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Development of validated UV spectroscopic method to estimate dexibuprofen from its formulation by hydrotrophy technique

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ABSTRACT

The present study was aimed to develop a hydrotrophy technique to increase the solubility of poorly water soluble drug. This technique is used to estimate the amount of Dexibuprofen in bulk drug and tablets by spectrophotometric method by using tri sodium citrate as hydrotropic agent. Beer's law was obeyed in the concentration range of 2-20µg/ml and showed maximum absorbance at 231nm. The solubility of Dexibuprofen in distilled water was found to be very less and then by adding hydrotropic agent solubility was increased as compared with distilled water. The analysis of tablets indicated good correlation between estimated and label claim. The LOD and LOQ of Dexibuprofen was found to be 0.0544µg/ml and 0.169µg/ml respectively indicated good sensitivity of proposed method. The percentage recovery was found to be 99.18%-99.607%. The proposed method is new, simple, accurate, non-toxic and precise method that can be successfully employed for estimation of drugs in routine analysis of tablets.

Key Words: Hydrotrophy technique, Dexibuprofen, Tri sodium citrate, solubilisation, UV spectrophotometry**.**

INTRODUCTION

Increasing the aqueous solubility of insoluble and slightly soluble drugs is major importance. This is because most of the newly developed drugs are highly lipophilic in nature and its analysis was mainly carried out using organic solvents like methanol, chloroform, ethanol, benzene, acetone, toluene, carbon tetrachloride, diethyl ether and acetonitrile. Most of these organic solvents are toxic, volatile and costlier. This may cause inaccuracy in analytical methods. Various techniques have been employed by the researchers to improve the aqueous solubility of lipophilic drugs and hydrotropy is one among them [1]. Hydrotropy can be considered to be potentially and industrially attractive technique since the observed increase in solubility is much higher than that affected by other solubilization method. Several works have been reported on use of hydrotropic solvents in estimation of various poorly water soluble drugs using some of the hydrotropic agents like sodium benzoate, sodium salicylate, niacinamide, sodium ascorbate, and urea [2-5]. But it was observed that hydrotropy is another type of cosolvency, which is utilized to improve the aqueous solubility of poorly water soluble drugs. Based on this approach to increase solubility of lipophilic model drug Dexibuprofen. These hydrotropic agents do not cause any toxicity and non-volatile in nature. In the present work the total concentration of hydrotropic agent was kept constant (30% w/v). Dexibuprofen is a non-steroidal anti-inflammatory drug. Its anti-inflammatory effects are believed to be due to inhibition of both COX-1and COX-2 which leads to the inhibition of prostaglandin synthesis. The chemical name is (2S)-2-[4-(2-methylpropyl) phenyl] propanoic acid. Fig1

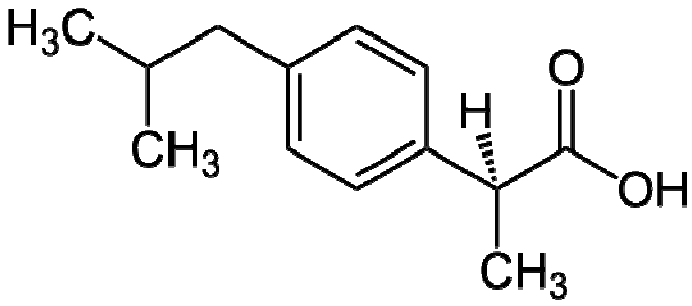

Figure 1: Structure of Dexibuprofen

It is slightly soluble in water, whereas freely soluble in methanol, chloroform and benzene. Literature survey revealed no hydrotropic solubilisation technique has been reported for analysis of Dexibuprofen [6-11]. Hence the current study aims at developing hydrotropic solubilisation technique and UV method for analysis of dexibuprofen from its bulk drug and formulations.

MATERIALS AND METHODS

Dexibuprofen bulk drug was gift sample from MSN Labs, Hyderabad, India. The Dexibuprofen formulation (capsules) was received from local market. Shimadzu UV/Visible recording spectrophotometer (model-UV-1601) with 1cm matched silica cells was employed. All other chemicals and solvents used were of analytical grade.

Selection of hydrotropic solubilising additive:
Various hydrotropic solubilising additives like Urea, Sodium acetate, Sodium benzoate, tri sodium citrate, Sodium salicylate etc. were tried. The Urea and sodium benzoate on addition to drug solution causes sedimentation of drug. Addition of niacinamide leads to turbidity. The tri sodium citrate renders complete solubilisation of drug. Hence tri sodium citrate was selected as hydrotropic solubilising additive. The volume of trisodium citrate added to solubilize dexibuprofen was optimized to be in the ratio of 4:1.

Preparation of the standard stock and calibration curve
An accurately weighed 100mg quantity of Dexibuprofen was transferred into a 100 ml volumetric flask. To this, 40ml of Tri sodium citrate solution was added and the flask was shaken for 1 mins to solubilise the drug and the volume was made up to the mark with Distilled water to get a standard stock solution of 1mg/ml. This stock solution used for further dilutions and by using distilled water as solvent for estimation.

The absorption maxima of dexibuprofen were found to be 231 nm (Fig.1). Working standard solutions ranging from concentration of 2 to10µg/ml was prepared with distilled water from the stock solution. The absorbances of resulting solutions were measured at wavelength of 231nm against solvent blank and a calibration curve was plotted to get the linearity and regression equation. Fig 2.

Analysis of dexibuprofen in capsules using mixed co solvents
Weigh accurately about 10 capsules powder and take 100mg equivalent quantity of Dexibuprofen and transfer into a 100ml standard flask. And add 40 ml of trisodium citrate and remaining volume make up to mark with distilled water by using ultrasonication. Then pipette out 1ml of solution and make up to 100ml leads to 10µg/ml concentration solution. The absorbance of the resulting solution was measured at 231nm against solvent blank and drug content was calculated.

Validation of the proposed method
The proposed method was validated for the following parameters. [12-15]

Precision
Precision was determined by studying the repeatability and intermediate precision. The standard deviation, coefficient of variance and standard error were calculated for the drug.

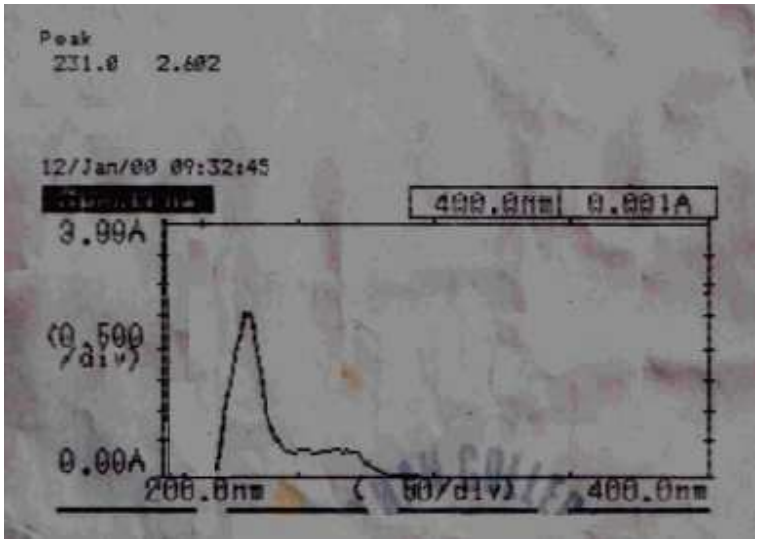

Fig.2

Inter- day and Intra- day precision

The intra-day concentration of the drug was calculated on the same day at an interval of two hour. Whereas the inter day concentration of drug was calculated on three different days within the laboratory conditions.

Table4: Intra-day and inter-day precision

Sample (µg/ml)	Intra-day precision		Inter-day precision	
	Absorbance	RSD	Absorbance	RSD
2	0.045 0.051 0.042	0.099	0.043 0.039 0.037	0.077
4	0.096 0.094 0.095	0.015	0.097 0.093 0.088	0.048

Linearity

The absorbance of appropriate dilutions of standard stock solutions were measured as per the developed method to confirm the linearity.

Limit of detection (LOD) and Limit of Quantitation (LOQ)

The LOD and LOQ of dexibuprofen by the proposed method were determined using calibration standards. LOD and LOQ were calculated as 3.3σ /S and 10σ/S, respectively, where S is the slope of the calibration curve and σ is the standard deviation of response

Accuracy

Accuracy is the percentage of analytes recovered by assay from known added amount. Analysis was performed at 80%, 100%, 120% levels.

Recovery studies

In order to check the accuracy and reproducibility of the proposed method, recovery studies were conducted. Recovery studies are done spiking method in this method the test sample having the concentration of 10µg/ml . to this the standard drug is spiked by adding into the test solution. A concentrations of 8, 10 and 12µg/ml are added to the sample solutions and the absorbance of the three spiked concentrations were taken. From this absorbance we can determine the amount of drug that can be recovered by the proposed method.

Molar Absorptivity

This is the important factor for determining the absorptive property of a drug in 1 mole concentration. And this value can be useful in determining the absorbance of drug in molar concentrations. This for identifying the shifts of the maximum absorbance of the drug during the method development.

RESULTS AND DISCUSSION

The solubility studies showed that aqueous solubility of dexibuprofen was increased by adding tri sodium citrate as hydrotropic solubilising agent. The Beer- Lambert's concentration range for dexibuprofen was between 2-10µg/ml. To check drug stability and precipitation of drug in solvent, a part of solution were kept in room temperature for 48 hours. The results revealed that estimation dexibuprofen can be done without substantial effect on drug stability as no precipitation was observed. From this study it is obvious that there was no interference of tri sodium citrate in estimation of dexibuprofen at the wavelength of 231nm.

Table1: Method Validation Parameters of Dexibuprofen

Parameters	Results
λ_{max}	231 nm
Beer's law limit	2-20 µg/ml
Molar absorptivity	x 10^4 L $mole^{-1}$ cm^{-1}
Regression equation (Y = mx + c)	y = 0.0206x + 0.00333
Slope (m)	0.0206
Intercept (c)	0.00333
Correlation coefficient (r)	0.992
Relative standard deviation (%)	0.099
LOD Value	0.0544
LOQ Value	0.169

Table 2: Recovery studies (accuracy parameter) of Dexibuprofen

Test µg/ml	Amount of standard drug added µg/ml	%Recovery	Standard deviation	%RSD
10	8	99.18	0.301	0.303
	10	99.607	0.331	0.331
	12	101.58	0.548	0.546

Table 3: Analysis of tablet formulations of dexibuprofen

Drug	Label claim mg/cap	Amount found	%Purity
Dexibuprofen	100	98.87 ±0.218	99.53 %w/w

The estimated label claim in the 30% mixed co-solvents was found to be 98.87 ± 0.218 indicating good correlation between estimated and those claimed by the manufacturers. The results of percent label claim were shown in Table 2. The recovery studies showed proposed method is accurate and reproducible. The results of recovery study revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed method. Accuracy, reproducibility and precision of the proposed methods were further confirmed by percent recovery values, which were close to 100 with low values of standard deviation as shown in Table 3. Repeatability results indicated the precision under the same operating conditions over a short interval time and inter-assay precision. Intermediate precision study expresses within laboratory variation in different days. In both intra and inter-day precision study for the method co-efficient of variation were not more than 1.0% indicates good intermediate precision. The low values of LOD and LOQ, 0.054 and 0.169 for dexibuprofen indicates good sensitivity of proposed method. (Table 1).

CONCLUSION

This current investigation is intended to use hydrotrophy technique to develop UV specrophotometric method to determine the assay of dexibuprofen. The method was validated, for both bulk and formulations. This method involves direct analysis without any extraction steps, thus it is performed faster, simple and easier. And this method is shown accurate and précised results. By these results this method found to be rapid, simple, accurate, economic method for analysis and quality determination.

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