RESEARCH ARTICLE

Stability Indicating UV Spectrophotometric Method for Loxoprofen Sodium: Method Development and Validation

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ABSTRACT

Loxoprofen sodium was analyzed using UV spectrophotometry, and the method was designed and validated in the present study in accordance with ICH Q2 recommendations. Loxoprofen sodium's stress degradation behavior was investigated using a newly discovered technique. Analysis was carried out at 223 nm by using distilled water as solvent. Stress degradation of drug was studied at acidic, basic and oxidative conditions. With a correlation coefficient of 0.999, linearity was found between 5 and 25 µg/mL. Intraday and interday precision studies showed RSD values of <2.0%, demonstrating the accuracy of the presented approach. Results obtained for LoD and LoQ are 0.012 and 0.037 µg/mL, respectively. For the ruggedness study, the absorbance value of six replicates was found to be 0.477 ± 0.004 with %RSD > 2.0% states that the developed method was found to be rugged. During the stress degradation study, it was observed that the drug is susceptible to basic and oxidative conditions with degradation of more than 10%.

Keywords: Loxoprofen sodium, Stress degradation, Method validation, UV-Spectrophotometric, Linearity.

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INTRODUCTION

Pharmaceutical analysis has its own importance in the maintenance of quality assurance and quality control of various pharmaceutical preparations. Loxoprofen sodium is a newly developed propionic acid deravative.[1] It is used as an NSAID drug to treat inflammation and reduce the pain in joints and muscles.[2] Loxoprofen is a precursor which shows its effects when absorbed in GIT by transforming to an active metabolite. Loxoprofen inhibits the synthesis of prostaglandin through its action on cyclooxygenase.[3] IUPAC name of loxoprofen sodium is "sodium-2-[4-(2-oxocyclopentyl1-methyl) phenyl] propionate dihydrate". In Japan, it is the most widely prescribed NSAID.[4] The structure of loxoprofen sodium is given in Figure 1.

Stress testing of drug products plays very important role in understanding the stability of pharmaceutical products.[5-7] It is studied at exaggerated conditions of temperature and humidity to understand the stability characteristics of drug products.[8] A stability study is a very useful tool in determining storage conditions of various existing as well as newly developing pharmaceutical dosage forms.[9]

Various liquid chromatographic methods have been developed and reported for loxoprofen sodium.[10] The reported chromatographic methods are complex and require costly instrumentation set-up and skilled personnel to operate. Many laboratories in the developing country cannot afford these costly instruments. In contrast, UV-Spectrophotomentry is considered as most convenient analytical technique in most quality control and quality assurance laboratories. Small-scale industries widely use spectrophotometry as the cost of the equipment is less and the results are reliable. Therefore, the purpose of this research was to create and verify an easy-to-use UV Spectrophotometric method for detecting loxoprofen sodium.

MATERIAL AND METHODS

Standard drug loxoprofen sodium is obtained from Dr. Reddy Labs, Hyderabad as a gift sample. Solvents required for UV Spectrophotometric estimation of selected drugs were obtained from store house of "KLE Society's College of Pharmacy, Belagavi". UV Spectrophotometer (Shimadzu-1800) was used.

Method Development

UV-Spectrophotometric method development began with solvent selection and λ_{max} determination. The solubility of ioxoprofen sodium was checked in various solvents. A literature survey revealed that loxoprofen is sodium soluble in

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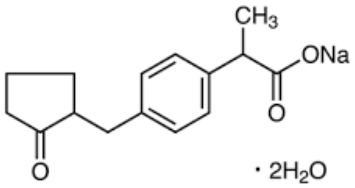

Figure 1: Chemical structure (Loxoprofen Sodium)

water as well as in methanol. In most of the studies, methanol is used as a solvent for UV spectroscopy. In our research work, we have used distilled water for estimation.

Selection of λ_{max}

The medication was precisely weighed out at 10 mg, and then diluted with distilled water to reach the desired concentration of 25 µg/mL. To find the λ_{max}, the solution was scanned from 200 to 400 nm.

Preparation of Standard Stock

Stock solution-I

A total of 10 mg of ioxoprofen sodium were accurately weighed and poured into a 100 mL volumetric flask. The medication was dissolved in distilled water, and the final volume was adjusted accordingly. From stock solution pipetted out 0.5–3.0 mL solutions and transferred them into 10 mL of volumetric flasks. Volume was made by adding distilled water up to the mark to get solutions with concentrations of 5 to 30 µg/mL. The prepared solutions were scanned for absorbance at 223 nm. Based on the results obtained, the calibration curve was plotted, and the correlation coefficient (r^2) was determined. The parameters of the developed method are given in Table 1.

Method Validation

Validation of the developed method was carried out in conditions of various parameters as per the current regulatory requirements.[11] The parameters studied during the validation of an analytical method include selectivity, specificity, LoQ, LoD, precision and ruggedness.[12]

Specificity and selectivity

The spectrum was obtained by keeping distilled water at blank and the sample position to check if any interference of solvent during routine analysis of the drug sample.

LoD and LoQ

The following formulae were used to calculate LoD and LoQ:

$$\mathbf{LoD} = \frac{3.3 \times Standard\ Deviation\ of\ Y\ intercept}{Slope\ of\ the\ calibration}$$

$$\mathbf{LoQ} = \frac{10 \times Standard\ Deviation\ of\ Yintercept}{Slope\ of\ the\ calibration}$$

Precision

In the intraday precision study, six replicates of drug solutions of 5, 15 and 25 µg/mL were prepared, and their absorbance were determined at three different times within the same day at 223 nm. Based on the results obtained, %RSD was determined.

Table 1: Developed UV method parameters for loxoprofen sodium

Parameter	*Details*
Method	UV-spectrophotometric Method
Instrument	UV-spectrophotometer
Analyte	Loxoprofen sodium
Wavelength Run	400–200 nm
Solvent	Distilled water
λmax	223 nm
Model	Shimadzu(UV-1800)
Software	UV-Probe

Ruggedness

By repeating six replicates of a 15 µg/mL solution by two different analysts, ruggedness was determined. Results obtained were compared, and %RSD was calculated.

Forced degradation studies

The stability of pure drug samples was accessed with a newly developed UV-spectroscopic method by exposing the drug to various stress conditions like acid, base and oxidation by using standard procedures.

RESULTS AND DISCUSSION

The UV spectrum obtained for loxoprofen sodium is as shown in Figure 2. The λ_{max} was found to be 223 nm which is in line with the available literature.

Method Validation

Linearity study

Figures 3 and 4 depict various absorbance values for respective concentrations. Linearity was observed between concentration and absorbance values within the studied range viz. 5–30 µg/mL. The correlation coefficient (r^2) was found to be 0.999. Results of Linearity are given in Table 2.

Specificity and selectivity

The spectrum obtained by keeping distilled water at blank was not show any absorbance at the maximum absorbance wavelength of the drug at 223 nm. It was determined that the solvent did not affect the results, leading researchers to conclude that the established approach was both specific and selective for the measurement of the medication.

LoD and LoQ

The results obtained for LoD and LoQ are as shown in Table 3.

Precision

%RSD values for intraday and interday precision study were found to be <2.0% which highlighted that the developed method was found to be precise for regular analysis.
The obtained results are shown in Table 4 and 5.

Ruggedness

The results obtained for the ruggedness study are as presented in Table 6. The absorbance value of six replicates was found

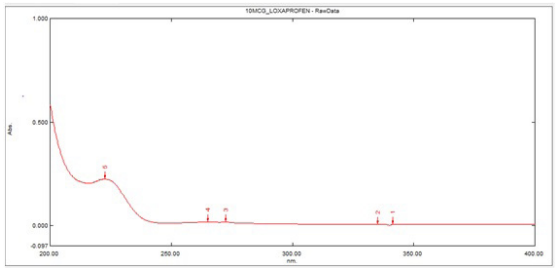

Figure 2: UV spectrum of loxoprofen sodium –λ^{max} at 223 nm

Table 2: Results of linearity and range study of loxoprofen sodium

S. No.	*Concentration (µg/mL)*	*Absorbance*
1	5	0.150
2	10	0.322
3	15	0.492
4	20	0.639
5	25	0.804
6	30	0.955
7	Slope	0.160
8	r^2	0.999

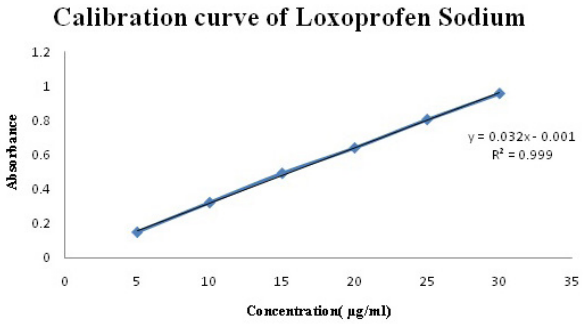

Figure 3: Standard calibration curve of loxoprofen sodium

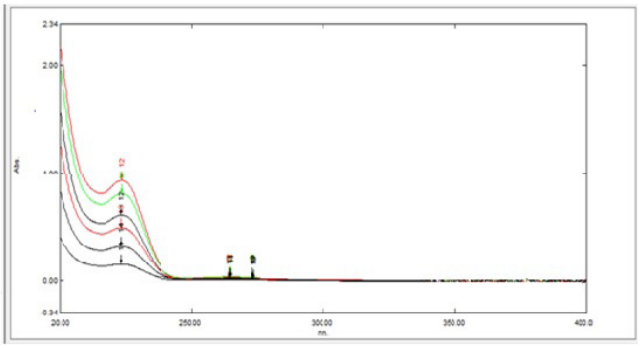

Figure 4: Overlay of UV –spectrum of loxoprofen sodium (5–30 µg/mL)

Table 3: LoD and LoQ data of loxoprofen sodium

S. No.	*Parameter*	*Values (µg/mL)*
1	LoD	0.012
2	LoQ	0.037

Table 4: Intraday-1, 2, 3 precision data of ioxoprofen sodium (15 µg/mL)

	Precision		
	Intraday -1	*Intraday -2*	*Intraday -3*
Concentration (µg/mL)	*Absorbance*	*Absorbance*	*Absorbance*
15	0.480	0.480	0.474
15	0.472	0.472	0.475
15	0.479	0.479	0.474
15	0.473	0.473	0.479
15	0.473	0.478	0.480
15	0.475	0.478	0.479
Mean	0.475	0.476	0.476
SD	0.003	0.003	0.002
%RSD	0.712	0.697	0.584

Table 5: Interday-1, 2, 3 precision data of loxoprofen sodium (15 µg/mL)

Precision	*Interday -1 precision*	*Interday - 2 precision*	*Interday -3 precision*
Concentration (µg/mL)	*Absorbance*	*Absorbance*	*Absorbance*
15	0.482	0.483	0.486
15	0.485	0.484	0.490
15	0.484	0.486	0.490
15	0.484	0.486	0.486
15	0.485	0.489	0.489
15	0.487	0.489	0.488
Mean	0.484	0.486	0.488
SD	0.001	0.002	0.001
%RSD	0.206	0.411	0.204

Table 6: Ruggedness data of loxoprofen sodium (15 µg/mL)

Ruggedness (change in analyst)	*15 µg/mL*	
Replicates	*Absorbance (Analyst I)*	*Absorbance (Analyst II)*
1	0.482	0.474
2	0.471	0.482
3	0.478	0.474
4	0.473	0.480
5	0.480	0.479
6	0.482	0.478
Mean	0.477	0.477
SD	0.004	0.003
%RSD	0.979	0.680

to be 0.477 ± 0.004 with %RSD values less than 2.0%. Thus developed method was established to be rugged.

Forced degradation studies

Forced degradation study results obtained are shown in Table 7.

Table 7: Forced degradation study data of loxoprofen sodium

Parameter	*Loxoprofen sodium at 223 nm*		
	Initial	*Final*	*%degradation*
Acid	0.428	0.420	1.86
Base	0.359	0.319	11.14
Oxidation	0.602	0.540	10.29

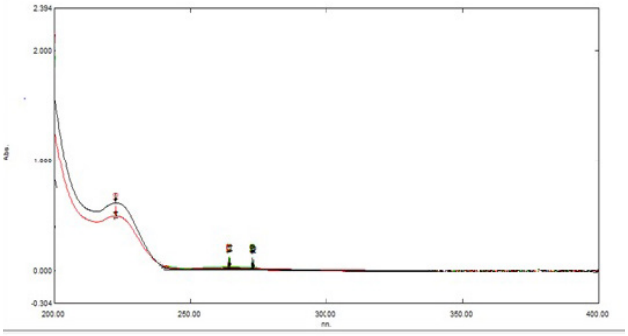

Figure 5: Overlay graph of loxoprofen sodium under basic condition

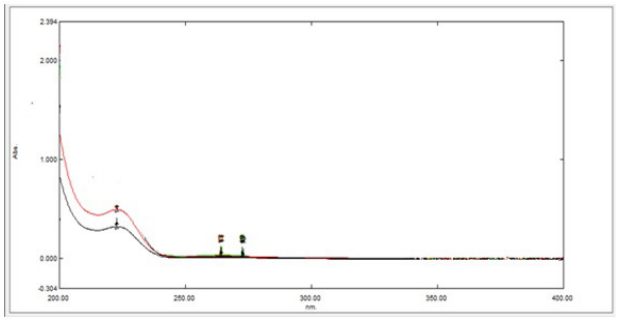

Figure 6: Overlay graph of loxoprofen sodium under oxidation degradation condition

- *Acid degradation study*

There were no any considerable changes observed in the spectra of drug solution after 2 hours of heating in acidic conditions. Thus it can be considered that drug is stable at acidic pH conditions.

- *Base degradation study*

The alkaline degradation study has revealed that drug is susceptible to basic conditions and within 2 hours of heating at 80°C, >10% drug was degraded. Comparative spectra of Initial and final drug solutions are as shown in Figure 5.

- *Oxidation degradation study*

The oxidative degradation study with 30% H_2O_2 has revealed that the drug is susceptible to oxidation and within 2 in hours of heating the presence of H_2O_2 more than 10% of the drug was found to be degraded. Spectral changes are shown in Figure 6.

CONCLUSION

The simple and accurate UV-spectroscopic method for analysis of loxoprofen sodium was developed and validated. Results obtained have highlighted the accuracy, specificity, linearity, precision and ruggedness of the method. Researchers looked at how loxoprofen sodium responded to a number of different types of stress and presented their findings. Studies on basic and oxidative degradation showed significant drug breakdown, but acidic conditions kept the medication stable. Small-scale industries might use the suggested method for monitoring the quality of bulk samples.

REFERENCES

1. Alqarni M, Namazi NI, Alshehri S, Naguib IA, Alsubaiyel AM, Venkatesan K, *et al*. Solubility Optimization of Loxoprofen as a Nonsteroidal Anti-Inflammatory Drug: Statistical Modeling and Optimization. Molecules. 2022; 27(14):4357.doi.org/10.3390/molecules27144357.
2. Ji C, Yu Y, Zhang M, Yu W, Dong S. Loxoprofen sodium alleviates oxidative stress and apoptosis induced by angiotensin II in human umbilical vein endothelial cells (HUVECs). Drug Design, Development and Therapy. 2020;14: 5087-96. doi.org/10.2147/dddt.s266175.
3. Kanazawa H, Tsubayashi A, Nagata Y, Matsushima Y, Mori C, Kizu J, *et al*. Stereospecific analysis of loxoprofen in plasma by chiral column liquid chromatography with a circular dichroism-based detector. Journal of Chromatography A. 2002;948(1-2):303-8. doi.org/10.1016/s0021-9673(01)01312-7.
4. Eissa MS, Abd El-Sattar OI. Identification and structure elucidation of forced degradation products of the novel propionic acid derivative loxoprofen: development of stability-indicating chromatographic methods validated as per ICH guidelines. Journal of Chromatographic Science. 2017;55(4):417-28.doi.org/10.1093/chromsci/bmw196.
5. Murakami T, Kawasaki T, Takemura A, Fukutsu N, Kishi N, Kusu F. Identification of degradation products in loxoprofen sodium adhesive tapes by liquid chromatography–mass spectrometry and dynamic pressurized liquid extraction–solid-phase extraction coupled to liquid chromatography–nuclear magnetic resonance spectroscopy. Journal of Chromatography A. 2008;1208:164-74. doi.org/10.1016/j.chroma.2008.08.076.
6. S.W. Baertschi, P.J. Jansen, in: S.W. Baertschi (Ed.), Pharmaceutical Stress Testing: Predicting Drug Degradation, Informa Healthcare, New York, USA, 2007, p. 13-19.
7. Uday TC, Shivabasappa PM, Sanjay SS, Maruti MS. Development and Validation of Stability Indicating UV-Spectrophotometric Method for the Simultaneous Estimation of Telmisartan and Metformin Hydrochloride in Bulk Drugs. Indian journal of pharmaceutical education and research. 2021;55(2):590-7.DOI: 10.5530/ijper.55.2.98.
8. Sneha K, Geetha M, Swapna B, Setty RS. Development and Validation of UV-spectrophotometric Method for Estimation of Gallic Acid in Acalypha indica Leaf Extract and its Cellulose Formulation. Indian journal of pharmaceutical education and research. 2022;56(3):881-7. DOI: 10.5505/ijper.56.3.141.
9. Kempwade A, Taranalli A, Jadhav K. Development and validation of UV Spectrophotometric method to study stress degradation behaviour of Rizatriptan Benzoate. Spectroscopy and Spectral Analysis. 2015;35(1):137-40. DOI: 10.3964/j.issn.1000-0593(2015)01-0137-04.
10. Farooq M, Shoaib MH, Yousuf RI, Siddiqui F, Hanif M, Naz S, Bashir L. Development and validation of liquid chromatographic

method for quantitative determination of Loxoprofen in mobile phase and in human plasma. Pak. J. Pharm. Sci. 2018;31(6):2629-33.
11. International Conference on Harmonization (ICH) Harmonized Tripartite Guideline: Validation of analytical procedures: text and methodology Q2 (R1), 2005.
12. Mujawar T, Ahmad S, Tajane P, Sable V, Gaikwad A, Tare H. Development and validation of ultraviolet spectrophotometric method for Saquinavir estimation in bulk and dosage form. Multidisciplinary Science Journal. 2023 Apr 9;5(2):2023020.