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Short communication

Voltammetric assay of Guaifenesin in pharmaceutical formulation

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Abstract

The electrochemical oxidation of Guaifenesin in a pharmaceutical formulation containing Guaifenesin has been carried out in Britton–Robinson buffer (BRB) (0.04 mol L^{-1}) on platinum electrode. Guaifenesin exhibits a well-defined irreversible oxidation peak at 0.924 V/ref. The influence of pH on the oxidation of Guaifenesin was studied in BRB (pH range 2-5). A method for the analysis of Guaifenesin in BRB (0.04 mol L^{-1}, pH 2), which allows quantification over the range 20–60 μg mL^{-1}, was proposed and successfully applied to the determination of Guaifenesin in syrup with mean recovery and relative standard deviation of 103.3% and 1.32%, respectively.

Keywords: Gauifenesin; Oxidation; Cyclic voltammetry; Platinum electrode; Irreversible

1. Introduction

Guaifenesin is a drug that reduces the thickness and stickiness of mucus. It is used for short-term relief of dry, non-productive cough and mucus in the breathing passages. Guaifenesin is used to treat symptoms of allergy, colds and upper respiratory infections. Several methods are reported in the literature proposing fast and reliable techniques for the determination of Guaifenesin in various cough-cold formulations [1–7]. Most of the methods reported for the analysis of Guaifenesin in different matrices, alone or with other active substances, rely on the use of chromatographic techniques. Vasudevan et al. developed and validated a method for the analysis of Guaifenesin in the presence of phenylpropanolamine HCl, diphenylpyraline HCl by HPLC on a C_8 column and a mobile phase consisting of acetonitrile–triethylamine (pH adjusted to 3.5 using orthophosphoric acid; 0.5%), (35:65, v/v) at a flow rate of 1.2 mL min^{-1}. Detection was carried out at 210 nm [8]. Another HPLC method has been developed by Wilcox and Stewart [9] for the simultaneous determination of Guaifenesin pseudoephedrine–dextromethorphan and Guaifenesin–pseudoephedrine in commercially available capsule dosage forms and Guaifenesin–codeine in a commercial cough syrup dosage form. Guaifenesin has been also analysed by spectrophotometric methods [10–12] and Micellar electrokinetic chromatography [13].

Electrochemical methods have proved to be very sensitive for the determination of organic molecules that undergo oxidation or reduction reactions, including drugs and related molecules in pharmaceutical dosage form and biological fluids [14–18]. The advance in experimental electrochemical techniques in the field of analysis of drugs is due to their simplicity, low cost and relatively short analysis time when compared with other techniques. To the best of our knowledge, no electrochemical method was developed for the analysis of Guaifenesin.

The aims of this study are to establish the experimental conditions and to optimize the conditions for the determination of this compound in a pharmaceutical dosage form using cyclic and differential pulse voltammetry (DPV) techniques.

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2. Experimental

2.1. Reagents

Guaifenesin were purchased from Sigma Chemical Co (St. Louis, MO). A stock standard solution of Guaifenesin at 2000 μg mL^{-1} was prepared in distilled water. BRB buffer 0.04 M was prepared from phosphoric acid, boric acid and acetic acid of analytical grade in distilled water. Tussipax (an adult syrup produced by Opalia, Tunisia) labeled to contain as active ingredients dextromethorphane bromhydrate and Guaifenesin at 3 and 10 mg mL^{-1}, respectively, and alcohol, sucrose, glycerol, menthol aroma as excipients. Tussipax was purchased from a commercial source.

2.2. Apparatus

Standard three-electrode potentiostatic circuitry was used, employing a PST 050 potentiostat and a high voltage booster HSB 100 (Radiometer Analytical). The counter electrode was a platinum wire (Φ = 500 μm) and the reference electrode was an Ag/AgNO$_3$ 0.1 mol L^{-1} reference electrode. All potentials are given versus the Ag/AgNO$_3$ 0.1 mol L^{-1}. The working electrode was a platinum wire (Φ = 250 μm, Φ = 500 μm or Φ = 1 mm). The system was controlled by Volta Master 4 software (Radiometer Analytical).

2.3. Calibration

Appropriate dilutions of the standard stock solution of Guaifenesin, were performed with water to obtain final concentrations of Guaifenesin 20–60 μg mL^{-1}. The voltammogram of each standard level were recorded. Calibration curves were constructed by plotting peak areas against concentration in μg mL^{-1} and the linear relationships was evaluated by calculation of regression lines by the method of least square.

2.4. Sample solution

Bottles were thoroughly mixed before sampling to ensure homogeneity. An aliquot of the syrup was then transferred to the electrolysis cell and diluted with BRB (0.04 mol L^{-1}). Voltammograms were recorded as described for pure Guaifenesin.

3. Results and discussion

3.1. Voltammetric behaviour

To elucidate the electrode reaction of Guaifenesin, a cyclic voltammogram at platinum electrode was recorded at different pH and at different scan rates. As an example, Fig. 1 shows the cyclic voltammogram of a 1.1 × 10^{-2} (mol L^{-1}) Guaifenesin in BRB (0.04 mol L^{-1}, pH 2) at a scan rate of 100 mV s^{-1}. The voltammogram exhibits one well-defined anodic peak, with no peak on the reverse scan, suggesting the irreversible nature of the electrode reaction.

The effect of potential scan rate, ν, on the peak current and the peak potential of Guafenesin was evaluated. A linear relationship was observed between log Ip and log ν over the scan range 20 and 200 mV s^{-1} (r = 0.9978) and corresponds to equation: log Ip (μA) = 0.4586 log ν + 1.3536, (ν in V s^{-1}). The slope of 0.45 is close to the theoretically expected value of 0.5 for a diffusive process [19]. On the other hand, as scan rate was increased, the potential shifted to less positive values as expected for an irreversible reduction process [20]. The dependence of peak potential of a 1.1 × 10^{-1} (mol L^{-1}) Guaifenesin in BRB (0.04 mol L^{-1}, pH 2) on the decimal logarithm of the scan rate was linear, followed the relationship Ep (V) = 0.096 log ν + 1.023, (ν in V s^{-1}). The shift of the peak potential to anodic value of about 96 mV per decade of the logarithm of the sweep rate indicates that the electron transfer is the determining step. Under these conditions, the average experimental $n\alpha$ value was 0.31.

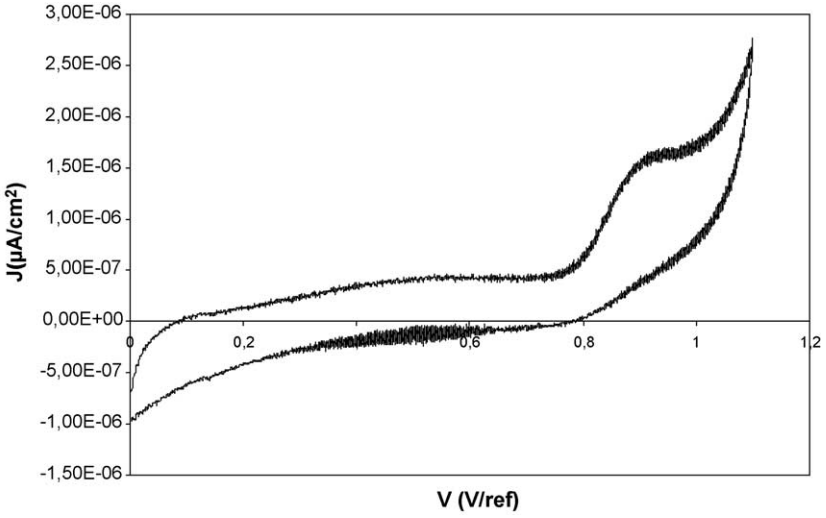

Fig. 1. Cyclic voltammogram of Guaifenesin in BRB (0.04 mol L^{-1}, pH 2) at platinum electrode. Scan rate 100 mV s^{-1}.

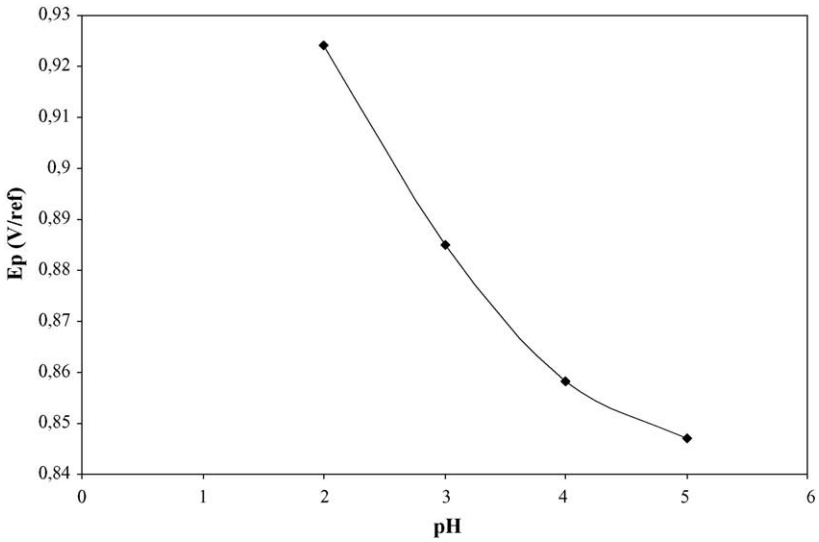

Fig. 2. Peak potential, Ep vs. pH. Guaifenesin (1.1×10^{-1} mol L^{-1}) in BRB (0.04 mol L^{-1}). Scan rate 100 mV s^{-1}.

The electroxidation of Guaifenesin was also studied over pH range 2–5 in BRB. The wave was well developed at pH < 5. The pH dependence of the peak potential is shown on Fig. 2. The potential of the anodic peak of Guaifenesin was shifted linearly towards less positive potential values with increasing the pH between 2 and 4 by 0.033 V/pH. At pH > 5, despite the fact that an oxidation wave was observed, the shape and the reproducibility were poor. The inhibition of Guaifenesin oxidation waves is obvious at those pHs. On the other hand, it was necessary to perform laborious electrode cleaning procedure before performing the next experiment. Because of the very fast poisoning of the electrode surface, it was not possible to investigate pHs higher than 6 especially with the scan rates available in our system.

3.2. Analytical application

In order to develop a voltammetric methodology for determining the drug, we selected the DPV mode, since the peaks were sharper and better defined than those obtained by cyclic voltammetry, with lower background current. A typical DPV for Guaifenesin concentration ranging between 20 and 60 μg mL^{-1} is reported on Fig. 3.

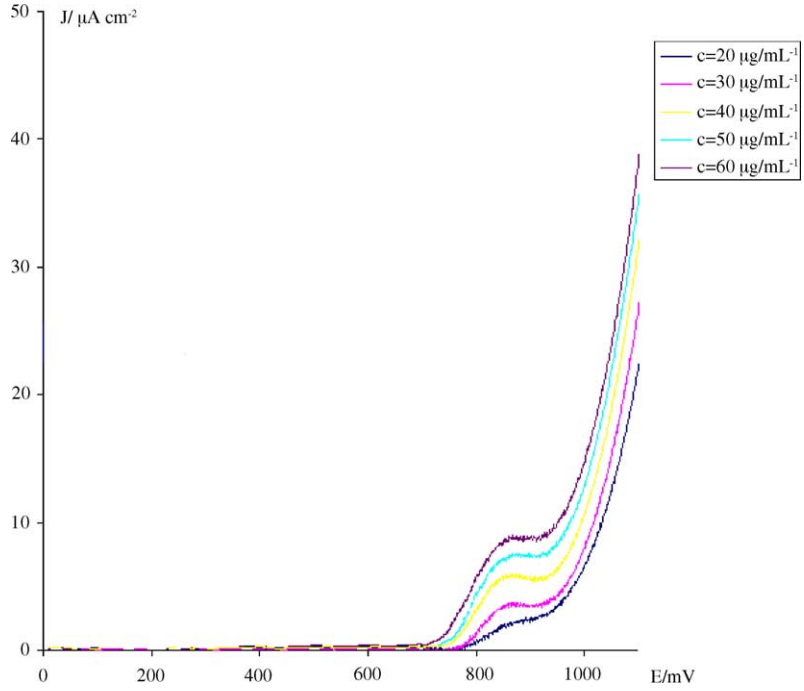

Fig. 3. DPV of Guaifenesin in BRB (0.04 mol L^{-1} pH 2) at platinum electrode (0.2 cm^2). Pulse height = 100 mV. Scan rate = 50 mV s^{-1}.

The optimized method was validated by a standard procedure to evaluate if adequate accuracy, precision, selectivity and linearity have been achieved [21].

Linearity was determined by representing the variation of Jp (current density, $\mu A\,cm^{-2}$) with standard concentrations ($\mu g\,mL^{-1}$) in BRB ($0.04\,mol\,L^{-1}$, pH 2) using DPV (pulse height 100 and scan rate $50\,mV\,s^{-1}$). Curve was represented by straight line equation Jp ($\mu A\,cm^{-2}$) = $-0.37 + 0.163C$, $r = 0.982$ ($n = 5$). The correlation coefficient, r values, were found to be significant ($t = 351.86$, $p < 0.05$) and intercepts was not significantly different from zero ($t = -1.00$, $p > 0.05$).

The LOD and LOQ were calculated using the equation LOD = $A \times$ S.D./a, where SD is the standard deviation of the blank and a is the slope of the calibration curve. A was taken as 3 for LOD and 10 for LOQ determinations, respectively.

Accuracy of the developed method was determined using spiked sample solutions, three preparations each, three analysis of each preparation. The percent recovery (%R) was 100.36–102.3% with a relative standard deviation (R.S.D.) in the range 0.23–0.40%.

Relative standard deviation values were calculated for repeated standard injections 0.34% ($n = 6$) (system precision) as well as repeated injections of multiple sample preparations 2.6% ($n = 6$) (method precision).

3.3. Determination in a pharmaceutical product

On the basis of these results, the proposed method was successfully applied to the direct determination of Guaifenesin in syrup without interference from dextromethorphane bromhydrate.

Six samples prepared to contain $40\,\mu g\,mL^{-1}$ Guaifenesin were analyzed by the proposed method. A mean value of $41.32\,\mu g/mL^{-1}$ with relative standard deviation of 1.32% was obtained.

4. Conclusion

The DPV on a platinum electrode can be used to determine Guaifenesin in pharmaceutical preparation without interference from dextromethorphane bromhydrate. The developed method has been validated for the quantitation of necessary components as shown by the accuracy, linearity, recovery, and precision data. Moreover, the proposed method is fast and easy to use. This method provides significant time-saving advantages in pharmaceutical laboratories analysis.

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