Application of oxidants to the spectrophotometric microdetermination of meclizine HCl in pure and pharmaceutical formulations

Abdel-Azem Mohammed, El-Sharkawy Talaat, Yonis Mohamed, and Sayed Ahmed Shama
Application of oxidants to the spectrophotometric microdetermination of meclizine HCl in pure and pharmaceutical formulations

Abdel-Azem Mohammed, El-Sharkawy Talaat, Yonis Mohamed, and Sayed Ahmed Shama

Faculty of Science, Chemistry Department, Benha University, Benha, Egypt.

Accepted 17th October, 2012

Two simple, rapid, sensitive and accurate methods (A and B) have been established and developed for the microdetermination of meclizine hydrochloride in pure form and in pharmaceutical formulations. These two methods are based on the oxidation of the cited drug with Fe (III) in acidic medium. The formed Fe (II) reacts with 1,10-phenanthroline (method A) and the ferroin complex is measured spectrophotometrically at λmax 510 nm against reagent blank. Method B is based on the reaction of the formed Fe (II) with 2,2'-bipyridyl to form a stable colored complex at λmax 521 nm. Optimization of the experimental conditions was described. Beer’s law was obeyed in the concentration range of 0.4-11 μg ml−1 by using method A and 0.5-21 μg ml−1 by using method B. The apparent molar absorptivity for method A is 4.76 x 10^4 and for method B is 3.66 x 10^4 L mol−1 cm−1, respectively. The suggested procedures can be used for the determination of meclizine hydrochloride in both pure and dosage forms without interference from common excipients.

Keywords: Spectrophotometric, meclizine hydrochloride, pharmaceutical formulation, 1,10-phenanthroline and 2,2'-bipyridyl.

INTRODUCTION

Meclizine HCl [piperazine 1-[(4-chlorophenyl)phenylmethyl]-4-[(3-methylphenyl)(methyl)dihydrochloride monohydrate] is an antiemetic agent used in postoperative vomiting. Several methods have been reported for the determination of meclizine HCl inducing HPLC (Kvist et al., 2000 and Zhijun et al., 2011), by using capillary electrophoresis (Hoy et al., 2003), spectrophotometrically (Hom and Ebert 2006) and the determination of the solubility of meclizine by using nonionic surfactants (Ahmed and Eur 2001). Fe (III)-1,10-phenanthroline and Fe (III)-2,2'-bipyridyl reagents are used for the determination of some drugs (Rahman et al., 2004 and Zhijun et al., 2010).

The present work describes the development of two simple and rapid spectrophotometric methods, by using 1.10-phenanthroline or 2,2'-bipyridyl reagent for the determination of meclizine HCl in pure or in dosage forms with good accuracy and sensitivity especially for a routine quality control analysis of pharmaceutical products containing meclizine hydrochloride.

MATERIALS AND METHODS

Apparatus

All the spectral measurements were made using JASCO V-530 (UV-VIS) spectrophotometer (Japan), with scanning speed 400 nm/min and band width 2.0 nm. They are also equipped with 10 mm matched quartz cells and a Metrohm (Switzerland) pH-meter was used for colorimetric pH measurements. A water bath, JOUAN, J18 Bain Universal (France) was used to carry out the temperature studies.

MATERIAL AND REAGENTS

All chemicals used were of analytical grade and all solutions were freshly prepared in doubly distilled water. - Pure meclizine HCl bulk powder was obtained from Delta Pharma S. A. E.10th of Ramadan City, Egypt. Meclizine HCl working solution was prepared by dissolving 0.01 g of pure meclizine HCl in 50 ml of
bidistilled water and was completed to 100 ml with bidistilled water to obtain the working standard solution. At least ten tablets of meclizine HC1 were weighed into a small dish, powdered and mixed well. A portion equivalent to 10 mg was weighed and dissolved in 100 ml bidistilled water, and was mixed well for 15 min by using a magnetic stirrer and filtered through a sintered glass crucible G4. A 0.8 ml aliquot of the test solution (100 µg ml-1 of meclizine HC1) was treated as described above.

**GENERAL PROCEDURE FOR BULK POWDER**

Aliquots of standard drug solution of meclizine HC1 were ranging from 0.04 to 1.1 ml (0.4-11 µg ml-1) for method A and from 0.05 to 2.1 ml (0.5-21 µg ml-1) for method B by using micropipette as shown in Figure 1. The developed methods are applied successfully for the determination of meclizine HC1 in pure form and in tablets without any interference of common excipients.

The oxidation process of meclizine HC1 is catalyzed by heating in water bath of 80±1 0C. The time required to complete the reaction is at 10 min. Then, the solution is left to cool at room temperature and the volume was made up to the mark with bidistilled water. The developed colored complexes were formed and measured at 510 nm for method A and at 521 nm for method B as shown in Figure 2.

**RESULTS AND DISCUSSION**

Ferric salts play a prominent role in the spectrophotometric determination of many pharmaceutical drugs. Acting as an oxidant, a ferric salt gets reduced to ferrous salt and this amount corresponds to drug concentration. The amount of Fe (II) can be determined by using reagents such as 1,10-phenanthroline and 2,2'-bipyridyl. These properties have been utilized to develop spectrophotometric methods for the determination of meclizine HC1. 1,10-phenanthroline and 2,2'-bipyridyl are organic bases similar to chemical structure, contain the iron (II) specific group (Marczenko., 1976).

The methods A and B are based on the formation of tris (o-phenanthroline) or tris (2,2'-bipyridyl) iron (II) chelate upon the reaction of meclizine HC1 with an iron (III) o-phenanthroline or iron (III) 2,2'-bipyridyl reagent. The reaction proceeds through the reduction of iron (III) to iron (II) and the subsequent formation of the intensive orange-red coloration of the complex.

The absorption spectra of the colored species in the proposed methods show characteristic λmax values as in Figure 2. The experimental conditions were established by varying each parameter individually (Massart et al., 1988) and observing its effect on the absorbance of colored species.

In order to establish the favorable experimental conditions for proposed methods, meclizine HC1 was allowed to react with Fe (II) in the presence of phenanthroline or bipyridyl.

**Effect of pH**

PROCEDURE FOR THE ASSAY OF FORMULATIONS

- The preparation of iron (III) o-phenanthroline reagent (Vishal and Sunil., 2010 and Amin et al., 1999) was prepared by mixing a 0.198 g of 1,10-phenanthroline monohydrate (Fluka, Swiss) with 2.0 ml of 1.0 M HCl and 0.16 g of ferric ammonium sulphate dodecahydrate (Fluka, Swiss) and, finally, this mixture was diluted with bidistilled water to 100 ml.

- Preparation of iron (III) bipyridyl reagent (Hapkin & williams, England) by dissolving a 0.16 g of 2,2'-bipyridyl in 2.0 ml of 1.0 M HCl and 0.16 g of ferric ammonium sulphate dodecahydrate.

- Sodium acetate-acetic acid buffer solutions were prepared as recommended previously (Britton., 1952).
The effect of pH on the reduction of Fe (III) by meclizine HC1 to form iron (II)-phenanthroline complex or iron (II) phenanthroline complex was studied over the range of 1.0-6.0 ml of acetate buffer. The highest absorbance was obtained at pH 2.6 (2.0 ml of acetate buffer) for method A and at pH 3.2 (2.0 ml of acetate buffer) for B.

Effect of concentration of reagent
The effect of reagent volume was studied in the range from 0.1 - 4.0 ml. The addition of 3.0 ml of iron (III) phenanthroline or 2.0 ml of iron (III) 2,2' bipyridyl reagent was sufficient to obtain a maximum reproducible absorbance as shown in Figure 3. Smaller volumes gave incomplete complex formation. A larger volume of reagent had no effect on the complex formation.

**Table 1**: Optical and regression characteristics of meclizine HC1 with different reagents.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>1, 10-Phenanthroline</th>
<th>2, 2'-Bipyridyde</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>2.6</td>
<td>3.2</td>
</tr>
<tr>
<td>$\lambda_{max}$ (nm)</td>
<td>510</td>
<td>521</td>
</tr>
<tr>
<td>Bear's law limits (µg ml$^{-1}$)</td>
<td>0.4-11</td>
<td>0.5-21</td>
</tr>
<tr>
<td>Ringbom limits (µg ml$^{-1}$)</td>
<td>0.5-10.7</td>
<td>0.7-20.4</td>
</tr>
<tr>
<td>Molar absorptivity (L mol$^{-1}$ cm$^{-1}$)</td>
<td>$4.04 \times 10^4$</td>
<td>$3.11 \times 10^4$</td>
</tr>
<tr>
<td>Sandell sensitivity (ng cm$^{-2}$)</td>
<td>11.9</td>
<td>15.5</td>
</tr>
<tr>
<td>Detection limits (µg ml$^{-1}$)</td>
<td>0.104</td>
<td>0.138</td>
</tr>
<tr>
<td>Quantitation limits (µg ml$^{-1}$)</td>
<td>0.347</td>
<td>0.461</td>
</tr>
<tr>
<td>Regression equation* Slope (b)</td>
<td>0.0839</td>
<td>0.0645</td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.016</td>
<td>0.0139</td>
</tr>
<tr>
<td>Correlation coefficient (r)</td>
<td>0.9996</td>
<td>0.998</td>
</tr>
<tr>
<td>RSD %</td>
<td>0.59</td>
<td>0.41</td>
</tr>
</tbody>
</table>

*With respect to $A = a + b C$ where $C$ is concentration of drug in µg ml$^{-1}$ and $A$ is absorbance.

**Table 2**: Evaluation of the accuracy and precision of the proposed procedure of meclizine HC1

<table>
<thead>
<tr>
<th>Dye</th>
<th>Taken µg ml$^{-1}$</th>
<th>Recovery %</th>
<th>RSD %</th>
<th>RE %</th>
<th>Confidence limits$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 10-Phenanthroline</td>
<td>4.0</td>
<td>101.3</td>
<td>0.46</td>
<td>0.81</td>
<td>4.05 ± 0.0327</td>
</tr>
<tr>
<td></td>
<td>6.0</td>
<td>99.2</td>
<td>0.49</td>
<td>0.52</td>
<td>5.95 ± 0.0304</td>
</tr>
<tr>
<td></td>
<td>8.0</td>
<td>99.8</td>
<td>0.74</td>
<td>0.78</td>
<td>7.98 ± 0.0619</td>
</tr>
<tr>
<td>2, 2'-Bipyridyde</td>
<td>8.0</td>
<td>100.3</td>
<td>0.65</td>
<td>0.68</td>
<td>8.02 ± 0.0546</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>99.8</td>
<td>0.40</td>
<td>0.42</td>
<td>11.98 ± 0.0504</td>
</tr>
<tr>
<td></td>
<td>18</td>
<td>100.1</td>
<td>0.22</td>
<td>0.23</td>
<td>18.01 ± 0.0416</td>
</tr>
</tbody>
</table>

$^a$ Relative standard deviation for six determinations, $^b$ 95% confidence limits and five degrees of freedom

**Figure 3**: Effects of reagents on the absorbances of complexes.
Effect of temperature and time

A preliminary investigation was carried out to determine

Abdel-Azem et al., 140

Table 3: Determination of meclizine HC1 in pharmaceutical formulations (Tablets).

<table>
<thead>
<tr>
<th>Pharmaceutical formulations</th>
<th>Proposed methods</th>
<th>Official method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1, 10-Phenanthroline</td>
<td>2, 2'-Bipyridyle</td>
</tr>
<tr>
<td></td>
<td>Recovery %</td>
<td>t- value</td>
</tr>
<tr>
<td>Vomidoxine 25 mg(^{11})</td>
<td>99.5</td>
<td>0.90</td>
</tr>
<tr>
<td>Navoproxine 25mg(^{12})</td>
<td>99.6</td>
<td>0.80</td>
</tr>
<tr>
<td>Ezadoxine 25 mg(^{13})</td>
<td>99.6</td>
<td>0.36</td>
</tr>
<tr>
<td>Dizirest B(_{2}) 25 mg(^{14})</td>
<td>100.5</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Theoretical value for t- and F- values for five degrees of freedom and 95 % confidence limits are 2.57 and 5.05 respectively.

- Pharaonia Pharmaceutical, Pharma-pharma Company, Cairo, Egypt.
- Delta Phama S A. E. 10\(^{th}\) of Ramadan City, Egypt.
- Multipharma for Pharmaceuticals and Chemicals Company, S. A. E., Egypt.
- Sigma Pharmaceutical Industries Company, S. A. E., Egypt.

the effect of temperature on the formation of the colored product. The reaction of color formation under the effect of meclizine HC1 proceeded very slowly at room temperatures. To accelerate the reaction, the temperature had to be increased till 80 oC. The maximum absorbance was obtained after heating for about 10 min on a water bath at 80 oC for A and 70 oC for B. The increase of temperature more than this degree had no appreciable effect on the formation of the colored compound.

**SENSITIVITY, ACCURACY AND PRECISION**

The mean molar absorptivity (\(\varepsilon\)) and Sandell sensitivity (S) as calculated from Beer’s law are presented in (Table 1). For more accurate results, Ringbom optimum concentration ranges were obtained (Table 1). Precision and accuracy of each method was tested by analyzing six replicate samples containing 6.0, 12 \(\mu\) g ml\(^{-1}\) of meclizine HC1 of pure drug for methods A and B, respectively. The measured standard deviations (s), relative standard deviations (Sr) and coefficient correlation (r) are given in (Table 1). The recoveries obtained with the proposed methods were compared with official method (The British Pharmacopoeia., 2005) (Table 2).

**ANALYTICAL APPLICATIONS**

The methods were applied to the spectrophotometric determination of meclizine HC1 in commercial pharmaceutical formulations. The results obtained were compared statistically by using the Students t-test and the variance ratio F-test with those obtained by an application of the reference method on samples of the same batches (Table 3). The proposed methods are suitable for the determination of meclizine HC1 in drug formulations without interference from excipients and additives such as cellulose, starch and magnesium stearate.

**CONCLUSION**

The two proposed methods were advantageous over other reported visible spectrophotometric and colorimetric methods. They showed their high reproducibility, high sensitivity, less time consuming and using simple and inexpensive reagents. Moreover, these methods allowed the determination of meclizine HC1 up to 0.4 and 0.5 \(\mu\) g ml\(^{-1}\); in addition to simplicity, rapidity, precision and stability of colored species for more than 48 h. The proposed method may be applied in routine analysis and in quality control laboratories for the quantitative determination of the meclizine HC1 in raw materials and in pharmaceutical formulations.

**REFERENCES**

Zhijun W, Shuai Q, Qizhi Z and Moses Chow SS, Journ of Nature Biotech, 0221(2010)