

**NEW SPECTROPHOTOMETRIC ESTIMATION OF NIMESULIDE IN THE TABLETS
USING MIXED SOLVENCY APPROACH****Sanjay Jain^{1*}, R. K. Maheshwari², Rajesh Kumar Nema³ and Indrajeet Singhvi⁴**¹Research Scholar, Faculty of Pharmacy, Pacific Academy of Higher Education & Research University, Udaipur.²Department of Pharmacy, Shri G.S. Institute of Technology and Science, Indore 452003, Madhya Pradesh, India.³Lakshmi Narain College of Pharmacy (RCP), Indore 453331, Madhya Pradesh, India.⁴Department of Pharmacy, Pacific Academy of Higher Education & Research University, Udaipur, Rajasthan, India.**Corresponding Author: Dr. Sanjay Jain**

Research Scholar, Faculty of Pharmacy, Pacific Academy of Higher Education & Research University, Udaipur.

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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. 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.^[1-31]

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. 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.

EXPERIMENTAL**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 (5000 µg/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)	Absorbtion
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

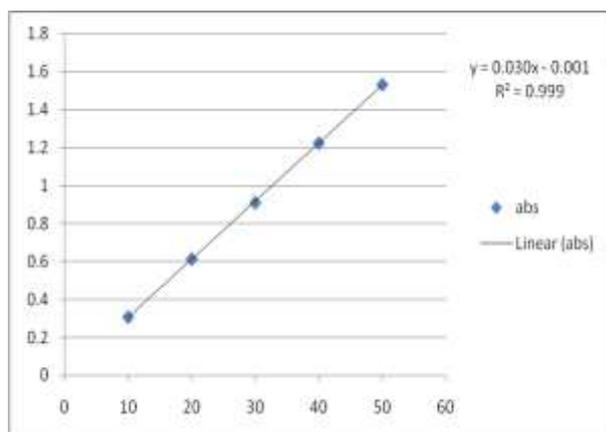


Figure 1: Calibration curve of Nimesulide.

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

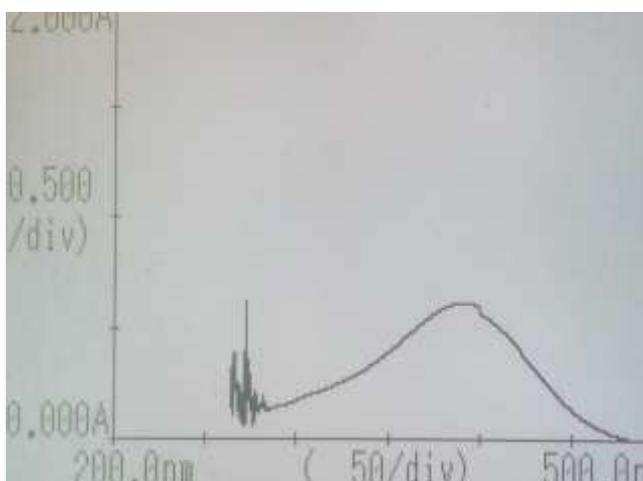
RESULTS AND DISCUSSION

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. R² 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	15% Sodium Benzoate and 25% phenol
Composition of Solvent	15% Sodium Benzoate and 25% phenol
Wavelength Maxima of Nimesulide	390 nm

**Figure 2: UV-Spectrum of Nimesulide.**

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 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 µg/ml and the limit of quantification was found to be 2.310 µg/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.

REFERENCES

1. Maheshwari RK. "Mixed-solvency approach"- Boon for solubilization of poorly water-soluble drugs. *Asian J Pharm*, 2010; 4(1): 60-3.
2. Maheshwari RK. Solubilization of ibuprofen by mixed solvency approach. *Indian Pharm*, 2009; 8(87): 81-4.
3. Maheshwari RK. "Mixed- solvency" – A novel concept for solubilization of poorly water-soluble drugs. *Delving J. Tech Eng Sci*, 2009; 1(1): 39-43.
4. Maheshwari RK. "Solid as solvent"- Novel spectrophotometric analysis of satranidazole tablets using phenol as solvent". *Indian Pharm*, 2014; 12: 37-40.
5. Maheshwari RK. "Solid as solvent"- Novel spectrophotometric analysis of norfloxacin tablets using phenol as solvent". *Int J Curr Pharm Res*, 2014; 6: 76-8.
6. Maheshwari RK. Potentiation of solvent character by mixed solvency concept: A novel concept of solubilization. *J Pharm Res*, 2010; 3(2): 411-3.
7. Maheshwari RK, Shilpkar R. Formulation development and evaluation of injection of poorly soluble drug using mixed solvency concept. *Int J Pharm Biosci*, 2012; 3(1): 179-89.
8. Maheshwari RK, Upadhyay N, Jain J, Patani M, Mathuria KC. New spectrophotometric estimation of naproxen tablet formulation employing mixed solvency concept (at 331 nm). *Int J Pharm Technol*, 2011; 3(4): 3618-23.
9. Maheshwari RK, Rajagopalan R. Formulation and evaluation of tinidazole syrup made by mixed-solvency concept. *Der Pharm Lett*, 2011; 3(6): 266-71.
10. Maheshwari RK, Karawande VU, Application of novel concept of mixed solvency in the design and development of floating microspheres of furosemide. *Int J Pharm Sci*, 2013; 15: 167-95.
11. Maheshwari RK, Upadhyay N, Jain J, Patani M, Pandey R. New spectrophotometric analysis of gatifloxacin tablets utilizing mixed solvency concept (at 288 nm). *Der Pharm Lett*, 2012; 4(1): 1-4.
12. Prashant B, Rawat S, Mahajan YY, Galgatte UC, Maheshwari RK. Formulation development and evaluation of aqueous injection of poorly soluble drug made by novel application of mixed solvency concept. *Int J Drug Delivery*, 2013; 2: 152-66.
13. Maheshwari RK, Rajagopalan R. Formulation and evaluation of paracetamol syrup made by mixed-solvency concept. *Der Pharm Lett*, 2012; 4(1): 170-4.
14. Chandna C, Maheshwari RK. Mixed solvency concept in reducing surfactant concentration of self emulsifying drug delivery systems of candesartan cilexetil using D-optimal mixture design. *Asian J Pharm*, 2013; 7(2): 83-91.
15. Maheshwari RK, Upadhyay N, Jain J, Patani M, Mathuria KC. New spectrophotometric estimation of naproxen tablet formulation employing mixed solvency concept (at 331 nm). *Int J Pharm Technol*, 2011; 3(4): 3618-23.
16. Agrawal A, Maheshwari RK. Formulation development and evaluation of in situ nasal gel of poorly water soluble drug using mixed solvency concept. *Asian J Pharm*, 2011; 5(3): 131-40.
17. Bhawsar N, Maheshwari RK, Ansari A, Saktawat Y. New spectrophotometric estimation of gatifloxacin in the tablets using mixed solvency approach. *Int J Pharm Sci*, 2011; 2(2): 270-4.
18. Soni LK, Solanki SS, Maheshwari RK. Solubilization of poorly water soluble drug using mixed solvency approach for aqueous injection. *Br J Pharm Res*, 2014; 4(5): 549-68.
19. Maheshwari RK, Gupta S, Gharia A, Garg SK, Shilpkar R. Simple eco-friendly spectrophotometric estimation of tinidazole tablets by application of mixed-solvency technique. *Bull Pharm Res*, 2011; 1(1): 22-5.
20. Maheshwari RK. "Solid as solvent"-Novel spectrophotometric analysis of tinidazole tablets using melted phenol as solvent. *Asian J Pharm Res*, 2015; 5(1): 21-24.
21. Maheshwari RK, Putliwala M, Padiyar A. Novel approach for spectrophotometric estimation of naproxen in tablet dosage form using solids (eutectic liquid of phenol and niacinamide) as solubilising agents. *Asian J Pharm Res*, 2015; 5(1): 25-28.
22. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Nifedipine in solid dosage formulation using mixed solvency concept. *World J of Pharm res*, 2017; 6(13): 1014-1021.
23. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Ondansetron hydrochloride in solid dosage formulation using mixed solvency concept. *International J of Pharm .sci. and drug research*, 2017; 9(5): 252-255
24. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Diazepam in solid dosage formulation using mixed

- solvency concept. International J of current Pharm res, 2017; 6(9): 15-17.
25. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Domperidone in solid dosage formulation using mixed solvency concept. A journal of drug design and discovery, 2017; 2(4): 19-23.
 26. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Domperidone in solid dosage formulation using mixed solvency concept. European journal of biomedical and pharmaceutical sciences, 2017; 4(12): 48-51.
 27. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. simultaneous estimation of ofloxacin and tinidazole in solid dosage form by u v Spectrophotometry using mixed solvency concept. European Journal of pharmaceutical and medical Research, 2017; 4(12): 413-418.
 28. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. simultaneous estimation of norfloxacin and tinidazole in solid dosage form by u v Spectrophotometry using mixed solvency concept. World Journal of pharmaceutical and medical Research, 2018; 4(1): 112-117.
 29. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Ornidazole in solid dosage formulation using mixed solvency concept. World journal of Pharmacy and pharmaceutical sciences, 2018; 1(7): 824-832.
 30. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. Development and validation of simple uv-spectrophotometric method of quantization of Indomethacin in solid dosage formulation using mixed solvency concept. The Pharma Innovation Journal, 2017; 6(12): 453-456.
 31. Jain Sanjay, Maheshwari RK, Nema RK, Singhvi I. New Spectrophotometric Estimation of Frusemide in the Tablets using mixed solvency concept Approach. International Journal of current Advanced Research, 2017; 6(12): 8510-8513.