Supporting Information

Chemico-Pharmaceutical Investigations of an Inclusion Complex formed with Valacyclovir and γ-Cyclodextrin Optimized by Molecular Docking for Innovative Applications as Topical Gel

Baishali Saha[a], Nibir Das[b], Paramita Paul[b], Sanjoy Barman[a], Modhusudan Mondal[a], Subhadeep Saha[c], Subhankar Choudhury[d], Niloy Roy[a], Salim Ali[a] and Mahendra Nath Roy*[a]

[a]Department of Chemistry, University of North Bengal, Darjeeling – 734013, India

[b]Department of Pharmaceutical Technology, University of North Bengal, Darjeeling, India

[c]Department of Chemistry, Government General Degree College at Pedong, Kalimpong-734311, India

[d]Department of Chemistry, Malda College, Malda, 732101, India

Corresponding Author's E-mail: mahendraroy2002@yahoo.co.in

Table S1: Composition of gel:

Composition	VC loaded gel	ICVC loaded gel
Carbopol 940 (g)	1	1
Propylene glycol (g)	10	10
Triethanolamine (g)	0.5	0.5
Isopropyl alcohol (g)	10	10
Double distilled water (mL)	100	100
Drug (mg)	VC (10 mg/g of gel)	ICVC (10 mg equivalent/g of gel)

Table S2. Data for the Job's plot performed by UV-Vis spectroscopy for VC+γ-CD system at 298.15 K[a].

VC + GAMMA - CYCLODEXTRIN							
VC(mL)	**γ-CD (mL)**	**VC (μM)**	**γ-CD (μM)**	**[VC]/ ([VC]+[γ-CD])**	**Absorbance (A)**	**ΔA**	**ΔA×[VC] /([VC]+[γ-CD])**
0	3	0	10	0	0.0000	1.3255	0.0000
0.3	2.7	1	9	0.1	0.16889238	1.1566	0.1157
0.6	2.4	2	8	0.2	0.36161852	0.9639	0.1928
0.9	2.1	3	7	0.3	0.45758152	0.8679	0.2604
1.2	1.8	4	6	0.4	0.59646225	0.7290	0.2916
1.5	1.5	5	5	0.5	0.70556307	0.6199	0.3100
1.8	1.2	6	4	0.6	0.83200979	0.4935	0.2961
2.1	0.9	70	30	0.7	0.96572685	0.3598	0.2518
2.4	0.6	80	20	0.8	1.11982346	0.2057	0.1645
2.7	0.3	90	10	0.9	1.16047287	0.1650	0.1485
3	0	100	0	1	1.32548428	0.0000	0.0000

[a]Standard uncertainties in temperature (T) = ±0.01 K.

Table S3: Chemical shifts data (in ppm) of various protons in the free state of VC and γ-CD and ICVC.

Guest	Position of Protons	Chemical shift of pure molecules[a] (ppm) (δ_1)	Chemical shift in inclusion complex[a] (ppm) (δ_2)	Change in chemical shift ($\delta_2 - \delta_1$)
Valacyclovir	A (C-H)	7.852	7.857	0.005
	B (CH_2)	5.391	5.414	0.023
	C (CH_2)	4.289	4.279	-0.010
	D (CH_2), E (C-H)	3.793	3.791	-0.002
	F (C-H)	1.988	1.968	-0.020
	G, G'(CH_3)	0.764	0.744	-0.020
γ-CD	H-1'	5.016	5.006	0.01
	H-3'	3.842	3.763	–0.079
	H-5'	3.777	3.740	–0.037
	H-2'	3.571	3.639	0.068
	H-4'	3.497	3.538	0.041

[a] Mean error in $\delta = \pm 0.001$

Table S4. Data for the conductivity study of VC+γ-CD system (concentration of stock solution of VC = 10 mM, concentration of stock solution of γ-CD = 10 mM) at 298.15 K[a].

Volume of γ-CD (mL)	Total volume (mL)	Conc of VC (mM)	Conc of γ-CD (mM)	Conductivity ($mS.cm^{-1}$)
0	10	10.000	0.000	0.452
1	11	9.091	0.909	0.424
2	12	8.333	1.667	0.396

3	13	7.692	2.308	0.368
4	14	7.143	2.857	0.344
5	15	6.667	3.333	0.323
6	16	6.250	3.750	0.304
7	17	5.882	4.118	0.287
8	18	5.556	4.444	0.272
9	19	5.263	4.737	0.255
10	20	5.000	5.000	0.247
11	21	4.762	5.238	0.24
12	22	4.545	5.455	0.23
13	23	4.348	5.652	0.23
14	24	4.167	5.833	0.23
15	25	4.000	6.000	0.227
16	26	3.846	6.154	0.227
17	27	3.704	6.296	0.227
18	28	3.571	6.429	0.224
19	29	3.448	6.552	0.224
20	30	3.333	6.667	0.224

[a]Standard uncertainty in temperature (T) = ±0.01 K.

Table S5. Data for the surface tension study of VC+γ-CD system (concentration of stock solution of VC = 10 mM, concentration of stock solution of γ-CD = 10 mM) at 298.15 K[a].

Volume of γ-CD (mL)	Total volume (mL)	Conc of VC (mM)	Conc of γ-CD (mM)	Surface tension ($mN.m^{-1}$)
0	10	10.000	0.000	65.9
1	11	9.091	0.909	67.2

2	12	8.333	1.667	68.6
3	13	7.692	2.308	69.6
4	14	7.143	2.857	70.4
5	15	6.667	3.333	71.2
6	16	6.250	3.750	71.9
7	17	5.882	4.118	72.4
8	18	5.556	4.444	72.9
9	19	5.263	4.737	73.3
10	20	5.000	5.000	73.6
11	21	4.762	5.238	73.8
12	22	4.545	5.455	74
13	23	4.348	5.652	74
14	24	4.167	5.833	74
15	25	4.000	6.000	74.1
16	26	3.846	6.154	74.1
17	27	3.704	6.296	74.2
18	28	3.571	6.429	74.2
19	29	3.448	6.552	74.2
20	30	3.333	6.667	74.3

[a]Standard uncertainties in temperature (T) = ±0.01 K.

Table S6. Data for the Benesi-Hildebrand double reciprocal plot performed by UV-Vis spectroscopy for VC+γ-CD system.

Temp /K[a]	**[VC] /μM**	**[γ-CD] /μM**	**Ao**	**A**	**ΔA**	**1/[γ-CD] /M^{-1}**	**1/ΔA**	**Intercept**	**Slope**	**K_a/M^{-1}**
298.15	10	10	1.351573	1.313484	0.038088	100000	26.25482	0.79308	0.00025178	3149.8928
	10	20		1.275345	0.076228	50000	13.11854			

	10	30		1.240223	0.111349	33333.33333	8.980764			
	10	40		1.180912	0.170661	25000	5.85957			
	10	50		1.175395	0.176178	20000	5.676094			
	10	60		1.167161	0.184412	16666.66667	5.422655			
	10	70		1.164854	0.186719	14285.71429	5.355643			
	10	80		1.130465	0.221108	12500	4.522678			
	10	90		1.119823	0.231749	11111.11111	4.315012			
	10	100		0.975751	0.375821	10000	2.66084			
	10	110		0.965727	0.385846	9090.909091	2.59171			

[a]Standard uncertainties in temperature (T) = ±0.01 K.

Table S7: Physicochemical characterization parameters of experimental VC and ICVC containing gel (n=3).

Parameter	VC-loaded gel	ICVC-loaded gel
Color	Translucent	Translucent
Odour	No bad odour	No bad odour
pH	5.8 ±0.3	9.1± 0.7
Viscosity (cP)	3548 ±232	3080 ± 354
Zeta potential (mV)	-3.8 ± 1.0	-5.7 ±0.9
Drug content assay (%)	99.02 ± 0.6	96.37 ± 0.8

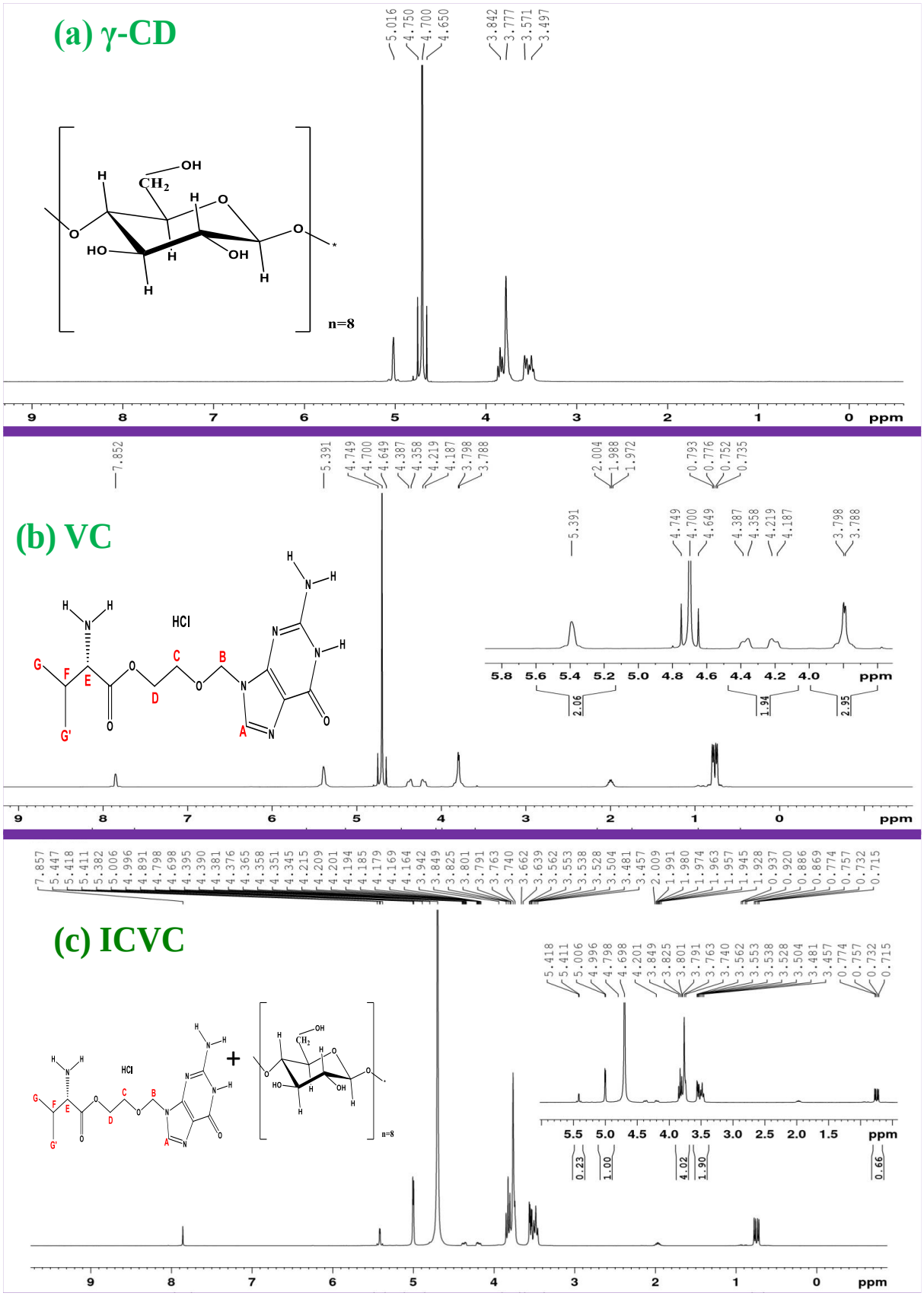

Figure S1: ^{1}H-NMR spectra of (a) γ-CD (b) VC and (c) ICVC in D_2O solvent.

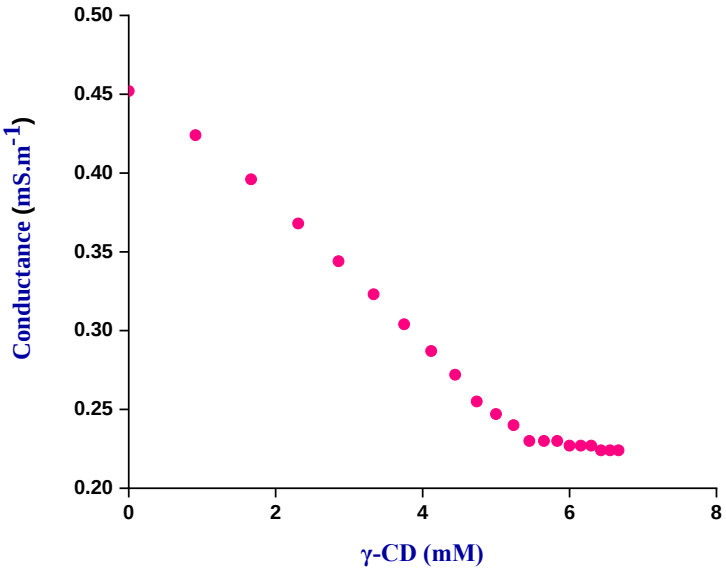

Figure: S2. Variation in the aqueous VC conductance with increasing concentration of γ-CD.

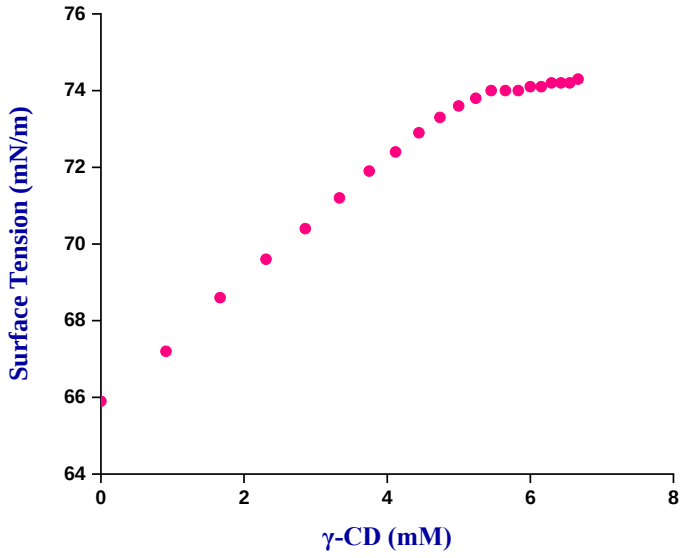

Figure: S3. Variation in the surface tension of aqueous VC with increasing concentration of γ-CD at 298.15 K.

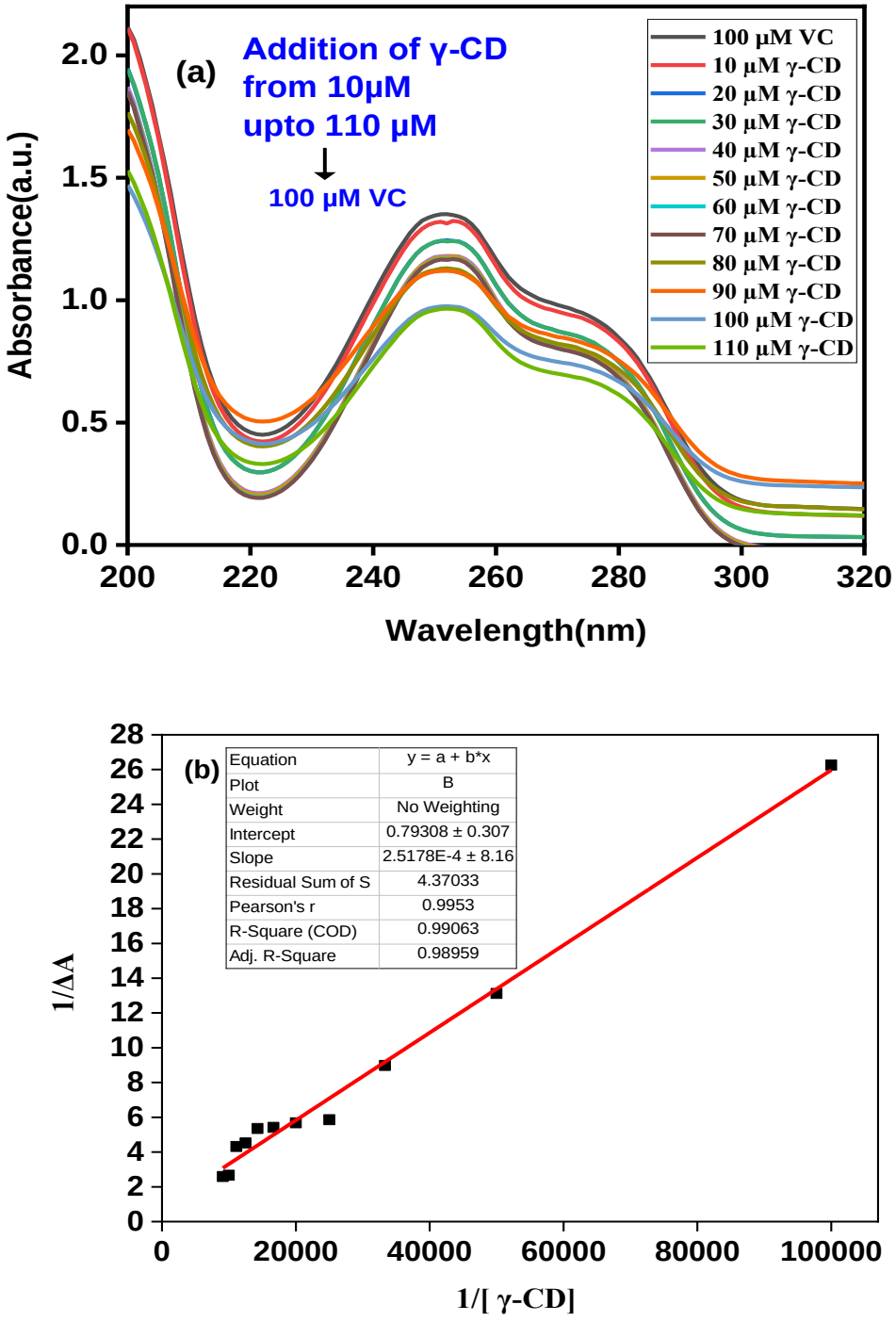

Figure: S4. (a) Absorption spectra of 100 μM VC in different concentrations (10 μM to 110 μM) of aqueous γ-CD (b) Benesi-Hildebrand double reciprocal plot for the effect of γ-CD on the absorbance of VC (λ_{max} = 252 nm) at 298.15 K (X-axis = 1/[γ-CD] and Y-axis = 1/ΔA).