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Development and validation of simple UV-Spectrophotometric method of quantization of indomethacin in solid dosage formulation using mixed solvency concept

Sanjay Jain, RK Maheshwari, Rajesh Kumar Nema and Indrajeet Singhvi

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 Indomethacin by use of mixed solvency concept. Indomethacin shows maximum absorbance in the concentration range of 10-50 μ g/ml at 320 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 101.25 \pm 0.05 and 100.78 \pm 0.10 respectively. The range of percent recoveries varied from 100.61 \pm 0.349 to 101.50 \pm 0.330. Sodium Benzoate, Niacinamide and sodium Caprylate do not interfere above 300 nm. The analytical method was found to be simple, safe (free from toxicity), economic and eco-friendly.

Keywords: Indomethacin, 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. Maheshwari^[1-6] 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 concept^[1-25].

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

Indomethacin is chemically 2-[1-(4-chlorobenzoyl)-5-methoxy-2-methylindol-3-yl] acetic acid. It is Pale-yellow to yellow-tan, crystalline powder. It is Soluble in ethanol, ether, acetone, castor oil; practically insoluble in water. Indomethacin is a non-steroidal anti-inflammatory agent (NSAID) that inhibits the enzyme cyclooxygenase necessary for the formation of prostaglandins and other autacoids. It also inhibits the motility of polymorphonuclear leukocytes.

Experimental

Chemicals and Reagents

Pharmaceutical grade Indomethacin was a gift from Modern Laboratories Pvt. Ltd. Indore and its dosage formulation Lasix 40 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 Indomethacin (5000µg/ml) was prepared by weighing 50 mg of Indomethacin and transferred to a 10 ml volumetric flask and was dissolved in sufficient

blend of 10% Sodium caprylate, 10% Sodium Benzoate and 10% Niacinamide. 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 330 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)	Absorbtion
1	10	0.2	100	0.165
2	20	0.4	100	0.329
3	30	0.6	100	0.493
4	40	0.8	100	0.658
5	50	1.0	100	0.828

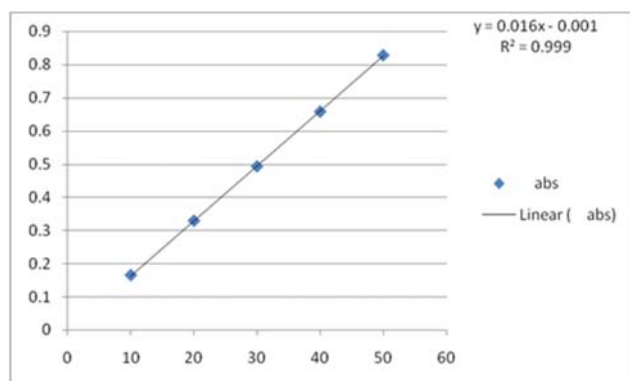


Fig 1: Calibration curve of Indomethacin

Preliminary solubility studies

To determine the solubility of the drug in distilled water and mixed solvent blend (containing 10% Sodium caprylate, 10% Sodium Benzoate and 10% Niacinamide) 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 330 nm against reagent blanks.

Proposed method of analysis

20 capsules of capsule formulation-I were accurately weighed and emptied to get powder. Amount of powder equivalent to 50 mg of bulk drug was transferred into 10 ml volumetric flask with 6 ml of blend (10% Sodium caprylate, 10% Sodium Benzoate and 10% Niacinamide) and the drug present in capsule 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 320 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 Indomethacin capsule formulations with statistical evaluation (n=3)

Drug	Batch	Label claim mg/cap	% Labeled claim estimated (mean ±SD)	Percent coefficient of variation	Standard Error
Indomethacin	I	25	101.25±0.050	0.049	0.028
Indomethacin	II	25	100.78±0.100	0.099	0.057

Recovery studies

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

analyzed tablet powder equivalent to 50 mg of Indomethacin 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 capsule powder(mg)	Amount of standard drug added(mg)	%Recovery estimated (mean±SD)	Percent coefficient of variation	Standard error
I	50	40	101.47±0.251	0.248	0.144
I	50	50	100.98±0.209	0.207	0.167
I	50	60	100.89±0.120	0.119	0.069
II	50	40	101.50±0.330	0.325	0.190
II	50	50	100.61±0.349	0.346	0.201
II	50	60	100.75±0.762	0.756	0.439

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 Indomethacin stock solution at concentration range of 10-50µg/ml. The absorbances of the resultant solutions were measured at 320

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)

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	10% Sodium caprylate, 10% Sodium Benzoate and 10% Niacinamide
Composition of Solvent	10% Sodium caprylate, 10% Sodium Benzoate and 10% Niacinamide
Wavelength Maxima of Indomethacin	320 nm

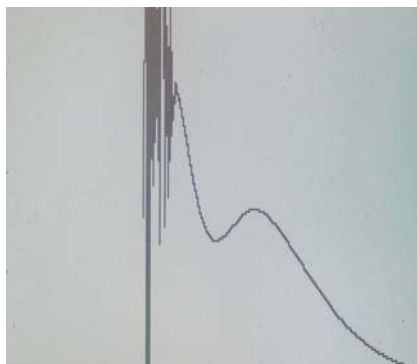


Fig 2: UV-Spectrum of Indomethacin

Specificity was performed to exclude the possibilities of interference of solvent in the region of maximum absorbance peaks of Indomethacin. The specificity of the method was tested under the normal conditions and results of the tests proved that the components other than Indomethacin 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 Indomethacin 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 Indomethacin, 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 Indomethacin 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 Indomethacin in distilled water at room temperature was found to be 0.009%. Approximate solubility of Indomethacin 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 101.25 ± 0.05 and 100.78 ± 0.10 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 100.61 ± 0.349 to 101.50 ± 0.330 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 $0.206 \mu\text{g/ml}$ and the limit of quantification was found to be $0.618 \mu\text{g/ml}$.

Conclusion

A rapid, simple, and non-toxic UV spectrophotometric method has been developed for the determination and quantification of Indomethacin. 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 Indomethacin in tablet dosage formulation in any laboratory.

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