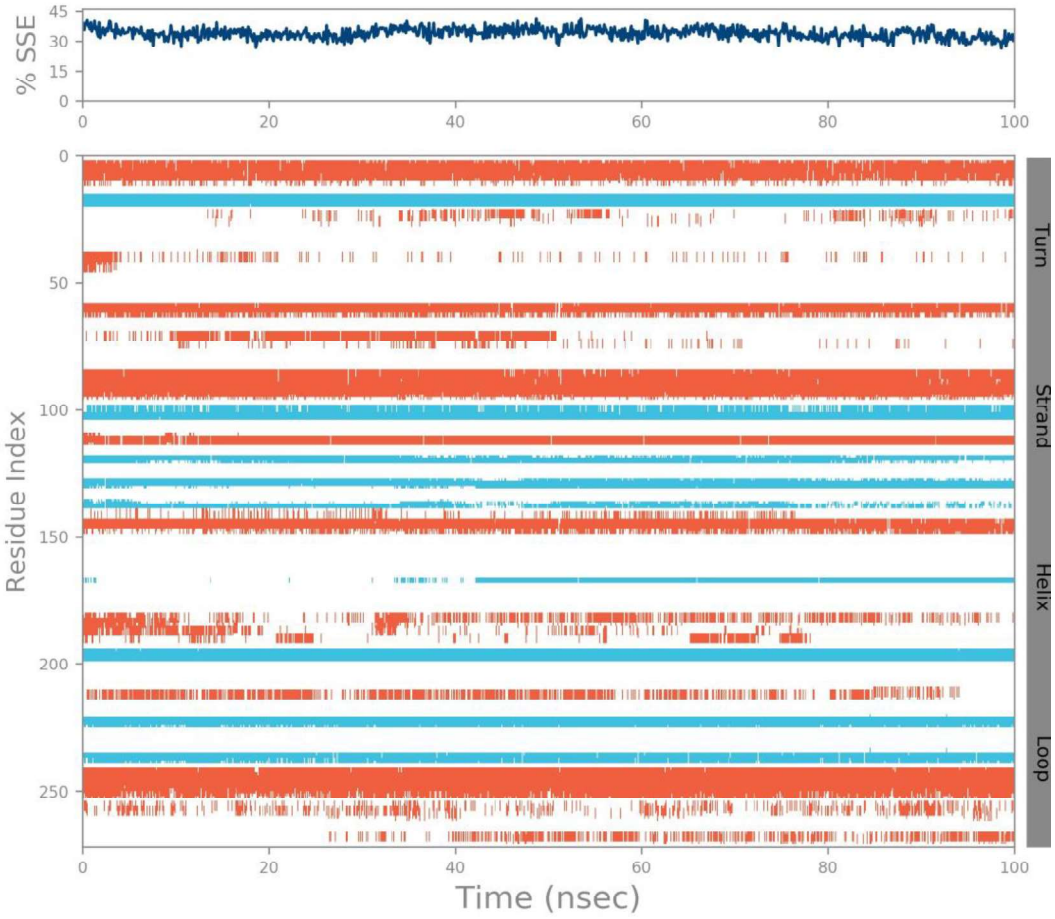

Figure S15: Protein secondary structure elements of **7**ba with SIRT1 (SSE) like alpha-helices and beta-strands are monitored throughout the simulation.

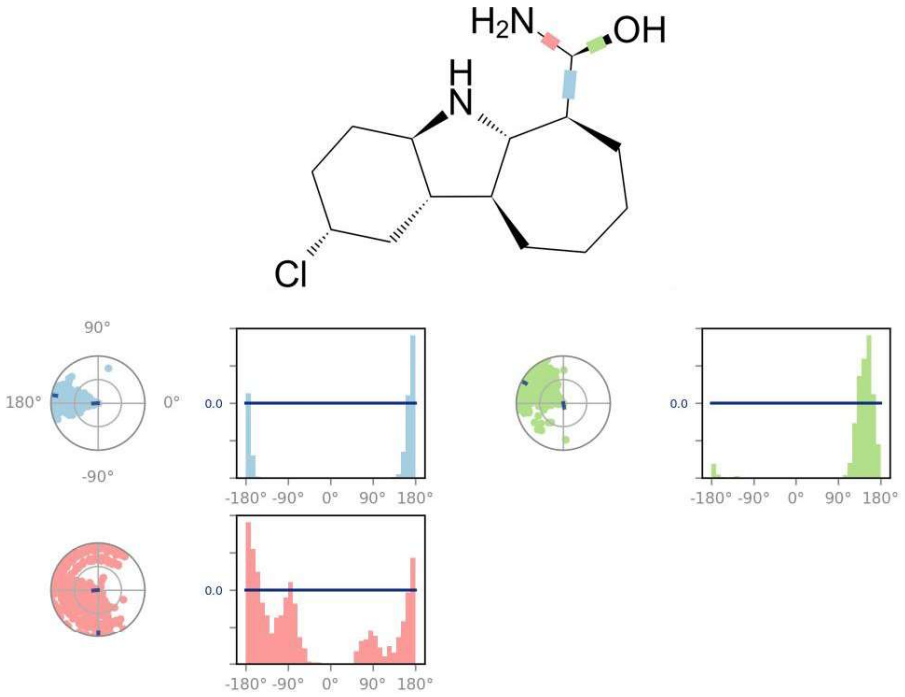

Figure S16: The ligand torsions plot of EX527 with SIRT1 summarizes the conformational evolution of every rotatable bond (RB) in the ligand throughout the simulation trajectory (0.00 through 100.00 nsec).

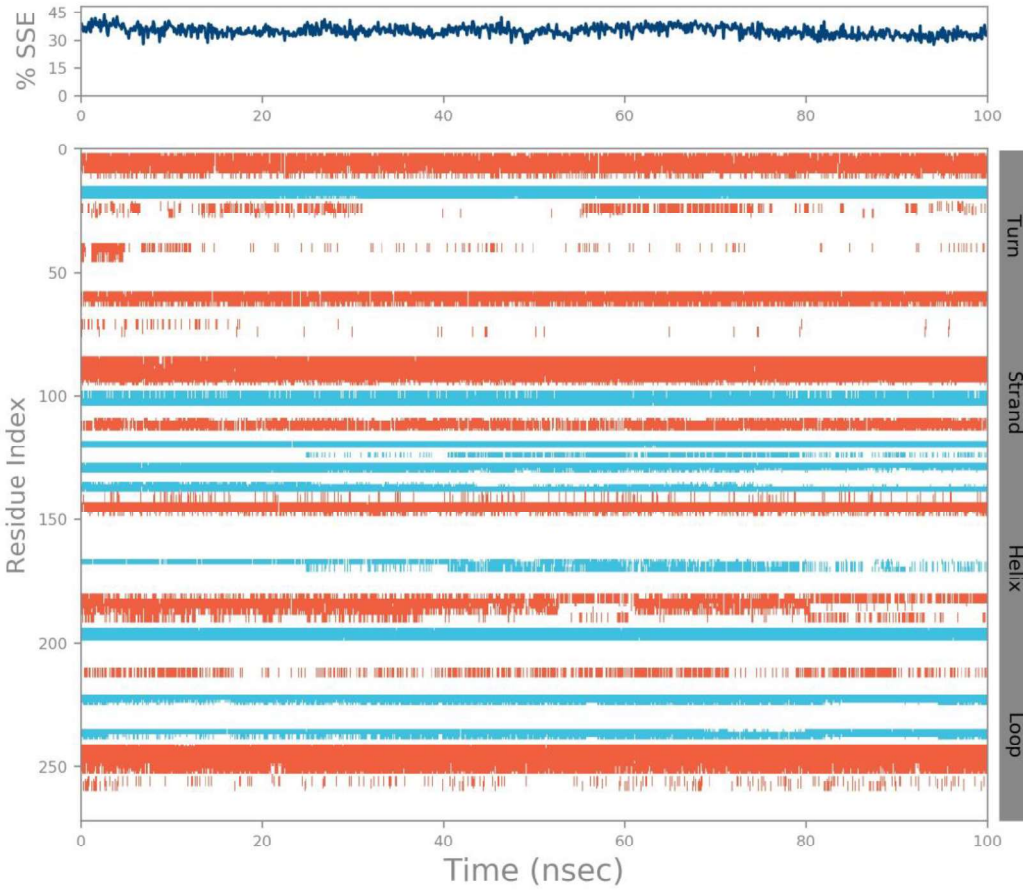

Figure S17: Protein secondary structure elements of EX527 with SIRT1 (SSE) like alpha-helices and beta-strands are monitored throughout the simulation.