

Host-guest Inclusion Complexation of 3-(2-Naphthyl)-D-Alanine with α - and β -Cyclodextrins Explored by Nuclear Magnetic Resonance, Fourier-transform Infrared, High-resolution Mass Spectrometry, Surface Tension, and Conductometric Studies

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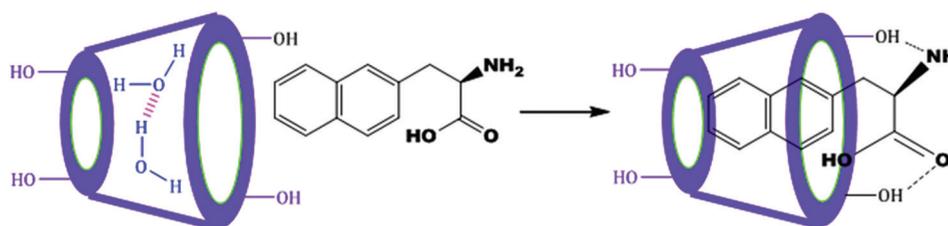
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ABSTRACT

Host-guest inclusion complex formation of α -cyclodextrin (α -CYD) and β -CYD with 3-(2-Naphthyl)-D-alanine has been investigated. Physicochemical and spectroscopic experimental data offer sufficient evidence about stabilization, carry, and regulatory release of the guest molecule. Surface tension and conductivity studies indicate 1:1 stoichiometry of the inclusion complexes. ^1H nuclear magnetic resonance and Fourier-transform infrared studies confirm the inclusion phenomena. The host-guest interactions have been explained on the basis of hydrogen bonding, Van der Waals force, hydrophobic effect, electrostatic force, and exceptional structural effect of host-guest molecules.

Key words: Inclusion complex, Cyclodextrin, 3-(2-Naphthyl)-D-Alanine, Spectroscopic investigation, Physicochemical studies.

GRAPHICAL ABSTRACT



In this article, one of the very important drugs, namely, 3-(2-Naphthyl)-D-alanine has been probed in solution and solid phase to encapsulate it within the cavity of α - and β -cyclodextrins. This inclusion phenomenon of the drug is exceedingly significant for its stabilization from external hazards, such as oxidation, sensitization, and photolytic cleavage, for regulatory release of an essential amount of drug at the targeted site for a period of time proficiently and accurately and for preventing overdose.

1. INTRODUCTION

In supramolecular chemistry the association of guest molecules into cyclodextrin (CYD), which has fairly rigid structure, hydrophobic inner cavities with unique hydrophilic outer surfaces. They can act as molecular receptors (hosts) for a wide variety of organic and inorganic, as well as biological and pharmaceutical guest molecules, forming noncovalent bonds under equilibrium condition with host molecules. Its potential applications are widespread such as drug delivery, solubility, bioavailability, safety, and stability. The guest is an amino acid derivative that has been used to synthesize cholecystokinin analog [1,2] and as a carrier may be achieved nutritional analysis and disease diagnosis. It is used in artificial receptors for an amino acid [3,4] (Scheme 1).

CYDs are cyclic oligosaccharide having six and seven glucopyranose units (unite bond together by α -(1-4) linkage) for α -CYD and β -CYD, respectively, creating a truncated conical structure which is favorable for inclusion. The electrochemical and spectroscopic studies show the interaction between 3-(2-Naphthyl)-D-alanine (D-NA) and CYD. In the

present article formation of inclusion, complexes have been explored by surface tension, conductivity, infrared (IR), and ^1H nuclear magnetic resonance (^1H NMR) study [5].

2. EXPERIMENTAL

2.1. Materials

D-NA, CYD α and β of high purity were purchased from Sigma-Aldrich. The purities of D-NA, α -CYD, and β -CYD were $\geq 99.1\%$.

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ISSN NO: 2320-0898 (p); 2320-0928 (e)

DOI: 10.22607/IJACS.2019.702001

Received: 05th November 2018;

Revised: 19th December 2018;

Accepted: 11th April 2019

2.2. Apparatus and Procedure

Experimentally, measure surface tensions of the solution were by tensiometer (K9, KRUSS; Germany) in platinum ring detachment technique using at 298.15 K. Accuracy of the study was $\pm 0.1 \text{ m. N m}^{-1}$. A circulating auto thermostated water through a double-walled glass vessel holding the solution 298.15 K.

The specific conductivities of the studied solutions were measured with a Mettler Toledo Seven Multi conductivity meter with an uncertainty of $\pm 1.0 \text{ mSm}^{-1}$. The experiments were carried out in an auto thermostated water bath held at 298.15 K using HPLC-grade water with a specific conductance of $6.0 \mu\text{Sm}^{-1}$. Calibration of the cell was achieved using a 0.01M aqueous KCl solution.

NMR spectra were recorded in D_2O unless otherwise stated. ^1H NMR spectra were recorded using Bruker AVANCE 350. Signals are quoted as δ values in ppm using residual protonated solvent signals as internal standard (D_2O : δ 4.79 ppm). Data are reported as a chemical shift.

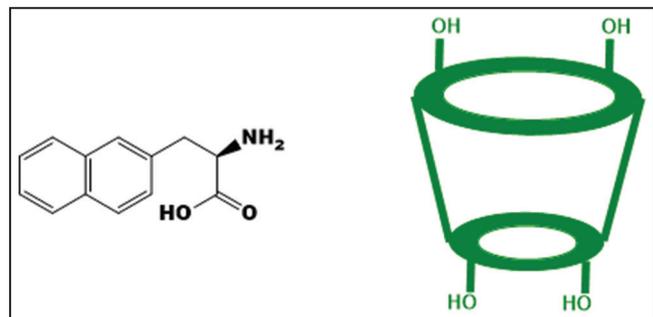
Fourier-transform IR (FT-IR) spectra were recorded in KBr disc method by Perkin-Elmer FT-IR Spectrometer. KBr discs were made in 1:100 ratio of sample and KBr. FT-IR studies were carried out in the scanning range of $4000\text{--}400 \text{ cm}^{-1}$ at room temperature.

HRMS analyses were performed by quadrupole time-of-flight high-resolution instrument with positive mode electrospray ionization taking the methanol solution of the solid integrated circuits (ICs).

3. RESULTS AND DISCUSSION

3.1. Surface Tension Study

The nature and formation of inclusion complex precious information are given by surface tension [13]. The aqueous solution of α - and β -CYD



Scheme 1: Molecular structures of 3-(2-Naphthyl)-D-alanine and cyclodextrin molecule.

does not show any considerable change of surface tension. The D-NA shows that COO^- , NH_2 group, and their side group being nonpolar show surfactant like behavior and it has a tendency to decrease the surface tension of aqueous solutions like other surfactants (Pineiro 2007).

Here surface tension (γ) is measured for a series of the solution with increasing concentration of both host α - and β -CYD at 298.15 K. The γ values show an increasing trend in case of both the guests (Table 1). Perhaps it is due to the formation of inclusion complex between D-NA and CYD because due to the removal of the surface-active D-NA molecules from the surface of the solution into the hydrophobic cavity α and β -CYD. In the two surface tension plots, the appearance of single breakpoint indicates the formation of inclusion complex in both cases (Figure 1). The values of surface tension with the corresponding concentration of α - and β -CYD and concentration of D-NA at each break are listed in Table 2. Overall, variation of γ and one beak point clearly shows that at a certain concentration of D-NA and CYD where their concentration ratio in solution was almost 1:1; thus, the study proves 1:1 ratio in both α - and β -CYD.

3.2. Conductance Study

Conductivity (κ) of an aqueous solution of D-NA has been measured with both α - and β -CYD solution to find out whether inclusion has been formed. During experiment k-value of the solution has been decreased in both cases encapsulation of the D-NA molecules inside into cavity of the CYD-molecule was observed (Table 1) [12]. In both cases, after certain concentration breaking of the curve was observed which

Table 1: Values of surface tension (γ) at the breakpoint with corresponding concentrations of cyclodextrins and D-NA and values of conductivity (κ) at the breakpoint with corresponding concentrations of cyclodextrins and D-NA at 298.15 K.

Conc. of α -CYD/mM	Conc. of D-NA/mM	γ/mNm^{-1}
4.75	5.25	70.25
Conc. of β -CYD/mM	Conc. of D-NA/mM	γ/mNm^{-1}
4.92	5.08	70.75
Conc. of α -CYD/mM	Conc. of D-NA/mM	κ/mSm^{-1}
4.86	5.14	0.245
Conc. of β -CYD/mM	Conc. of D-NA/mM	κ/mSm^{-1}
4.93	5.07	0.228

CYD: Cyclodextrin

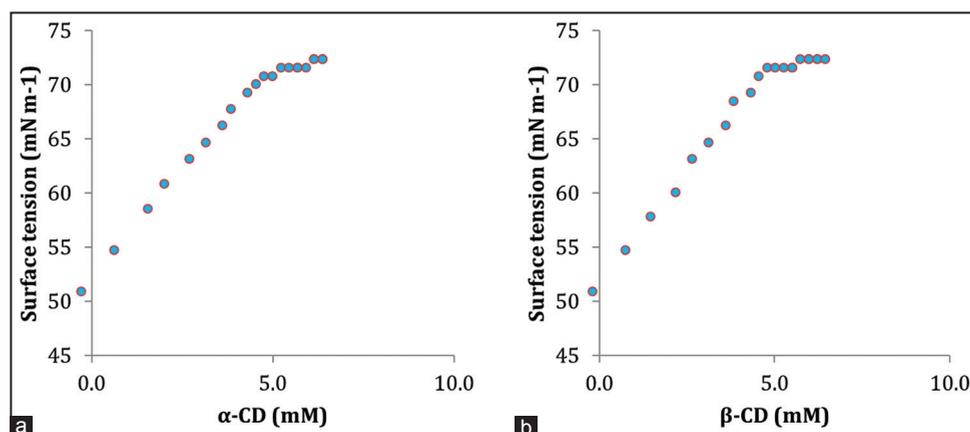


Figure 1: Variation of surface tension of aqueous (a) 3-(2-Naphthyl)-D-alanine α -cyclodextrin (CYD) and (b) 3-(2-Naphthyl)-D-alanine β -CYD systems, respectively, at 298.15 K.

Table 2: Data for surface tension study of aqueous 3-(2-Naphthyl)-D-alanine with α -CYD and β -CYD system at 298.15 K^a.

Volume of CYD (mL)	Total volume D-NA (mL)	Conc. of D-NA (mM)	Conc. of CYD (mM)	Surface tension in α -CYD (mNm ⁻¹)	Surface tension in β -CYD (mNm ⁻¹)
0	10	10.000	0.000	50.5	50.5
1	11	9.091	0.909	53.8	53.9
2	12	8.333	1.667	57.6	57.4
3	13	7.692	2.308	60.1	59.7
4	14	7.143	2.857	62.5	62.2
5	15	6.667	3.333	64	63.7
6	16	6.250	3.750	65.5	65.4
7	17	5.882	4.118	67.2	67.4
8	18	5.556	4.444	68.7	68.9
9	19	5.263	4.737	69.5	70.1
10	20	5.000	5.000	70.2	70.7
11	21	4.762	5.238	70.3	70.8
12	22	4.545	5.455	70.5	71
13	23	4.348	5.652	70.7	71.1
14	24	4.167	5.833	70.8	71.2
15	25	4.000	6.000	71	71.3
16	26	3.846	6.154	71.2	71.4
17	27	3.704	6.296	71.3	71.5
18	28	3.571	6.429	71.3	71.6
19	29	3.448	6.552	71.4	71.7
20	30	3.333	6.667	71.5	71.8

^aStandard uncertainties in temperature u are: $u(T)=\pm 0.01$ K. CYD: Cyclodextrin

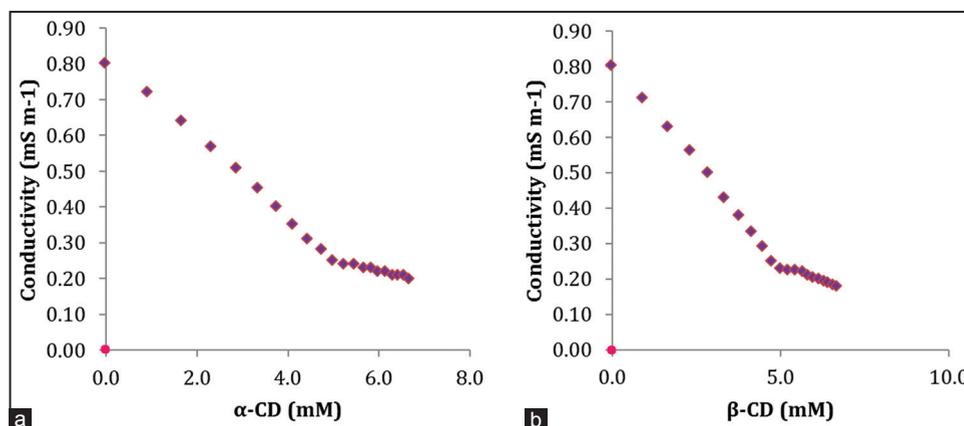


Figure 2: Variation of conductivity of aqueous (a) 3-(2-Naphthyl)-D-alanine α -cyclodextrin (CYD) and (b) 3-(2-Naphthyl)-D-alanine β -CYD systems, respectively, at 298.15 K.

may indication of the formation of inclusion complex (Figure 2). The experimental curve showed only one beak, which indicates 1:1 inclusion in both α - and β -CYD cases, suggesting the host-guest ratio to be 1:1.

At certain concentration, the breakpoint is found where maximum inclusion occurs through dynamic equilibrium between the host and the guest molecules [12].

3.3. ¹H NMR Study

¹H NMR spectrum of D-NA/ α -CYD and D-NA/ β -CYD is small shifts to higher frequencies that are observed for D-NA signals. The protons of the CYD molecule show considerable chemical shift due

to the inclusion of the guest D-NA into the hydrophobic cavity. In CYD structure H3 and H5 are situated inside the wider rim of the cavity, while H1, H2, and H6 are found narrow rim cavity of the CYD molecule [15]. During the insertion naphthyl group of the D-NA molecule inside the cavity of CYD, the H3 and H5 protons show upfield chemical shifts which conform the interaction of the host-guest molecule occurs [13]. The COO⁻, NH₂ group of D-NA interact with H5 and H3 of the CYD molecules. All guest aromatic protons move upfield considerable shift, illuminating deep insertion of the naphthyl group inside the cavity. On the other hand, the proton H¹ and one of the CH₂ protons of D-NA move downfield slightly, which indicates that they are located outside the cavity. The aromatic peaks are completely

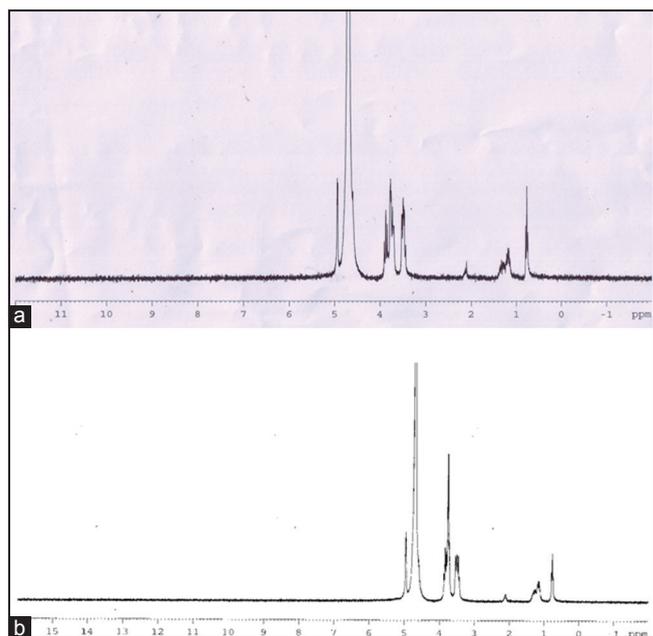


Figure 3: ^1H nuclear magnetic resonance spectra of solid inclusion complexes of (a) N-DA+ α -cyclodextrin (CYD) and (b) N-DA+ β -CYD in D_2O at 298.15 K.

shifted upfield. These observations suggest that the naphthyl moiety of the D-NA guest was encapsulated into the cavity of CYD formation of the inclusion compound (Figure 3).

3.4. FT-IR Study

The formation of inclusion complex of 3-(2-Naphthyl)-D-alanine with α - and β -CYD in solid state is supported by FT-IR study. There are many changes in the FT-IR spectra of solid inclusion complexes due to the changes of bending and vibrating peaks of the guest also aroused due to the symmetrical and anti-symmetrical stretching vibrations of the COO^- grouping. The various frequencies of D-NA, α -CYD, β -CYD, D-NA + α -CYD, and D-NA + β -CYD are reported in Tables 3 and 4. The $-\text{O}-\text{H}$ frequency of both α - and β -CYD is shifted to the lower region most likely due to the involvement of the $-\text{O}-\text{H}$ groups of the host molecules in hydrogen bonding molecule after complexation. The IR spectra of D-NA with the hosts presented in Figures 4 and 5. The spectrum was measured in the solid-state of the sample as a KBr dispersion. The following bands in cm^{-1} are assigned in Table 5. The inclusion complex formation due to strong bands is caused by overlapping of C-H stretching vibrations of various methyl and naphthyl groups of the guest molecule with CYDs. Moreover, strong bands included in the tables and figures with the guest molecule. Moreover, the spectra of the two inclusion complexes are dissimilar to CYD. Additional peaks are recognized in the solid inclusion complexes, which mean chemical reaction, occurred between the guest and CYD. However, quite a lot of peaks of D-NA are absent or somewhere shifted which is due to the change in environment after inclusion in the cavity of α -CYD, these changes were more appropriately noticed in β -CYD than α -CYD. Hence, we conclude that the encapsulation is better with β -CYD.

3.5. Electrospray Ionization (ESI)-mass Spectrometric Analysis of Inclusion Complexes

The solid ICs of D-NA with α - and β -CYD were further analyzed by ESI-mass spectrometry by dissolving these in methanol. The spectra are shown in Figure 6. The peaks at m/z 1188.42 and 1350.47 correspond to $[\text{D-NA}+\alpha\text{-CYD}+\text{H}]^+$ and $[\text{D-NA}+\beta\text{-CYD}+\text{H}]^+$, respectively. The spectra confirm that the desired ICs D-NA+ α -CYD and D-NA+ β -CYD

Table 3: Estimated vibrational frequencies for α -CYD+3-(2-Naphthyl)-D-alanine complex formation

Wavenumber/ cm^{-1}	Group
3-(2-Naphthyl)-D-alanine	
3082-2875	$-\text{C}-\text{H}$ from various $-\text{CH}_3$ and methylene groups
1700.60	Stretching for $-\text{C}=\text{O}$
1560.01	Symmetrical stretching of $-\text{COO}^-$
1412.45	Anti-symmetrical stretching of $-\text{COO}^-$
α-CYD	
3412.10	Stretching of $-\text{O}-\text{H}$
2930.79	Stretching of $-\text{C}-\text{H}$ from $-\text{CH}_2$
1406.76	Bending of $-\text{C}-\text{H}$ from $-\text{CH}_2$ and bending of $\text{O}-\text{H}$
1154.39	Bending of $-\text{C}-\text{O}-\text{C}$
1030.39	Stretching of $-\text{C}-\text{C}-\text{O}$
952.36	Skeletal vibration involving α -1,4 linkage
α-CYD+[D-NA]	
3366.45	Stretching of $-\text{O}-\text{H}$ of α -CYD
2948.52	Symmetrical stretching of $-\text{C}-\text{H}$ from $-\text{CH}_3$ of D-NA
1662.75	$-\text{C}=\text{O}$ from D-NA
1538.74	Stretching of $-\text{COO}^-$ from D-NA
1046.03	Bending of $\text{C}-\text{C}-\text{O}$ of α -CYD
984.46	stretching of $\text{C}-\text{C}-\text{O}$ of α -CYD
D-NA: 3-(2-Naphthyl)-D-alanine	

have been formed in solid state and the stoichiometric ratio of the host and guest is 1:1 (Scheme 2).

3.6. Structural Features of CYD and 3-(2-Naphthyl)-D-alanine

The structural suitability CYD provides great opportunity to act as a host molecule due to the inner hydrophobic cavity and hydrophilic rims. A nonpolar part of guest molecules inside the cavity and polar part of the guest molecule makes an association with the polar rims, forming a stable inclusion complex (Scheme 2). The apolar cavity diameter of α -CYD is 4.7–5.3 Å and β -CYD is 6–6.5 Å, respectively [11]. The D-NA size and a polar part of naphthyl group and polar part COO^- , NH_3^+ can be easily encapsulated inside the cavity of CYD [16]. The formation of inclusion complex no covalent bond formation or breaking occur [17]. The polar water molecules are present inside the slightly a polar cavity, which generally energetically unflavored. Hence, the polar water molecules are readily substituted by hydrophobic naphthyl group of the N-DA. This results in a more stable energy state. The stoichiometry of the inclusion complex is found as 1:1, which is supported by conductivity and surface tension measurements [17]. Hence, after inclusion of one N-DA molecule COO^- , NH_2 the zwitterionic part blocks the rim by making hydrogen bonding with the rim $-\text{OH}$ groups, so the second molecule cannot enter. Naphthyl group hydrophobic part of D-NA was found to be inserted through the wider rim of CYD [18].

4. CONCLUSION

We reached the conclusion with the help of spectroscopic and physicochemical studies such as surface tension, conductance, NMR,

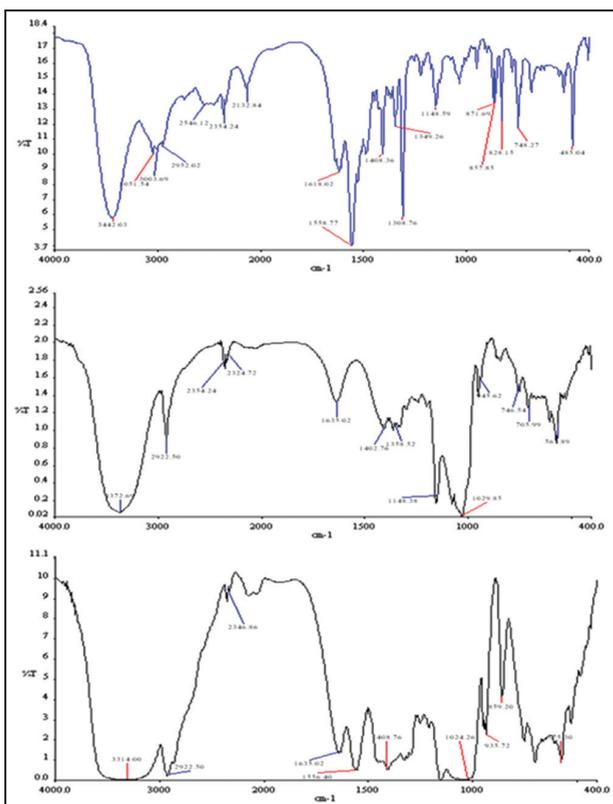


Figure 4: Fourier-transform infrared spectra of N-DA (top), α -cyclodextrin (CYD) (middle), and N-DA- α -CYD inclusion complex (bottom).

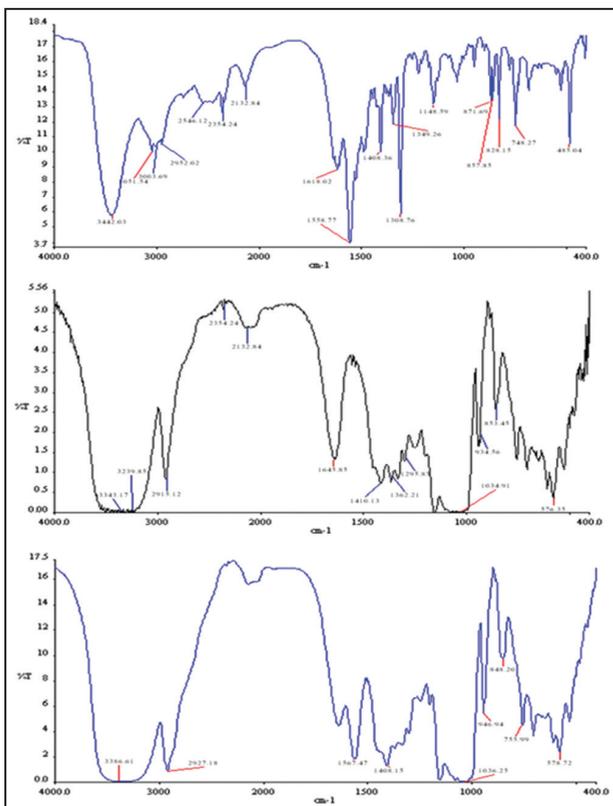


Figure 5: Fourier-transform infrared spectra of N-DA (top), β -cyclodextrin (CYD) (middle), and N-DA- β -CYD inclusion complex (bottom).

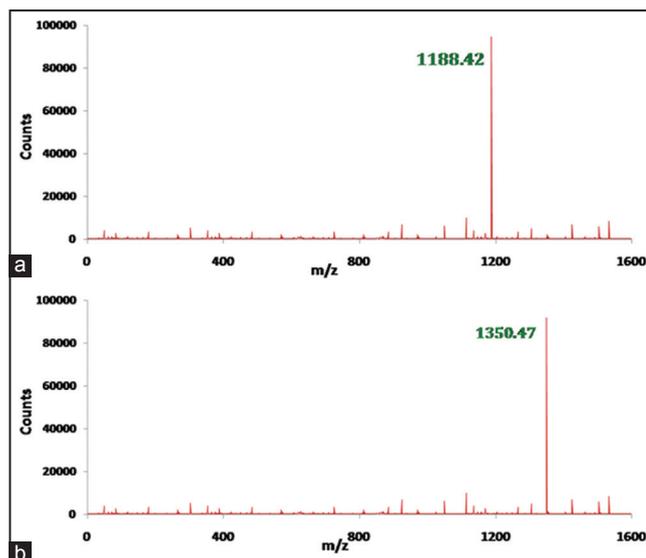
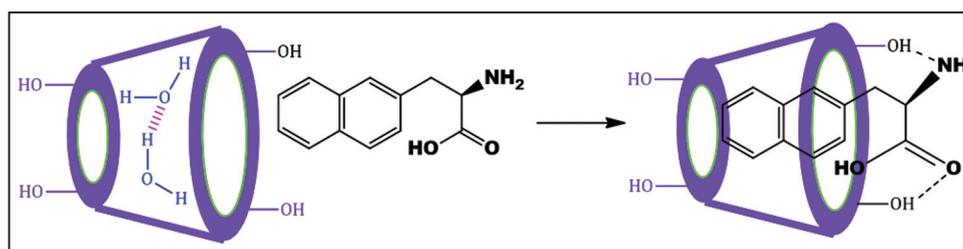


Figure 6: Electrospray ionization mass spectra of (a) N-DA- α -cyclodextrin (CYD) inclusion complex and (b) N-DA- β -CYD inclusion complex.

Table 4: Estimated vibrational frequencies for β -CYD+3-(2-Naphthyl)-D-alanine complex formation

Wavenumber/cm ⁻¹	Group
3-(2-Naphthyl)-D-alanine	
3000-2800	-C-H from various -CH ₃ and methylene groups
1700	Stretching for C=O
1560	Symmetrical Stretching of -COO ⁻
β-CYD	
3349.23	Stretching of O-H
2919.12	Stretching of -C-H from -CH ₂
1409.18	Bending of -C-H from -CH ₂ and bending of O-H
1153.17	Bending of C-O-C
1033.02	Stretching of C-C-O
938.64	Skeletal vibration involving α -1,4linkage
β-CYD+[D-NA]	
3326.18	Stretching of O-H of β -CYD
2958.13	Stretching of -C-H from -CH ₃ and -CH ₂ Of D-NA
1722.67	Stretching for C=O of D-NA
1678.56	Symmetrical stretch of -COO ⁻ of D-NA
1384.41	Anti- symmetrical Stretching of COO ⁻ of D-NA
1158.05	Bending of C-O-C of β -CYD
1072.56	Stretching of C-C-O of β -CYD

FT-IR, and mass saws that the 3-(2-Naphthyl)-D-alanine form host-guest ICs with both α - and β -CYD both in solution and the solid state. ¹H NMR confirms the inclusion in the a polar cavity of both CYD molecules, while surface tension and conductivity measurements suggest a 1:1 stoichiometry. Solid state characterizations have been



Scheme 2: Plausible schematic presentation of mechanism for the formation of 1:1 inclusion complex between 3-(2-Naphthyl)-D-alanine and cyclodextrin.

Table 5: Data for conductivity study of aqueous 3-(2-Naphthyl)-D-alanine with α and β -CYD system at 298.15 K^a.

Volume of CYD (mL)	Total volume of D-NA (mL)	Conc. of D-NA (mM)	Conc. of α -CYD (mM)	Conductance of α -CYD (mSm ⁻¹)	Conductance of β -CYD (mSm ⁻¹)
0	10	10.000	0.000	0.80	0.80
1	11	9.091	0.909	0.72	0.71
2	12	8.333	1.667	0.64	0.63
3	13	7.692	2.308	0.57	0.56
4	14	7.143	2.857	0.51	0.50
5	15	6.667	3.333	0.45	0.43
6	16	6.250	3.750	0.40	0.38
7	17	5.882	4.118	0.35	0.33
8	18	5.556	4.444	0.31	0.29
9	19	5.263	4.737	0.28	0.25
10	20	5.000	5.000	0.25	0.23
11	21	4.762	5.238	0.24	0.225
12	22	4.545	5.455	0.24	0.223
13	23	4.348	5.652	0.23	0.220
14	24	4.167	5.833	0.23	0.210
15	25	4.000	6.000	0.22	0.205
16	26	3.846	6.154	0.22	0.200
17	27	3.704	6.296	0.21	0.195
18	28	3.571	6.429	0.21	0.190
19	29	3.448	6.552	0.21	0.185
20	30	3.333	6.667	0.20	0.180

^aStandard uncertainties in temperature u are: $u(T) = \pm 0.01$ K. CYD: Cyclodextrin

carried out by FT-IR, confirming their formation also in the solid state. Considerately of electrostatic interaction, multiple C-H...O interactions, hydrogen bond D-NA encapsulated into the cavity of both CYD. The inclusion phenomenon has been found to be more favorable in the case of β -CYD than the α -CYD. In the present study, we investigate the nature of formation and stoichiometry of inclusion complexes of α - and β -CYD with D-NA in the aqueous medium can be useful in specific amino acid, peptides with suitable binding group as controlled delivery systems in the field of modern biomedical sciences.

5. ACKNOWLEDGMENT

The authors are highly thankful to the SAP, Department of Chemistry, University of North Bengal under University Grants Commission for financial assistance and instrumental convenience to facilitate the research work. One of the authors, Prof. M. N. Roy, is thankful to University Grant Commission, New Delhi, Government of India, for

being awarded One Time Grant under Basic Scientific Research via the Grant-in-Aid No. F.4-10/2010 (BSR) regarding his active service for enhancement of research facilities to facilitate further research work.

6. REFERENCES

- Z. Z. Gao, R. L. Lin, D. Bai, Z. Tao, J. X. Liu, X. Xiao, (2017) Host-guest complexation of cucurbit uril with two enantiomers, *Scientific Reports*, **7(1)**: 44717.
- C. U. Johannessen, (2000) Mechanisms of action of valproate: A commentary, *Neurochemistry International*, **37(2-3)**: 103-110.
- A. L. Abuhijleh, C. J. Woods. (1996) Synthesis, characterization, and oxidase activities of copper (II) complexes of the anticonvulsant drug valproate, *Journal of Inorganic Biochemistry*, **64(1)**: 55-67.
- Z. Z. Gao, R. L. Lin, D. Bai, Z. Tao, L. Jing-Xin, X. Xin, (2017) Host-guest complexation of cucurbit uril with two enantiomers, *Scientific Reports*, **10(1)**: 1038.

5. S. Saha, T. Ray, S. Basak, MN. Roy, (2016) Surface tension and conductivity studies to determine the inclusion mechanism: Thermodynamics of host guest inclusion complexes of natural amino acids in aqueous cyclodextrins, *New Journal of Chemistry*, **40**: 651-661.
6. K. Klokkers, (1996) U.S. Patent, No. 6,204, p255.
7. J. G. Hardman, (1996) *Goodman and Gilman: The Pharmacological Basis of Therapeutics*. 9th ed. New York: McGraw-Hill, p461.
8. K. J. Szejtli, (1998) Introduction and general overview of cyclodextrin chemistry, *Chemical Reviews*, **98**: 1743-1754.
9. T. Pralhad, K. J. Rajendrakumar, (2004) Study of freeze-dried quercetin cyclodextrin binary systems by DSC, FT-IR, X-ray diffraction and SEM analysis, *Journal of Pharmaceutical and Biomedical Analysis*, **34(2)**: 333-339.
10. A. Roy, S. Saha, B. Datta, M. N. Roy, (2016) Insertion behavior of imidazolium and pyrrolidinium based ionic liquids into α and β -cyclodextrins: Mechanism and factors leading to host guest inclusion complexes, *RSC Advances*, **6(1)**: 100016-100027.
11. A. Roy, S. Subhadeep, M. N. Roy, (2016) Study to explore host-guest inclusion complexes of cyclodextrins with biologically active molecules in aqueous environment, *Fluid Phase Equilibria*, **425(1)**: 252-258.
12. M. N. Roy, E. Deepak, S. Saha, M. C. Host-guest inclusion complexes of α and β -cyclodextrins with α -amino acids, *RSC Advances*, **4(80)**: 42383-42390.
13. M. N. Roy, M. C. Roy, K. Roy, (2015) Investigation of an inclusion complex formed by ionic liquid and β -cyclodextrin through hydrophilic and hydrophobic interactions, *RSC Advances*, **5(70)**: 56717-56723.
14. M. N. Roy, A. Roy, S. Saha, (2016) Probing inclusion complexes of cyclodextrins with amino acids by physicochemical approach, *Carbohydrate Polymers*, **151**: 458-466.
15. M. N. Roy, S. Saha, M. Kundu, S. Saha, S. Barman, (2016) Exploration of inclusion complexes of neurotransmitters with β -cyclodextrin by physicochemical techniques, *Chemical Physics Letters*, **43**: 655-656.
16. L. R. Teixeira, R. D. Sinisterra, R. P. Vieira, A. Scarlatelli-Lima, M. F. Moraes, M. C. Doretto, H. Beraldo, (2006) An inclusion compound of the anticonvulsant sodium valproate into α -cyclodextrin: Physicochemical characterization, *Journal of Inclusion Phenomena and Macrocyclic Chemistry*, **54(1-2)**: 133-138.
17. A. Roy, S. Saha, M. N. Roy, (2016) Study to explore host-guest inclusion complexes of cyclodextrins with biologically active molecules in aqueous environment, *Fluid Phase Equilibria*, **425**: 252-258.
18. M. N. Roy, M. C. Roy, K. Roy, (2015) Investigation of an inclusion complex formed by ionic liquid and β -cyclodextrin through hydrophilic and hydrophobic interactions, *RSC Advances*, **5**: 56717-56723.

Author Query???

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*Bibliographical Sketch



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