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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, 5µm) column using Methanol and Water in the ratio of 70:30 (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 2.845 min and linearity was observed in the concentration range of 10-80 µg/ml. The percentage recovery was in good agreement with the labelled amount in the pharmaceutical formulations and the method was simple, precise and accurate for the determination of Zaltoprofen in bulk and pharmaceutical formulations.

Keywords: Zaltoprofen, RP-HPLC, Validation.

1. 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.

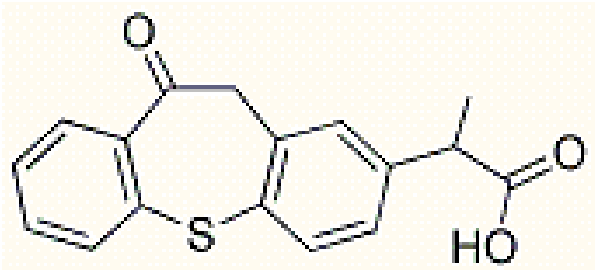

Figure - 1: Structure of Zaltoprofen

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 forms.

2. EXPERIMENTAL

2.1. HPLC instrumentation

The HPLC system consists of Enable ODS reverse phase (250mm x 4.6mm, 5µm 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 methanol and water in the ratio of 70:30 v/v i.e. 70 volumes of methanol and 30 volumes of water. It was then filtered through 0.45 µm membrane 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 (methanol and water, 70:30 v/v) and sonicated for 5 minutes. 10 ml of this solution was taken and

further diluted to 100 ml with mobile phase to get a working standard concentration of 100 µg/ml.

2.5. Chromatographic conditions

The mobile phase consists of methanol and water in the ratio of 70:30 v/v and was pumped at a flow rate of 1.0 ml/min, while the detection was monitored at a wave 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 was 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 40 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 solvent system yielded a symmetric peak for the drug with retention time 2.845 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 10-80 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 table 1.

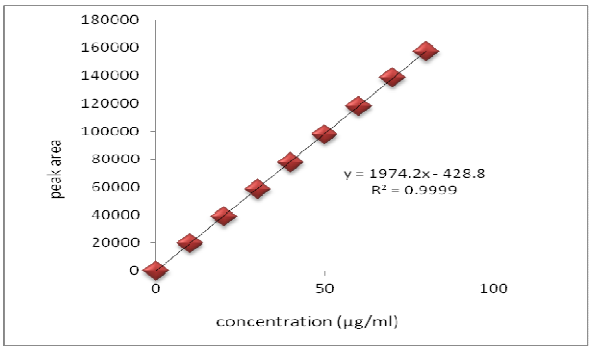

Figure - 2: Linearity curve for Zaltoprofen.

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 interday precision were shown in table 2, 3 & 4.

Table - 1: Data of linearity

Concentration (µg/ml)	Peak area	Statistical Analysis
0	0	**Regression equation**
10	19486	Y=1974x-428.8
20	38921	**Slope,m**
30	58712	1974
40	77842	
50	97836	**y-intercept**
60	117865	428.8
70	138758	
80	157416	**Correlation coefficient**
		0.999

Table - 2: System Precision results for Zaltoprofen

Injection	Concentration (µg/ml)	Peak area	% Assay
1	40	78484	99.94
2	40	78673	100.17
3	40	77796	99.06
4	40	78162	99.53
5	40	78098	99.45
6	40	77995	99.32
%RSD =0.4083			

Table - 3: Intraday Precision results for Zaltoprofen

Injection	Concentration (µg/ml)	Peak area	% Assay
1	40	78541	100.01
2	40	77923	99.22
3	40	78317	99.72
4	40	78196	99.57
5	40	78457	99.90
6	40	77842	99.12
%RSD =0.3612			

Table - 4: Interday Precision results for Zaltoprofen

Day	Concentration (µg/ml)	Peak area	% Assay
1	40	78398	99.83
2	40	78011	99.34
3	40	77865	99.15
4	40	77903	99.20
5	40	78492	99.95
6	40	78264	99.66
7	40	78586	100.06
% RSD = 0.3612			

Table - 5: Accuracy results for Zaltoprofen

(%) level (µg/mL)	Actual Conc. (µg/mL)	Conc. added (µg/mL)	Conc. found	% Recovery ± SD	% Mean recovery ± SD
80%	40	32	31.92	99.75±0.578	99.67±0.145
100%	40	40	39.9	99.77±0.452	99.74±0.342
120%	40	48	47.76	99.5±0.116	99.56±0.221

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 ± SD
Zaltokin80	100	99.45	99.45±0.2907

Table - 7: Results from robustness study

Parameter	Condition	Peak area	% Assay ± SD
Flow rate ±10% of optimum flow rate	0.9 ml	78351	99.22±0.234
	1.1 ml	78969	100.01±0.312
Wavelength±5nm of optimum wavelength	326 nm	78745	99.72±0.276
	336 nm	78624	99.57±0.439
Mobile phase ±5% of optimum mobile phase composition	66.5:33.5 v/v	78885	99.9±0.361
	73.5:26.5 v/v	78270	99.12±0.423

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.

3.5. Assay

The assay of the method was performed to determine the % recovery of formulation. A 40 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.The chromatogram was shown in figure 3.

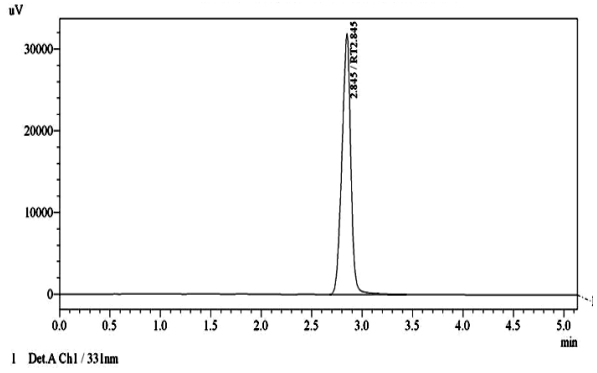

Figure - 3: Chromatogram of the drug Zaltoprofen.

3.6 Robustness

To evaluate the robustness of the developed method, small variations in the optimized method parameters were done. The effect of change in flow rate, wavelength and mobile phase composition were studied. The method was found to be unaffected by small changes in the mobile phase composition (± 5%), flow rate (± 10%), changing the wavelength (± 5 nm). The results are shown in table 7.

4. CONCLUSION

The RP – HPLC method proposed for the determination of Zaltoprofen, is simple 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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