Determination of Naproxen and Ibuprofen in Pharmaceutical Formulations by using Atomic Absorption Spectrometry

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Abstract

Two simple, accurate, precise and sensitive methods for Naproxen and Ibuprofen have been developed using atomic absorption spectrometer. These methods are based on reaction of both the drugs with Copper (II) chloride and Cobalt (II) chloride to give purpursion blue colour and light pink colour metal complexes respectively. These complexes are readily extracted with dichloromethane and estimated via determination of copper and cobalt content in the formed complexes after digestion with 0.1 M Sulphuric acid by atomic absorption spectrometer. Naproxen and Ibuprofen can be determined in the concentration ranges 2.5-25.0 and 1.5-22.5 µg ml⁻¹ with mean percentage recovery 100.06 ± 0.13 and 100.05 ± 0.08% respectively. The proposed methods were also applied for analysis of pharmaceutical formulations and the results obtained were statistically analyzed.

Key word: Atomic absorption spectrometry, Naproxen, Ibuprofen, Triethanolamine, Copper Chloride, Cobalt Chloride.

Introduction

Naproxen and Ibuprofen are important pharmaceutical compounds. Ibuprofen was prototype in propionic acid derivatives to become available in the United States. Latter on; it was followed by Naproxen, fenoprofen, ketoprofen, flurbiprofen and oxaprozin. All the drugs have anti-inflammatory, analgesic and antipyretic activity and have gained acceptance in the treatment of disorders like rheumatoid and osteoarthritis because of less gastrointestinal effect as compared to aspirin [1]. Ibuprofen is supplied as tablets containing 200 to 800 mg; only the 200mg tablets are available without a prescription [2]. Both the drugs are in the list of top 200 prescription drugs in the United States [3].

Several methods like Spectrophotometric [4-7], HPLC [8-11], HPTLC [12], GC [13-14], Capillary Isotachophoresis [15-16] and Fluorimetric methods [17-18] have been reported for
the quantitative estimation of Naproxen and Ibuprofen. In addition to these Colorimetric [19], Chemiluminescence [20], Voltametry [21], and Liquid Phosphorimetry [22] methods have also been reported for Naproxen.

The proposed atomic absorption spectrometric methods are simple, sensitive, less expensive and hence more suitable for application in quality control laboratories for analysis of both the drugs.

Result and Discussion

Atomic Absorption spectrometry provided a new and alternate route for analysis of propionic acid derivatives like Naproxen and Ibuprofen. In the present work investigated drugs are found to react with Copper and Cobalt (II) chlorides to form suitable molecular complexes. These complexes are insoluble in aqueous phase, but are readily extractable with dichloromethane. It is not possible to aspirate the organic extract of metal complexes directly into atomic absorption spectrometer because of inflammable nature. Therefore they were extracted with dilute Sulphuric acid and measured their atomic absorptions at 324.8 nm and 240.7 nm for copper and cobalt respectively. In Copper (II) chloride method; Naproxen and Ibuprofen can be determined in the concentration ranges 2.5-25.0 and 1.5-22.5 µg ml\(^{-1}\) with mean percentage recovery 100.06 ± 0.13 and 100.05 ± 0.08% respectively. (Table 1)

Table: 1 Quantitative parameters for determination of Naproxen and Ibuprofen with Copper (II) chloride method

<table>
<thead>
<tr>
<th>Bulk drug</th>
<th>Linearity range observed (µg ml(^{-1}))</th>
<th>Intercept</th>
<th>Slope</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen</td>
<td>2.5-25.0</td>
<td>0.032</td>
<td>0.018</td>
<td>0.998</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>1.5-22.5</td>
<td>0.039</td>
<td>0.017</td>
<td>0.997</td>
</tr>
</tbody>
</table>

Table: 2 Quantitative parameters for determination of Naproxen and Ibuprofen with Cobalt (II) chloride method

<table>
<thead>
<tr>
<th>Bulk drug</th>
<th>Linearity range observed (µg ml(^{-1}))</th>
<th>Intercept</th>
<th>Slope</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen</td>
<td>3.5-23.5</td>
<td>0.042</td>
<td>0.014</td>
<td>0.994</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>3.0-25.0</td>
<td>0.054</td>
<td>0.034</td>
<td>0.996</td>
</tr>
</tbody>
</table>

Table: 3 Determination of the investigated drugs in tablets by copper (II) chloride method.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Label Claimed (mg / tablet)</th>
<th>Amount Found (mg/ tablet)</th>
<th>%age of Label Claimed Found</th>
<th>Coefficient of Variation*</th>
<th>Percentage Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand A</td>
<td>275</td>
<td>275.17</td>
<td>100.34</td>
<td>0.38</td>
<td>100.19</td>
</tr>
<tr>
<td>Brand B</td>
<td>250</td>
<td>249.88</td>
<td>99.76</td>
<td>0.27</td>
<td>99.94</td>
</tr>
<tr>
<td>Brand C</td>
<td>400</td>
<td>400.37</td>
<td>100.74</td>
<td>0.31</td>
<td>100.13</td>
</tr>
<tr>
<td>Brand D</td>
<td>400</td>
<td>400.70</td>
<td>100.14</td>
<td>0.57</td>
<td>99.94</td>
</tr>
<tr>
<td>Brand E</td>
<td>400</td>
<td>400.90</td>
<td>100.38</td>
<td>0.68</td>
<td>100.08</td>
</tr>
</tbody>
</table>

*Mean of three estimations.
Brand A & B – Naproxen Tablets. Brand C, D & E – Ibuprofen Tablets

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In Cobalt (II) chloride method; Naproxen and Ibuprofen can be measured in the concentration ranges 3.5.0-23.5 and 3.0-25.0 µgml\(^{-1}\) with mean percentage recovery 100.05 ± 0.24 and 99.99 ± 0.12% respectively. (Table 2)

These methods were also applied for the analysis of pharmaceutical formulations of both the drugs as shown in Table (3&4) along with recovery studies. These methods can be employed for routine analysis of Naproxen and Ibuprofen in quality control laboratories.

### Table: 4 Determination of the investigated drugs in tablet dosage form by cobalt (II) chloride method

<table>
<thead>
<tr>
<th>Sample</th>
<th>Label Claimed (mg/ tablet)</th>
<th>Amount Found (mg/ tablet)</th>
<th>%age of Label Claimed Found</th>
<th>Coefficient of Variation*</th>
<th>Percentage Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand A</td>
<td>275</td>
<td>275.82</td>
<td>100.29</td>
<td>0.37</td>
<td>100.29</td>
</tr>
<tr>
<td>Brand B</td>
<td>250</td>
<td>249.53</td>
<td>99.81</td>
<td>0.21</td>
<td>99.81</td>
</tr>
<tr>
<td>Brand C</td>
<td>400</td>
<td>399.89</td>
<td>99.97</td>
<td>0.11</td>
<td>99.97</td>
</tr>
<tr>
<td>Brand D</td>
<td>400</td>
<td>399.56</td>
<td>99.89</td>
<td>0.87</td>
<td>99.89</td>
</tr>
<tr>
<td>Brand E</td>
<td>400</td>
<td>400.37</td>
<td>100.09</td>
<td>0.48</td>
<td>100.12</td>
</tr>
</tbody>
</table>

*Mean of three estimations.

Brand A & B – Naproxen Tablets. Brand C, D & E – Ibuprofen Tablets

### Materials and Methods

Naproxen and Ibuprofen were obtained as gift samples from Brown & Burk Pharmaceuticals (INDIA) and Knoll Pharmaceutical limited (INDIA) respectively. Market samples of Naproxen and Ibuprofen were procured from Market for analysis. All other chemicals used were of analytical grade.

Their standard stock solutions containing 0.5mgml\(^{-1}\) were prepared in methanol. Each was further diluted to five dilutions ranging from 10 to 250 µgml\(^{-1}\) with distilled water.

### Copper (II) chloride method

One ml of each dilution was transferred to 10 ml volumetric flasks. Added 5 ml (1%) Copper (II) chloride solution and shaken vigorously for 5 minutes. All volumes were made up to mark with distilled water. These were transferred quantitatively to separating funnels and extracted with (3x10 ml) dichloromethane. Dichloromethane extracts were evaporated to dryness and digested with 5ml (0.1 M) Sulphuric acid. Aspirated the acid extracts directly in the atomic absorption spectrometer and measured their absorbance at 324.8 nm for copper metal. Regression analysis was applied for generating standard curves for both the drugs (Table 1).

### Cobalt (II) chloride method

One ml of each dilution was transferred to 10 ml volumetric flasks. Added 5 ml (1%) Cobalt (II) chloride reagent and heated at 60°C for 5 minutes. Added 1ml (0.5%) triethanolamine reagent and made volume up to mark with distilled water. Transferred quantitatively to separating funnels and extracted with (3x10 ml) dichloromethane. These dichloromethane
extracts were evaporated and digested with 5 ml (0.1 M) sulphuric acid. Aspirated the acid extracts directly in the atomic absorption spectrometer and measured their absorbance at 240.7 nm for cobalt metal. Regression analysis was applied for generating standard curves for both the drugs (Table 2).

Analysis of Pharmaceutical Formulations
Twenty tablets of each market sample were weighed and crushed to fine powder separately for Naproxen and Ibuprofen. An amount of powdered tablets equivalent to 10 mg were weighed accurately for each drug, shaken with (3x10 ml) methanol; filtered and washed. Alcoholic extracts were combined and evaporate to dryness and made volume up to 10ml with distilled water. Suitable dilutions were made to carry out analysis on AAS as shown in both the methods for bulk drugs (Table3-4).

Conclusion
Atomic Absorption spectrometry provided a new route for analysis of propionic acid derivatives like Naproxen and Ibuprofen in pharmaceutical formulations. Naproxen and Ibuprofen can be determined in the concentration ranges 2.5-25.0 and 1.5-22.5 µg ml⁻¹ with mean percentage recovery 100.06 ± 0.13 and 100.05 ± 0.08% respectively. Hence, these methods can be employed for routine analysis of Naproxen and Ibuprofen in quality control laboratories.

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References


