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Development and validation of visible spectrophotometric method for the estimation of zaltoprofen in tablet dosage form

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ABSTRACT

A novel, simple, sensitive, precise and accurate visible spectrophotometric method has been developed for the estimation of Zaltoprofen in Pharmaceutical tablet dosage form. Zaltoprofen with 2, 4-dinitrophenyl hydrazine reagent (2,4 DNP) forms orange-red colored complex that exhibited maximum absorbance at 446.5 nm. The linearity dynamic response was found to be in the concentration range of 5-55 µg/ml and correlation coefficient was found to be 0.999. The results of analysis for the method have been validated statistically and by recovery studies indicate the accuracy and precision of the method. The proposed method was simple, accurate, and precise hence can be applied for the analysis of Zaltoprofen in pharmaceutical tablet dosage form.

Keywords: Zaltoprofen, Visible Spectrophotometric, 2,4-DNP, Tablet dosage form, Validation.

INTRODUCTION

Zaltoprofen, 2 - (10, 11 – dihydro – 10 – oxodibenzo [b, f] thiepin – 2 - yl) propionic acid is a potent nonsteroidal anti-inflammatory drug (NSAID)[1]. It is a preferential COX-2 inhibitor, exhibited a potent inhibitory action on the nociceptive responses induced by a retrograde infusion of bradykinin into the right common carotid artery in rats[2] It is used in the treatment of rheumatoid arthritis, osteoarthritis, and other chronic inflammatory pain conditions.

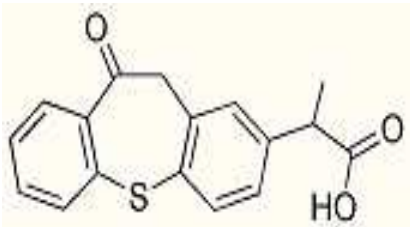

Figure 1: Structure of Zaltoprofen

Literature review revealed the drug estimation by HPLC in plasma[3-7] .There is a chiral HPLC method for enantioselective analysis[8-10] , Stability-Indicating LC method in bulk drug and formulations[11] and UV spectrophotometric method[12-13] and RP-HPLC method[14]. There were no visible spectrophotometric methods reported so far. So there is a need to develop visible spectrophotometric method for the estimation of zaltoprofen in

tablet dosage form. The present work aims to develop a novel, simple, sensitive, precise and accurate visible spectrophotometric method for the determination of Zaltoprofen in tablet dosage form.

MATERIALS AND METHODS

Instrumentation

All spectral measurements were made on ELICO UV/VIS SL-210 Double beam UV- Visible spectrophotometer with 1cm matched quartz cells.

Materials and Reagents

Tablet formulation Zaltokin 80 (Zaltoprofen Tablets) containing Zaltoprofen 80 mg was used in present study. Methanol and distilled water is of E Merck Limited, 2, 4-DNP is of SD fine chemicals were used in the analysis.

Preparation of (0.08 %w/v) 2, 4 -Dinitro phenyl hydrazine reagent (2, 4-DNP)

Accurately weighed and transferred 0.08 g of 2,4- dinitro phenyl hydrazine reagent into a 100 ml calibrated flask, dissolved in 10 ml distilled water, and the volume was made up to the mark with distilled water to obtain a solution of 0.08 % (w/v). The solution was freshly prepared during the use and protected from light during the use.

Preparation of standard stock solution (100 µg/ml)

Standard solution of Zaltoprofen was prepared by transferring accurately weighed 100 mg of pure drug in 100 ml of volumetric flask , dissolved it in little quantity of methanol and volume was made up to the mark methanol. Diluting 10 ml of the above solution to 100 ml with the methanol to get a concentration of 100 µg/ml.

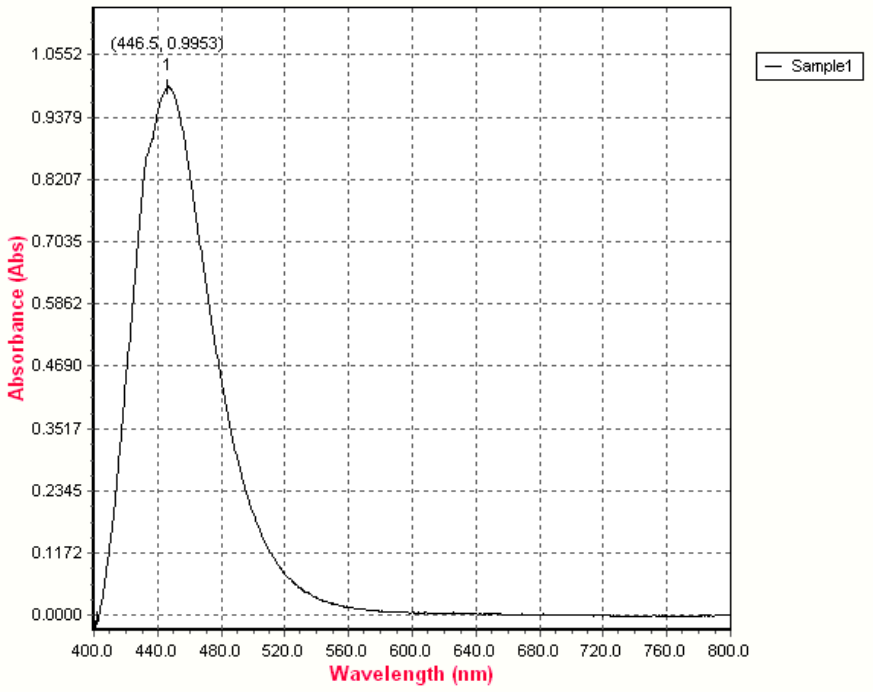

Figure: 2 Absorption spectrum of Zaltoprofen with 2,4 DNP reagent

Determination of λ_{max}

Standard solution of 55 µg/ml of Zaltoprofen was prepared from 100 µg/ml stock solution by transferring 5.5 ml of drug solution to 10 ml calibrated flask and to it 2 ml of 0.08% w/v 2,4-DNP reagent was added and allowed to react for 15 minutes and the volume was made up to the mark with distilled water. The orange red colored complex was formed and the absorption spectrum of the complex was determined against reagent blank solution and the wavelength of maximum absorption was determined by scanning the resulting solution in UV-Vis

spectrophotometer from 400-800 nm. Absorption maximum wavelength (λ max) was found to be at 446.5 nm (figure 2).

Procedure for Pharmaceutical Formulation

Accurately 20 tablets of Zaltoprofen were weighed and triturated to fine powder. Tablet powder equivalent to 100 mg of Zaltoprofen was weighed and dissolved in 10 ml of methanol with shaking, sonicated for 10 min and final volume was made up to 100 ml with methanol. This was then filtered through whatmann's filter paper No.41 to get concentration of 1 mg/ml solution. This solution was then diluted to make the concentration of 100 µg/ml with methanol. From the above solution 10 µg/ml was prepared and the absorbance was measured at 446.5 nm using reagent blank. The content of Zaltoprofen in pharmaceutical preparation was calculated by means of calibration curve (Table 1).

Table: 1 Assay of marketed formulation

Formulation	Amount of drug taken from tablet(mg)	Mean amount of drug found from tablet (mg)	% Mean Assay±%RSD
Zaltokin 80 (Tablets)	100	100.046	100.046±0.4005

VALIDATION

The proposed method was validated according to International Conference on Harmonization (ICH) guidelines [15].

Linearity and Range

Aliquots (0.5 – 5.5 ml) of Zaltoprofen from standard stock solution (100 µg/ml) were transferred into a series of 10 ml calibrated volumetric flasks. To these, 2 ml of 0.08 % w/v 2, 4-DNP reagent solution was added and allowed to react for 15 minutes. Then the volumes were made up to the mark with distilled water to get the concentrations in the range of 5-55 µg/ml and the absorbance of the resulting solutions were measured at 446.5 nm against the reagent blank and the calibration curve was plotted (figure 3). The regression parameters were shown in table 2.

Table: 2 Optical Characteristics of Zaltoprofen

S.No.	Parameter	Values
1.	Absorption maxima (nm)	446.5
2.	Linearity range (µg/ml)	5-55
3.	Regression Equation(y=bx+c)	y=0.018x+0.002
4.	Slope(b)	0.018
5.	Intercept(c)	0.002
6.	Correlation Coefficient(r^2)	0.999
7.	%RSD	0.77
8.	Molar Absorptivity(lit.mol^{-1} cm^{-1})	0.546414×10^4
9.	Sandell's Sensitivity(µg/cm^2/ 0.001 abs unit)	0.0177906
11.	Limit of Detection (µg/ml)	1.118
12.	Limit of Quantification (µg/ml)	3.383

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. The precision of analytical method was usually expressed as the standard deviation or relative standard deviation (coefficient of variation) of series of measurement. The precision of the method studied as system precision, interday and intraday precision (Table 3 and Table 4).

Table: 3 System Precision

Amount taken (µg/ml)	(n=6)Repeatability ± S.D	(n=6)%RSD
30 µg/ml	99.66±0.405	0.406

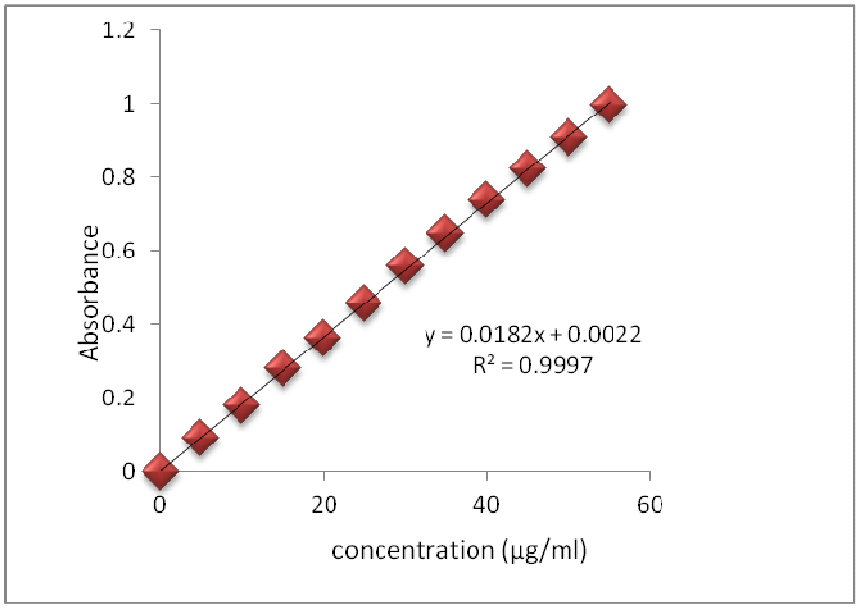

Figure: 3 Beer's law plot of Zaltoprofen

Table: 4 Intraday and Interday Precision

	Intraday		Interday	
Con. taken (µg/ml)	**Con. found* (µg/ml)**	**%RSD**	**Con. found* (µg/ml)**	**%RSD**
24	23.98	0.94	23.95	0.96
30	29.93	0.86	29.91	0.91
36	35.95	0.96	35.94	0.93

**average of six determinations*

Accuracy

To assess the accuracy of the proposed method, recovery studies were carried out at three different levels i.e. 80%, 100% and 120%. To the preanalysed sample solution a known amount of standard drug solution was added at three different levels, absorbance was recorded. Solutions were prepared in triplicates and accuracy was indicated by % recovery. (Table 5)

Table: 5 Accuracy

S.No.	(%) level	Actual conc. (µg/ml)	Conc. Added (µg/ml)	Conc. found (µg/ml)	(n=3) %Recovery ±%RSD	%Mean Recovery ±%RSD
1.	80%	30	24	23.8	99.16±0.161	99.57±0.171
2.	100%	30	30	29.91	99.72±0.206	
3.	120%	30	36	35.95	99.85±0.146	

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 triplicates. When the effect of altering one set of conditions was tested, the other conditions were held constant at the optimum values. Assay for all deliberate changes of conditions should be within 98.0–102.0 % for the proposed method (Table 6).

Table: 6 Results from Robustness study

Formulation	Amount of drug taken from tablet(mg)	At 444.5 nm	At 448.5 nm
		(n=3)%assay±%RSD	(n=3)%assay±%RSD
Zaltokin 80	100	99.87±0.613	99.62±0.586

Ruggedness

Ruggedness of the proposed method is determined by analysis of aliquots from homogeneous slot by two analysts using same operational and environmental conditions (Table 7).

Table: 7 Results for Ruggedness studies

Formulation	Amount of drug taken from tablet(mg)	Analyst 1 (n=3)%assay±%RSD	Analyst 2 (n=3)%assay±%RSD
Zaltokin 80	100	100.01±0.732	99.92±0.457

Limit of Detection and Limit of Quantitation

Limit of detection (LOD) and Limit of quantitation (LOQ) were determined by using the formula based on standard deviation of the response and the slope. Limit of detection (LOD) and limit of quantitation (LOQ) were calculated by using the equations LOD = 3 σ /S and LOQ= 10 σ /S, where σ is standard deviation of intercept, S is slope of the line (Table 1).

RESULTS AND DISCUSSION

The developed visible spectrophotometric method is based on condensation of Zaltoprofen with 2, 4 -DNP resulting in the formation of orange red colored hydrazones for which the absorption peak appears at 446.5 nm. Linearity of the method was observed in the concentration the range of 5-55 µg/ml. Statistical analysis of the calibration curve was done with correlation co-efficient (r^2 = 0.999) shows the validity of beers law. The proposed method was applied to pharmaceutical formulation and percent amount of drug estimated was found in good agreement with the label claim. The excipients used in the pharmaceutical preparation do not interfere in this analysis. The recovery experiment was carried out at three different levels i.e., 80%, 100% and 120%. The percentage recovery was found to be in the range 99.1-99.8 % indicates of accuracy of the method . The precision of the method was studied as system, intra-day and inter-day precision. The % RSD value < 1% indicates the precision of the method. Ruggedness of the proposed method was studied with the help of two analysts and robustness for the method was studied by variation in wavelength both of which show low values of % RSD indicates the ruggedness and robustness of the method. The limits of Detection and Quantification for Zaltoprofen were 1.118 µg/ml and 3.383 µg/ml respectively indicates the sensitivity of method.

CONCLUSION

The developed visible spectrophotometric method for the determination of Zaltoprofen was novel, simple, accurate, precise and sensitive. 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 the drug Zaltoprofen in its pharmaceutical dosage forms.

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