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ORIGINAL RESEARCH ARTICLE

Spectrophotometric Determination of Ibuprofen in Visible Region of Spectrum

Naveed Aslam Dogar *[1], Islam Ullah Khan [2], Bilal Bashir [2], Naeem Asghar Khan[3]

1. Department of Chemistry, Govt. Islamia College, Civil Lines, Lahore, Pakistan
2. Department of Chemistry, Govt. College University, Lahore, Pakistan
3. Department of Chemistry, Govt. Shalimar College for Boys, Lahore, Pakistan

ABSTRACT

Ibuprofen reacts with α – naphthylamine and sodium nitrite to give orange color having maximum absorbance at 460 nm. The reaction is specific for Ibuprofen and provides a basis for its spectrophotomertic determination. The color reaction obeys Beer's law from 0.1 mg to 10 mg/10 ml of Ibuprofen. The relative standard deviation is 1.25%. The quantitative assessments of tolerable amount of other drugs have also been studied.

Keywords: Ibuprofen, Calibration Curve, Pharmaceutical Preparation, Spectrophotometer.

INTRODUCTION

Ibuprofen is a white or almost white crystalline powder with a characteristic odour and a slight taste. It has analgesic, anti-inflammatory and antipyretic actions. It is used in the treatment of rheumatoid arthritis and other musculoskeletal disorders. It has also been used in the treatment of acute gout. Ibuprofen is a derivative of Propionic acid.[1] Many analytical techniques have been employed for the detection and determination of ibuprofen. The complex reversed phase HPLC and high field proton NMR spectroscopy have been used for the detection and identification of the urinary metabolites of ibuprofen.[2] The ibuprofen solution in chloroform was treated with Cu (II) solution at pH 5.5 forming a blue compound which was extractable in the organic phase. This complex was spectrophotometically measured at 675 nm obeying Beer's law in a range of 0.5 – 3.2 mg/ml.[3] A coupled HPLC – NMR method has been used for the detection and identification of ibuprofen, fluribiprofen, antipyrine and paracetamol.[4] The

Address for correspondence:
Naveed Aslam Dogar *
Department of Chemistry, Govt. Islamia College, Civil Lines, Lahore, Pakistan
E-mail: naveeddogar_33@yahoo.com

second order UV derivative spectrophotometry has been used for the quantitative determination of ibuprofen in tablets. The second order derivative spectrophotometry presented a good definition of spectra when compared to the zero order UV spectrophotometry. Derivative data were collected by the tangent method and 0.1N NaOH solution was used as solvent of all samples.[5] Gas chromatography mass spectrometry (GC – MS) method has been used for the detection of plasma ibuprofen.[6] Two simple, accurate and reproducible methods for simultaneous estimation of ibuprofen and pseudoephedrine in combined dosage have been developed. The first method was based on the solving of simultaneous equations by using 263.8 and 257.6 nm as 2 wavelengths. The second method involved first derivative UV spectroscopy. Two wavelengths selected for this method were 265 and 257 nm.[7] A new extractive spectrophotometric method has been developed for the detection of ibuprofen. The method involves the formation of coloured electron donor acceptor complex between ibuprofen and safranine in aqueous phase extractable into chloroform, which is measured at 520 nm.[8]

During a systematic study of pharmaceutical drugs, it was found that ibuprofen reacts with α – naphthylamine and sodium nitrite to give orange color at a value of 460 nm. The reaction is specific for ibuprofen and has 0.01 mg/ml as the visual limit of quantitation. This indicates that this color reaction has not been reported previously. The present method is simple not requiring many chemicals, accurate, precise and other organic compounds like Mefenamic acid, indomethacin, Baclofen, Nitrazepam, salicylic acid, Nefopam do not interfere even if present as 100, 200, 15, 100, 200, 150 folds respectively.

MATERIALS AND METHODS

A description of materials and methods used throughout for this work is given as under:

INSTRUMENTS

(a) Electrical Balance

Meter H10, made in Switzerland.

Maximum 160 grams with 0.0001 accuracy

(b) Spectrophotometer

HITACHI U – 1100 Spectrophotometer, Made in Japan

Silica glass cells with 1 cm thickness.

(c) Hot Plate

Maximum temperature 400 °C

Made in England

(d) Glass Apparatus

(i) Micropipettes with 0.1 ml graduation and pipettes of 1mL, 2mL and 20 ml were used.

(ii) Measuring flasks of 25 ml, 50 ml, 250mL and 500mL of Pyrex glass were also used.

(iii) Microburette of 5.0 ml graduated at intervals of 0.05 ml.

All apparatus and flasks were officially calibrated.

CHEMICALS

All chemicals were of analytical grade, which were used during spectrographotometric determination.

Sodium Nitrate	BDH
α – naphthylamine	E. Merck
Ibuprofen	Basf pharma
Ethyl alcohol	E. Merck
Mefenamic acid	Efroze chemists
Hydroxyzine – HCL	Zafa Pharma
Indomethacin	Searle Pak Ltd.
Nefopam	Ciba – Geigy
Phenytoin sodium	French pharma
Chlopromazine HCL	Glaxo
Baclofen	Medimpex
Nitrazepam	Fazal Din & Sons
Salicylic acid	E. Merck
Amitryptyline – HCL	Pfizer pharma
Clonazepam	Roche
Piroxicam	Pfizer pharma

PREPARATION OF REAGENTS:

All reagents and stock solutions required for these spectrophotometric studies were prepared in double distilled water and ethyl alcohol, which were of analytical grade.

Ibuprofen Solution (1mg/mL)

100 mg of pure ibuprofen was dissolved in 10 ml ethanol and 40 ml distilled water and then in a 100 ml measuring flasks the volume was made up to the mark. The solution was stored in airtight and protected from light.

α – Naphtylamine Solution (0.05%)

0.05g of α – naphthylamine was dissolved in 1.5 ml ethanol in a 100 ml measuring flask and the volume was made up to the mark with distilled water.

Sodium Nitrite Solution (2.0%)

2g of sodium nitrite was dissolved in distilled water in a 100 ml measuring flask and the volume was made up to the mark with distilled water.

Stock Solutions of Various Organic Compounds for Checking Interferences

Stock solutions of strength 1 mg/ml of various organic compounds were prepared by dissolving 100 mg of the organic compounds in distilled water, ethyl alcohol, methyl alcohol etc. in 100 ml measuring flasks and the volumes of the solutions were made up to the mark with the above solvents

in order to check the interferences of these compounds in the determination of ibuprofen.

PROCEDURES

Ibuprofen reacts with α – naphthylamine and sodium nitrite to give orange color. The reaction is specific for Ibuprofen and this provides a base for a new spectrophotometric method for the determination of Ibuprofen in tablets. Effect of different reagents, heating time, temperature and color stability was studied along with interferences of different organic compounds in the determination of Ibuprofen.

Procedures for the complete study of the reactions are given below:

Procedure for the determination of

To 1 ml Ibuprofen (1 mg/ml), 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%) was added.

The mixture was heated at 70 °C for 80 seconds in a water bath. The mixture was cooled down and the volume of the solution was made up to 10 ml by adding alcohol. Absorbance measurements of the resulting colored solution were made with a spectrophotometer at different wavelengths in the visible region using distilled water as blank. The spectrum shows maximum absorbance at 460 nm.

Procedure to Study the Effect of Temperature

To study the effect of temperature on the color of the reaction, 1 ml Ibuprofen (1 mg/ml) was mixed with 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%). About 7 test mixtures were prepared and each mixture was heated for 2 minutes in a water bath at different temperature (30 – 100 °C). The volume of each mixture was made up to 10 ml by dilution with ethyl alcohol. Absorbance of the resulting colored solutions was measured at 460 nm with spectrophotometer using distilled water as blank. A graph was plotted between the absorbance and temperature.

Procedure to Study the Effect of Heating Time

To study the effect of heating time on the color reaction, 1 ml Ibuprofen (1 mg/ml) was mixed with 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%) and the mixture was heated at 70 °C in a water bath for different time intervals. About 15 mixtures were studied.

After cooling, the volumes of the mixtures were made up to 10 ml using ethyl alcohol. Absorbance of these colored solutions was measured at 460 nm with spectrophotometer using distilled water as blank.

A graph was plotted between the heating time and the absorbance of the resulting colored solutions.

Procedure to Study the Effect of Colour Producing Agents

(a) α – Naphthylamine

To study the effect of concentration of α – Naphthylamine on the color of the reaction, various concentrations of α – Naphthylamine were mixed with 1 ml of Ibuprofen (1 mg/ml) and 1 ml of sodium nitrite (2%). The resulting mixtures were heated at 70 °C for 80 seconds in a water bath. These mixtures were cooled down and the volume of each was made up to 10 ml with ethanol. Absorbance of the resulting orange colored solutions was measured at 460 nm with spectrophotometer using distilled water as blank. A graph was plotted between the concentrations of α – Naphthylamine and absorbance,

(b) Sodium Nitrite

To study the effect of concentration of sodium nitrite on the color of the reaction, various concentrations of sodium nitrite were mixed with 1 ml of Ibuprofen (1 mg/ml) and 2 ml of α – naphthylamine (0.05%). The resulting mixtures were then cooled down and the volume of each was made up to 10 ml with ethanol. Absorbance of the resulting orange colored solutions was measured at 460 nm with spectrophotometer using distilled water as blank. A graph was plotted between the concentration of sodium nitrite and absorbance.

Procedure for the Construction of Calibration Curve for Ibuprofen

The different concentrations of Ibuprofen (0. α – 10) were mixed with 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%). These mixtures were heated at 70 °C for 80 seconds in a water bath. On getting cooled the volume of each mixture was made up to 10 ml using ethyl alcohol. The absorbance of each colored solution was measured at 460 nm using distilled water as blank. A graph was plotted between the concentration of Ibuprofen and absorbance obtaining a straight line. This was calibration curve for Ibuprofen.

Procedure to Study the Stability of Color with Time

To study the stability of color, 1 ml of Ibuprofen (1 mg/ml) was mixed with 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%) and the mixture was heated at 70 °C for 80 seconds in a water bath. The mixture was then cooled down and dilution was made up to 10 ml with ethyl alcohol.

Absorbance was noted after 20 minutes, 40 minutes, 60 minutes, 80 minutes, 100 minutes, 120 minutes and 140 minutes A graph was plotted between the time and abservance.

Procedure for the Determination of Ibuprofen from available Pharmaceutical Preparations

The contents of tablets containing Ibuprofen were dissolved in water and their solution was prepared by dissolving 100 mg of ibuprofen in 100 ml of water and alcohol (90 ml + 10 ml) to get (1 mg/ml)

solution. The solution was filtered and used for the determination of Ibuprofen present in tablets using the developed method. The amount of Ibuprofen determined by the developed method was compared with the amounts present in different pharmaceutical preparations and percentage error was calculated.

Procedure to Study the Interferences of various Organic Compounds

1 ml of Ibuprofen (1 mg/ml) was mixed with 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%) and different amounts were heated at 70 °C for 80 seconds in a water bath. After cooling the volume was made up to 10 ml with ethyl alcohol for each reading. Absorbance was measured at 460 nm with a spectrophotometer using distilled water as blank. The amount of each interfering organic compound was increased or decreased till it showed the absorbance range of the test solution. Percentage amounts of various organic compounds which do not interfere during the determination of Ibuprofen by the developed method were calculated.

Procedure for Calculation of Relative Standard Deviation

For the calculation of the relative standard deviation, various concentrations of Ibuprofen were mixed with 2 ml of α – naphthylamine (0.05%) and 1 ml of sodium nitrite (2%). These mixtures were heated at 70 °C for 80 seconds in a water bath. The mixtures were cooled down and the volume of each mixture was made up to 10 ml using ethyl alcohol. The absorbance was measured at 460 nm using distilled water as blank. The absorbance was measured for five times after going through same procedure and the amount of Ibuprofen was found for each determination. Mean amount of Ibuprofen was determined and then the relative standard deviation was calculated.

RESULTS

Results of various investigations made to develop a Spectrophotometric method for the determination of Ibuprofen are given below:

Determination of λ_{max}

A graph was plotted between absorbance and wavelength. It showed maximum absorbance at 460 nm as shown by figure 1.

Effect of Temperature

The results are show by figure 2. Maximum colour results when reaction mixture is heated at 70 °C and the absorbance are taken at 460 nm wavelengths.

Effect of Heating Time

The results are show by figure 3. The maximum colour is obtained by heating the mixture for 80 seconds at 70 °C.

Effect of Reagent α - Naphthylamine

1 mg/10ml of (0.05%) α – Naphthylamine gives maximum color. It is shown by figure 4.

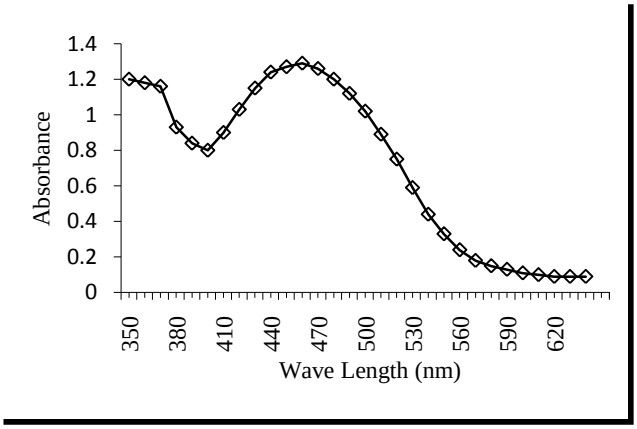

Figure 1: Absorption Spectra of Ibuprofen with α - Naphtylamine and Sodium Nitrite

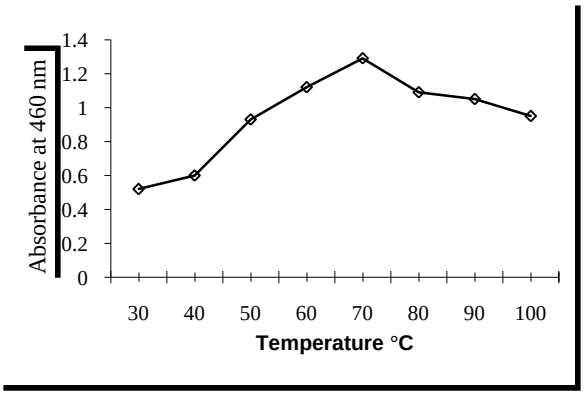

Figure 2: Effect of Temperature

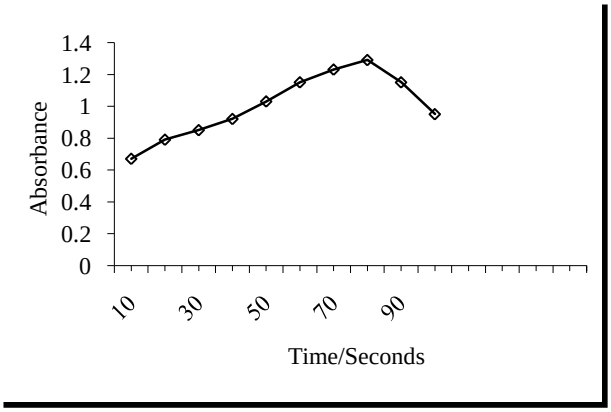

Figure 3: Effect of heating time

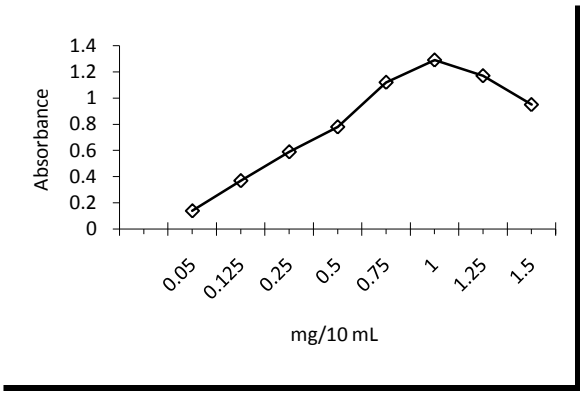

Figure 4: Effect of α - Naphthylamine

Effect of Reagent, Sodium Nitrite

It is clear that 20mg/10ml of Sodium Nitrite gives maximum color as shown by figure 5.

Calibration Curve for Ibuprofen

A graph was plotted between the amount of Ibuprofen per 10 ml and absorbance. A straight line was obtained up to 10mg/10 ml as shown in figure 6.

This indicates that Beer's law is valid in the concentration range 0. α – 10 mg/10 ml.

Stability of colour with time

Figure 7 show that there is no effect of time on stability of colour, and the colour is stable over a wide range of time.

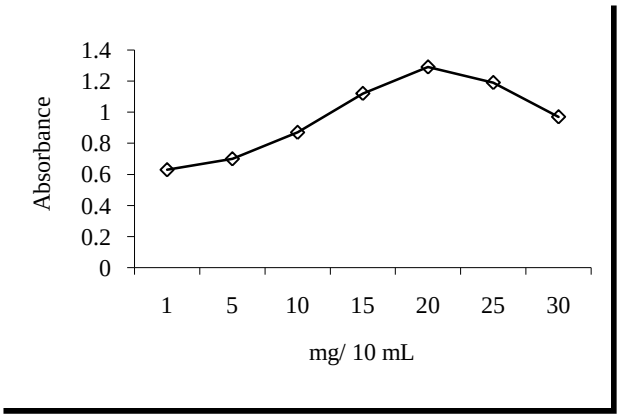

Figure 5: Effect of Sodium Nitrite

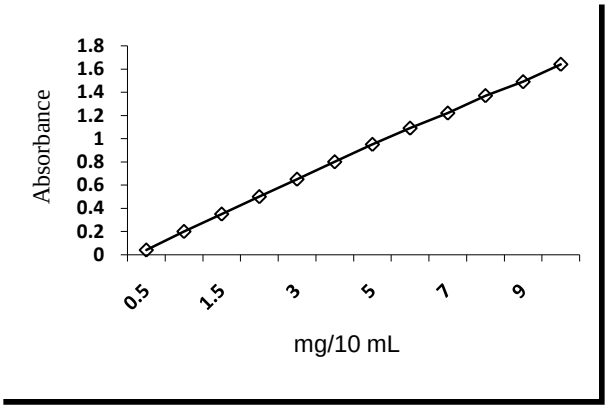

Figure 6: Calibration Curve of buprofen with 1 - Naphthylamine and Sodium Nitrite

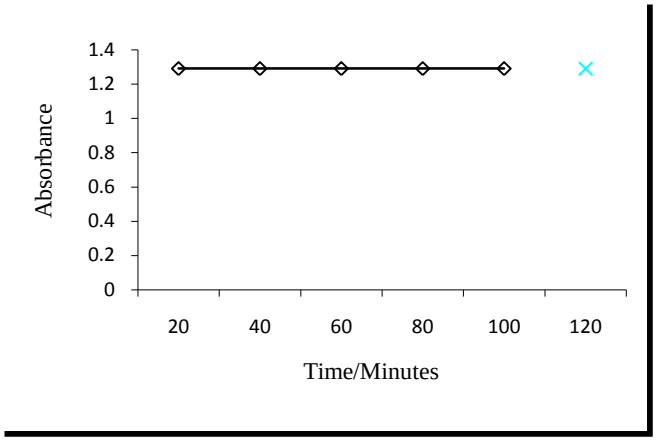

Figure 7: Effect of Time on Color Stability

Determination of Ibuprofen from Pure Solution

It is shown in Table 1.

Table 1:

Ibuprofen Taken (mg/mL)	Ibuprofen found (mg/mL)	Relative Standard Deviation* (%)
0.1	0.126	1.25
0.2	0.201	0.78
0.3	0.305	0.51
0.4	0.400	0.00
0.5	0.500	0.00
1.0	1.04	0.15
2.0	2.02	0.078
3.0	3.00	0.00

* Every reading is an average of five readings.

Determination of Ibuprofen from available Pharmaceutical Preparations

The amount of the Ibuprofen present in pharmaceutical preparations by the developed method was determined. The results are shown in the table 2.

Table 2:

Trade Name	Amount present Manufacturer's Specification (mg)	Amount Found (mg)	Relative Standard Deviation* (%)
Dolofen (Ali Gohar Pharmaceutics)	400	400.5	0.18
Brufen (Knoll Pharmaceutics)	50	49.96	0.15
Brufen (Knoll Pharmaceutics)	200	198.9	.30
Brufen Retard(Knoll Pharmaceutics)	400	400	0.00

* Every reading is an average of five readings.

Quantitative Assessment of Tolerable Amounts of Other Drugs

The interference of various organic compounds in the determination of Ibuprofen was studied. The results are given in table 3.

Table 3:

Drugs	**Maximum Amount* not interfering (%)**
Mefenamic Acid	100
Piroxicam	75.0
Hydroxyzime – HCL	50.0
Indomethacin	200
Nefopam	150
Phenytoin Sodium	25.0
Chlorpromazine – HCL	75.0
Baclofen	15.0
Nitrazepam	100
Salicylic acid	200
Amitryptyline – HCl	150
Clonazepam	25.0

*To an aliquot containing 1 mg/ml of Ibuprofen, different amounts of various interfering drugs were added individually under experimental conditions. The value is the percentage of the drugs with respect to the amount of Ibuprofen.

Optical Characteristics, Precision and Accuracy of the Proposed Method

The statistical parameters which show reproducibility, sensitivity, validity and reliability for the calibration curve were calculated. These are summarized in the table given below in Table 4.

Table 4:

Parameters	***Values***
λ_{max} (nm)	460
Beer's Law limits (mg/10ml conc.)	0.α – 10
Molar Absorptivity ($mol^{-1}cm^{-1}$)	2.65×10^2
Limit of Detection (mg/ml)	0.01
Regression Equation (Y)* Slope (m) Intercept (b)	 0.132 0.0353
Correlation Coefficient (r)	0.9992
RSD** (%)	1.25
% Range of Error (confidence limits) at 95% confidence level	49.95 $\pm$ 0.025
Optimum Photometric Range (mg/10 ml)	0.α – 10

*Y=mX + b, where X is the concentration of analyte (mg/10ml) and Y is the absorbance unit.

**Calculated from five determinations.

DISCUSSION

Ibuprofen reacts with α–naphthylamine and sodium nitrite when heated for 80 seconds at 70 °C to give an orange complex, the absorption spectrum of which, under optimum conditions lies at 460 nm (Figure 1).

So, all the measurements were carried out at the wavelength 460 nm. It was found that heating for 80 seconds at 70 °C in a water bath gave maximum color intensity (Figure 3).

The effect of color producing reagents α – naphthylamine and sodium nitrite is shown in Figure 4 and Figure 5 respectively. It was found that 1 mg/ 10ml of α – naphthylamine and 20 mg/10 ml of sodium nitrite gave maximum color intensity. Above and below these concentration ranges in color intensity was decreased.

Beer's Law was obeyed between the concentration range 0.01 mg/ml to 1 mg/ml as shown in Figure 6.

Effect of time on the stability of color is shown in Figure 7. It was found that the color is stable for more than 120 minutes. So, all the readings were carried out within this time period. During all the experiments total volume of test solutions was made up to 10 ml with alcohol.

The developed method was applied for the determination of Ibuprofen from pure solution as shown in table 1 and 4 which show the repeatability, sensitivity and validity of the method. It is also reasonably precise and accurate, as the amount of the above procedure does not exceed the relative standard deviation 1.25% which is the replicate of five determinations of table 1. The optimization has been done at lower analyte concentration.

The quantitative assessment of tolerable amounts of different organic compounds (w/v) under the experimental conditions is given in table 3. Various amounts of diverse interfering organic compounds were added to a fixed amount of Ibuprofen (1mg/ml) and the recommended procedure for the spectrophotometric determination was followed. The proposed method is successfully applied for the quality control of pure Ibuprofen and in pharmaceutical dosage form as shown in table 2.

CONCLUSION

The spectrophotometric method for the determination of Ibuprofen is simple, reliable and sensitive. There is no need for pH control. The color reaction does not require stringent conditions nor many reagents or solvents. It is specific for Ibuprofen.

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