Spectrophotometric Determination of Diclofenac sodium in Pharmaceutical preparations

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Summary:
A simple and sensitive spectrophotometric method is described for the determination of Diclofenac sodium, in pure form and pharmaceutical formulations. The method is based on the reaction of drug with iron(III)chloride to form iron(II) which reacts with potassium hexacyanoferrate(III) forming a blue color product measurable spectrophotometrically at 710nm. Linearity was in the range (1.00-6.00 μg. ml⁻¹). A linear response was observed over the tested range of drug with correlation coefficient of 0.9980, a relative standard deviation of (0.396-0.934%) and recovery of (97.83 -104.9%). The method was successfully applied to the determination of this drug in their dosage forms.

Introduction:
The determination of small amounts of diclofenac in pharmaceutical preparations is very important for medical and pharmaceutical needs where it is used for the treatment of various diseases. Therefore it is crucial to develop a simple, selective and cost-effective method to determining the microamounts of diclofenac in different pharmaceutical formulations.

Diclofenac [2-(2,6-dichloroamino)phenyl]acetic acid is a non-steroidal anti-inflammatory drug. It is usually found as a sodium or potassium salt (Fig.1) It is used for the treatment of rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and sport injuries.  The pharmacological effects of this drug are thought to be related to the inhibition of the conversion of arachidonic acid to prostaglandins, which are the mediators of the inflammatory process. It is employed mainly in oral formulations, and the some extent, also for intramuscular injection and topical formulation for topical formulations, one of the most wildly used is Voltaren® emulgel, Diclogel® and Dosanac® emulsiongel. The advantage for this type of dosage form found to be effective for the treatment of local inflammatory. However, the disadvantage was also observed due to careless of the patients which may wipe the drug out shortly after applied to the skin.

Several types of analytical procedures have been proposed for the analysis of diclofenac in pharmaceutical formulation. These procedures include potentiometry, fluorimetry, HPLC, GC, gravimetry, UV spectrophotometry, and spectrofluorometric methods. Some of these procedures are cumbersome and too costly for routine analysis. The spectrophotometric method provides sensitivity, precision and accuracy of analysis, thus it offers practical and economical advantages over other techniques. There are numerous publications dedicated to the determination of small amounts of pharmaceutical compounds with the help of base coloring agents. Base dyes are often used as reagents for the extractive spectrophotometric determination of many inorganic and organic substances.

This trend of analytical chemistry is of current interest and holds much promise. This work describes a new spectrophotometric method based on the reduction properties of the studied drugs.
Fig. 1. Structures of diclofenac sodium or potassium salt.

**Experimental**

**Apparatus:**
- A shimadzu UV–Vis 1800 Spectrometer (Japan) was used equipped with a quarts cell of 1.0 cm width for the \( \lambda_{\text{max}} \) determination and all absorbance measurements.
- Labtech water bath manufacture of lab instruments.
- Denver sensitive balance instrument ISO 9001.

**Reagents and Materials:**
- Analytical reagents grade chemicals and distilled water were used throughout. Pure drug samples were provided by SDI.
- Standard solution of Diclofenic 100 µg. ml\(^{-1}\) was prepared in distilled water. Working standard solutions were prepared by appropriate dilution immediately before use.
- Dosage forms containing the studied drug being purchased from commercial sources provided by SDI.
- Iron chloride(III) 3.00x10\(^{-2}\)M solution: was prepared by dissolving 0.4866 gm of FeCl\(_3\) in 1ml concentrated HCl and made up to 100 ml of distilled water.
- Potassium hexacyanoferrate(III) 1.00X10\(^{-3}\) M solution: was prepared by dissolving 0.0329gm of K\(_3\)Fe(CN)\(_6\) in 100 ml of distilled water.

**Recommended procedure:**

In to a series of 25ml volumetric flask, transfer increasing volumes of diclofenac sodium solution (100µg.ml\(^{-1}\)) to cover the range of calibration curve(1.00-6.00µg.ml\(^{-1}\)), added 1ml (0.03M) of FeCl\(_3\) and shake well. Add 1.5ml (0.001M) of K\(_3\)Fe(CN)\(_6\), dilute the solution to the mark with distilled water, and allow the reaction to stand for 15min. Measure the absorbance at 710nm against a reagent blank prepared in the same way but containing no diclofenac sodium. The color of the Prussian Blue product is stable for 30min.

**Procedure for pharmaceutical preparations:**
- Diclofenac sodium tablets (25mg):
  Weight and finally powdered (10 tablets), extract an accurately weight portion of the powder equivalent to about 100mg of diclofenac sodium (total average Wight of four tablets) in 100ml distilled water using 100ml volumetric flask to obtained 1000µg.ml\(^{-1}\) of diclofenac sodium, filter the solution and 10ml from the above solution was transferred into 100ml volumetric flask and complete to the mark with distilled water to obtained 100µg.ml\(^{-1}\). This solution was suitable to analyze by taking a convenient volumes in the range of calibration curve under a general procedure.

**Results and discussion:**

**Absorption Spectra of the Colored Complex:**

The diclofenac sodium drug reacts with iron(III) to produce iron(II) which in the presence of potassium hexacyanoferrate(III) forms a blue product measurable at 710 nm (Fig. 2). The absorbance of the blue product is directly related to the concentration of the diclofenac sodium and...
can be used for its spectrophotometric determination. The development of the color depends very much on the reaction conditions. Therefore it is very important to optimize the reaction conditions.

Fig. 2: Spectrum of the blue complex resulted from (2.00 μg. ml⁻¹) of diclofenac sodium with (1.2x10⁻³ M) FeCl₃ and (6x10⁻⁵ M) K₃Fe(CN)₆ measured against a blank solution.

**Effect of Iron(III) Chloride:**

The effect of iron(III) chloride concentration on the absorbance of the Prussian blue color product was investigated in the range of (2.4x10⁻²-3x10⁻³ M) in a final volume 25ml, (1.2x10⁻³ M) gave the highest absorbance as shown in Fig. 3.

![Graph](image)

Fig. 3: Effect of Iron(III) chloride concentration.

**Effect of Potassium Hexacyanoferrate(III):**

The effect of potassium hexacyanoferrate(III) concentration was similarly studied in the range (2x10⁻³-2x10⁻⁶ M) in a final volume 25ml. The absorbance increased with increasing K₃Fe(CN)₆ concentration up to 6x10⁻⁵ M, above which it stable as shown in Fig. 4. Therefore it is chosen for anthers uses.
**Effect of Temperature:**

The effect of temperature on the color intensity of the product was studied. In practice the same absorbance or very closed was obtained when the color was developed at room temperature (25°C) or when the calibrated flask was placed in an water bath (50°C). While a decreased in absorbance was observed when the solution was places in an ice-bath (0°C). Therefore, it is recommended that the reaction should be carried out at room temperature as shown in table .1.

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 °C</td>
<td>0.094</td>
</tr>
<tr>
<td>25 °C</td>
<td>0.215</td>
</tr>
<tr>
<td>50 °C</td>
<td>0.220</td>
</tr>
</tbody>
</table>

**Effect of order of addition:**

The effect of order of addition on the absorbance of the Prussian blue color product was studied. Table.2, shows there is no effect for order of addition on the absorbance. Therefore, the order of addition could be followed, drug : FeCl₃ : K₃Fe(CN)₆.

<table>
<thead>
<tr>
<th>Order of addition</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug : FeCl₃ : K₃Fe(CN)₆</td>
<td>0.220</td>
</tr>
<tr>
<td>Drug : K₃Fe(CN)₆ : FeCl₃</td>
<td>0.215</td>
</tr>
<tr>
<td>K₃Fe(CN)₆ : FeCl₃ : Drug</td>
<td>0.211</td>
</tr>
<tr>
<td>K₃Fe(CN)₆ : Drug : FeCl₃</td>
<td>0.215</td>
</tr>
<tr>
<td>FeCl₃ : Drug : K₃Fe(CN)₆</td>
<td>0.213</td>
</tr>
<tr>
<td>FeCl₃ : K₃Fe(CN)₆ : Drug</td>
<td>0.211</td>
</tr>
</tbody>
</table>

**Effect of reaction time:**

The color intensity reached a maximum after mixing the diclofenac sodium with FeCl₃ and K₃Fe(CN)₆ for 15min. Therefore, 15min development time was selected as optimum in the general procedure. The color obtained was stable for at least 30min as shown in Fig.5.
**Calibration Gragh:**

Under the described experimental conditions, standard calibration curve for the studied diclofenac sodium were constructed by plotting the absorbance versus concentration. Conformity to Beer’s Law was evident over the concentration range of (1.00-6.00µg.ml⁻¹) Fig.6, with the mean correlation coefficient of 0.9980 and an intercept of 0.0572. The conditional molar absorptivity of the Prussian blue color product was found to be (3.057x10⁴L.mole⁻¹.cm⁻¹) and the sandell sensitivity was (1.040x10⁻⁴µg.cm²⁻¹).

**Accuracy and Precision:**

Diclofenac sodium was determined at three different concentrations with five replicated. The results obtained are shown in table(3). A satisfactorily precision and accuracy could be obtained using the proposed method.

**Table.3:** Accuracy and precision of the proposed method.

<table>
<thead>
<tr>
<th>Concentration of diclofenac sodium (µg.ml⁻¹)</th>
<th>Recovery %</th>
<th>R.S.D %</th>
<th>Error %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taken</td>
<td>Found</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.00</td>
<td>2.098</td>
<td>104.9</td>
<td>0.934</td>
</tr>
<tr>
<td>4.00</td>
<td>4.12</td>
<td>103</td>
<td>0.577</td>
</tr>
<tr>
<td>6.00</td>
<td>5.87</td>
<td>97.83</td>
<td>0.396</td>
</tr>
</tbody>
</table>

* Average of five replicated
Pharmaceutical Applications:

In order to evaluate the analytical usefulness of the proposed method, it was applied to the determination of studied diclofenac sodium in pharmaceutical formulations. The results were listed in Table 4. The results showed a good recoveries obtained.

Table 4: Application of the proposed method for the determination of diclofenac sodium in pharmaceutical tablets.

<table>
<thead>
<tr>
<th>Drug sample</th>
<th>Concentration of diclofenac sodium (µg.ml⁻¹)</th>
<th>Recovery %</th>
<th>R.S.D %</th>
<th>Error %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voltaren(25mg) SDI</td>
<td>Taken 2.00 Found 2.05</td>
<td>102.62</td>
<td>1.38</td>
<td>2.50</td>
</tr>
<tr>
<td></td>
<td>Taken 4.00 Found 4.20</td>
<td>105.00</td>
<td>0.64</td>
<td>5.00</td>
</tr>
</tbody>
</table>

*Average of three replicated.

Conclusion:

The new method provides a simple and sensitive means of determining the studied diclofenac sodium in pharmaceutical preparations. It has also the advantages of acceptable accuracy and precision. This method is also easier and cheaper to perform than HPLC separations and do not require expensive reagents or organic solvents. These advantages coupled with acceptable precision make the method suitable for routine quality control. The diclofenac sodium reacts with iron(III) chloride and the resulting iron(II) reacts with potassium hexacyanoferrate(III) and a blue product is resulted.

REFERENCES: