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RESEARCH ARTICLE

DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR THE DETERMINATION OF ZALTOPROFEN IN BULK AND PHARMACEUTICAL TABLET DOSAGE FORM

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ABSTRACT

A new RP-HPLC method was developed and validated for determination of Zaltoprofen in bulk and tablet dosage form. The estimation was carried out on Enable C18G (250 mm ×4.6 mm, 5 µm) column using Acetonitrile and Water in the ratio of 95:5 (v/v) as mobile phase. The flow rate was 1.0 ml/min and the effluent was monitored by UV detector at 331 nm. The retention time was 3.653 min and linearity was observed in the concentration range of 10-50 µg/ml. The percentage recovery was in good agreement with the labelled amount in the pharmaceutical formulation and the method was simple, precise and accurate for the determination of Zaltoprofen in bulk and pharmaceutical formulation.

Key words: Zaltoprofen, RP-HPLC, 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.

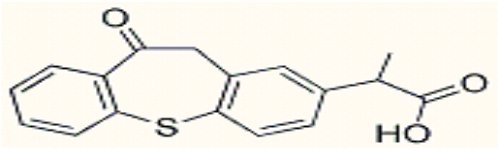

Figure 1: Structure of Zaltoprofen

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]. The present work aims to develop a novel, simple, specific, sensitive, precise and accurate RP-HPLC method for the determination of Zaltoprofen in pure form and in tablet dosage form.

2. EXPERIMENTAL:

2.1 HPLC instrumentation:

The HPLC system consists of Enable ODS reverse phase (250 mm x 4.6 mm, 5 µm particle size) C_{18} column, a Rheodyne valve injector equipped with a 20 µl sample loop, variable wavelength programmable UV Detector SPD-20A VP with manual mode of injection. The HPLC system equipped with LC solutions software.

2.2 Materials and Reagents:

Tablet formulation Zaltokin–80 (Zaltoprofen Tablets) containing Zaltoprofen 80 mg that was purchased from local market was used in present study. All reagents and chemicals used were of HPLC Grade.

2.3 Preparation of mobile phase:

The mobile phase was prepared by using acetonitrile and water in the ratio of 95:5 v/v i.e. 95 volumes of acetonitrile and 5 volumes water. It was then filtered through 0.45 µm nylon filter to remove any particles if present and kept for sonication for 15 minutes and was then used.

2.4 Preparation of zaltoprofen standard stock solution (100 µg/ml):

Standard solution of Zaltoprofen was prepared by accurately weighing and dissolving 100 mg of the drug in 100 ml of mobile phase (acetonitrile and water, 95:5 v/v) and sonicated for 5 minutes. 10 ml of this solution was taken and further diluted to 100 ml with the mobile phase to get a standard concentration of 100 µg/ml.

2.5 Chromatographic conditions:

The mobile phase consists of acetonitrile and water in the ratio of 95:5 (v/v) and was pumped at a flow rate of 1.0 ml/min, while the detection was monitored at a wave

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length of 331 nm on Enable ODS reverse phase (250 mm x 4.6 mm, 5 µm particle size) C_{18} column. The mobile phase was degassed and vaccum filtered prior to use.

2.6 Preparation of sample drug solution from Pharmaceutical formulation:

Accurately 20 tablets of Zaltoprofen were weighed, average weight of twenty tablets were calculated and triturated to fine powder. Tablet powder equivalent to 100 mg of Zaltoprofen was weighed and dissolved in 10 ml of mobile phase with shaking, sonicated for 15 min and final volume was made up to 100 ml with the mobile phase. This was then filtered through whatmann's filter paper No.41 to get concentration of 1 mg/ml solution. This was then diluted to prepare the working concentration of 100 µg/ml with mobile phase. From the above solution 30 µg/ml was prepared, filtered through 0.2 µm membrane filter, sonicated and then the sample was injected.

3. RESULTS AND DISCUSSION:

The developed method was validated[15] as per ICH guidelines, and accordingly the parameters were evaluated for Linearity, Specificity, Accuracy, Precision and Robustness.

3.1 Specificity:

The optimized mobile phase system yielded a symmetric peak for the drug with retention time 3.653 min. The peak for the bulk drug was identified by comparing the retention time and also comparing its peak area with that obtained from standard drug. Peak purity values were good for the drug, which shows that the analyte peaks were pure and there were no interferences from excipients in the analyte peak. Therefore, it could be said that developed method was highly specific.

3.2 Linearity and Range:

Various concentrations from standard solution of Zaltoprofen were prepared and the calibration graph was plotted by the values of the peak area versus concentration (µg/ml) which were found to be linear over the concentration ranges of 10-50 µg/ml and the linearity data was shown in the figure 2. From the data obtained, co-relation coefficient, slope and y-intercept were calculated and the results were shown in Table1.

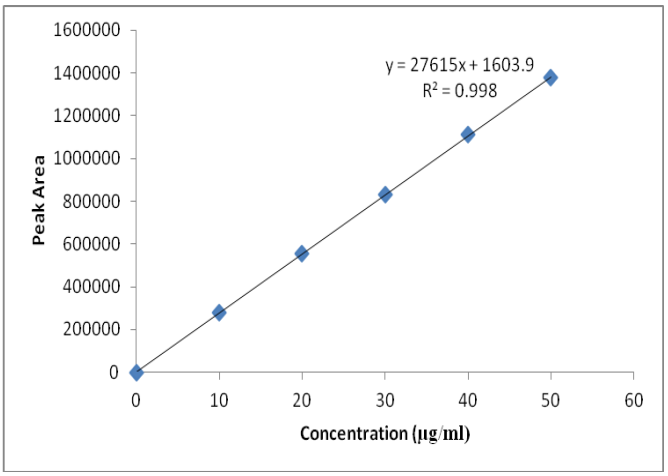

Figure: 2 Linearity Plot of Zaltoprofen

Table 1: Data for Linearity

Concentration (µg/ml)	Peak area	Statistical Analysis
10	278026	Regression equation Y=27615X+1603.9 Correlation coefficient 0.998 Slope,m 27615 y-intercept 1603.9
20	555073	
30	829932	
40	1109851	
50	1378976	

3.3 Precision:

The precision of analytical procedure expresses the closeness of agreement between a series of measurement obtained from multiple sampling of the same homogenous sample under the prescribed condition. It was analysed by 6 different solutions of same concentration and peak areas were noted. The result was indicated by % RSD. The results for system, intraday and inter-day precision were shown in Table – 2,3&4.

Table: 2 System Precision results for Zaltoprofen

Injection	Concentration (µg/ml)	Peak area	%Assay
1	30	831962	100.21
2	30	829874	99.96
3	30	831736	100.18
4	30	830451	100.03
5	30	828921	99.84
6	30	828142	99.75
%RSD			0.1827

Table: 3 Intraday Precision results for Zaltoprofen

Injection	Concentration (µg/ml)	Peak area	%Assay
1	30	830738	99.97
2	30	827981	99.73
3	30	826873	99.60
4	30	830934	100.08
5	30	829852	99.95
6	30	828674	99.81
%RSD			0.176

Table: 4 Inter-day Precision results for Zaltoprofen

Day	Concentration (µg/ml)	Peak area	%Assay
1	30	825723	99.46
2	30	826541	99.56
3	30	827924	99.72
4	30	827262	99.64
5	30	828145	99.75
6	30	828976	99.85
7	30	829647	99.93
%RSD			0.1633

3.4 Accuracy:

To determine the accuracy of the proposed method, different amounts of drug samples (80%, 100%, and 120%) of Zaltoprofen within the linearity range were taken. Solutions were prepared in triplicates and accuracy was indicated by % recovery. The results were recorded in table –5.

Table: 5 Accuracy results for Zaltoprofen

S.No.	(%) level	Actual conc. (µg/ml)	Conc. Added (µg/ml)	Conc.found (µg/ml)	%Recovery ±%RSD	%Mean recovery ±%RSD
1.	80%	30	24	23.94	99.77±0.77	100.03±0.242
2.	100%	30	30	30.02	100.07±0.396	
3.	120%	30	36	36.09	100.25±0.279	

3.5 Assay:

The assay of the method was performed to determine the % recovery of formulation. A 30 µg/ml of sample solution was prepared and injected. The amount of drug present per tablet was calculated by comparing the peak area of the sample solution with that of the standard solution. The results were shown in table-6.

Table: 6 Estimation of Zaltoprofen in Tablets

Formulation	Amount of drug taken from tablet(mg)	Mean amount of drug found from tablet (mg)	% Mean assay±%RSD
Zaltokin 80 (Tablets)	100	100.03	100.03±0.142

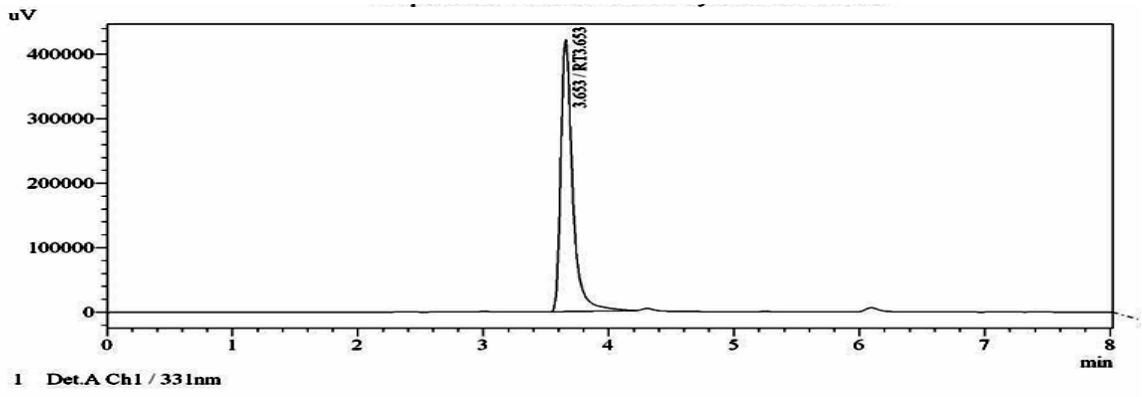

Figure 3: Chromatogram of the drug Zaltoprofen

3.6 Robustness:

To evaluate the robustness of the developed method, small variations in the optimised method parameters were done. The effect of change in flow rate and wavelength were studied. The method was found to be unaffected by small changes in the mobile phase flow rate (± 10%) and changing the wavelength (± 5 nm).

Table: 7 Results from robustness study

Parameter	Condition	Peak area	%Assay±%RSD
Flow rate±10% of optimum flow rate	0.9 ml	830738	99.97±0.334
	1.1 ml	830508	99.94±0.482
Wavelength±5nm of optimum wavelength	326 nm	832646	100.2±0.217
	336 nm	827728	99.7±0.279

3.7 Sensitivity:

The LOD and LOQ values of the developed method were found to be 0.293 µg/ml and 0.88 µg/ml respectively indicating that the method was sensitive.

4. CONCLUSION:

The RP – HPLC method proposed for the determination of Zaltoprofen, is simple,sensitive and economical with reasonable precision and accuracy. Parameters and statistical comparison justify this method for application in estimation of Zaltoprofen in bulk and tablet dosage form. Commercial formulation of Zaltoprofen was successfully analysed and results were calculated.There was no interference of additives or excipients for the assay and evaluation of Zaltoprofen in pharmaceutical tablet dosage form.

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