RESEARCH PAPER

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Spectrophotometric and Thermodynamic Parameters of Albendazole – Chloranilic Acid Complex in Dioxane

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Albendazole–chloranilic acid complex in dioxane was analysed spectrophotometrically. The optimum conditions for the complexation were determined. The stoichiometry for the complex was found to be 1:1 through Job's methods of continuous variation. Benesi- Hildebrand equation was used in the determination of the association constant, molar absorptivity and hence free energy for the complex was calculated.

Albendazole (methyl-5-propylthiobenzimidazol-2-ylcarbamate) is an anthelmintic with activity against most nematodes and round worms.[1] It is also effective against some larval stages and ova of the susceptible worms. The drug is official in the USP 20th revision.[2] This official compendium describes chromatographic and potentiometric assays of the drug. The physical and chemical properties of albendazole have been described.[3] It is a white powder freely soluble in formic acid and slightly soluble in chloroform but practically insoluble in water, dilute mineral acids, alcohol and ether.

The interaction between π -acceptors and electron donors results in the formation of molecular complexes. Some of these interactions give coloured complexes resulting in the use of this reaction in the detection of drugs and other compounds on TLC plates.[4-5] It has equally resulted in the formation of products that absorb at longer wavelength from those of the reactants, enhancing the spectrophotometric determination of those compounds.[6-10] P-Acceptors are compounds that have electron withdrawing substituents or have empty molecular orbital that are capable of accepting or sharing electron with an electron rich system (electron donors). The detail of the charge–transfer interaction has been discussed.[11] The forces involved in typical charge-transfer interaction are not more than 30 kJ mol^{-1}, which is not surprising in view of their long range character compared with covalent bond length.[12] Charge–transfer complexation occurs from the Highest Occupied Molecular Orbital (HOMO) of the donor to the Lowest Empty Molecular Orbital (LEMO) of the acceptor. The extent of charge-transfer being determined by whether the complex is in ground or excited state. In the ground state, the usual intermolecular physical forces apply and the extent of charge-transfer is comparatively small. The complex, however, may be raised to the excited state by the absorption of light energy of suitable wavelength at which electron is wholly transferred from donor to acceptor.

EXPERIMENTAL

SP8-100UV spectrophotometer, product of Pye Unicam, England; was used for the spectral determination. Chloranilic acid was procured from BDH, England, while 1,4-dioxane and 98% formic acid were procured from M&B, England. Albendazole and Zentel® were obtained from SmithKline Beecham, France. Albendazole was certified to be 99.8% pure through potentiometric tritration.[2]

Preparation of standard solution:

Six hundred milligrams of albendazole was accurately weighed out and dissolved in 50 ml of formic acid to

prepare 45.2 mM of the solution. The Zentel® solution was prepared by weighing out 0.673 g of Zentel® corresponding to 0.2 g of albendazole and soaking it in 20 ml of formic acid. The suspension was filtered, washed with formic acid and the volume was made up to 50 ml with formic acid to prepare 15.2 mM solution. Solution of chloranilic acid in dioxane, 3.54 mM, was made by dissolving suitable quantity of chloranilic acid in exact volume of dioxane. Other necessary standard solutions were obtained by dilutions.

Optimal conditions for the complexation:

Absorption spectrum of chloranilic acid was obtained by scanning suitable concentration of chloranilic acid in dioxane against a blank, dioxane. Suitable concentration of albendazole-choloranilic acid complex was scanned in the spectrophotometer against formic acid in dioxane. The absorbances at different time intervals using the same concentration of the complex were measured at λ–max. At different temperatures, absorbances were measured for the complex at λ–max and optimum time for complexation against a blank, formic acid in dioxane.

Determination of stoichiometry for the complex:

Suitable volumes of 23.9 mM of albendazole and suitable volumes of 23.9 mM of chloranilic acid were mixed in such a way that the molar fraction of albendazole is 1 to 0 in the mixtures. Their absorbances were measured at the above detected optimal conditions.

Determination of association constant and molar absorptivity for the complex:

Different volumes of 45.2 mM of mebendazole were mixed with each of 1 ml of 1.53 mM of chloranilic acid and their absorbances measured at room temperature and at λ-max after 60 min of mixing against a blank of formic acid in dioxane.

Calibration graph and assay of Zentel®:

Different concentrations of the complex containing 0.5-14 mg of abendazole in 100 ml but maintaining 1:1 mebendazole chloranilic acid molar ratio were prepared. Their absorbances were measured against a blank of formic acid in dioxane. The Zentel® solution was assayed using the above generated standards.

RESULTS AND DISCUSSION

Mixing albendazole in formic acid with chloranilic acid in dioxane resulted in the formation of a purple solution. This colour development can be attributed to the formation of charge-transfer complex between albendazole as the electron donor (D_o) and cholranilic acid as π–acceptor (A_o). The general reaction is shown in equation I.

$$nD_o + mA_o = [D_o nA_o m] \qquad I$$

The complexation was substantiated by the mixture absorbing at longer wavelengths from that of the original materials. It had a λ-max at 540 nm different from and higher than those of albendazole and chloranilic acid. The absorption spectra of chloranilc acid and albendazole-chloranilic acid complex are shown in fig. 1.

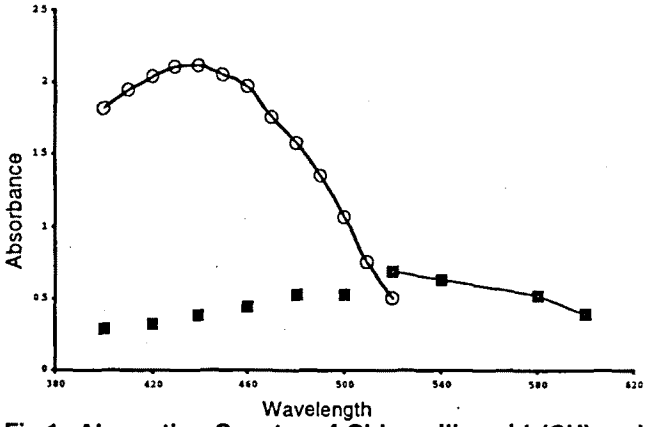

Fig.1: Absorption Spectra of Chloranilic acid (CH) and albendazole-chloranilic acid [AICH] complex

CH-represents chloranilic acid spectrum; while

AICH - represents albendazole-chloranilic acid complex spectrum.

At 30 min from time of mixing, complexation was found to be maximum. Fig. 2 shows the time absorbance relationship at room temperature. From fig. 3 it was observed that 30-50° seems to favour this complexation. The stoichiometry for the complex was determined using Job's method of continuous variation.[13] In a donor-acceptor reaction represented as in equation I, the absorbances measured have a large value for the complex than for A or D. From fig. 4 the stoichiometry is 1:1.

Benesi-Hildebrand method[14] was used in the determination of association constant and molar absorptivity. This method is centered on equation II.

$$\frac{[A_o]}{A_c} = \frac{1}{k_c E_\lambda D_o} + \frac{1}{E_\lambda} \qquad II$$

Where $[A_o]$ and $[D_o]$ are concentration of the acceptor and donor respectively. Aλ Eλ, k_c are the absorbance, molar absorptivity and association constant for the com-

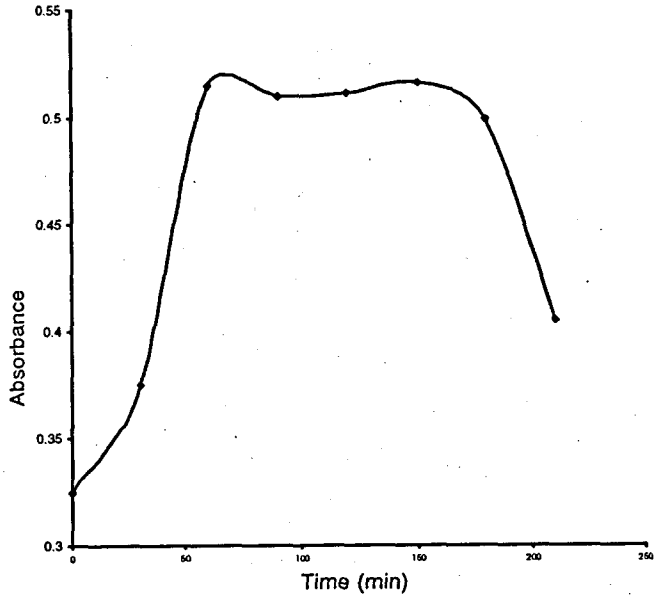

Fig. 2: Time-related changes in the albendazole-chloranilic acid complex formation
Figure shows the absorbance of albendazole-chloranilic acid complex in a mixture of formic acid and dioxan measured at different time intervals

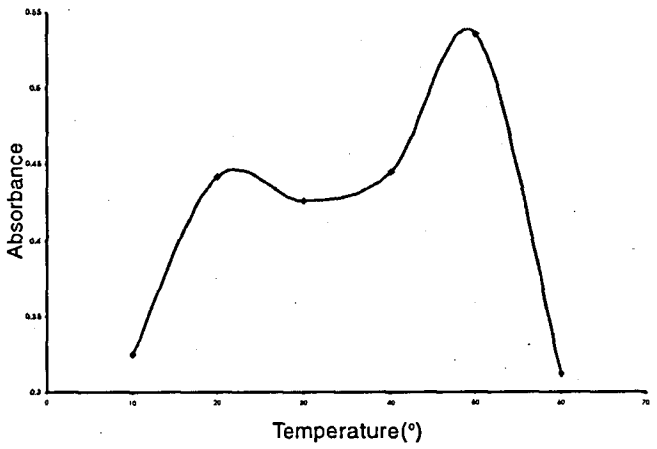

Fig.3: Effect of temperature on the formation of albendaozle-chloranilic acid complex
Figure shows the absorbance of albendazole-chloranilic acid complex in a mixture of formic acid and dioxan measured at different temperatures

plex at wavelength (λ) respectively. The result is shown in fig. 5 and Table 1. The standard free energy charge ΔG° for complexation is related to association constant, k_c, as in equation III.[15]

$$\Delta G^\circ = - 2.303\ RT \log k_c \ldots \quad III$$

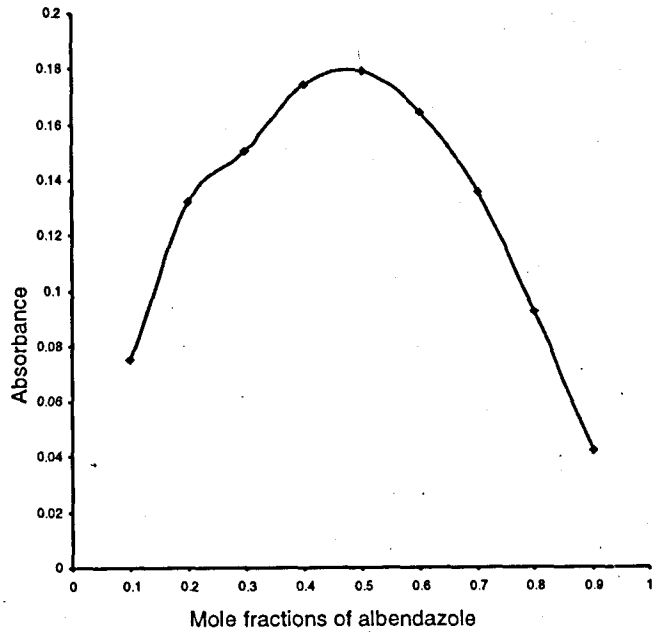

Fig. 4: Job's plot of continous variation for albendazole-chloranilic acid complex
The mole fractions of albendazole were prepared by mixing suitable volumes of 23.9 mM of albendazole with suitable volumes of 23.9 mM of chloranilic acid and absorbances were measured at λ_{max}

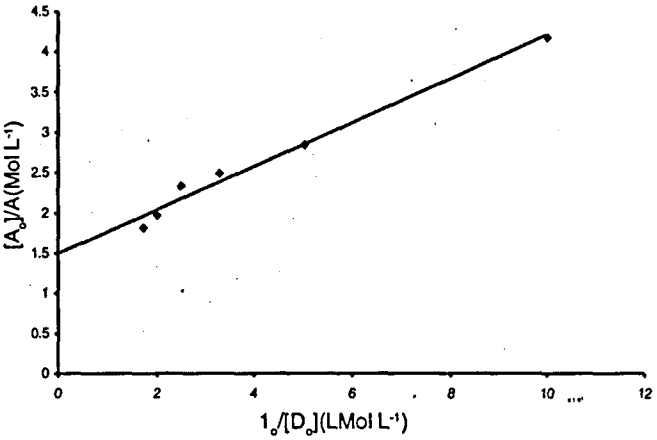

Fig.5: Benesi - Hildebrand plot for albendazole -chloranilic acid complex
[Ao], [Do] and A represent concentration of chloranilic acid, concentration of albendazole and absorbance, respectively

where, R is the universal gas constant, T is temperature in Kelvin. The result and other statistical data of the regression equation for the complex are shown in Table 1.

TABLE 1: OPTICAL AND THERMODYNAMIC PARAMETERS AND REGRESSION EQUATION FOR THE COMPLEX

Maximum wavelength (nm)	540
Association constant (l mol^{-1}.)	0.947
Free energy charge (kcal mol^{-1}.)	– 4.78
Beer's law limits (mg% w/v)	2–12
Regression equation Intercept (a)	0.932
Slope	0.054
Percentage recovery (%)	97.35 ± 3.23*
Molar absorptivity (l mol^{-1} cm^{-1})	909.1

* mean ± standard deviation of seven determinations, percentage recovery from the label claim amount of Zentel® (200 mg of albendazole)

Within the described experimental conditions, the graph obtained by plotting absorbances at λ-max against the concentrations found to be linear over the Beer's law range given in Table 1. This method was applied to assay Zentel. The results obtained were in agreement with those given in the official procedure since the calculated mean percentage recovery was 98.26%, which was in agreement with the theoretical value.

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