

Physical Properties and Phase Solubility Studies of Sulfadiazine Schiff Bases Inclusion Complexes with β -Cyclodextrine

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Abstract

A novel inclusion Complex of Sulfadiazine Schiff bases with β Cyclodextrine were Prepared , the formation of inclusion Complexes has been studied by IR ,HNMR ,SEM and XRD methods , The improvement of Solubility of Schiff bases and the 1:1 stoichiometry of the Complexes was Confirmed followed Higuchi and Connors method . The amorphous nature of the resulting inclusion Complexes were confirmed by SEM and XRD . The crystallite size of Schiff bases and the corresponding inclusion complexes were determined using Willamson –Hall method

Keywords: Sulfa drugs; Freezdrying; Higuchi-Connors; Willamson –Hall; SEM

Introduction

Schiff bases are compounds containing azomethine group resulting from condensation of primary amines with carbonyl compounds. Schiff bases exhibit many applications such as used to development various bioactive compounds that are used in pharmaceutical industry. They are used as antimicrobial, antioxidant, anticonvulsant ets . Schiff bases also used in industry as a catalyst, anticorrosion inhibitors and in dye and pigments industries [1].

β -Cyclodextrine is one of macrocyclic oligosaccharides consist of seven glucopyranose units joined together via α -1,4 glycosidic bonds to formation a cone shaped structure with a hydrophobic nature cavity and hydrophilic outer surface , by this coracterstic structure cyclodextrines are able to formation inclusion Complexes , and the purpose of Preparation of inclusion Complexes to improved chemical , physical and biological properties compared to the guest molecules , for example increase the aqueous solubility increase the stability against oxidation or photo decomposition ets . [2].

Materials and Methods

Materials: Sulfadiazine was purchased from Sigma – Aldrich Company, Salcildehyde and 2- hydroxy naphthaldehyde were purchased from BDH, β -CD was obtained from Across Organic Company. All solvent used are of analytical grad and used as received without further Purification [3].

Spectral measurement: IR spectra were recorded as KBr Pellets on Shimadzu FTIR-8300 spectrophotometer in the region 4000–400 cm^{-1} . ^1H NMR were recorded as DMSO- d_6 solution at room temperature on a Bruker 500 (500 MHz) TMS as internal reference. EI - Mass Spectra were recorded on Agilent Technologies 5975C Spectrometer. XRD Patterns were recorded on Panalytical X ' PERT Panalytical X ' PERT PRO ,(Panalytical Company) , Netherlands using Cu $K\alpha$ radiation ($\lambda=1.54060 \text{ \AA}$) and analyzed from $2\theta(0-60^\circ)$ [4].

Scanning Electron Microscopy (SEM) of free and complexes were performed using ZEISS SIGMA VP from Carl Zeiss Microscopy , Germany , the images were obtain through secondary electrons with attention of 15 KV and the magnifications 10-20 KX and the samples was coated with gold to render them electrically conductive [5].

Preparation

Preparation of Schiff bases : 5 mmole (1.25 g) from Sulfadiazine dissolved 50 ml hot absolute ethanol in R.B.F and add to this solution 5 mmole(0.67 g) of Salcildehyde dissolved in 10 ml absolute ethanol . 2 drops of conc. H_2SO_4 was added and the resulting mixture refluxed for 3 hrs and the reaction pathway was monitored by was used as eluent. The reaction mixture was left overnight in refrigerator and the resulting precipitate filtered and drying in oven, to afford the yellow precipitate, m.p 184-185 $^\circ\text{C}$ yield 62% [6].

Preparation of: 4-(((2- hydroxynaphthalen-1-yl)methylene)amino)-N-(pyrimidine-2-yl)benzenesulfonamide (SDHN) by the same above method the compound SDHN was prepared after refluxing for 5 hrs to afford a yellow crystals , m.p 241-243 $^\circ\text{C}$ yield 70% [7].

Preparation of Schiff bases - β -Cyclodextrine inclusion Complexes freeze drying method was employed to synthesis the inclusion Complexes were 1:1 molar ratio of β -CD and Schiff base was mixed in deionized water and the resulting mixture was stirring for 72 hrs at room temperature , The solution freezing and then lyophilized in a freeze drying type CHRIST , modle alpha LD plus . until completely drying and the resulting fine powder kept in desiccator over silica gel [8] .

Results and Discussion

The two Schiff bases which prepared in this study are stable and nonhygroscopic, springily soluble in most common organic solvent but soluble in DMF and DMSO. The compounds and mode of interactions between Schiff base as a guest and β -CD as a host were investigated by IR and ^1H NMR spectra.

IR : The IR spectrum of SDS a strong band at 1621.21 cm^{-1} which attributed to C=N stretching and indicate the formation of Schiff base , another strong band at \acute{u} 1581 cm^{-1} attributed to C=N stretching of Sulfadiazine moiety the strong bands at 1492 cm^{-1} and 1446 cm^{-1} attributed to skeletal C=C stretching , two very strong bands at 1340 cm^{-1} and 1166 cm^{-1} attributed to asymmetric and symmetric stretching of SO_2 group and very strong band at 943 cm^{-1} attributed to S-N. A Comparison of IR spectrum of SDS with corresponding inclusion Complexes, the azomethine band shifted to high frequency ($\Delta\nu = + 1.92 \text{ cm}^{-1}$

1) and decrease the intensity of the band, while the position of C=N of diazine moiety remain in the same position which indicated the interrupted of azomethine inside the cavity, also a significant change in position of band attributed to SO₂ and C=C. The IR spectrum of SDHN show a strong band at 1624 cm⁻¹ attributed to azomethine (C=N) group stretching, strong bands attributed to C=C at 1556.77 ,1449 and 1442.7 cm⁻¹ , two very strong band at 1340.5 and 1157.29 cm⁻¹ which attributed to SO₂ asymmetric and symmetric stretching respectively . A Comparison of these data with IR of corresponding inclusion Complexes SDHN-β-CD, no change was observed in the position of O=S=O bands and S-N band which indicated that these group don't interped in the cavity of β-CD and small change (+1.93) in the position of azomethine group which indicated the week interaction between the guess and the β-CD cavity [9].

HNMR: HNMR spectrum of SDS which indicated the formation of Schiff base where the singlet signal attributed to (HC=N) proton where a observed at δ 8.95, a broad signal at δ11.85 and δ12.5 attributed to NH and OH protons respectively. The aromatic protons signals appear in the expected region at δ 6.98 -8.5 ppm. A comparison of 1HNMR of SDS with corresponding inclusion Complexes SDS-β-CD a significant change in all aromatic position of SDS after Complexation which indicated the interaped of aromatic ring inside the cavity , als a significant change in the H3 and H5 of the β-CD moiety which lay inside the cavity.

HNMR of SDHN and their inclusion Complexes: The 1HNMR spectrum of SDHN show a singlet signal at δ 8.53 ppm attributed to azomethine proton, broad signal at δ11.86 attributed to NH proton, singlet signal down field at δ 15.34ppm which indicated the presence of OH proton. And a series of signals attributed to aromatic proton in the region δ6.98 to δ8.06 ppm . A comparison of these data with HNMR spectrum of SDHN-β-CD a significant change of H3 and H5 of the β-CD were shifted to high field , Δ δ for H3 = -0.18 and for H5=-0.38 ppm , also the azomethine show a small change Δ δ=-0.06 ppm , the change in aromatic protons chemical shift was depicted [10].

Mass spectra: EI mass spectrometry analysis of both SDS and SDHN show the molecular ions at m/z which in agreement with the suggested structure, where the SDS show a molecular ions at354 m/z and SDHN show a molecular ions 404 at m/z.

XRD: The diffractograms of the guest, β-Cyclodextrine and inclusion complexes. Both the guest (SDS) and β-Cyclodextrine shows a crystalline nature the intense peaks of crystalline nature of while the inclusion complexe diffractogram show the amorphous nature. The crystallite size and lattice strain was calculated from Williamson –Hall plot, the slope represent the lattice strain and the crystallite size in nm determined from the intercept using the following equation (Table 1).

Table (1): The results of Williamson-Hall method Comp.

Comp.	crystallite size	lattice strain
SDS	68.96	0.0031
SDHN	39.13	0.003

SEM: The images of β-CD show amorphous and heterogeneous character ,while SDS image show similar to clumped rocks shape .The image of SDS- β-CD inclusion complexe revealed morphological differences which indicate the formation of the inclusion complexes whereas the complexe show plate like shape with irregular edges . with size average D= 99nm where the

size average of SDS equal $D=130\text{nm}$. SDHN image two shapes can be seen parallelepiped shape and cone shape with size average $D=352\text{ nm}$, while the inclusion complexes image showing a few particle similar to the original shape of SDHN which indicated that the complexion has not been complete but all image have amorphous shape with average size $D=238\text{ nm}$.

Phase solubility studied

The Phase solubility of SDS and SDHN were performed according to the Higuchi and Connors method. excess (25 mg) of SDS or SDHN was added to the aqueous solution of different concentration of β -CD ranging from 0.001 to 0.015 M. The resulting suspension were shaken at room temp. for 72 hrs. After that the suspensions were filtered through Whatman No.1 filter paper and the concentration of SDS or SDHN was determined by UV spectrophotometer at λ 259 for SDS and at λ 263 for SDHN. The solubility constant was calculated from the straight line slope of the experimental diagrams using the relation Where S_0 is the solubility of SDS or SDHN in the absence of β -CD determined from intercept. The resulting linear curve can be classified as AL for both SDS and SDHN. It should be noted that the solubility of SDS solubility increase by 4.033 fold and SDHN increase by 13.05 folds. The binding constant of SDS or SDHN complexes were calculated according to the eq.1 and it was found to be 962 M^{-1} for SDS complex and 1607 M^{-1} for SDHN.

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