



**“SOLID AS SOLVENT” - NOVEL APPROACH FOR
SPECTROPHOTOMETRIC ESTIMATION OF SOLID DOSAGE FORM
OF NALIDIXIC ACID USING SOLIDS (EUTECTIC LIQUID OF
PHENOL AND NIACINAMIDE) AS SOLUBILIZING AGENTS (MIXED
SOLVENCY CONCEPT)**

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ABSTRACT

The pollution and toxicity caused by most of the organic solvents is a big challenge. The researchers are doing much work to give eco-friendly solutions for this challenge. Maheshwari has given a nice concept, known as mixed-solvency concept. By application of this concept, innumerable solvent systems can be developed. Maheshwari is of the opinion that each substance possesses solubilizing power. He has given several eco-friendly methods in the area of drug estimations and formulations precluding the use of toxic organic solvents. The

present research work also provides an eco-friendly method to estimate spectrophotometrically, the nalidixic acid drug in tablet formulations without the help of organic solvent. The present investigation is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents. The main objective of the present study is to demonstrate the solvent action of solid. In the present study, a eutectic liquid (PNM 2510) obtained by triturating phenol crystals and niacinamide in 25:10 ratio on weight basis was employed to extract (dissolve) nalidixic acid drug from fine powder of tablets. Dilution was made with distilled water to carry out spectrophotometric estimation at 330 nm without the help of organic solvent. The solubility of nalidixic acid in distilled water at room temperature was found to be 0.21 mg/ml. The solubility of nalidixic acid in PNM

2510 was more than 138 mg per ml (of PNM 2510). Proposed spectrophotometric analytical method is novel, economic, eco-friendly, rapid, free from toxicity of organic solvent, accurate and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. The presence of tablet excipients, phenol and niacinamide did not interfere in the spectrophotometric estimation at 330 nm. Phenol and niacinamide do not interfere above 300 nm.

Keywords- Mixed-solvency concept, nalidixic acid, phenol, niacinamide, spectrophotometric analysis, eutectic liquid.

INTRODUCTION

Majority of drugs show the problem of poor solubility, whether in the case of their analytical estimations or in the field of liquid dosage forms in the form of solutions. Commonly used organic solvents for spectrophotometric analysis of water insoluble drugs include methanol, ethanol, chloroform, benzene, dichloromethane, dimethyl formamide, acetonitrile, ethyl acetate, toluene, carbon tetrachloride, acetone, hexane etc. The main drawbacks of organic solvents include high cost, toxicity and pollution. Organic solvents have innumerable adverse effects caused by single exposure like dermatitis, headache, drowsiness, nausea, eye irritation and long term exposure causes serious effects such as neurological disorders, chronic renal failure, liver damage, necrosis, mutagenesis disorder. They should be replaced by other eco-friendly alternative sources. The researchers are doing much work to give eco-friendly solutions for this challenge. Maheshwari ^[1-3] has given a nice concept, known as mixed-solvency concept. By application of this concept, innumerable solvent systems can be developed. Maheshwari is of the opinion that each substance possesses solubilizing power. He has given several eco-friendly methods in the area of drug estimations and formulations precluding the use of toxic organic solvents. The solubility of a large number of poorly soluble drugs has been enhanced by mixed solvency concept. ^[1-21]

The present investigation is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents. The main objective of the present study is to demonstrate the solvent action of solids. In the present study, a eutectic liquid obtained by triturating phenol crystals and niacinamide in 25:10 ratio on weight basis was employed to extract (dissolve) nalidixic acid drug from fine powder of its tablets. Dilution was made with distilled water to carry out spectrophotometric estimation at 330 nm without the help of organic solvent. Proposed method is novel, economic, eco-friendly, rapid, free from toxicity

of organic solvent, accurate and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. The presence of tablet excipients, phenol and niacinamide did not interfere in the spectrophotometric estimation at 330 nm. Phenol and niacinamide do not interfere above 300 nm.

MATERIALS AND METHODS

Nalidixic acid bulk drug sample was a generous gift by M/S Ranbaxy Laboratories Limited, Dewas (India). All other chemicals used were of analytical grade. Commercial tablets of nalidixic acid were procured from local market.

A Shimadzu-1700 UV visible spectrophotometer with 1 cm matched silica cells was used for spectrophotometric analysis.

Preparation of eutectic liquid - Phenol and niacinamide were triturated in 25:10 ratio on weight basis to obtain a eutectic liquid (PNM 2510).

Calibration curve- Accurately weighed 40 mg of nalidixic acid standard drug was transferred to a 10 ml volumetric flask. Eight ml of PNM 2510 was added and the flask was shaken to dissolve the drug. Then, the volume was made up to 10 ml with PNM 2510 and the flask was shaken to homogenize the contents. Then, 1 ml of this solution was transferred to another 10 ml volumetric flask and sufficient PNM 2510 was added to make the volume up to 10 ml producing a stock solution containing 400 µg/ml. This stock solution was suitably diluted with distilled water to obtain standard solutions of 10, 20, 30 and 40 µg/ml. The absorbances of these standard solutions were noted at 330 nm against respective reagent blank.

Preliminary solubility studies

To determine the solubility of the drug (nalidixic acid) in distilled water at room temperature, sufficient excess amount of the drug was added to a 25 ml capacity vial containing distilled water. After putting the vial cap and applying the aluminium seal, the vial was shaken mechanically for 12 hours at room temperature in an orbital flask shaker (Khera Instrument Pvt. Ltd., India). 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.

In order to determine the approximate solubility of drug in PNM 2510, 1 ml of PNM 2510 was transferred to a 10 ml volumetric flask. The weight of the stoppered volumetric flask (initial weight) was noted. About 5 mg of drug was added and the flask was shaken to solubilize the drug. As soon as a clear solution was obtained again about 5 mg of drug was added and the flask was shaken to solubilize the drug to get a clear solution. Same process was repeated till the liquid was saturated with the drug. Again the weight of volumetric flask was noted (final weight). Difference in these two weights (initial and final) gave the approximate amount of drug which saturates (nearly) one ml of PNM 2510.

Proposed method of analysis

Twenty tablets of tablet formulation I were weighed and crushed to get a fine powder. Tablet powder equivalent to 40 mg nalidixic acid was transferred to a 10 ml volumetric flask. Then, 8 ml of PNM 2510 was transferred to it and the flask was shaken vigorously for 10 min by hand shaking to extract (solubilize) the drug from the tablet powder. Then, the volume was made up to 10 ml with PNM 2510 and the flask was shaken for few min to homogenize the contents. Again, 1 ml of this liquid was diluted up to 10 ml with PNM 2510. After this, 2.5 ml of this liquid of the flask was transferred to a 100 ml volumetric flask and 80 ml of distilled water, was added and the flask was again shaken for 5 min by hand to solubilize phenol, niacinamide and drug in the distilled water. Then, sufficient distilled water was added to make up the volume up to 100 ml. Filtration was carried out through Whatmann filter paper # 41 to remove the tablet excipients. Then, the absorbance of the filtrate was noted at 330 nm against the reagent blank. The drug content was calculated using the calibration curve. Same procedure was repeated for tablet formulation II. The results of analysis are reported in table 1.

Recovery studies

To perform the recovery studies, standard nalidixic acid drug was added (10 mg and 20 mg , separately) to the pre-analyzed tablet powder equivalent to 40 mg nalidixic acid and the drug content was determined by the proposed method. Results of analysis are reported in table 2 with statistical evaluation.

Table 1: Analysis data of nalidixic acid tablet formulations with statistical evaluation (n=3)

Tablet formulation	Label claim (mg/tablet)	Percent drug estimated (mean \pm SD)	Percent coefficient of variation	Standard error
I	500	98.49 \pm 0.764	0.776	0.441
II	500	100.41 \pm 1.467	1.461	0.847

Table 2: 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 \pm SD)	Percent coefficient of variation	Standard error
I	40	10	101.74 \pm 1.202	1.181	0.694
I	40	20	100.31 \pm 0.339	0.338	0.196
II	40	10	99.81 \pm 1.666	1.669	0.962
II	40	20	99.77 \pm 1.993	1.998	1.151

RESULTS AND DISCUSSION

The solubility of nalidixic acid in distilled water at room temperature was found to be 0.21 mg/ml. The solubility of nalidixic acid in PNM 2510 was more than 138 mg per ml (of PNM 2510).

It is evident from table 1 that the percent drug estimated in tablet formulation I and II were 98.49 \pm 0.764 and 100.41 \pm 1.467, respectively. The values are very close to 100.0, indicating the accuracy of the proposed analytical method. Small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (table 1) further validated the method. Further, table 2 shows that the range of percent recoveries varied from 99.77 \pm 1.993 to 101.74 \pm 1.202 which are again very close to 100.0, indicating the accuracy of the proposed method. Proposed analytical technique is further supported by significantly small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (table 2).

CONCLUSION

In the present study, a eutectic liquid obtained by triturating phenol crystals and niacinamide in 25:10 ratio on weight basis was employed to extract (dissolve) nalidixic acid drug from fine powder of its tablets. Dilution was made with distilled water to carry out spectrophotometric estimation at 330 nm without the help of organic solvent. Proposed method is novel, economic, eco-friendly, rapid, free from toxicity of organic solvent, accurate

and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. The presence of tablet excipients, phenol and niacinamide did not interfere in the spectrophotometric estimation at 330 nm. Phenol and niacinamide do not interfere above 300 nm. The eutectic liquid PNM 2510 can also be used with other water insoluble drugs provided the spectrophotometric analysis is carried out at a wavelength above 300 nm.

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