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Research Article

# "SOLID AS SOLVENT"- NOVEL SPECTROPHOTOMETRIC ANALYSIS OF NORFLOXACIN TABLETS USING PHENOL AS SOLVENT

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**ABSTRACT**

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 innumerous 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 present investigation is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents. In a separate study, author has attempted soxhelation using phenol as solvent. The vapours of boiling phenol got condensed in extraction chamber to effect the extraction of active constituents from powder of crude drugs. The main objective of the present study is to demonstrate the solvent action of solids. Solid excipients can nicely be employed as solubilizers in the development of pharmaceutical dosage forms in solution form of poorly soluble drugs (mixed solvency concept). Present study describes the application of solvent character of melted phenol (at 50-60°C) for spectroscopic estimation of norfloxacin tablets. Solubility of norfloxacin in distilled water is 0.88 mg/ml. More than 100 mg of nofloxacin dissolves in one gram of melted phenol (at 50-60°C). In the present investigation, melted phenol (at 50-60°C) was utilized to extract out (dissolve) the drug from powder of norfloxacin tablets. Distilled water was used for dilution purpose. Absorbances of standard solutions containing 5, 10, 15, 20, and 25 µg/ml were noted at 324 nm against reagent blanks to obtain calibration curve. 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 and phenol did not interfere in the spectrophotometric estimation at 324 nm.

**Keywords**: Mixed-solvency concept, Norfloxacin, Phenol, Spectrophotometric analysis.

## INTRODUCTION

There are very few safe liquids e g propylene glycol, glycerin, tweens, ethanol, liquid polyethylene glycols (like PEG 200, 300 etc) which are employed by pharmaceutical industries in various dosage forms for making solution type dosage forms of poorly soluble drugs. Mixed solvency concept, proposed by Maheshwari[1-3] provides a means to develop innumerable solvent systems employing combination of the pharmaceutical excipients in small concentrations. Each substance present on the earth has got solubilizing power. By combining the excipients, additive solvent actions and synergistic solvent actions can be obtained. The problem of toxicity issue due to high concentration of a solvent can be solved in this manner. The solubility of a large number of poorly soluble drugs has been enhanced by mixed solvency concepst[1-19].

Commonly used organic solvents for spectrophotometric analysis of water insoluble drugs include methanol, ethanol, chloroform, benzene, dichloromethane, dimethyl formamide, actonitrile, ethyl acetate, toluene, carbon tetrachloride, acetone, hexane etc. The main drawbacks of organic solvents include high cost, toxicity and pollution. Organic solvents have innumerous 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 present investigation is an attempt to show that solids can also be wisely used to act as solvent precluding the use of organic solvents. In a separate study, author has attempted soxhelation using phenol as solvent. The vapours of boiling phenol got condensed in extraction chamber to effect the extraction of active constituents from powder of crude drugs. The main objective of the present study is to demonstrate the solvent action of solids. Solid excipients can nicely be employed as solubilizers in the development of pharmaceutical dosage forms in solution form of poorly soluble drugs (mixed solvency concept).

Present study describes the application of solvent character of melted phenol (at 50-60°C) for spectroscopic estimation of norfloxacin tablets. Solubility of norfloxacin in distilled water is 0.88 mg/ml. More than 100 mg of nofloxacin dissolves in one gram of melted phenol (at 50-60°C). In the present investigation, melted phenol (at 50-60°C) was utilized to extract out (dissolve) the drug from powder of norfloxacin tablets. Distilled water was used for dilution purpose. Absorbances of standard solutions containing 5, 10, 15, 20, and 25 µg/ml were noted at 324 nm against reagent blanks to obtain calibration curve. 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 and phenol did not interfere in the spectrophotometric estimation at 324 nm.

## MATERIALS AND METHODS

Norfloxacin bulk drug sample was a generous gift by M/S Alkem Laboratories Limited, Mumbai, (India). All other chemicals used were of analytical grade. Commercial tablets of norfloxacin were procured from local market.

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

**Calibration curve**- 50 mg of norfloxacin standard bulk drug was transferred to a 500 ml volumetric flask. Phenol (10 g) was added and the flask was heated on a water bath (50-60°C) to melt the phenol. Then the flask was shaken to dissolve the drug. After complete dissolution, about 400 ml distilled water (at 50-60°C) was poured in the volumetric flask and the contents were shaken for about 5 min to give a clear solution. The flask was allowed to cool to room temperature and sufficient distilled water was added to make up the volume (500 ml). From this stock solution (100µg/ml), standard solutions containing 5, 10, 15, 20 and 25 µg/ml were prepared by suitable dilution with distilled water. The absorbances of these solutions were noted at 324 nm against respective reagent blank.

**Preliminary solubility studies**

To determine the solubility of the drug 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 (27±1°C) 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 Whatman filter paper # 41. The filtrate was appropriately diluted with distilled water to measure the absorbance at 324 nm.

In order to determine the approximate solubility of drug in melted phenol, 1 g phenol was transferred to a 10 ml volumetric flask. The weight of the stopered volumetric flask (initial weight) was noted. Then, the flask was heated on the water bath to melt the phenol (at 50-60°C). 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 melted phenol (at 50-60°C) was saturated with 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 gram of melted phenol (at 50-60°C).

**Proposed method of analysis**

Twenty tablets of tablet formulation I were weighed and crushed to get a fine powder. Tablet powder equivalent to 50 mg norfloxacin was transferred to a 500 ml volumetric flask and 10 g phenol was added. The flask was heated on a water bath (at 50-60°C) to melt the phenol. Then the flask was shaken vigorously for 10 min by hand shaking to extract (solubilize) the drug from the tablet powder. Then 400 ml distilled water (at 50-60°C) was added and the flask was again shaken for 5 min by hand to solubilize phenol and drug in water. The flask was allowed to cool to room temperature and sufficient distilled water was added to make up the volume (500 ml). Filtration was carried out through Whatman filter paper # 41 to remove the tablet excipients. Ten ml filtrate was diluted to 50 ml with distilled water and the absorbance was noted at 324 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 norfloxacin drug sample was added (15 mg and 30 mg, separately) to the pre-analyzed tablet powder equivalent to 50 mg norfloxacin and the drug content was determined by the proposed method. Results of analysis are reported in table 2.

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

| Tablet formulation | Label claim (mg/tablet) | Percent drug estimated (mean ± SD) | Percent coefficient of variation | Standard error |
|---|---|---|---|---|
| I | 400 | 101.37 ± 0.744 | 0.733 | 0.430 |
| II | 400 | 99.49 ± 1.407 | 1.414 | 0.812 |

**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 ± SD) | Percent coefficient of variation | Standard error |
|---|---|---|---|---|---|
| I | 50 | 15 | 97.81 ± 1.921 | 1.964 | 1.109 |
| I | 50 | 30 | 99.70 ± 1.007 | 1.010 | 0.581 |
| II | 50 | 15 | 99.12 ± 1.222 | 1.233 | 0.706 |
| II | 50 | 30 | 98.65 ± 0.881 | 0.893 | 0.509 |

**RESULTS AND DISCUSSION**

The solubility of norfloxacin in distilled water at room temperature was found to be 0.88 mg/ml. The solubility of norfloxacin in melted phenol (at 50-60°C) was more than 100 mg/gm of phenol.

It is evident from table 1 that the percent drug estimated in tablet formulation I and II were 101.37 ± 0.744 and 99.49 ± 1.407, 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 further validated the method. Further, table 2 shows that the percent recoveries varied from 97.81±1.921 to 99.70±1.007 which are again very close to 100.0, indicating the accuracy of the proposed method which is further supported by significantly small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error (Table 2).

**CONCLUSION**

The proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of norfloxacin tablets. Melted phenol can also be tried with other water insoluble drugs which are estimated above 300 nm. Phenol does not interfere above 300 nm.

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