



Estimation of Nimesulide using mixed solvency approach

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Abstract

Organic solvents are most frequently employed in spectrophotometric analyses. They may be sources of pollution. Some of them may be toxic while others may be costlier. Volatility may be a source of inaccuracy in spectrophotometric estimations. In the present investigation, it was proposed to solubilize Nimesulide by use of mixed solvency concept. Nimesulide shows maximum absorbance in the concentration range of 10-50 µg/ml at 390 nm. Method of analyses have been validated for different parameters like linearity, accuracy, precision, LOD and LOQ. The percent drug estimated in tablet formulation of Batch-I and of Batch-II were 100.16±0.260 and 99.96±0.283 respectively. The range of percent recoveries varied from 100.36±0.175 to 101.23±0.371. Sodium Benzoate and phenol do not interfere above 300 nm. The analytical method was found to be simple, safe (free from toxicity), economic and eco-friendly.

Keywords: Nimesulide, UV-Spectrophotometry, solid dosage formulation, mixed solvency concept

Introduction

Increasing the aqueous solubility of Insoluble and slightly soluble drugs has been done by various methods to avoid the usage of organic solvents. Because of toxicity, volatility, and also high cost of organic solvents, an alternative method has been developed. Mixed solvency concept is one of the methods to enhance the aqueous solubility of less water soluble drugs. Mixed solvency concept may be a proper choice to preclude the use of organic solvents. So there is a broad scope for mixed solvency concept in quantitative estimation of other less water soluble drugs.

By application of this concept, innumerable solvent system can be developed. Maheshwari¹⁻⁶ is one of the opinions that each substance possesses solubilizing power. He has given

several ecofriendly methods in the area of drug estimations and formulations precluding the use of toxic organic solvents. The solubility of large number of poorly soluble drugs has been enhanced by mixed solvency concept¹⁻³¹.

The present research work also provides an ecofriendly method to estimate spectrophotometrically, the Nimesulide drug in tablet formulations without the help of organic solvent.

Nimesulide is chemically N-(4-nitro-2-phenoxyphenyl) methane sulfonamide. It is Odorless yellow crystalline powder.

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Nimesulide is soluble in ethanol, DMSO AND DMF, practically insoluble in water. Nimesulide is a nonsteroidal aryl sulfonamide with anti-inflammatory properties. The drug Nimesulide in distilled water at room temperature was found to be practically insoluble. Approximate solubility of Nimesulide in blend (15% Sodium Benzoate and 25% phenol) was more than 2.5% w/v.

Material and Methods

Chemicals and Reagents

Pharmaceutical grade Nimesulide was a gift from Modern Laboratories Pvt. Ltd. Indore and its dosage formulation Nicip was purchased from local market. All other chemicals were of analytical grade.

Instrumentation

UV Visible spectrophotometer (Model 1800, Shimadzu, Japan) with 10 –mm path length connected to a computer was used for spectrophotometric analysis.

Calibration curve

Standard stock solution of Nimesulide (5000µg/ml) was prepared by weighing 50 mg of Nimesulide and transferred to a 10 ml volumetric flask and was dissolved in sufficient blend of 15% Sodium Benzoate and 25% phenol. Then finally volume was made up to 10ml with the same blend to get a concentration of 5000 µg/ml. Appropriate volumes of this solution were further diluted with distilled water to obtain final concentrations in the range of 10-50 µg/ml. The absorbances of these standard solutions were noted at 390 nm against respective reagent blanks.

Table 1: Data of calibration curve

S. No.	Concentration (µg/ml)	Stock Solution in (ml)	Final volume with distilled water(ml)	Absorption
1	10	0.2	100	0.307
2	20	0.4	100	0.613
3	30	0.6	100	0.910
4	40	0.8	100	1.224
5	50	1.0	100	1.532

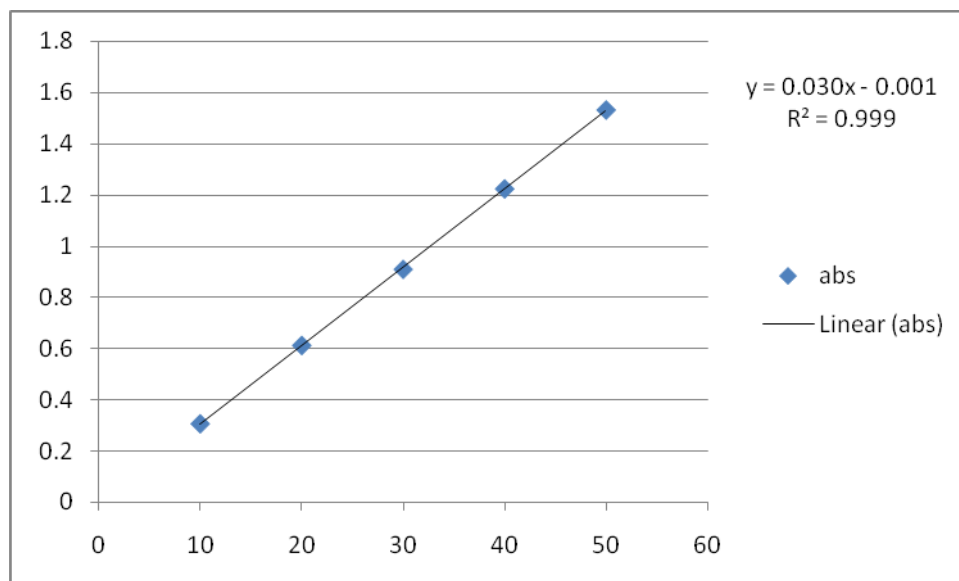


Fig. 1: Calibration curve of Nimesulide

Preliminary solubility studies

To determine the solubility of the drug in distilled water and mixed solvent blend (containing 15% Sodium Benzoate and 25% phenol) at room

temperature sufficient excess amount of the drug was added to a 25 ml capacity vial containing distilled water and the mixed solvent blend. After putting the vial cap and applying the aluminum seal, the vial was shaken mechanically for 12 hours at room temperature (27°C) in an orbital flask shaker. The solution was allowed to equilibrate for 24 hours undisturbed and then filtration was done through Whatmann filter paper#41. The filtrate was appropriately diluted with distilled water to measure the absorbance at 390 nm against reagent blanks.

Proposed method of analysis

20 tablets of tablet formulation-I were accurately weighed and finely powdered. Amount of powder equivalent to 50 mg of bulk drug was transferred

into 10 ml volumetric flask with 6 ml of blend (15% Sodium Benzoate and 25% phenol) and the drug present in tablet powder was dissolved by sonication for 20 minutes. The flask was filled to the mark with the same blend and the resulting solution was filtered through Whatmann filter paper no.41. One ml of the above filtrate was diluted to 100 ml. Method was followed as described under analytical procedure and the absorbance was noted at 390 nm against the reagent blank. The drug content was calculated using the calibration curve. Same procedure was repeated for the tablet formulation II. The results of analysis are reported in Table-2. All analyses were performed thrice.

Table 2: Analysis data of Nimesulide tablet formulations with statistical evaluation (n=3)

Drug	Batch	Label claim mg/tab	% Labeled claim estimated (mean ±SD)	Percent coefficient of variation	Standard Error
Nimesulide	I	100	100.16±0.260	0.260	0.150
Nimesulide	II	100	99.96±0.283	0.283	0.163

Recovery studies

To perform the recovery studies, standard Nimesulide drug was added (40mg, 50mg and 60mg separately) to the pre-analyzed tablet

powder equivalent to 50 mg of Nimesulide and the drug content was determined by the proposed method. Results of analysis were reported in Table3.

Table 3: Results of recovery studies with statistical evaluation (n=3)

Tablet Formulation	Drug in Pre-Analyzed tablet powder(mg)	Amount of standard drug added(mg)	% Recovery estimated (mean±SD)	Percent coefficient of variation	Standard error
I	50	40	100.66±0.378	0.376	0.218
I	50	50	100.50±0.254	0.252	0.145
I	50	60	100.36±0.175	0.175	0.101
II	50	40	100.98±0.095	0.094	0.054
II	50	50	101.23±0.371	0.369	0.215
II	50	60	100.98±0.627	0.621	0.362

Results and Discussion

The developed UV-spectrophotometric method was validated as per ICH guidelines in terms of linearity, and range, specificity, precision, sensitivity and accuracy.

In order to determine linearity range of developed method, a series of solutions were prepared using Nimesulide stock solution at concentration range

of 10-50µg/ml. The absorbances of the resultant solutions were measured at 390 nm against reagent blank. The calibration curves were

constructed by plotting concentration on X axis and absorbance on Y axis. R^2 value not less

than 0.999 was regarded as acceptance criteria (Figure 1)

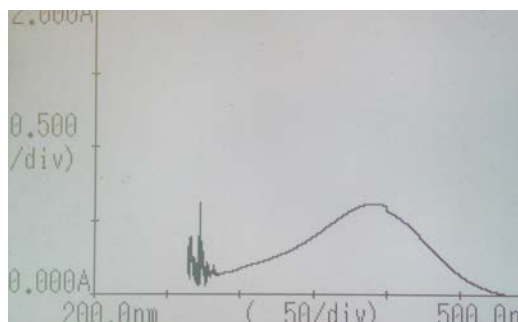


Fig. 2: UV Spectrum of Nimesulide

Table 4: Developed UV method specification

Instrument and specification	UV-Spectrophotometer Shimadzu 1800
Scanning Range	200 nm to 400 nm
Solvent Used	Hydrotropic solvent
Strength of Solvent	15% Sodium Benzoate and 25% phenol
Composition of Solvent	15% Sodium Benzoate and 25% phenol
Wavelength Maxima of Nimesulide	390 nm

Specificity was performed to exclude the possibilities of interference of solvent in the region of maximum absorbance peaks of Nimesulide. The specificity of the method was tested under the normal conditions and results of the tests proved that the components other than Nimesulide did not produce the deductible peaks at the maximum absorbance peaks of the drug.

Accuracy of the developed method was determined by recovery studies at three different levels. The pre analyzed samples were spiked with 80, 100 and 120% of mixed standard solution. The mixtures were analyzed and the recoveries were determined. The recovery study was carried out in triplicate. The mean % recovery of the Nimesulide at each level should not be less than 98% and not more than 102% was considered as the acceptance criteria.

Precision was studied to find out intra- day and inter-day variations in the test method of Nimesulide, Intra- day assay precision was found by analysis of standard drug thrice on the same day in different intervals of time. Inter-day assay

precision was carried out on three different days and percentage relative standard deviation (%RSD) was calculated. The %RSD should not be more than 2.0%.

Sensitivity of proposed method was estimated in terms of limit of Detection (LOD) and Limit of quantification (LOQ). The LOD and LOQ of Nimesulide by proposed methods were determined using calibration standards. LOD and LOQ were calculated as $3.3s/S$ and $10s/S$ respectively, where S is the slope of calibration curve and s is standard deviation of response.

The solubility of Nimesulide in distilled water at room temperature was found to be very less. Approximate solubility of Nimesulide in blend was more than 2.5% w/v.

It is evident from table-2 that the percent drug estimated in tablet formulation of Batch-I and of Batch-II were 100.16 ± 0.260 and 99.96 ± 0.283 respectively. The values are very close to 100, indicating the precision of the proposed analytical method. Further table-3 shows that the range of percent recoveries varied from 100.36 ± 0.175 to 101.23 ± 0.371 which are again very close to 100, indicating the accuracy of the proposed method. Proposed analytical method is further supported by significantly small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (table 3).

The limit of detection was found to be $0.770 \mu\text{g/ml}$ and the limit of quantification was found to be $2.310 \mu\text{g/ml}$.

Conclusion

A rapid, simple, and non toxic UV spectrophotometric method has been developed for the determination and quantification of Nimesulide. The present method also validated as per ICH guidelines for linearity, precision, accuracy. The results of all these parameter shows that the present UV spectrophotometric methods found to be precise, linear, rapid, and accurate and can be used for routine quality control analysis of Nimesulide in tablet dosage formulation in any laboratory.

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