Original Article

Economical spectrophotometric method for estimation of zaltoprofen in pharmaceutical formulations

Abstract

Aim: A simple, rapid, precise, and economical spectrophotometric method has been developed for quantitative analysis of zaltoprofen (ZLT) in pharmaceutical formulations. **Materials and Methods:** A mixture of methanol and water was used as a solvent. Initial stock solution of ZLT was prepared in methanol and subsequent dilution was done in water. The standard solution of ZLT in water showed two absorption maxima, one at 243.5 nm and another at 338.0 nm. **Results:** The drug obeyed Beer–Lambert's law in the concentration range of 1–40 μg/mL with regression 0.9999 at 243.5 nm and 5–100 μg/mL with regression 0.9999 at 338.0 nm. The overall % recovery was found to be 99.53% and 99.77% at 243.5 nm and 338.0 nm, respectively, which reflect that the method is free from interference of the impurities and other additives used in tablet formulation. Relative standard deviations of absorbance from six measurements were always less than 2%. **Conclusions:** The results of analysis have been validated as per ICH guidelines. Both the wavelengths can be adopted in routine analysis of ZLT in tablet dosage form.

Key words: ICH guidelines, UV Spectrophotometric, validation, zaltoprofen

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Access this article online

Website: www.phmethods.org

DOI: 10.4103/2229-4708.84443

Quick response code

INTRODUCTION

Zaltoprofen (ZLT) is a non-steroidal anti-inflammatory drug and has excellent effects even on postsurgery or posttrauma chronic inflammation. The chemical name of ZLT is (±)-2-(10, 11-dihydro-10-oxodibenzo [b,f] thiepin-2-yl) propionic acid [Figure 1].[1] ZLT selectively inhibits cyclooxygenase-2 activity and prostaglandin E2 production.[2] It is used in the treatment of rheumatoid arthritis, osteoarthritis, and other chronic inflammatory pain conditions.[3,4] It is a unique compound that also has anti-bradykinin activity.[5] It is not only cyclooxygenases but also bradykinin-induced 12-lipoxygenase inhibitor.[6]

Earlier publications have described high-performance liquid chromatography (HPLC) methods useful for the quantification of ZLT in human plasma.[7-10] However, these methods involve arduous sample preparation and long chromatographic run times for biological samples.

So far to our present knowledge, no UV spectrophotometric analytical method is available in the literature for analyzing ZLT in pharmaceutical tablet dosage form or bulk drug samples. It was felt necessary to develop a simple, precise, and rapid spectrophotometric method for the quantitative determination of ZLT. The current research work deals with the development of spectrophotometric method and its validation as per International Conference on Harmonisation (ICH) guidelines. The developed method was found to be selective, accurate, precise, reliable, and economical.

MATERIALS AND METHODS

Materials

ZLT bulk drug was obtained from Macleods Pharmaceuticals (Mumbai, India),

methanol (HPLC grade) from Merck Fine Chemicals (Mumbai, India), and Whatman filter paper number 1 from Qualigens Fine Chemicals (Glaxo, Mumbai, India). The commercially available Zalto® tablets (B. No KL0947 and KL0948 of Intas Pharmaceuticals Ltd., Sikkim) containing 80 mg of ZLT were used and procured from the local market. Milli-Q water was used throughout the work. Other chemicals used were analytical or HPLC-grade and glassware used were Class A grade.

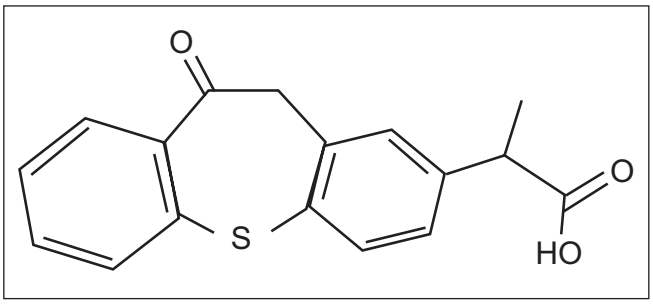

Figure 1: Chemical structure of ZLT

Instruments

Shimadzu UV - 1700 UV/VISIBLE spectrophotometer with UV probe 2.10 software and 1 cm matched quartz cells were used for absorbance measurements. Analytical balance used for weighing standard and sample was Make-Mettler Toledo, Model-XP 105.

Preparation of standard stock solution

One hundred milligrams of ZLT working standard was accurately weighed and transferred into a 100 mL volumetric flask and dissolved with minimum quantity of methanol and volume was made up to 100 mL with methanol to give the solution containing 1000 µg/mL of ZLT.

Selection of λ_{max}

The standard stock solution was further diluted with Milli-Q water to get a 10 µg/mL of concentration. The solution was scanned between 200 and 400 nm using Milli-Q water as blank. The UV spectrum of ZLT in Milli-Q water had shown two λ_{max}, one at 243.5 nm and other at 338.0 nm. Hence, both λ_{max} were selected for the analysis of ZLT [Figure 2].

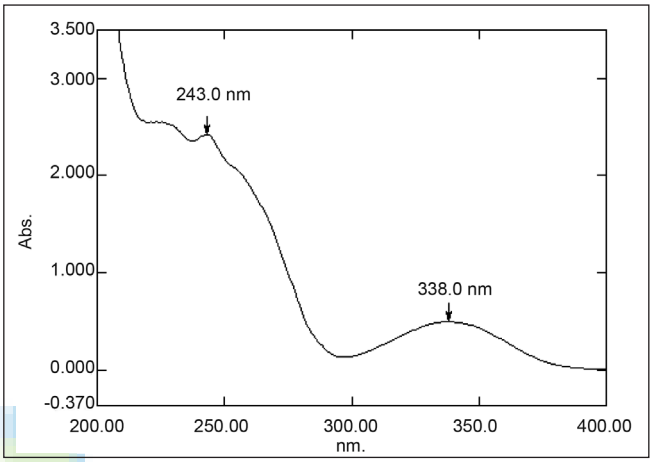

Figure 2: UV spectrum of pure drug ZLT in water

Preparation of the calibration curve

Aliquots of standard stock solution were further diluted with Milli-Q water to get the solutions of concentration 1–100 µg/mL. The absorbances were measured at 243.5 and 338.0 nm against Milli-Q water as blank. All measurements were repeated three times for each concentration. The calibration curve was constructed by plotting mean of absorbance against corresponding concentration.

Preparation of the sample solution

Two commercial tablet preparations of different batch number were assayed. These were labeled to contain 80 mg of ZLT per tablet, respectively.

Twenty tablets of formulation (Zalto® tablet) containing 80 mg of ZLT were accurately weighed and powdered. The powder equivalent to 100 mg of ZLT was weighed and transferred to a 100 mL volumetric flask; 80 mL methanol was added and sonicate for 10 min. The volume was made to 100 mL with methanol. The solution was filtered through Whatman filter paper No. 01. From this filtrate, 1 mL was transferred to a 100 mL volumetric flask and diluted with Milli-Q water to 100 mL in order to obtain the final concentration of 10 µg/mL. The absorbance was measured at 243.5 and 338.0 nm using Milli-Q water as blank. This procedure was repeated for six times. The amount of ZLT present in formulation was calculated by comparing it with standard absorbance. The results obtained are shown in Table 1.

Method validation

The developed method was validated as per ICH guidelines for following parameters.[11,12]

Linearity

The linearity was studied in the concentration range of 1–40 µg/mL and 5–100 µg/mL at 243.5 and at 338.0 nm, respectively. Linear regression data are shown in Table 2.

Specificity and selectivity

The spectra obtained from tablet solutions were identical with that obtained from standard solution

Table 1: Assay of marketed formulations

Formulation	B. No	Method wavelength (nm)	Amount of drug taken from tablet (mg)	% Mean assay*	%RSD
Zalto® tablet (Intas)	KL0947	243.5	100	99.23	0.43
		338.0	100	100.12	0.23
	KL0948	243.5	100	99.63	0.86
		338.0	100	99.86	0.34

*Mean of six determinations

Table 2: Linear regression data

Parameters	243.5 nm	338.0 nm
Beer's law limit (µg/mL)	1–40	5–100
Correlation coefficient	0.9999	0.9999
Molar extinction coefficient (L/mol cm)	210642.2	35952.4
Regression equation ($y = mx + c$)	$y = 0.058x + 0.089$	$y = 0.012x + 0.006$
Slope (m)	0.058	0.012
Intercept (c)	0.089	0.006

Table 3: Results of recovery studies

Method wavelength (nm)	Amount of std drug added (µg/mL)	Amount recovered (µg/mL)*	% Recovery*	% RSD	Mean % recovery
243.5	8	8.01	100.13	0.18	99.83
	10	9.92	99.20	0.22	
	12	12.02	100.16	0.62	
338.0	8	7.98	99.75	0.04	99.74
	10	9.98	99.80	0.75	
	12	11.96	99.67	0.86	

*Mean of three determinations

containing an equivalent concentration of ZLT. This showed that there was no any interference from excipients. Therefore, it could be said that developed method is highly selective.

Recovery studies

To ensure accuracy of the method, recovery studies were performed by standard addition method at 80%, 100%, and 120% level to preanalyzed samples and subsequent solutions were reanalyzed. At each level, three determinations were performed. The absorbances were measured at 243.5 and 338.0 nm using Milli-Q water as blank and the amount of drug recovered from the formulation were calculated, and the results obtained are shown in Table 3.

Precision

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Precision of the method was determined in terms of repeatability and intraday and interday precisions.

Repeatability

Repeatability of the method was determined by analyzing six samples of same concentrations of drug. Chromatographs were recorded, and the area of each chromatograph was measured. The results of this determination are reported in Table 4.

Intraday and interday precision

Intraday precision was determined by analyzing the drugs at three different concentrations and each concentration for three times, on the same day. Interday precision was determined similarly, but the analysis being carried out daily, for three consecutive days. The results are summarized in Table 4.

Robustness

The robustness of a method is its capacity to remain unaffected by small changes in conditions. To determine the robustness of the method, the experimental conditions were deliberately altered and assay was evaluated. The effect of detection wavelength was studied at ±2 nm. For changes of conditions, the sample was assayed in triplicate. When the effect of altering one set of conditions was tested, the other conditions were held constant at

Table 4: Result of repeatability, intraday, and interday precision studies

Method wavelength (nm)	Intraday		Interday		Repeatability	
	% Labeled claim ± SD *	% RSD	% Labeled claim ± SD *	% RSD	% Labeled claim ± SD *	% RSD
243.5	99.18 ± 0.50	0.51	99.08 ± 0.42	0.43	99.97 ± 0.025	0.26
338.0	100.11 ± 0.47	0.45	100.04 ± 0.49	0.51	100.24 ± 0.012	0.95

*Mean of six determinations.

Table 5: Result of robustness studies

Method wavelength (nm)	Condition (nm)	% Assay*	% RSD
243.5	226.5	98.57	0.67
	230.5	99.02	0.46
338.0	332.0	100.21	0.23
	328.0	99.85	0.34

*Mean of three determinations.

Table 6: Result of ruggedness studies

Parameter	Analyst I		Analyst II	
	243.5 nm	338.0 nm	243.5 nm	338.0 nm
Label claim (mg)	80	80	80	80
% Assay*	99.27	99.36	99.51	99.93
% RSD	0.26	0.43	0.76	0.68

*Average of three determinations.

Table 7: Stability data

Method wavelength (nm)	Time (h)	% Assay*	% RSD
243.5	1	99.37	0.34
	4	99.21	0.79
	8	98.77	1.12
338.0	1	100.10	0.23
	4	99.77	0.34
	8	99.67	1.03

*Average of three determinations.

the optimum values. Assay of ZLT for all deliberate changes of conditions was within 98.0–102.0 %. The results are shown in Table 5.

Ruggedness

To determine ruggedness, two different analyst performed assay on marketed tablets of the drug in similar operational and environmental conditions using developed method. The results are summarized in Table 6.

Solution stability

The stability of the standard solution was tested at intervals of 1, 4, and 8 h. The stability of solutions was determined by comparing absorbance of ZLT. The absorbance values were within 0.5% after 8 h. These results indicate the solution was stable for 8 h at ambient temperature, because there was no change in assay value. The %RSD of assay was 1.12% and 1.03% at 243.5 and 338.0 nm, respectively, after 8 h. The results are shown in Table 7.

RESULTS AND DISCUSSION

The overlay UV spectra of standard and tablet solutions of ZLT in Milli-Q water were found to be same. The UV spectrum of ZLT in Milli-Q water has two maximum absorption (λ_{max}), one at 243.5 nm and another at 338.0 nm. The absorbance of excipients in tablet solution did not interfere with ZLT at 243.5 and 338.0 nm. As a result, both wavelengths were selected for quantitative analysis and validation. The developed method was found to be precise as the %RSD values for intraday and interday precision were found to be less than 2%. The method was also found to be accurate, indicated by % recoveries ranging from 99.20 to 100.16%.

CONCLUSIONS

The developed UV spectrophotometric method for the determination of ZLT has the advantage of being fast, simple, inexpensive, and applicable over a wide concentration range with high precision and accuracy. The method was validated as per the guidelines laid by ICH. The results of the validation tests were found to be satisfactory and therefore this method can be applied successfully to analyze drug formulations.

ACKNOWLEDGMENT

We would like to thank Macleods Pharmaceuticals Ltd, Mumbai, India, for providing pure drug samples for this study and the Amrutvahini Sheti and Shikshan Vikas Sanstha, Sangamner, M.S., India, for providing us the research facility.

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How to cite this article: Aher KB, Bhavar GB, Joshi HP, Chaudhari SR. Economical spectrophotometric method for estimation of zaltoprofen in pharmaceutical formulations. Pharm Methods 2011;2:152-6.
Source of Support: Nil, **Conflict of Interest:** None declared.