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Inclusion of hydrazinophthalazine insight into the cavity of β-cyclodextrin: A study of surface tension and UV-vis spectroscopy

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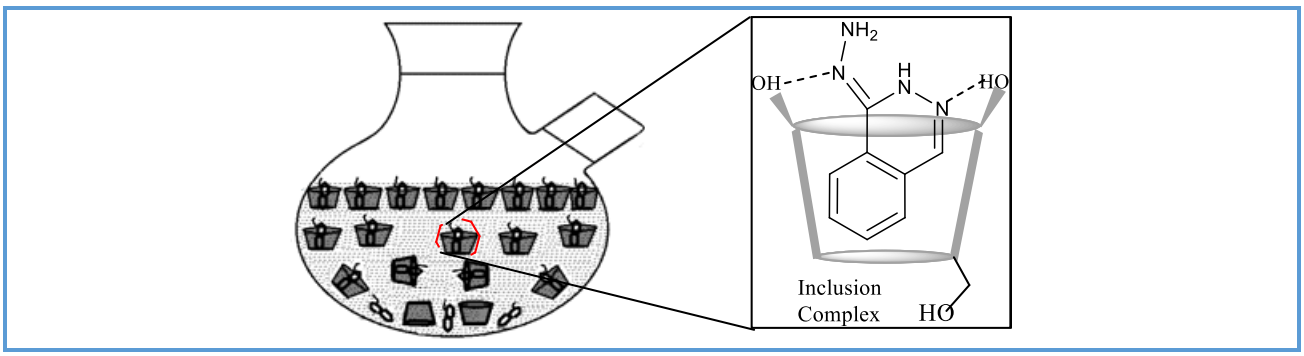
ABSTRACT

Surface tension, conductivity, and ultraviolet spectroscopic methods have been employed to study the dimensional fit molecular encapsulation of hydrazinophthalazine hydrochloride insight into the cavity of β-cyclodextrin in aqueous media. The equilibrium constant and 1:1 stoichiometry of the complex has been analyzed by surface tension (plot against reciprocal of concentration), and Job's plot (drawn from UV-vis data). The binding constants computed from the tensiometric and spectroscopic method were found to be 59.91 μM^{-1} and 12.02-96.58 μM^{-1}, respectively, that return the comfort zone of the results. The noteworthy upshot has also come out from standard Gibbs energy for inclusion complex formation. The free energy for inclusion complex is negative and lower in magnitude than adsorption by 6.11 kJ mol^{-1}. ^{1}HNMR and SEM picture also certified the formation of the inclusion complex. The results demonstrated that the driving force for formation of the inclusion complex inside the bucket-like cavity of β-cyclodextrin was a combination of hydrophobic effect and reduction of the surface energy, while in adsorption is only hydrophilic effect.

Graphical Abstract



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Introduction

Inclusion complex formation is a dimensional fit of host molecule insight into the host cavity, and the phenomena can also termed as molecular recognition [1, 2]. Cyclodextrin and its derivatives inclusion phenomena achieved broad range of application in *in-vivo* and *in-vitro* [3-6]. Its inner cavity is principally hydrophobic while the outer phase is hydrophilic good response in aqueous solubility. The polarity difference between the interior and exterior of the cavity provide it encapsulating power. On the other side, poorly bounded two molecules of water present in the cavity [7] of β-cyclodextrin (βCD), provide it excellent driving force to encapsulate the hydrophobic moiety of the guest molecule. This property enhances it as one of the outstanding drug carrier [8, 9]. It is also utilized as solubility enhancer, [10-12] stabilizing agent, [13, 14] hydrophobic group protector, [15] toxicity reducing agent [16, 17] catalysts for green synthesis [18, 19].

Hydrazinophthalazine hydrochloride [20] molecule (also known as hydralazine or l(2H)-Phthalazinone hydrazone) is belongs to the cyclic hydrazine family. It is one of the potential therapeutic drug for hypertension, [21] which composed of 10, 25, 50, and 100 mg tablets for oral dose [22]. The main function of the drug is, in midbrain it clams the pituitary hormone that acts to promote the retention of water by the kidneys and increase the blood pressure. Its hydrochloride salt is effective drug, whose condign dose reduce the arterial blood pressure and peripheral vascular resistance, whereas increases rate of heart beat and the amount of blood pumped out by the ventricles in a given time period [23]. Therefore, it is often prescribe to minimize abnormally high blood pressure in large number of patients. Albeit, it used as tumorigenic effect in mice, [23] to control on hypertensive preeclampsia [24], as waste water treatment [25], for synthesis of chemosensor NNI [26].

A fruitful understanding of the mechanism and basic principles that govern the host-guest complexation between the hydrazinophthalazine hydrochloride and β-cyclodextrin helps us to customize the composition, to design a better drug delivery system coupled with increased therapeutic potential. After the thorough survey, it has been seen that there is no article has published on this topic. Therefore, to make the clear knowledge about the mechanism of encapsulation between hydrazinophthalazine and β-cyclodextrin, in the present investigation we have employed to surface tension and UV-vis spectroscopic data. In this research study we have deduced the stoichiometry of the complex, binding constant, standard free energy change and binding nature; and there after discuss them with reference to molecular recognition.

This work aimed at synthesizing and controlling the release of 4-chloro-1-napthol (4C1N) by inclusion complex with host cyclodextrin molecules without any chemical and biological distortion.

Experimental

Materials and methods

1-hydrazinophthalazine hydrochloride and β-cyclodextrin of puris grade were purchased from the Sigma-Aldrich and were utilized without any further purification. Triple distilled water having the conductance $1 \cdot 10^{-6}$ $S \cdot m^{-1}$ was used to prepare the solution.

Apparatus

Surface tension of the solutions was measured using the platinum ring detachment technique with a K9 digital tensiometer (Krüss

GmbH, Hamburg, Germany) at the experimental temperature. The accuracy of measurement was ±0.1 mN·m^{-1}. Temperature was controlled using a circulation of auto thermostat water through a double-walled glass vessel containing the solution. UV−visible spectra were recorded using a JASCO V-530 UV−VIS spectrophotometer having a wavelength accuracy of ±0.5 nm. A digital thermostat was used to maintain the cell constant and temperature. METTLER TOLEDO-7 multi conductivity meter has used for the measurement of specific conductivity values with an uncertainty of ±1.0 μS m^{-1} .

^{1}H NMR spectra has been recorded in D_2O using Bruker Avance 400 MHz instrument. Signals have been cited as δ values in ppm with reference to residual protonated solvent signal as the internal standard (HDO, δ 4.79 ppm). Data have presented in chemical shifts. FTIR spectra have recorded by means of Perkin-Elmer FTIR spectrometer using KBr disk cell within the range of 4000−500 cm^{-1} at room temperature. Using JEOL JSM-IT 100 Scanning Electron Microscope (SEM), the surface morphologies of host, guest and complexes have recorded. The pictures were taken at an excitation voltage of 30kV with a magnification of 2000X.

Procedure

Before execute the practical experiment the solubility of host and guest molecules have been checked. 1-hydrazinophthalazine hydrochloride and β-cyclodextrin both are soluble in water (triple distilled). The solutions were prepared by mass measurements (accomplished using a Mettler AG-285 electronic balance with a precision of ±0.0003x10^{-3} kg) in aqueous solution. Precautions were taken to minimize the weight loss and the uncertainty in molality of solution was found to be ±0.0001 mol kg^{-1}. All the solutions were prepared freshly before performing experimental measurement.

Results and Discussion

Surface tension method

Inclusion, adsorption and thermodynamic parameters

The experiment were carried out at pH 3.4 - 4.9 to ensure the predominant presence of the guest and involved in complexation with βCD. The assumption was taken as only hydrazinophthalazine (HP) is contributing for inclusion, and the hydrochloride or chloride are stabilising the complex or act as a counter ion. Incoming hydrazinophthalazine molecules in aqueous solution of βCD experience two scenarios, (a) adsorption at air-water interfaces and (b) inclusion complex formation or other associative behavior.

$$\gamma = f([\mathrm{HP\beta CD}]_n) \qquad \text{air}$$

$$\text{adsorption}\updownarrow\text{behavior} \qquad \text{water}$$

$$\mathrm{HP} + n\beta\mathrm{CD} \xleftrightarrow{K_a} \mathrm{HP\beta CD}_n$$

$$\text{association}\updownarrow\text{ behavior} \qquad \text{complexation}$$

$$\text{bulk solution}$$

The rest non-associative phase has been conjecture as bulk solution. Both the scenarios surface adsorption and inclusion are manifested by surface tension, association or binding constant and free energy change. The surface tension (γ) results are represented in Figure 1.

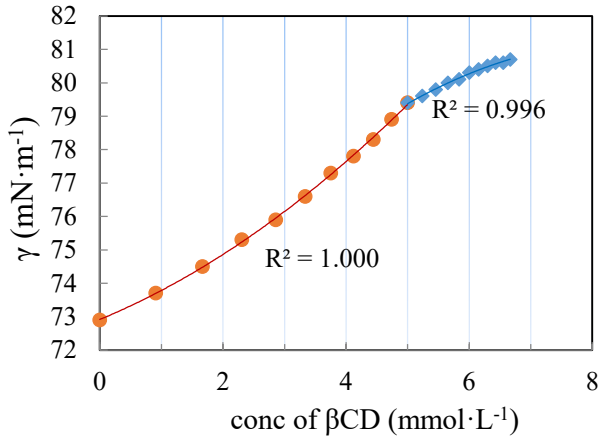
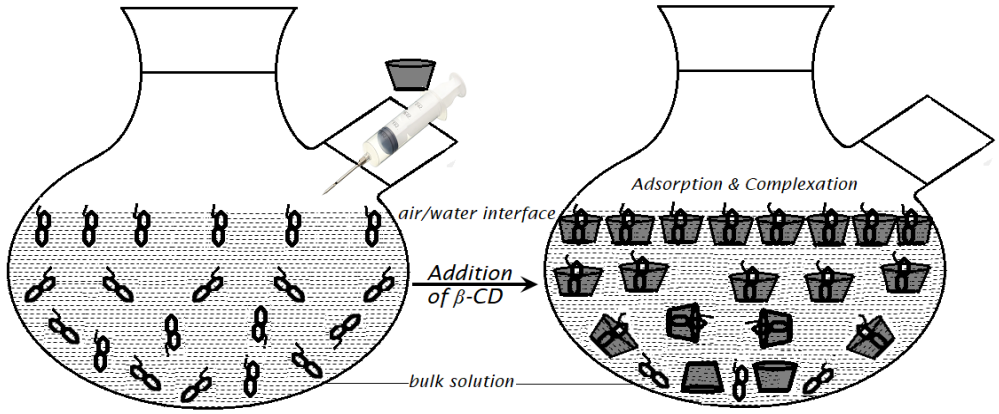


Figure 1. Plot of surface tension of hydrazinophthalazine as a function of βCD concentration

Figure 1 demonstrates two types of nature of γ, where both the curves intersecting at a same point, that kink has been considered as saturation point of inclusion complex (γ_{ic}). The corresponding concentration is called as saturation point of inclusion complex concentration (C_{ic}). Here, the γ_{ic} and C_{ic} are 79.4 mN·m² and 5.01 mM respectively (Table 1). Below the C_{ic}, the incorporation of hydrazinophthalazine are occurring insight into the apolar cavity of βCD, in addition to adsorption, so, the results are continues positive variation corresponding to concentration. The adsorption considered here is a physical adsorption instates of chemical adsorption. At this juncture, the inclusion is surface active; the number of surface adsorption at the air/water interface is increase upon injection of βCD (Scheme 1). In addition, the variation was almost parallel to *x* axis, this is due to the absence of guest molecules for inclusion. The graph has shown only for aqueous βCD; we know that cyclodextrin is surface inactive compound, so, in aqueous solution it does not significantly changed the surface tension [27].



Scheme 1. Schematic representation of inclusion complex between the hydrazinophthalazine and βCD in aqueous media

Surface tension data have plotted with logarithm of concentration and determine the surface excess (Γ) using the Gibbs isotherm equation

$$|\Gamma| = \frac{1}{RT}\frac{d\gamma}{dlnC} \quad (1)$$

Equation 1 can also be rearranged as

$$d\gamma = RT\,|\Gamma|\,dlnC \quad (2)$$

On integration, Equation 2 demonstrates the surface tension is a function of concentration. We have assumed that the change of adsorption enthalpy unaltered. Therefore, the Langmuir isotherm [28] can be write as

$$\theta|\Gamma| = \frac{K_{ad}C}{1+K_{ad}C} \quad (3)$$

Where, θ and K_{ad} are the cross-section area of the hydrazinophthalazine molecules at the surface and equilibrium constant for adsorption. Evaluate the surface excess from Equation 3, substituting into Equation 2 and after integration gives the Szyszkowski equation [29] in positive variant.

$$\gamma = \gamma_o + \frac{RT}{\theta}\ln(1 + K_{ad}C) \quad (4)$$

Here, the surface tension of pure water is γ_o(70.8 mN·m^{-1}). Fitting the data of know parameters to Equation 4, the cross-section area occupied by hydrazinophthalazine molecules at the surface and surface adsorption equilibrium constant below the saturation of complexation has been determined. For simplifying the calculation of Equation 4, we have predefined the value of K_{ad}, so that the intercept has been fitted to 70.8 mN·m^{-1}. Then θ has been evaluated from slope. As seen in Table 1, the considerable cross-section area occupied the molecules with a strong adsorption constant at the surface event there are complex has formed. The standard Gibbs energies for adsorption and inclusion complex formation have been computed using surface adsorption equilibrium constant and inclusion complex concentration (C_{ic}) respectively [30].

$$\Delta G^o_{ad} = -RT\ ln\, K_{ad} \ \ and\ \Delta G^o_{ic} = -RT\ ln\, C_{ic} \quad (5)$$

The standard Gibbs energy for inclusion complex formation is more negative than for adsorption by 6.11 kJ mol^{-1}. That make sense, the driving force in adsorption is only hydrophilic effect, while in formation of inclusion complex it is a combination of hydrophobic effect and reduction of the surface energy.

Guest: host binding stoichiometry and binding constant

The argument on the binding stoichiometry between hydrazinophthalazine and βCD has been taken into account in discussion. The major conflict is whether the binding ratio is 1:1 or 2:1. The ratio has been optimized by employing the surface tension data on modified Benesi-Hildebrand equation. The equation has modified on the complex formation between hydrazinophthalazine and βCD as follow:

$$HP + n\,\beta CD \xrightarrow{K_a} \mathrm{HP}\beta CD_n$$

The binding constant K_a is given by

$$K_a = \frac{[\mathrm{HP}\beta CD_n]}{[HP][\beta CD]^n} \quad (6)$$

where, n is the number of cyclodextrin participating to complex formation with respect to one molecule of hydrazinophthalazine. If the analytical concentration of the host ([HP]$_o$)and guest ([βCD]$_o$) are respectively

$$[HP]_o = [HP] + [\mathrm{HP}\beta CD_n]$$

and $[\beta\mathrm{CD}]_o = [\beta\mathrm{CD}] + [\mathrm{HP}\beta CD_n]$

then K_a can be rewritten as

$$K_a = \frac{[\mathrm{HP}\beta CD_n]}{\{[HP]_o - [\mathrm{HP}\beta CD_n]\}\{[\beta CD]_o - [\mathrm{HP}\beta CD_n]\}^n} \quad (7)$$

In experiment, we have used large excess of βCD (100 mM) relative to constant concentration of hydrazinophthalazine (10 mM). Thus, we may assume $[\beta CD]_o \gg [\mathrm{HP}\beta CD_n]$ or $\{[\beta CD]_o - [\mathrm{HP}\beta CD_n\} \approx [\beta CD]_o$. Then, equation 7 reduces to

$$K_a = \frac{[\mathrm{HP}\beta CD_n]}{\{[HP]_o - [\mathrm{HP}\beta CD_n]\}\,[\beta CD]_o{}^n} \quad (8)$$

As a low concentration of hydrazinophthalazine, it has obtained that the surface tension is proportional to complex concentration.

$$\gamma_{[\mathrm{HP}\beta CD_n]} = r\,[\mathrm{HP}\beta CD_n] \quad (9)$$

Where, r is the proportionality constant. Substituting the $[\mathrm{HP}\beta CD_n]$ from equation 9 into equation 8, and rearranging we have

$$\frac{[HP]_o}{\gamma_{[\mathrm{HP}\beta CD_n]}} = \frac{1}{r\,K_a}\frac{1}{[\beta CD]_o{}^n} + \frac{1}{r} \qquad (10)$$

Substituting $\gamma_{[\mathrm{HP}\beta CD_n]} = \gamma - \gamma_o$ (here, γ_o and γ are surface tension of the solution in absence and presence of βCD), equation 10 reduced to

$$\frac{[HP]_o}{\gamma-\gamma_o} = \frac{1}{r\,K_a}\frac{1}{[\beta CD]_o{}^n} + \frac{1}{r} \qquad (11)$$

Plot $\frac{[HP]_o}{\gamma-\gamma_o}$ against $\frac{1}{[\beta CD]_o{}^n}$ for n=1, 2, 3 etc (Figure 2) and find out the nature of the curve. Linear plot play the best fit whole number binding stoichiometry (n), while the nonlinear plot is diverge the correct stoichiometry. Perusal of Figure 2 disclose that the modified Benesi-Hildebrand plot is linearly fit only for n=1, and curve for n=2 and higher. So, it is confirmed that only 1:1 stoichiometric complexation are occurring; in other word, at a time only one hydrazinophthalazine molecule can integrated insight into the cavity of βCD. The binding constant (K_a) has computed from the ratio of intercept to the slope; and free energy change (ΔG_a^o) from K_a. From Table 1, the K_a is 14 time higher than K_{ad}; in contrast to ΔG_a^o is 20% and 45% lesser than ΔG_{ic}^o and ΔG_{ad}^o, respectively. These findings reveal that the inclusion complex is formed by strong binding between incorporated hydrazinophthalazine and βCD. The complexation has stabilized in lower energy even than adsorption. Comparing the considerable these three types of standard free energy (ΔG_{ic}^o, ΔG_{ad}^o, and ΔG_a^o,), it can be say that both the adsorption and incorporation are occurring in a same extent from end to end via opposite direction.

Table 1. Thermodynamic parameters computed from surface tension and uv spectroscopy

Parameters	Numerical values	Parameters	Numerical values
C_{ic}	: 5.01 mmolL^{-1}	Average λ_{max}	: λ_1 = 208 nm
ΔG_{ic}^o	: -19.24 kJ mol^{-1}		: λ_2 = 245 nm
K_{ad}	: 4.26×10^{-4} molL^{-1}		: λ_3 = 299 nm
θ	: 3.53×10^{-5} m^{2}mol^{-1}	$^{\#}K_a$ at 208 nm	: 12.03×10^3 molL^{-1}
ΔG_{ad}^o	: -13.13 kJ mol^{-1}	$^{\#}K_a$ at 245 nm	: 96.58×10^3 molL^{-1}
$^{*}K_a$	: 59.91 ×10^{-3} molL^{-1}	$^{\#}K_a$ at 299 nm	: 22.84×10^3 molL^{-1}
ΔG_a^o	: -24.10 kJ mol^{-1}	$\Delta G_{\lambda 1}^o$	: -23.29 kJ mol^{-1}
		$\Delta G_{\lambda 2}^o$	: -28.45 kJ mol^{-1}
		$\Delta G_{\lambda 3}^o$	: -24.88 kJ mol^{-1}

*surface tension and using C^{-n} method

$^{\#}$ uv spectroscopy method

UV-vis spectroscopic method

The UV-vis spectral data plays an incomparable method for analysis of inclusion behavior of host-guest complex. Here, UV-vis spectral data have been employed to evaluate the stiochiometry of the complexation and binding association. Stiochiometry had manifested by dint of Job's method which known as continuous variation method, while binding association with the help of Benesi-Hildebrand equation.

Job's plot for determination of stoichiometry of guest: host inclusion complex

A set of stock solutions (hydrazinophthalazine + βCD) have been formulated separately by varying the mole fraction (x) of the hydrazinophthalazine within the range x = 0 to x = 1 with keeping the total concentration of the species are constant. The absorption spectra at λ_{max} has observed for each set of solution at room temperature (T=298.15K). Then, Job's plot has generated by

plotting ($x \cdot \Delta A$) against mole fraction (x), where ΔA is absorption difference of hydrazinophthalazine in presence and absence of βCD, and $x = [HP]/\{[HP]+[\beta CD]\}$. This fraction ($x$) provides the stiochiometry of the complexes. As for example, when x = 0.25, the ratio of the guest and host complex is 1:3; similarly, the mole fraction 0.33, 0.50, 0.66, and 0.75, assigned 1:2, 1:1, 2:1, and 3:1 respectively. In Figure 3 we have shown a plot of $x \cdot \Delta A$ *vs* x for with corresponding absorption maxima at 271 nm.

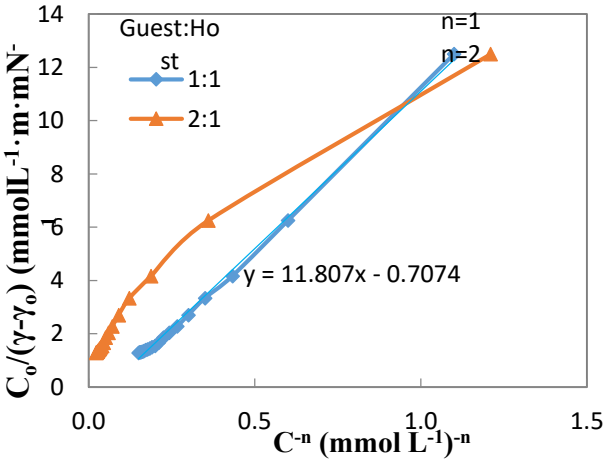


Figure 2. Plot of $C_o/(\gamma-\gamma_o)$ of hydrazine-phthalazine against concentration of βCD (C^{-n}; n=1 or 2)

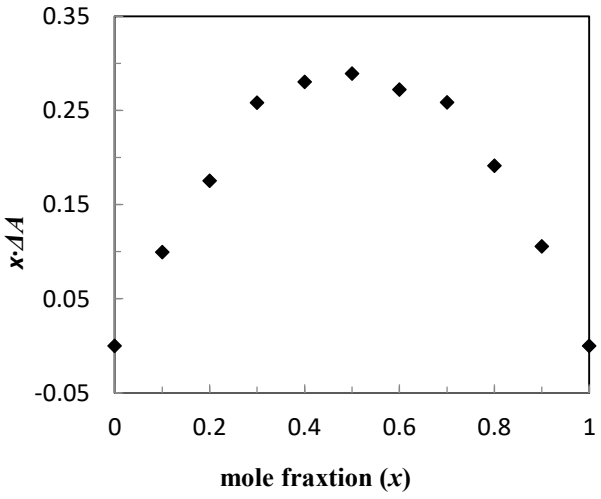


Figure 3. Jobs plot of hydrazinophthalazine + βCD

A half oval-shaped was observed from in Figure 3, where $x \cdot \Delta A$ is maximum at x = 0.50. This implies, 1:1 stiochiometric dimensional (or volume) fit guest-host inclusion complex has formed.

Binding constant and free energy change

The degree of encapsulation and retention of the guest molecule in the interior cavity of βCD can be explained by stability of the complex, binding nature, binding strength and standard free energy change. Binding potency in term of constant (K_a) of inclusion were explored by Benesi-Hildebrand method for 1:1 complex. The double reciprocal plot was obtained using the Equation.

$$\frac{1}{\Delta A} = \frac{1}{\Delta\varepsilon\,[HP]K_a}\frac{1}{[\beta CD]} + \frac{1}{\Delta\varepsilon\,[HP]} \qquad (12)$$

Where, ΔA attributes the difference of guest absorbance before and after complexation with βCD. In order to compute the binding constant changes in absorbance (ΔA) were plotted against wave length (λ) at different concentration (0 to 2.8 mM) of βCD (Figure 4). Inspection of Figure 4, the absorbance maxima have observed at 208 nm, 245 nm and 299 nm. If we notice the λ_{max} of hydrazinophthalazine is at 211, 240, 260, 304, and 315 nm (where, βCD is UV inactive), the absorbance maxima of complex at 208 nm is blue shift with respect to 211 nm; and 245 nm and 299 nm are red shift with respect to 240 nm and 260 nm respectively. The effect observed can be expressed that this is due to π - π* electron transition between the aromatic ring. Double reciprocal plot of $\frac{1}{\Delta A}$ vs $\frac{1}{[\beta CD]}$ has been plotted at 208 nm, 245 nm and 299 nm and represented at Figure 5. Binding constant (K_a) has been calculated from intercept by dividing slope at 208 nm. Similar way has employed at 245 nm and 299 nm and the magnitudes have listed in Table 1. After that standard free energy changes

(ΔG_{λ}^{o}) have been work out by means of K_a. Scrutiny of the Table 1, expose very high values of K_a than estimated from surface tension; on the other hand these are extremely high than adsorption constant. The results are in line with surface measurement that association/binding capacity of inclusion is higher than adsorption. Alternatively, the standard free energy changes (ΔG_{λ}^{o}) are more or less lie within the range, as obtained from surface tension computation. Overall, it can attribute that 1:1 ratio is powerful complexation with great stability and feasible at lower energy.

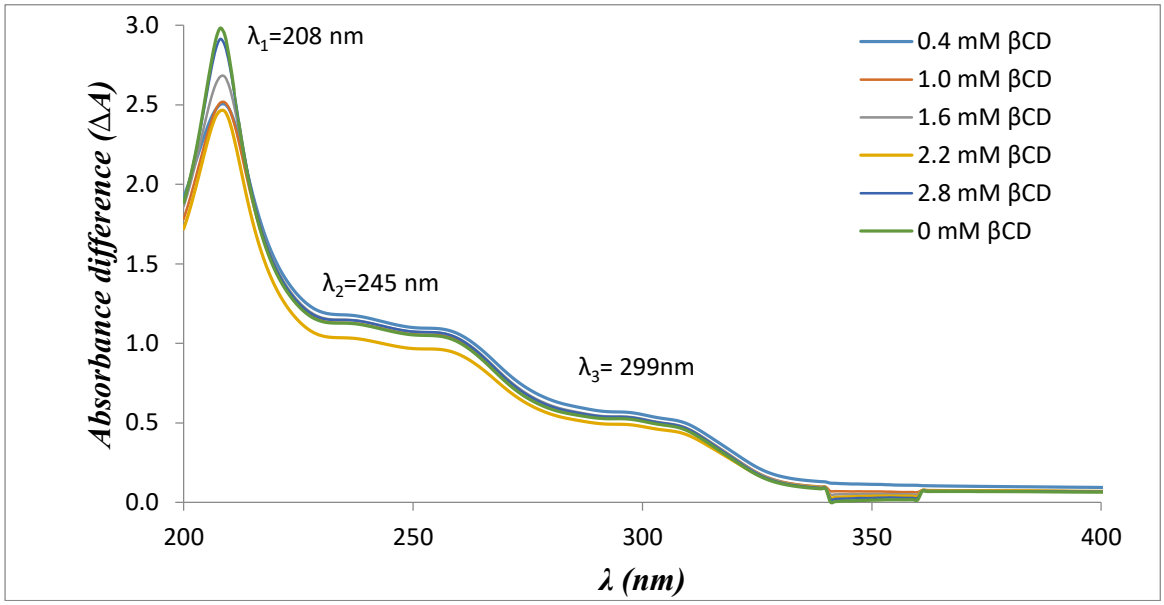


Figure 4. Absorption spectra of hydrazinophthalazine in presence and absence of βCD

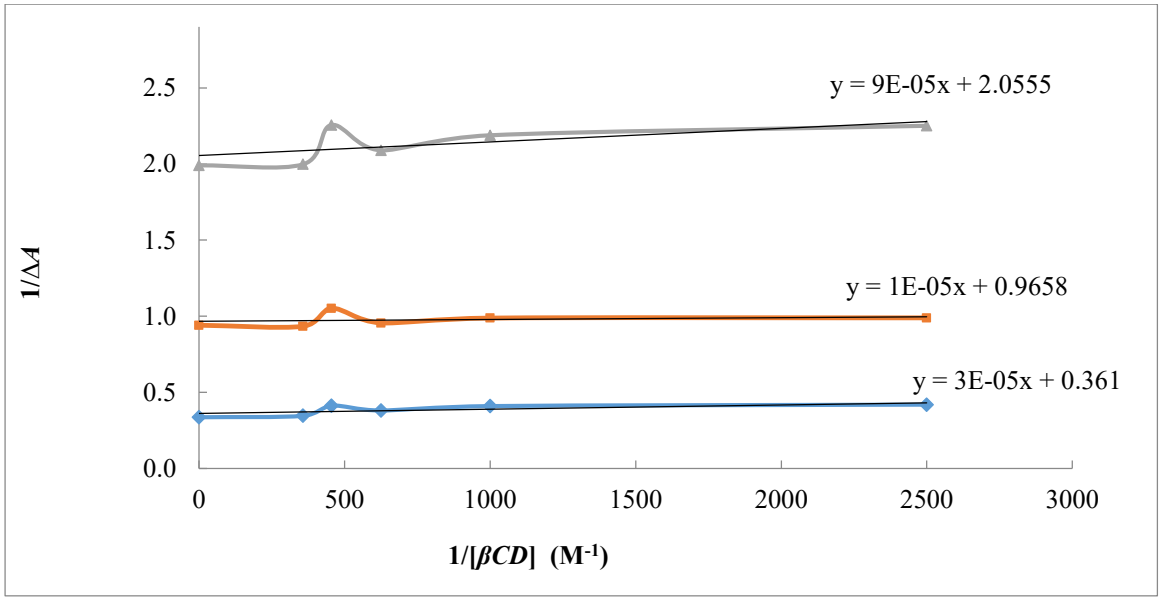


Figure 5. Double reciprocal plot of $\frac{1}{\Delta A}$ vs $\frac{1}{[\beta CD]}$

Conductivity

Conductivity data is also an important tool to elucidate the inclusion phenomenon in the solution [31]. From the scrutiny of the data, it is obvious that the specification conductance (κ) is decreasing gradually, due to the fact of encapsulation of charged HPHC molecules into the β-CD cavity (Figure 6). Single break in the conductivity curve, at 5 mM of β-CD, suggests that hydrazinophthalazine and β-CD complex with equimolar ratio; and therefore, the host-guest stiochiometry of the complaxation is 1:1.

Structural feature of guest and host molecules

Complex formation between the guest hydrophobicity and the host apolar cavity can only make the clear sense if we demonstrate the fitting with respect to their molecular dimension or volume. The noticeable feature of the inner cavity size is 6.0Å – 7.0Å (6.0-6.5Å [7]) of the β-cyclodextrin molecule provides a potential environment, in which appropriate size apolar moiety of the guest meet and form stable complex [32]. The qualified dimension of hydrazinophthalazine [33] is 5.25Å (apolar benzene ring) and 6.6 Å (two unit of benzene ring+side chain of hydrazine part) (Scheme 2), where the apolar moiety benzene rings are eligible for incorporation in the cavity. According to the dimensional fitting approach or in view of the dimension of both the apolar part of guest and space of cavity, it is confirmed that only one hydrazinophthalazine moity can occupied the cavity of one cyclodextrin molecule. In other word we may say that there is only 1:1 stiochiometric complaxation are occurring. The tendency of the occupation is driven by the water molecules present into the cavity of cyclodextrin [34]. Because the water molecules present into the cavity are highly energetic and unfavourable, consequently they are substituted and pull the hydrophobic moiety of guest insight into cyclodextrin cavity. Inside the cavity, they undergo hydrophobic-hydrophobic interactions and cyclodextrin ring strain is diminished, as a result the complex becomes stable with lower energy. But, it should be note that during the complex formation there are no covalent bonds breaking or forming. The complexation occurs with retention of configuration of cyclodextrin. They are attached via non-covalent bonds like hydrogen bond, van der Waal force, electrostatic force, hydrophobic interactions etc. While, the $-NH=NH_2$ is arrested at the periphery by secondary –OH groups of cyclodextrin through H-bond or electrostatic force or hydrophilic-hydrophilic interactions. Hence, the plausible formation of 1:1 guest-host ratio as if by magic molecular encapsulation is remarkably agree with the experiment and observed data analysis from surface tension and UV-vis spectroscopy.

^{1}H NMR analysis of complexes

The protons in βCD are in different environments. From the side of cavity, $H^{3'}$ and $H^{5'}$ proton is located near the wider and narrower rim respectively; whereas $H^{1'}$, $H^{2'}$ and $H^{4'}$ were oriented at the exterior of CD molecule (Scheme 3).

^{1}HNMR spectra of complex, β-CD, and pure hydrazinophthalazine are represented in Figure 7. Where, the signals of the interior $H^{3'}$ and $H^{5'}$ protons of CD as well as the interacting aromatic protons of hydrazinophthalazine showed down-field shifts (Table 2 and Figure 7), that confirms the formation of complex.

Higher value of the chemical shift (δ) in case of $H^{3'}$ proton than $H^{5'}$, also provide the information that the guest choose the wider rim to incorporate into the cavity of β-CD (Scheme 2).

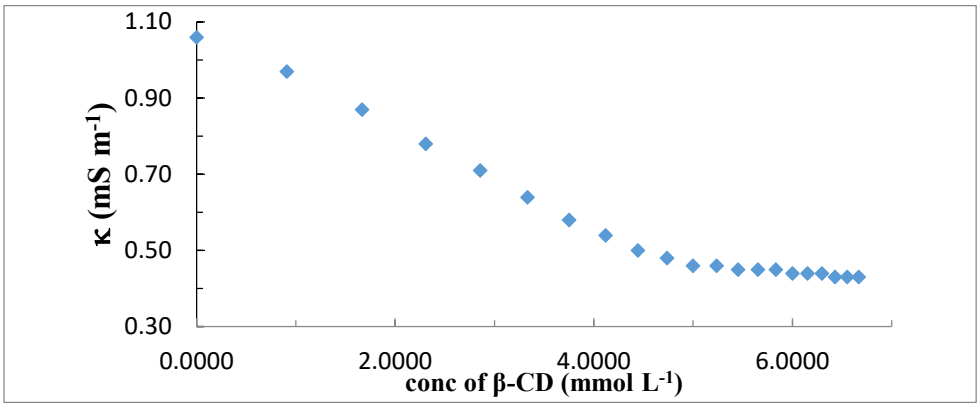
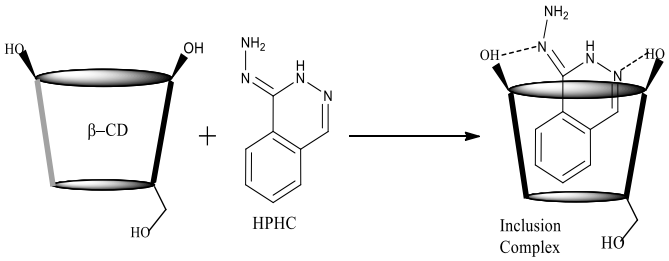
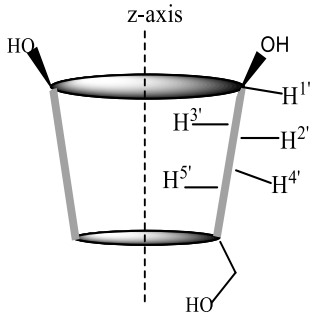


Figure 6. Plot of specific conductivity (κ) corresponding to conc. of β-CD

Scheme 2. Schematic representation of 1:1 inclusion complex



Scheme 3. Interior and exterior proton of β-cyclodextrin



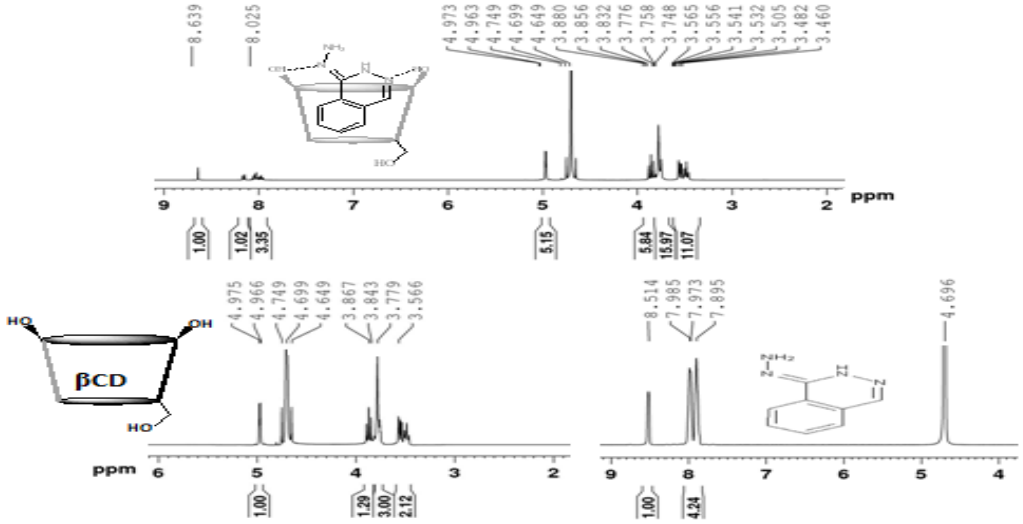


Figure 7. [1]HNMR spectra of complex, β-CD, and pure hydrazinophthalazine in D_2O respectively

Table 2. Chemical shifts (**δ**/ppm) of protons of β-Cyclodextrin after complex formation

Protons	**δ** βCD	**δ** (βCD+HP)	**Δδ** (βCD+HP)
$H^{3'}$	3.867	3.832	0.35
$H^{5'}$	3.779	3.758	0.21

Scanning electron microscopy (SEM)

Scanning Electron Microscopy (SEM) used to analyze the surface texture and particle size of the complex. The surface morphology of pure hydrazinophthalazine, pure β-CD, and inclusion complex are shown in Figure 7. A vast difference has seen between the morphological structures of pure hydrazinophthalazine or β-CD and the complex. So, this is one of the evidence that indicating the strong complexation (Figure 8).

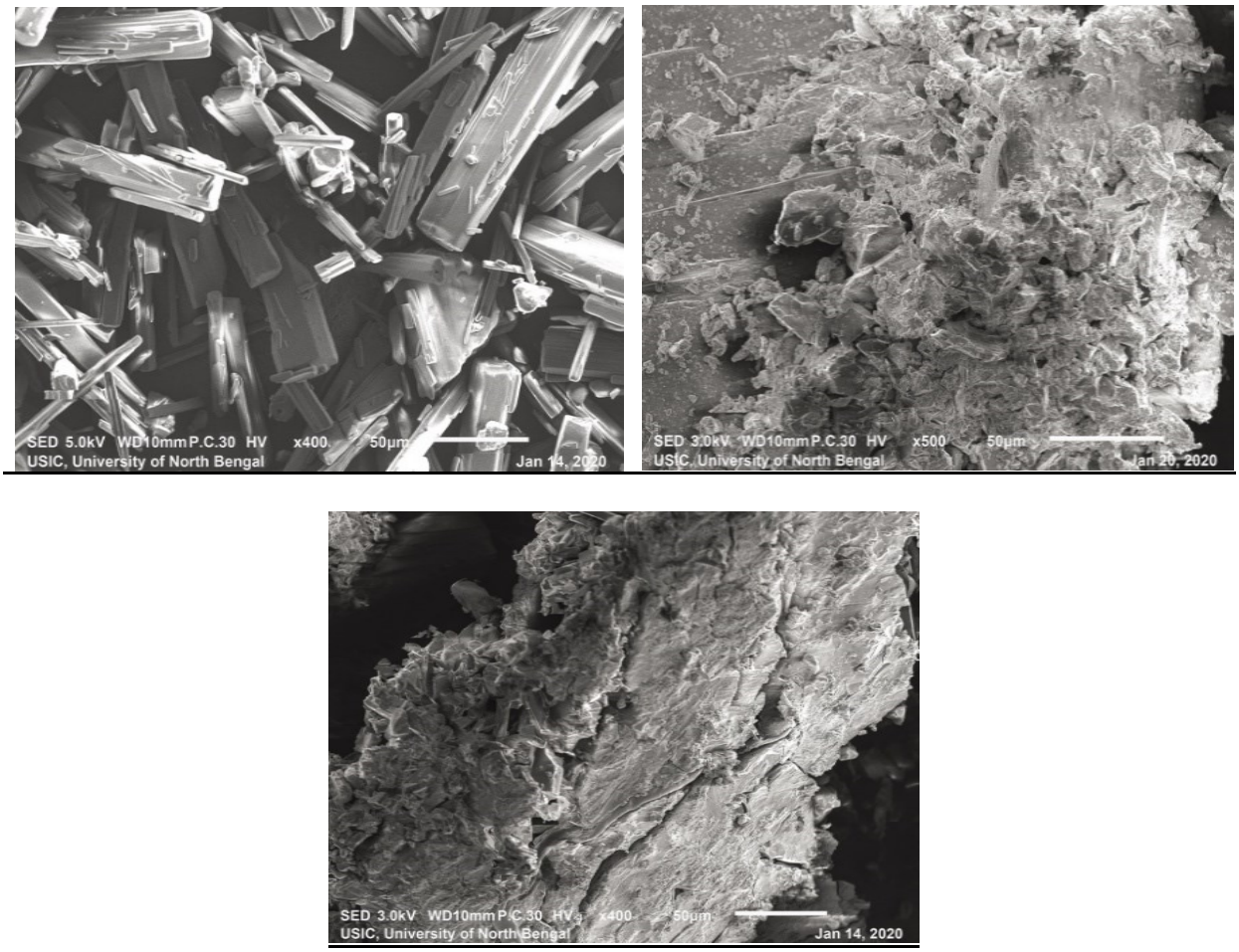


Figure 8. SEM picture of hydrazinophthalazine, β-CD, and inclusion complex respectively

Conclusions

This study demonstrated that the hydrazinophthalazine molecule is incorporated insight into the truncated cone type hydrophobic cavity of β-cyclodextrin molecule and form 1:1 stiochiometric complex. Binding the stiochiometry and constants observed from both the surface tension and UV-vis spectroscopy are demonstrating the same

observation that the host-guest inclusion complex formed with great stability. Conductivity, ^{1}HNMR, and SEM picture also support and agree with this result. The complex was formed by replacing the water molecules present into the cavity of cyclodextrin (which make a driving force for incorporation of guest molecule) and becomes stable with non-covalent interaction. The formed inclusion balance both surface and bulk properties of the solution by adsorption and inclusion phenomena. However, the inclusion phenomena are dominant over the surface adsorption.

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