Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2014, 6(8):301-304

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Optimization and validation of a method for determination of ibuprofen by HPLC in different pharmaceutical forms: Tablet, syrup, gel and suppository

M. Radi*[1], Y. Ramli*[2], M. El Karbane[1], A. Elalami[1], K. Karrouchi[1], A. Bekkali[3], B. Benaji[3], S. Issmaili[1] and K. Bakhous[1]

[1]*Physicochemical Service, Drugs Quality Control Laboratory, Division of Drugs and Pharmacy, Ministry of Health, Rabat, Morocco*
[2]*Medicinal Chemistry Laboratory, Faculty of Medicine and Pharmacy, Mohammed V University- Rabat, Morocco*
[3]*Team for Research in Pharmacology and Toxicology, Faculty of Sciences, Hassan II University- Casablanca, Morocco*

ABSTRACT

A simple, fast, economical, accurate, precise and reproducible RP – HPLC method was developed for the determination of Ibuprofen. The method was validated in terms of specificity, linearity, precision accuracy, and robustness. The proposed method's results were found to be satisfactory and are suitable for determination of Ibuprofen for routine quality control of drugs in bulk drug and formulation.

Keywords: Ibuprofen, HPLC, method validation.

INTRODUCTION

Ibuprofen or alpha-methyl-[4 - (2-methylpropyl) phenyl] propanoic acid (Fig. 1) is a non-steroidal analgesic and anti-inflammatory drug (NSAID) used to relieve the symptoms of arthritis, primary dysmenorrhoea, pyrexia.

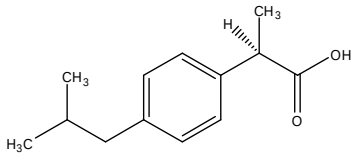


Fig. 1: Structure of Ibuprofène

Medicines ibuprofen base are available in different dosage forms such as tablet, syrup, gel and suppository. Currently, the determination of this molecule in the finished products is done by various methods [1-9].

In this work, we developed and validated according to ICH guidelines strategy (International Conference on Harmonisation) [10] a simple and fast method RP-HPLC, able to determine ibuprofen in different pharmaceutical forms. The validation of this method is based on a statistical analysis based on a number of criteria leading to an analytical method to give reliable results and demonstrate that it corresponds to the use for which it is given.

EXPERIMENTAL SECTION

2.1 Apparatus

Two chromatographic systems used: consisted of Waters 2695 pump, auto sampler and Waters 2998 photodiode-

array detector (PDA) with Spectra Manager software and Empower Software data registration. were used for all absorbance measurements and a PERKINELMER SERIE 200 photodiode-array detector (PDA). Data acquisition was performed by the Totalchrom Software data registration (USA), the Mettler Toledo scale made in Switzerland.

2.2 Reagents and samples

The ibuprofen standard (99,7% %) was obtained from European Pharmacopeias (Eur Ph) .The ibuprofen generic (tablet, syrup, gel and suppository) were purchased from local market.

The placebo used in validation procedure is composed by the usual excipients found in the commercial formulation (Saccharose, Sodium citrate, citrique acid, sodium saccharine, gomme xanthane, lécithine, potassium sorbate, Colouringyellow orange, propylene glycol, corn starch, colloïdale silice, magnésium stéarate , povidone K30, méthyle parahydroxybenzoate, propyle parahydroxybenzoate, sodium benzoate, tutti frutti flavor, polysorbate 60, witepsol, Sorbitol Glycérol).

Acetonitrile HPLC grade was from Sigma - Aldrich (Germany). Phosphoric acid 85% (H_3PO_4) was supplied from Labosi.

2.3 Chromatographic Conditions

The separation was achieved using a Zorbax SB-C18 (150 mm×4,6mm 5µm) column. The mobile phase was composed of acetonitrile and acidified water (0,7 ml of H_3PO_4 in 1000ml of water**)** (50/50) at a flow rate of 1ml/min. Detection was performed at 220 nm and all assays were performed at room temperature conditions. The auto sampler was programmed to inject 20µl. The mobile phase was filtered through a 0.45-µm Millipore filter and degassed by vacuum prior to use.

RESULTS AND DISCUSSION

3.1 Specificity of the chromatographic method

The selectivity of the method was confirmed by observing potential interferences caused by excipients in formulations.The chromatogram of the excipients (Fig. 2) shows that there were no interference of peaks to the determination of ibuprofen.

The peak purity indices for ibuprofen were found to be better (purity angle < purity threshold) indicating that no additional peaks were co-eluting with the analytes and also evidencing the ability of the method to assess unequivocally the analytes of interest in the presence of potential interference.

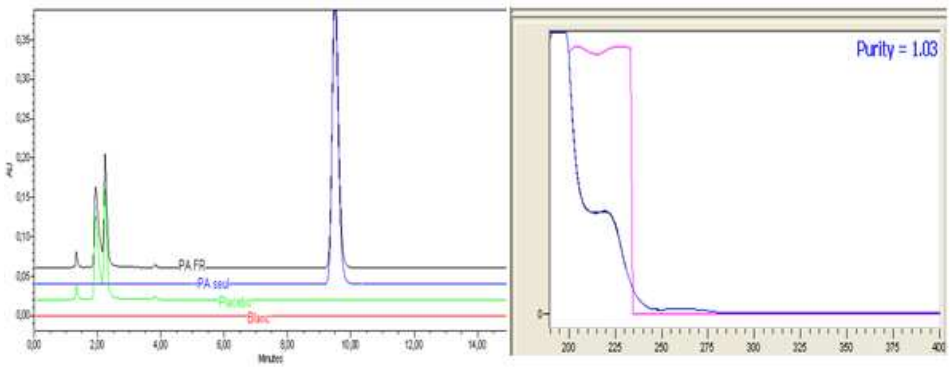
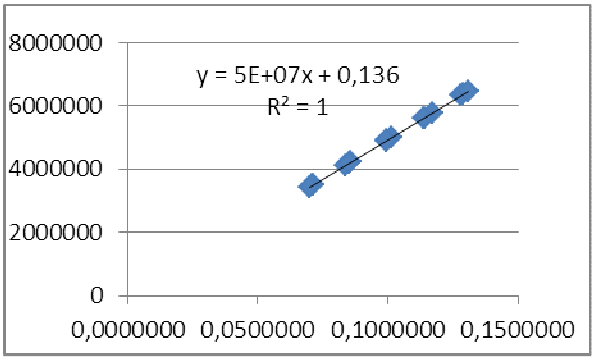


Fig.2: Specificity of the chromatographic method

3.2 Linearity

The linearity of the method was determined by preparing serial dilutions of minimum 5 concentrations of standard stock solutions and 5 concentrations of the reconstituted form each in duplicate. Take the average area of each injection and plot the graph of average peak area versus actual concentration of each solution in µg/ml.



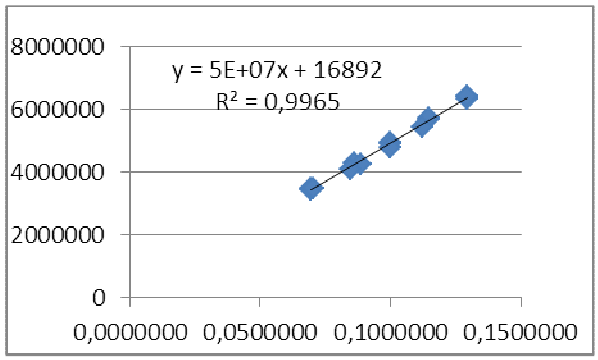


Fig 3a: Linearity of ibuprofen (active ingredient alone) **Fig 3b: Linearity of ibuprofen (reconstituted form)**

A linear regression equation was obtained:

For active ingredient alone (y =49331952,8 x + 0.135981) with a regression coefficient (r^2=1)

With confidence intervals (CI) of the slope (a_1) and directed at the origin (b1), 49331950,01< a_1 < 49331955,54 and - 0,147733403 < b_1 <+0,419695338.

For reconstituted form (y= 48939654,2 x + 16892,34) with a regression (r^2= 0,998)

With confidence intervals (CI) of the slope (a_2) and directed at the origin (b_2), 47512970, 35 < a_2 <50366338, 03 and -128777,43 < b_2 <162562,11

3.3 Precision (repeatability and intermediate precision)

The repeatability (within-day precision) was validated as described on the ICH Q2R1 guidelines[10], by performing six replicate samples of 0.1mg /ml of ibuprofen in the same conditions. The calculated mean relative standard deviation (R.S.D) was 1.58%

The intermediate precision (day-to-day precision) was assessed by the CV% calculated from data obtained by performing six measurements for the nominal concentration (0.1mg /ml) for three independent series. The CV % was 1.79 which confirmed the reproducibility of the HPLC assay.

3.4 Accuracy

The accuracy of the method was determined by spiking the placebo with standard ibuprofen at five concentration levels, covering the range of 50 - 140 % of the target concentration. The mean percent recovery 99.24 % falls inside the 95 % confidence interval of 98.82%-100.35%.

3.5 Robustness

The robustness of the method was studied by changes in the method like alteration in flow rate (0.1 ml/min of set value i.e. 0.9 ml/min and 1.1 ml/min), column temperature (5°of set value i.e. 20°c and 30°c), composition of the mobile phase (acetonitrile and acidified water45/55 and 55/45), detection wavelength (210 and 220) and column (A new column and B old one) . (Table1)

Table1: Robustness of the method

	Number of theoretical plates **N > 8000**	**Asymmetry factor** **1.1% < F < 1.4%**	**Content (%)** **95% < T(%) <105%**	**RSD (%)** C < 2.5%
Temperature T=20°C	10061	1.282	103.30	1,11
Temperature T=25°C	1 0752	1.132	101.13	
Temperature T=30°C	9789	1.352	101.63	
Mobile phase: 45% /55%	8448	1.281	101.35	0,15
Mobile phase: 50% /50%	10752	1.132	101.13	
Mobile phase: 55% /45%	11293	1.253	101.41	
Flow: 0,9 ml/min	10944	1.245	100.36	0.44
Flow : 1,0 ml/min	10752	1.132	101.13	
Flow : 1,1ml/min	9789	1.234	101.11	
λ= 210nm	9889	1.272	101.36	0.16
λ= 220nm	10752	1.132	101.13	
Column A	10752	1.132	101.65	0.36
Column B	9789	1.352	101.13	

3.6 Application of the developed method (Determination of Ibuprofen in formulations)

The validated method was applied to the determination of Ibuprofen in different pharmaceutical forms such as tablet, syrup, gel and suppository.

The results are shown in table 2 indicating that the amount of drug in samples met with requirements.

Table2: Result of Analysis of Ibuprofen in marketed formulations

Pharmaceutical form	Content (%)
Tablet	95.31
Gel	98.05
Syrup	98.51
Suppository	98.49

CONCLUSION

The proposed method was found to be simple and rapid for determination of ibuprofen from pure and pharmaceutical formulations. The mobile phase is simple to prepare and the run time was less than 9min which consumes only less than 9ml of mobile phase. So the method was demonstrated to be economical. The sample recoveries in all formulations were in good agreement with their respective label claims suggested non-interference in the estimation. Hence, the method can be easily and conveniently adopted for routine analysis of ibuprofen dosage forms .The simplicity ensures that the RP-HPLC method can be applied for estimation of ibuprofen in syrup, gel, suppository and tablet dosage forms, the method was found to be accurate, precise, linear, robust and rugged.

Acknowledgements
The authors thank the Moroccan National Drug Control Laboratory (Laboratoire Nationale de Contrôle des Médicaments LNCM) and IPharma for supporting this study.

REFERENCES

[1] USP34-NF29,**2011**, 3099-3102 .
[2] Pharmacopée européenne 7.0, **2011**, 2385-2387.
[3]J. Sochor, J. Klimeš, M. Zahradníček, J. Sedláček *Journal of Chromatography B: Biomedical Sciences and Applications*, Volume 654, Issue 2, 1 April, **1994**, Pages 282-286
[4]N. Oi, H. Kitahara, F. Aoki and N. Kitsu, *J. Chromatogr.* B, 689 ,**1995**, 195.
[5]R. Mehvar, F. Jamali and F.M. Pasutto, *Clin. Chem*., 34 ,**1988**, 493.
[6]H.Y. Ahn, S.T. Wu, G.K. Shiu, T.D. Doyle, C.A. Brunner and W.F. Trafton, *Pharm. Res.*, 8 ,**1992**, 31.
[7]K. Iwaki, T. Bunrin, Y. Kameda and M. Yamazaki, *J. Chromatogr.* A, 662, **1994**, 87.
[8]W.H. Pirkle and C.J. Welch, *J. Liq. Chromatogr*., 15, **1992**, 1947.
[9]J. Goto, N. Goto, A. Hikichi, T. Nishimaki and T. Nambara, *Anal. Chim. Acta*, 120, **1980**, 187.
[10]ICH-Q2B, Validation of Analytical, Procedures: Methodology, November **1996**