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Physical properties and phase solubility studies of Schiff base and their inclusion complexe

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ABSTRACT: The inclusion complex between Schiff base and β-cyclodextrin was prepared and the mode of interaction between guest and host was confirmed by IR-HNMR and XRD methods. The important advantages of these interaction are the enhancement of the aqueous solubility of Schiff base and increase of zeta potential and these two characteristics are important in pharmaceutical industries.

Keywords:Schiff base, inclusion complexes, zeta potential, phase solubility.

I. INTRODUCTION:

Schiff base are compounds resulting from condensation of primary amines with carbonyl compounds, exhibit many applications one of them in pharmaceutical industry due to their antimicrobial, antioxidant activities[1, 2].

Cyclodextrins (CD) are cyclic oligosaccharides consisting of glucopyranosyl units linked by α-(1,4) bonds[3]. The widely used natural cyclodextrins are α-, β- and γ-cyclodextrin consisting of 6,7 and 8 glucopyranose units, respectively.The toroid shape of cyclodextrins which differ in the size of cavity and the same height. The host-guest system which occurs through a physicalforce such as vander waals, electrostatic and hydrogen bonding[4, 5].

the advantages of inclusion complex formation between cyclodextrin as a host and the drugs or organic and inorganic compounds as guest are enhancement of the aqueous solubility[6], increase the thermal or photo stability, controller the drag release, ete[7, 8].

II. MATERIAL AND METHODS:

6-methyl-3-formylchromone was purchased from Merck (Germany), benzocaine was purchased from ChemCenter and used as received β-CD was purchased from Across organic chemical company. Ethanol absolute was supplied byJ.T.Baker.

Spectral measurement:IR spectra were recorded as KBr pellets on Shimadzu FT-IR 8300 Spectrophotometer in the ring 4000-400 cm^{-1}. HNMR spectra were recorded DMSO-d_6 solution at room temperature on the Bruker 500(500 MHz).TMS as internal reference. EI-mass spectrum of Schiff basewas recorded on Agilent technologies 5975c. spectrometer XRD pattern were recorded on PERT Panalytical(Netherland)using Cu Ka radiation(λ=1.54060 A°) and analyzed from 2θ (0-60°). SEM images were performed using ZEISS SIGMA (Carl Zeiss microscopy) the images were obtain through secondary electrons with attention of 15 KV and the magnification 10-20 Kx and the sample was cooled with gold to render them electrically conductive. Zeta potential was recorded as aqueous solution after sonicated for 20 min at room temperature using nano particle analyzer model sz-100 Horiba(Japan).

Phase solubility studies:

The phase solubility studies were performed according to Higuchi and Connors method[9]. An excess amount of Schiff base was added to10 mL aqueous solution of βCD in different concentration (0, 0.001, 0.003, 0.006, 0.009, 0.012, 0.015) $mol.L^{-1}$. The samples were mixed at room temperature for 24 h. After that the suspination were filtered through a Whatman paper and filtrate concentration were determined by UV-visible after diluted for 25 times.

Preparation of Schiff base:

In 50 mL R.B.F 30 mL of absolute ethanol was heated and 0.595 g(5 mmol) of benzocaine and 0.745 g(5 mmol) of 3-formyl-6-methylchromone, 2 drops of conc.$H_2SO_4$was added and the resulting mixture was refluxed for 8 h [10]. The reaction was monitored by TLC using ethyl acetate : chloroform 7:3 as eluent until the reaction complete. then the solution cooled to room temperature and the solid product was filtered and recrystallized from ethanol to obtained Light yellow precipitation, m.p.155-157°C yield 72.7%

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Preparation of Inclusion complex:

The freeze-drying method was employed to prepare the inclusion complex as following an equimolar of Schiff bases and β-CD were mixed in 50 ml deionized water and the mixture was stirred at room temperature for 72 h, then the solution lyophilized in a freeze dryer. The resulting fine powder was collected and kept in a desiccator over silica gel[11-14].

III. RESULT AND DISCUSSION

The Schiff base which prepared in this study are stable non hygroscopic, insoluble in water and sparingly soluble in common organic solvent but soluble in DMSO and DMF. The inclusion complexresulting from Schiff bases and β-CD is lightyellow powder,stable,non hygroscopicsparingly soluble in water.

The Schiff base was characterized by mass spectra where the mass spectrum show an intense peak at m/z = corresponding to molecular ion [M^+]. In agreement with proposed structural formula and indicated the condensation of 3-formyl-6-methylchromone with benzocaine in 1:1 molar ratio.

IR spectra of Schiff base and its inclusion complex:

The IR spectrum of Schiff base show a characteristic band at 1606 cm^{-1} which attributed to stretching vibration of azomethine group HC=N which indicate to formation of Schiff base in addition the following bands at 1691,1660 and1278cm^{-1} which attributed to C=O (ester group),C=O (ketonic) and C-O respectively. When compared these data with the IR spectrum of its inclusion complex noted that a significant shift in the position of bands as shown in fig.(1) and the data in Table (1).

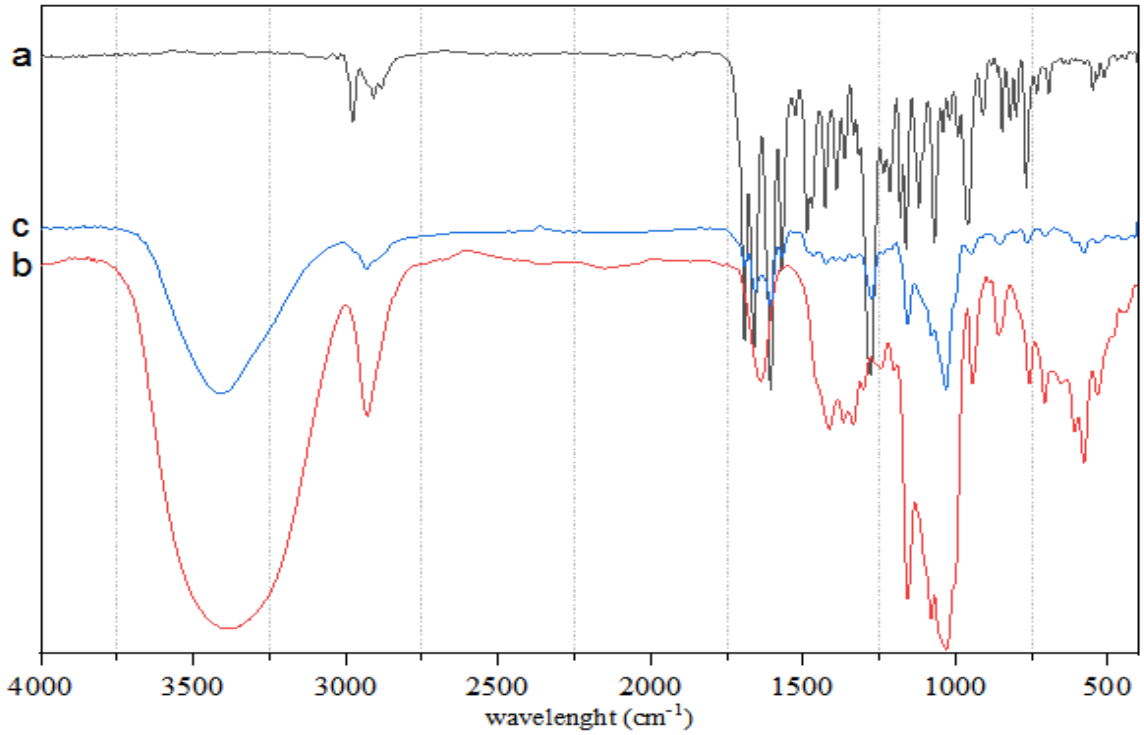

Fig.1.FTIR spectra of (a) Sb (b) βCD (c) Sb:βCDinclusion complex

Table 1 Important position (υ) and Δυ for Sb,βCD and Sb:βCD inclusion complex

Band	βCD	Sb	Sb:βCD	Δυ
OH	3377	-	3414	+37
$-CH_2$	2929	-	2931	+3

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C-O-C	1155	-	1157	+2
O-H bending	1029		1031	+2
C=O aster	-	1691	1691	-
C=N	-	1606	1606	-
C=C	-	1570	1568	-2
C-O	-	1278	1274	-4
C=O ketone	-	1660	1656	-4

HNMR Spectra:

The Of Schiff Base Confirmed By The HNMR Spectrum Result Where The Signal Of Azomethine Proton Appeared At 8.12 Ppm. All Signal Are Listed (Table 2) Together With The Spectra Of Free Bcd And Inclusion Complex. The Change In The Chemical Shift Of Signals Of Schiff Base As Well As H_5 And H_3 Protons Of Bcd Indicated The Formation Of Inclusion Complex (Fig. 2).

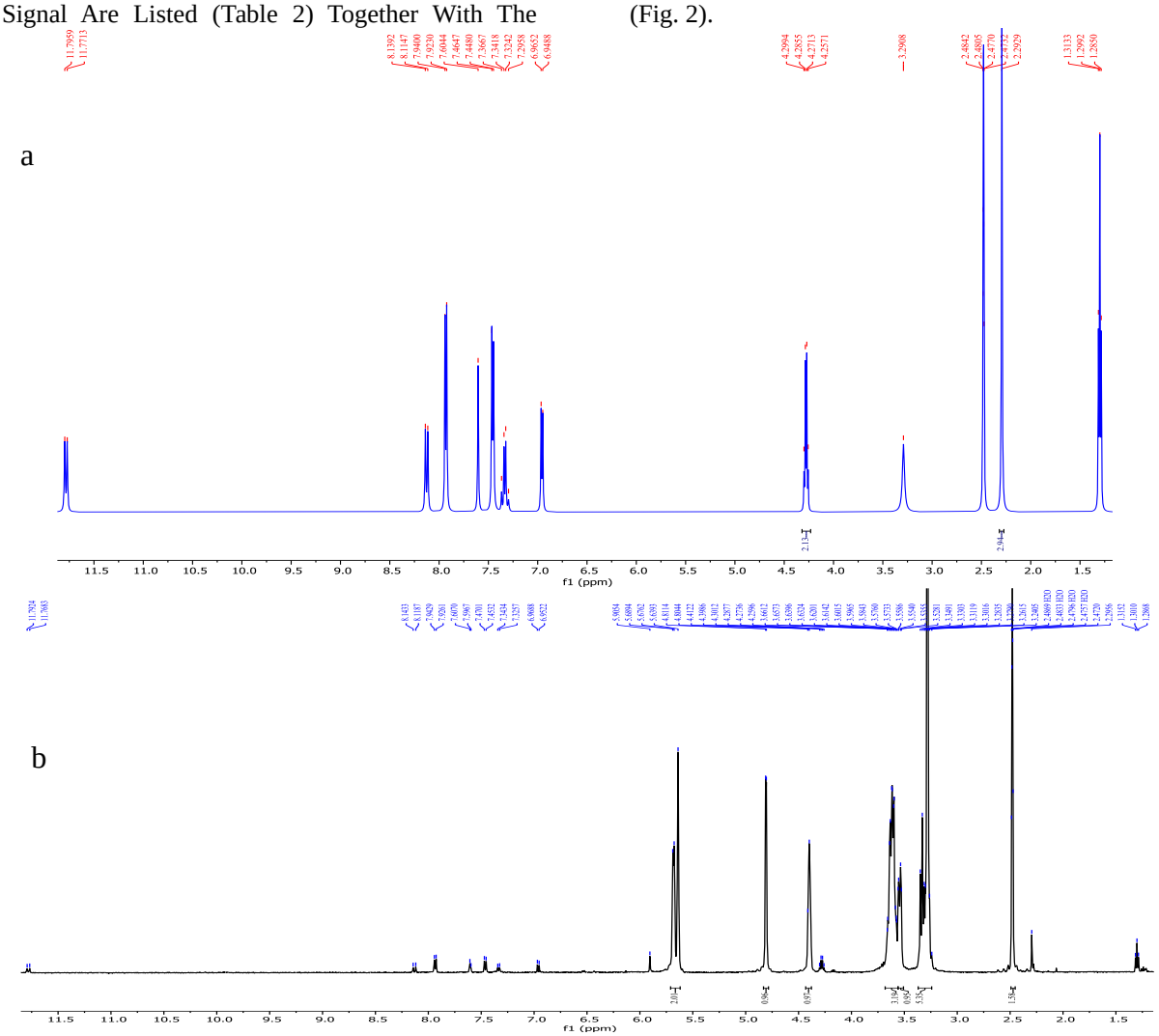

Fig.2.HNMR spectra of (a) Sb (b) Sb:βCD inclusion complex

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Fig.3. Chemical structure of Schiff base.

Table 2 Chemical shifts (**δ**) and **Δδ** for Sb, βCD and Sb:βCD inclusion complex

proton	Free Sb	Free βCD	complex	**Δδ**
a	1.2988		1.3010	0.0022
b	4.2777		4.2807	0.0030
c	7.9312		7.9342	0.0030
d	7.4566		7.4615	0.0049
e	8.1272		8.1313	0.0041
f	11.7835		11.7801	-0.0034
g	6.9568		6.9603	0.0035
h	7.2312		7.2354	0.0042
j	2.2927		2.2956	0.0029
i	7.6059		7.6064	0.0005
OH-2		5.765	5.682	-0.083
OH-3		5.707	5.639	-0.068
H1		4.822	4.808	-0.014
OH-6		4.510	4.399	-0.111
H3		3.624	3.617	-0.007
H5		3.551	3.545	-0.006
H2,H4		3.332	3.340	0.008

X-ray powder diffraction (XRD):

The diffractograms of Sb andSb:βCD inclusion complex are presented in Fig.4.Thediffractogram of the inclusion complex differs from the Schiff base diffractogram[15]. The appearance of new peaks, as well as the shifts of some peaks of Schiff base were noticed in the diffractogram of theinclusion complex[16, 17]. On the otherhand, the high crystallinity of the synthesized Schiff base was confirmed based on very significant peaks in the diffractogram.

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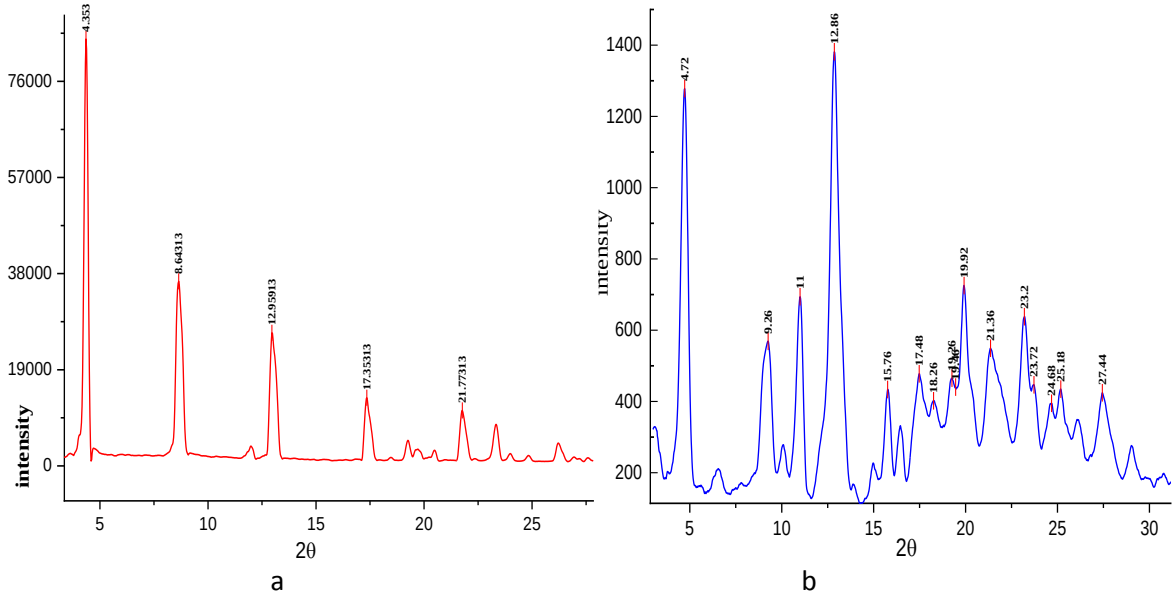

a b

Fig.4. Diffractogram of (a) Sb (b) Sb:βCD inclusion complex

Zeta potential:

Zeta potential is an important property inpharmaceutical industry[18] where the dispersion system stability is possible Zeta potential value close to ± 30 mV. The Zeta potential of pure Schiff base(Sb) was negative (-29.9 mV) and Zeta potential of its inclusion complex was more negative (-46.6 mV) Fig.5.

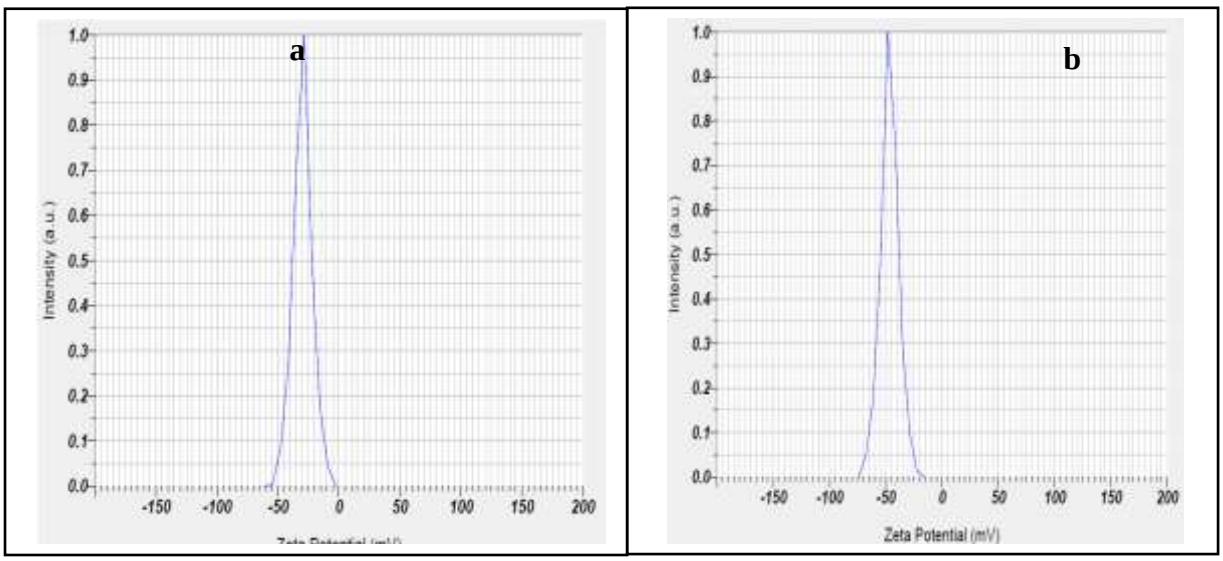

Fig.5. Zeta potential of (a) Sb (b) Sb:βCD inclusion complex

Phase solubility studies:

The stability constant (K_s)was calculated from the straight line (fig.6) of the phase solubility diagram. The resulting linear curve can be classified as "A_L" type.It should be noted that the solubility of Schiff base increase by 3.9fold and the stability constant which determined from Higuchi and Connors relation.

$$\mathbf{K = slope/S_\circ(1 - slope)}$$

Where $S_\circ$ is the solubility of Sb in the absence of βCD and from intercept. The K_s was calculated and found to be 0.222 M^{-1}.

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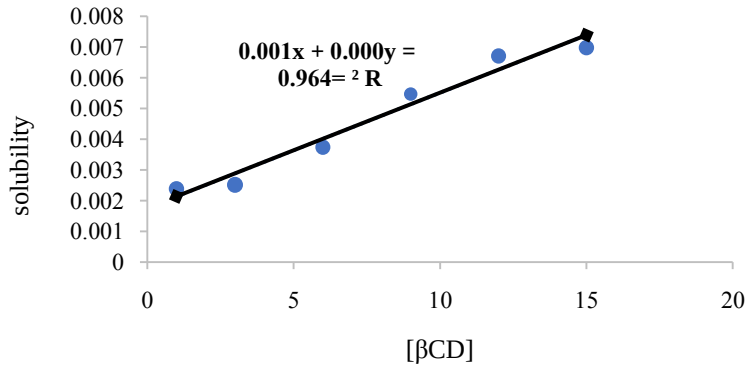

Fig.6: Phase solubility study of Sb and βCD

SEM analysis:

SEM image of Sb and Sb:βCD inclusion complex as show in Fig.7. A drastic change in morphology and crystalline nature was observed which confirmed the interaction between the Schiff base and βCD during the formation of inclusion complex[19].

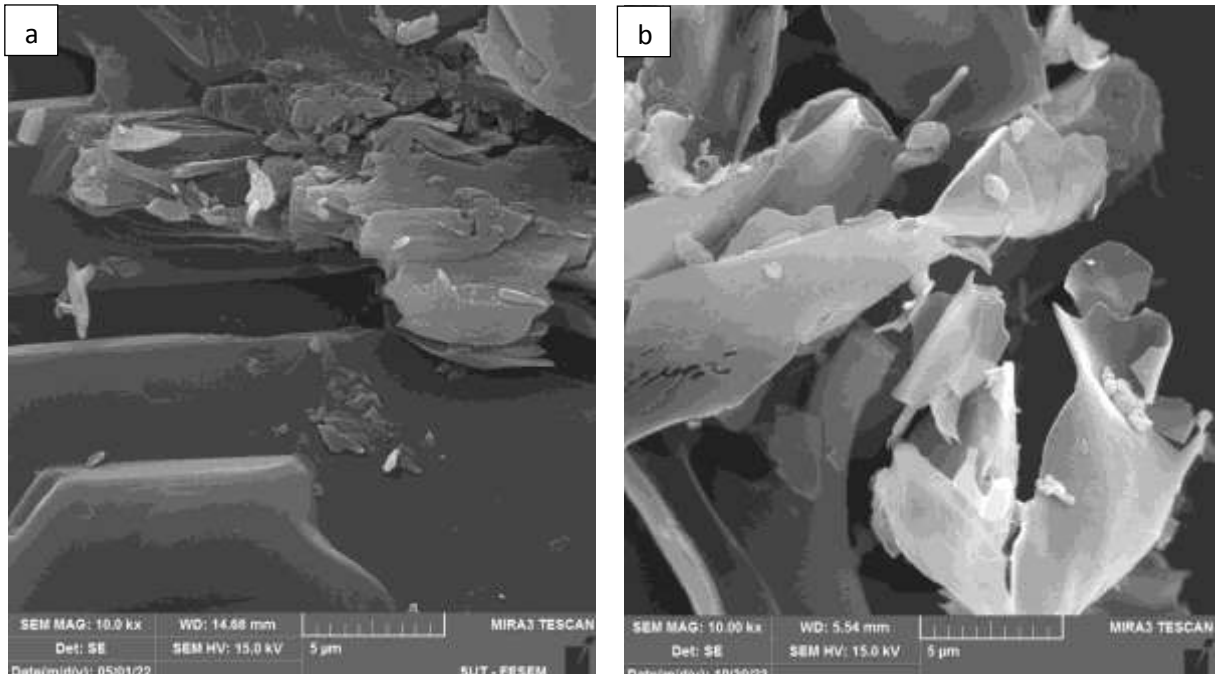

Fig.7 SEM of (a) Sb (b) Sb:βCD inclusion complex

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