



Eco-friendly and Economical Spectrophotometric Estimation of the Low Water-Soluble Drug (Norfloxacin) Applying the Concept of Mixed Hydrotrophy

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Abstract

Objectives The main aim of the research was to analyze an economical and eco-friendly approach to improve the solubility of norfloxacin. The current analysis was to utilize the hydrotropic solutions to extract the drugs from their dosage forms, avoiding the use of costlier and harmful organic solvents.

Materials and Methods In this study, an ultraviolet–visible spectrophotometer (model 1800, Shimadzu Corporation) was used to analyze the norfloxacin drug. The mixed hydrotrophy approach was used to determine the solubility of norfloxacin. In this work, a blend solution (20% of urea + 20% of sodium benzoate) was used as a hydrotropic solubilizing agent.

Results The solubility of norfloxacin drug in water was very low at ~0.88 mg/mL and the solubility of norfloxacin drug in the blend solution was 11 mg/mL. From 98.96 (tablet II) to 99.35 (tablet I), the percent estimation value was achieved. This value was nearly 100, so the proposed method was correct. Standard deviation (0.2540–0.4156), percentage coefficient of variation (0.2566–0.4183), and the value of standard error (0.1481–0.2415) are also very low; hence, we can say that the proposed method is accurate.

Conclusion To avoid the use of organic solvents, the mixed hydrotrophy concept can be used for spectrophotometric estimation of low water-soluble drugs from bulk drug samples. It provides an economical and environmentally friendly mechanism.

Keywords

- norfloxacin
- mixed hydrotrophy
- estimation
- solubility
- sodium benzoate

Introduction

Solubility plays a very important role in drug formulation development and estimation, but most drugs have very low water solubility.^{1–3} Increasing the solubility of such drugs is a

challenging task. There are many methods to increase the solubility of such drugs; however, there are many disadvantages in those methods such as some methods change the physical and chemical properties of the drug, in addition to some modifications in the drug, thereby increasing the

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drug's solubility.^{4,5} Therefore, there is a need for a method that increases the solubility of the drug without its modification.

Hydrotropy and mixed hydrotropy are techniques that can increase the solubility of low water-soluble drugs.⁶ Many techniques such as TLC, HPLC, and spectrophotometric analysis, are used in drug studies, and some organic solvents are used in all these techniques.⁷⁻¹¹ Methanol, ethanol, benzene, toluene, and other organic solvents are both costly and dangerous. As a result, to replace these solvents, non-toxic and conveniently available solvents must be employed. The idea of hydrotropy can be realized.¹²⁻¹⁷ Green chemistry can benefit from the ideas of hydrotropy and mixed hydrotropy.¹⁸ Norfloxacin is a kind of antibiotic. It has extremely poor solubility in water (0.88 mg/mL).¹⁹ Hence, it is a poorly water-soluble drug and its solubility must be improved. The solubility of this drug can be increased with the help of hydrotropy and the mixed hydrotropy method.²⁰⁻²³ Hydrotropic agents are required to increase the solubility of drugs with the help of these methods. Hydrotropic agents are ionic organic salts that help to increase the solubility of any solute substance.²⁴⁻²⁶ These hydrotropic agents are less expensive and readily available as compared with organic solvents and have no harmful effects. Hydrotropic agents, such as urea, sodium benzoate, sodium citrate, sodium acetate, sodium caprylate, and others, can easily increase the solubility of a drug.²⁷⁻³⁰

In this study, we increased the solubility of norfloxacin using mixed hydrotropic techniques. Mixed hydrotropic techniques require two or more hydrotropic agents. As a hydrotropic agent, we utilized a blend solution (20% urea + 20% sodium benzoate) in this investigation.

Materials and Methods

Materials and Instrument

A bulk drug sample of norfloxacin was collected from the M/S Alkem Laboratories Limited, Mumbai (India). Norfloxacin tablets of two separate firms were purchased from the local market. Analytical-grade chemicals and reagents were utilized.

The UV-visible spectrophotometer (Model 1800, Shimadzu) was used for spectrophotometric estimation of norfloxacin.

Determination of Solubility

The solubility of the norfloxacin drug was determined at room temperature. An additional quantity of norfloxacin drug was added to a 20 mL glass bottle involving blend solution (20% urea + 20% sodium benzoate solution). At room temperature, the bottle was shaken for 12 hours in an orbital flask shaker. After 24 hours, the solution of the bottle was filtered using a Whatman filter paper. The filtrate was diluted properly and the absorbance was reported spectrophotometrically at 324 nm against a reagent blank.

Determination of Solubility Improvement

It was determined using the following formula (→Table 1).

Table 1 Solubility of norfloxacin drug in hydrotropic blend solution

Solvent	Absorbance	Solubility in mg/mL	Solubility improvement ratio
Hydrotropic solution (20% of urea + 20% of sodium benzoate solution)	0.335	11	$11/0.88 = 12.5$

Table 2 Data of analysis curve

Concentration in µg/mL	Absorbance
0	0.000
10	0.324
20	0.612
30	0.880
40	1.090

Solubility improvement ratio = solubility in hydrotropic solution/solubility in distilled water

Calibration Curve of Norfloxacin Drug

A 10 mL volumetric flask was filled with 50 mg of the standard drug (norfloxacin) and 8 mL of the blend (20% urea + 20% sodium benzoate solution). The flask was stirred until the drug was completely soluble, then the volume was made up to 10 mL with the help of a blend solution. Various standard solutions of different concentrations (10, 20, 30, and 40 µg/mL) were prepared from this stock solution by desirable dilution with distilled water. The absorbance was reported (at 324 nm) of these solutions versus the specific reagent blank (→Table 2).

Proposed Research Method of Analysis

The tablet (I) powder equal to 50 mg of norfloxacin and 8 mL of a blend solution was transferred to 10 mL of the volumetric flask. The vial was stirred quickly for 15 minutes and a mixture solution was added to complete the volume up to 10 mL. The solution was filtered through a Whatman 41 filter paper to remove the tablet excipients. Next, 0.6 mL of the filtrate was diluted to 100 mL distilled water, then the absorbance was recorded at 324 nm compared with the reagent blank. A similar procedure was applied to the tablet (II). Results were reported in →Table 3.

Recovery Studies

The drug content was assessed using the indicated technique after adding 20 mg and 40 mg of norfloxacin (standard drug

Table 3 Analysis of norfloxacin tablet with statistical evaluation ($n = 3$)

Tablet of norfloxacin drug	Claimed amount of drug mg/tablet	% drug estimated (mean \pm standard deviation)	% coefficient of variation	Standard error
I (Alkem laboratory Ltd.)	100	99.35 \pm 0.4156	0.4183	0.2415
II (Cipla Ltd.)	100	98.96 \pm 0.2540	0.2566	0.1481

Table 4 Statistically analyzed results of recovery experiments

Tablet of norfloxacin drug	Amount of drug in mg presented in preliminarily investigated tablet powder	Quantity of standard drug added (mg) (spiked)	% drug estimated (mean \pm standard deviation)	% coefficient of variation	Standard error
I (Alkem laboratory Ltd.)	50	20	99.02 \pm 0.3579	0.3614	0.2086
I (Alkem laboratory Ltd.)	50	40	99.26 \pm 0.3522	0.3548	0.2048
II (Cipla Ltd.)	50	20	100.34 \pm 0.2830	0.2820	0.1628
II (Cipla Ltd.)	50	40	98.61 \pm 0.03464	0.0351	0.0202

sample) to the pre-analyzed tablet powder (equal to 50 mg norfloxacin drug). The same procedure was repeated for tablet-II and results are reported in ►Table 4 ($n = 3$).

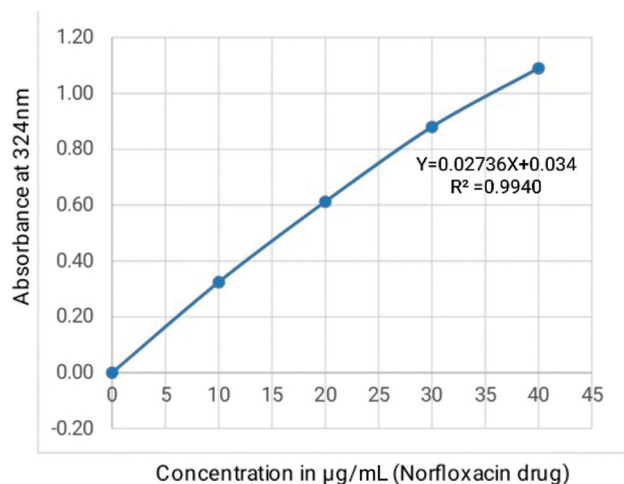
Results and Discussion

In the previous study done by Maheshwari et al,¹⁹ norfloxacin was observed to be 0.88 mg/mL soluble in distilled water at room temperature. In the present investigation, the solubility of norfloxacin in the blend solution (20% urea + 20% sodium benzoate solution) was found to be 11 mg/mL. The solubility improvement ratio was found to be 12.5, which is given in ►Table 1. The absorbance obtained for the calibration curve is given in ►Table 2 and the calibration curve of norfloxacin is shown in ►Fig. 1. ►Table 3 displays the percent estimate values. Spectrophotometric investigation using the mixed hydrotropy methodology yielded values ranging from 98.96

(tablet I) to 99.35 (tablet II). These values were close to 100; hence, the recommended procedure was valid. The low values of standard deviation (0.173–0.346), percentage coefficient of variation (0.175–0.350), and standard error (0.101–0.202) indicate the accuracy of the proposed method. ►Table 4 shows the value of the recovery studies that have been achieved from 97.8 to 99.3. This value is also close to 100, which shows the precision of the proposed method, as well as the standard deviation (0.101–0.519), percentage coefficient of variance (0.108–0.526), and the standard error (0.063–0.303) value also very low, which shows the validation of the proposed method. In earlier studies,¹⁹ the solubility of norfloxacin was improved using a mixed solvency technique in which melted phenol was employed to promote solubility. In this research, a blend solution (20% urea + 20% sodium benzoate solution) was used to increase the solubility of norfloxacin. In this research, the solubility of norfloxacin was increased by ~12.5 times (►Table 1) with the help of the mixed hydrotropy method. Also, this is an eco-friendly and profitable method because no toxic organic solvent has been used in this method. Because of its distinctive qualities, such as quick availability, quick recovery, lack of fire hazards, and eco-friendly design, hydrotropic solutions are in great demand in the industrial sector. The mixed hydrotropic technique can be assigned efficiently in the pharmaceutical sector. It may be used for spectrophotometric analysis of weakly water-soluble drugs from bulk drug samples to remove the need for organic solvents, resulting in a quick, inexpensive, environmentally friendly, and safe analytical method.

Conclusion

Different technologies have been used for enhancing the solubility of poorly water-soluble drugs. It may be assumed that it is possible to use the mixed hydrotropy strategy to

**Fig. 1** Calibration curve of norfloxacin drug.

replace the use of an organic solvent that is more expensive and harmful for our atmosphere. In comparison to distilled water, the solubility of norfloxacin in the hydrotropic solution was found to be more than 12.5 times higher. According to the findings, the spectrophotometric technique for determining norfloxacin in bulk and formulations employing a blend solution of 20% sodium benzoate and 20% urea as a hydrotropic agent is accurate and eco-friendly. This method can be successfully utilized in the routine analysis of norfloxacin in bulk drug and dosage formulations. For the spectrophotometric study of other poorly water-soluble drugs avoiding the use of organic solvents, there is a further scope of sodium benzoate and urea solution as a hydrotropic solubilizing agent.

Conflict of Interest

None declared.

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