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Spectrophotometric Determination of Captopril Through Charge-Transfer Complexation

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Captopril was quantitatively determined using chloranilic acid through charge-transfer complexation. Favourable conditions like time and temperature for the complex formation were determined. The wavelength for maximum absorption of light by the complex was 520 nm. The complex formation was maximum 30 min after mixing the reactants and room temperature was favourable for the complex formation. Captopril and chloranilic acid formed 1:1 complex in a mixture of dioxan:chloroform activated with dimethylsulphoxide. The association constant, molar absorptivity and free energy change for the complex were 0.6971 l/mol, 2.2462x10² l/mol.cm and 8.828 kcal/mol, respectively. Beer-Lambert's law was obeyed in the concentration range of 0.4–1.4 mg% (w/v) of captopril. This method was employed in the analysis of captopril in dosage forms and the mean percentage recovery was 96.7%.

Charge-transfer complexation is a term used to describe certain types of interaction with distinctive features that arises from the formation of weak complexes, one acting as an electron acceptor and the other as an electron donor. The standard free energy change for the complexes is typically in the order of few kcal/mole[1]. The complex exists in two states; a ground state and an excited[2]. In the ground state, the two molecules involved in the interaction experience the normal physical forces one would expect for two molecules in close proximity such as Van der Waals forces, and in addition, a small amount of charge is transferred from the donor to the acceptor. The excited state results when the complex in ground state absorbs light of suitable energy and the electrons which is only slightly shifted towards the acceptor is almost wholly transferred. It is the transfer of electrons on absorption of light that gives the characteristics colours to these complexes. The widely accepted mechanism of charge transfer complexation is that of the Mulliken's[3]. Weak interactions between an electron donor and acceptor exist. For such interaction to occur there is a jump of on pair of electron initially occupying a molecular orbital in the donor to an unoccupied molecular orbital in the acceptor in such a way that the excited electron still remains paired to its original electron partner. The electron donor and acceptor moieties then tend to orient themselves relative to one another in such a way as to make a maximum overlap. The contribution of the ground state to the charge transfer structure is usually very small. The theory of charge-transfer complexation has been thoroughly discussed[4]. Charge-transfer complexation has been employed in quantitative determination of albendazole[5], famotidine[6], promethazine hydrochloride[7], and ketamine hydrochloride[8]. The interaction has assisted in location of famotidine[9] and cimetidine on chromatogram.

Captopril [1-(3-mercapto-2-methyl-1-oxopropyl)-L-proline] is an angiotensin converting enzyme inhibitor. It is a white or off-white crystalline powder with characteristic sulphide-like odour. The melting point is within 104–110°. It is freely soluble in water, alcohol, chloroform and methanol. Other physical and chemical properties have been discussed[10,11]. The pharmacokinetics, pharmacodynamic and pharmacology of the compound have been studied[12,13]. Captopril was qualitatively detected on chromatogram using dimethylamino benzaldehyde[14] and was equally determined titrimetrically[11]. This study aims at quantitative determination of captopril though charge-transfer complexation using

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chloranilic acid as titrant. The physico-chemical parameters of the complex formed are to be determined. The favourable conditions for the complexation are to be determined.

MATERIALS AND METHODS

The materials used were sourced commercially and were of analytical grade. P-Chloranilic acid and 1,4-dioxan were products of BDH chemicals Ltd. England while chloroform was product of May and Baker, England. Captopril tablets were products of Approved Prescription Service Ltd, Eastbourne England. SP10-100 ultraviolet spectrophotometer (Pye Unicam, England) was used to measure absorbances.

Preparation of standard solutions:

A quantity of chloranilic acid (0.1045 g) was dissolved in 100 ml of 1,4-dioxan to prepare 5.0 mM solution of chloranilic acid. Other concentrations of chloranilic acid were obtained by dilution. Thirty tablets of captopril (unbranded, 25.0 mg per tablet, and product of Approved Prescription Services Ltd, Eastbourne, England) were pulverised and extracted with enough quantity of chloroform. The filterate was evaporated to dryness and the residue recrystallized twice with chloroform and decolourised with bone charcoal. This gave a white crystalline powder with melting point of 105°. A stock solution of captopril (5 mM) was prepared by weighing out 0.025 g of captopril and dissolving in 50 ml of chloroform. Other solutions were obtained by dilution with chloroform.

Determination of absorption spectra for chloranilic acid, captopril and chloranilic acid-captopril complex:

Two millilitres of 5.0 mM of chloranilic acid was made up to 4 ml with dioxan and was scanned over a wavelength range of 400 nm to 600 nm against, a blank of dioxan. Two millilitres of 5.0 mM of captopril was made up to 4 ml with chloroform and the solution was scanned over a wavelength range of 200–500 nm against a blank of chloroform. Two millilitres of 5.0 mM of captopril was mixed with 2 ml of 5.0 mM of chloranilic acid and a drop of dimethylsulphoxide was added into the mixture. The mixture was scanned at room temperature against a blank containing 2 ml, each, of dioxan and chloroform plus a drop of dimethylsulphoxide.

Determination of favourable conditions for the complex formation:

The absorbances of a mixture of 2 ml of 5.0 mM of chloranilic acid and 2 ml of 5.0 mM of captopril plus a drop of dimethylsulphoxide were measured at various time intervals, at 520 nm and at room temperature against a blank of a mixture of the solvents in the ratio they occur in the mixture. A similar mixture was prepared and the absorbances of the mixture were measured at different temperatures and at 520 nm, after the complex has stood for 30 min.

Stoichiometric determination for the complex:

Job's method of continuous variation[15] was used to determine the stoichiometry for the complex. Equal concentrations (5.0 mM) of captopril and chloranilic acid were used. Different molar ratios of captopril and chloranilic acid were prepared and their absorbances measured at room temperature and at 520 nm against a blank of dioxan and chloroform in the ratio they occure in the mixture, after the mixture had stood for 30 min. Each of the reaction medium was activated with a drop of dimethylsulphoxide.

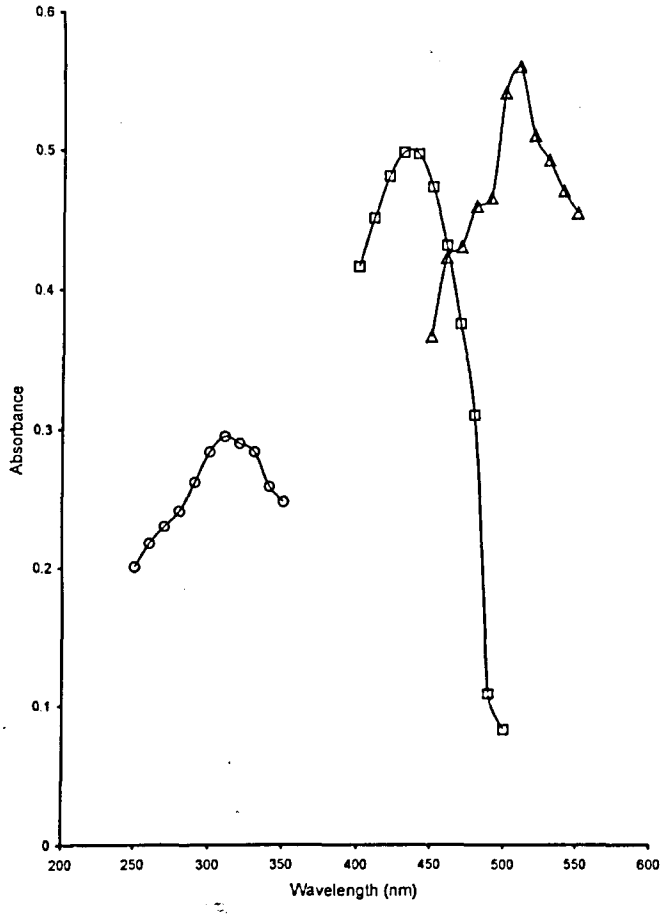

Fig. 1: Absorption spectra of captopril, chloranilic acid and captopril:chloranilic acid complex.

The graph shows spectra of captopril (-○-) chloranilic acid (-□-) and captopril:chloranilic acid complex (-△-).

Determination of association constant, molar absorptivity and free energy for the complex:

Benesi-Hildebrand method[16] was used in these determinations. Serial volumes (0.4, 0.8, 1.2, 1.6, 1.8, 2.0 ml) of 2.3 mM of captopril were transferred into different test tubes and 1.0 ml of 5.0 mM of chloranilic acid was added to each of the test tube. The mixtures were made up to 4 ml with chloroform and activated with a drop of dimethylsulphoxide. The mixtures were left at room temperature for 30 min and their absorbances were measured at 520 nm against the mixture of the solvents in the ratio they occurred in the reaction medium.

Assay of captopril tablets:

Absorbances of different concentrations of captopril-chloranilic acid complex were measured at room temperature and at 520 nm against a mixture of dioxan chloroform and dimethylsulphoxide in the ratio they occurred in the reaction medium. The media stayed 30 min after mixing the reactants before the absorbances were measured. The values were used to prepare Beer's plot.

An amount of pulverised captopril tablets equivalent to 10 mg of captopril was exhaustively extracted with chloroform and the extract was made up to 100 ml with chloroform. Required volume of standard chloranilic acid solution was added to a known concentration of the captopril solution and a drop of dimethylsulphoxide was added. The absorbance of the mixture was measured at 520 nm, observing the detected favourable conditions for the complex

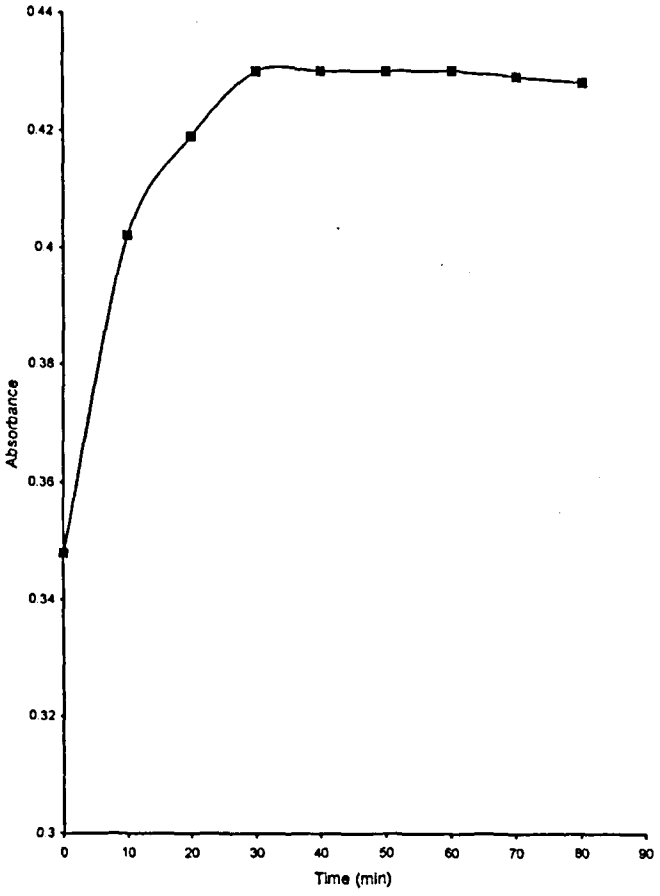

Fig. 2: Effect of time on captopril:chloranilic acid complex formation.

Absorbances of a mixture of captopril:chloranilic acid activated with a drop of dimethylsulphoxide at different time intervals.

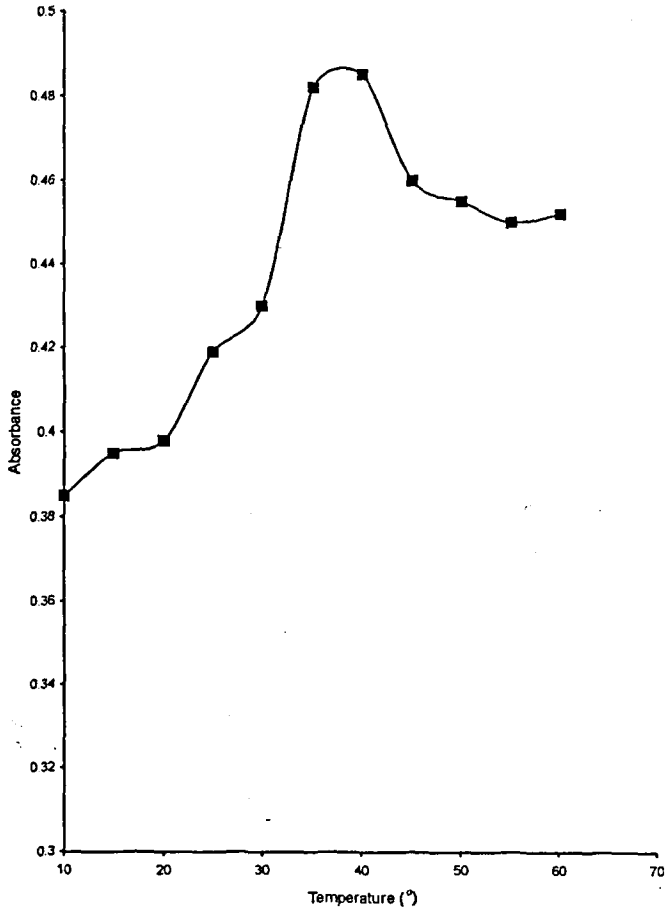

Fig. 3: Effect of temperature on captopril-chloranilic acid complex formation.

Absorbances of a mixture of captopril:chloranilic acid activated with a drop of dimethylsulphoxide at different temperature.

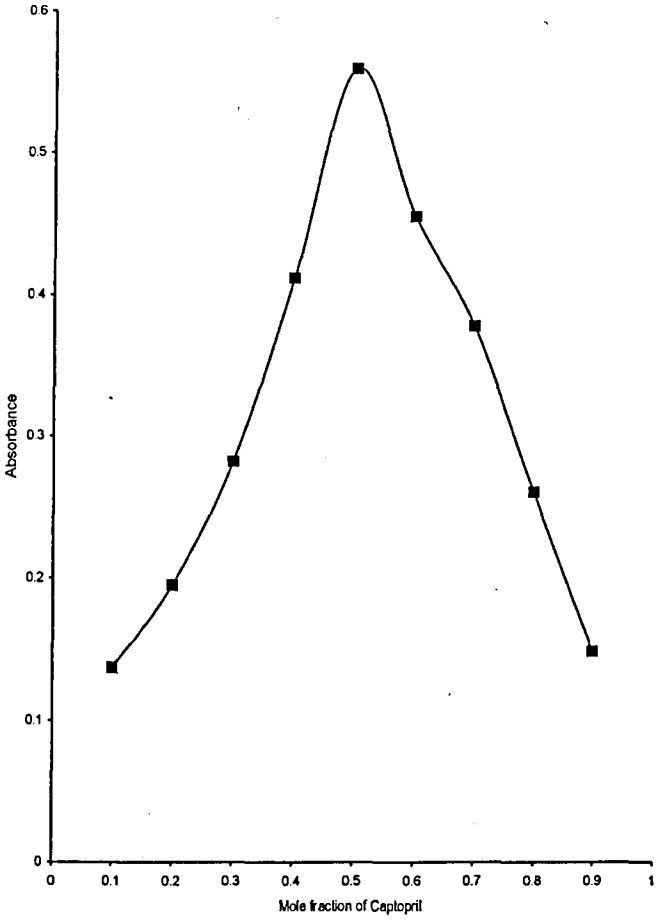

Fig. 4: Job's plot of continuos variation for captopril-chloranilic acid complex.

Absorbances of mixtures containing different molar ratios of captopril:chloranilic acid activated with a drop of dimethylsulphoxide.

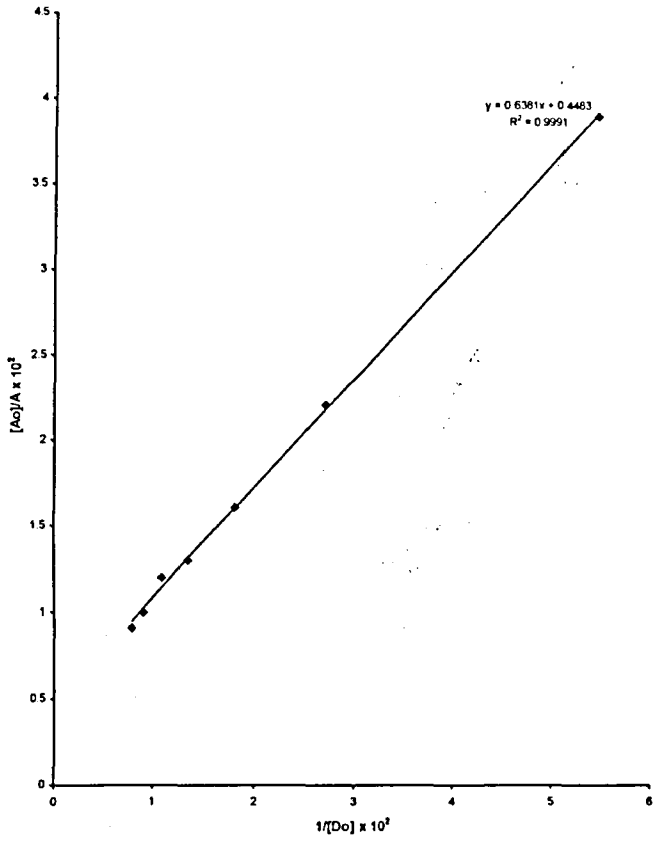

Fig. 5: Benesi-Hildebrand plot for captopril-chloranilic acid complex.

Where [Do], [Ao] and A represent the concentrations of captopril, chloranilic acid and absorbance, respectively

formation, against a mixture of the solvents in the ratio they occurred in the reaction medium.

RESULTS AND DISCUSSION

On mixing captopril in chloroform with chloranilic acid in dioxan, no colour change was observed. But on addition of a drop of dimethylsulphoxide into the mixture there was instantaneous golden purple colour observed. This colour development is an indication of stronger charge–transfer complex formation. It has been stated that polar medium favours charge-transfer complex formation.

The wavelength of maximum absorption of light by captopril, chloranilic acid and captopril chloranilic acid complex are 430, 310 and 520 nm, respectively. The spectra are given in fig. 1. The complex formation was maximum 30 min after mixing the reactants (fig. 2). It was observed that room temperature is favourable for the complex formation but maximum absorbance was observed at 39°. The temperature effect on the complex formation is shown as fig. 3. Through Job's method[15] of continuous variation, the stoichiometry was found to be 1:1 captopril: chloranilic acid, shown as fig. 4.

From the Benesi-Hildebrand plot[16], the association constant and molar absorptivity were determined. This plot depends on the fact that one of the components of the reactants should be in excess so that its concentration is virtually unaltered on formation of a complex. Here chloranilic acid is in excess. The molar absorptivity and association constant for the complex are 2.2462×10^2 l/mol.cm and 0.6971 l/mol, respectively. The standard free energy change, ΔG of the complex is related to the association constant as

indicated in Eqn. 1, $-\Delta G=2303$ RT log K, where, R, T and k are universal gas constant, absolute temperature in Kelvin and association constant, respectively.

Their values show that the complex is stable. Using the above equation ΔG was calculated to be 8.828 kcal/mol. The value of ΔG supported charge transfer complexation and indicates that the reaction is spontaneous since it has a negative value.

The complex obeyed Beer's law in the concentration range of 0.4–1.4 mg% of captopril in the complex. This method was employed in the analysis of captopril in dosage forms and the mean percentage recovery was 96.7%. This method is simple, precise, accurate and reproducible for the analysis of captopril even in dosage forms. When compared with titrimetric method it can determine captopril in lower concentration.

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