

## Spectrophotometric determination of drugs with iodine

T Karuna<sup>1</sup>, K Neelima<sup>1</sup>, G Venkateshwarlu<sup>2</sup> and P Yadagiri Swamy<sup>1,\*</sup>

<sup>1</sup>Department of Chemistry, University College of Engineering, Osmania University, Hyderabad 500 007

<sup>2</sup>Department of Chemistry, Nizam College, Hyderabad 500 001

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Spectrophotometric method is described for the determination of drugs through charge transfer complex formation with iodine acceptor. This method is based upon molecular interaction between drugs and iodine to form charge transfer complexes in which iodine acts as a sigma acceptor ( $\sigma$ ). Iodine was found to form charge transfer complex in 1:1 stoichiometry with all the drugs selected for study. Colored products were quantified spectrophotometrically by using absorption bands. Thermodynamic parameters and spectral characteristics of these complexes have been evaluated. A complete detailed investigation of the formed complex was made with respect to its composition, formation constant and free energy change. Electronic absorption bands are found shifted towards shorter wavelengths upon complex formation with iodine along with well-known blue shift of visible iodine band. The values of formation constants and thermodynamic parameters show a strong donor-acceptor interaction, which helps to study the possible site of interaction between the donors and the acceptors and also provides a tool for the estimation of drugs at both iodine band at 512 nm and blue shift band, which are sensitive to the drugs up to the concentration of  $10^{-3} M$ .

**Keywords:** Drugs, Iodine, Spectrophotometric determination

### Introduction

Iodine forms molecular complexes with a variety of aromatic, aliphatic and heterocyclic compounds<sup>1-3</sup> containing lone pair (non bonding) of electrons on oxygen, sulphur and nitrogen atoms, respectively, which act as electron donors and iodine itself acts as a  $\sigma$ -acceptor<sup>4-6</sup>. Bonding type involved in iodine is n- $\sigma$ . Complexation results in intensity decrease of iodine band with a simultaneous appearance of blue shift iodine band (BSB) and provides a significant, time saving, practical and economic method for the estimation of donors from intensities of iodine band and BSB. Formation of isosbestic point confirms that stoichiometry of drug complexes is 1:1. Origin<sup>7-9</sup> of BSB and charge transfer (CT) bands are explained in terms of valence band theory (VBT) and molecular orbital theory (MOT). Formation of CT complexes<sup>10,11</sup> is due to excitation of electrons from orbital of donor to orbital of acceptor. In present communication, UV spectrophotometric study provides an estimation method of therapeutic drugs<sup>12</sup> possessing antifungal, antidepressant, antihistamine,  $\beta$ -adrenergic properties from study of their complexes with iodine.

### Materials and Methods

Fisher certified iodine was repurified by sublimation twice under nitrogen atmosphere and was kept in a desiccator with calcium chloride and protected from the light. The solvent used was chloroform of spectro grade. The standard solution of iodine was prepared in chloroform. The pharmaceutical grade drugs were supplied by Arabindo Pharmaceuticals and Heterodrugs Pvt Ltd, Hyderabad in the form of acid salts.

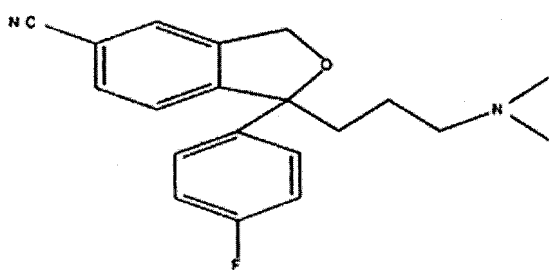
Spectrophotometric analysis for the study of electron spectral measurements was carried out on a SL-164 UV double beam spectrophotometer (Elico) having a fixed slit width with 1cm quartz cells, which is attached to the computer loaded with software and equipped with a printer.

### Preparation of Experimental Solutions

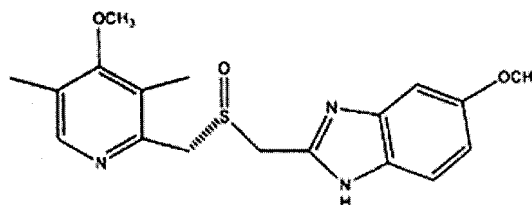
The concentration of iodine was held constant at  $9 \times 10^{-4} M$ . The drug was neutralized with 20% ammonium hydroxide solution and made the concentration up to  $10^{-3} M$  so as to produce a distinct decrease in the intensity of iodine band and BSB with sizable change in the intensity.

In volumetric flasks (10 ml each) sample solutions (1, 2, 3, 4 and 5 ml) were transferred by pipette and 5 ml of iodine solution were added in each flask. The

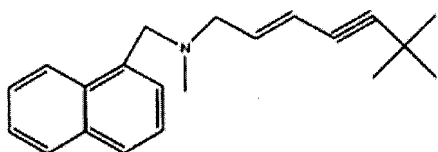
\*Author for correspondence  
E-mail: swamypy2003@yahoo.co.in



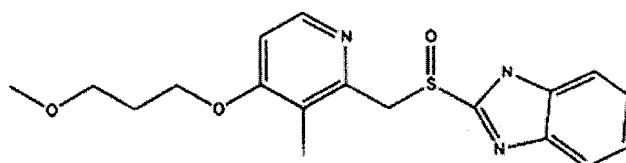
Escitalopram oxalate



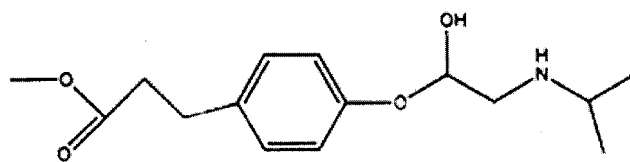
Esomeprazole



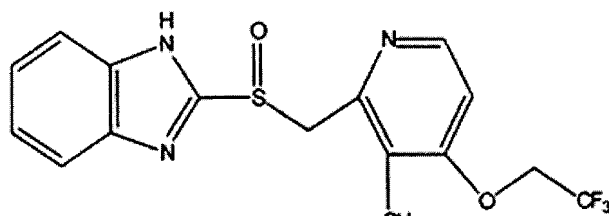
Terbinafine



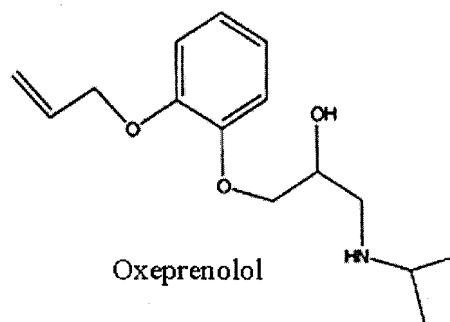
Rubeprazole



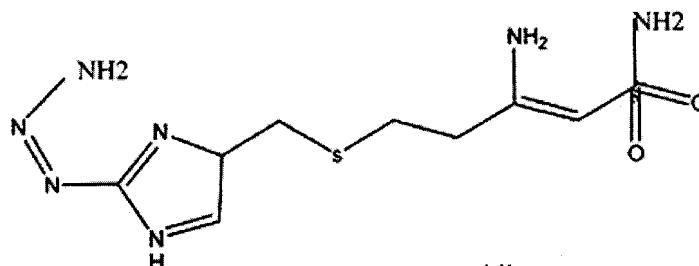
Esmolol



Lansoprazole



Oxeprenolol



Fam etidine

Fig. 1—Structure of drugs

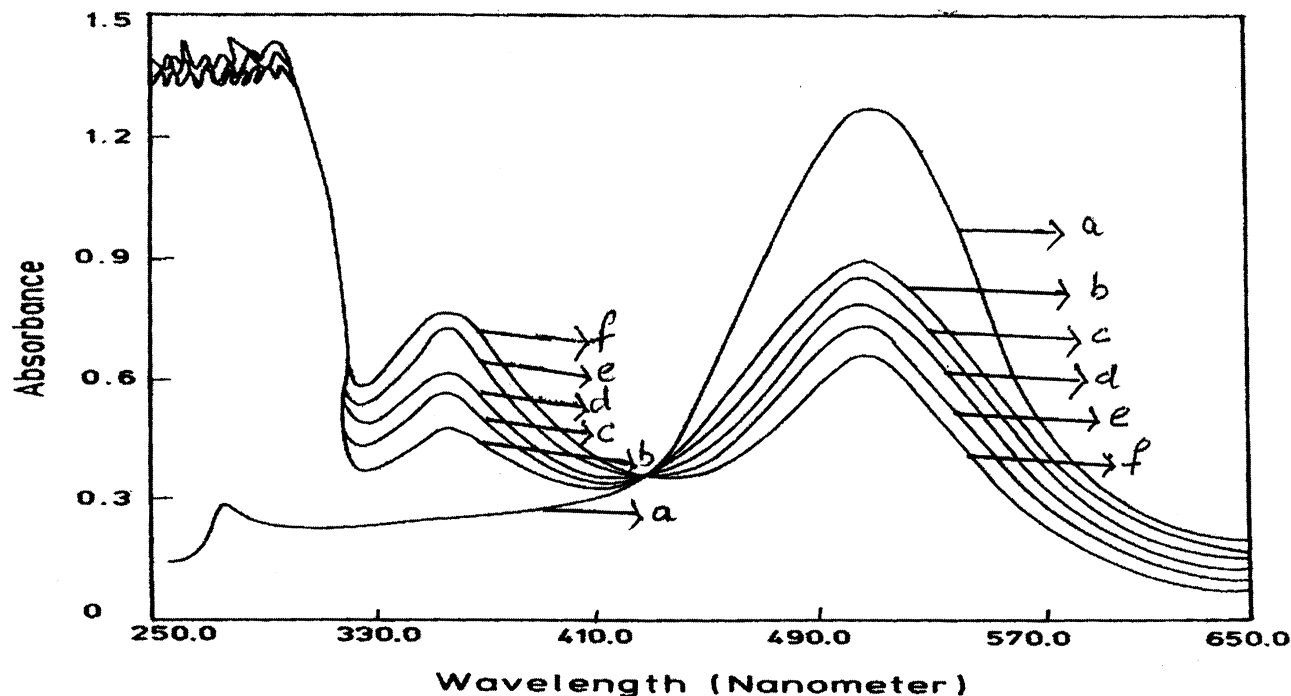


Fig. 2—Molecular complexes of iodine with terbinafine

solutions were well mixed and allowed to stand at 20°C for 20 min. The solutions were diluted with chloroform and the absorbances were measured against blank using chloroform as solvent. Drugs used in the study were omeprazole, lansoprazole, rabeprazole, fametidine, terbinafine, escitalopram oxalate, esmolol and oxeprenolol (Fig 1).

### Results and Discussion

Experimental Drugs (Fig. 1) were basic nitrogen compounds, which act as n-donors to form CT complexes with iodine ( $\sigma$  acceptor). Donors ( $10^{-3}$ - $10^{-4}$  M) were completely transparent to visible light while iodine absorbs at 513 nm to shorter wavelength (hypsochromic shift). Drugs showed negligible absorption in 300-700 nm. Mixing chloroformic solution of iodine resulted in the change of violet colour of iodine to different colour. As a consequence, absorption of iodine shifted to shorter wavelength (Fig. 2). In Fig. 2, *a* is the concentration of iodine in chloroform whereas *b*, *c*, *d*, *e* and *f* are the increasing concentrations of terbinafine-iodine complex.

Formation constants ( $K_c$ ) of complexes are determined<sup>13</sup> from iodine band using Eq. (1)

$$K_c = [C] / ([I_2] - [C]) ([N] - [C]) \quad \dots (1)$$

where,  $[C]$  = molar concentration of the complex,  $[N]$  = molar concentration of donor,  $[I_2] - [C]$  = molar concentration of free iodine, and  $[N] - [C]$  = molar concentration of free donor.

The  $K_c$  of the complexes is determined from iodine and BSB using Rose-Drago method<sup>14</sup>. Free energy change ( $\Delta G$ ) is obtained from  $K_c$  using Eq. (2).

$$\Delta G = -2.303 RT \log K_c \quad \dots (2)$$

$K_c$  of the complexes of lansoprazole, omeprazole, rabeprazole and fametidine have benzimidazole moiety in their structure and are comparable with literature values<sup>15</sup>. Terbinafine and escitalopram oxalate has tertiary amine moiety containing nitrogen atom as a donor site and its  $K_c$  values are comparable with that of literature<sup>16</sup>.  $K_c$  values for escitalopram oxalate are found to be lower than that of terbinafine, because the presence of electron withdrawing cyanide group in its ring structure. Esmolol and oxeprenolol have a secondary amine moiety in common as donor site and are expected to act as n-donors and their  $K_c$  values are in good agreement with that of literature<sup>17</sup>. Experimental  $K_c$  values are also determined from BSB using Rose-Drago method and the values agreed well with each other. Rose-Drago equation is

$$K^1 = A / \epsilon - ([A_0] + [D_0]) + [A_0 D_0] \epsilon / A. \quad \dots (3)$$

Table 1—Spectral data and thermodynamic constants

Drugs	$K$ from iodine method	$K$ from R D method	$\epsilon$	$\lambda$ of BSB	$-\Delta G$ (KJ/mole)
Omeprazole	183	198	700	378.2	12.6
Lansoprazole	163	152	950	358.5	12.8
Rabeprazole	178	150	1000	398	12.9
Famotidine	315	329	1550	361	14.2
Terbinafine	1065	1050	909	372	17.5
Escitalopram oxalate	915	909	1300	356	16.9
Esmolol	6221	6250	700	350	21.5
Oxeprenolol	6642	6666	950	375	24.8

$\Delta G$  values are accurate up to  $\pm 0.1$  KJ/mole.

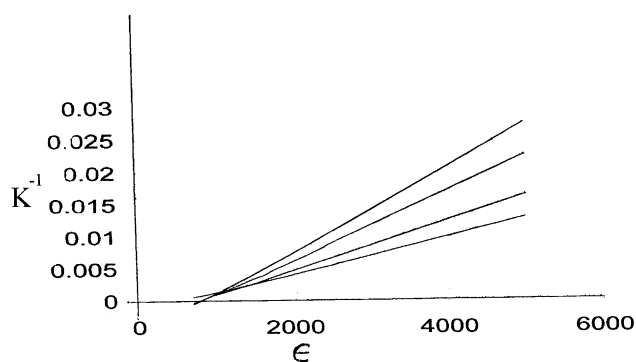


Fig. 3—Rose-Drago plot of terbinafine

where,  $K_c$  is formation constant,  $A$  is absorbance,  $\epsilon$  is molar extinction coefficient of the complex and  $A_0$  and  $D_0$  are initial concentrations of acceptor and donor respectively.

Rose-Drago method involves a random selection of  $\epsilon$  (molar extinction coefficient) values of the complex and calculating  $K^{-1}$  from a set of experimental data, namely absorbance  $A$ ,  $[D_0]$ ,  $[A_0]$  and then  $K^{-1}$  is plotted against the selected  $\epsilon$  values (Fig. 3). Procedure is repeated with different sets of donor and acceptor concentrations. All the plots intersect at a common point, from which experimental value  $K$  and  $\epsilon$  are determined. Plots normally intersect in small triangular area near common point. The  $\epsilon$  values are selected from 200 to 3000. Epsilon values (Table 1) are also obtained from Rose-Drago method<sup>18</sup>.

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