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Simple and Economic method development of Dexketoprofen by RP-HPLC: An application to routine quality control analysis

Selvadurai Muralidharan*, Jayarajakumar, Subramani Parasuraman and Sokkalingam Arumugam Dhanaraj

Faculty of Pharmacy, AIMST University, Semeling-08100, Bedong, Kedah, Malaysia

***Corres. Author: murali23pharm@hotmail.com**
Phone: +60164953594, Fax: +6044298009

Abstract: Simple, economic, precise, rugged, sensitive and validated RP-HPLC method has been developed to determine dexketoprofen (DKP) tablet. Chromatographic separation was achieved isocratically on Thermo, C18 column (250mm × 4.6 mm, 5 µm) and acetonitrile: ammonium acetate buffer (pH 5.0) in the ratio of 400:60 (v/v) using mobile phase, at a flow rate of 1.0 ml/min. Detection was carried out at 225 nm. The retention time for DKP was found to be 4.25 min respectively. The method was validated as per ICH guidelines. The method was linear in the concentration range of 100-600 ng/ml for with correlation coefficient of 0.99 respectively. The mean recoveries obtained for DKP was 98.14 % respectively. The correlation coefficients for all components are close to 1. The present developed and validated method was found to be more accurate, precise, selective, rapid and easily adapted to bioanalytical method.
Keywords: Dexketoprofen, RP-HPLC, method development and validation.

Introduction

Dexketoprofen, chemically, (2S)-2-[3-(benzoyl) phenyl] propanoic acid is non-steroidal anti-inflammatory drug and is used for the management of mild to moderate pain [1]. Only limited method has been published for Dexibuprofen alone which is stability indicating HPTLC and HPLC method [2, 3]. To access the reproducibility and wide applicability of the developed method was validated as per ICH guidelines, [4]. The developed method can be useful for all the aspects of analytical and bioanalytical method development and application to quality control analysis.

Materials and Methods

Instrumentation

HPLC chromatographic separation was performed on a Shimadzu liquid chromatographic system equipped with a LC-20AD solvent delivery system (pump), SPD-20A photo diode array detector, and SIL-20ACHT injector. LC solution version 1.25 was applied for data collection and process (Shimadzu, Japan).

Reagent and materials

Gift sample of dexketoprofen was obtained from Emcure Pharmaceuticals Ltd, Pune, India. Acetonitrile (HPLC grade) was obtained from Merck, Germany. Ammonium acetate (molecular biology reagent

grade) was obtained from Systerm Malaysia. Methanol obtained from QREC and HPLC grade water was used throughout.

Chromatographic conditions

The isocratic mobile phase consisted of acetonitrile-ammonium acetate buffer (pH 5.0) in the ratio of (60:40v/v), flowing through the column at a constant flow rate of 1.0 ml/min. A Thermo, C_{18} column (5µm, 250 × 4.6 mm) was used as the stationary phase. The chromatographic parameter, sensitivity and selectivity of the method for two drugs, 225 nm was selected as the detection wavelength for UV-PDA detector. The HPLC system was operated at a room temperature.

Standard solution preparation

Standard solutions (stock) were prepared by dissolving 100 mg of DKP drug in 100 ml of diluent which was a mixture of acetonitrile and water in the ratio of 1:1 to get a concentration of 1000 µg/ml.

Results and Discussion

Chromatography

The mobile phase was chosen after optimization of chromatographic conditions such as wavelength, mobile phase ratio, pH, flow rate and buffer strength. A mobile phase consisting of acetonitrile: ammonium acetate (60:40, v/v, pH 5.0) was selected to achieve maximum separation and sensitivity. A flow rate of 1 ml/min gave an optimal signal-to-noise ratio with a reasonable separation time. Using a reversed-phase C18 column, the retention time for DKP was observed to be 4.25 min, respectively. Total time of analysis was less than 5 min. [Figure 1].

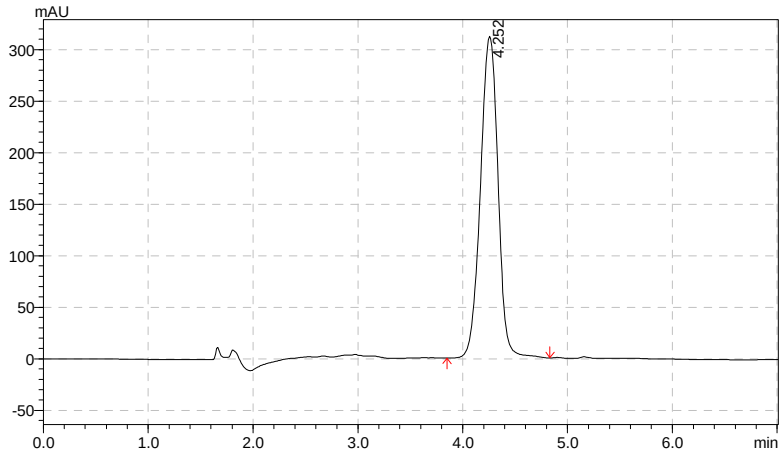

Figure 1: Typical chromatogram of Dexketoprofen

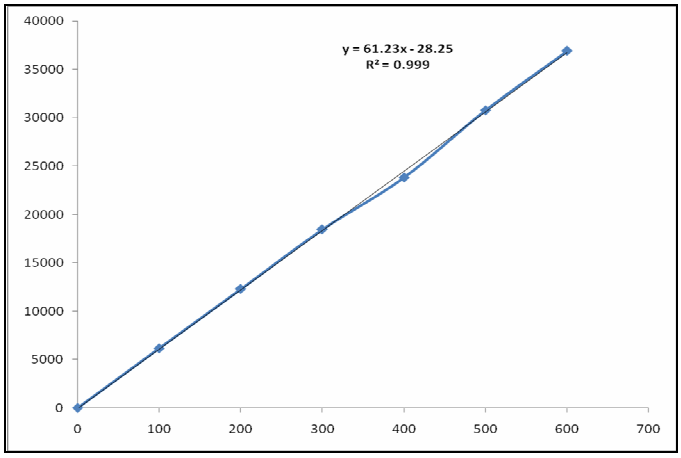

Figure 2: Calibration curve of Dexketoprofen

System suitability

The column efficiency, resolution and peak asymmetry were calculated for the standard solutions (Table 1). The values obtained demonstrated the suitability of the system for the analysis of this drug combination and the system suitability parameters fall within ± 3 % standard deviation range during routine performance of the method.

Linearity

The calibration curve was linear over the concentration range of 100–600 ng/ml for DKP. The linearity was represented by a linear regression equation as follows:

$Y = 61.23x \times -28.25$ ($r^2 = 0.999$)

Accuracy and precision

The accuracy of the method was determined by recovery experiments. The studies were carried out six times and the percentage recovery and standard deviation of the percentage recovery were calculated and presented in Table 2. From the data obtained, added recoveries of standard drugs were found to be accurate.

The precision of the method was demonstrated by inter day and intra day variation studies. In the intra day studies, six repeated injections of standard and sample solutions were made and the response of drug peaks and % CV were calculated and presented in Table 2. In the inter day variation studies, six repeated injections of standard and sample solutions were made for three consecutive days and response factor of drug peaks and percentage % CV were calculated and presented in Table 2. From the data obtained, the developed RP-HPLC method was found to be precise.

Table 1: System suitability

S. No.	Parameters	Dexketoprofen
1	Theoretical plate/meter	4859
2	Asymmetric factor	0.92
3	LOD (ng/ml)	25
4	LOQ (ng/ml)	100

Table 2: Intraday and interday precision studies of Dexketoprofen

	Intraday studies			Interday studies		
	100	400 (ng/ml)	600	100	400 (ng/ml)	600
Mean	98.76	398.95	599.24	98.85	399.29	599.56
SD	0.62	0.64	0.61	0.70	0.48	0.59
%CV	0.63	0.32	0.20	0.68	0.12	0.10
%Accuracy	98.70	99.47	99.74	98.85	99.82	99.91

Ruggedness and Robustness

The ruggedness of the method was determined by carrying out the experiment on instruments like Shimadzu HPLC by different operators using different columns of similar type like LichroCART C_{18}, Thermo C_8 and Thermo C_{18}. Robustness of the method was determined by making slight changes in the chromatographic conditions. It was observed that there were no marked changes in the chromatograms, which demonstrated that the RP-HPLC method developed, are rugged and robust.

Solutions stability

The stability of both standard solutions during analysis, were analyzed over a period of 5 h at room temperature. The results shown standard solution, the retention time and peak area of dexketoprofen remained

almost unchanged and no significant degradation within the mentioned period, thus indicated that both solutions were stable for 5 h, which was sufficient to complete the whole analytical process.

Conclusion

A simple precise, economic, rapid, sensitive, and accurate RP-HPLC method has been developed for the standard of dexketoprofen. A high percentage of recovery and the run time of less than 5 minutes allow its application for the routine analysis of dexketoprofen in any dosage form. The proposed method could be useful for the quality control laboratories in developing countries.

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