World Journal of Chemistry 5 (1): 67-70, 2010
ISSN 1817-3128

Determination of Ketoprofen in Tablet Dosage Form by Gas Liquid Chromatography

Gurupadayya V. Bannimath, Madhusudan N. Purohit and Gurubasavaraj V. Pujar

Department of Pharmaceutical Chemistry, JSS College of Pharmacy, JSS University, Mysore-570 015, India

Abstract: The present work describes the methodology and validation of gas chromatography with flame ionization detection (GC-FID) for the determination of ketoprofen using internal standard (IS) (ibuprofen) in pharmaceutical preparations. The standard curve was linear (R = 0.998) over the concentration range of 20 100 μg mL^{-1} with a detection limit of 0.75 μg mL^{-1} and a quantification limit of 1.00 μg mL^{-1}. Intra-day and inter-day precision and accuracy of the method were established according to the current ICH guidelines. Intra-day RSD values at three levels (25, 50 and 75 μg mL^{-1}) were 0.25- 0.52 %, based on the peak area. The developed method was successfully applied for the assay of ketoprofen in tablet dosage form and method does not require any prior separation or treatment of samples.

Key words: Ketoprofen · Gas chromatography · Flame ionization detection · Solid dosage form

INTRODUCTION

Ketoprofen (KPF) ((RS)-2-(3-benzoylphenyl) propionic acid) (Fig. 1) is a non-steroidal anti-inflammatory drug (NSAID) of the propionic acid class, which also includes pharmaceuticals such as ibuprofen, naproxen and fenoprofen. It is widely used in the treatment of rheumatoid arthritis, osteoarthritis and a variety of other acute and chronic musculoskeletal disorders [1].

Several methods for the determination of KPF in pharmaceutical dosage forms and standard solution have been reported. These include spectrophotometric [2], HPLC method in plasma [3-6], electron-capture gas chromatography [7] and luminescence method [8]. Holzer *et al*. [9] have examined flurbiprofen and ketoprofen toxicity in rat model experiments. In another study determination method of ketoprofen and parabens simultaneously in a commercial gel formulation by reversed phase high performance liquid chromatography was developed with a UV detection at 254 nm [10]. Ketoprofen and mefenamic acid were analysed by high-performance liquid chromatography in combined dosage forms [11]. The GC method for determination ketoprofen together with florbiprofen in patches has been reported [12].

The present work describes a newly developed, gas liquid chromatography with flame ionization detector (GC-FID) method for the determination of KPF in pure and pharmaceutical dosage form (tablet).

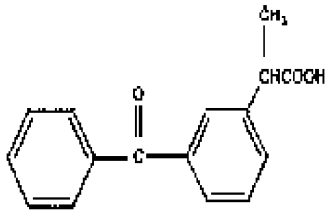

Fig. 1: Structure of KPF

Experimental

Chemicals and Reagents: All chemicals and reagents used were of analytical grade and obtained from s.d. fine-chem., Mumbai, India. KPF and IPF were obtained as a gift sample from BEC Chemicals Pvt. Ltd., Roha, India. Pharmaceutical dosage forms (Rhofenid and Ketofen) containing KPF were obtained commercially from a pharmacy.

Stock and Standard Solutions: The stock standard solution of KPF was prepared to 1000 μg mL^{-1} concentration in methanol. The standard solutions contain 20, 40, 60, 80, 100 μg mL^{-1} with 10 μg mL^{-1} IPF were prepared daily from the stock solution that prepared from 1000 μg mL^{-1} stock solution in methanol. The solutions were stored at 4°C when not in use.

Instrumentation and Analytical Conditions: A gas chromatograph (Shimadzu GC 2014) equipped with a flame ionization detector (FID) was used for the present research work. Shimadzu Lab solution software was used

Corresponding Author: Gurupadayya V. Bannimath, Department of Pharmaceutical Chemistry, JSS College of Pharmacy, JSS University, Mysore-570 015, India E-mail: bm_guru2004@yahoo.co.in

to analyze the samples. Separation was achieved using an cross bond 30 m, packed capillary column 5% diphenyl/95% dimethyl polysiloxane (0.25 mm x 0.25 µm particle size). The split mode (5:1) was used with nitrogen carrier gas at flow rate of 2 mL min^{-1}. Hydrogen and synthetic air were used as auxiliary gases for the detector (FID). Manual split injection (split ratio 5:1) of approximately 2 µL samples was performed at an inlet temperature of 250°C. The detector temperature was maintained at 270°C. The oven temperature programme: initial temperature 100°C, hold for 1 min, then raise the temperature to 220°C with the increment of 20°C min^{-1} and then hold same temperature for 5 min.

Preparation of Tablet Solutions: 20 tablets of KPF were weighed to obtain the average tablet weight and were powdered by trituration. A quantity of tablet powder equivalent to 100 mg of KPF was accurately weighed into a 100 mL calibrated flask and mixed with 50 mL of methanol. The mixture was allowed to stand with intermittent sonication to ensure complete solubility of drug. Further the resulted solution was passed through 0.45 µm membrane filter followed by adding of methanol to obtain a stock solution of 2 mg mL^{-1}.

RESULTS AND DISCUSSION

Method Development: The method development for the assay of KPF was based on its chemical properties. Methanol was used as solvent. The gas liquid chromatography parameters used in the method development were based on the boiling point (228°C) of KPF. The different temperature programmes were investigated for exception of matrix interferences. At the end of this investigation, best temperature programme was selected for a good resolution and thus for all experiments was used the oven temperature programme described above. As shown in Fig. 2, good separation of KPF from internal standard IPF was performed and no further matrix interfering peaks at the retention times of KPF (t_R= 5.3 min) and internal standard (IS) IPF (t_R= 3.37 min) were observed.

Linearity: The calibration curve (Fig. 3) was established by plotting the ratio of the peak areas of KPF and ISI versus the concentrations of KPF samples. Linear correlations were found between peak ratio and KPF concentration and are described by the regression equations:

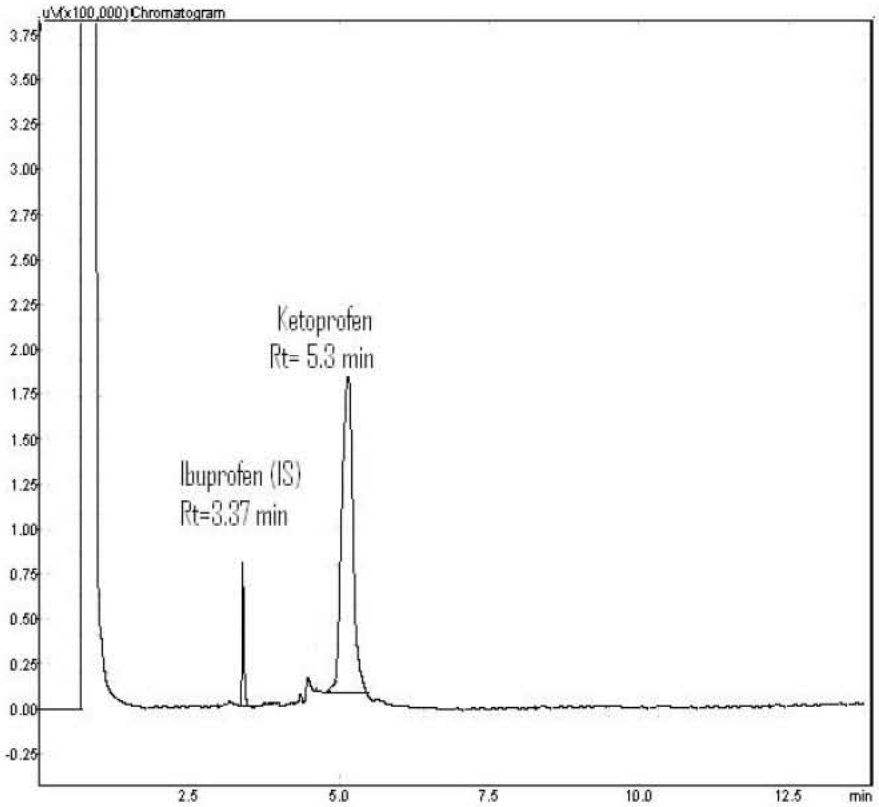

Fig. 2: GC-FID chromatogram of standard solutions of KPF with Internal standard (IS) IBF

Table 1: Intra-day, inter-day precision and accuracy of ketoprofen

Added µg mL^{-1}	Intra-day Found ± SD[a] µg mL^{-1}	Precision RSD %[b]	Accuracy	Inter-day Found ± Sd[a] µg mL^{-1}	Precision RSD %[b]	Accuracy
25	24.82 ± 03	0.46	-0.72	23.35 ± 05	4.20	-6.6
50	50.89 ± 02	0.25	1.78	50.58 ± 06	2.84	1.16
75	75.75 ± 04	0.52	1.00	74.24 ± 02	1.02	-1.01

[a] Average of six replicate determinations

[b] Accuracy (% relative error); (found-added/added) x 100

[c] SD standard deviation of six replicate determinations, RSD relative standard deviation

Table 2: Recovery study percentage for Ketoprofen and Rhofenid

Formulation studied	KPF in formulation (µg mL^{-1})	Pure KPF added (µg mL^{-1})	Total found (µg mL^{-1})	Pure KPF recovered (%)[a]
Ketofen	100	15	114.79	99.82± 1.5
	100	20	119.85	99.88± 1.2
	100	25	124.92	99.94± 1.9
Rhofenid	100	15	113.75	98.91± 2.7
	100	20	118.89	99.05± 2.2
	100	25	125.91	100.73± 1.5

[a] Mean ± SD, n = 6

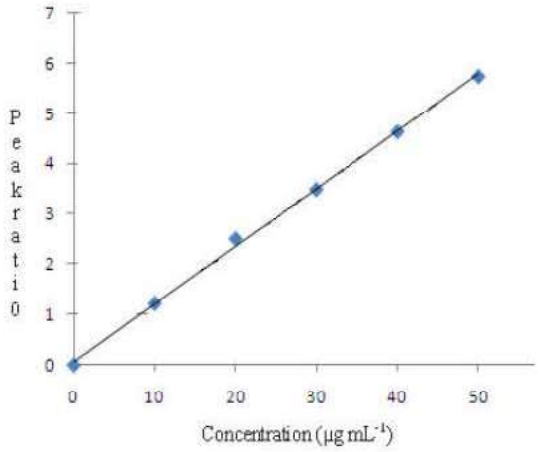

Fig. 3: Calibration curve of KPF

$$Y = 0.080 + 0.114\ x;\ R = 0.998,\ n = 6$$

Where y is the ratio of peak areas of and IPF and IPF and x is the concentration in µg mL^{-1} R is the correlation coefficient and n is the number of measurement levels. Beer's law is obeyed for 20-100 µg mL^{-1}. The limit detection (LOD) and Limit of quantification (LOQ) were found to be 0.75 and 1.00 µg mL^{-1} respectively. Both accuracy and precision of these values were well within the proposed criteria (RSD % < 20%).

Precision: Precision of the method was evaluated in terms of intra-day and inter- day precision. Three different concentrations of KPF were analyzed in six replicates on the same day (intra-day precision) and in five consecutive days (inter-day precision). Within each series, every solution was injected in triplicate. The peak-area based intra-day RSD values were 0.25–0.52%. The inter-day precision showed higher RSD values of 1.02–4.20 %. The results of the study compiled are quite satisfactory (Table 1).

Accuracy/ Recovery: The accuracy was determined by recovery of known amounts of KPF reference standard adding the tablet samples at the beginning of the process. In the first recovery study, 20 µg mL^{-1} tablet solutions were added in 25, 50 and 75 µg mL^{-1} KPF standard solutions with IS. In the second recovery study, 15, 20, 25 µg mL^{-1} tablet solutions were added in 50 µg mL^{-1} KPF standard solutions with internal standard. The percentage recovery of added KPF standard was calculated by comparing with found and added concentrations (C_{found}/C_{added} x100) in each case. The mean recoveries for both recovery studies ranged from 99.82 to 99.94 % (kitofen) and 98.91 to 100.73 % (Rhofenid) (Table 2).

CONCLUSION

The suggested gas liquid chromatographic method was applied to the analysis of two dosage form containing KPF without interference from excipients encountered in pharmaceutical preparations using internal standard methodology.

The linear concentration range of the proposed method was 20-100 µg mL^{-1}. The average recovery value for KPF in 200 mg tablet composites ranged from

98.78 to 99.75 for the proposed method and confidence interval was found to be 210.59-187.31 for (kitofen) and 205.59-186.84 (Rhofenid). The RSD values obtained from recovery studies ranged from 0.75 to 3.5%, which indicated high accuracy and precision. The developed method was validated by using linearity, stability, precision, accuracy and sensitivity parameters according to ICH guidelines [13].

In the present study, we report a highly selective gas liquid chromatography method for the determination of the KPF of substance used as anti inflammatory drugs without derivatisation in pharmaceutical formulation. The gas liquid chromatography method was high recovery and excellent reproducibility. For this reasons, it can be used for the determination for pharmaceutical preparation of KPF in routine quality control measurement. The method involves with simple sample preparations without derivatisation in pharmaceutical preparations using ibuprofen (IPF) as internal standard (IS) [14].

ACKNOWLEDGEMENT

The authors express their gratitude to BEC Chemicals Pvt. Ltd., Roha, India, for the gift samples of pure KPF and IPF. Thanks are also extended to Dr. H.G. Shivakumar, Principal, JSS College of Pharmacy for providing necessary facilities and his constant support.

REFERENCES

1. Anderson, T., E. Bredberg, P.O. Lagerstrom, J. Naesdal and I. Wilson, 1998. Eur. J. Clin. Pharmacol., 54: 399.
2. Kormosha, Z., I. Hunkaa and Y. Baselb, 2009. Acta Poloniae Pharmaceutica Drug Res., 66(1): 3.
3. Chi-yin Wong, Ming-kung Yeh and Da-peng Wang, 1992. Journal of Liquid Chromatography & Related Technologies, 15(8): 1215.
4. Dvorak, J., R. Hajkova, L. Matysova, L. Novakova, M.A. Koupparis and P.S. Solich, 2004, J. Pharm. Biomed. Anal., 36: 625.
5. Jefferies, T.M., W.O.A. Thomas and R.T. Parfitt, 1979. J. Chromatogr, 162: 122.
6. Bannier, A., J.L. Brazier and C. Quincy, 1979. Feuill. Biol., 106: 91.
7. Royer, R.J., F. Lapicque, P. Netter, C. Monot, B. Bannwarth and M.C. Cure, 1986. 40(3): 100.
8. Salma, M.Z., Al-Kindy, Zakiya Al-Harasi, F.E.O. Suliman, A. Al-Hamadi and A. Pillay, 2009, J. Fluoresc, 19: 249.
9. Holzer, P., M. Jocic, F. Cabré and D. Mauléon, 2001. Inflamm. Res., 50: 602.
10. Bertini, M.J., A. Cocchini, A. Perico, F. Salvagnini, and A. Triolo, 1992. J. Liquid Chromatography & Related Technologies, 15(2): 327.
11. Hung, C.Y. and C.C. Hwang, 2008. J. Chromatogr Sci., 46(9): 813.
12. Man-Jeong Paik, Duc-Toan Nguyen and Kyoung-Rae Kim, 2004. Arch Pharm. Res., 27(12): 1295.
13. ICH harmonized Tripartite Guideline. Validation of Analytical procedures: Text and Methodology Q2(R1). International Conference on Harmonization. 1997.
14. Rau, H.L. and P.G. Rao, 1990. Indian J. Pharm. Sci., 52(5): 253.