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Development and validation of a stability-indicating RP-HPLC method for estimation of Ciclopirox olamine in bulk drug and cream formulation

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ABSTRACT

A simple, economic, selective, precise, and stability-indicating HPLC method has been developed and validated for estimation of ciclopirox olamine (CPO) both in bulk drug and in cream formulation. Reversed-phase chromatography was performed on a phenomenex C_{18} column with mobile phase acetonitrile-phosphate buffer 6.5 pH (70:30 v/v) at a flow rate of 1.0 ml min^{-1}. Detection was performed at 305 nm and a sharp peak was obtained for CPO at a retention time of 7.190 ± 0.045 min. The method was validated for accuracy, precision, specificity and selectivity, robustness, detection and quantification limits, and system suitability in accordance with ICH guidelines. Linear regression analysis data for the calibration plot showed there was a good linear relationship between response and concentration in the range 2 - 16 µg ml^{-1}; the regression coefficient was 0.9980 and the linear regression equation was y = 10035x - 20400. The detection (LOD) and quantification (LOQ) limits were found to be 0.005 and 0.01 µg ml^{-1}, respectively. Statistical analysis proved the method was precise, reproducible, selective, specific, and accurate for analysis of CPO. In order to determine whether the analytical method and assay were stability-indicating, CPO cream was stressed under various conditions to conduct forced degradation studies. The wide linearity range, sensitivity, accuracy, short retention time, and simple mobile phase imply the method is suitable for routine quantification of CPO with high precision and accuracy.

Keywords: stability-indicating; reversed-phase chromatography; ciclopirox olamine; forced degradation studies; cream formulation

INTRODUCTION

Ciclopirox olamine (CPO) is the ethanolamine salt of ciclopirox, which is a 6-cyclohexyl-1-hydroxy-4-methyl-2(1*H*)-pyridone having an empirical formula of $C_{12}H_{17}NO_2$ßC_2H_7NO[1,2]. It is a broad spectrum antifungal agent and effective against *Trichophyton equinum*[3], *T. mentagrophytes*[3,4,5], *T. rubrum*[3,4,5], *T. schoenleinii*[3,5], *T. tonsurans*[3,5], *T. verrucosum*[5], *T. violaceum*[3,5], *Epidermophyton floccosum*[3,4,5], *Microsporum audouinii*[3,5], *M. Canis*[3,5], *M. furfur* (*P. orbiculare*) and *Candidacies species*[3,5]. It acts against a wide range of bacteria including many gram-positive and gram-negative species pathogenic for humans[6]. Assay method based on UV spectrometry has been developed to determine the concentration of CPO[7]. Polarographic determination of CPO in pure substance and in different pharmaceutical preparations has also been reported[8]. A few methods were reported for the determination of CPO in raw material and in dosage form[9-14]. But those methods are complex and need special attention. There was a need to develop simple and conventional method for the determination of CPO. The aim of the present work is to develop an accurate, selective, precise and robust RP-HPLC method for the determination of CPO both in bulk drug and in cream formulation. The proposed method was validated as per ICH guidelines[15,16] and its updated international convention[17].

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MATERIAL AND METHODS

Materials

Pure ciclopirox olamine (CPO) was purchased form Sigma Lab, New Delhi. Acetonitrile and methanol (HPLC grade) were purchased from S. D. FineChemicals Ltd., Mumbai, India. Nylon 0.45 µm- 47 mm membrane filter were procured from Gelman laboratory, Mumbai, India and formulation was procured from local pharmacy. All other chemichals and reagents were of AR grade.

Preparation of standard stock solution

Accurately weighed 10 mg CPO was transferred to 100 ml volumetric flask, dissolved in 50 ml methanol and diluted up to mark with methanol.

Preparation of sample stock solution

A portion of the cream, equivalent to 10 mg of CPO was transferred into a 100 ml volumetric flask and 20 ml methanol was added. The content of the flask was sonicated for 30 min and diluted to volume with the mobile phase. The above sample solution was filtered through

Whatmann filter paper No. 41 prior to injection. To ensure, the solution was filtered again through 0.45 µ filter paper.

Method development

A Shimadzu's HPLC (LC-2010 CHT) with photodiode array (PDA) detector and manual injector of 20- µl loop was used. Separation was performed on phenomenex C_{18} column (250 mm x 4.6 mm i.d., 5 µm particle size) maintained at 27?C temperature. A variety of mobile phases were investigated in the development of an HPLC method suitable for analysis of CPO in the bulk drug and in cream. It consisting of different ratio of acetonitrile-water and acetonitrile-phosphate buffer 6.5 pH. The mobile phase was filtered through nylon 0.45 µm - 47 mm membrane filter and was degassed before use. Flow rate was adjusted to 1.0 ml min^{-1} and wavelength was set to 305 nm (? max of ciclopirox olamine).

Method validation

Linearity and range

Solutions of different concentration (2 - 16 µg ml^{-1}) for construction of calibration plots were prepared from the standard stock solution. The mobile phase was filtered through a 0.45 µ membrane filter and delivered at 1.0 ml min^{-1} for column equilibration; the baseline was monitored continuously during this process. The detection wavelength was 305 nm. The prepared dilutions were injected in series, peak area was calculated for each dilution, and concentration was plotted against peak area. Data was analyzed through linear regression.

Accuracy (as % Recovery)

Accuracy was determined by the standard addition method. Previously analyzed samples (CPO 4 µg ml^{-1}) were spiked with 50, 100 and 150% extra CPO standard and the mixtures were analyzed by the proposed method. The experiment was performed in triplicate. Recovery (%), SD (%) and % CV were calculated for each concentration.

Precision

Precision was determined as both repeatability (Method precision) and intermediate precision, in accordance with ICH recommendations. The repeatability was checked by repeatedly injecting (n = 6) solution of CPO (5 µg ml^{-1}). The results were reported in term of % coefficient of variance (% CV) should not more than 2 %.

Intermediate precision was evaluated in terms of intra-day and inter-day precision. For both intra-day and inter-day variation, replicate analysis of solutions of CPO at three different concentrations (6, 8 and 10 µg ml^{-1}) were carried out for six times. The results were reported in terms of % coefficient of variance (% CV).

Specificity and selectivity

The specificity of the method was established through resolution factor of the drug peak from the nearest resolving peak and also among all other peaks. Selectivity was confirmed through peak purity data using a PDA detector. To assess the method specificity, cream without CPO (placebo) was prepared with the excipients as for commercial preparation and compared with respective CPO standard to evaluate specificity of the method. Representative chromatograms of placebo and standard were compared for retention time, resolution factor and purity.

Robustness

The robustness of the developed method was determined to assess the effect of small but deliberate variation of the chromatographic conditions on the determination of CPO. Robustness was determined by changing ratio of mobile phase, column own temperature, wavelength, and injection volume.

Detection (LOD) and Quantification (LOQ) Limits

LOD and LOQ were determined by the standard deviation (Sy/x) method. Blank samples were injected in triplicate and the peak area of this blank was calculated. LOD and LOQ were determined from the slope, S, of the calibration plot and the standard deviation of the response for the blank sample, Sy/x, by use of the formulae LOD = 3.3 × Sy/x/S and LOQ = 10 × Sy/x/S[18].

System suitability

As system suitability test was an integral part of chromatographic methods development and was used to verify that the system is adequate for the analysis to be performed; the system suitability parameters for CPO were evaluated. The suitability of the chromatographic system was demonstrated by comparing the obtained parameter values, with the acceptance criteria of the CDER guidance document.

Solution stability

The stability of the drug in solution during analysis was determined by repeated analysis of samples during the course of experimentation on the same day and also after storage of the drug solution for 24 h under laboratory bench conditions (32 ± 1°C) and under refrigeration (8 ± 0.5°C).

Forced degradation study

In order to determine whether the analytical method and assay were stability-indicating, CPO cream was stressed under various conditions to conduct forced degradation studies[1,2]. Methanol was used as solvent in all studies, as CPO is practically insoluble in water and is freely soluble in methanol[1,2]. In all cases, cream contents equivalent to 10 mg CPO was accurately weighed and solutions were prepared as previously described using suitable solvent, to yield starting concentration 100 µg ml^{-1} of CPO for analysis. Sample solution was exposed to hydrolytic (neutral, acid and base), thermal (dry heat), oxidative and photolytic stress conditions and, the stressed samples were analyzed by the proposed method.

Acid degradation

To check the stability in acidic condition hydrochloric acid was used in different strength. Solution of CPO (100 µg ml^{-1}) for acid degradation study was prepared using 0.1N to 5 N hydrochloric acid in

methanol and the resultant solution was refluxed at 60 ºC for around 12 hours to facilitate acid degradation of CPO.

Alkali degradation

To check the stability in alkaline condition sodium hydroxide was used in different strength. Solution of CPO (100 µg ml^{-1}) for alkali degradation study was prepared using 0.1N to 5 N sodium hydroxide in methanol and the resultant solution was refluxed at 60 ºC for around 12 hours to facilitate alkali degradation of CPO.

Wet heat (Hydrolysis)

Solution of CPO (100 µg ml^{-1}) for wet heat degradation study was prepared using HPLC grade water and the resultant solution was refluxed at 60 ºC for 12 hours to facilitate hydrolysis of CPO.

Dry heat

Solution for dry heat study were prepared by exposing approximately 50 mg of cream in aluminium foil to dry heat in an oven at 60 ºC for 24 hour to facilitates dry heat degradation of CPO. The cream was removed from oven and the content of powder equivalent to 10 mg of CPO was accurately weighed and transferred to volumetric flask to make the final concentration 100 µg ml^{-1} of CPO.

Oxidation

To check the stability in oxidative condition hydrogen peroxide was used in different strength. Solution of CPO (100 µg ml^{-1}) for oxidation study was prepared using 3 % to 30 % H_2O_2 in methanol and the resultant solution was refluxed at 60 ºC for 12 hours to facilitate oxidation of CPO.

Photo stability (Sun light and UV light)

Cream was exposed to sunlight and UV radiation to determine the effects of light irradiation on the stability of CPO in the solid state. Approximately 100 mg of CPO cream was spread on a glass dish in a layer that was less than 2 mm thick. All samples for photo stability testing were placed in direct sunlight exposed for 12 hours and under UV cabinet (At 25 ?C with both UV radiation shorter and higher wavelength 254 and 310, respectively) for 12 hours. The cream were removed from the sun and UV light and the contents of powder equivalent to 10 mg of CPO was accurately weighed and transferred to volumetric flask to make the final concentration 100 µg ml^{-1} of CPO. Control samples which were protected with aluminium foil were also placed in the light cabinet and exposed concurrently. Following removal from the light cabinet, all samples were prepared for analysis as previously described.

Analysis of ciclopirox olamine in cream

LOPROX® (1 %) cream was used for analysis. Appropriate three different aliquots from sample solution (100 µg ml^{-1}) were suitably diluted with mobile phase in such a way to get concentrations in a range of 2 to 16 µg/ml for CPO. The finally prepared solutions were analysed under proposed chromatographic condition. The amount of CPO present in sample solution was determined by fitting the area response into the regression equation of CPO in the method.

RESULTS AND DISCUSSION

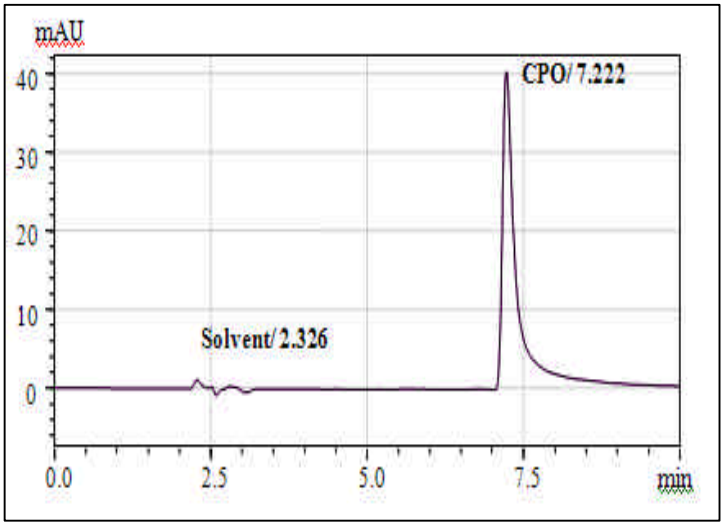
Method optimization

Initial studies to develop the method involved the use of C_{18} column with various mobile phases ratio containing acetonitrile and water. In almost every system studied, while the separation of more polar compounds was in some instance obtained, CPO showed a retention time greater than 6 min. Chromatograms with good peak shape with a steady baseline required for the analysis of CPO in presence of degraded impurities with an acceptable retention time. It was observed that satisfactory resolution of CPO and its degradation products formed under various conditions and present in the mixture of stressed samples were achieved. The method was optimized to separate major degradation products formed under various conditions. The optimized chromatographic conditions are mentioned in Table 1. Resolution was also checked on mixture of the degradation samples to confirm the separation behaviour. It indicates that the gradient method was successful in separation of drug and all chromophoric degradation products. A representative chromatogram is shown in Figure 1, which satisfies all the system suitability criteria, better resolution of the peak from solvent peak with clear base line separation was found.

Table 1:Optimized chromatographic conditions for estimation of Ciclopirox olamine

Parameters	Description
Column	Phenomenex C_{18} column (250 x 4.6 mm id, 5 µm particle size)
Column temperature	27 ± 1?C
Mobile phase	Acetonitrile: Phosphate buffer 6.5 pH (70:30, v/v)
Detection	Photodiode array detection at 305 nm
Injection volume	20 µl
Flow rate	1.0 ml min^{-1}

Figure 1:Chromatogram of CPO (1 µg m-1) standard with corresponding retention time at 305 nm by stability indicating RP-HPLC method



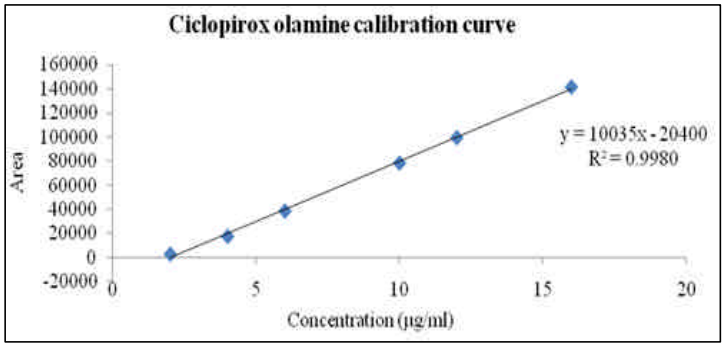
Ciclopirox olamine (CPO) with corresponding retention time (tR) of 7.222 min was detected at 305 nm. Peak of solvent observed at tR of 2.326 min is well separated from peak of drug

Method validation

Linearity and range

Linearity of the method was evaluated at seven concentration levels by diluting the standard stock solution to give solutions in the concentration range from 2 to 16 µg ml^{-1}. The results show that an excellent correlation existed between the peak area and concentration of analyte. The calibration curve was prepared by plotting the area under the response from the detector (AUC) line versus the concentration and analyzed through linear regression [Figure 2]. The response for the drug was linear (r^2 = 0.9980) in the concentration range between 2 and 16 µg ml^{-1}. The linearity was observed in the expected concentration range, demonstrating its suitability for analysis.

Figure 2:Calibration curve of CPO at 305 nm by stability indicating RP-HPLC method



Accuracy

Good recovery of the spiked drug was obtained at each added concentration, indicating that the method was accurate. A known amount of CPO (50, 100, and 150 %) of standard powder was added to the pre analysed solution of formulation. This solution was analyzed as previously described. The assay was repeated over 3 consecutive days to obtain intermediate precision data. The resultant % CV for this study was found to be < 2.0 % with a corresponding percentage recovery value. The recoveries obtained by RP-HPLC method for CPO shown in Table 2.

Table 2:Accuracy (% Recovery) study of Ciclopirox olamine by stability indicating RP-HPLC method

Ciclopirox olamine µg ml^{-1}	Added Concentration µg ml^{-1}	Intra-day measured % recovery ± S.D.[a], % CV[b] (n[c]=6)	Inter-day measured % recovery ± S.D.[a], %CV[b] (n[c]=6)
0.4	0.2 (50%)	99.476 ± 1.275, 1.281	99.460 ± 1.674, 1.683
0.4	0. 4 (100%)	101.475 ± 1.320, 1.300	100.58 ± 1.786, 1.75
0.4	0.6 (150%)	100.576 ± 1.343, 1.335	101.47 ± 1.806, 1.799

S.D[a] is standard deviation and % CVb is coefficient of variance for nc = 6 observations

Precision

The results of repeatability (method precision) experiment are shown in Table 3. Method precision was determined by repeatedly injecting 5.0 µg ml^{-1} concentration of CPO. The developed method was found to be precise as the % CV values for repeatability study was < 1.0 %. The results of intermediate precision experiment for both intraday and inter-day are shown in Table 4. Replicate analyses of three concentrations (6, 8 and 10 µg ml^{-1}) of the standard solution show good reproducibility. The developed method was found to be precise as the % CV values for intermediate precision study was < 2.0 %.

Table 3:Method precision data of Ciclopirox olamine by stability indicating RP-HPLC method

Ciclopirox olamine 5.0 µg ml^{-1} (n[c]=6)	Retention time (Min.)	Area
1	7.228	30214
2	7.104	29786
3	7.187	29976
4	7.199	29587
5	7.202	29685
6	7.222	39943
Mean	7.19	29881.83
S.D.[a]	0.0449	236.656
% CV[b]	0.624	0.791

S.D[a] is standard deviation and % CVb is coefficient of variance for nc = 6 observations

Table 4:Intermediate precision data of Ciclopirox olamine by stability indicating RP-HPLC method

Ciclopirox olamine µg ml^{-1}	Intra-day measured mean area ± S.D.[a], %CV[b] (n[c]=6)	Inter-day measured mean area ± S.D.[a], %CV[b] (n[c]=6)
6	40046.240 ± 486.048,1.213	39573.370 ± 687.704, 1.737
8	60247.580 ± 717.162,1.190	59237.230 ± 961.63, 1.623
10	89452.500 ± 1175.303,1.131	88964.880 ± 1432.506, 1.610

S.D[a] is standard deviation and % CVb is coefficient of variance for nc = 6 observations

Specificity

The resolution factor for the CPO from the nearest resolving solvent peak was > 4 in all forced degradation samples. The placebo shows no detector response near retention time of 7.229 min, while the CPO standard display good resoluted peak [Figure 1]. No interference from excipients present in the formulation [Figure 3] indicate specific nature of the method. The purity curve [Figure 4] and data [Table 5] of CPO shows that no other excipients are co-eluted with the drug and the peak is pure in nature.

Figure 3:Chromatogram of CPO (1 µg ml-1) cream at 305 nm by stability indicating RP-HPLC method

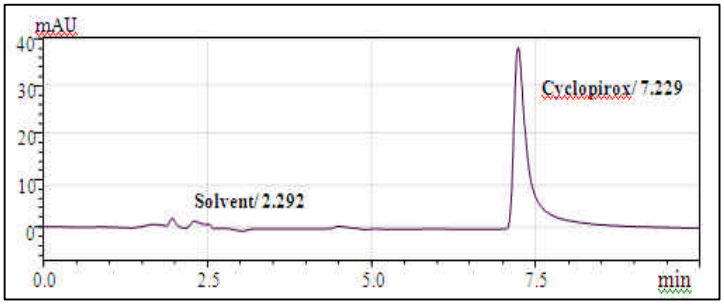


Figure 4:Purity plot of CPO at 305 nm by stability indicating RP-HPLC method

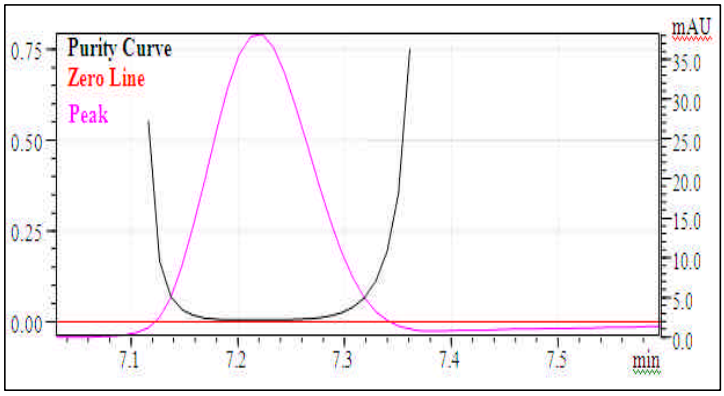


Table 5: Peak purity data of Ciclopirox olamine by stability indicating RP-HPLC method

Drug/degradation Products	Peak purity Index	Single point threshold	Minimum peak purity threshold
Ciclopirox olamine	0.99996	0.99657	7685

Robustness
To determine the robustness of the developed method, experimental conditions were deliberately altered and the response of the CPO was recorded. The results of change in ratio of mobile phase, column own temperature, wavelength, and injection volume were within the limit. System suitability criteria are also satisfied in deliberated condition.

Limit of detection (LOD) and quantitation (LOQ)
The detection (LOD) and quantification (LOQ) limits were found to be 0.005 and 0.01 µg ml^{-1}, respectively.

System suitability
The suitability of the chromatographic system was demonstrated by comparing the obtained parameter values, reported in Table 6, with the acceptance criteria of the CDER guidance document.

Table 6:System suitability parameters of Ciclopirox olamine by RP-HPLC method

Parameter	Value
Retention time (Min)	7.229
Resolution	2.43
Theoretical plates	2867
Tailing factor	1.32
Asymmetric factor	1.26
Capacity factor	3.254

Solution stability
The % CV of the assay of CPO during solution stability experiments were within 2 %. No significant changes were observed in the content of standard drug during solution stability and mobile phase stability experiments when performed using the method. The solution stability and mobile phase stability experiment data confirms that the sample and standard in solvent and mobile phases used during assay and the related substance determination were stable for at least 24 hours.

Force degradation of ciclopirox olamine
Ciclopirox olamine showed slight degradation in acidic, basic, wet and oxidative condition within very short time. Table 7 indicates the extent of degradation of CPO under various stress conditions. Stability data for the degradation of CPO were analysed according to the ICH guidelines.

Table 7:Force degradation summary of Ciclopirox olamine by stability indicating RP-HPLC method

Stress condition/ state	Time	% Assay ± S.D.[a] (n^b=6)
Acidic 5 N HCL (60ºC)/solution	12 hr	97.574 ± 1.675
Alkali 5 N NaOH (60ºC)/solution	12 hr	96.375 ± 1.767
Wet heat (60ºC)/solution	12 hr	97.897 ± 1.275
Oxidative 30 % H_2O_2 (60ºC)/solution	12 hr	96.057 ± 1.368
Dry hear (60ºC)/solid	24 hr	99.376 ±1. 573
Photo light (Sun light) /solid	2 hr	13.287 ± 1.305
UV Light 254 and 366 nm/solid	2 hr	32.074 ± 1.064

S.D.[a] is standard deviation for n^b = 6 observations

Degradation behaviour of ciclopirox olamine
In total, many degradation products were detected by LC on decomposition of the drug under specific stress conditions. CPO showed extensive degradation in sunlight and UV light condition. The degradation behaviour of the drug in individual stress conditions is outlined below. HPLC studies of CPO samples obtained from different stress conditions, using acetonitrile: phosphate buffer pH 6.5 (60:40 v/v) as the mobile solvent system suggested for the following degradation behaviour.

Acid degradation
It was observed that around 2 – 4 % of the drug degraded on refluxing it in methanolic 5 N HCL for 12 hr and there was no corresponding formation of degradation products as compared to the chromatogram of drug in formulation. This indicates that the drug was stable in acidic condition.

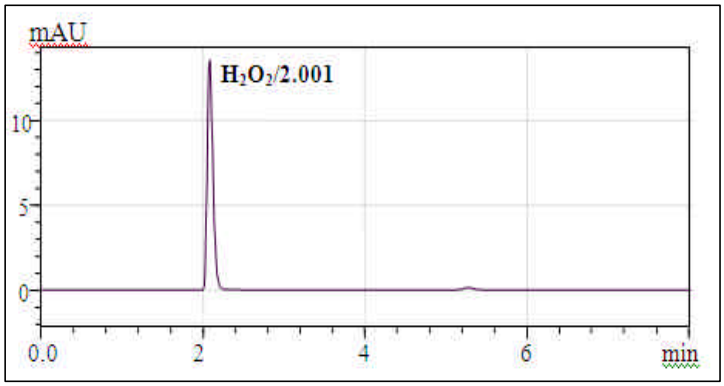
Alkali degradation
The results obtained on degradation of ciclopirox olamine in alkaline conditions were found to be very similar to those reported for acidic condition. 2 - 4 % degradation was observed within 12 hr refluxing in methanolic 5 N NaOH. No degraded impurities were separated from the drug. The product was seen during HPLC analyses of alkali-degraded samples with drug and compared with chromatogram of drug in formulation and standard, respectively. The drug was found to be highly stable to alkaline condition. The rate of degradation in alkali was same as acid condition.

Wet heat (Hydrolysis)
In neutral condition, only 2–3 % degradation of the drug was seen after refluxing at 60ºC at the end of 12 hr, degradation of the drug was observed with decreasing in area but no new degradation product was separated. The degradation observed in the wet degradation was not differing from the degradation of acid and alkali. The chromatogram was compared with standard and formulation.

Oxidation

Almost 2-5 % drug degradation was observed on exposure to 30 % H_2O_2 for 12 h. No degradation product peaks was seen, and also there was significant decrease in the height and area of the parent peak with time. The major peak observed at retention time of 2.001 RT is compared with blank chromatogram of 30 % H_2O_2 [Figure 5] shows that peak was of H_2O_2 not of impurity. This showed that the drug was stable in oxidative conditions, resulting in products are same as acid, alkali and wet degradation.

Figure 5:Chromatogram of blank 30% H_2O_2 at 305 nm by stability indicating RP-HPLC method



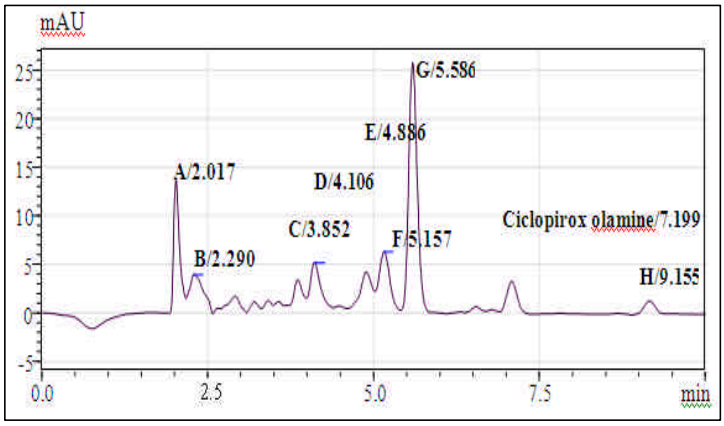
Dry heat

Ciclopirox olamine was found to be stable as compare to acid, base and wet degradation after exposing the drug to 60ºC for 24 hours. The exposure of the solid drug to 60ºC for 24 hours shows no degradation. It indicated that CPO was stable to dry heat than other force degradation condition.

Photo stability (Photo and UV light)

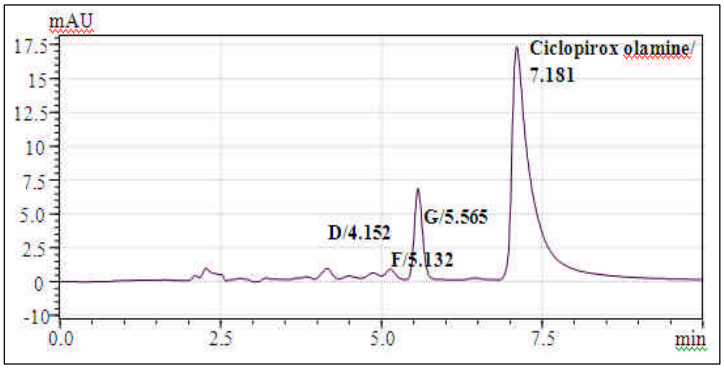
Ciclopirox olamine proved labile on exposure to sunlight and UV light (256 and 366 nm). In solid and methanolic solution 70-90 % degradation was observed. Under the conditions, the drug decomposed to the same major degradation product [Figure 6 and 7]. No degradation

Figure 6:Chromatogram of sunlight degradation of CPO at 305 nm by stability indicating RP-HPLC method



Degradation products found and separated after sunlight degradation are shown as alphabet A-H with their retention time. Observed peak of degradation products are well separated from the peak of drug

Figure 7:Chromatogram of UV light degradation of CPO at 305 nm by stability indicating RP-HPLC method



Degradation products found and separated after UV light degradation are shown as alphabet A-H with their retention time. Observed peak of degradation products are well separated from the peak of drug

was observed in control samples in the dark chamber. Many degradation products were observed after exposure of drug solution in sunlight and UV light for 2 hr. Almost 70-90% of the drug degraded in 2 hours with formation of a two minor degradation products between retention time ranges of 2 to 10 minute. This peak was found to increase with time. In this case, the fall in drug peak was in correspondence with the rise in degradation product peaks. Summary of photo degradation is indicated with corresponding retention time and ?max in Table 8.

Table 8:Photo degradation summary of Ciclopirox olamine by stability indicating RP-HPLC method

Impurity		Retention time (min)		lmax (nm)	
Sunlight	UV light	Sunlight	UV light	Sunlight	UV light
A	—	2.017	—	—	—
B	—	2.29	—	—	—
C	—	3.852	—	236	—
D	D	4.102	4.152	295	296
E	—	4.886	—	301	—
F	F	5.157	5.132	298	296
G	G	5.586	5.565	300	300
H	—	9.155	—	256	—

Degradation products found and separated after photo degradation are shown as alphabet A-H with their retention time and absorption maxima.

Analysis of ciclopirox olamine in cream

The proposed method was applied for the determination of CPO in cream (LOPROX®). A typical chromatogram obtained following the assay of suspension powder is depicted in Figure 3. The results of assay were from 98 to 101 % of label claim for the formulation. The results of the assay indicate that the method is suitable for the assay of ciclopirox olamine without interference from the excipients used in the cream [Table 9].

Table 9:Assay of Ciclopirox olamine in cream by stability indicating RP-HPLC method

Ciclopirox olamine µg ml^{-1}	Intra-day measured % Assay ± S.D^a, (n^b=5)	Inter-day measured % Assay ± S.D^a, (n^b=5)
5	98.574 ± 1.435	98.574 ± 1.664
10	99.572 ± 1.254	100.684 ± 1.764
15	98.352 ± 1.543	99.574 ± 1.574

S.D.^{a} is standard deviation for n^b = 5 observations

CONCLUSION

The results of stress testing undertaken according to the International Conference on Harmonization (ICH) guidelines reveal that the method is selective and stability-indicating. The proposed method is simple, accurate, precise and has ability to separate drug from degradation products and excipients found in the dosage forms.

The RP-HPLC method developed meets the system suitability criteria, peak integrity and resolution from the parent drug and its degraded products. Two major degradation products were observed at RT 3.187, and 3.879 minute. Detection and quantification limits achieved, describe the method is very sensitive. High recovery and acceptable % CV values confirm established RP-HPLC method is accurate and precise. The complete separation of the analytes was accomplished within 7 minutes. The method has been successfully applied to perform accelerate stability study of ciclopirox olamine. Hence, the method is recommended for routine quality control analysis of ciclopirox olamine.

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