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EFFECT OF pH ON 4-AMINOSALICYLIC ACID : α-CD/ HP -CD INCLUSION COMPLEXES

Chemistry

KEYWORDS: α-cyclodextrin, Hydroxy propyl α-cyclodextrin, UV- spectrophotometry, Fluourometry, pH meter, NaOH, H_2SO_4

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ABSTRACT

The characteristics of host – guest complexation between 4- Aminosalicylic acid with α-CD / HPα-CD at pH~2 and pH~7 were investigated by spectrometric method. In pH~2 the absorption is shifted to longer wavelength than pH~7. As the concentration of α-CD / HP**α**-CD increases, the emission wavelength is bathochromically shifted for both the pH. The study reveals that in both pH 4-ASA forms 1:1 inclusion complex. Benezi- Hildebrand plot confirms that 1:1 stoichiometric ratio was present in the inclusion complex. The association constant value is higher at pH~2 for HPα-CD. This confirms that at pH~2, 4-ASA was tightly included in the HP**α**-CD cavity than **α**-CD.

Introduction

4-Aminosalicylic acid, is an antibiotic used to treat tuberculosis. This organic compound has also been use since 1940s for the treatment of Inflammatory Bowel Diseases (IBDs), where it has shown greater potency in ulcerative colitis and Crohn's disease[1]. IUPAC name 4-amino-2-hydroxy-benzoic acid. The chemical formula $C_7H_7NO_3$. The molar mass 153.135g/mol.

Cds are cyclic oligosaccharides consisting of 6,7 and 8 units of D-(+) glucopyranose referred to as **α**,**β** and **ϒ** CD respectively, that may encapsulate a wide variety of guest molecules in their hydrophobic cavity(2-7).

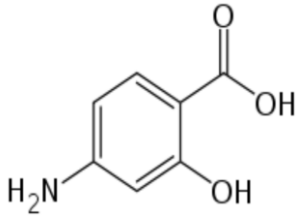


Fig: 1 Structure of 4-Amino salicylicacid

Experimental

The selected organic compound was weighed accurately and dissolved in suitable acids. All solvents used were the highest grade commercially available. Triply distilled water was used for the preparation of aqueous solutions. pH ~ 2. was made by mixing H2SO4 – H2O mixture solution and pH~7 was prepared using water. The solutions were prepared just before taking the measurements.

Characterization Equipments

Absorption spectral measurements were carried out with a Double beam Spectrophotometer smart 2203. Fluorescence spectral measurements were carried out with a fluorimetry Jasco spectroflurometer FP 8200. The pH values were measured by Elico pH meter.

Results and Disscussion

Table: 1.1

Absorption and Fluorescence maxima of 4-ASA with α – Cyclodextrin and Hydroxy propyl α – Cyclodextrin at pH~2

Alpha Cyclodextrin					**Hydroxy Propyl alpha Cyclodextrin**			
[α-CD]/[HPα-CD]	**λmax** nm	Abs	**λflu** nm	Intensity	**λmax** nm	Abs	**λflu** nm	Intensity
0	276.3	0.197	402	237.690	276.3	0.197	402	237.690
0.002	278.4	0.220	403	294.260	277.9	0.232	404	268.914
0.004	279.8	0.244	405	335.360	279.1	0.269	405	288.218
0.006	284.1	0.265	407	365.894	280.5	0.337	408	310.248
0.008	286.4	0.304	408	380.121	284.9	0.356	409	318.288
0.01	287.8	0.328	410	425.384	286.8	0.395	411	345.793

Table: 1.2 Absorption and Fluorescence maxima of 4-ASA of α – Cyclodextrin and Hydroxy propyl α – Cyclodextrin at pH~7

Alpha Cyclodextrin					Hydroxy Propyl 3 alpha Cyclodextrin			
[α-CD]/ [HPαCD]	**λmax** nm	Abs	**λflu** nm	Intensity	**λmax** nm	Abs	**λflu** nm	Intensity
0	262.3	0.460	393	376.576	262.3	0.460	393	376.576
0.002	263.7	0.542	394	442.078	263.1	0.576	394.8	420.484
0.004	264.4	0.570	395	482.312	263.9	0.655	395.6	430.536
0.006	265.8	0.657	397	525.299	264.4	0.680	398	465.269
0.008	266.6	0.675	398	536.383	266.2	0.736	399	474.666
0.01	268.2	0.758	399	578.382	267.9	0.769	400	520.289

The absorption maxima of 4-ASA appears at 276.3nm at pH~2. Upon increasing concentration of **α** – CD and HP**α**-CD the absorption value is red shifted to 287.8nm and 286.8nm respectively. The intensity of absorbance also increases as the concentration of **α**-CD / HP**α**-CD increases. In pH ~7 the absorption wavelength appears at 262.3nm. By the addition of **α**-CD / HP**α** –CD the wavelength is bathochromically shifted to 268.2nm and 267.9nm. This is because of the formation of mono anion, deprotonation takes place in the OH group [8]. Clear isobestic point is present in both the pH, which indicate that well defined 1 : 1 inclusion complex is formed. In pH~2 the absorption is shifted to longer wavelength than pH~7. This shows that at acid medium 4-ASA is completly dissociated.

4-ASA shows an emission maxima of 402nm and 393nm at pH~2 and pH~7 respectively. As the concentration of **α**-CD / HP**α**-CD increases, the emission wavelength is bathochromically shifted for both the pH. The emission intensity increases with increase in concentration of **α**-CD / HP**α**-CD. This shows that the solubility of the fluorophore increases by the addition of both **α**-CD / HP**α**-CD.

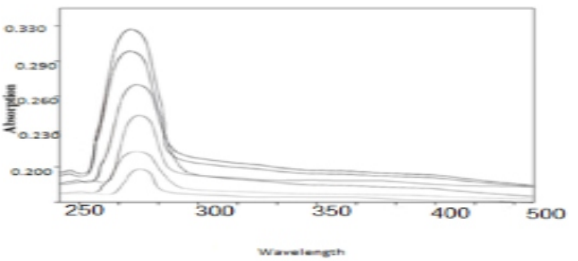


Fig: 2.1 The absorption spectra of 4-ASA with **α**-CD at pH ~2

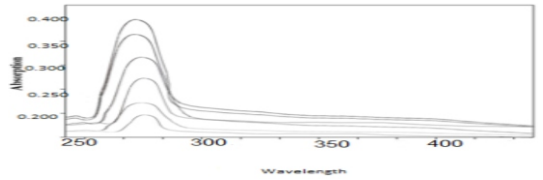


Fig:2.2 The absorption spectra of 4-ASA with HP**α**-CD at pH ~2

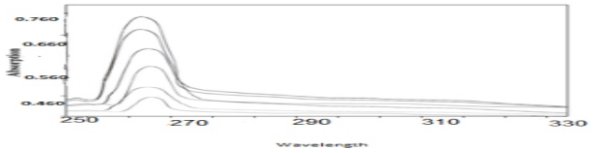


Fig:2.3 The absorption spectra of 4-ASA with **α**-CD at pH ~7

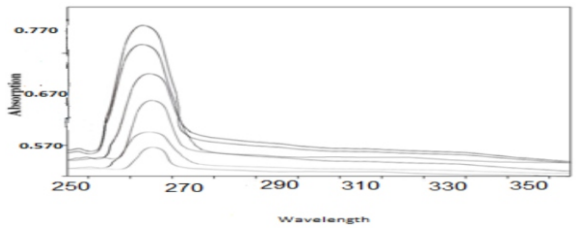


Fig: 2.4 The absorption spectra of 4-ASA with HP**α**-CD at pH ~7

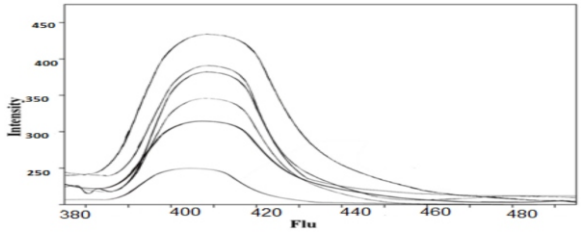


Fig: 2.5 The fluorescence spectra of 4-ASA with **α**-CD at pH ~2

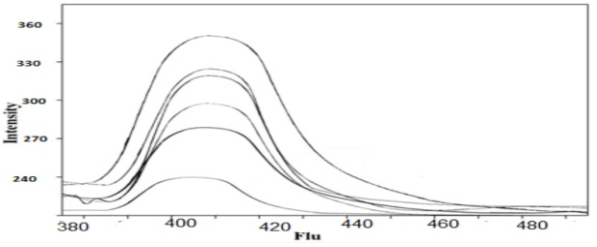


Fig: 2.6 The fluorescence spectra of 4-ASA with HP**α**-CD at pH ~2

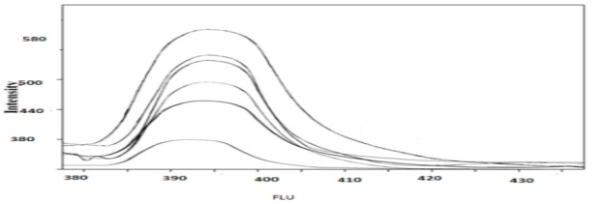


Fig:2.7 The fluorescence spectra of 4-ASA with **α**-CD at pH~7

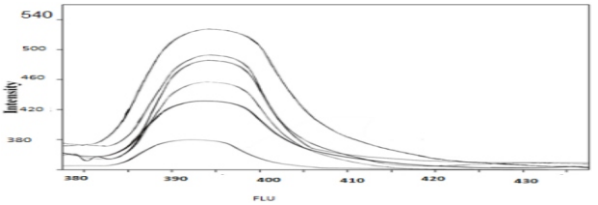


Fig: 2.8 The fluorescence spectra of 4-ASA with HP**α**-CD at pH~7

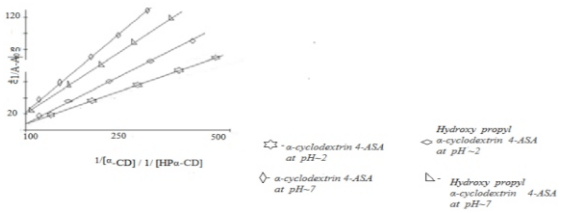


Fig: 2.9 Benzi – hilde brand diagram for absorption

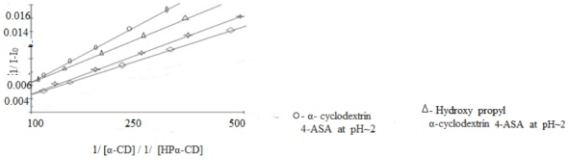


Fig: 2.10 Benzi – Hilde brand diagram for emission

The formation constant for the **α**-CD / HP**α**-CD :4-ASA complex formation has been determined by analysing the changes in the intensity of absorption and fluorescence maxima with the **α**-CD/ HP**α**-CD concentrations. The association constant(K) is determined by using Benesi- Hildebrand relation (9) indicates 1:1 complex is formed between α-CD/ HPα-CD and 4-ASA.

Absorption

$$1/A\text{-}A_0 = 1/A\text{-}A_0 + 1/K(A'\text{-}A0)[\ \text{-CD}]$$

Fliorescence

$$1/I\text{-}I0 = 1/I\text{-}I0 + 1/K(I\text{-}I0)[\ \text{-CD}]$$

In the above equation,

A0/I0= intensity of absorption / fluorescence of drug without α-CD/ HPα-CD

A/I= Absorption / fluorescence intensity with a particular concentration of α-CD/HPα-CD

A'/I'= Absorption / fluorescence intensity at the maximum concentration of α-CD/ HPα-CD used

k= Association constant

Linearity is obtained in the plot of 1/A-A0 or 1/I-I0 verses 1/ [α-CD] / [HPα-CD] for 1:1 complex. The association constant (K) was calculated from the slope of Benesi- Hildebrand plot using the equation

K=1/ slope (A'-A0) for absorbance

K= 1/ slope (I'-I0) for fluorescence

The plot of 1/ A-A0 verses 1/ [α-CD] / [HPα-CD] and 1/ I-I0 verses 1/ [α-CD]/ [HPα-CD] gives a straight line as shown in Fig 2.9 and 2.10. Good linear correlation was obtained which confirming the formation of a 1:1 complex. The formation constant of 4-ASA at pH~2 and pH~7 are 161.117M-1 , 319.560 M-1 respectively for α-CD and 170.78M-1, 331.030M-1 respectively for HPα-CD . In fluorescene spectra the formation constant was 374.105M-1 , 229.055M-1 at pH~2 and pH~7 for α-CD. The formation constant value for HPα-CD was 126.386M-1 at pH~2 and 167.70M-1 at pH~7. The higher formation constant value for HPα-CD indicates 4-ASA is included tightly in the cavity of HPα-CD than α-CD.

Conclusion

As the pH of the solution increases, the absorption wavelength of 4-ASA decreases. The host molecule α-CD and HPα-CD shows

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the same behavior. As the concentration of the host molecule increases the intensity of absorbance also increases. The emission wavelength decreases with pH of the solution for both α-CD and HPα-CD. The formation constant(K) is determined by using Benesi- Hildebrand relation indicates 1:1 complex is formed between α-CD/ HPα-CD and 4-ASA. Good linear correlation was obtained which confirms the formation of a 1:1 complex. The association constant value is higher for 4-ASA : HPα-CD complex at pH~2. This proves 4-ASA is included tightly in the cavity of HPα-CD than α-CD. The inclusion is best at pH~2 than pH~7.

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