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Simultaneous determination of tinidazole and ciprofloxacin hydrochloride in combined formulation of the two using differential pulse polarography

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ABSTRACT

A simple and precise method for the simultaneous determination of Tinidazole and Ciprofloxacin hydrochloride in a combined formulation of the two has been developed using differential pulse polarography. Both tinidazole and ciprofloxacin produce a cathodic wave at -0.48 V and -1.30 V vs S.C.E in a solution of pH = 6.5 (Britton Robison buffer). The dynamic range for Tinidazole, is 0.833-354.0 $\mu gcm^{-3}$and for Ciprofloxacin, it is 13.04-230.0 μgcm^{-3}.The method has been validated and applied successfully for the simultaneous determination of the two in the combined drug formulation.

KEYWORDS

Tinidazole;
Ciprofloxacin hydrochloride;
Differential-pulse polarography;
Combined formulation.

INTRODUCTION

Tinidazole (TNZ) [1-(2-ethylsulfonylethyl)-2-methyl-5-nitro-imidazole] is a 5-nitroimidazole derivative, an anti-parasitic drug used against protozoan infections. It is also used in the treatment of a variety of amoebic and parasitic infections. Ciprofloxacin Hydrochloride (CIPRO) [1-cyclopropyl- 6-fluoro- 4-oxo- 7-piperazin- 1-yl- quinoline- 3-carboxylic acid] is used in the treatment of bacterial infections. It is a second generation Floroquinolone antibacterial. A combination of these two is prescribed to the patients so as to have an added advantage[1-3].

The simultaneous determination of TNZ and CIPRO, has been reported by UV/Visible spectrophotometry[4], HPLC[5-7] and HPTLC[8]. However, their simultaneous as well as individual determination by electro analytical methods has not been reported[9-21]. The present paper reports successful application of the technique differential pulse polarography for the simultaneous determination of the two in a combined formulation.

MATERIALS AND METHODS

Equipments

Differential pulse polarography was carried out using an Autolab PGSTAT 30 with 663 VA electrode stand of Metrohm. The three- electrode system consisted of saturated calomel electrode as a reference electrode, HMDE as a working electrode and platinum electrode as an auxiliary electrode. The pH measurements were made with an Equip-Tronic pH meter model no. 610.

Chemicals

TNZ and CIPRO standards were obtained from Mayer Organics Pvt. Ltd. and formulations used for analysis were Ciplox- TZ (Cipla) and Cifran-CT

(Ranbaxy). 1M KCl was used as supporting electrolyte and Britton-Robinson buffer of pH 6.5 as a buffer solution in cell. All the solutions were prepared in distilled water and analytical-reagent grade chemicals (Merck) were used.

Sample preparation

A stock solution of 1000 μgcm^{-3} for both was prepared by dissolving 25mg of both the standards and making up the volume to 25 cm^3 in a volumetric flask. Britton-Robinson buffer was prepared by mixing 0.04M boric acid, 0.04M phosphoric acid and 0.04M glacial acetic acid and adjusting the pH to required value with 1M NaOH.

Development of polarographic method and calibration curve

The optimization of experimental condition and parameters has been done to get uniform, less tailing, less broadening peak shape with normal baseline. The polarographic response for TNZ and CIPRO was examined in different buffer solutions such as Britton-Robinson, phosphate, carbonate and acetate buffer. The Britton-Robinson buffer of pH 6.5 was chosen as a best, as both the analytes give well defined peak in the same pH condition. The polarogram was also observed with different supporting electrolyte like KNO_3, KCl, NaCl and peak height was found to be maximum in presence of KCl.

The peak current is linearly related to the pulse amplitude between 10 and 100mV. Pulse amplitude of 50mV was chosen as a optimum, as there is a distorted peak at high pulse amplitude value. The differential pulse polarogram of TNZ and CIPRO were recorded at various scan rates. At the scan rate higher than $15mVs^{-1}$ the width of the peak shape increases and gives distorted peak. At lower scan rate than $15mVs^{-1}$ the peak height is small as when compared with the $15mVs^{-1}$ scan rate.

No significance interference was observed from excipients which are commonly used in the formulation.

An aliquot of ($18cm^3$) of the Britton-Robinson buffer of pH 6.5 was placed in the voltammetric cell, 1M KCl ($2cm^3$) was added as a supporting electrolyte. The solution in cell was purged with nitrogen gas for 180 seconds. The recording of polarogram was carried out in voltage range of 0.0V to -2.0V vs SCE with scan rate of $15\ mVs^{-1}$ and pulse amplitude of 50 mV. After recording blank polarogram, aliquot of definite volume was added to the system. It was observed that TNZ and CIPRO give a well defined cathodic peak at -0.48V and -1.30V respectively. The calibration curves were constructed for the concentration added against the current obtained for each addition.

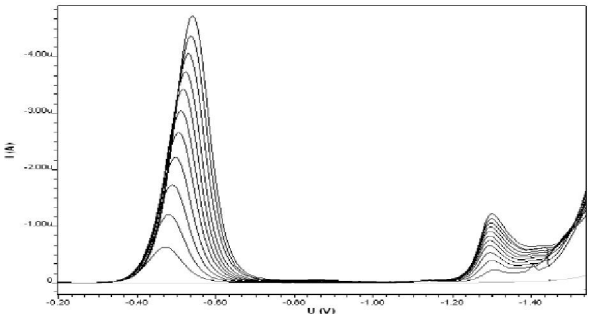

Figure 1 : A typical polarogram shows a linear response of TNZ and CIPRO simultaneously

Analysis of tablets

The two commercially available formulations Ciplox-TZ (Cipla) and Cifran-CT (Ranbaxy) were used for simultaneous determination. Each contained 300mg of TNZ and 250mg of CIPRO. Ten tablets were weighed at a time and powdered. The weight of the powder equivalent to 25 mg CIPRO was weighed and transferred to a 25 cm^3 volumetric flask and the volume was made up to the mark with distilled water. The solution was subjected to vigorous shaking for 5 minutes, then 0.5 cm^3 volume of the supernatant solution was transferred in to a volumetric cell containing de-aerated Britton-Robinson buffer of pH 6.5. The polarograms were recorded under the optimum experimental conditions. The amount of TNZ and CIPRO were calculated from resulting current values using already constructed calibrations graphs.

RESULTS AND DISCUSSION

In simultaneous determination of TNZ and Cipro, TNZ gives wide range of linearity from 0.833-354.0 μgcm^{-3} where as linearity for Cipro is 13.04 – 230.0 μgcm^{-3}. The working range selected for both the analytes

Full Paper

TABLE 1 : Assay and recovery study for the drug samples

Brand name (Label Claim)	Amount of sample in a cell (μgcm^{-3})		% Assay ± RSD (n =6)	
	TNZ	CIPRO	TNZ	CIPRO
Ciplox – TZ (TNZ – 300mg, CIPRO -250mg)	29.38	24.39	97.57 ± 0.34	99.58 ± 1.14
Cifran- CT (TNZ – 300mg, CIPRO -250mg)	29.38	24.39	98.47 ± 0.24	98.56 ± 1.15

was 14.28-100.0 μgcm^{-3}. The quantitative determination of both the analytes has been done by both calibration and the standard addition method. The validation parameters and results for both analytes are shown tabulated in TABLE 1. The method is validated as per ICH guidelines[22].

Validation parameters

(1) Specificity

The specificity of method was confirmed by observing the polarograms of both the combined standard solution and the drug sample solutions.

The polarograms obtained from the drugs sample solution were found to be identical to those obtained for standard solution.

The addition of the standard solution to the drug sample solution did not change the characteristics of differential pulse polarogram. This gives the validity of method for the determination of both drugs from combined pharmaceutical formulation.

(2) Linearity

The linearity for TNZ and CIPRO was observed simultaneously by frequent addition of standard solution. TNZ gives a wide linear response from 0.83 to 354 μgcm^{-3} where as for CIPRO it was from 13.04 to 230 μgcm^{-3}. The calibration curves were constructed with concentration (C) against peak current (I_p). Coefficient of correlation for both the curves was found to be 0.999. The simultaneous linear polarogram for TNZ and CIPRO is shown in figure 1.

Limit of detection and limit of quantification

Stock solution containing two analytes were diluted to series of appropriate concentration with distilled water and aliquots of diluted solutions were subjected to polarographic analysis. The limit of detection (LOD) and limit of quantification (LOQ) for the TNZ was calculated on the basis of signal-to- noise ratio (S/N) of 3 and 10 respectively. Limit of detection and quantification for TNZ was 0.24 μgcm^{-3} and 0.83 $ugcm^{-3}$ where as for CIPRO it was 9.09 $ugcm^{-3}$ and 13.04 μgcm^{-3} respectively.

Precision and repeatability

About ten concentrations in the working range of 14.28-100.00 μgcm^{-3} were selected as a set and analyzed three times for intra-day and inter-day precision. The mean RSD value of intra-day precision for TNZ and CIPRO was 0.44 and 0.72 respectively where as for inter-day it was found to be 1.17 and 2.03.

Robustness

The robustness of the method was tested by the measuring the peak height by bringing deliberately small changes in the experimental parameters. A slight changes in the pH value from the optimum, did not change the peak height for both analytes also, a small change in scan rate and pulse amplitude was examined to be correct.

Accuracy

The accuracy of the method for the simultaneous determination of both was tested by standard addition method. Recovery of both analytes has performed at three levels, 20, 120 and 220 % of amount of sample added, as shown in TABLE 1.

CONCLUSION

The advantage of this method for the analytical purposes lie in the rapid determination TNZ and CIPRO simultaneously in combined pharmaceutical formulation, easy sample preparation, good reproducibility and use of inexpensive instrumentation. The suggested method is cheaper and is accurate as other spectrometric and chromatographic methods. Therefore the present method can be recommended for routine analysis of TNZ and CIPRO simultaneously in combined formulation.

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