Quantitative Determination of drugs & pharmaceuticals by using iodine as analytical reagent: A spectrophotometric study

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Abstract: Sensitive, accurate and precise methods for the quantitative determination of Seven drugs viz., Cyclobenzaprine HCl (CYC), Ciproheptadine HCl (CYP), Dobutamine HCl (DOB), Moxifloxacin HCl (MOX), Pamiprioxole HCl (PAM), Sumatriptan succinate (SUM) and Trimetazadine 2HCl(TRI) have been developed. The methods are based on the charge transfer interaction of iodine with drugs which resulted in the formation of I⁻ ion with absorption maximum at 366nm. The absorbance of the band increased with increasing concentration of the drug and formed basis for the quantitative determination of the drugs. The methods have been validated in terms of ICH guidelines and parameters affecting the absorbance are optimised. The stoichiometry of each of the CT complex is found to be 1:1 by Job’s continuous variation methods and the formation constants are determined by drawing tangents to the Job’s plots.

Key words: Drugs; Determination; Iodine; spectrophotometry; validation

I. Introduction

1.1 Cyclobenzaprine HCl (CYC)
Cyclobenzaprine, -(5H-dibenzo[a,d]cyclohept-5-ylidene)-N,N-dimethyl-1-propanamine (Fig. 1a), was first introduced in 1977 and is a widely prescribed skeletal muscle relaxant with proven efficacy and safety profile in the treatment of acute muscle spasm, acute cervical strain and myofascial pain in occidental populations [1,2]. The important and recent references reported for quantitative determination of this drug included a vast number of references thus far reported for the assay of the drug and pharmaceuticals [3,6].

1.2 Ciproheptadine HCl (CYP)
Ciproheptadine hydrochloride, chemically known as 4-(5H-dibenzo[a,d]-cyclohept-5-ylidene)-1-methylpiperidine hydrochloride (Fig. 1b) is a sedating antihistamine with antimuscarinic, serotonin antagonist, and calcium-channel blocking action in pancreatic islet cells and smooth muscle [7]. It is used to treat some hormonal disorders and may also be used for treating side effects of taking antidepressants [8]. CPH is also used in clinical and veterinary medicine as an antiserotonergic and antihistaminic agent with sedative and anticolinergic effects, as well as to stimulate appetite and weight gain in human and veterinary medicine.

It is important to emphasize that there are a huge number of analytical procedures reported and these references cited almost all earlier methods of analysis of this drug [9-12].

1.3 Dobutamine HCl (DOB)
Dobutamine hydrochloride, C18H23NO3HCl, chemically: 4-(2-((1-methyl-3-(4-hydroxybenzene)propyl)amido) ethyl)-1,2-di-hydroxybenzene hydrochloric salt (Fig. 1c) is an adrenalin receptor concussion medicine indicated obvious curative effect for coronary heart disease, acute myocardial infarction, and expansionary cardiomyopathy [13-14]. The physiological importance of Dobutamine hydrochloride initiated several reports on its determination, both in pharmaceuticals and in biological fluids. Several methods have been employed [15-18] for estimation of this drug.

1.4 Moxifloxacin HCl
Moxifloxacin (Fig. 1d) chemically known as 1-cyclopropyl-6-fluoro-1, 4-dihydro-8-methoxy-7-[(4aS, 7aS)-octahydro-6H-pyrrolo-[3, 4-b] pyridin-6-yl]-4-oxo-3-quinolinecarboxylic acid hydrochloride is a new generation, 8-methoxyquinolone derivative of fluoroquinolone antibacterial agent, synthetic, active against a broad spectrum of pathogens, encompassing Gram-negative and Gram-positive bacteria. However, most of fluoroquinolones show minor side effect one of these is skin reaction including photosensitivity. This response is inhibited by co-administration with H2 receptor antagonist [19-20].

The therapeutic importance of Moxifloxacin required the development of sensitive, simple and reliable methods for industrial quality control of pharmaceutical preparations and clinical monitoring of the drug in...
toxicological studies. It is important to emphasize that there are a large number of analytical procedures reported and these references cited almost all earlier methods of analysis of this drug [21-24].

1.5 Pramipexole HCl (PAM)

Pramipexole dihydrochloride (PPD), a nonergot dopamine agonist approved in the US (1997), is used as an antidyskinetic for treatment of Parkinson’s disease. Its chemical name is (S)-N6-propyl-4,5,6,7-tetrahydro-1,3-benzoazole-2,6- diaminedihydrochloride (Fig. 1e). The ability of PPD to alleviate the signs and symptoms of Parkinson’s disease is supposed to be linked to its ability to stimulate dopamine receptors in the striatum [25-26].

Because of its physiological significance, the drug attracted the attention of Scholars. Several analytical methods have been reported for the determination of Pramipexole, either in pharmaceutical preparations or in biological fluids [27-30]. The references cited here have exhaustively enumerated the earlier analytical methods on this drug.

1.6 Sumatriptan succinate (SUM)

Sumatriptan succinate is chemically, 3-[2-(dimethylamino) ethyl]-N-methyl-indole-5-methanesulfonamide succinate (Fig.1f). Sumatriptan is a selective 5-hydroxytryptne1 receptor subtype agonist. Sumatriptan is a triptan drug including a sulfonamide group for the treatment of migraine headaches [31-32].

Because of physiological significance of Sumatriptan, there is much interest in its determination for the purpose of pharmaceutical quality control. Hence it attracted the attention of pharmaceutical analysts. Literature survey assembled a number of methods, which have been used for analysis of Sumatriptan in bulk and in pharmaceutical preparation, the recent ones being [33-36] which collected a large number of other methods for the analysis of the drug.

An exhaustive survey of literature revealed that no reports are available for quantification of above drugs using Iodine as analytical reagent. This prompted author to develop the same.

1.7 Trimetazadine 2HCl

Trimetazidine (TRMZ); 1-[2,3,4-trimethoxyphenyl]methyl] piperazine dihydrochloride (Fig. 1g) is a clinically effective antianginal agent that has been used in the prophylaxis and management of angina pectoris, and in ischemia of neurosensorial tissues as in Meniere’s disease [37]. The antianginal efficacy of TRMZ is comparable to propranolol but it does not reduce cardiac rate–pressure product or coronary blood flow [38].

Because of physiological significance of Trimetazadine, there is much interest in its determination for the purpose of pharmaceutical quality control. Hence it attracted the attention of pharmaceutical analysts. Literature survey assembled a number of methods, which have been used for analysis of Trimetazadine in bulk and in pharmaceutical preparation, the recent ones being [39-42] which collected a large number of other methods for the analysis of the drug.

Through survey of literature revealed that the above mentioned seven drugs have not been quantified by iodine as analytical reagent. The successful results obtained are reported in the present communication

II. Experimental

2.1 Instruments

The UV-Vis. spectra required for the study have been recorded on SHIMADZU 140 double beam spectrophotometer, Thermo Nicolet 1000 and also on ELICO 159 UV-Visible single beam spectrophotometers using quartz cells of 10 mm path length.. A Dhona 200 single pan electrical balance is used for weighing the samples.

2.2 Materials

Iodine (BDH, Poole, UK) was twice sublimed and preserved in vacuum desiccators (mp 113.6°C). The drugs analysed were procured from Dr. Reddy’s laboratories, Hetero drugs private limited, Kekule Pharma Limited and Symed laboratories ltd. as gift samples.

Stock solution of iodine, (4.003×10⁻³ M) in analytical grade 1, 2- dichloroethane was freshly prepared (daily) to avoid errors due to the liberation of iodine. A stock solution of each drug containing 1000 µg ml⁻¹ was initially prepared and further diluted to get working concentrations (table 1).

2.3 About the method

Iodine forms ion- pair charge transfer complexes with a variety of aromatic, aliphatic and heterocyclic compounds containing lone pair (non – bonding) of electrons on oxygen, sulphur and nitrogen atoms which act as electron donors and iodine itself acts as σ-acceptor. Bonding involved in iodine is n-σ type. Donors are completely transparent to visible light while iodine absorbs at 510 nm.
Mixing the solutions of iodine and drugs results in a change of violet color of iodine into light brown to pale yellow and as a consequence, absorption spectra exhibited a band at 366nm (Fig.2). This is attributed due to I$_3^-$ ion formed by the interaction of iodine with drugs and the same is shown below as Scheme 1.

\begin{align*}
D + I_2 & \rightarrow D.I_2 \quad \text{(outer complex)} \quad \text{fast} \quad \cdots \quad 1 \\
D.I_2 \text{(outer complex)} & \rightarrow (D.I^+) I \text{(inner complex)} \quad \text{slow} \quad \cdots \quad 2 \\
(D.I^+)I \text{(inner complex)} + I_2 & \rightarrow (D.I^+) + I_3 \quad \text{fast} \quad \cdots \quad 3 \\
\end{align*}

Scheme 1

The absorbance of the band at 366 is a function of concentration of the drugs and formed a basis for quantitative determination of drugs and attracted the attention of many pharmaceutical analysts [43-52].

2.4 Method development

Different aliquots of solution of drugs were transferred to 10ml calibrated standard flask containing a constant volume of reagent solution and volume was made to 10ml by the solvent. The concentration of drug was varied (Table 1) so as to produce charge transfer complexes with absorbance between 0.06 to 1.2 absorbance units.

2.5 Procedure for Assay of pure drug

To test the accuracy and precision of the methods developed pure sample solutions containing drug in the Beer’s law limit were chosen. For this study 4, 8, 12 and 16 μg ml$^{-1}$ of CYC; 4, 8, 12 and 16 μg ml$^{-1}$ of CYP; 4, 8, 12 and 16 μg ml$^{-1}$ of DOB; 80, 160, 240 and 320 μg ml$^{-1}$ of MOX; 4, 8, 12 and 16 μg ml$^{-1}$ of PAM; 8, 16, 24 and 32 μg ml$^{-1}$ of SUM; and 4, 8, 12 and 16 μg ml$^{-1}$ of TRI have been taken.

2.6 Procedure for analysis of Pharmaceuticals

2.6.1. Cyclobenzaprine HCl (CYC)

Twenty tablets of Flexeril each containing 10 mg of CYC were weighed and finely powdered in a mortar. A quantity of powder equivalent to 100 mg of CYC was weighed accurately and dissolved in 100 ml of double distilled water. The solution was then filtered through Whatman filter paper and neutralized with NaOH. It was extracted into 1,2-Dichloro ethane and was further diluted with the same solvent to get working concentrations of the drug.

2.6.2. Cyproheptadine HCl (CYP)

Eighty tablets (Practin-4mg) were powdered, weighed and average weight of the tablets was determined. An amount of powder equivalent to 30mg of CYP was weighed accurately and dissolved in 100 ml of double distilled water. The solution was then filtered through Whatman filter paper and neutralized with NaOH. It was extracted into 1,2-Dichloro ethane and was further diluted with the same solvent to get working concentrations of the drug.

2.6.3. Dobutamine HCl (DOB)

2 vials of Dobutrox injection containing 12.5mg/vial of DOB were placed in a boiling tube and neutralized with NaOH and worked out to get working concentrations of drugs in solution of 1,2-dichloro ethane.

2.6.4. Moxifloxacin HCl (MOX)

A tablet of Moxicip-420mg was crushed into powder and worked out as mentioned for earlier tablets to get working concentrations of drugs in solution of 1,2-dichloro ethane.

2.6.5. Pramipexole HCl (PAM)

Fifty tablets of Parpex-1mg were crushed into powder and worked out as mentioned for earlier tablets to get working concentrations of drugs in solution of 1,2-dichloro ethane.

2.6.6. Sumatriptan succinate (SUM)

The powdered content of two tablets of Sumatriptan-50mg was weighed and worked out as mentioned for earlier tablets to get working concentrations of drugs in solution of 1,2-Dichloro ethane.

2.6.7. Trimetazadine 2HCl (TRI)

Twenty tablets of Carvidon each containing 20mg of TRI were weighed and powdered. Accurately weighed quantity of tablet powder equivalent to 25mg of TRI was transferred into 50.0 ml volumetric flask and
dissolved in 25ml of double distilled water. The solution was then neutralized with NaOH and extracted into 1,2-dichloro ethane to get required working concentrations.

III. Results And Discussion

3.1 Construction of calibration curves

The absorbance of each solution was measured against blank (without drug). The absorbance to concentration of the drug called the relative response has been calculated. The average relative response of five replicates was evaluated. The relative responses falling within 95% to 105% of average were only considered for construction of calibration curves (Fig. 3). The limits of Beer’s law, slope, intercept, correlation coefficient, molar absorptivity, Sandell’s sensitivity, formation constants and regression equation for each drug are tabulated in Table 2.

3.2 Method validation

The method developed for quantification of drugs has been validated in terms of precision, accuracy, limit of detection, limit of quantification, linearity, selectivity and ruggedness. Calibration curves were drawn and are used to assess the recovery of the drug. To assess the precision, each experiment was repeated at least 5 times and accuracy is estimated in terms of percent recovery and %RSD. Excellent percent recovery and RSD being less than 2 for each drug demonstrates accuracy and precision of the methods. Further t-test and F-test values have also been calculated using a standard reference method. The t-test and F-test values are less than their permissible range indicating high accuracy of the methods (Table 3).

Limits of linearity of calibration curves were mentioned in the Table 1 under the title Beer’s law limit. To test the selectivity, known excipients of each drug were added to the pure drug sample and recovery experiments were performed. The ruggedness of the method was examined by collecting absorbance data using 3 different instruments and 2 analysts. No significant changes were observed either by change of instrument or analyst, hence the method may be taken as rugged.

3.3 Optimization of the parameters of quantification

3.3.1. Effect of concentration of reagent

When varying volumes of Iodine (0.2, 0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0, 2.2, 2.4 ml) were added to fixed concentration of various drugs viz., 20µg ml⁻¹ of CYP, 22.5 µgml⁻¹ of CYC, 31.5µg ml⁻¹ of DOB, 450µg ml⁻¹ of MOX, 22.5µg ml⁻¹ of PAM, 57.6µg ml⁻¹ of SUM and 22.5µg ml⁻¹ of TRI. 0.7 - 0.9ml of Iodine was sufficient to produce maximum absorbance after which it remained constant. Hence 1 ml of reagent is used uniformly for all the drugs (Fig 4).

3.3.2 Effect of time

The interaction of Iodine with drugs resulted in the formation of colored product which stabilized immediately after mixing. The developed color remained stable at room temperature for about an hour. After two hours many solutions turned purple. After a day all solutions turned black, hence the measurements were made immediately after mixing the solutions.

3.3.3. Effect of organic solvent

Various solvents such as carbon tetrachloride, chloroform, 1,2- dichloro ethane, methanol and acetonitrile have been tried to select suitable solvent for the analysis of the drug. 1,2- dichloroethane is found to be the suitable solvent as it produces maximum optical density with a fixed concentration of drug while other solvents mentioned above are found to be unsuitable as they produced lower absorbances due to incomplete dissociation of complex. Methanol and acetonitrile turned Iodine brown even before addition of any drug. Hence 1,2- dichloroethane is used throughout the work.

3.3.4 Determination of stochiometry

The stochiometry of each of the complexes has been determined from Job’s continuous variation method and found to be 1:1 in each case (Fig. 5). The Job’s plots have also been used to evaluate the formation constants of complexes[53,54].

3.3.5 Analysis of pharmaceuticals

To test the applicability of the method developed, solutions of pharmaceutical tablets containing drug in the Beer’s Law limit were chosen and charge transfer complexation was studied. For this study 4, 8, 12 and 16 µg ml⁻¹ of CYC; 4, 8, 12 and 16 µg ml⁻¹ of CYP; 4, 8, 12 and 16 µg ml⁻¹ of DOB; 80, 160, 240 and 320 µg ml⁻¹ of MOX; 4, 8, 12 and 16 µg ml⁻¹ of PAM; 8, 16, 24 and 32 µg ml⁻¹ of SUM; and 4, 8, 12 and 16 µg ml⁻¹ of TRI were chosen for charge transfer complexation other experimental details being common. To assess the precision
and accuracy, each tablet analysis was repeated at least 5 times and accuracy is estimated in terms of percent recovery and percent RSD. Excellent percent recovery and RSD being less than 2 for each drug demonstrates applicability of the methods for pharmaceutical analysis. Further t-test and F-test values have also been calculated using a standard reference method. The t-test and F-test values are less than their permissible range indicating excellent applicability of the methods for pharmaceutical analysis (Table 4). The excellent recovery studies indicate that methods developed can be applied to pharmaceutical analysis without hesitation.

Sandell’s sensitivity of the analyte capable of producing a change 0.001 absorbance units is a measure of sensitivity of the method. Lower the Sandell’s sensitivity higher is the sensitivity of the method developed. Sandell’s sensitivity values of drugs presented in Table 18 indicate CYC has the lowest Sandell’s sensitivity and hence has the highest sensitivity towards the method, they are in the order CYC < DOB < CYP < TRI < PAM < SUM < MOX.

IV. Conclusions

Iodine is found suitable for the analysis of drugs and acts as analytical reagent through charge transfer complexation. The stoichiometry is found to be 1:1. The factors effecting the optical density have been optimised and methods developed are applied to the analysis of both drugs and pharmaceuticals

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Quantitative Determination of drugs & pharmaceuticals by using iodine as analytical reagent: A

a. Cyclobenzaprine HCl

b. Cyproheptadine HCl

c. Dobutamine HCL

d. Moxifloxacin HCl

e. Pramipexole HCl

f. Sumatriptan succinate

g. Trimetazadine 2HCl

Fig 1 Structures of the drugs

Table 2. Analytical Parameters for the charge transfer complexes of Iodine with Drugs.

<table>
<thead>
<tr>
<th>Name of Drug</th>
<th>CYC</th>
<th>CYP</th>
<th>DOB</th>
<th>MOX</th>
<th>PAM</th>
<th>SUM</th>
<th>TRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>a max (nm)</td>
<td>366</td>
<td>366</td>
<td>366</td>
<td>366</td>
<td>366</td>
<td>366</td>
<td>366</td>
</tr>
<tr>
<td>Beer’s law limits (μg mL^{-1})</td>
<td>2.5-20</td>
<td>2.5-22.5</td>
<td>3.5-31.5</td>
<td>50-450</td>
<td>2.5-22.5</td>
<td>6.4-57.6</td>
<td>2.5-22.5</td>
</tr>
<tr>
<td>Molar absorptivity (L·mol^{-1}·cm^{-1})</td>
<td>1176</td>
<td>1075</td>
<td>18581</td>
<td>689.7</td>
<td>880</td>
<td>901</td>
<td>14317</td>
</tr>
<tr>
<td>Formation constant, K, (M^{-1})</td>
<td>410</td>
<td>340</td>
<td>350</td>
<td>260</td>
<td>280</td>
<td>270</td>
<td>360</td>
</tr>
<tr>
<td>Sandell’s sensitivity (μg cm^{-2})</td>
<td>0.0153</td>
<td>0.0078</td>
<td>0.0131</td>
<td>0.5</td>
<td>0.0222</td>
<td>0.0555</td>
<td>0.0212</td>
</tr>
<tr>
<td>Std. Dev. of intercepts</td>
<td>0.0105</td>
<td>0.0081</td>
<td>0.0163</td>
<td>0.00624</td>
<td>0.00929</td>
<td>0.0102</td>
<td>0.0102</td>
</tr>
<tr>
<td>LOD (μg mL^{-1})</td>
<td>0.534</td>
<td>0.652</td>
<td>0.994</td>
<td>14.21</td>
<td>0.652</td>
<td>1.881</td>
<td>0.718</td>
</tr>
<tr>
<td>LOQ (μg mL^{-1})</td>
<td>1.604</td>
<td>1.936</td>
<td>2.984</td>
<td>42.653</td>
<td>2.064</td>
<td>5.701</td>
<td>2.17</td>
</tr>
<tr>
<td>Slope, b</td>
<td>0.085</td>
<td>0.049</td>
<td>0.053</td>
<td>0.092</td>
<td>0.045</td>
<td>0.038</td>
<td>0.047</td>
</tr>
<tr>
<td>Intercept, a</td>
<td>0.074</td>
<td>-0.0264</td>
<td>-0.014</td>
<td>0.065</td>
<td>-0.0191</td>
<td>-0.009</td>
<td>0.07</td>
</tr>
<tr>
<td>Correlation coefficient</td>
<td>0.990</td>
<td>0.989</td>
<td>0.993</td>
<td>0.997</td>
<td>0.994</td>
<td>0.980</td>
<td>0.989</td>
</tr>
<tr>
<td>Regression equation</td>
<td>Y=mx+b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.065=</td>
<td>0.074X</td>
<td>0.049=</td>
<td>0.020X</td>
<td>0.053=</td>
<td>0.014X</td>
<td>0.002=</td>
</tr>
</tbody>
</table>

X = concentration of the drug, (μg/mL^{-1})
Table 3. Recovery studies to evaluate accuracy and precision for the determination of drugs by proposed method.

<table>
<thead>
<tr>
<th>Name of the Drug</th>
<th>Amount Taken (µg ml(^{-1}))</th>
<th>Amount Found (µg ml(^{-1}))</th>
<th>% Recovery</th>
<th>RSD %</th>
<th>Proposed method Mean ± SD</th>
<th>Ref method Mean ± SD</th>
<th>t-test (*)</th>
<th>F-test (**)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYC</td>
<td>4 8 12 16</td>
<td>3.97 7.95 12.01 16.02</td>
<td>99.32</td>
<td>0.429</td>
<td>99.75 ± 0.43</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.86 7.97 11.98 16.01</td>
<td>96.56</td>
<td>1.657</td>
<td>99.01 ± 1.64</td>
<td>[199] 101.4 ± 1.63</td>
<td>0.066</td>
<td>1.014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.05 7.94 11.97 15.94</td>
<td>101.25</td>
<td>0.894</td>
<td>99.96 ± 0.893</td>
<td>[206] 100.10 ± 0.86</td>
<td>0.053</td>
<td>1.97</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80 160 320</td>
<td>99.00</td>
<td>0.718</td>
<td>100.05 ± 0.72</td>
<td>[130] 100.21 ± 0.56</td>
<td>0.403</td>
<td>1.648</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.022 8.039 12.05 16.04</td>
<td>100.55</td>
<td>0.131</td>
<td>100.51 ± 0.76</td>
<td>[212] 102.6 ± 0.78</td>
<td>-1.803</td>
<td>0.0326</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.112 24.16 32.2</td>
<td>101.39</td>
<td>0.392</td>
<td>101.39 ± 0.398</td>
<td>[218] 99.92 ± 0.28</td>
<td>0.491</td>
<td>2.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.02 8.02 12.0 16.0</td>
<td>100.54</td>
<td>0.169</td>
<td>100.29 ± 0.170</td>
<td>[145] 99.80 ± 0.11</td>
<td>0.664</td>
<td>2.393</td>
</tr>
</tbody>
</table>

Table 4. Application of proposed method for the analysis of drugs in pharmaceutical formulations by proposed method.

<table>
<thead>
<tr>
<th>Name of the Drug</th>
<th>Amount Taken (µg ml(^{-1}))</th>
<th>Amount Found (µg ml(^{-1}))</th>
<th>% Recovery</th>
<th>RSD %</th>
<th>Proposed method Mean ± SD</th>
<th>Ref method Mean ± SD</th>
<th>t-test (*)</th>
<th>F-test (**)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYC (Flexiril)</td>
<td>4 8 12 16</td>
<td>3.98 8.03 12.05 16.11</td>
<td>99.50</td>
<td>0.514</td>
<td>100.24 ± 0.515</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>3.91 8.14 11.94 16.06</td>
<td>97.75</td>
<td>1.677</td>
<td>99.843 ± 1.675</td>
<td>[199] 99.16 ± 1.31</td>
<td>0.297</td>
<td>1.63</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.06 7.97 12.11 16.26</td>
<td>101.50</td>
<td>0.906</td>
<td>100.916 ± 0.914</td>
<td>[206] 99.60 ± 0.98</td>
<td>-0.153</td>
<td>0.871</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80 160 240 320</td>
<td>100.37</td>
<td>0.2586</td>
<td>100.05 ± 0.2587</td>
<td>[130] 100.68 ± 0.17</td>
<td>0.657</td>
<td>2.317</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.022 8.039 12.05 16.04</td>
<td>100.55</td>
<td>0.131</td>
<td>100.51 ± 0.76</td>
<td>[212] 102.6 ± 0.78</td>
<td>-1.802</td>
<td>0.0326</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.06 16.06 23.96 32.13</td>
<td>100.57</td>
<td>0.375</td>
<td>100.314 ± 0.378</td>
<td>[218] 99.76 ± 0.37</td>
<td>0.0322</td>
<td>1.048</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.02 8.05 12.11 15.97</td>
<td>99.00</td>
<td>0.862</td>
<td>100.088 ± 0.863</td>
<td>[145] 99.98 ± 0.59</td>
<td>0.584</td>
<td>2.134</td>
</tr>
</tbody>
</table>

* t-test and ** F-test values from literature
Table 1. The range of concentration of the drugs used for charge transfer complexation with Iodine

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Working concentration</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclobenzaprine HCl</td>
<td>2.5 µg ml⁻¹</td>
<td>2.5-20 µg ml⁻¹</td>
</tr>
<tr>
<td>Cyproheptadine HCl</td>
<td>2.5 µg ml⁻¹</td>
<td>2.5-22.5 µg ml⁻¹</td>
</tr>
<tr>
<td>Dobutamine HCL</td>
<td>3.5 µg ml⁻¹</td>
<td>3.5-31.5 µg ml⁻¹</td>
</tr>
<tr>
<td>Moxifloxacin HCl</td>
<td>50 µg ml⁻¹</td>
<td>50-450 µg ml⁻¹</td>
</tr>
<tr>
<td>Pramipexole HCl</td>
<td>2.5 µg ml⁻¹</td>
<td>2.5-22.5 µg ml⁻¹</td>
</tr>
<tr>
<td>Sumatriptan succinate</td>
<td>6.4 µg ml⁻¹</td>
<td>6.4-57.6 µg ml⁻¹</td>
</tr>
<tr>
<td>Trimetazadine 2HCl</td>
<td>2.5 µg ml⁻¹</td>
<td>2.5-22.5 µg ml⁻¹</td>
</tr>
</tbody>
</table>

Fig. 2 Typical absorption spectra of iodine and its CT complex(b) with drug(a)

Fig. 4 Influence of the volume of Iodine (typical)

Fig. 5 Job’s Continuous-variation study of drug-Iodine system (typical)