Voltammetric determination of prifinium bromide in a pharmaceutical formulation

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ABSTRACT

For the first time voltammetric methods have been applied and optimized for prifinium bromide (PRF) determination in pharmaceutical formulation. Cyclic voltammetry (CV) study has shown that PRF is an electroactive compound with quasi-revisable voltammograms. Optimization of voltammetric parameters indicated that platinum is the proper working electrode and (KNO₃ 1 M) is the proper supporting electrolyte. All applied voltammetric methods have shown high precession and accuracy. Square wave voltammetry (SWV) has shown the best limit of detection and limit of quantitation of 45.6 and 58.1 µg mL⁻¹, respectively. Recoveries of SWV are 99.06% and 98.60% for 0.30 and 0.60 mg mL⁻¹, respectively, using PRF tablet Riabal® 30 mg. CV with relative standard deviation values of 0.135 and 0.322 of intra-day repeatability and inter-day reproducibility, respectively, has the best precision.

1. Introduction

Prifinium bromide (PRF) is a quaternary ammonium compound (Figure 1), IUPAC name of this compound is 3-(diphenylmethylene)-1,1-diethyl-2-methylpyrroloidinium bromide. PRF is an anticholinergic and antimuscarinic agent that is used in the treatment of irritable bowel syndrome [1] and irritable colon syndrome [2]. The number of articles dealing with the determination of PRF is quite few, Sa’sa et al. used the reversed-phase High Performance Liquid Chromatography (RF-HPLC) method for the determination of PRF in six different pharmaceutical formulations [3]. Lateifeh and Wedian developed the HPLC method for the quantitation of PRF combined with Paracetamol in the pharmaceutical dosage form, the limit of detection (LOD) for PRF with the HPLC method was 0.75 µg mL⁻¹ and its limit of quantification was 2.30 µg mL⁻¹ [4]. Tokuma et al. developed the HPLC-UV method for PRF analysis in human serum and urine. Detection limit of PRF is 0.5 ng mL⁻¹ of prifinium ion for serum samples and 5 ng mL⁻¹ for urine [5].

Abu-Nameh studied the spectroscopic method, for the determination of PRF in Pharmaceutical Preparations, which showed the dynamic range at concentrations of 0.149074–0.447222 mg mL⁻¹ [6]. Standard methods, used for pharmaceutical compounds assay in pharmaceutical companies, rely basically on chromatographic and spectroscopic methods. These methods have some disadvantages such as sample preparation and analysis time, high instrumental and running cost, method analysis waste disposed to the environment. Electrochemical determinations of pharmaceutical compounds become a comparable alternative to chromatographic and spectroscopic methods [7,8]. Potentiometric membrane ion selective electrodes have been applied for in vitro and in vivo assays of pharmaceutical products [9,10]. Voltammetric analysis methods are simple and rapid, in addition to high accuracy and precision [7–11]. Furthermore, voltammetric methods required lower instrumental and operation cost. According to the chemicals used and disposed to the environment in the pharmaceutical compound analysis, voltammetric methods are considered greener methods than chromatographic and spectroscopic methods. In the present work voltammetric methods have been used and optimized for PRF quantitation in pharmaceutical formulation.

2. Results and discussion

2.1. Method development and optimization

2.1.1. Optimization of working electrode

Cyclic voltammetry (CV) has been used to study the electroactivity of PRF and optimize working electrode and supporting electrolytes. Figure 2 voltammograms indicated that PRF is an electroactive compound involved in redox reaction. Platinum (Pt) and glassy carbon (GC) electrodes have been studied in this work, cyclic voltammograms in Figure 2(b,c) illustrated that Pt is a better working electrode than the GC electrode since Pt electrode has shown sharper anodic
and cathodic peaks than the GC electrode with higher difference between the supporting electrolyte and PRF anodic and cathodic currents (Figure 2(b,c)).

2.1.2. Optimization of supporting electrolytes
Two supporting electrolytes were studied in this work Na₂SO₄ (1 M) and KNO₃ (1 M). Cyclic voltammograms in (Figure 2(a,c)) indicated that when KNO₃ (1 M) is used as a supporting electrolyte it showed a higher anodic and cathodic current peak for PRF than when Na₂SO₄ (1 M) is used (Figure 2(a,c)). It can be concluded that PRF has shown quasi-reversible voltammograms when Pt is used as a working electrode and KNO₃ (1 M) as a supporting electrolyte.

2.1.3. Optimization of voltammetric methods
Pt working as an electrode and KNO₃ (1 M) as a supporting electrolyte have been used for voltammetric method optimization of the PRF analysis. Cyclic voltammograms of pure PRF pharmaceutical formulation samples (0.2–1.0 mg mL⁻¹) (Figure 3) have shown a quasi-reversible redox cycles with oxidation current peak at 1.02 V and reduction current peak at 0.71 V. Calibration curve slope indicated high sensitivity of the method with a good correlation $R^2$ of 0.9827.

Figure 1. Chemical structure of PRF.

Figure 2. Comparison between cyclic voltammograms (a) Pt working electrode, Na₂SO₄ (1 M) supporting electrolyte (blue line), PRF 1 mg mL⁻¹ in Na₂SO₄ (1 M) (red line). (b) GC working electrode, KNO₃ (1 M) supporting electrolyte (blue line), PRF 1 mg mL⁻¹ in KNO₃ (1 M) (red line). (c) Pt working electrode, KNO₃ (1 M) supporting electrolyte (blue line), PRF 1 mg mL⁻¹ in KNO₃ (1 M) (black line).
Figure 3. CV study of PRF (0.2–1.0 mg mL\(^{-1}\)), Pt working electrode, KNO\(_3\) (1 M) supporting electrolyte, scan rate 0.1 V s\(^{-1}\), each concentration has been done triplicate.

Figure 4. DPV study of PRF (0.2–1.0 mg mL\(^{-1}\)), Pt working electrode, KNO\(_3\) (1 M) supporting electrolyte, each concentration has been done triplicate.

Table 1. Linearity of PRF (0.20–1.00 mg mL\(^{-1}\), KNO\(_3\) 1 M).

| Method | LR \(y = \) | \(R^2\) | LOD (µg mL\(^{-1}\)) | LOQ (µg mL\(^{-1}\)) |
|--------|-------------|--------|----------------------|----------------------|
| CV     | \(73.326x + 7.3116\) | 0.9827 | 66.2 | 86.4 |
| DPV    | \(54.928x + 1.9316\) | 0.9845 | 61.8 | 74.4 |
| SWV    | \(83.266x - 2.5157\) | 0.9909 | 45.6 | 58.1 |

Note: LR: linear regression, \(R^2\): correlation coefficient, LOD: limit of detection, LOQ: limit of quantification.

2.2. Precision

Intra-day repeatability and inter-day reproducibility have been studied for PRF voltammetric analysis (Table 2). Repeatability was tested by triplicate analyses of pure preparations of PRF (0.60 mg mL\(^{-1}\), KNO\(_3\) 1 M) within the same day. Reproducibility was tested for PRF voltammetric analysis for three consecutive days. Table 2 has shown that CV with relative standard deviation (RSD) values of 0.135 and 0.322 of intra-day and inter-day, respectively, has the best precision method. Furthermore, both intra-day repeatability and inter-day...
Figure 5. SWV study of PRF (0.2–1.0 mg mL\(^{-1}\)), Pt working electrode, KNO\(_3\) (1 M) supporting electrolyte, each concentration has been done triplicate.

Table 2. Precision of PRF (0.60 mg mL\(^{-1}\), KNO\(_3\) 1 M).

| Method | Intra-day RSD% | Inter-day RSD% |
|--------|----------------|----------------|
| CV     | 0.135          | 0.322          |
| DPV    | 0.510          | 0.734          |
| SWV    | 1.735          | 1.852          |

Note: Intra-day (repeatability) RSD: relative standard deviation of triplicate determinations on the same day, inter-day (reproducibility) RSD: relative standard deviation of three consecutive days.

reproducibility fall within the accepted range for all applied voltammetric methods.

2.3. Accuracy

The accuracy of voltammetric techniques was measured using 0.30 and 0.60 mg mL\(^{-1}\) prepared from PRF tablet Riabal\(^\text{®}\) 30 mg. The voltammetric determination was carried out three times for each concentration level. Recovery in Table 3 reflects the accuracy of the applied voltammetric methods. Recovery values in Table 3 have indicated that SWV has the best accuracy. Furthermore, the accuracy of all applied methods falls within the desired range.

Table 3. Accuracy and precision of commercial preparation of PRF (Riabal\(^\text{®}\) 30 mg) Pt electrode (KNO\(_3\) 1 M).

| Method | 0.30 mg mL\(^{-1}\) | 0.60 mg mL\(^{-1}\) |
|--------|---------------------|---------------------|
| CV     | Found ± SD 0.3101 ± 0.0004 | 0.6098 ± 0.0051 |
|        | Recovery% 103.36 | 101.63 |
| DPV    | Found ± SD 0.2949 ± 0.0013 | 0.5869 ± 0.0091 |
|        | Recovery% 98.31 | 97.81 |
| SWV    | Found ± SD 0.2972 ± 0.0056 | 0.5916 ± 0.0181 |
|        | Recovery% 99.06 | 98.60 |

Note: SD: standard deviation of triplicate determinations, RSD: relative standard deviation, recovery = found/added × 100.

3. Materials and methods

3.1. Materials and reagents

The standard pharmaceutical formulation of PRF was obtained from Hikma pharmaceuticals (Jordan). A commercial PRF Riabal\(^\text{®}\) 30 mg tablet, manufactured by The Arab Pharmaceutical Manufacturing Company, Jordan, was bought from the Jordanian local market. Potassium nitrate (KNO\(_3\), ACS reagent, Fluka), Sodium sulphate anhydrous (Na\(_2\)SO\(_4\) Janssen Chemica). Supporting electrolytes of 1.0 M KNO\(_3\) and 1.0 M Na\(_2\)SO\(_4\) were prepared using Milli-Q water.

3.2. Standard solutions

Standard stock solutions of 1.0 mg mL\(^{-1}\) PRF were prepared by dissolving 100 mg of PRF standard pharmaceutical formulation powder in the 100 mL supporting electrolyte solution. Supporting electrolytes were used to prepare stock solutions and in the dilution of stock solutions to prepare the standard working solutions. Sample solutions using The Riabal\(^\text{®}\) 30 mg tablets were weighed and grounded by a mortar and a pestle and a water bath sonicator was used to dissolve a certain mass of tablet powder in the supporting electrolyte solution. Next, undissolved substance was removed by applying a simple filtration method. Supporting electrolytes were used for washing the filter paper used in the filtration; then they were used to complete solution volume to the mark.

3.3. Apparatus

All voltammetric methods were carried out using the potentiostat (Metrohm Autolab) PGSTAT 204. Ag/AgCl (3 M KCl) was used as reference electrode. A GC or Pt was applied as a working electrode and a Pt sheet as a counter electrode.
4. Conclusion

Voltammetric analysis of PRF in pharmaceutical formulation has indicated that it is an electroactive compound. All the applied voltammetric methods have shown accuracy and precision within the accepted range. According to the study results SWV is the recommended method since it has shown the best sensitivity, recovery, LOD, LOQ and $R^2$.

Disclosure statement

No potential conflict of interest was reported by the author.

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