WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 13, 1014-1021. Research Article ISSN 2277–7105

DEVELOPMENT AND VLAIDATION OF SIMPLE UV-SPECTROPHOTOMETRIC METHOD OF QUANTIZATION OF NIFEDIPINE IN SOLID DOSAGE FORMULATION USING MIXED SOLVENCY CONCEPT.

Sanjay Jain[1]*, R. K. Maheshwari[2], Rajesh Kumar Nema[3] and Indrajeet Singhvi[4]

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

[2]Department of Pharmacy, Shri G.S. Institute of Technology and Science, Indore 452003, Madhya Pradesh, India.

[3]Lakshmi Narain College of Pharmacy (RCP), Indore 453331, Madhya Pradesh, India.

[4]Department of Pharmacy, Pacific Academy of Higher Education & Research University, Udaipur, Rajasthan, India.

Article Received on
31 August 2017,

Revised on 21 Sept. 2017,
Accepted on 11 October 2017

DOI: 10.20959/wjpr201713-9919

***Corresponding Author**
Dr. Sanjay Jain
Research Scholar, Faculty of Pharmacy, Pacific Academy of Higher Education & Research University, Udaipur.

ABSTRACT

Commonly used organic solvents for spectrophotometric analysis of water insoluble drugs are methanol, ethanol, chloroform, benzene, toluene etc. The main drawbacks of organic solvents include high cost, toxicity and pollution. Organic solvents have numerous adverse effects caused by single exposure like dermatitis, headache, drowsiness, nausea, eye irritation and long term exposure causes serious effects such as neurological disorder, chronic renal failure and liver damage. They should be replaced by other ecofriendly alternative sources. The present study is an attempt to show that solid can also be used to act as solvent precluding the use of organic solvents. A simple, safe and sensitive method of spectrophotometric determination of Nifedipine obeyed beers law in the concentration range of 10-50 µg/ml at 340 nm. The results of analyses have been validated statistically for Linearity, accuracy, precision, LOD and LOQ. The results of validation parameters also indicated that proposed method was found to be accurate, precise, reproducible, sensitive, and suitable for routine quality control analysis for estimation of Nifedipine in solid dosage formulation.

KEYWORDS: Nifedipine, 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.[1,21]

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

Nifedipine is chemically 3, 5-dimethyl 2, 6-dimethyl-4-(2-nitrophenyl)-1, 4-dihydropyridine-3, 5-dicarboxylate. It is present as a yellow crystalline substance that can be dissolved in ethanol but not water. Nifedipine is classified in pharmacies as a calcium channel blocker. It effectively dilates blood vessels to lower blood pressure. It is also useful for chest pains, especially those diagnosed as vasopastic angina or chronic staple angina.

EXPERIMENTAL

Chemicals and Reagents

Pharmaceutical grade Nifedipine was a gift from Modern Laboratories Pvt. Ltd. and its dosage formulation Cardipin Retard (two different batches) were purchased from local market. All other chemicals were of analytical grade and obtained from BDH labs.

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 Nifedipine was (500µg/ml) prepared by weighing 50 mg of Nifedipine and transferred to a 100 ml volumetric flask and was dissolved in20 ml blend of 25% phenol and 15% sodium benzoate then finally volume was made up to 100ml with distilled water to get a concentration of 500 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 absorptions of these standard solutions were noted at 340 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	2	100	0.159
2	20	4	100	0.312
3	30	6	100	0.450
4	40	8	100	0.591
5	50	10	100	0.719

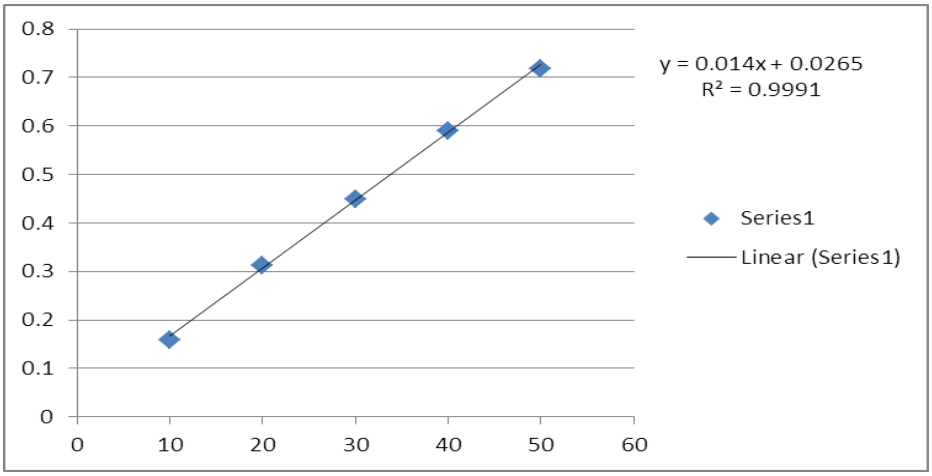

Figure 1: Calibration curve of Nifedipine at 340nm.

Preliminary solubility studies

To determine the solubility of the drug in distilled water and mixed solvent blend (containing 25% phenol and 15% sodium benzoate) 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 vials were shaken mechanically for 12 hours at room temperature (27^0C) 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 340 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 100 ml volumetric flask with 20 ml of blend (25%phenol and 15% sod. benzoate) and the drug present in tablet powder was dissolved by sonication for 20 minutes. The flask was filled to the mark with distilled water and the resulting solution was filtered. Five ml of the above filtrate was diluted to 100 ml. Method was followed as describe under analytical procedure and the absorbance was noted at 340 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.

Table 2 Analysis data of Nifedipine tablet formulations with statististical evaluation (n=3).

Drug	Batch	Label claim mg/tab	% Labeled claim estimated (mean ±SD)	Percent coefficient of variation	Standard Error
Nifedipine	**I**	**20**	**99.68±2.26**	**2.267**	**1.204**
Nifedipine	**II**	**20**	**100.06±1.06**	**1.050**	**0.612**

Recovery studies

To perform the recovery studies standard Nifedipine drug was added (40mg, 50mg and 60mg separately) to the pre-analyzed tablet powder equivalent to 50 mg of Nifedipine 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	99.97±0.845	0.845	0.487
I	50	50	101.32±0.596	0.588	0.344
I	50	60	100.73±0.239	0.237	0.137
II	50	40	101.34±0.578	0.570	0.333
II	50	50	100.56±0.472	0.469	0.272
II	50	60	101.15±0.222	0.219	0.128

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 Nifedipine stock solution at concentration range of 10-50µg/ml. The absorbances of the resultant solutions were measured at 340nm against reagent blank. The calibration curves were constructed by plotting concentration on X axis and absorbance on Y axis. R^2 value not less than0.999 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	25%phenol and 15% sod. benzoate
Composition of Solvent	25%phenol and 15% sod. benzoate
Wavelength Maxima of Nifedipine	340 nm

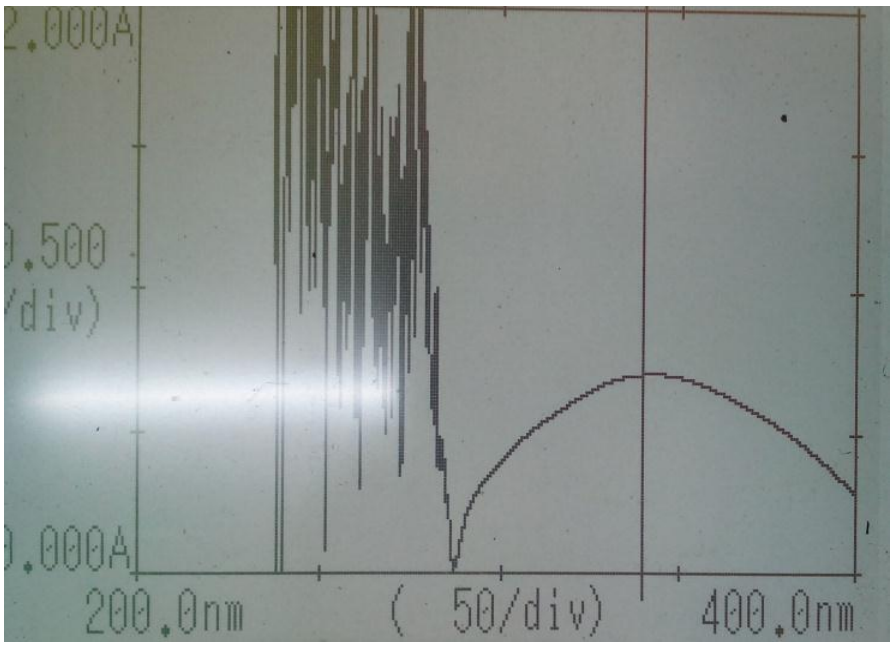

Fig.(2): UV-Spectrum of Nifedipine

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

Nifedipine is practically insoluble in distilled water at room temperature. The solubility of Nifedipine in blend was more than 5mg/ml.

It is evident from table-2 that the percent drug estimated in tablet formulation of Batch-I and of Batch-II were 99.68±2.26 and 100.06±1.06respectively. The values are very close to100, indicating the precision of the proposed analytical method. Further table-3 shows that the range of percent recoveries varied from 99.97±0.845 to 101.34±0.578 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 (table3).

The limit of detection was found to be 0.153 µg/ml and the limit of quantification was found to be 0.465 µg/ml.

CONCLUSION

A rapid, simple, and non toxic UV spectrophotometric method has been developed for the determination and quantification of Nifedipine. 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 Nifedipine in tablet dosage formulation in any laboratory. Phenol does not interfere above 300nm.

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.