Indirect spectrophotometric determination of some biologically important phenothiazines using potassium dichromate, iron(II) and 1,10-phenanthroline

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A sensitive method is presented for the spectrophotometric determination of phenothiazine derivatives of biological importance. The drugs namely, chlorpromazine hydrochloride (CPH), promethazine hydrochloride (PH), trifluoperazine hydrochloride (TFPH), prochlorperazine maleate (PCPM) and fluphenazine hydrochloride (FPH) are reacted with a fixed amount of dichromate in acidic conditions. After the reaction is complete, the unreacted dichromate is determined by treating with iron(II) and ortho-phenanthroline at a raised pH and measuring the absorbance at 510 nm. The amount of dichromate reacted corresponds to the drug content. The linearity ranges are found to be 5-30, 2.5-25, 5-45, 7.5-60 and 5-50 μg mL⁻¹ for CPH, PH, TFPH, PCPM and FPH, respectively. The apparent molar absorptivity values are in the range 3.46×10³-6.47×10³ L mol⁻¹ cm⁻¹ and the limits of determination range from 0.49 to 1.87 μg mL⁻¹ and the relative standard deviation is less than 2%. The proposed method has been applied for the determination of these drugs in pure form and in pharmaceutical formulations with recoveries in the range 96.28-103.24%. The method was further validated by parallel determination by the official British Pharmacopoeial procedure and by recovery studies.

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Phenothiazines are a very significant class of organic compounds with potent physiological activity. They are used as antipsychotics, anticholinergics and antihistamines. The development of simple, sensitive and rapid methods for their determination is, therefore, of importance. Various techniques including spectrophotometry reported upto 1992 have been reviewed by Puzanowska-Tarasiewicz and Karpinska. Spectrophotometry, because of its simplicity, selectivity, sensitivity and cost-effectiveness, continues to be widely used in pharmaceutical analysis including in the assay of phenothiazines. Spectrophotometric methods for the determination of phenothiazines reported in the last one decade are generally based on redox, ion-pair complex formation, binary complex formation, ternary complex formation, diazo-coupling and oxidative-coupling reactions. Many spectrophotometric methods found in the literature are reasonably rapid and selective, but suffer from one or the other disadvantage such as low sensitivity, narrow dynamic range, heating step, extraction step, poor stability of the coloured species and instrumental or procedural complications (Table 1).

The intensely coloured radical cation formed as a result of one-electron loss oxidation of phenothiazine drugs by iron(III) salts in acidic conditions has previously been used as the basis for the spectrophotometric determination of these drugs. However, these procedures suffer from deficiencies such as low sensitivity, critical working conditions, critical contact time, or an unstable coloured species. Indirect spectrophotometric determination of phenothiazine and pH in which iron(III) was used as the oxidant and the iron(II) formed was measured as its 1,10-phenanthroline complex at 500 nm, has been reported by Buhl and Chwistek. Since iron(III) is a mild oxidising agent, the reaction mixture must be heated for 40 min at 60°C to effect the oxidation of drugs.

In an attempt to overcome this limitation, the author has simplified the above procedure by using dichromate as the oxidant. In the present work, the phenothiazine drugs were oxidised by a known excess of dichromate, the unreacted dichromate reduced by a measured excess of iron(II) under acidic conditions, and the residual iron(II) was determined by measuring...
the absorbance of iron(II)-1,10-phenanthroline complex after raising the pH. This method offers the advantages of speed, sensitivity, long dynamic linear range of response, and makes use of a highly stable coloured species produced under milder conditions without heating or extraction. The method was validated by determining the drugs in their dosage forms, and by recovery studies.

**Experimental Procedure**

**Apparatus**

A Systronics model 106 digital spectrophotometer provided with 1-cm matched quartz cells was used for absorbance measurements.

**Reagents and solutions**

All chemicals used were of analytical reagent grade and double distilled water was used throughout the study. A 100 μg mL⁻¹ potassium dichromate solution was obtained by first preparing 1000 μg mL⁻¹ solution by dissolving 100 mg of reagent (S.d. Fine Chem., India, 99.9% pure) in water and diluting to volume in a 100 mL volumetric flask, and subsequently effecting a 10-fold dilution with water. An approximately 0.02 M solution of iron(II) ammonium sulphate was prepared by dissolving 0.7899 of the reagent (S.d. Fine Chem., India, 98.5% pure) in 1 mL of 1 M sulphuric acid and diluting to 100 mL with water. This solution was standardised using pure dichromate. This was appropriately diluted to get 700 μg mL⁻¹ solution. A 0.25% aqueous solution of ortho-phenanthroline was prepared by dissolving 0.25 g of reagent (Ranbaxy Chem., India, 99.5% pure) in hot water and diluting to 100 mL. A 10 M sulphuric acid solution was prepared by adding 278 mL of concentrated acid, (Sp Gr 1.84) (S.d. Fine Chem., India, 95% pure) to 222 mL of water with cooling. An aqueous ammonia solution (1:1) was prepared by diluting the chemical (Sp Gr 0.91) (S.d. Fine Chem. India, 25% assay) with water. Pharmaceutical grade phenothiazine derivatives were procured from British Pharmaceuticals (CPH), Rhone-Poulenc (PH and PCPM), SmithKline Beecham (TFPH) and Sarabhai Chemicals (FPH). Stock standard solution containing 1000 μg mL⁻¹ CPH, PH, TFPH, PCPM or FPH was

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**Table 1—Comparison of the existing spectrophotometric methods with the proposed method**

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Reagent</th>
<th>Linear range µg mL⁻¹ (∈)</th>
<th>Remarks</th>
<th>Ref No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cerium(IV)</td>
<td>5-400</td>
<td>Uses Fia assembly and an unstable coloured species</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>Cerium(IV)</td>
<td>60-200</td>
<td>Uses Fia assembly and an unstable coloured species</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>N-Bromophthalimide</td>
<td>50-140</td>
<td>Uses Fia assembly and an unstable coloured species</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>K₂Cr₂O₇</td>
<td>40-250</td>
<td>Uses Fia assembly and an unstable coloured species</td>
<td>11</td>
</tr>
<tr>
<td>5</td>
<td>Iron(III) nitrate</td>
<td>20-240</td>
<td>Longer contact time and unstable coloured species</td>
<td>10</td>
</tr>
<tr>
<td>6</td>
<td>Iron(III) chloride</td>
<td>3-15</td>
<td>Involves heating at 60°C for 10 min</td>
<td>13</td>
</tr>
<tr>
<td>7</td>
<td>Cerium(IV) sulphate</td>
<td>1-500</td>
<td>Uses an unstable coloured species</td>
<td>12</td>
</tr>
<tr>
<td>8</td>
<td>Ammonium molybdate</td>
<td>1-60</td>
<td>Involves boiling for 15 min and the coloured species in unstable</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>Amaranth &amp; Fast Red E</td>
<td>5-50</td>
<td>Involves extraction and use of an organic solvent</td>
<td>15</td>
</tr>
<tr>
<td>10</td>
<td>Methyl orange</td>
<td>20-120</td>
<td>Involves extraction and use of an organic solvent</td>
<td>16</td>
</tr>
<tr>
<td>11</td>
<td>Bromocresol green</td>
<td>2-18</td>
<td>Involves extraction and use of an organic solvent</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(∈ = 2×10⁶)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Bromothymol blue</td>
<td>20-140</td>
<td>Involves extraction and use of an organic solvent</td>
<td>18</td>
</tr>
<tr>
<td>13</td>
<td>Chlorophenol red</td>
<td>-</td>
<td>Involves extraction and use of an organic solvent</td>
<td>19</td>
</tr>
<tr>
<td>14</td>
<td>Picric and flavianic acids</td>
<td>20-70</td>
<td>Involves extraction and use of an organic solvent</td>
<td>20</td>
</tr>
<tr>
<td>15</td>
<td>Palladium(II)</td>
<td>0-130</td>
<td>Fia assembly, less sensitive</td>
<td>21</td>
</tr>
<tr>
<td>16</td>
<td>Vanadate-H₂O₂</td>
<td>0-500</td>
<td>Less sensitive</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(∈ = 5×10⁵)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Beryllium(II)-Chrome azurol S</td>
<td>1.0×10⁴</td>
<td>Involves extraction and use of an organic solvent</td>
<td>23</td>
</tr>
<tr>
<td>18</td>
<td>Antimonoyl(III)-H₂O₂</td>
<td>20-1250</td>
<td>Least sensitive</td>
<td>24</td>
</tr>
<tr>
<td>19</td>
<td>Niobium(V)-KSCN</td>
<td>20-200</td>
<td>Involves extraction and use of an organic solvent</td>
<td>25</td>
</tr>
<tr>
<td>20</td>
<td>Diazotised dapsone</td>
<td>10-80</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>21</td>
<td>NBS-diphenylamine</td>
<td>-</td>
<td>Absorbance measured at 395 nm where the interference is more</td>
<td>27</td>
</tr>
<tr>
<td>22</td>
<td>K₂Cr₂O₇-iron(II) Orthophenanthroline</td>
<td>2.5-60.0</td>
<td>Uses a novel reaction scheme, a stable coloured species fairly sensitive, no heating or extraction step.</td>
<td>Present method</td>
</tr>
</tbody>
</table>
prepared in water, kept in amber coloured bottle and stored in a refrigerator (A few drops of 0.1 M hydrochloric acid were used to aid dissolution of PCPM). Working solutions equivalent to 100 μg mL⁻¹ CPH and PH, 200 μg mL⁻¹ of TFPH and FPH, and 300 μg mL⁻¹ PCPM were prepared by appropriate dilution of the stock solutions with water before use.

**General methods**

**Method for bulk drugs**

A 1 mL portion of 100 μg mL⁻¹ potassium dichromate solution was placed in a series of 10 mL calibrated flasks followed by 1 mL of 10 M sulphuric acid. After adding 0.25-3.00 mL of CPH, 0.25-2.50 mL of PH (each 100 μg mL⁻¹), 0.25-2.25 mL of TFPH, 0.25-2.50 mL of FPH (each 200 μg mL⁻¹) or 0.25-2.00 mL of PCPM (300 μg mL⁻¹), the overall volume was adjusted to 6 mL by adding water, mixed well and was allowed to stand for 15-30 min (Table 2) i.e., till the disappearance of the purple, red or orange colour. Subsequently, 1 mL of 700 μg mL⁻¹ iron(II) ammonium sulphate solution was added to each flask and mixed well, after 1 min, 1 mL of 0.25% 1,10-phenanthroline solution was added followed by 2 mL of 1:1 ammonia, the volume was diluted to 6 mL by adding water, mixed well and absorbance was measured at 510 nm against a water blank, 10 min after diluting to the final volume. The calibration graph in each case was constructed by plotting the absorbance measured versus the concentration of drug in μg mL⁻¹. Concentration of the unknown was read from the calibration graph or calculated from the regression equation in each case.

**Method for dosage forms**

Twenty tablets were weighed and ground into a fine powder. A portion of the powder equivalent to 100 mg of phenothiazine drug was accurately weighed into 100 mL calibrated flask, 60 mL water were added (plus 5 mL of 0.1 M hydrochloride in the case of Stemetil tablets) and shaken thoroughly for about 20 min to extract the drug. The contents were diluted to the mark, mixed well and filtered using Whatman No 41 filter paper. The tablet extract (1000 μg mL⁻¹) was diluted appropriately to get working concentration of 100 μg mL⁻¹ (CPH and PH), 200 μg mL⁻¹ (TFPH and FPH) or 300 μg mL⁻¹ (PCPM). A convenient volume was then subjected to analysis.

In the case of injections, the contents of ten ampoules were mixed and an accurately measured volume equivalent to 100 mg of drug was transferred into a 100 mL volumetric flask and diluted to volume with water, and proceeded further as described under tablets (in the case of anatensol and prolinate injections, a few mL of absolute alcohol were used to aid dissolution).

**Results and Discussion**

When varying amounts of phenothiazine drug are reacted with a known and fixed amount of dichromate in sulphuric acid medium, proportionate amounts of dichromate will be used for the oxidation of the drug, and there will be a concomitant fall in dichromate concentration. When the unreacted dichromate is reduced by a fixed amount of iron(II) in the same acidic conditions, there will be a concomitant increase in the concentration of iron(II). The residual iron(II) is reacted subsequently with 1,10-phenanthroline after raising the pH to form an intense red coloured complex, ferroin³⁹, and measured at 510 nm. The absorbance is linearly depende nt on the concentration of phenothiazine drugs studied, forming the basis for determination.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CPH</th>
<th>PH</th>
<th>TFPH</th>
<th>PCPM</th>
<th>FPH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer’s law limits, μg mL⁻¹</td>
<td>5-30</td>
<td>2.5-25</td>
<td>5-45</td>
<td>7.5-60</td>
<td>5-50</td>
</tr>
<tr>
<td>Detection limit, μg mL⁻¹</td>
<td>0.33</td>
<td>0.16</td>
<td>0.62</td>
<td>0.41</td>
<td>0.57</td>
</tr>
<tr>
<td>Quantification limit, μg mL⁻¹</td>
<td>1.02</td>
<td>0.49</td>
<td>1.87</td>
<td>1.24</td>
<td>1.74</td>
</tr>
<tr>
<td>Molar absorptivity, L mol⁻¹ cm⁻¹</td>
<td>4.17×10³</td>
<td>6.47×10³</td>
<td>3.46×10³</td>
<td>4.17×10³</td>
<td>3.52×10³</td>
</tr>
<tr>
<td>Sandell sensitivity, ng cm⁻² per 0.001 A unit</td>
<td>85</td>
<td>49</td>
<td>139</td>
<td>145</td>
<td>145</td>
</tr>
<tr>
<td>Regression equation (A*)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>-0.005</td>
<td>0.009</td>
<td>-0.008</td>
<td>-0.006</td>
<td>0.035</td>
</tr>
<tr>
<td>Slope (b)</td>
<td>0.012</td>
<td>0.019</td>
<td>0.007</td>
<td>0.007</td>
<td>0.006</td>
</tr>
<tr>
<td>Regression coefficient (r)</td>
<td>0.9997</td>
<td>0.9962</td>
<td>0.9997</td>
<td>0.9995</td>
<td>0.9916</td>
</tr>
<tr>
<td>Reaction time, min</td>
<td>15</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>30</td>
</tr>
</tbody>
</table>

*A=A + b C, where A is the absorbance for concentration C in μg mL⁻¹.*
Optimization of experimental variables

The optimal conditions were established for each phenothiazine drug based on the formation of maximum colour through variation of parameters such as acid strength, reaction time and volume of ammonia solution.

Since the oxidation of phenothiazines to sulphoxides by dichromate was slow in hydrochloric acid and phosphoric acid media, sulphuric acid was chosen to effect oxidation. A 1 mL volume of 10 M sulphuric acid was found optimum in a total volume of 6 mL to effect oxidation in 15-30 min (Table 2).

Fixing 10 μg mL⁻¹ as the upper limit of iron(II) that could be determined by 1,10-phenanthroline method, 700 μg of iron(II) ammonium sulphate was used in this study. Stoichiometrically, this would react with 87.46 μg of potassium dichromate. However, a slightly higher amount, i.e., 100 μg of the oxidant was used to ensure the complete oxidation of iron(II) and to produce a colourless blank.

The volume of 1:1 ammonia was not critical since the sensitivity and stability of ferroin are unaffected over a wide pH range. However, 2 mL of 1:1 ammonia were used to raise the pH to ~ 4. Under the described experimental conditions, the ferroin complex was found to be stable for 24-48 h depending upon the individual phenothiazine drug.

Linear range and sensitivity

A linear relationship was obtained for the absorbance of the complex when the concentrations of the drugs were in the range given in Table 2. The graphs showed negligible or zero intercepts and are described by the relation: A=a+bC (A is the absorbance of a 1-cm layer solution; b, slope; a, intercept; and C, concentration in μg mL⁻¹) obtained by the method of least-squares. The apparent molar absorptivities were calculated to be in the range of 3.46×10³-6.47×10³ L mol⁻¹ cm⁻¹ and the Sandell sensitivities were in the range of 49-145 ng cm⁻². These values together with the limits of detection and quantification compiled in Table 2 indicate the reasonably high sensitivity of the method. Table 2 also contains the linear equations for absorbance versus concentration, together with correlation coefficients, indicating excellent lineairities.

Validation of the method

Accuracy and precision

The precision and accuracy of the method were evaluated by performing seven replicate analyses on pure drug solutions at three different concentration levels (within the Beer’s law limits). The percent error and relative standard deviation (RSD) values presented in Table 3 indicate the high accuracy and precision of the method. For a better picture of

<table>
<thead>
<tr>
<th>Phenothiazine drug</th>
<th>Taken, μg mL⁻¹</th>
<th>Found*, μg mL⁻¹</th>
<th>Range, μg mL⁻¹</th>
<th>Relative error, %</th>
<th>SD, μg mL⁻¹</th>
<th>RSD, %</th>
<th>ROE, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPH</td>
<td>5.0</td>
<td>4.82</td>
<td>0.25</td>
<td>3.60</td>
<td>0.03</td>
<td>0.68</td>
<td>± 0.63</td>
</tr>
<tr>
<td></td>
<td>15.0</td>
<td>15.36</td>
<td>0.36</td>
<td>2.40</td>
<td>0.05</td>
<td>0.34</td>
<td>± 0.31</td>
</tr>
<tr>
<td></td>
<td>25.0</td>
<td>24.67</td>
<td>0.74</td>
<td>1.32</td>
<td>0.24</td>
<td>0.94</td>
<td>± 0.87</td>
</tr>
<tr>
<td>PH</td>
<td>5.0</td>
<td>5.16</td>
<td>0.28</td>
<td>3.20</td>
<td>0.04</td>
<td>0.72</td>
<td>± 0.67</td>
</tr>
<tr>
<td></td>
<td>15.0</td>
<td>14.86</td>
<td>0.32</td>
<td>0.93</td>
<td>0.19</td>
<td>1.26</td>
<td>± 1.16</td>
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<td></td>
<td>20.0</td>
<td>20.23</td>
<td>0.46</td>
<td>1.15</td>
<td>0.31</td>
<td>1.54</td>
<td>± 1.42</td>
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<td>TFPH</td>
<td>10.0</td>
<td>9.85</td>
<td>0.21</td>
<td>1.50</td>
<td>0.03</td>
<td>0.28</td>
<td>± 0.26</td>
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<tr>
<td></td>
<td>25.0</td>
<td>25.26</td>
<td>0.62</td>
<td>1.04</td>
<td>0.11</td>
<td>0.42</td>
<td>± 0.39</td>
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<td></td>
<td>40.0</td>
<td>40.34</td>
<td>0.56</td>
<td>0.85</td>
<td>0.05</td>
<td>0.12</td>
<td>± 0.11</td>
</tr>
<tr>
<td>PCPM</td>
<td>20.0</td>
<td>20.26</td>
<td>0.32</td>
<td>1.30</td>
<td>0.20</td>
<td>1.02</td>
<td>± 0.94</td>
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<td>30.0</td>
<td>30.40</td>
<td>0.28</td>
<td>1.33</td>
<td>0.23</td>
<td>0.75</td>
<td>± 0.69</td>
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<td>50.0</td>
<td>50.16</td>
<td>0.32</td>
<td>0.32</td>
<td>0.26</td>
<td>0.52</td>
<td>± 0.48</td>
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<tr>
<td>FPH</td>
<td>10.0</td>
<td>9.92</td>
<td>0.28</td>
<td>0.80</td>
<td>0.16</td>
<td>1.56</td>
<td>± 1.44</td>
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<td>20.0</td>
<td>19.74</td>
<td>0.35</td>
<td>1.30</td>
<td>0.07</td>
<td>0.34</td>
<td>± 0.31</td>
</tr>
<tr>
<td></td>
<td>40.0</td>
<td>40.31</td>
<td>0.56</td>
<td>0.78</td>
<td>0.72</td>
<td>1.79</td>
<td>± 1.65</td>
</tr>
</tbody>
</table>

*Averedge value of seven determinations.
SD. Standard deviation.
RSD. Relative standard deviation.
ROE. Range of error.
Table 4—Results of analysis of dosage forms

<table>
<thead>
<tr>
<th>Drug and dosage form&lt;sup&gt;ψ&lt;/sup&gt;</th>
<th>Label claim, mg/tablet or mg/mL</th>
<th>% found * ±SD</th>
<th>Student’s t-value (2.78)&lt;sup&gt;$&lt;/sup&gt;</th>
<th>F-value (6.39)&lt;sup&gt;$&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPH tablets&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25</td>
<td>98.76±0.86</td>
<td>99.12±0.56</td>
<td>1.25</td>
</tr>
<tr>
<td>Megatil tablets&lt;sup&gt;b&lt;/sup&gt;</td>
<td>50</td>
<td>101.28±0.36</td>
<td>102.14±0.63</td>
<td>2.47</td>
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<tr>
<td>Emetil tablets&lt;sup&gt;c&lt;/sup&gt;</td>
<td>100</td>
<td>97.84±0.92</td>
<td>98.36±0.38</td>
<td>1.26</td>
</tr>
<tr>
<td>Megatil injections&lt;sup&gt;b&lt;/sup&gt;</td>
<td>25</td>
<td>101.76±0.74</td>
<td>102.88±0.94</td>
<td>2.10</td>
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<td>PH</td>
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<td></td>
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<tr>
<td>Phenergan tablets&lt;sup&gt;a&lt;/sup&gt;</td>
<td>10</td>
<td>99.26±1.26</td>
<td>100.58±0.64</td>
<td>2.19</td>
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<tr>
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<td>25</td>
<td>101.37±0.52</td>
<td>99.84±0.28</td>
<td>6.04</td>
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<td>TPH</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Trazine tablets&lt;sup&gt;d&lt;/sup&gt;</td>
<td>5</td>
<td>103.24±1.48</td>
<td>102.56±0.74</td>
<td>0.97</td>
</tr>
<tr>
<td>Neocalm tablet&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5</td>
<td>98.12±0.76</td>
<td>98.96±0.42</td>
<td>2.25</td>
</tr>
<tr>
<td>PCPF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emidoxin tablet&lt;sup&gt;e&lt;/sup&gt;</td>
<td>5</td>
<td>99.64±0.92</td>
<td>101.14±0.63</td>
<td>3.03</td>
</tr>
<tr>
<td>Stemetil tablet&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5</td>
<td>97.72±1.26</td>
<td>99.28±0.72</td>
<td>2.46</td>
</tr>
<tr>
<td>FPH</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Prolinate injection&lt;sup&gt;d&lt;/sup&gt;</td>
<td>25</td>
<td>96.28±0.84</td>
<td>95.36±0.42</td>
<td>2.30</td>
</tr>
<tr>
<td>Anatenosol injection&lt;sup&gt;f&lt;/sup&gt;</td>
<td>25</td>
<td>97.42±1.04</td>
<td>97.74±0.38</td>
<td>2.93</td>
</tr>
</tbody>
</table>

* Mean value of five determinations.
<sup>$</sup> Figures in the parenthesis are the tabulated values at 95% confidence level.
<sup>ψ</sup> Marketed by: a. Rhone –Poulenc (India) Ltd., Mumbai
Intas Lab Pvt, Ltd., Ahmedabad.
LA Pharmaceuticals, Ahmedabad.
Sun Pharma Ind. Ltd., Mumbai.
Rallis India Ltd., Mumbai
Sterling Pharm Products co-Pvt. Ltd., Calcutta

Table 5—Results of recovery studies by the standard-addition technique

<table>
<thead>
<tr>
<th>Dosage form studied</th>
<th>Drug present in the dosage form, µg</th>
<th>Pure drug added, µg</th>
<th>Total found, µg</th>
<th>Recovery* of pure drug added, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Megatil tablets (50 mg)</td>
<td>101.28</td>
<td>120</td>
<td>225.45</td>
<td>102.64</td>
</tr>
<tr>
<td></td>
<td>101.28</td>
<td>150</td>
<td>283.70</td>
<td>97.85</td>
</tr>
<tr>
<td></td>
<td>101.28</td>
<td>180</td>
<td>283.70</td>
<td>101.34</td>
</tr>
<tr>
<td>Megatil injections (25 mg)</td>
<td>101.76</td>
<td>120</td>
<td>226.13</td>
<td>103.64</td>
</tr>
<tr>
<td></td>
<td>101.76</td>
<td>150</td>
<td>256.04</td>
<td>102.85</td>
</tr>
<tr>
<td></td>
<td>101.76</td>
<td>180</td>
<td>289.57</td>
<td>104.34</td>
</tr>
<tr>
<td>Phenergan tablets (25 mg)</td>
<td>50.69</td>
<td>75</td>
<td>123.65</td>
<td>97.28</td>
</tr>
<tr>
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<td>50.69</td>
<td>125</td>
<td>180.24</td>
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<td></td>
<td>50.69</td>
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<td>232.06</td>
<td>103.64</td>
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<tr>
<td>Trazine tablets (5 mg)</td>
<td>103.24</td>
<td>150</td>
<td>251.32</td>
<td>98.72</td>
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<tr>
<td></td>
<td>103.24</td>
<td>175</td>
<td>302.52</td>
<td>99.64</td>
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<tr>
<td></td>
<td>103.24</td>
<td>200</td>
<td>401.95</td>
<td>102.57</td>
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<td>Stemetil tablets (5 mg)</td>
<td>195.44</td>
<td>200</td>
<td>391.96</td>
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<tr>
<td></td>
<td>195.44</td>
<td>300</td>
<td>493.88</td>
<td>99.48</td>
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<tr>
<td></td>
<td>195.44</td>
<td>400</td>
<td>599.64</td>
<td>101.05</td>
</tr>
<tr>
<td>Prolinate injections (25 mg)</td>
<td>96.28</td>
<td>150</td>
<td>239.32</td>
<td>95.36</td>
</tr>
<tr>
<td></td>
<td>96.28</td>
<td>200</td>
<td>291.54</td>
<td>97.63</td>
</tr>
<tr>
<td></td>
<td>96.28</td>
<td>250</td>
<td>336.58</td>
<td>96.12</td>
</tr>
</tbody>
</table>

* Average of three determinations.
precision on a day-to-day basis, pure drug solution at concentration levels used to assess the accuracy and intra-day precision were analysed over a period of five days. The day-to-day RSD values were in the range of 0.64-1.85%.

**Application to dosage forms**

The proposed method was applied to the determination of the studied drugs in tablets and injections. The results presented in Table 4 reveal excellent recoveries in the range of 96.28-103.24% and low RSD values (<2%) indicate the high accuracy and repeatability of the method. The same batch tablets and injections were analysed simultaneously by the official British Pharmacopoeial method and these results are also contained in Table 4. The performance of the proposed method was judged by calculating the Student’s t-value and F-value. At 95% confidence level, the calculated t- and F-values did not exceed the tabulated values inferring that there is no significant difference between the proposed method and the official method in respect of accuracy and precision.

To further establish the validity and accuracy of the method, recovery tests through standard-addition technique were performed. Known amounts of pure drug at three levels were added to a fixed amount of tablet powder or injection solution (pre-analysed) and the total was found by the proposed method. Each test was repeated three times. The results compiled in Table 5 reveal good recoveries (95.36-104.34) and non-interference from common additives (to formulations) such as starch, talc, gum acacia, alginate, stearate, lactose, calcium gluconate, calcium dihydrogen-octohosphate and sulphite. This is also clear from results obtained for dosage forms presented in Table 4.

**Conclusions**

A new method based on oxidation-complexation reaction for five neuroleptic phenothiazine drugs using the spectrophotometric technique has been developed. It has no procedural or instrumental complications and the analytical performance is characterised by high accuracy and precision. It provides a wide dynamic range, highly stable coloured species, and a better sensitivity than that of many earlier methods. The method was applied to the analysis of dosage forms with recoveries of 96.28 – 103.24%. Many common inactive ingredients do not interfere. This is the first attempt at the determination of phenothiazine drugs based on oxidation followed by complexation reaction.

**References**