Supporting Information

Mechanistic investigation of inclusion complexes of a sulfa-drug with α and β-cyclodextrins

Subhadeep Saha, Aditi Roy and Mahendra Nath Roy*

*Department of Chemistry, University of North Bengal, Darjeeling-734013, India

E-mail: *mahendraroy2002@yahoo.co.in*

Tables:

Table S1 Data for the Job plot performed by UV-Vis spectroscopy for aqueous SS-*α*-CD system at 298.15K[a]

SS (mL)	*α*-CD (mL)	SS (μM)	*α*-CD (μM)	[SS]/([SS]+[*α*-CD])	Absorbance (A)	ΔA	ΔA×[SS]/([SS]+[*α*-CD])
0.0	1.0	0	100	0.0	0.0000	1.6225	0.0000
0.1	0.9	10	90	0.1	0.1394	1.4831	0.1483
0.2	0.8	20	80	0.2	0.3062	1.3163	0.2633
0.3	0.7	30	70	0.3	0.4758	1.1467	0.3440
0.4	0.6	40	60	0.4	0.6443	0.9782	0.3913
0.5	0.5	50	50	0.5	0.7955	0.8270	0.4135
0.6	0.4	60	40	0.6	0.9728	0.6497	0.3898
0.7	0.3	70	30	0.7	1.1298	0.4927	0.3449
0.8	0.2	80	20	0.8	1.3181	0.3044	0.2435
0.9	0.1	90	10	0.9	1.4774	0.1451	0.1305
1.0	0.0	100	0	1.0	1.6225	0.0000	0.0000

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S2 Data for the Job plot performed by UV-Vis spectroscopy for aqueous SS-*β*-CD system at 298.15K[a]

SS (mL)	*β*-CD (mL)	SS (μM)	*β*-CD (μM)	[SS]/([SS]+[*β*-CD])	Absorbance (A)	ΔA	ΔA×[SS]/([SS]+[*β*-CD])
0.0	1.0	0	100	0.0	0.0000	1.6225	0.0000
0.1	0.9	10	90	0.1	0.1405	1.4820	0.1482
0.2	0.8	20	80	0.2	0.3107	1.3118	0.2624
0.3	0.7	30	70	0.3	0.4834	1.1391	0.3417
0.4	0.6	40	60	0.4	0.6509	0.9716	0.3886
0.5	0.5	50	50	0.5	0.8074	0.8151	0.4075
0.6	0.4	60	40	0.6	0.9808	0.6417	0.3850
0.7	0.3	70	30	0.7	1.1346	0.4879	0.3415
0.8	0.2	80	20	0.8	1.3189	0.3036	0.2429
0.9	0.1	90	10	0.9	1.4812	0.1413	0.1272
1.0	0.0	100	0	1.0	1.6225	0.0000	0.0000

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S3 Data for surface tension and conductivity study of aqueous SS-*α*-CD system at 298.15K[a]

Volm of *α*-CD (mL)	Total volm (mL)	Conc of SS (mM)	Conc of *α*-CD (mM)	Surface tension (mN m^{-1})	Conductuvity (mS m^{-1})
0	10	10.000	0.000	61.9	0.960
1	11	9.091	0.909	63.4	0.892
2	12	8.333	1.667	64.7	0.830
3	13	7.692	2.308	65.8	0.771
4	14	7.143	2.857	66.7	0.720
5	15	6.667	3.333	67.5	0.674
6	16	6.250	3.750	68.3	0.640
7	17	5.882	4.118	68.9	0.598
8	18	5.556	4.444	69.6	0.569
9	19	5.263	4.737	70.1	0.538
10	20	5.000	5.000	70.6	0.510
11	21	4.762	5.238	70.7	0.493
12	22	4.545	5.455	70.8	0.485
13	23	4.348	5.652	70.9	0.481

14	24	4.167	5.833	71.0	0.475
15	25	4.000	6.000	71.1	0.469
16	26	3.846	6.154	71.2	0.465
17	27	3.704	6.296	71.3	0.459
18	28	3.571	6.429	71.3	0.455
19	29	3.448	6.552	71.4	0.450
20	30	3.333	6.667	71.4	0.446

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S4 Data for surface tension and conductivity study of aqueous SS-*β*-CD system at 298.15K[a]

Volm of *β*-CD (mL)	Total volm (mL)	Conc of SS (mM)	Conc of *β*-CD (mM)	Surface tension (mN m^{-1})	Conductuvity (mS m^{-1})
0	10	10.000	0.000	61.9	0.960
1	11	9.091	0.909	63.4	0.874
2	12	8.333	1.667	64.7	0.811
3	13	7.692	2.308	65.8	0.760
4	14	7.143	2.857	66.7	0.709
5	15	6.667	3.333	67.6	0.670
6	16	6.250	3.750	68.4	0.629
7	17	5.882	4.118	69.1	0.601
8	18	5.556	4.444	69.7	0.564
9	19	5.263	4.737	70.3	0.531
10	20	5.000	5.000	70.8	0.505
11	21	4.762	5.238	71.0	0.492
12	22	4.545	5.455	71.1	0.485
13	23	4.348	5.652	71.2	0.479
14	24	4.167	5.833	71.3	0.474
15	25	4.000	6.000	71.3	0.469
16	26	3.846	6.154	71.4	0.465
17	27	3.704	6.296	71.4	0.461
18	28	3.571	6.429	71.5	0.455
19	29	3.448	6.552	71.5	0.451
20	30	3.333	6.667	71.5	0.445

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S5 Data for the Benesi-Hildebrand double reciprocal plot performed by UV-Vis spectroscopy for aqueous SS-*α*-CD system

Temp /K[a]	[SS] /μM	[α-CD] /μM	Ao	A	ΔA	1/[α-CD] /M^{-1}	1/ΔA	Intercept	Slope	K_a /M^{-1}
	50	30		0.8092	0.0073	33333	137.0			
	50	40		0.8115	0.0096	25000	104.2			
288.15	50	50	0.8019	0.8134	0.0115	20000	87.0	6.9170018	0.0039110	1768.60
	50	60		0.8157	0.0138	16667	72.5			
	50	70		0.8182	0.0163	14286	61.4			
	50	30		0.8084	0.0065	33333	153.8			
	50	40		0.8102	0.0083	25000	120.5			
293.15	50	50	0.8019	0.8121	0.0102	20000	98.0	6.9619200	0.0044582	1561.60
	50	60		0.8142	0.0123	16667	81.2			
	50	70		0.8165	0.0146	14286	68.5			
	50	30		0.8079	0.0060	33333	166.7			
	50	40		0.8094	0.0075	25000	133.3			
298.15	50	50	0.8019	0.8112	0.0093	20000	107.5	6.6989797	0.0048941	1368.79
	50	60		0.8134	0.0115	16667	87.3			
	50	70		0.8155	0.0136	14286	73.5			
	50	30		0.8073	0.0054	33333	185.2			
	50	40		0.8089	0.0070	25000	142.9			
303.15	50	50	0.8019	0.8104	0.0085	20000	117.6	6.4918606	0.0054087	1200.26
	50	60		0.8122	0.0103	16667	97.1			
	50	70		0.8143	0.0124	14286	80.8			
	50	30		0.8066	0.0047	33333	212.8			
	50	40		0.8081	0.0062	25000	161.3			
308.15	50	50	0.8019	0.8094	0.0075	20000	133.3	6.5801710	0.0062032	1060.77
	50	60		0.8110	0.0091	16667	109.9			
	50	70		0.8126	0.0107	14286	93.5			
	50	30		0.8059	0.0040	33333	250.0			
	50	40		0.8071	0.0052	25000	192.3			
313.15	50	50	0.8019	0.8083	0.0064	20000	156.2	6.9107879	0.0073459	940.77
	50	60		0.8096	0.0077	16667	129.9			
	50	70		0.8111	0.0092	14286	108.9			

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S6 Data for the Benesi-Hildebrand double reciprocal plot performed by UV-Vis spectroscopy for aqueous SS-*β*-CD system

Temp /K[a]	[SS] /μM	[β-CD] /μM	Ao	A	ΔA	1/[β-CD] /M^{-1}	1/ΔA	Intercept	Slope	K_a /M^{-1}
	50	30		0.8098	0.0079	33333	126.6			
	50	40		0.8122	0.0103	25000	97.1			
288.15	50	50	0.8019	0.8145	0.0126	20000	79.4	6.7600021	0.0036022	1876.63
	50	60		0.8170	0.0151	16667	66.2			
	50	70		0.8191	0.0172	14286	58.2			
	50	30		0.8093	0.0074	33333	135.1			
	50	40		0.8114	0.0095	25000	105.3			
293.15	50	50	0.8019	0.8136	0.0117	20000	85.5	6.4280917	0.0038959	1649.96
	50	60		0.8159	0.0140	16667	71.4			
	50	70		0.8184	0.0165	14286	60.6			
	50	30		0.8085	0.0066	33333	151.5			
	50	40		0.8106	0.0087	25000	114.9			
298.15	50	50	0.8019	0.8125	0.0106	20000	94.3	6.2717644	0.0043613	1438.05
	50	60		0.8145	0.0126	16667	79.6			
	50	70		0.8167	0.0148	14286	67.6			
	50	30		0.8079	0.0060	33333	166.7			
	50	40		0.8096	0.0077	25000	129.9			
303.15	50	50	0.8019	0.8113	0.0094	20000	106.4	6.1369214	0.0048727	1259.45
	50	60		0.8134	0.0115	16667	87.2			
	50	70		0.8156	0.0137	14286	73.1			
	50	30		0.8074	0.0055	33333	181.8			
	50	40		0.8090	0.0071	25000	140.8			
308.15	50	50	0.8019	0.8107	0.0088	20000	114.3	5.9663108	0.0053241	1120.62
	50	60		0.8124	0.0105	16667	95.2			
	50	70		0.8145	0.0126	14286	79.5			
	50	30		0.8068	0.0049	33333	205.3			
	50	40		0.8084	0.0065	25000	153.8			
313.15	50	50	0.8019	0.8099	0.0080	20000	125.0	5.8429417	0.0059699	978.73
	50	60		0.8112	0.0093	16667	107.5			
	50	70		0.8130	0.0111	14286	89.9			

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S7 Data of the van't Hoff equation for calculation of thermodynamic parameters ΔH^o and ΔS^o of different SS-cyclodextrin inclusion complexes

	Temp /K[a]	K_a /M^{-1}	1/T	lnK_a	Intercept	Slope	ΔH^o /kJ mol^{-1}	ΔS^o /J $mol^{-1}K^{-1}$
α-cyclodextrin	288.15	1769	0.00347	7.478	-0.4748	2293.40	-19.07	-3.95
	293.15	1562	0.00341	7.353				
	298.15	1369	0.00335	7.222				
	303.15	1200	0.00330	7.090				
	308.15	1061	0.00325	6.967				
	313.15	941	0.00319	6.847				
β-cyclodextrin	288.15	1877	0.00347	7.537	-0.5958	2345.06	-19.50	-4.95
	293.15	1650	0.00341	7.409				
	298.15	1438	0.00335	7.271				
	303.15	1259	0.00330	7.138				
	308.15	1121	0.00325	7.022				
	313.15	979	0.00319	6.886				

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S8 Data of the van't Hoff equation for calculation of thermodynamic parameters $\Delta H^{o\phi}$ and $\Delta S^{o\phi}$ of different SS-cyclodextrin inclusion complexes

	Temp /K[a]	K_a^{ϕ} /M^{-1}	1/T	lnK_a^{ϕ}	Intercept	Slope	$\Delta H^{o\phi}$ /kJ mol^{-1}	$\Delta S^{o\phi}$ /J $mol^{-1}K^{-1}$
α-cyclodextrin	288.15	1831	0.00347	7.513	-0.4622	2297.99	-19.11	-3.84
	293.15	1601	0.00341	7.378				
	298.15	1399	0.00335	7.244				
	303.15	1234	0.00330	7.118				
	308.15	1092	0.00325	6.996				
	313.15	969	0.00319	6.876				
β-cyclodextrin	288.15	1938	0.00347	7.569	-0.6642	2374.37	-19.74	-5.52
	293.15	1706	0.00341	7.442				
	298.15	1485	0.00335	7.303				
	303.15	1295	0.00330	7.166				
	308.15	1142	0.00325	7.041				
	313.15	1009	0.00319	6.917				

[a] Standard uncertainties in temperature *u* are: *u*(T) = ±0.01 K.

Table S9 ^{1}H NMR data of Sulfacetamide sodium salt, α-CD, β-CD and solid inclusion complexes

Sulfacetamide sodium salt (300 MHz, Solv: D_2O) δ /ppm	
1.77 (3H, s), 6.63-6.66 (2H, d, *J* = 8.7 Hz), 7.47-7.50 (2H, d, *J* = 8.7 Hz)	
α-Cyclodextrin (500 MHz, Solv: D_2O) δ /ppm	β-Cyclodextrin (400 MHz, Solv: D_2O) δ /ppm
3.48-3.51 (6H, t, *J* = 9.00 Hz), 3.53-3.56 (6H, dd, *J* = 10.00, 3.00 Hz), 3.74-3.83 (18H, m), 3.87-3.91 (6H, t, *J* = 9 Hz), 4.96-4.97 (6H, d, *J* = 3 Hz)	3.49-3.54 (7H, t, *J* = 9.2 Hz), 3.57-3.60 (7H, dd, *J* = 9.6, 3.2 Hz), 3.79-3.84 (21H, m), 3.87-3.92 (7H,t, *J* = 9.2 Hz), 5.00-5.01 (7H, d, *J* = 3.6 Hz)
SS-α-CD inclusion complex (300 MHz, Solv: D_2O) δ /ppm	SS-β-CD inclusion complex (300 MHz, Solv: D_2O) δ /ppm
1.77 (3H, s), 3.39-3.51 (12H, m), 3.61-3.67 (6H, m), 3.71-3.82 (18H, m), 4.90-4.92 (6H, d, *J* = 3.6 Hz), 6.60-6.62 (2H, d, *J* = 8.4 Hz), 7.43-7.46 (2H, d, *J* = 8.4 Hz)	1.77 (3H, s), 3.39-3.51 (14H, m), 3.61-3.66 (7H, m), 3.71-3.82 (21H, m), 4.91-4.92 (7H, d, *J* = 3.6 Hz), 6.59-6.62 (2H, d, *J* = 8.4 Hz), 7.42-7.45 (2H, d, *J* = 8.4)

Table S10 The observed peaks at different m/z with corresponding ions for the solid inclusion complexes

SS-α-CD inclusion complex		SS-β-CD inclusion complex	
m/z	Ion	m/z	Ion
237.03	$[SS+H]^+$	237.03	$[SS+H]^+$
259.01	$[SS+Na]^+$	259.01	$[SS+Na]^+$
973.32	$[α\text{-}CD+H]^+$	1135.38	$[β\text{-}CD+H]^+$
995.31	$[α\text{-}CD+Na]^+$	1157.36	$[β\text{-}CD+Na]^+$
1209.35	$[SS+α\text{-}CD+H]^+$	1371.40	$[SS+β\text{-}CD+H]^+$
1231.33	$[SS+α\text{-}CD+Na]^+$	1393.38	$[SS+β\text{-}CD+Na]^+$

Table S11 Frequencies at FTIR spectra of Sulfacetamide sodium salt, α-CD, β-CD and solid inclusion complexes

Sulfacetamide sodium salt			
wave number / cm^{-1}	group	wave number / cm^{-1}	group
3433.76	N-H stretching	1322.43	S=O asymmetric stretching
1874.65	out of plane C-H bending combination/overtone	1132.63	S=O symmetric stretching
1626.42	>C=O stretching	1086.51	C-N stretching
1598.20	N-H bending	836.89	out of plane C-H bending
1375.35	(aromatic)-C-N stretching	690.32	out of plane C-H bending
α-Cyclodextrin		β-Cyclodextrin	
wave number / cm^{-1}	group	wave number / cm^{-1}	group
3412.10	O-H stretching	3349.84	O-H stretching
2930.79	–C-H stretching	2921.52	–C-H stretching
1406.76	–C-H bending and O-H bending	1412.36	–C-H bending and O-H bending
1154.39	C-O-C bending	1157.57	C-O-C bending
1030.39	C-C-O stretching	1033.51	C-C-O stretching
952.36	skeletal vibration involving α-1,4linkage	938.53	skeletal vibration involving α-1,4linkage

SS-α-CD inclusion complex		SS-β-CD inclusion complex	
wave number / cm^{-1}	group	wave number / cm^{-1}	group
3406.25	O-H stretching	3417.91	O-H stretching
2933.57	–C-H stretching	2932.95	–C-H stretching
1633.94	>C=O stretching	1634.83	>C=O stretching
1594.92	N-H bending	1593.38	N-H bending
1417.51	–C-H bending and O-H bending	1416.52	–C-H bending and O-H bending
1330.58	S=O asymmetric stretching	1329.43	S=O asymmetric stretching
1152.07	S=O symmetric stretching	1154.61	S=O symmetric stretching
1080.79	C-N stretching	1080.79	C-N stretching
1031.75	C-C-O stretching	1031.10	C-C-O stretching
951.71	skeletal vibration involving α-1,4linkage	948.07	skeletal vibration involving α-1,4linkage
846.98	out of plane C-H bending	844.09	out of plane C-H bending
685.55	out of plane C-H bending	684.45	out of plane C-H bending

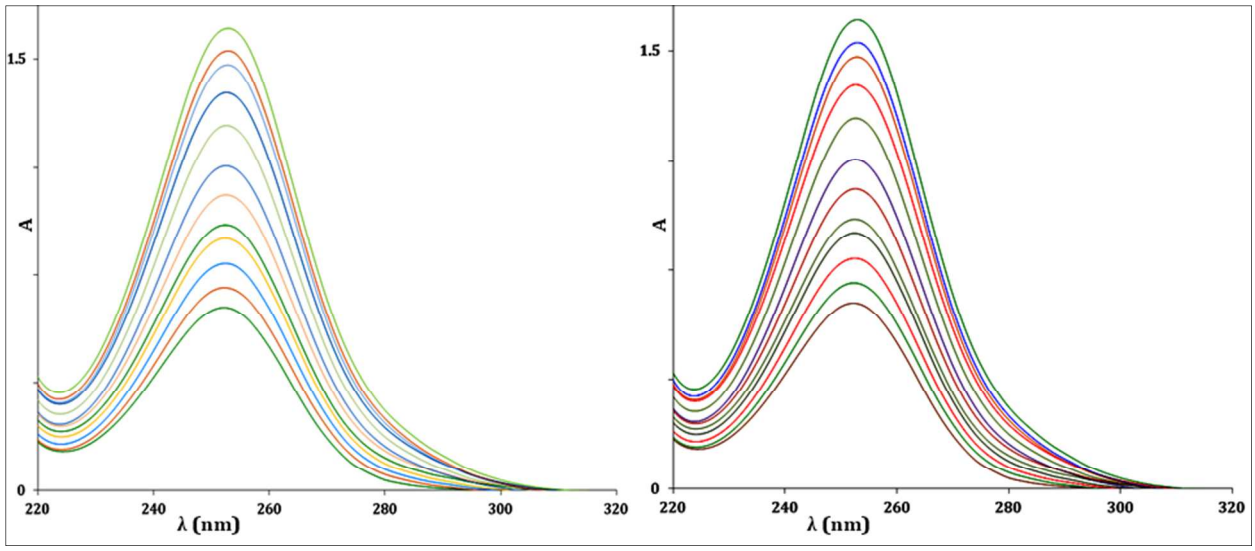
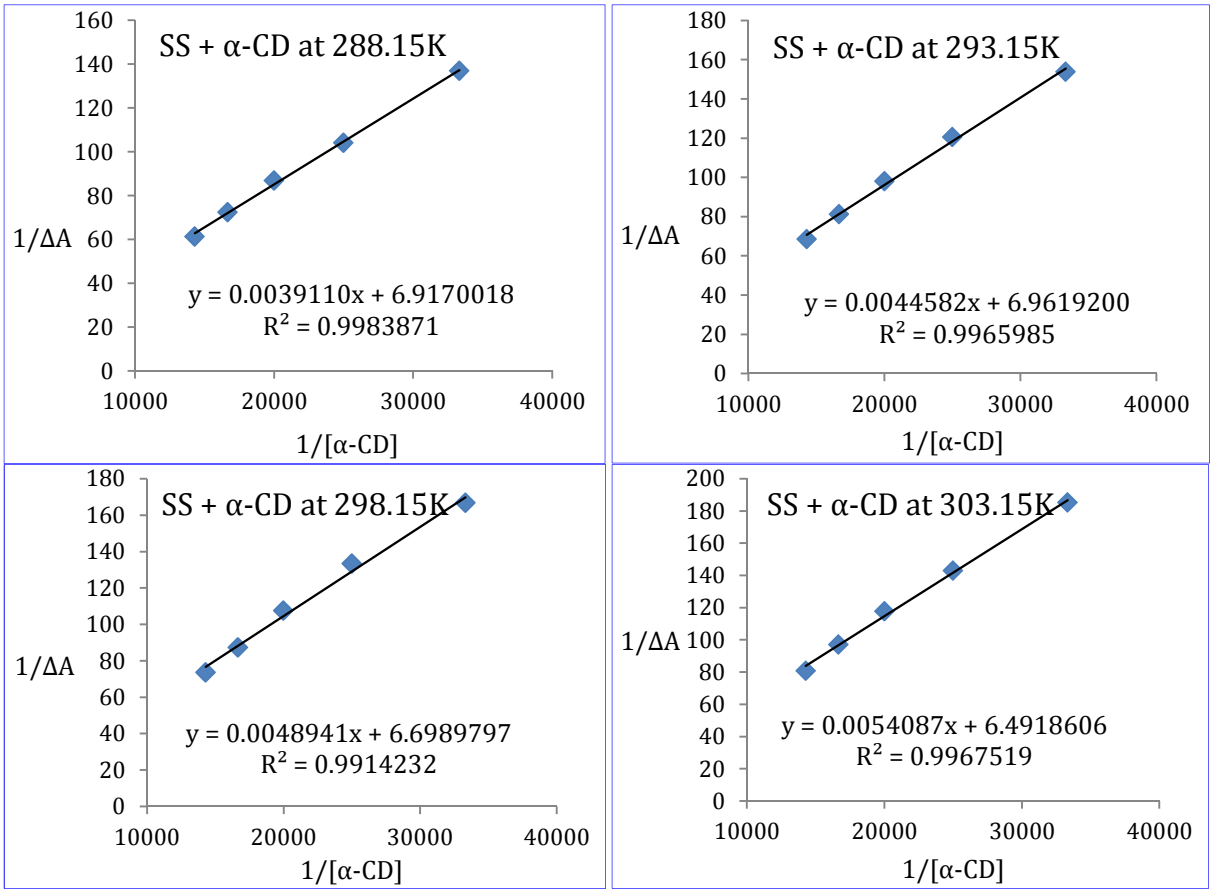
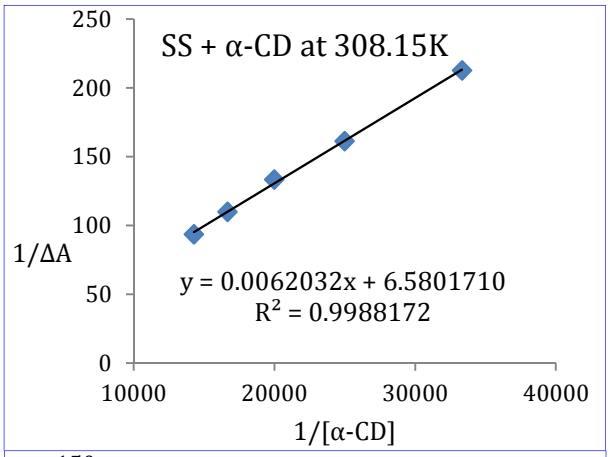
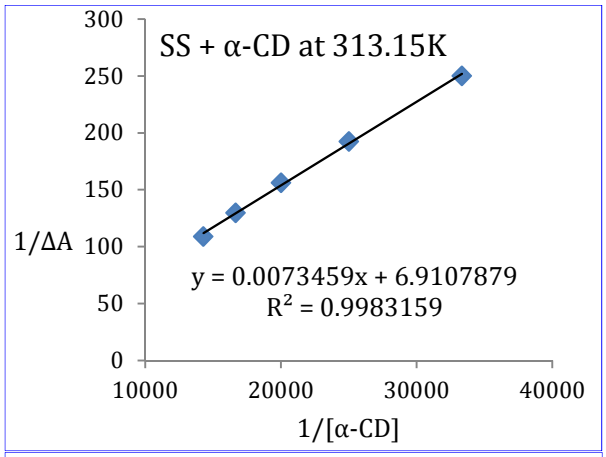
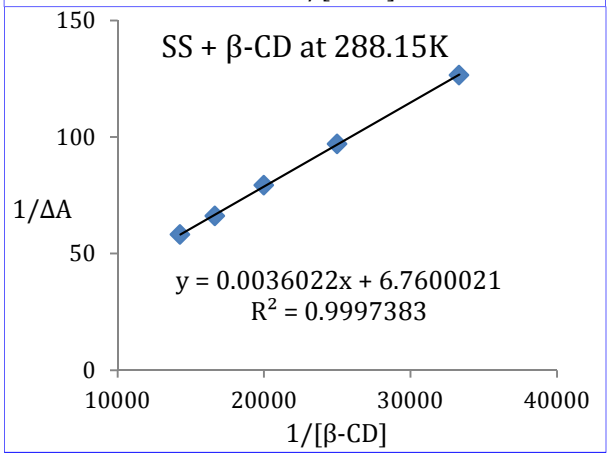


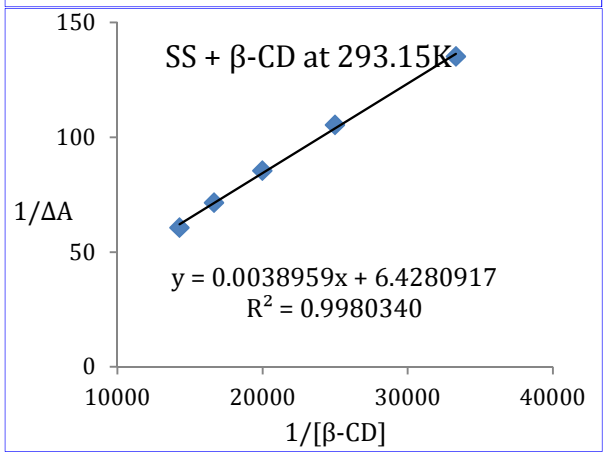
Figure S1 UV-visible spectra of SS with α and β-CD respectively for generation of Job plots.




SS + α-CD at 308.15K
y = 0.0062032x + 6.5801710
R² = 0.9988172
1/ΔA
1/[α-CD]
250
200
150
100
50
0
10000
20000
30000
40000


SS + α-CD at 313.15K
y = 0.0073459x + 6.9107879
R² = 0.9983159
1/ΔA
1/[α-CD]
300
250
200
150
100
50
0
10000
20000
30000
40000


SS + β-CD at 288.15K
y = 0.0036022x + 6.7600021
R² = 0.9997383
1/ΔA
1/[β-CD]
150
100
50
0
10000
20000
30000
40000


SS + β-CD at 293.15K
y = 0.0038959x + 6.4280917
R² = 0.9980340
1/ΔA
1/[β-CD]
150
100
50
0
10000
20000
30000
40000

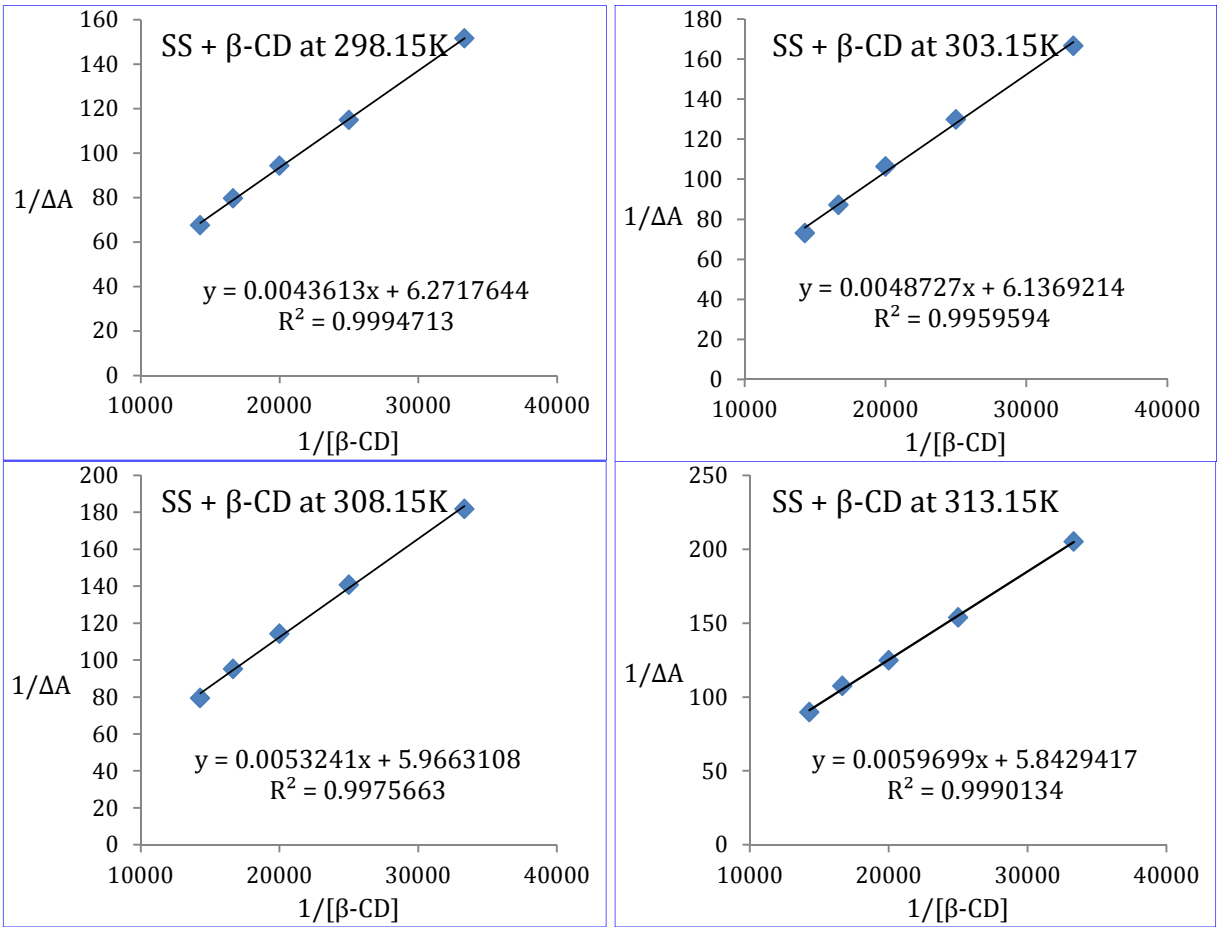


Figure S2 Benesi-Hildebrand double reciprocal plots for the effect of α and β-CD on the absorbance of SS (256 nm) at different temperatures.

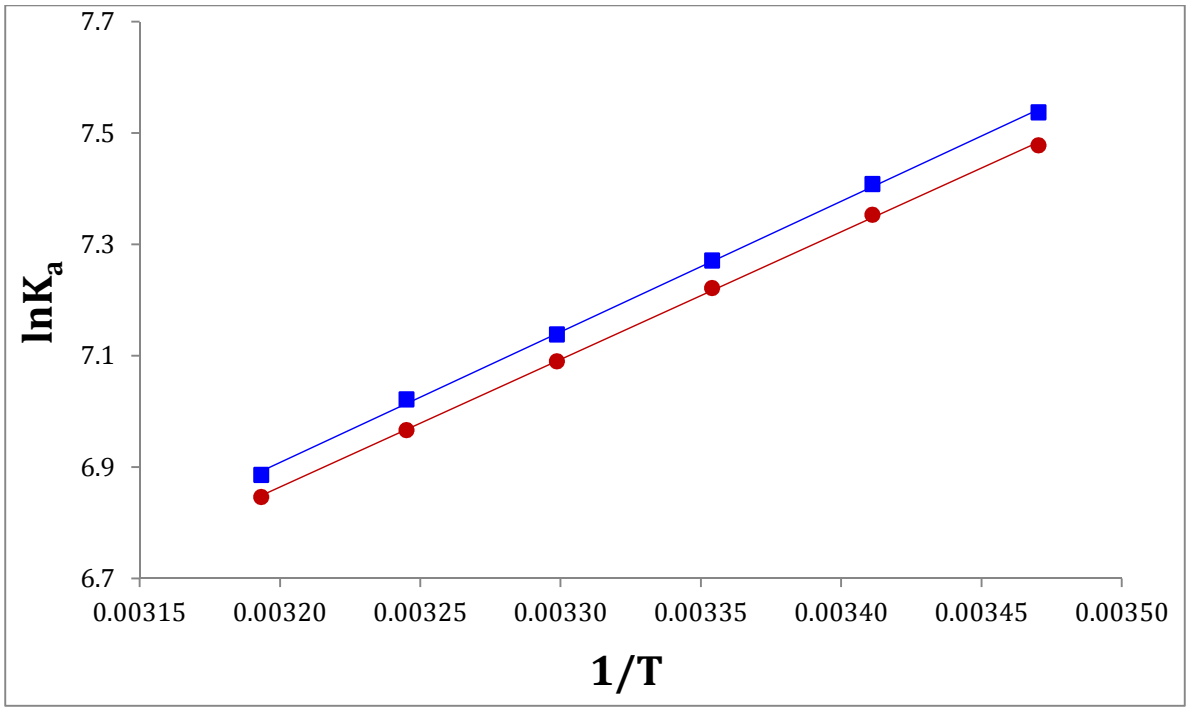


Figure S3 Plot of $\ln K_a$ vs 1/T for the interaction of SS with α-CD (●) and β-CD (■).

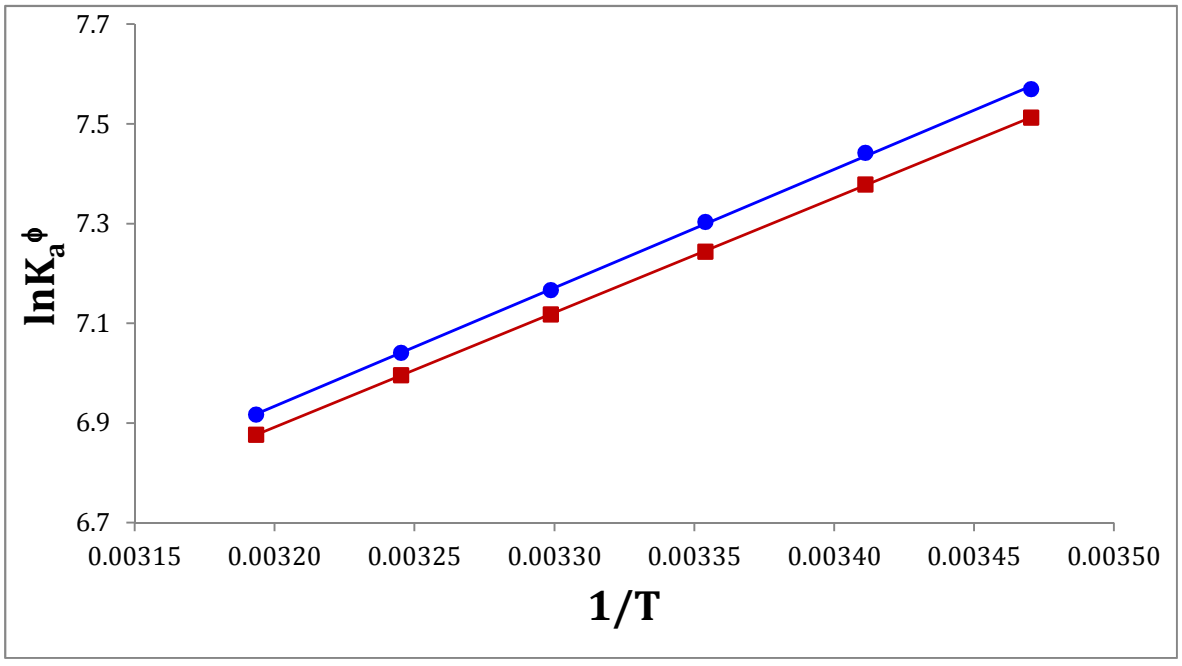


Figure S4 Plot of $\ln K_a^{\phi}$ vs 1/T for the interaction of SS with α-CD (■) and β-CD (●).

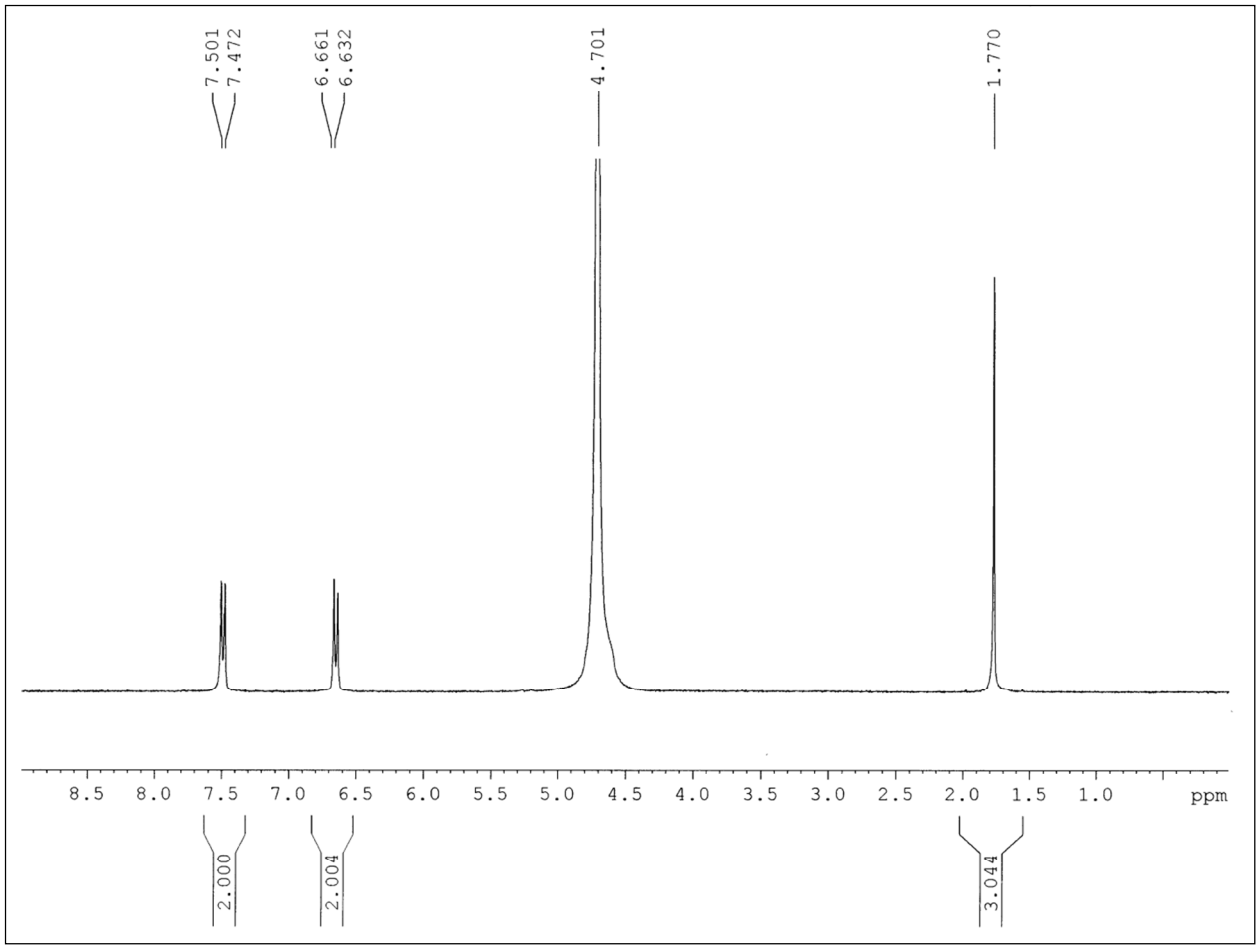


Figure S5 ^{1}H NMR spectra of sulfacetamide sodium salt in D_2O at 298.15K.

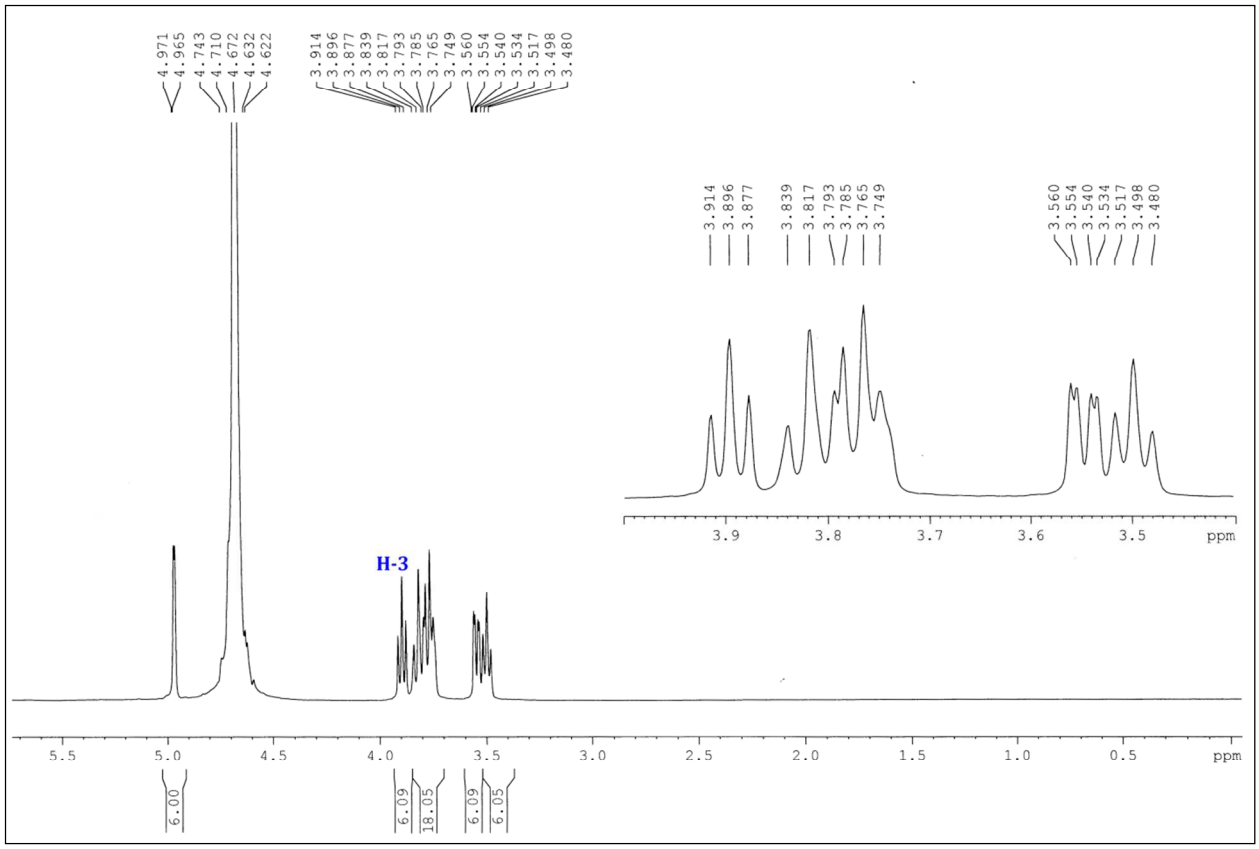


Figure S6 ^{1}H NMR spectra of α-cyclodextrin in D_2O at 298.15K.

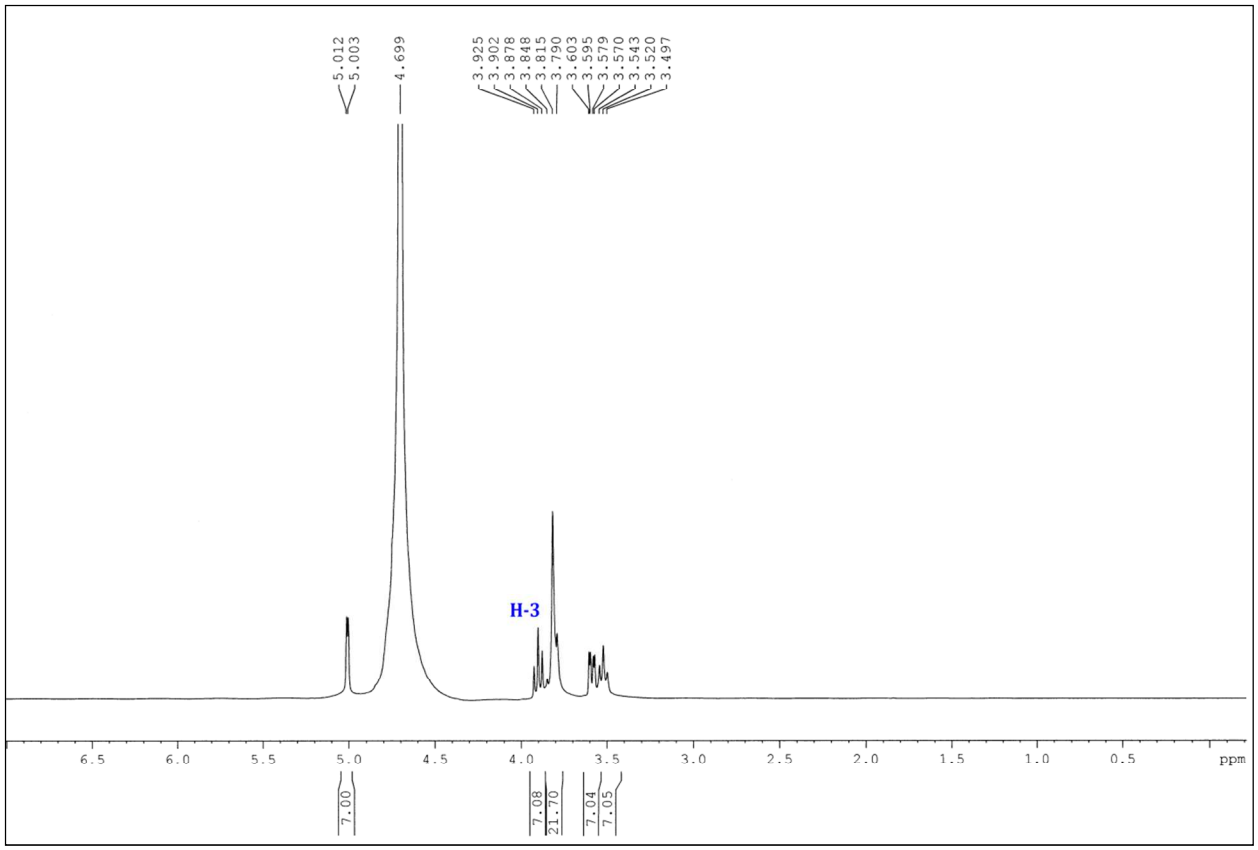


Figure S7 ^{1}H NMR spectra of β-cyclodextrin in D_2O at 298.15K.

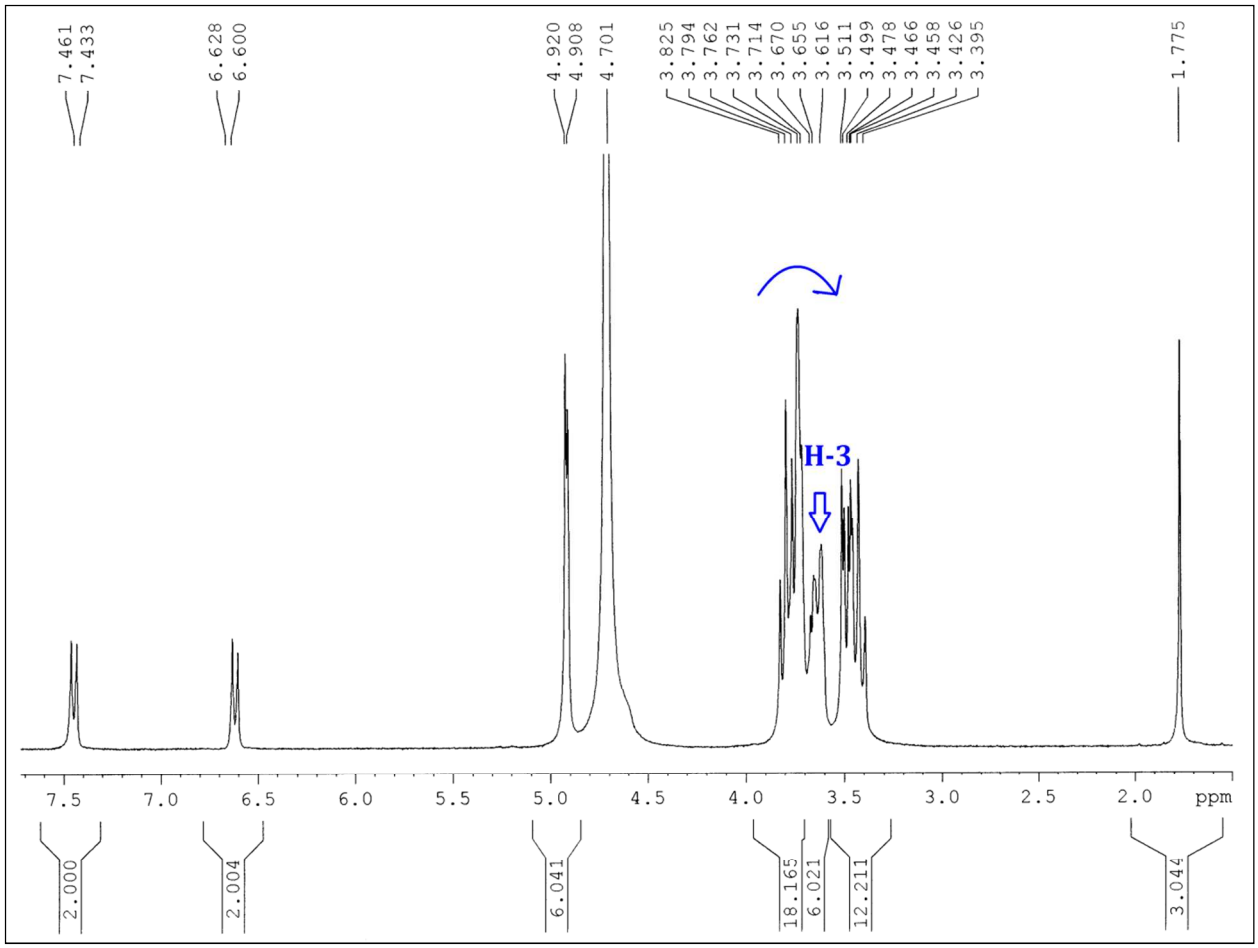


Figure S8 ^{1}H NMR spectra of solid inclusion complex of SS and α-CD in D_2O at 298.15K.

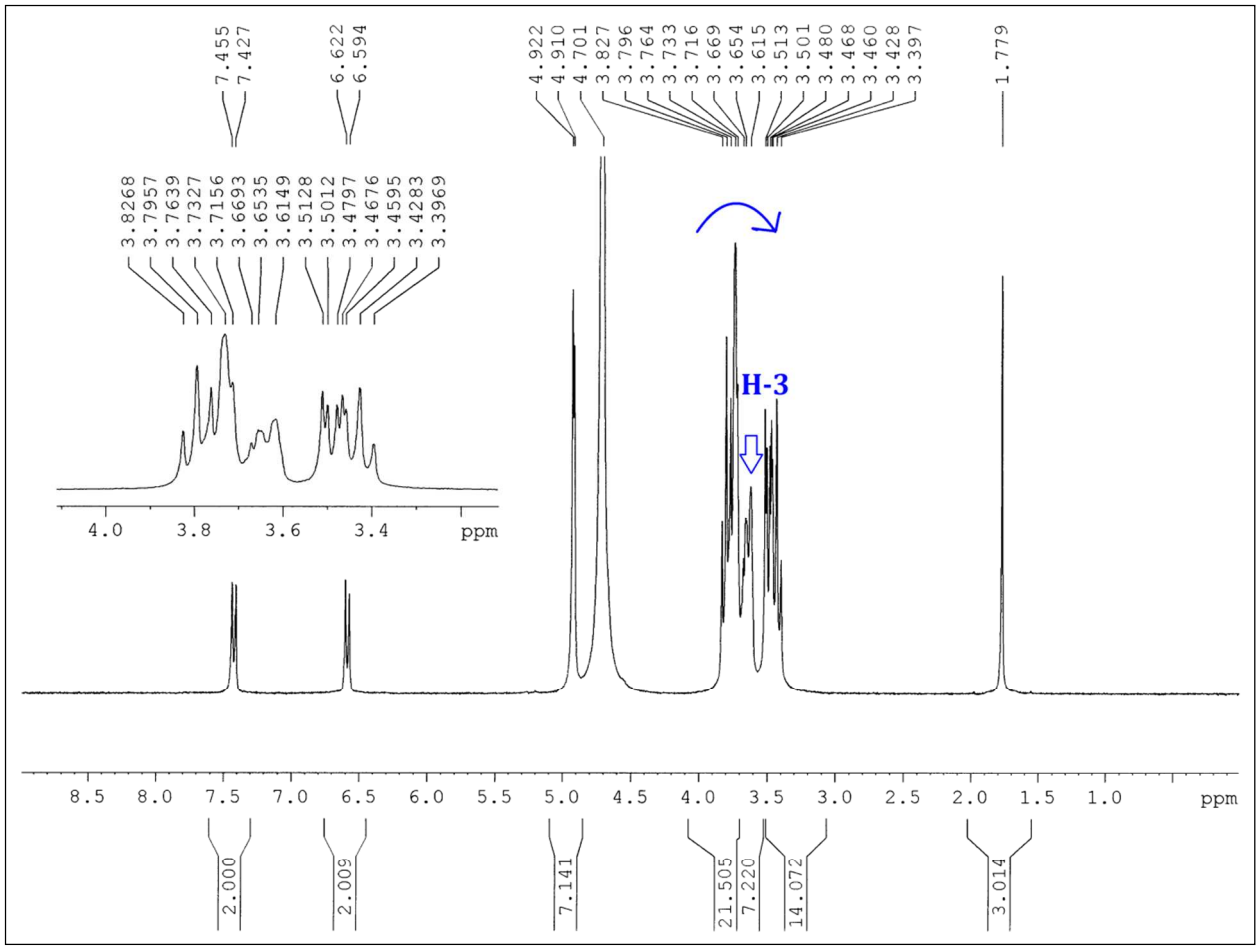
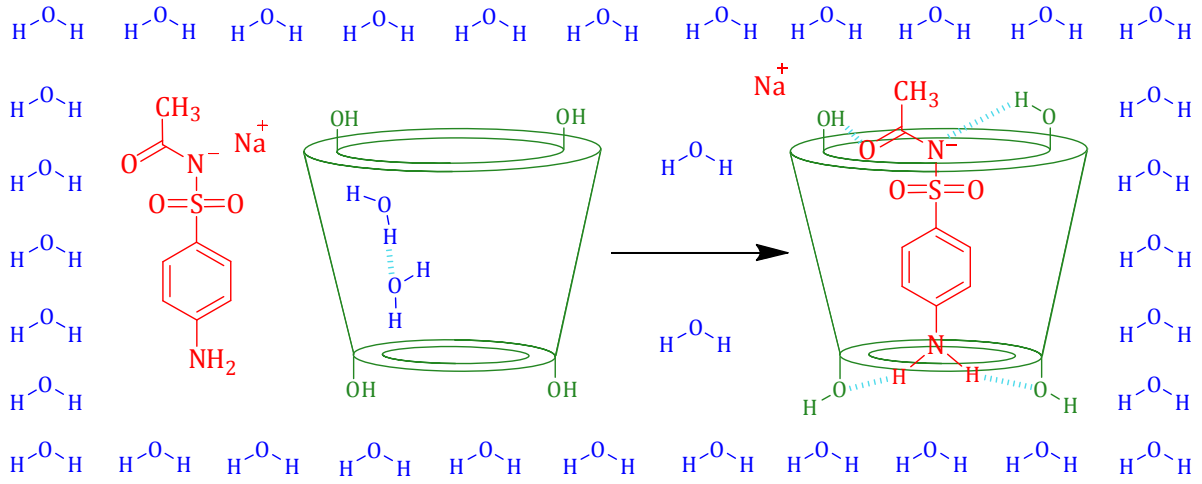


Figure S9 ^{1}H NMR spectra of solid inclusion complex of SS and β-CD in D_2O at 298.15K.



Scheme S1 Plausible schematic presentation of mechanism for formation of 1:1 inclusion complex between sulfacetamide sodium salt and cyclodextrin.