Determination of olanzapine by spectrophotometry using permanganate

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Two new spectrophotometric methods using permanganate as the oxidimetric reagent for the determination of olanzapine (OLP) were developed and validated as per the current ICH guidelines. The methods involved the addition of known excess of permanganate to OLP in either acid or alkaline medium followed by the determination of unreacted permanganate at 550 nm (method A) or bluish-green color of manganate at 610 nm (method B). The decrease in absorbance in method A or increase in absorbance in method B as a function of concentration of OLP was measured and related to OLP concentration. Under optimized conditions, Beer’s law was obeyed over the ranges 2.0 to 20 and 1.0 to 10 µg mL⁻¹ in method A and method B, respectively. The calculated molar absorptivity values were 1.34 x 10⁴ and 2.54 x 10⁴ l mol⁻¹ cm⁻¹ for method A and method B respectively, and the respective Sandell sensitivities were 0.0233 and 0.0123 µg cm⁻². The LOD and LOQ for method A were calculated to be 0.37 and 1.13 µg mL⁻¹ and the corresponding values for method B were 0.16 and 0.48 µg mL⁻¹. Intermediate precision, expressed as RSD was in the range 0.51 to 2.66 %, and accuracy, expressed as relative error ranged from 0.79 to 2.24 %. The proposed methods were successfully applied to the assay of OLP in commercial tablets with mean percentage recoveries of 102 ±1.59 % (method A) and 101 ±1.53 % (method B). The accuracy and reliability of the methods were further confirmed by performing recovery tests via standard addition procedure.

**Uniterms:** Olanzapine/determination. Spectrophotometry. Permanganate. Pharmaceuticals.

INTRODUCTION

Olanzapine (OLP), chemically known as 2-methyl-10-(4-methyl-piperazin-1-yl)-4H-3-thia-4,9-diazabenzof[\textregistered]azulene (Figure 1), is an atypical antipsychotic drug that belongs to the thienobenzodiazepine class. It shows high receptor affinity binding in vitro at serotonin, dopamine, muscarinic and histamine receptors. Since its introduction in 1997, it has been approved in 84 countries for treating schizophrenia and related disorders (Shen, 1999).

Several analytical methods have been reported for the determination of OLP in biological fluids and in pharmaceutical preparations, and they include high performance liquid chromatography (HPLC) with ultraviolet (Olesen et al., 1998; Boulton et al., 2001; Harald et al., 2001; Concetta et al., 2006; Dusci et al., 2002; Olesen et al., 2001; Raggi et al., 2000; Saracino et al., 2007; Shah et al., 2007; Reddy et al., 2007; Xuejun et al., 2004); electrochemical (Saracino et al., 2006; Raggi et al., 2000; Bao, Potts., 2001; Raggi et al., 2001; Kasper et al., 1999) or mass spectrometric (Thieme, Sachs., 2003; Berna et al., 2002; Titier et al., 2003; Dusci et al., 2002) detection, gas chromatography (Sabbioni et al., 2004), capillary zone electrophoresis (Raggi et al., 2000), UV-spectrophotometry and non-aqueous titrimetry (Firdous et al., 2005). However, there are only three reports on the visible spectrophotometric methods (Jasinska, Nalewajko, 2004; Mohamed, 2008; Krebs et al., 2006) based on redox reaction using hexacyanoferrate (III), cerium (IV), N-bromosuccinimide (NBS) or potassium iodate. However, these methods suffer from one or the other disadvantage such as poor sensitivity, unstable color and rigid experimental conditions (Table 1).

The aim of the present work is to develop simple, sensitive and cost-effective spectrophotometric methods for the determination of OLP in pharmaceutical formulations. The methods make use of potassium permanganate as the oxidimetric reagent, and have been demonstrated to be superior to the existing spectrophotometric methods in terms of sensitivity, color stability, working conditions, and accuracy and precision. We have found that potassium permanganate has earlier been used in pharmaceutical analysis in the determination of thio-oxanthines, for example (Tammilehto, 1980), isoniazid (Murugesan, Venkappaya, 1983) methyl thiouracil (Kucharski, Sikorska-Tomica, 1982) chloramphenicol (Fedchenko, 1985) amidopyrine (Stepnayuk and Bala-gorazumnya, 1989), valdecoxb (Suganthi et al., 2006), nicotine (Al-Tamrah, 1999) tramadol HCl (Abdellatef, 2002) cefuroxime (Reddy et al., 2002), diloxamide (Al-Ghanman, Belal., 2001) and pentacoze (Sastry et al., 1998), to mention a few.

In our studies OLP was found to react with permanganate in H\textsubscript{2}SO\textsubscript{4} medium consuming the oxidant in proportion to its concentration. This reaction was used for the indirect assay of OLP by measuring the decrease in the absorbance at 550 nm as a function of the OLP concentration. On the other hand, in alkaline medium, the reaction yielded a bluish-green manganate with a \(\lambda_{\text{max}}\) at 610 nm. This color reaction was studied for the direct spectrophotometric determination of the drug. Optimum conditions were established and both the methods were validated for linearity, sensitivity, accuracy and precision as well as robustness and ruggedness. The validated methods when applied to the determination of OLP in tablets yielded results which were in agreement with the label claim.

MATERIAL AND METHODS

Apparatus

Absorbance measurements were made with a Systronics model 106 digital spectrophotometer equipped with 1 cm matched quartz cells.

Reagents and standards

All chemicals used were of analytical grade and solutions were made in distilled water.

Potassium permanganate (600 \(\mu\)g mL\(^{-1}\))

An approximately 0.002 M solution was prepared by dissolving 79.00 mg of KMnO\(_4\) (Merck, Mumbai, India) in water and diluting to 250 mL in a calibrated flask, and standardized using H.A Bright’s procedure (Vogel, 1961). The standard solution was then diluted appropriately with water to get 600 \(\mu\)g mL\(^{-1}\) working concentration for method A. A separate 0.2 % aqueous solution was prepared for use in method B.
Sulphuric acid (0.1 and 2 M)

Concentrated acid (S.D. Fine Chem, Mumbai, India, sp. gr. 1.84) was appropriately diluted with water to get the required concentrations.

Sodium hydroxide (1 M)

Prepared by dissolving 4 g of the chemical (Merck, Mumbai, India) in 100 mL of water.

Standard OLP solution

Pharmaceutical grade OLP certified to be 99.85% pure was kindly provided by Cipla India Ltd., Mumbai, India; and was used as received. A 500 µg mL⁻¹ stock standard solution was prepared by dissolving accurately weighed 50 mg of pure OLP in 0.1 M H₂SO₄ and diluting to the mark in a 100 mL calibrated flask with the same acid. It was subsequently diluted to 50 µg mL⁻¹ OLP for method A. Twenty mg of OLP were weighed separately and dissolved in 5 mL of 0.5 M acetic acid and diluted to 100 mL in a calibrated flask with water. The solution was then diluted with water to get a working concentration of 20 µg mL⁻¹ for use in method B.

Tablets

Three brands of tablets claimed to contain 2.5, 5.0 and 20 mg OLP per tablet were purchased from local market for investigation.
Procedure

Method A

Aliquots of standard OLP solution (50 µg mL⁻¹) in the range 0.0-4.0 mL were accurately measured and transferred to a series of 10 mL calibrated flasks and the volume was adjusted to 4.0 mL with 0.1 M H₂SO₄. Two mL of 2 M H₂SO₄ were added to each flask followed by 1 mL of 600 µg mL⁻¹ KMnO₄ solution. The content was mixed and the flasks were let stand for 15 min before diluting to the mark with water. The absorbance of each solution was measured at 550 nm against a reagent blank.

Method B

Known volumes of standard OLP solution (0.0, 1.0,…..5.0 mL) were accurately delivered into a series of 10 mL calibrated flasks and the volumes were adjusted to 5.0 mL with water. To each flask were added 1 mL each of 1 M NaOH and 0.2 % KMnO₄ solutions. The content was mixed well and flasks were allowed to stand for 15 min with occasional shaking. Then, the volume was made up to the mark with water and absorbance measured at 610 nm against a reagent blank.

Calibration graphs were prepared by plotting either the decreasing absorbance values in method A or increasing absorbance values in method B versus concentrations of OLP. The unknown concentration was read from the respective calibration graph or deduced from the regression equation desired using the Beer’s law data.

Procedure for tablets

Twenty tablets were weighed accurately and pulverized. A quantity of the powder containing 20 mg of OLP was accurately weighed into a 100 mL calibrated flask, added 60 mL of 0.1 M H₂SO₄ and shaken for 20 min. Then, the volume was diluted to the mark with 0.1 M H₂SO₄, mixed and filtered using a Whatman N° 42 filter paper. First 10 mL of the filtrate were discarded and a suitable aliquot of the subsequent portion (200 µg mL⁻¹ in OLP) was diluted with 0.1 M H₂SO₄ to obtain 50 µg mL⁻¹ solution and the analysis was completed using the procedure described earlier (method A). However, for method B, a portion of the tablet powder equivalent to 20 mg of OLP was accurately weighed into a 100 mL beaker. The powder was extracted with three 10 mL portions of chloroform and each time the extract was filtered with a Whatman N° 42 filter paper. The filtrate was collected in 100 mL calibrated flask, chloroform was evaporated over a water bath and the residue was dissolved in 5 mL 0.5 M acetic acid and the solution was diluted to the mark with water. The solution was appropriately diluted before applying the procedure for the assay of drug content.

Placebo for analysis

A placebo blank of the composition: starch (10 mg), acacia (15 mg), hydroxyl cellulose (10 mg), sodium citrate (10 mg), talc (20 mg), magnesium stearate (15 mg) and sodium alginate (10 mg) was made and its solution was prepared as described under ‘tablets’, and then subjected to analysis.

RESULTS AND DISCUSSION

The proposed methods are based on the redox reaction between permanganate and OLP in acid (method A) or in alkali (method B) medium. In method A, a known excess of KMnO₄ was added to OLP in H₂SO₄ medium followed by the determination of the residual oxidant by measuring its absorbance at 550 nm. The decrease in absorbance at 550 nm with respect to the reagent blank was taken as the measure of OLP concentration. In method B, KMnO₄ resulting from the reduction of KMnO₄ by OLP in NaOH medium was measured at 610 nm and related to OLP concentration. The possible reaction scheme of both the methods is given in Scheme 1 and Scheme 2.

Method development: Optimization of experimental variables

Method A

Preliminary experiments were performed to determine the permanganate concentration which would give a reasonable maximum absorbance at 550 nm and in H₂SO₄ medium; and this was found to be 60 µg mL⁻¹ (0.811 absorbance unit). Hence, different concentrations of OLP were reacted with 1 mL of 600 µg mL⁻¹ KMnO₄ in H₂SO₄ medium, and after elapsed the contact time, the absorbance of the residual permanganate was measured and related to OLP concentration.

When a fixed concentration of KMnO₄ (60 µg mL⁻¹) was reacted with varying concentrations of OLP, the former was consumed in proportion to OLP concentration and there occurred a concomitant fall in the concentration of KMnO₄ as shown by the decreasing absorbance values at 550 nm with increase in the OLP concentration. This is depicted in Figure. 2. This facilitated the evaluation of the linear range over which the method is applicable to the determination of OLP.

Since oxidation reactions with permanganate are usually performed in H₂SO₄ medium (Basset et al., 1978),
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The reaction of the oxidant with the drug was carried out in H$_2$SO$_4$ medium. Experiments were performed with H$_2$SO$_4$ concentrations in the range 0.5-1.5 M and it was found that maximum and constant absorbance readings were obtained in the range studied (Figure 3a). Hence, 2 mL of 2 M H$_2$SO$_4$ in a total volume of ~7 mL was fixed as the optimum. The reaction time selected for the recommended method was fixed by carrying out the experiment using 10 µg mL$^{-1}$ OLP. Maximum absorbance was obtained in 15 min and it remained constant for the next 45 min (Figure 3b) at room temperature.

Method B

This method is based on the reduction of permanganate to manganate by OLP in the presence of NaOH.

\[ \text{OLP} + \text{Known excess of KMnO}_4 \xrightarrow{H^+} \text{OLP-sulfoxide} + \text{Reacted KMnO}_4 \] (measured at 550 nm)

\[ \text{OLP} + \text{Excess of KMnO}_4 \xrightarrow{OH^-} \text{K}_2\text{MnO}_4 \] (Bluish-green colour measured at 610 nm)

The reaction of the oxidant with the drug was carried out in H$_2$SO$_4$ medium. Experiments were performed with H$_2$SO$_4$ concentrations in the range 0.5-1.5 M and it was found that maximum and constant absorbance readings were obtained in the range studied (Figure 3a). Hence, 2 mL of 2 M H$_2$SO$_4$ in a total volume of ~7 mL was fixed as the optimum. The reaction time selected for the recommended method was fixed by carrying out the experiment using 10 µg mL$^{-1}$ OLP. Maximum absorbance was obtained in 15 min and it remained constant for the next 45 min (Figure 3b) at room temperature.

**FIGURE 2** - Effect of OLP concentration on the absorbance of 60 µg mL$^{-1}$ KMnO$_4$ (A.0.0; B.5.0; C.10.0; D.15.0 and E.20 µg mL$^{-1}$ OLP).
thereby producing the reduced species - the bluish-green colored chromogen (Mann, Sounders, 1974; Sharma, 1994) having the absorption maximum at 610 nm (Figure 4). The formation of the colored product and the sensitivity of the reaction were found to be influenced by the alkali and permanganate concentrations. Maximum and constant absorbance readings were observed when an overall NaOH concentration of 0.06-0.5 M was maintained at a drug concentration of 6 µg mL\(^{-1}\). Two mL of 2 M NaOH in a total volume of 7 mL were hence used for the redox reaction (Figure 5a). The reaction was somewhat rapid compared to method A, taking 10 min for completion, and the bluish-green manganate color was stable for 40 min thereafter (Figure 5b). When a separate experiment was conducted to study the permanganate concentration, it was found that maximum absorbance associated with a minimum blank reading was obtained when 1 mL of 0.2 % KMnO\(_4\) in a total volume of 10 mL was used. Higher concentrations of permanganate, no doubt, resulted in increased sensitivity but the blank absorbance simultaneously showed an increasing trend.

**Method validation**

- Linearity, sensitivity, limits of detection and quantification

Calibration graphs were constructed from nine and six points covering the concentration ranges 2.0-20.0 and 1-10 µg mL\(^{-1}\) for method A and method B, respectively (Figure 6). In method A, Beer’s law was obeyed in the inverse manner. Regression analysis of the Beer’s law data indicated a linear relationship between absorbance and concentration (Table II), which is corroborated by high values (close to unity) of the correlation coefficients. The small values of the variance speak about the negligible scattering of the calibration data points around the line of regressions for both the proposed procedures. The significance of correlation coefficients was evaluated by calculating the t-values using the following formula (Miller, Miller, 2000):

\[
t = \frac{|r|\sqrt{n-2}}{\sqrt{1-r^2}}
\]

The calculated values were found to be 30.26 and 48.45 for method A and method B, respectively. Thus,
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it can be concluded that there is significant relationship between the concentration of OLP and the parameters used in the development of regression equations.

The calculated molar absorptivity and Sandell sensitivity (Zavis et al., 1976) values are summarized in Table II. The limits of detection (LOD) and quantification (LOQ), calculated according to the ICH (ICH guidelines 1996) guidelines using the formulae:

\[
\text{LOD} = 3.3 \frac{S}{b} \quad \text{and} \quad \text{LOQ} = 10 \frac{S}{b},
\]

(where S is the standard deviation of seven blank absorbance values, and b is the slope of the calibration plot) are also summarized in Table II. The high values of ε and low values of Sandell sensitivity and LOD indicate the high sensitivity of the proposed methods. The reaction stoichiometry for method B was determined by the Job’s method of continuous variations and was found to be 1:4 (OLP:KMnO₄).

precision and accuracy

The assays described under “general procedures” were repeated seven times within the day to determine the repeatability (intra-day precision) and six times on different days to determine the intermediate precision (inter-day precision) of the methods. These assays were performed for three levels of analyte. The results of this study are summarized in Table III. The percentage relative standard deviation (%RSD) values were <2 % (intra-day) and <3 % (inter-day) indicating high precision of the methods. The accuracy of the methods was determined by the percent mean deviation from known concentration, bias % = \([\frac{(\text{Concentration found} - \text{known concentration}) \times 100}{\text{known concentration}}]\). Bias was calculated at each concentration and these results are also presented in Table III.
A systematic study was performed to determine the effect of matrix by analyzing the placebo blank and synthetic mixture containing OLP. A placebo blank of the composition described earlier was prepared and analyzed. The absorbance of the placebo solution in each case was almost equal to the intercept of the calibration graph, which revealed no interference. To assess the role of the inactive ingredients on the assay of OLP, a synthetic mixture was separately prepared by adding 20 mg of OLP to the placebo mentioned above. The drug was extracted and solution prepared as described under the general procedure for tablets. The solution after appropriate dilution were analyzed following the recommended procedures. The absorbance resulting from 10 µg mL\(^{-1}\) (method A) and 6 µg mL\(^{-1}\) (method B) were nearly the same as those obtained for pure OLP solutions of identical concentrations. This unequivocally demonstrated the non-interference of the inactive ingredients in the assay of OLP. Further, the slopes of the calibration plots prepared from the synthetic mixture solutions were about the same as those prepared from pure drug solutions. In method B (alkaline medium) a strong interference was noticed from some tablet excipients causing erratic results. To overcome this interference, after several trials, it was found that OLP in the synthetic mixture or the tablet should be extracted with chloroform, before applying the method following the steps involved in the assay procedure.

### Robustness and ruggedness

To determine the robustness of the methods, two experimental variables, acid/alkaline concentration and reaction time, were altered deliberately in small increments. Intermediate precision expressed as %RSD was calculated and found to be <1%. Method ruggedness was demonstrated having the analysis done by four analysts, and also by a single analyst performing analysis on three different instruments in the same laboratory. Intermediate precision values in both instances were in the range 0.85-3.06% indicating acceptable ruggedness. These results are summarized in Table IV.

### TABLE II - Sensitivity and regression parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Method A</th>
<th>Method B</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\lambda_{max}), nm</td>
<td>550</td>
<td>610</td>
</tr>
<tr>
<td>Color stability, min.</td>
<td>45</td>
<td>40</td>
</tr>
<tr>
<td>Linear range, µg mL(^{-1})</td>
<td>2.0-20.0</td>
<td>1.0-10.0</td>
</tr>
<tr>
<td>Molar absorptivity(e), L mol(^{-1}) cm(^{-1})</td>
<td>1.34 x 10(^4)</td>
<td>2.54 x 10(^4)</td>
</tr>
<tr>
<td>Sandell sensitivity*, µg cm(^2)</td>
<td>0.0233</td>
<td>0.0123</td>
</tr>
<tr>
<td>Limit of detection (LOD), µg mL(^{-1})</td>
<td>0.37</td>
<td>0.16</td>
</tr>
<tr>
<td>Limit of quantification (LOQ), µg mL(^{-1})</td>
<td>1.13</td>
<td>0.48</td>
</tr>
<tr>
<td>Regression equation, (Y^{**})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.8111</td>
<td>0.0310</td>
</tr>
<tr>
<td>Slope (b)</td>
<td>-0.0411</td>
<td>0.0965</td>
</tr>
<tr>
<td>Standard deviation of a ((S_a))</td>
<td>0.0998</td>
<td>0.0998</td>
</tr>
<tr>
<td>(\pm tS_a/\sqrt{n})</td>
<td>0.077</td>
<td>0.071</td>
</tr>
<tr>
<td>Standard deviation of b ((S_b))</td>
<td>0.0052</td>
<td>0.0111</td>
</tr>
<tr>
<td>(\pm tS_b/\sqrt{n})</td>
<td>0.004</td>
<td>0.008</td>
</tr>
<tr>
<td>Variance ((S^2))</td>
<td>9.96 x 10(^{-3})</td>
<td>9.96 x 10(^{-3})</td>
</tr>
<tr>
<td>Regression coefficient (r)</td>
<td>-0.9962</td>
<td>0.9983</td>
</tr>
</tbody>
</table>

*Limit of determination as the weight in µg per mL of solution, which corresponds to an absorbance of A = 0.001 measured in a cuvette of cross-sectional area 1 cm\(^2\) and l = 1 cm. \(Y=a+bX\), Where Y is the absorbance, X is concentration in µg mL\(^{-1}\), a is intercept, b is slope, \(\pm tS/\sqrt{n}\) = confidence limit for intercept, \(\pm tS_b/\sqrt{n}\) = confidence limit for slope.

**Regression equation, \(Y=a+bX\), Where Y is the absorbance, X is concentration in µg mL\(^{-1}\), a is intercept, b is slope, ± \(tS/\sqrt{n}\) = confidence limit for intercept, ± \(tS_b/\sqrt{n}\) = confidence limit for slope.

### TABLE III - Evaluation of accuracy and precision

<table>
<thead>
<tr>
<th>Method</th>
<th>OLP taken, µg mL(^{-1})</th>
<th>Intra-day accuracy and precision (n=7)</th>
<th>Inter-day accuracy and precision (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>OLP found µg mL(^{-1})±CL</td>
<td>%RE</td>
</tr>
<tr>
<td>A</td>
<td>5.00</td>
<td>4.92±0.08</td>
<td>1.60</td>
</tr>
<tr>
<td></td>
<td>10.0</td>
<td>10.2±0.11</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>15.0</td>
<td>14.8±0.09</td>
<td>1.33</td>
</tr>
<tr>
<td>B</td>
<td>2.00</td>
<td>2.02±0.01</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>4.00</td>
<td>4.05±0.06</td>
<td>1.25</td>
</tr>
<tr>
<td></td>
<td>6.00</td>
<td>5.90±0.09</td>
<td>1.67</td>
</tr>
</tbody>
</table>

%RE. Percent relative error, %RSD. relative standard deviation and CL. Confidence limits were calculated from: CL \(= \pm tS/\sqrt{n}\). (\(t = 2.44\) for six degrees of freedom at the 95% confidence level; \(S = \) standard deviation and \(n = \) number of measurements).
TABLE IV - Method robustness and ruggedness expressed as intermediate precision (% RSD)

<table>
<thead>
<tr>
<th>Method</th>
<th>OLP taken µg/mL</th>
<th>Parameter altered</th>
<th>Robustness</th>
<th>Ruggedness</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Reaction time*</td>
<td>H₂SO₄/NaOH concentration**</td>
<td>Inter-Analysts (% RSD)</td>
</tr>
<tr>
<td>A</td>
<td>5.00</td>
<td>0.76</td>
<td>0.66</td>
<td>1.04</td>
</tr>
<tr>
<td></td>
<td>10.0</td>
<td>0.82</td>
<td>0.74</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>15.0</td>
<td>0.97</td>
<td>0.52</td>
<td>0.92</td>
</tr>
<tr>
<td>B</td>
<td>2.00</td>
<td>0.56</td>
<td>0.66</td>
<td>0.78</td>
</tr>
<tr>
<td></td>
<td>4.00</td>
<td>0.83</td>
<td>0.48</td>
<td>0.92</td>
</tr>
<tr>
<td></td>
<td>6.00</td>
<td>0.78</td>
<td>0.78</td>
<td>0.85</td>
</tr>
</tbody>
</table>

*In method A, the reaction times were 13, 15 and 17 min, and the same were 8, 10 and 12 min in method B. **In method A, H₂SO₄ concentrations were 0.5, 0.6 and 0.7 M, and NaOH concentrations in method B were 0.1, 0.2 and 0.3 M.

Application

The proposed methods are applied for the quantification of OLP in commercial tablets. The results were compared with those obtained using a published non-aqueous titrimetric method (Firdous et al., 2005). Statistical analysis of the results did not detect any significant difference between the performance of the proposed methods and reference titrimetric method, with respect to accuracy and precision as revealed by the Student’s t-value and variance ratio F-value (Inczedy et al., 1998). The results of assay are given in Table V.

Recovery study

To further assess the accuracy of the methods, recovery experiments were performed by applying the standard-addition technique. The recovery was assessed by determining the agreement between the measured standard concentration and added known concentration to the sample. The test was done by spiking the pre-analyzed tablet powder with pure OLP at three different levels (50, 100 and 150%) of the content present in the tablet powder (taken), and the total was found by the proposed methods. Each test was repeated three times. In all the cases, the recovery percentage values ranged between 99.4 and 104.1%, with relative standard deviation in the range 1.35-1.78%. Closeness of the results to 100% showed the fairly good accuracy of the methods (Table VI).

CONCLUSIONS

The methods proposed herein, based on the use of spectrophotometry with permanganate, can reliably determine olanzapine in pharmaceuticals, with good accuracy and precision. Furthermore, the methods are more sensitive, as compared to many published spectrophotometric method-
TABLE VI - Results of recovery study via standard-addition method

<table>
<thead>
<tr>
<th>Tablet studied</th>
<th>OLP in tablet, µg mL(^{-1})</th>
<th>Pure OLP added, µg mL(^{-1})</th>
<th>Total found, µg mL(^{-1})</th>
<th>Pure OLP recovered (Percent±SD(^{*}))</th>
<th>OLP in tablet, µg mL(^{-1})</th>
<th>Pure OLP added, µg mL(^{-1})</th>
<th>Total found, µg mL(^{-1})</th>
<th>Pure OLP recovered (Percent±SD(^{*}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oleanz-20</td>
<td>4.96</td>
<td>2.5</td>
<td>7.52</td>
<td>102.3±1.76</td>
<td>3.0</td>
<td>4.49</td>
<td>99.47±1.46</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.96</td>
<td>5.0</td>
<td>10.17</td>
<td>104.1±1.45</td>
<td>3.0</td>
<td>4.5</td>
<td>103.3±1.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.96</td>
<td>7.5</td>
<td>12.59</td>
<td>101.7±1.57</td>
<td>3.0</td>
<td>7.56</td>
<td>101.4±1.35</td>
<td></td>
</tr>
</tbody>
</table>

\(^{*}\)Mean value of three determinations.

ds (Jasinska, Nalewajko., 2004; Mohamed., 2008; Krebs et al., 2006) and also some HPLC methods (Olesen et al., 1998; Harald et al., 2001; Concetta et al., 2006; Dusci et al., 2002; Olesen et al., 2001; Raggi et al., 2001; Raggi et al., 2000; Shah et al., 2007; Reddy et al., 2007; Xuejun et al., 2004). The methods are simpler as compared to published methods (Jasinska, Nalewajko, 2004; Mohamed, 2008; Krebs et al., 2006) with respect to experimental conditions, instrumental setup and the stability of the measured species. An all important advantage is the cost-effectiveness, since analysis can be performed with an inexpensive instrument as compared to methods (Jasinska, Nalewajko, 2004; Mohamed, 2008; Krebs et al., 2006) which require expensive devices and/or reagents (Table I). The methods are rapid and allow the determination of the drug in tablets without any interference from the common tablet excipients. The limitation of method B (in alkaline medium) is that it cannot be applied directly to the tablets, and involves extraction of the drug into chloroform and evaporation of the organic solvent before other steps are applied for the assay.

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