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Research Article

"SOLID AS SOLVENT": NOVEL SPECTROPHOTOMETRIC ANALYTICAL TECHNIQUE FOR QUANTITATIVE ESTIMATION OF TINIDAZOLE IN TABLETS USING SOLIDS (EUTECTIC LIQUID OF PHENOL AND LIGNOCAINE HYDROCHLORIDE) AS SOLUBILIZING AGENTS (MIXED SOLVENCY CONCEPT)

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ABSTRACT

As per the mixed solvency concept, every substance present in this universe has got solubilizing power. The substance may be a gas, liquid or solid. The present research work is an attempt to demonstrate the solubilizing property of solids. Also, the present research work is one of the examples which prove that solids can also be employed for spectrophotometric analysis of poorly soluble drugs in place of organic solvents. Tinidazole has got poor solubility in distilled water, while, significantly 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 eutectic liquid was employed to act as solvent to extract out the drug, tinidazole, from the fine powder of its tablets for spectrophotometric estimation at 318 nm. Necessary dilutions were done using distilled water. The solubility of tinidazole in distilled water is 5.38 mg/ml at room temperature while the approximate solubility in PL 41 is more than 200 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 analytical method employed. Tablet excipients together with phenol and lignocaine hydrochloride did not interfere at 318 nm.

Keywords - Spectrophotometric analysis, mixed-solvency concept, tinidazole, phenol – lignocaine hydrochloride eutectic liquid

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INTRODUCTION

Most frequently employed common techniques of solubility enhancement include cosolvency, hydrotropy, micellar solubilization, complexation, pH modification and salt formation. A novel technique of solubility enhancement by use of mixed solvency concept has been proposed by Maheshwari [1-6]. 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 [7-17], 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 of the drug can be solved. Maheshwari [5] utilized mixed solvency concept to potentiate the solvent character of a weaker solvent. In this research work it has been shown that a weaker solvent can be made a strong solvent by incorporation of

a solid solubilizer. The solubility of frusemide in ethanol was enhanced about three fold in the presence of 15% w/v niacinamide (a solid solubilizer). Frusemide is sparingly soluble in ethanol and pharmacopoeial method requires dimethyl formamide (a class II organic solvent) for titrimetric analysis of frusemide bulk drug. In this research work 15% w/v solution of niacinamide in ethanol was successfully employed to carry out titrimetric analysis of frusemide bulk drug, giving an ecofriendly method of analysis because ethanol is a class III organic solvent (relatively safe in comparison to dimethyl formamide). The solubilities of a large number of poorly soluble drugs have been nicely improved utilizing the mixed solvency concept [1-30].

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 tinidazole tablets. Tinidazole 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, tinidazole, from the fine powder of its tablets for spectrophotometric estimation at 318 nm. Distilled water was used for dilution purpose. The solubility of tinidazole in distilled water is 5.38 mg/ml at room temperature while the approximate solubility in PL 41 is more than 200 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 318 nm.

MATERIALS AND METHODS

- The gift sample of tinidazole bulk drug was procured from M/S Alkem Laboratories Limited, Mumbai (India). Chemicals used were of analytical grade.
- Commercial tablets of tinidazole were purchased from the local market.
- A Shimadzu-1700 UV visible spectrophotometer with 1 cm matched silica cells was used for spectrophotometric analysis.

1. Preparation of eutectic liquid

Phenol crystals and lignocaine hydrochloride powder were triturated with the help of pestle and mortar in 4:1 ratio on weight basis to obtain a eutectic liquid, PL 41.

2. Calibration curve

To a 500 ml volumetric flask, accurately weighed 50 mg of tinidazole standard drug sample was transferred. Eutectic liquid, PL 41 (10 ml) was transferred to this volumetric flask and the volumetric flask was shaken for few minutes to obtain a clear solution. Now 400 ml of distilled water was added and the flask was shaken for about 5 minutes to get a clear solution. Sufficient of distilled water was added to make up the volume to 500 ml. In this way a stock solution of drug (100 µg/ml) was obtained. After suitable dilutions with distilled water, the standard solutions containing 10, 20, 30 and 40 µg/ml of drug were prepared. Calibration curve was obtained by using the absorbance of these standard solutions, measured against their respective reagent blanks at 318 nm.

3. Preliminary solubility studies

The equilibrium solubility of drug in distilled water was determined. For this, excess amount of drug sample was added to a 25 ml capacity vial containing distilled water. After putting the vial cap and applying the aluminium seal properly, the vial was shaken mechanically for 12 hours at room temperature in an orbital flask shaker (Khera Instrument Pvt. Ltd., India). The vial was kept undisturbed for 24 hours. Then, the filtration was carried out using Whatmann filter paper # 41. The filtrate was appropriately diluted with distilled water and the absorbance was noted at 318 nm. The result of solubility was computed using the calibration curve.

Then, the approximate solubility of drug was determined in PL 41 liquid. For this, 1 ml of PL 41 was taken in a 10 ml volumetric flask and the weight of this flask was noted. About 5 mg of drug was added in the volumetric flask and the flask was shaken to solubilize the drug. As soon as a clear solution was obtained, again about 5 mg of drug was transferred to the flask and the flask was shaken to solubilize the drug. Same procedure was repeated till the liquid PL 41 was nearly saturated with the drug (at this stage, slight turbidity was observed). Then, the final weight of the flask was noted. Difference in these two weights provided the approximate amount of drug solubilized by 1 ml of PL 41. In this way, the approximate solubility of drug in PL 41was determined.

4. Proposed method of analysis

For determination of drug content, twenty tablets of tablet formulation I were weighed accurately. With the help of pestle and mortar, the tablets were crushed to get a fine powder. The powder of tablets equivalent to 50 mg tinidazole was transferred to a 500 ml volumetric flask. Ten ml of PL 41 liquid was added in the flask and the flask was shaken continuously for 10 minutes manually. This step ensured the complete dissolution of drug (present in the powder taken) in the 10 ml of PL 41 liquid. Then, 400 ml of distilled water was added in the flask and the flask was shaken for 5 minutes. This step helps to retain the drug (tinidazole), phenol and

lignocaine hydrochloride in the solution form. Then, the volume was made up to 500 ml with distilled water. After filtration through Whatmann filter paper # 41 (discarding the first few ml of the filtrate), 10 ml of the filtrate was diluted with distilled water up to 50 ml and the absorbance was noted at 318 nm against the reagent blank. This procedure was applied thrice (n=3). Exactly the same procedure was used for assay of tablet formulation II. The drug contents were determined using the calibration curve and the results of analysis were recorded in Table 1.

5. Recovery studies

Recovery studies were performed on the pre-analyzed tablet powders. Standard tinidazole drug was added (15 mg and 30 mg, separately) to the pre-analyzed tablet powder equivalent to 50 mg tinidazole 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 of tinidazole 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	300	99.39 ± 1.424	1.433	0.822
II	300	100.97 ± 1.807	1.790	1.043

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	98.22±1.755	1.787	1.013
I	50	30	99.84±1.421	1.423	0.820
II	50	15	100.14±1.907	1.904	1.101
II	50	30	98.84±1.423	1.440	0.822

RESULTS AND DISCUSSION

The results of solubility studies revealed that the equilibrium solubility of tinidazole in distilled water at room temperature was found to be 5.38 mg/ml while the approximate solubility of tinidazole drug in PL 41 liquid was found to be more than 200 mg/ml.

Table 1 demonstrates that the percent drug estimated in tablet formulation I and formulation II were 99.39 ± 1.424 and 100.97 ± 1.807, respectively. Since, these values are very close to 100; this indicates the accuracy of the proposed analytical method. Small values of statistical parameters, viz. standard deviations (1.424 and 1.807 for tablet formulation I and formulation II, respectively), percent coefficient of variation (1.433 and 1.790, for tablet formulation I and formulation II, respectively) and standard error (0.822 and 1.043, for tablet formulation I and formulation II, respectively) further validated the proposed analytical method.

Further, Table 2 shows that the range of percent recoveries varied from 98.22±1.755 to 100.14±1.907. These values are again very close to 100, confirming 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.

CONCLUSION

The proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of tinidazole tablets. The use of PL 41can also be done to estimate other water insoluble drugs which are estimated above 310 nm. Phenol and lignocaine hydrochloride do not interfere above 310 nm. Obtained accuracy of the proposed analytical method is also indicative of the proof that the solids possess solvent character.

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