Journal of Pharmaceutical and Biomedical Analysis 47 (2008) 929–933

Contents lists available at ScienceDirect

Journal of Pharmaceutical and Biomedical Analysis

journal homepage: www.elsevier.com/locate/jpba

Short communication

Fast and simple method for assay of ciclopirox olamine by micellar electrokinetic capillary chromatography

Junmei Li, Ye Jiang*, Ting Sun, Shumeng Ren

Department of Pharmaceutical Analysis, School of Pharmacy, Hebei Medical University, 361 East Zhongshan Road, Shijiazhuang City, PR China

ARTICLE INFO

Article history:
Received 12 November 2007
Received in revised form 16 February 2008
Accepted 22 February 2008
Available online 29 February 2008

Keywords:
Ciclopirox olamine
Assay
Forced degradation
Optimization
Micellar electrokinetic capillary chromatography

ABSTRACT

A rapid, simple and specific method has been developed and validated for the assay of ciclopirox olamine in pharmaceutical formulations using micellar electrokinetic capillary chromatography (MEKC). The key factors, including pH, buffer concentration and buffer additive, sodium dodecyl sulfate (SDS) concentration, applied voltage and injection time have been systematically investigated in a fused silica capillary (i.d. 50 μm, total length 45 cm and effective length 38 cm) with UV detection at 298 nm. Optimized conditions have been established on the basis of the experimental results. The buffer contains 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA at pH 8.0 and the applied voltage is 20 kV with hydrodynamics sample injection (15 cm high for 5 s). The method has been validated with respect to its specificity, linearity, limits of detection, and quantification, precision and accuracy. The total analysis time was less than 10 min with good peak shape for ciclopirox olamine, which eluted at 3.6 min. Degradation of the ciclopirox olamine was forced using different conditions. These were using hydrogen peroxide, acidic and basic conditions, heat and light. The degradation products so produced showed no interference with ciclopirox olamine. A linear standard curve was established over the concentration range 31.3–2.00 × 10^3 μg mL^{-1} of ciclopirox olamine in running buffer with a correlation coefficient (r) of 0.9999. The limits of quantification and detection were 31.3 and 9.36 μg mL^{-1}, respectively. The proposed method has been successfully used for the quantitative determination of ciclopirox olamine in pharmaceutical suppository and cream formulations.

1. Introduction

Ciclopirox olamine, the 2-aminoethanol salt of 6-cyclohexyl-1-hydroxy-4methyl-2(1H)-pyridone (Fig. 1) is a broad spectrum-antifungal agent with excellent activity against most pathogenic fungi, including *Dermatophytes* and *Candida* albicans. It has a powerful sterilization effect with low toxicity and strong osmolarity. This compound is very effective against the fungi that cause the keratinization of skin [1–3]. So far, several assays including spectrophotometric [4], chromatographic [1–7], microbiological [8,9] and polarographic methods [10,11] have been established. Although acknowledged as the universal and authoritative methods for the determination of ciclopirox olamine, they still have some real disadvantages. In the United States Pharmacopoeia (USP) [4] an HPLC method was used to determine ciclopirox olamine related compounds. Under these conditions, the ciclopirox olamine peak tailed badly, because the hydroxyl groups have a strong chelating effect with metal cations. In order to reduce the chelating effect, the chromatographic column is rinsed with a mixture of water, acetonitrile, glacial acetic acid and acetylacetone (500:500:1:1) for at least 15 h followed by the mobile phase for at least 5 h before the experiment. It was found that this method could not be successfully used for assay determination of ciclopirox olamine even after this long rinsing time had been employed. Some literature references cite HPLC with pre-column derivatization [1–3,6,7] for the quantitative assay of ciclopirox olamine. However, because of the complicated procedures required, the method is only suitable for trace analysis of biological samples and not appropriate for fast quality control to support pharmaceutical production processes. Thin layer chromatography (TLC) [5] is another means used to determine ciclopirox olamine quantitatively. This method has poor specificity because neither the free acid nor its aminoethanol salt migrate as a uniform spot during the development and severe tailing is also observed.

Ibrahim and El-Enany [10,11] developed the polarographic method for the determination in different dosage forms by the reduction of the carbonyl group in ciclopirox olamine at the dropping mercury electrode in Britton Robinson buffer, but this method

* Corresponding author. Tel.: +86 311 86266069; fax: +86 311 86265623.
E-mail addresses: jiangye@hebmu.edu.cn, jiangye1@126.com (Y. Jiang).

0731-7085/$ – see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jpba.2008.02.023

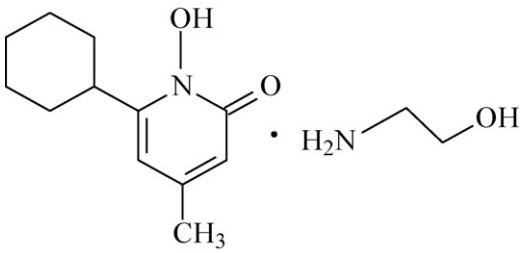

Fig. 1. Ciclopirox olamine.

has a narrow linearity range for detection and also has poor specificity. The spectrophotometric method [4] is still the most commonly used technique for assay of ciclopirox olamine, but because precise quantitation and simultaneous analysis of related compounds and assay determination are not possible, it is unsuitable for stability research and fast quality control in pharmaceutical production processes. Thus, a simple, fast and specific approach for the stability research and fast quality control in pharmaceutical production processes is of great interest.

In this paper, we describe a simple, rapid and specific micellar electrokinetic capillary chromatography method for the simultaneous analysis of the drug and its forced degradation products of ciclopirox olamine in fast quality control in process of pharmaceutical production. The total analysis time was less than 10 min with good peak shape for ciclopirox olamine, which eluted at 3.6 min. A good separation was achieved.

2. Experiments

2.1. Instrumentations

A CL1020 capillary electrophoresis instrument (Beijing Cailu Scientific Inc., Beijing, China) equipped with a UV detector was used for the experiments. Electrophoresis was performed in an uncoated fused-silica capillary column (Yongnian Photoconductive Fibre Factory, Hebei, China) with 45 cm (effective length 38 cm) and 50 μm i.d. A pHS-25 acidity meter (Shanghai REX Instrument Factory, Shanghai, China) was used for the pH measurements.

2.2. Chemicals

The standard of ciclopirox olamine was obtained from the National Institute for Control of Pharmaceutical and Biological Products (Beijing, China). The ciclopirox olamine cream, containing 10 mg of ciclopirox olamine per 1 g cream, was provided by Beijing Shuangji Pharmaceutical Company (Beijing, China). Each suppository, containing 100 mg of ciclopirox olamine, was purchased from the Science and Technology General Company of Hebei Medical University (Hebei, China). Absolute alcohol was supplied by Tianjin Hengxing Chemical Reagent Limited Company (Tianjin, China). Sodium tetraborate and boric acid were purchased from Baoding Chemical Reagent Factory (Hebei, China). EDTA was from Tianjin Chemical Reagent Factory (Tianjin, China). Sodium dodecyl sulfate (SDS) was from Shenyang Chemical Reagent Factory (Shenyang, China). Ultra pure water was used for the preparation of the solutions.

2.3. Preparation of standard solutions

A standard stock solution (4.00×10^3 μg mL^{-1}) of ciclopirox olamine was prepared in absolute alcohol. Before the analysis, the ciclopirox olamine solution (31.3–2.00×10^3 μg mL^{-1}) was prepared by diluting appropriate volume of stock solution with the running buffer.

2.4. Sample preparation

Ciclopirox olamine suppository: Twenty suppositories were milled and mixed. A portion of the powder equivalent to 5 mg of ciclopirox olamine was transferred into a 10 mL volumetric flask and 5 mL of absolute alcohol was added. The content of the flask was sonicated for 15 min and diluted to the volume with the same solvent. The solution was filtered and 5 mL of the filtered solution was transferred into a 10 mL volumetric flask and diluted to volume with running buffer.

Ciclopirox olamine cream: A portion of the cream, equivalent to 5 mg of ciclopirox olamine was transferred into a 10 mL volumetric flask and 5 mL of absolute alcohol was added. The content of the flask was sonicated for 15 min and diluted to volume with the same solvent. The solution was filtered and 5 mL of the filtered solution was transferred into a 10 mL volumetric flask and diluted to volume with running buffer.

Both the above sample solutions were filtered through 0.45 μm membrane filters prior to injection into the capillary electrophoresis system.

2.5. Preparation of the degraded samples

A stock solution containing 200 mg ciclopirox olamine in 100 mL absolute alcohol was prepared for the forced degradation test.

2.5.1. Preparation of hydrogen peroxide-induced degradation product

To 50 mL of absolute alcohol stock solution, 10 mL of hydrogen peroxide (30%, v/v) was added. The solution was heated in boiling water bath for 5 h to remove the excess of hydrogen peroxide.

2.5.2. Photochemical degradation product

The photochemical stability of the drug was studied by exposing the stock solution to direct ultraviolet light (wavelength range: 200–400 nm; power: 90 μW/cm^2; distance: 2 cm) for 24 h.

2.5.3. Preparation of acid-induced degradation product

To 50 mL of absolute alcohol stock solution, 10 mL of 5 M HCl was added. This mixture was heated in a water bath at 80 °C for 24 h. The forced degradation in acidic condition was performed in the dark to prevent any possible light degradation.

2.5.4. Preparation of base-induced degradation product

To 50 mL of absolute alcohol stock solution, 10 mL of 5 M sodium hydroxide was added. This mixture was heated in a water bath at 80 °C for 24 h. The forced degradation in this basic environment was carried out in the dark to prevent the potential of light degradation.

2.5.5. Preparation of high temperature-induced degradation product

50 mL of absolute alcohol stock solution was transferred to an ampoule and the ampoule sealed. The solution was heated in a constant temperature cabinet at 110 °C for 24 h.

2.6. CE conditions

The running buffer contained 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA at pH 8.0. It was prepared by dissolving a calculated amount of borate, SDS and EDTA in ultra pure water. The pH was adjusted to 8.0 with 0.1 M sodium hydroxide. The solution was then filtered through a 0.45 μm membrane before use. At

the beginning of each experimental session, the capillary column was washed with 0.1 M sodium hydroxide for 10 min followed by a 10 min rinse with ultra pure water and finally the running buffer for 10 min. Prior to each injection, the capillary was purged for 3 min with the running buffer. A constant voltage of 20 kV was applied and the UV detector was set at 298 nm. The capillary column was maintained at 25 °C. Samples were injected hydrodynamically using a height of 15 cm for 5 s.

3. Results and discussion

3.1. Development of the MEKC method

3.1.1. Effect of the running buffer pH

Control of buffer pH is key to optimizing the separation of the ionizable analytes in MEKC, because the buffer pH determines the degree of ionization and electrophoretic mobility of the solutes. The effect of pH was investigated in the range from 5.0 to 9.0 at a buffer concentration of 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA. In the pH range from 5.0 to 7.0, ciclopirox olamine migrated closely with the electroosmotic flow (EOF). In the higher pH range of 7.0–9.0, the theoretical plate number increased until pH 8.0 was reached and then it decreased above pH 8.0. The migration time of ciclopirox olamine decreased slowly up to pH 8.0 and then increased rapidly (Fig. 2a) above this. Therefore pH 8.0 was chosen as the optimum pH value of the running buffer as it gave a suitable migration time and good peak shape.

3.1.2. Effect of buffer concentration

The effect of running buffer concentration was studied by varying the borate concentration from 50 to 250 mM with 20 mM SDS and 2 mg mL^{-1} EDTA at a constant pH 8.0 (Fig. 2b). An increase in the borate concentration resulted in an increase in the migration time of ciclopirox olamine. Peak efficiency increased with increasing borate concentration until 200 mM was reached and then decreased. Above 200 mM a higher current and baseline shift occurred. Therefore, the borate concentration was set at 200 mM for all the analyses.

3.1.3. Effect of SDS

To compare the results produced by different methods a preliminary study using capillary zone electrophoresis (CZE) was attempted before the MEKC experiments. It was found that there was poor resolution between forced degradation product peaks of ciclopirox olamine and the EOF peak. The MEKC method was first reported by Terabe et al. [12], and since then, it has been applied successfully to the separation of many compounds [13,14]. A negative charged surfactant such as SDS is usually added to the background electrolyte to improve selectivity for the separation [15,16]. In this experiment, the effect of SDS on the separation was investigated within the range of 10–30 mM (Fig. 2c). The migration times of both the ciclopirox olamine and its forced degradation products increased with increasing SDS concentration. Ciclopirox olamine was completely separated from the forced degradation products using 10–30 mM SDS, however, higher SDS concentrations produced a poor baseline and prolonged the analysis time. Therefore, 20 mM SDS was chosen for this work.

3.1.4. Effect of EDTA

When 200 mM borate and 20 mM SDS at pH 8.0 were used in the running buffer, the ciclopirox olamine peak tailed. Theoretically this was expected as ciclopirox olamine forms a complex with the extractable and soluble metal ions from the system, chemicals and solvents. To prevent the interference of these metal ions, 2 mg mL^{-1}

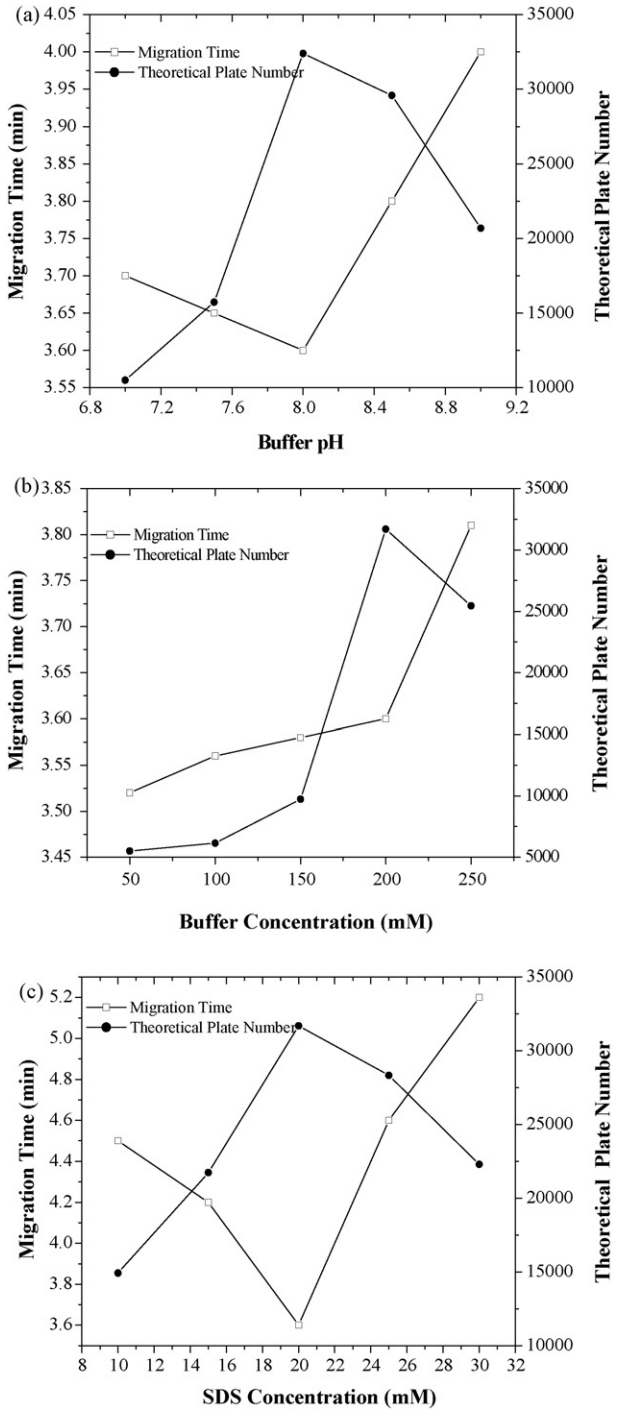

Fig. 2. (a) Effect of buffer pH on migration time and theoretical plate number of ciclopirox olamine. The electrolyte was 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA of various pH. The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C. (b) Effect of buffer concentration on migration time and theoretical plate number of ciclopirox olamine. The electrolyte was 20 mM SDS and 2 mg mL^{-1} EDTA (pH 8.0) of various buffer concentrations. The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C. (c) Effect of SDS concentration on migration time and theoretical plate number of ciclopirox olamine. The electrolyte was 200 mM borate and 2 mg mL^{-1} EDTA (pH 8.0) of various SDS concentrations. The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C.

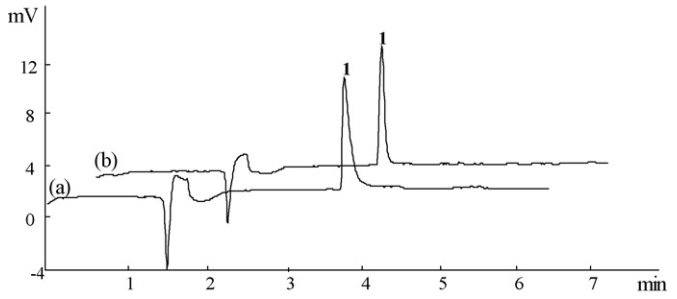

Fig. 3. The electropherograms of ciclopirox olamine solutions (a) without 2 mg mL^{-1} EDTA in running buffer and (b) with 2 mg mL^{-1} EDTA in running buffer. (a) The electrolyte was 200 mM borate and 20 mM SDS (pH 8.0). The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C. (b) The electrolyte was 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA (pH 8.0), The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C; peak: **1**, ciclopirox olamine.

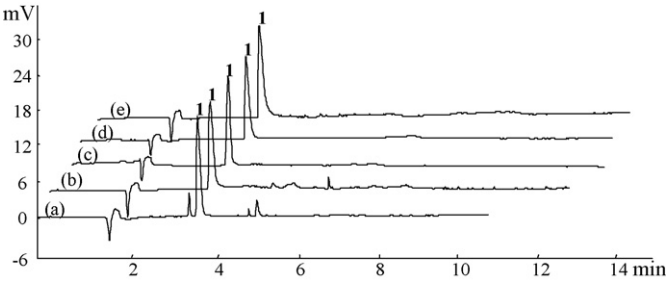

Fig. 4. The electropherograms of (a) hydrogen peroxide-induced degradation solution, (b) Photochemical degradation solution, (c) acid–base-induced degradation solution, (d) alkali-base-induced degradation solution and (e) high temperature-induced degradation solution. The electrolyte was 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA (pH 8.0), The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C; peak: **1**, ciclopirox olamine.

EDTA was added to the running buffer, as EDTA will preferentially form a complex with the metal ions, to keep the ciclopirox olamine free. This improved the peak shape (Fig. 3).

3.1.5. Effect of the applied voltage

The applied voltage had a great effect on the migration time, current strength and resolution. The impact of changing the applied voltage from 10 to 30 kV with the buffer of 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA at pH 8.0 was studied. The results indicated that the increase of applied voltage led to the decrease of the migration time due to the increasing EOF. However, it also resulted in poor peak resolution as well as deterioration in the baseline due to the much higher Joule's heating and electric current at higher voltage. A voltage of 20 kV yielded the best compromise in terms of the run time and separation current and it was used in all experiments.

3.1.6. Effect of the injection time

The injection time affected the peak width and height. In order to improve the sensitivity, the injection time was varied from 3 to 7 s. The peak area increased with the increasing injection time. At greater than 5 s, the peak shape of ciclopirox olamine deteriorated. Therefore 5 s was selected as the optimum injection time.

In summary the final and optimum conditions chosen for the measurements were a running buffer containing 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA (pH 8.0). Hydrodynamics sample injection was employed with a height of 15 cm for 5 s. The analysis were carried out at 20 kV with UV detection at 298 nm.

3.2. Results of the forced degradation studies

Three degradation products were observed in the hydrogen peroxide (30%, v/v) experiment. This indicated that the drug was unstable when degradation was forced using hydrogen peroxide (Fig. 4(a)).

Forced degradation of the drug in direct ultraviolet light for 24 h produced an extra later eluting peak, which showed that the drug was unstable against photochemical forced degradation. This was in line with USP's suggestion that ciclopirox olamine should be stored away from light. But there is no further information on degradation behavior or degradation products of ciclopirox olamine in the USP

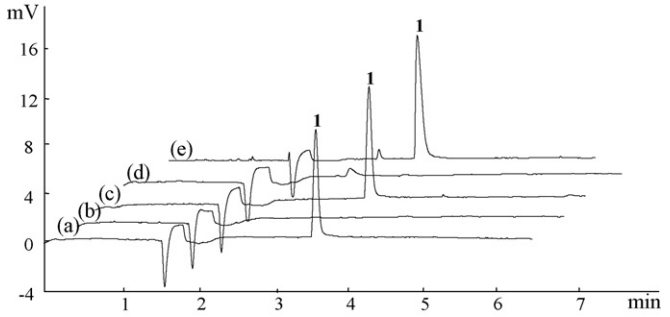

Fig. 5. The electropherograms of (a) ciclopirox olamine solution, (b) excipients placebo in suppository solution, (c) pharmaceutical suppository solution, (d) excipients placebo in cream solution and (e) pharmaceutical cream solution. The electrolyte was 200 mM borate, 20 mM SDS and 2 mg mL^{-1} EDTA (pH 8.0), The effective capillary length was 45 cm, the total length 38 cm and the applied voltage 20 kV. Hydrodynamic injection was performed for 5 s at 15 cm high. Detection wavelength, 298 nm; detection temperature, 25 °C; peak: **1**, ciclopirox olamine.

(Fig. 4(b)).

No degradation products were detected in either the acidic or basic conditions at 80 °C for 24 h or in the high temperature condition at 110 °C for 24 h. This indicated that the drug was stable under these conditions (Fig. 4(c)–(e)).

3.3. Method validation

The specificity of the method was tested by comparing the standard solution, excipients placebo solutions and pharmaceutical solutions. The excipients placebo solutions (solutions without the drug) were prepared by mixing proportions of the common excipients to the pharmaceutical formulations. From the electropherograms of standard solution, excipients solutions and pharmaceutical solutions it was clear that no significant interference occurred with the drug peaks during analysis (Fig. 5).

Table 1
Analytical characteristics of proposed method ($n = 7$)

Analyte	Ciclopirox olamine
Regression equation	$A = 3.90 \times 10^4 C + 4.00 \times 10^2$
Correlation coefficient (r)	0.9999
Linearity range (μg mL^{-1})	31.3–2.00 × 10^3
Number of data points	7
LOD (μg mL^{-1})	9.36
LOQ (μg mL^{-1})	31.3

Table 2
Intra- and inter-day R.S.D.of peak areas for proposed method

Concentration ($\mu g\,mL^{-1}$)	Intra-day R.S.D. (%) ($n=5$)	Inter-day R.S.D. (%) ($n=5$)
2.00×10^3	0.9	1.3
250	1.0	1.2
31.3	1.2	1.3

Table 3
The results of percentage recovery value in synthetic mixture of ciclopirox olamine for proposed method (added ciclopirox olamine for suppository and cream)

Theoretical concentration ($\mu g\,mL^{-1}$)	Suppository ($n=3$)		Cream ($n=3$)	
	Recovery (%)	R.S.D. (%)	Recovery (%)	R.S.D. (%)
200	100.1	0.5	100.7	0.8
250	99.4	1.1	99.5	1.1
300	100.2	0.5	100.7	1.3

Table 4
Results of analysis of ciclopirox olamine in different pharmaceutical formulations ($n=3$)

Pharmaceutical preparations	Proposed method		USP method	
	Assay (%)	R.S.D. (%)	Assay (%)	R.S.D. (%)
Suppository-batch-1	100.2	1.0	100.1	1.2
Suppository-batch-2	100.1	0.6	99.9	0.9
Suppository-batch-3	99.4	1.0	99.4	1.1
Cream-batch-1	100.4	1.0	100.2	1.3
Cream-batch-2	99.8	0.7	99.8	0.9
Cream-batch-3	99.5	0.9	99.4	1.0

To test the linearity of the MEKC method, a seven-point ciclopirox olamine standard curve was constructed with the concentration range from 31.3 to 2.00×10^3 $\mu g\,mL^{-1}$. The correlations of peak area versus the concentrations of ciclopirox olamine were obtained with a correlation coefficient (r) of 0.9999. In Table 1, the analytical characteristics were summarized for the proposed MEKC method. The limit of detection (LOD) and the limit of quantification (LOQ) were determined separately in five replicates at a signal-to-noise ratio (S/N) of 3 and 10, respectively. The LOD and LOQ were 9.36 and 31.3 $\mu g\,mL^{-1}$ for the proposed method. The measurements of intra- and inter-day precisions with multiple concentrations were performed to assess the repeatability and reproducibility of the developed method. Five replicates of three ciclopirox olamine solutions with concentration of high, middle and low were injected. The relative standard deviation (%R.S.D.) values of the peak areas for intra-day precision were 0.9, 1.0 and 1.2%, respectively. The inter-day precision of the method was evaluated by assessing higher, middle and lower linearity ranges on 3 consecutive days. The R.S.D. values of inter-day precision were 1.3, 1.2 and 1.3% (Table 2). The accuracy of the proposed method was studied by using percentage recovery experiments. These were performed by adding ciclopirox olamine of three different concentrations ranging from 80 to 120% to a constant mixture of excipients within the linearity range. Three samples were prepared for each recovery concentration level. The results showed excellent recovery ranging from 99.4 to 100.2% with an R.S.D. of less than 1.1% for suppository and 99.5–100.7% with an R.S.D. of less than 1.3% for the cream (Table 3).

3.4. Analysis of ciclopirox olamine in suppositories and creams

The applicability of the proposed method to the assay of ciclopirox olamine in suppository and cream was tested. The results obtained are presented in Table 4. The proposed method was assessed by comparing the results obtained with those generated by the official USP method (Table 4). These results were found to be consistent with those produced by the USP referenced method.

4. Conclusions

This is the first report of this kind on the simultaneous analysis of the drug ciclopirox olamine and its forced degradation products by MEKC. It is simple and rapid. The validation experiments showed that the method is selective, linear, precise, and accurate for quantitating ciclopirox olamine in the two pharmaceutical preparations. Ciclopirox olamine was separated from degradation products produced under forced degradation conditions. The total analysis time was less than 10 min with a good ciclopirox olamine peak shape at 3.6 min. A wide linear range for ciclopirox olamine was achieved. Compared to the published methods, such as HPLC, TLC, spectrophotometry, etc., this method has better separations and higher specificity. This study highlights the benefit of using simultaneous analysis of the drug ciclopirox olamine and its forced degradation products by saving drug manufacturers from unnecessary applications of complex procedures. This method had been adopted for the quality control of ciclopirox olamine in pharmaceutical production processes.

Acknowledgements

We thank Mike Duffin and Yucheng Gu of Syngenta Jealott's Hill International Research Centre in the UK for the proof reading of this manuscript.

References

[1] F. Belliardo, A. Bertolino, G. Brandolo, C. Lucarelli, J. Chromatogr. 553 (1991) 41–45.
[2] K. Lehr, P. Damm, J. Chromatogr. 339 (1985) 451–456.
[3] G. Coppi, S. Silingardi, IL Farmaco. 47 (1992) 779–786.
[4] United States Pharmacopoeia 28-NF23, United States Pharmacopoeia Convention, Inc., Rockville, MD, 2005, p. 470.
[5] H.M. Kellner, C. Arnold, O.E. Eckert, J. Herok, I. Hornke, W. Rupp, Arzneim. Forsch. 31 (1981) 1337–1353.
[6] H. Koch, Pharm. Int. 3 (1982) 46–47.
[7] S.A. Qadripur, G. Horn, T. Hohler, Arzneim. Forsch. 31 (1981) 1369–1372.
[8] C.J. Nithman, Pharm. West. 107 (1995) 15–19.
[9] A.V. Samtsov, Voen. Med. Zh. 323 (2002) 39–41.
[10] F. Ibrahim, N. El-Enany, IL Farmaco. 58 (2003) 1313–1318.
[11] F. Ibrahim, N. El-Enany, J. Pharm. Biomed. Anal. 32 (2003) 353–359.
[12] S. Terabe, K. Otsuka, K. Ichikawa, Anal. Chem. 56 (1984) 111–113.
[13] S. Fujiwara, S. Honda, Anal. Chem. 59 (1987) 2773–2776.
[14] Q.P. Dang, Z.P. Sun, D.K. Ling, J. Chromatogr. 603 (1992) 259–266.
[15] N. Öztekin, S. Başkan, F.B. Erim, J. Chromatogr. B 850 (2007) 488–492.
[16] X. Zhao, Y. Wang, Y. Sun, J. Pharm. Biomed. Anal. 44 (2007) 1183–1186.