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Determination of ketoprofen in tablet dosage forms by derivative IR spectroscopy

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Abstract

The study as a simple and rapid method has been described for determination of ketoprofen depending upon normal and first derivative IR Spectroscopy. The aim of this study is to develop a specific, precise and accurate spectroscopic methods that could be applied in quality control for the determination of ketoprofen in pharmaceutical formulations. Ketoprofen has been determined quantitatively in the range of (1000 to 4000)µg/ml depending on the measurement of transmittance for normal and its first derivative spectrum against the concentration with relative error+4.33% and 4.78% and RSD 1.15% and 1.37%, respectively. The values of r^2 of the both methods were 0.993 and 0.978, respectively. The methods have been applied for determination of ketoprofen in some pharmaceutical samples with recovery 97.691%.The obtained results were statistically compared to those of a reported HPLC technique and t-student's and F- tests at P=0.05 are calculated2SA1`

Keywords: Ketoprofen, First Derivative, IR Spectroscopy

1. Introduction

Ketoprofen is a 2-(3-benzolphenyl)propionic acid an important non-steroidal anti-inflammatory drug with anti-inflammatory, analgesic and antipyretic properties (Fig.1). Recent studies have shown that ketoprofen has therapeutic potential in the prevention of various cancers including colorectal and lung cancers, in addition to its potential in the treatment of neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease [1,2]. Moreover, different formulation of ketoprofen has been used to treat several acute and chronic inflammatory diseases. Ketoprofen has been used in treating diseases such as osteoarthritis, rheumatoid arthritis, abdominal cramps associated with menstruation, and ankylosing spondylitis [3-6].
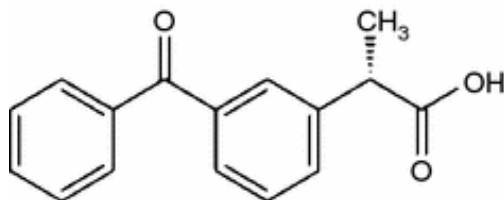

Figure 1: Ketoprofen Chemical structure [7].

A range of different analytical methods have been used for the determination of ketoprofen in pharmaceutical formulations. These techniques including UV- spectrophotometry[8-12], capillary zone electrophoresis [13], high-performance liquid chromatography[14-18], voltametric methods [19,20], electrokinetic chromatography [21], and quantitative Fourier transform infrared spectroscopy using attenuated total reflectance analysis [22]. In addition, flow injection technique conjugated with other techniques have been also used for determination of ketoprofen, such as flowinjection technique with chemiluminescence [23, 24] and flow injection with UV-detection [25].

IR spectroscopy is inexpensive and sensitive technique and is applicable with fast and easy. Moreover, the majority of samples can be prepared, scanned, and the results plotted in less than five minutes [26].In a recent study byHabib and Kamel Near infra-red reflectance spectroscopic has been used for the determination of metformin in tablets [27].

The aim of this study is to develop a specific, precise and accurate normal and derivative IR spectroscopic method, that could be applied in quality

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control for the determination of ketoprofen in some pharmaceutical formulation samples.

2. Experimental

2.1 Instruments

FTIR analysis for the samples was performed by using FTIR spectroscopy (Shimadzu, FTIR-8400) in the frequency range of 400 cm^{-1} to 4000 cm^{-1}.using spatial cells for liquid samples.

2.2 Reagents and Solutions

All chemicals and solvents used were of analytical grade.

2.2.1 Preparation of stock standard ketoprofen solution (100.0 μg/ml):

A 100.0 μg/ml ketoprofen stock solution was prepared in CCl$_4$. The stock solution was kept protected from light using amber colored flasks and refrigerated. After being diluted with solvent, increasing volumes of ketoprofen stock solutions were quantitatively transferred to prepare solutions within the 1000–9000 ppm concentration range. Final standard solutions were kept in the fridge.

2.2.2 Preparation of sample solutions:

Two tablet samples(Turkey market)(Bi-Profenid 100 mg(batch no. A10676) and (Erbil market)Profenid 100 mg (batch no. 7KP5C), both manufactured by SANOFI) were accurately weighed, finely pulverized, and thoroughly mixed. An accurately weighed portion of seven pulverized tablets equivalent to 1.2236g of Erbil tablets (7 x0.1748 g).From this 0.4369 g of the powder was dissolved in CCl$_4$ to prepare 10000 ppm ketoprofen in final volume 25ml CCl$_4$. Anaccurately weighed portion of seven pulverized tablets equivalent to 3.5707 g of Turkey tablets (7 x 0.5101 g).From this 1.2754 gm of powder was dissolved in CCl$_4$ to prepare 10000 ppm ketoprofen in finalvolume 25ml CCl$_4$.thenboth solutions sonicated for 10 min. All sample solutions were filtered through 0.22 μm analytical Nylon filters. Ketoprofen sample solutions were used to prepare solutions in the range of 1000–4000 ppm.

2.3. Analysis by normal and derivative IRspectroscopy:

Normal and derivative IR spectrophotometry techniques have been applied effectively for the quantification of ketoprofen. In this investigation, the normal IR spectrum of the ketoprofen has been used for the quantitative determination depending on the measurement of the transmittance values of the carbonyl group at wave numbers 1710 cm^{-1} and 1666 cm^{-1}. While, in the first derivative IR the analysis depends on measuring the amplitudes at the wave number 1718cm^{-1},1705cm-1,1670cm^{-1},1660cm^{-1} and 1651cm^{-1} .

2.4. Construction of normal and derivative IR calibration curve

In the normal IR the calibration curve was constructed by plotting the measured transmittance values against the respective concentration (1000–4000 ppm). Regression analysis data was calculated using excel formula:

$$Y= a+bx$$

Where b is the slope,anda is the intercept.

While in the first derivative the same expression has been used for the construction of the calibration curve by plotting the measured transmittance values of the peak to the base line against the respective concentrations.

3. Results and discussion

3.1. Optimization of chemical parameters

Various solvents have been studied to optimize the solubility of ketoprofen. CCl$_4$ was chosen as the best solvent because it can produce clear solution and the ketoprofen was completely dissolved. After preparation the ketoprofen solutions were stored in a dark and cool condition to sustain the stability of ketoprofen.

3.2. Selection of optimum apparatus conditions

Three different sample holders with different thickness have been used, these including 1.0 mm, 0.5 mm, and 0.05 mm KBr sample holder. It was found that the 0.5 mm KBr discs shows the best result.

3.3. Normal spectra of ketoprofen

Figure (2) shows the normal spectra of Standard, Erbil and Turkey ketoprofen solutions, using CCl$_4$ as a solvent blank with a characteristic peak of carbonyl group at wave number 1710 cm^{-1}.

3.4. Derivative spectra of ketoprofen

Figure (2) also shows the derivative spectra of Standard, Erbil and Turkey ketoprofen solutions, using CCl$_4$ as a solvent blank with two characteristic peaks of carbonyl groups at 1718 cm^{-1} as a positive peak and at 1705 cm^{-1} as a negative peak.
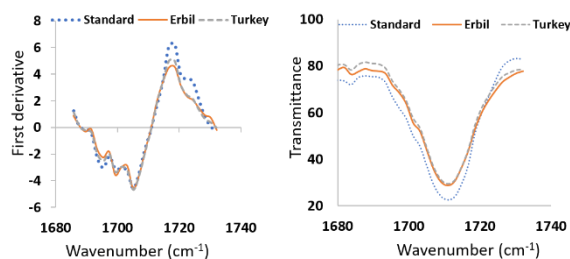

Figure 2: first derivative and normal spectra of Standard, Erbil and Turkey ketoprofens.

3.5 Calibration curves and statistical data for standard ketoprofen

Ketoprofen spectrum shows absorption bands of C=O stretching vibration of carboxylic group and C=O stretching vibration of ketene group appeared at

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1710 cm^{-1}and 1666 cm-1, respectively. According to Beer-Lambert's law there is an inverse proportional relationship between the T% and the concentration.

The proportional relationship between the peak height and concentration was evaluated by constructing a linear regression of fourconcentrations (1000-4000 ppm) at1710 cm^{-1}. While the sensitivity of the linearity at the second wave number at1666 cm^{-1}was less than the first one.

Detection limit (LOD) for normal spectrum was found to be208.5 ppm

The good linearity obtained was indicated by the correlation coefficient value for normal and derivative standard ketoprofen (fig. 4 and 5). 3.6 Statistical Analysis

all regression parameters of normal and first derivative calibrations of slope, intercept, correlation coefficient, standard deviation of intercept (Sa), standard deviation of slope (Sb), Sandell's sensitivity, limits of detection, and quantification for wave numbers 1710 cm^{-1} (normal) and 1718 cm-1 (derivative) are shown in Table1.

Table 1: Summary of statistical data

Method	Normal IR	1stderivative IR
Regression equations	Y=-0.015x +84.29	Y=0.001x +1.9
Sensitivity	0.015	0.001
Intercept	+84.29	+1.9
r^2	0.993	0.978
S(a)	3.624991	0.285
S(b)	0.002315	0.00016
LOD	208.5 ppm	237.6 ppm
LOQ	632 ppm	720 ppm
Sandell's sensitivity	5.89*10^{-5}	3.93*10^{-6}

The obtained results were statistically compared to those of a reported HPLC technique and t-student's and F- tests at P=0.05 are calculated; where the results are less than theoretical, no significant difference was observed in terms of accuracy and precision, (Table2).

Table2: Statistical comparison of the proposed methods with the reported one [28] for determination ofketoprofen in pharmaceutical formulation

Methods	Normal spectra	1stDerivative spectra	Reported method[1]
	Standard(Normal spectrum)	Standard(1st-derivative spectrum)	Standard(HPLC)
Mean	101.4	99.75	99.11
%RSD	1.1525	1.3737	1.32
n	4	4	4
Student t-test [2] (2.262)	0.827	0.138	

F-value [2] (9.38)	1.323	2.427	

[1] HPLC reported method the determinations were carried out on a Luna C18 analytical column (250mm ×4.6mm I.D., 5 mm particle size) thermostatted at 30ºC. The mobile phase was a 48:9:43 (v/v/v) mixture of MeOH, 2-propanol and 50mM sodium phosphate (pH =5.5), pumped at 1.0 mL.min^{-1}. Detection wavelength was 225 nm. All samples were filtered through 0.45 mm nylon filters before injection.
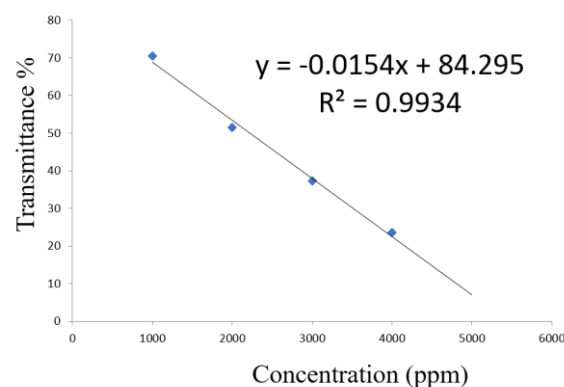
[2]Theoretical values of t and F at (P= 0. 05).

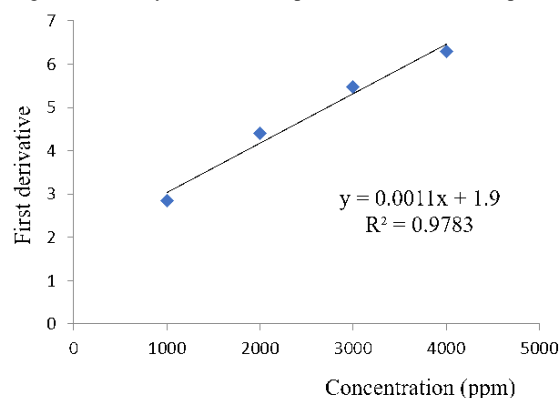Figure 4: linearity of normal IR spectrum of standard ketoprofen.

Figure 5: linearity of derivative spectrum of standard ketoprofen.

3.6 Precision

Precision usually is reported as a relative standard deviation, s, which we define as

$$s = \sqrt{\frac{\sum (x_i - \bar{x})^2}{n-1}}$$

where x$^-$ is the average, or mean result, and xi is one of the n different results.

The precision of the method was evaluated by both interday and intraday variation studies (four concentration/ four replications) as well as the relative standard deviation (%RSD).

RSD was 1.15% and 1.37%, for normal standard ketoprofen and 1st derivative ketoprofen respectively

3.7 Accuracy

Accuracy usually is reported as a percent error

$$\% \text{ error} = \frac{\text{actual value} - \text{expected value}}{\text{expected value}} \times 100$$

The accuracy of the normal and derivative IR methods were calculated upon the values of E% values and they were found to be +4.33 and + 4.78 respectively.

3.8. Application of the proposed methods for quantification/determination of Erbil and Turkey ketoprofen samples

The normal and derivative spectra of ketoprofensamples were carried out. The methods have beenapplied for determination of ketoprofen in somepharmaceutical samples obtained from Erbil andTurkey markets with recovery 97.691%.

4. Conclusion

The proposed first derivative IR spectroscopic method is considered as a green, non-destructive, low cost, fast, sensitive, accurate and precise technique for the quantitative analysis of ketoprofen in its pure and tablet dosage formulation and can be easily applied for quantitative determination and quality control.

5. Conflicts of interest

There are no conflicts to declare.

6. Formatting of funding sources

7. References

[1] Weder, JE, Dillon, CT, Hambley, TW, Kennedy, BJ, Lay, PA, Biffin, JR, Regtop, HL, Davies, NM. Copper complexes of non-steroidal antiinflammatory drugs: an opportunity yet to be realized, Coordin Chem Rev 232: 95-126, 2002.

[2] Hirohata, M, Ono, K, Morinaga, A, Yamada, M. Non-steroidal anti-inflammatory drugs have potent anti-fibrillogenic and fibrildestabilizing effects for a-synuclein fibrils in vitro, Neuropharmacology 54: 620-627, 2008.

[3] Katzung, BG. Basic and Clinical Pharmacology, Eighth Edition, San Francisco, p.605, 2000.

[4] Okai Tettey-Amlalo, RN. In Vitro Release of Ketoprofen from Proprietary and Extemporaneously Manufactured Gels, Rhodes University, A Thesis of Master, 2005.

[5] Tayade, PT, Vavia, PR. Inclusion Complexes of Ketoprofen with ß- Cyclodextrins: Oral Pharmacokinetics of Ketoprofen in Human, Indian J Pharm Sci 68: 164-170, 2006.

[6] Patrono, C. and Rocca, B., Nonsteroidal antiinflammatory drugs: Past, present and future. Pharm Res, 59: 285-289, 2009.

[7] Oliveira, L.J., Stofella, N.C.F., Veiga, A. et al. Physical–chemical characterization studies of ketoprofen for orodispersible tablets. J Therm Anal Calorim 133, 1521–1533 (2018).

[8] Pomykalski, A. and Hopkata, H. Application of derivative UV spectrophotometry for the determination of fenbufen and ketoprofen in

pharmaceutical preparations. Acta Pol Pharm, 62: 171-176, 2005.

[9] Kormosh, Z., Hunka, I. and Basel Y. Spectrophotometric determination of ketoprofen and its application in pharmaceutical analysis. Acta Pol. Pharm.- Drug research, 66: 3-9, 2009.

[10] Dvorac, J., Hajkova,R., Matysova, L., Novakova, L., Koupparis, M. and Solich, P. Simultaneous determination of ketoprofen and its degradation products in the presence of preservatives in pharmaceuticals. J Pharm Biomed Anal, 36: 625-629, 2004.

[11] El-Sadec, M., El-Adi, S. and Abou-Kull, M. Spectrophotometric determination of ketoprofen in pharmaceutical preparations by means of charge transfer complex formation. Talanta, 40: 585-588, 1993.

[12] Blanko, M., Coello, J., Iturriaga, H., Maspoch, S. and Alaoui-Ismaili S. UVspectrophotometric determination of ketoprofen and paraben in a gel preparation by partial least-squares calibration. Fresenius' J Anal Che., 357: 967-972, 1997.

[13] Blanko, M., Coello, J., Iturriaga, H., Maspoch, S. and Perez-Maseda, C. Chiral and nonchiral determination of ketoprofen in pharmaceuticals by capillary zone electrophoresis. J Chromatogr A, 799: 301- 307, 1998.

[14] Wong, C., Yeh, M. and Wang, D. High performance liquid chromatographic determination of ketoprofen in pharmaceutical dosage forms and plasma. J Liquid Chromatography, 15: 1215-1225, 1992.

[15] Novakova, L., Matysova, L., Solichova, D., Koupparis, M. and Solich, P. Comparison of performance of C18 monolithic rod columns and conventional C18 particle packed columns in liquid chromatographic determination of Estrogel and Ketoprofen gel. J Chromatogr B, 813: 191-197, 2004.

[16] Labbozzetta, S., Valvo, L., Bertocchi, P., Alimouti, S., Gandiano, M. and Manna, L. Focused microwave-assisted extraction and LC determination of ketoprofen in the presence of preservatives in a pharmaceutical cream formulation. Chromatographia, 69: 365-368, 2009.

[17] Bempong, D. and Bhattacharyya, L. Development and validation of a stabilityindicating high-performance liquid chromatographic assay for ketoiprofen topical penetrating gel. J Chromatogr A, 1073: 341-346, 2005.

[18] Mannucci, C., Bertini, J., Cocchini, A. and Perico, F. High performance liquid chromatography simultaneous quantitation of ketoprofen and parabens in a commercial gel formulation. J Liquid Chromatography, 15: 327-335, 1992.

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[19] Emara, K., Ali, A. and Maali, N. The polarographic behaviour of ketoprofen and assay of the capsules using spectrophotometric and voltammetric methods. Talanta, 41: 639-645, 1994.

[20] Amaukwa, L. and Chatten, L. Electrochemical reduction of ketoprofen and its determination on pharmaceutical dosage forms by differential-pulse polarography. Analyst, 109: 57-60, 1989.

[21] Safra, J. and Pospisilova, M. Separation and determination of ketoprofen, methylparaben and propylparaben in pharmaceutical preparation by micellar electrokinetic chromatography. J Pharm Biomed Anal, 48: 452-455, 2008.

[22] Overbeke A, Bossche W, (1995) Quantitative Fourier transform infrared/attenuated totalreflectance analysis of ketoprofen in some pharmaceutical formulations, Vibrational Spectroscopy, ,9, 121-130.

[23] Zhuang, Y., Cao, D. and Ge, D. Flow injection analysis of ketoprofen based on the order transform second chemiluminiscence reaction. Spectrochim Acta part B, 85: 139- 144, 2012.

[24] Zhuang, Y. and Song, H. Sensitive determination of ketoprofen using flow injection with chemiluminiscence detection. J Pharm Biomed Anal, 44: 824-828, 2007.

[25] Aboul-Enein, H., Dal, A. and Tuncel, M. A validated method development for ketoprofen by a flow-injection analysis with UV-detection and its application to pharmaceutical formulations. Il Pharmaco, 58: 419-422, 2003.

[26] Rhee, YS, Choi, JG, Park, ES, Chi, SC. Transdermal delivery of ketoprofen using microemulsions, Int J Pharm 228: 161-170, 2001.

[27] Habib, I. H. and Kamel, M. S. (2003) Near infra-red reflectance spectroscopic determination of metformin in tablets. Talanta, 28;60(1):185-90. doi: 10.1016/S0039-9140(03)00123-1.

[28] Tsvetkova, B. and Peikova, L. (2013) Hplc Determination Of Ketoprofen In Tablet Dosage Forms, Trakia Journal of Sciences, No 1, pp 55-59, 2013.

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