



**“SOLID AS SOLVENT”- NOVEL SPECTROPHOTOMETRIC ANALYTICAL METHOD
FOR QUANTITATIVE ESTIMATION OF GATIFLOXACIN TABLETS USING SOLIDS
(EUTECTIC LIQUID OF PHENOL AND LIGNOCAINE HYDROCHLORIDE AS
SOLUBILIZING AGENTS (MIXED SOLVENCY CONCEPT))**

Rajesh Kumar Maheshwari¹, Nupur Maheshwari², Neelesh Maheshwari³, Tilotma Sahu^{4*} and Jitendra Jain⁵

^{1,2}Department of Pharmacy, Shri G S Institute of Technology and Science, Indore.

³School of Pharmaceutical Sciences, RGPV, Bhopal.

⁴Shri Rawatpura Sarkar Institute of Pharmacy, Kumhari, Durg, Chattisgarh.

⁵IPS Academy, Indore.

***Corresponding Author: Prof. Tilotma Sahu**

Shri Rawatpura Sarkar Institute of Pharmacy, Kumhari, Durg, Chattisgarh.

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ABSTRACT

Solubility enhancement of various poorly soluble compounds is a challenging task for researchers and pharmaceutical scientists in today's scenario. Solubility is one of the important parameter to achieve preferred concentration of drug in systemic circulation to obtain desired pharmacological response. 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. 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 eutectic liquid consisting of phenol and lignocaine hydrochloride in 4:1 ratio (PL-41) on the weight basis for spectrophotometric estimation of gatifloxacin tablets. Solubility of gatifloxacin in distilled water was found to be 1.31 mg/ml at room temperature. More than 120 mg of gatifloxacin dissolves in 1 ml of PL-41. In the present investigation, PL-41 was utilized to extract out (dissolve) the drug from tablet powder of gatifloxacin tablets. Distilled water was used for dilution purpose. Absorbance was noted at 333 nm against reagent blank to calculate the amount of drug in the tablets. Proposed method is novel, 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 phenol, lignocaine hydrochloride and tablet excipients did not interfere in the spectrophotometric estimation of gatifloxacin at 333 nm. Phenol and lignocaine hydrochloride do not interfere at 333 nm in spectrophotometric analysis.

KEYWORDS - Mixed-solvency concept, gatifloxacin, phenol, lignocaine hydrochloride, eutectic liquid, spectrophotometric analysis.

INTRODUCTION

Solubility enhancement of various poorly soluble compounds is a challenging task for researchers and pharmaceutical scientists in today's scenario. Solubility is one of the important parameter to achieve preferred concentration of drug in systemic circulation to obtain desired pharmacological response.

Gatifloxacin is a third-generation quinolone antimicrobial drug mainly used for the treatment of acute exacerbations of chronic bronchitis and community-acquired pneumonia. It inhibits the bacterial enzymes DNA gyrase and topoisomerase IV. It has excellent activity against *Streptococcus pneumoniae*, many atypical respiratory pathogens & certain anaerobes.

Some of the common techniques of solubility enhancement include micellar solubilization, complexation, pH modification, salt formation, hydrotrophy and cosolvency. A novel technique of solubility enhancement by use of mixed solvency concept has been proposed by Maheshwari.^[1-5] All the substances (whether liquids, gases or solids) have solubilizing power. Innumerable solvent systems may be developed using mixed solvency concept. By application of mixed solvency concept^[6-16], the drug loading in various pharmaceutical formulations, including NDDS, may be improved and by combining the excipients in appropriate amounts, synergistic solvent actions and additive solvent actions can be obtained and also the problem of toxicity issue due to high concentration of a

solvent for desired solubility can be solved. Chandan and Maheshwari^[14] utilized mixed solvency concept to improve the drug loading and to reduce the surfactant concentration in SEDDS of candesartan cilexetil. The solubilities of a large number of poorly soluble drugs have been nicely improved utilizing the mixed solvency concept.^[1-39]

Several organic solvents are employed for spectrophotometric analysis of dosage forms of poorly water soluble drugs. Methanol, ethanol, chloroform, acetonitrile, dichloromethane, dimethyl formamide, ethyl acetate, toluene, carbon tetrachloride, acetone and hexane are the most common examples of such solvents. High cost, toxicity and pollution are serious drawbacks of organic solvents. The present investigation is an attempt to show that solids can also be wisely employed for spectrophotometric estimation of poorly soluble drugs without using the organic solvents.

Present study describes the application of solvent character of eutectic liquid (PL 41) of two solid solubilizers, namely, phenol and lignocaine hydrochloride for spectrophotometric estimation of gatifloxacin tablets. Gatifloxacin has got poor solubility in distilled water while very high solubility in a eutectic liquid of two solids, namely phenol and lignocaine hydrochloride. Phenol and lignocaine hydrochloride were employed in 4:1 ratio to give eutectic liquid (PL 41). This liquid was used to act as solvent to extract out the drug, gatifloxacin, from the fine powder of its tablets for spectrophotometric estimation at 333 nm. Distilled water was used for dilution purpose. The solubility of gatifloxacin in distilled water is 1.31 mg/ml at room temperature while the solubility in PL 41 is more than 120 mg/ml. Proposed method is novel, accurate, rapid and free from toxicity of organic solvents and reproducible. Recovery studies and statistical data proved the accuracy, reproducibility and precision of the proposed method. There was no interference of tablet excipients, phenol and lignocaine hydrochloride at 333 nm.

MATERIALS AND METHODS

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

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

Calibration curve- Accurately weighed 50 mg of Gatifloxacin standard drug was transferred to a 500 ml volumetric flask. Ten ml of PL-41 was added and the flask was shaken to dissolve the drug. Then, about 400 ml of distilled water was added and the flask was shaken for 5 min to solubilize the contents. Then, the volume

was made up to 500 ml with distilled water to get a stock solution of 100 µg/ml. The stock solution was suitably diluted with distilled water to prepare standard solutions of 20, 40, 60, 80 and 100 µg/ml. The absorbances of these standard solutions were noted at 333 nm against respective reagent blanks.

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 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 333 nm.

In order to determine the approximate solubility of drug in PL-41, one ml of PL-41 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 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 PL-41.

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 gatifloxacin was transferred to a 500 ml volumetric flask. Then, 10 ml of PL-41 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, about 400 ml distilled water was added and the flask was shaken for about 5 min for proper solubilization of phenol, lignocaine hydrochloride and drug in the distilled water. Then, sufficient distilled water was added to make up the volume up to 500 ml. Filtration was carried out through Whatmann filter paper # 41 to remove the insoluble tablet excipients. Then, the absorbance of the filtrate was noted at 333 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

In order to validate the proposed analytical method, recovery studies were performed for which standard gatifloxacin drug was added (15 mg and 30 mg, separately) to the pre-analyzed tablet powder equivalent to 50 mg gatifloxacin and the drug content was

determined by the proposed method. Results of analysis with statistical evaluation are reported in table 2.

Table 1: Analysis data Gatifloxacin 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	400	101.34 $\pm$ 1.337	1.319	0.772
II	400	99.73 $\pm$ 1.848	1.853	1.067

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	50	15	99.33 $\pm$ 0.864	0.870	0.499
I	50	30	98.08 $\pm$ 1.228	1.252	0.709
II	50	15	99.49 $\pm$ 1.656	1.664	0.956
II	50	30	98.81 $\pm$ 1.192	1.206	0.688

RESULTS AND DISCUSSION

1.31mg/ml was the observed solubility of gatifloxacin in distilled water at room temperature. The solubility of gatifloxacin in PL-41 was more than 120 mg per ml.

It is evident from table 1 that the percent drug estimated in tablet formulation I and II were 101.34 $\pm$ 1.337 and 99.73 $\pm$ 1.848, 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 98.08 $\pm$ 1.228 to 99.49 $\pm$ 1.656, which are again very close to 100.0, indicating the accuracy of the proposed method. The accuracy of the proposed analytical method is further supported by significantly small values of statistical parameters viz. standard deviation, percent coefficient of variation and standard error.

CONCLUSION

The proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of gatifloxacin tablets. The use of PL-41 can also be done to estimate other water insoluble drugs which are estimated above 333 nm. Phenol and lignocaine hydrochloride do not interfere above 333 nm. Obtained accuracy of the proposed analytical method is also indicative of the proof that the solids possess solvent character.

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