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Modification ofPhotophysical Properties of Benzoic Acids upon Inclusion into Per-6-amino-□- cyclodextrin Cavity and its Impact

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Abstract - Cyclodextrins (CDs), a class of cyclic oligosaccharides, form complexes of inclusion with various organic compounds in water through non-covalent interactions through their well-defined hydrophobic inner cavities. CDs have been widely used in organic synthesis, because they can bind substrates and catalyze high selectivity chemical reactions, as well as for sensor applications. The microenvironment of chromophores within CD usually results in adjustments in the properties of their absorption and fluorescence. Although native CDs are of great interest to many visitor species as hosts themselves, there are many limitations in their structural features regarding the scale, shape and availability of chemically useful functional groups. Therefore, they need to be updated in such a way that the size and shape can be changed and new functional groups, catalytically active groups or chromophore can be added to expand their applications and the specificity of host-guest. Chemical modification of CDs provides both tremendous possibilities and challenges for chemists as the modified cyclodextrins are exquisite molecules that are invaluable in investigations at the limits of chemistry ranging from enzyme-like catalytic activity and antibody-like binding to esthetically pleasing molecules. UV-visible, FT-IR, ICD and molecular modeling techniques study the binding activity and mode of inclusion of benzoic acid, 4-nitrobenzoic acid, 4-hydroxybenzoic acid and 4-N, N-dimethylaminobenzoic acid in per-6-NH2-β-CD at two different pH values (3.5 and 7). All the five acids form stable 1:1 inclusion complexes and the binding constants obtained for per-6-NH_2-β-CD complexes are compared with that of reported binding constants for β-CD complexes and striking differences are noticed. The significant enhancement in binding constants at pH 7.0 clearly highlights the importance of electrostatic interactions in determining CD complexation. These factors are vital ingredients in choosing the right CD for biological applications, where solubility and modulations of luminescence for monitoring the guest are very important. This research paper more discuss about the Modification ofPhotophysical Properties of Benzoic Acids upon Inclusion into Per-6-amino-□- cyclodextrin Cavity

KEYWORD: Modification, Photophysical Properties, Benzoic Acids, Inclusion, Per-6-amino-□- cyclodextrin Cavity

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I. INTRODUCTION

Cyclodextrins have been studied extensively in various reactions as biomimetic catalysts. CDs catalytic reactions require reversible formation by non-covalent bonding of host-guest complexes with substrates. Cyclodextrins selectively bind substrates, and catalyze high selectivity chemical reactions. Cyclodextrincomplexation exercises geometric control over the traffic of the trapped molecular species resulting in excellent selectivity in a number of reactions. Besides this it can also cause asymmetry in organic reactions with the CD cavity being chiral.

Cyclodextrin inclusion complexes are found to changes the physical and chemical properties of guest molecule.[1]The acid base balance of many organic compounds is detected as being moved[2] in the presence of cyclodextrins. The change is seen as a measure of complex formation, as the constants of stability related to the forms of conjugate acid and base are different. Cyclodextrins have usually been found to interact preferentially with the neutral forms of both aliphatic and aromatic carboxylic acids[3] andwith the ionized form of 4-substituted phenols.[4] In our community, the inclusion complexation activity of plant growth regulators such as indole-3-acettic acid and its derivatives indole-3-propionic acid, indole-3-acrylic acid and pyridyl-3-acrylic acid with native a-, b- and g-cyclodextrins is studied using different analytical techniques.[5]

The chemical modification of cyclodextrins can be adjusted according to the form of hydroxyl group replaced.[6]The literature recorded the synthesis of cyclodextrins with primary hydroxyls, alone or entirely replaced by amino groups.[7]The effect of substituting CD hydroxyl groups with other moieties on the complexation characteristics of CDs is an area of active research resulting from the modification of the complexation characteristics and solubility of CDs resulting from such substitution.[8]Peramino-CDs are CD derivatives which are changed by persuasion on the primary face with amino pendant groups which display compromised hydrophobic binding but additional electrostatic binding of guest molecules relative to native CDs.

The association of cyclodextrins with organic acids has long back been studied by Schlenk and Sand.[9] The solubility of benzoic acid is greatly enhanced in presence of a- and b-cyclodextrins as it associates very strongly with both cyclodextrins. From the optical rotation measurement studies, it is evident that the organic acids form strong inclusion complexes with cyclodextrins. Pitchumani*et al.*[10] have studied Specific structure of some x-cyclodextrinnitrobenzoic acids, benzoic acids and several naphthalene derivatives. In the presence of cyclodextrins the acid-baseequilibria of organic compounds is changed. They stated that cyclodextrins in general associate preferentially with the neutral types of carboxylic acids than the corresponding conjugate bases. Only 4-nitrobenzoic acid forms a stronger complex in ionized form due to a

greater stability of the inclusion complex of the 4-nitrobenzoate anion in relation to 4-nitrobenzoic acid in terms of dipolar interactions, London dispersion forces and also increased mesomeric interactions between the carboxylate anion and the nitro group, which increases the electron density and polarizability of the anion.

Owing to their use in medicine, the spectroscopic properties of 4-aminobenzoic acid derivatives (PABA) have been extensively studied. This compound is also used as a sulfonamide antagonist in the clinical laboratory, and is most widely used as a sunscreen agent.[11] It is used as an intermediate in bacterial synthesis of folate.[12]As an antioxidant, PABA protects against ozone, smoking and other air pollutants that harm the structures of cells and membranes via oxidative stress.[13] It has some therapeutic effect against vitiligo, scleroderma, arthritis, herpes, typhus andother ricketisial diseases.[14]The therapeutic benefit from using PABA as complexes with cyclodextrins can be expected to be improved. Furthermore, PABA's luminescence features are of interest based on many solid matrices, such as filter paper,[15] polyvinyl alcohol substrate,[16] sodium acetate,[17] sodium acetate/sodium chloride[18] and CD/NaCl.[19]Specially increased emissions of fluorescence or phosphorescence are observed on a solid CD / NaCl substrate.

Since the harmful effects of sunbeams are prevented or minimized by 4- *N*,*N*-dimethylaminobenzoic acid [DMABA], it is considered as an important material in cosmetic industry.[20] The DMABA and its co-polymers absorb ultra violet beams.[21] Especially metal salts or complexes of DMABA are used to cosmetic industry. In 1996, Yoon *et al*. demonstrated that the specific H- bonding of DMABA[22] and its derivative[23] with water in aqueous cyclodextrin (CD) solutions played an important role in Creating an ICT State. They also recorded that the ICT process is greatly impacted by the guest molecule 's orientation in the CD cavity. Jiang is studying the impact of β-cyclodextrin inclusion complex formation on the twisted transfer of intramolecular charge (TICT) of the included p-dimethylaminobenzoic acid system.[24]

II.MATERIALS AND METHODS

Materials

Cyclodextrin modifications were performed under nitrogen atmosphere using pre-dried and distilled solvents. Solvents for chromatography and extractions were distilled prior to use. DMF was supplied by Merck. It was further purified by distillation after drying with activated molecular sieves.2 n-Hexane; 2-propanol, acetonitrile and methanol were of HPLC grade and were used as received.

Method

A saturated solution of CD in water was added dropwiseequimolar quantity of substratum dissolved in minimum quantity of acetonitrile, an immediate turbid solution emerged and was stirred at room temperature for 24 h. To extract any uncomplexed substrates, the resulting precipitate was cooled, filtered, washed with diethyl ether. It was then dried up in an air oven at 60oC for 4 h. We used the dried crystalline powder for further studies.

Chromatographic methods

Thin layer chromatography was carried out with Merck grade silica gel 60 F254 plates. Compounds were detected at 254 nm (UV) or by using iodine. Analytical HPLC was performed on Thermo Finningon HPLC system with Surveyor plus solvent degasser, Surveyor autosampler plus, Thermostatic column housing or Shimadzu LC-10AT series and Shimadzu SPD-10AT vp

Spectroscopic methods

A JASCO V-550 double beam spectrophotometer with PMT detector was used to record ultraviolet-visible absorption spectra (UV-Vis). Vis-UV. Analyzes were carried out using JASCO-Spectral Manager and measurements were made using Microsoft Excel 2003 Software.

FT-IR spectra ofSolid CD complexes of the guest molecules were prepared in 1: 1 ratio and analysed by pressed KBr pellet technique. As the guest molecules contain several chromophores giving IR active vibrations, FT-IR spectra were found to be highly useful in characterisation of CD complexes of the guest molecules chosen.

Host-Guest ratio

Complex composition was also demonstrated by a gravimetric method of evaluating the molar host-guest ratio.[7] The host-guest ratio was determined by implementing the following technique. In a minimum amount of distilled water a known quantity of the solid CD inclusion complex was dissolved and the guest molecule was removed with warm chloroform. After chloroform evaporation the volume of the guest recovered was measured gravimetrically.

Determination of binding constants Stock solution of the substrate (1×10^{-3} or 2×10^{-3} M) was prepared by weighing and dissolving a specified quantity of the substrate in a minimum amount of pure acetonitrile / ethanol. For water-soluble compounds, the substrate was dissolved in doubly distilled water and then sonicated. 0.1 or 0.2 mL of this was added to a known volume of appropriate CD (1×10^{-2} M stock solution in water) and diluted to 10 mL by using respective buffers of appropriate pH values. The solution was stirred for 6 h unless noted otherwise. Absorption was recorded to calculate the equilibrium constants for the complexes.

ICD spectral studies

When guest molecules (chiral/achiral) are included in chiral macrocyclic CD molecules, chirality is induced in it, which is observed by the changes in its ICD spectral pattern. According to Harata's rule, the ICD of a chromophore located inside the cyclodextrin cavity will always be positive when its electric transition dipole moment is parallel to the principal axis of the cyclodextrin. According to Kodaka's rule, the sign of ICD is reversed when a chromophore is situated outside the cavity. The ICD spectrum of the solvent was recorded first and automatically eliminated from the dichroism of the complexes. The ICD spectra are helpful to understand the mode of inclusion of the guest chromophores into the CD cavity. Solutions were of higher concentration than

Molecular modeling studies **were** carried out using Insight II. Energyminimized structure of the complexes were obtained by Molecular Mechanics calculations using Insight II/Discover programs on Silicon Graphics IRISworkstation. Energies of structures were minimized by using CVFF (for neutral molecule) or AMBER (for charged molecule) force field and RMS derivative0.001 is achieved in each case. Complexation energies were calculated by using the following equation:

□E = □Ecomplex- □Ehost- □Eguest

III. RESULTS AND DISCUSSION

The above compounds are weakly acidic. At a pH below their pK_a value, these compounds will exist in neutral (-COOH) form and the pH above the pK_a value, they will be in anionic ($-COO^-$) form. Hence pH values of 3.5 (except for **2**) and 7 are chosen for recording UV absorption and Induced Circular Dichroism (ICD) spectra of these acids. For the acid **2**, pH 2.2 is chosen because its pK_a value is 3.4. The pK_a values of these acids are given Table 1.

Table 1 pK_a values of acids 1-5 in water

Acid	**pK_a**
1	4.19
2	3.41
3	4.48 & 9.6

4 2.50 &4.87

5 5.0

The reported pK_a values of per-6-amino-β-cyclodextrin (per-6-NH_2-β- CD) in protonated forms are around 6.1-8.5(±0.5).[25] The pK_a values of primary ammoniums in sugars are very much sensitive to chirality and possible hydrogen bonding.[26] Per-6-NH_2-β-CD exists as the polyvalent cation (per-6- NH_3^+-β-CD) at pH<6 and exists as the neutral from above the pH value ~8.5.[27] Per-6-NH_2-β-CD is reported to exist in the partially protonated form even under neutral conditions

In order to get an insight into the interactions between acids **1-5** and per-6-NH_2-β-CD, UV-Visible, FT-IR and Induced Circular Dichroism (ICD)] spectra of acids **1-5** are recorded and the observed results are discussed below.

Characterization of per-6-NH_2-β-CD inclusion complexes of acids 1-5

FT-IR spectra

It was found that the inclusion complex formation is confirmed when the bands resulting from the incorporated ''guest'' molecule are generally shifted or their intensities altered. FT-IR spectra of pure acids **1-5** and their per-6-NH_2-β-CD complexes and the respective spectral values are given in table 2. It is clear from table 2, entry 1, that the FT-IR frequencies of functional groups such as C=O and C=C stretching vibrations of **1** are shifted significantly when complexed with per-6-NH_2-β-CD. The sharp peak at 1687 cm^{-1} corresponding to C=O stretching is shifted to lower frequency ($\Delta\nu$ = -19 cm^{-1}). The aromatic C=C stretching vibrations at 1618 cm^{-1} and 1581 cm^{-1} of **1** are shifted to higher frequencies ($\Delta\nu$ = +11 cm^{-1}& +15 cm^{-1}). From the above observations**,** it may be concluded that significant host-guest inclusion complex formation of the substrate **1** has taken place inside per-6-NH_2-β-CD cavity.

In 4-nitrobenzoic acid **2 (**Table 2)**,** the peak at 1693 cm^{-1} corresponding to C=O stretching is shifted very much to 1625 cm^{-1} ($\Delta\nu$ = -68 cm^{-1}) when included in per-6-NH_2-β-CD. The sharp peak at 1600 cm^{-1}corresponding to C=C (aromatic) stretching decreases ($\Delta\nu$ = -27 cm^{-1}). The asymmetric N=O stretching frequency of nitro group at 1523 cm^{-1} decreases ($\Delta\nu$ = -22 cm^{-1}) while the symmetric stretching vibration at 1340 cm^{-1} is shifted to higher frequency ($\Delta\nu$ = +44 cm^{-1}). The peak at 867 cm^{-1} corresponding to C-N stretching frequency is shifted to higher frequency ($\Delta\nu$ = +20 cm^{-1}). From the above observations, it is concluded that significant host-guest inclusion of acid **2** has taken place inside the per-6-NH_2-β-CD cavity.

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Table 2 FT-IR spectral data (ν in cm-1) of benzoic acids **1-5** and their per-6- NH2-β-CD complexesa

Acid Functional group	Free Acid	Per-6-NH2-β-CD complex of acid
C=O stretching	1687	1668
C=C stretching	1618 1581	1629 1596
C=O stretching	1693	1625
C=C stretching	1600	1573
N=O stretching	1535	1523
	1340	1384
C-N stretching	867	887
C=O stretching	1676	1670
C=C strecthing	1596	1595
	1510	1500
O-H stretching	3388	Merges in CD
N-H stretching	3361	Merges in CD
C=O stretching	1664	1640
N-H bending	1627	1604
C=C stretching	1570	1539
C-N stretching	1317	1371
C=O stretching	1668	1663
C=C stretching	1598	1602
	1533	1531
C-H bending	1369	1371
C-N stretching	1319	1336

The spectral data of **3** in table 2 shows that the C=O and C=C stretching frequencies of 4-hydroxybenzoic acid **3** are considerably shifted when complexed with per-6-NH_2-β-CD. The peak at 1676 cm^{-1}corresponding to C=O stretching frequency is shifted to 1670 cm^{-1} in the presence of per-6- NH_2-β-CD. The C=C stretching frequencies are also shifted inside per-6-NH_2-β-CD. These changes in the stretching frequencies of **3** confirm the formation of inclusion complex between the acid **3** with per-6-NH_2-β-CD.The spectral data of **4** in table 2 reveals that

when complexed with per- 6-NH_2-β-CD, the peak at 3361 cm^{-1} (N-H stretching frequency) of 4-aminobenzoic acid **4** has merged with the per-6-NH_2-β-CD's amino groups. The peak at 1676 cm^{-1} corresponding to C=O stretching frequency undergoes a considerable decrease in frequency in per-6-NH_2-β-CD. (Δν□ □6 cm^{-1}). The peak observed at 1317 cm^{-1} (O-H bending) exhibits a shift in frequency to higher value (Δ□ □20cm^{-1}). Comparison of FT-IR frequencies of free DMABA **5** and its per-6-NH_2-β-CD complex (Table 2) also confirms the complexation between **5** and the per-6-NH_2-β-CD, as the vibrational stretching frequencies of the functional groups (C=O, C=C and C-N) and the bending frequency of C-H have been considerably changed. While the C=O stretching and C-H bending frequencies are shifted to lower value, the C-N stretching frequency is shifted to a higher value in the presence of per-6-NH_2-β-CD. These spectral changes reveal that a strong host-guest complexation has also taken place between **5** and per-6-NH_2-β-CD.

Host-guest ratio

It was observed that the complex formation is also evidenced from the determination of molar host-guest ratio by a gravimetric method.[29] The H-G ratio of the inclusion complexes of acids **1-5** with per-6-NH_2-β-CD is determined by a gravimetric method and the observed values are displayed in table 3. These values clearly indicate that only a 1:1 complex is formed between the host and guest.

Table 3 Host-guest ratios for complexes of acids with per-6-NH_2-β-CD [a]

Guest	H-G ratio
1	1: 0.98
2	1: 0.93
3	1: 0.95
4	1: 0.94
5	1:0.96

[a] *determined by a gravimetric method*

UV-Visible absorption spectra

The host-guest inclusion complexation between per-6-NH_2-β-CD and acids **1-5** can be evidenced and established by UV-Vis. spectrophotometric method.[30] UV-Vis. absorption spectra of the acids **1-5** are recorded with varying amounts of per-6-NH_2-β-CD at two different pH values (one below and another above the pK_a value). The details of UV-absorption wavelengths at which maximum absorptions are observed (λ_{max} in nm). In all the cases, at a given pH value,

addition of per-6-NH_2-β-CD increases the intensity of UV-Vis. absorption along with a small blue shift, which is more pronounced in the case of 4-aminobenzoic acid at pH=3.5 (□λ=-14 nm).

Binding constants

The binding constant values for acids **1-5** with per-6-NH_2-β-CD at two different pH values are calculated from the UV absorption maxima by a linear method using the Benesi-Hildebrand (B-H plot) double reciprocal plot and also by a non-linear regression method using Graphpad prism software (Trial) and are given in table 4. The values reflect the strength of supramolecular host-guest inclusion complexes of the substrates in per-6-NH_2-β-CD. These binding constant values are also compared with the reported binding constant values of their β-CD complexes.

Table 4 Binding constant values of per-6-NH_2-β-CD complexes of acids **1-5**

K [dm^3 mol^{-1}] for PABCD complexReported K [dm^3 mol^{-1}]For β-CD complex

Acid	Unionized form (below the pKa value)[a]	Ionized form (above the pKa value)[b]	Unionized form (below the pKa value)	Ionized form (above the pKa value)
1	412	1408	1380 [19]	174[19]
2	1174[c]	1277	220[19]	1470[19]
3	543	2677	910 ± 90[33]	75±15[25], 56[34]
		941[d]	2526	
4	773	3417	600±44[35] 33 [36]	

Induced circular dichroism (ICD) spectral studies

Direct and concrete evidence for the formation of complexes and mode of inclusion are obtained from the circular dichroism studies. Chiral per-6-NH2- β-CD induces circular dichroism (ICD), when an achiral guest molecule is included in its cavity. The shape and signs of these spectra provide valuable information regarding the structure of the host–guest complex. To compare the orientation of these acids in per-6-NH_2-β-CD with β-CD, the ICD spectra of the acids **1-5** are recorded in β-CD also. In the case of **1** in per-6-NH_2-β-CD at pH values 3.5, +ve Cotton effect curves are obtained at 268 nm corresponding to π- π*(COOH-Ph)and at 235 nm corresponding to π- π*(Ph). Similar pattern is observed for **1** in β-CD, which confirms that the orientation of the phenyl and COOH chromophores (mode I) in both the CD's is same. In these cases, the aryl

chromophore stays inside the CD cavity resulting in positive chirality at both the λ_{max} values. Similarly, the ICD spectra of acid **1** at pH= 7 in both the CD's have two positive Cotton effect curves at 272 nm (Fig. 5.15) corresponding to n - π*(COO^--Ph) and 222 nm corresponding to π - π*(Ph), indicating the same orientation (mode I) in both the CD's. These positive peaks confirm that both the phenyl and COO^- moieties are present inside the CD cavity and their transition dipole is parallel to the CD axis.

Energy minimization studies using molecular modeling

Molecular modeling is a powerful tool used to study the nature, mode of inclusion of the guest molecule inside the host cavity, hydrogen-bonding and other possible non-covalent interactions such as van der Waals forces, Londondispersion forces *etc.* The energy minimization for a particular molecular model explains the stability of a particular mode of molecular inclusion inside a host cavity. Molecular modeling studies are carried out in vacuum with IRIX system. Energy minimization of the acids **1-5** (neutral and ionic form) in per- 6-NH_2-β-CD in two possible modes are carried out and the observed results are presented in Table 5. The molecular modeling snapshots are given in figs 1a–5b, which reveal that all the acids form favourable 1:1 H-G complexes with per-6-NH_2-β-CD with one or more H-bonding.

Table 5 Complexation energies (ΔE) in kcal.mol^{-1} for per-6-NH_2-β-CD complexes of **1-5** from energy minimization studies.

Acid	**pH**	**ΔE[a] (kcal. mol^{-1})**	
		Mode I	**Mode II**
	3.5	**-30.66313**	-23.98170
1			
	7	**-309.41816**	-288.22158
	2.2	-24.44420	**-29.79645**
2			
	7	**-306.17025**	-258.37329
	3.5	**-54.72696**	-49.42801
3			
	7	**-320.94523**	-271.91408
	3.5	**-22.49505**	-18.32454
4			
	7	**-327.88872**	-273.56322
	3.5	**-43.13612**	-37.19361

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5

7 **-315.24146** -283.36005

a Binding energy of the complex □**E = □Ecomplex- □Ehost- □Eguest**Mode I-COOH/COO^- inside the cavity; Mode II-COOH/COO^- outside the cavity. Energy of each complex was minimized using CVFF force field. RMS derivative for each substrate was 0.0001.

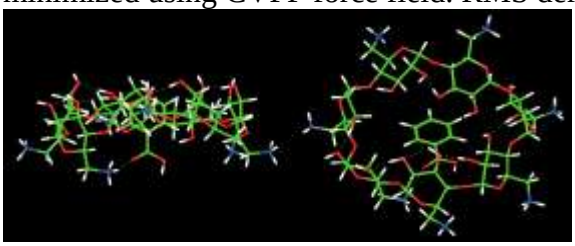

Fig. 1a *Energy minimized structure of benzoic acid in per-6-NH_2-β-CD by* ***mode I*** *at pH=3.5*

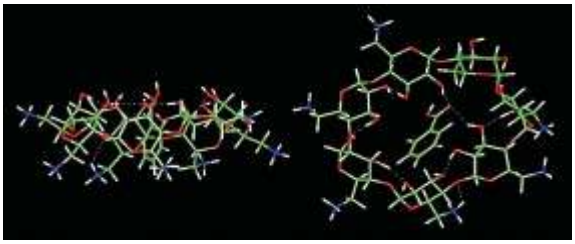

Fig. 1b *Energy minimized structure of benzoic acid in per-6-NH_2-β-CD by* ***mode II*** *at pH=3.5*

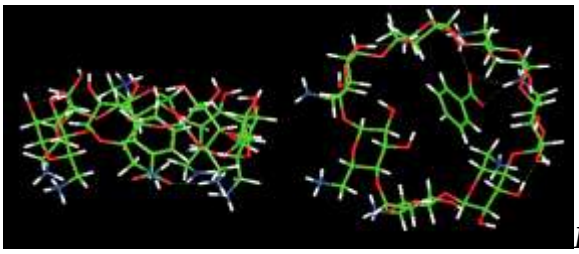

Fig. 2a *Energy minimized structure of benzoate ion in per-6-NH_2-β-CD by* ***mode I*** *at pH=7*

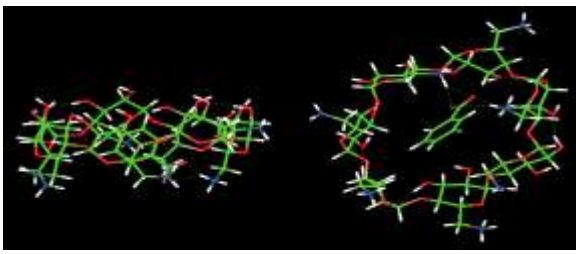

Fig. 2b *Energy minimized structure of benzoate ion in per-6-NH_2-β-CD by* ***mode II*** *at pH=7*

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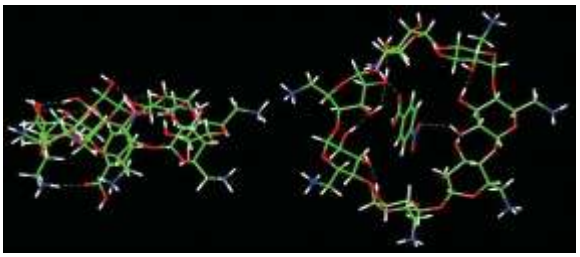

Fig. 3a *Energy minimized structure of 4-nitrobenzoic acid in per-6-NH_2-β-CD by* ***mode I*** *at pH=2.2*

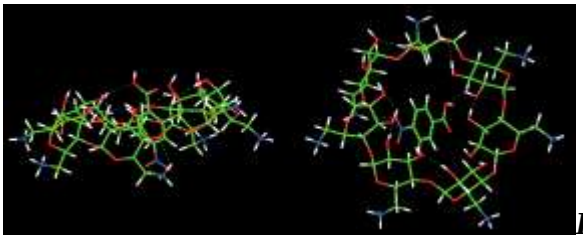

Fig. 3b *Energy minimized structure of 4-nitrobenzoic acid in per-6-NH_2-β-CD by mode* ***II*** *at pH=2.2*

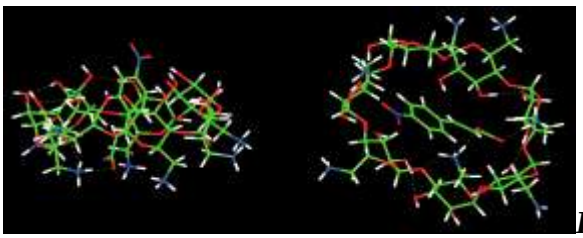

Fig. 4a *Energy minimized structure of 4-nitrobenzoate ion in per-6-NH_2-β-CD by* ***mode I*** *at pH=7*

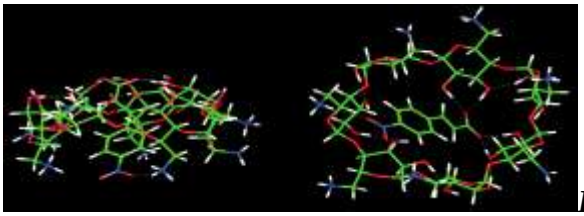

Fig. 4b *Energy minimized structure of 4-nitrobenzoate ion in per-6-NH_2-β-CD by* ***mode II*** *at pH=7*

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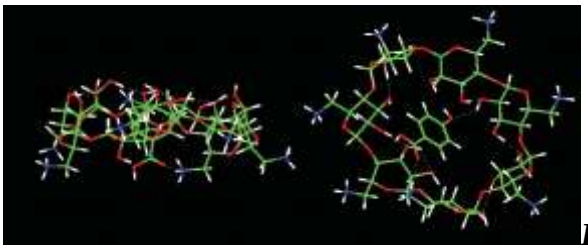

Fig. 5a *Energy minimized structure of 4-hydroxybenzoic acid in per-6-NH_2-β-CD by* ***mode I*** *at pH=3.5*

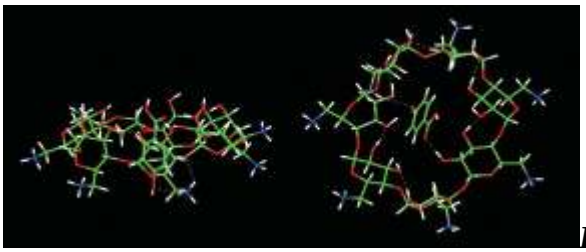

Fig. 5b *Energy minimized structure of 4-hydroxybenzoic acid in per-6-NH_2-β-CD by* ***mode II*** *at pH=3.5*

While comparing the binding energies and modes of benzoic acids and substituted benzoic acids (**1-5**), it is found that all the acids (**1-5**) in the neutral and ionized form (pH=3.5 & 7) prefer mode I than mode II except for the acid **2** at pH 2.2, in which mode II has lower binding energy than mode I. In addition, ionic forms of **1-5** have resulted in more stable CD complexes thanthe neutral forms. This may be due to facile electrostatic interaction and hydrogen bonding interactions between the ammonium group of CD and carboxylate ion. These features clearly show that electrostatic and hydrogen bonding interactions play key roles in complex stability. In addition, as evident from the binding energy values, it is clear that benzoic acids with electron releasing substituents have lower binding energy that benzoic acid with electron withdrawing substituents.

V. CONCLUSION

The observed results of present study indicate clearly that acids **1-5** form stable 1:1 inclusion complexes with per-6-NH_2-β-CD. The complexes are characterized by various spectral techniques like UV-Vis. absorption, FT-IR and ICD. The 1:1 stoichiometry of the complex is confirmed by Job's continuation variation method and gravimetric method. In addition, binding constants, modes and stability order at different pH values and their arrangement inside CD cavity are also evidenced. The observed results are alsosupported by molecular modeling studies. The binding constant values obtained for per-6-NH_2-β-CD complexes are also compared with that of reported binding constant values for β-CD complexes and striking differences are noticed. The binding constants are significantly enhanced at pH 7.0. This may be attributed to the

existence of electrostatic and hydrogen bonding interactions between the carboxylate ion and NH_3^+ of partly protonated per-6-NH_2-β-CD. But in β-CD, the neutral form of these acids form stronger inclusion complex than the anionic form except 4-nitrobenzoic acid **2,** where the anionic form binds strongly with β-CD due its different orientation inside the β-CD cavity.

The results also clearly highlight the importance of electrostatic interactions in determining CD complexation (which is predominantly reported so far involving hydrophobic interactions). The present study also highlights the significant role of nature of CD in determining complex formation, mode and stability. These factors are vital ingredients in choosing the right CD for biological applications, where solubility and modulations of luminescence for monitoring the guest are very important.

Aminocyclodextrins have been shown to selectively recognize various glycosaminoglycan sulphate (GAGs) and to inhibit and/or provide a substratum for neurite growth in primary cell culture, showing selectivity for small anionic guest molecules, such as nucleotides and aryl phosphates. These studies indicate that aminocyclodextrins are substantially different from other CD derivatives. Researchers recorded that aminocyclodextrins inhibit the self-assembly of a potentially neurotoxic component of π-amyloid protein (Aπ) involved in Alzheimer's disease by means of a specific immunoassay conducted by Aÿ. Aminocyclodextrins inhibit Aπ's self-assembly into diffusible ligands (ADDLs) derived from neurotoxic amyloids with nanomolar potency by integrating electrostatic and hydrophobic identification. Amino-cyclodextrins can be interpreted to offer a binding site topology similar to an antibody-like binding pocket but without the inherent problems in antibody therapy

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