RESEARCH ARTICLE

Ecofriendly spectrophotometric estimation of tinidazole in tablets using lignocaine hydrochloride as a hydrotropic solubilizing agent

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A novel, safe and sensitive method of spectrophotometric estimation in the ultraviolet region has been developed using 1M lignocaine hydrochloride (an economic drug) as a hydrotropic solubilizing agent for the quantitative determination of tinidazole, a sparingly water-soluble antiprotozoal drug in tablet dosage form. Beer's law was obeyed in the concentration range of 5-25 μg/ml. Lignocaine hydrochloride does not interfere above 280 nm. There was more than a six-fold enhancement in aqueous solubility of tinidazole in 1M lignocaine hydrochloride solution as compared with the solubility in distilled water. Commonly used tablet excipients and lignocaine hydrochloride did not interfere in spectrophotometric estimation. Results of the analysis were validated statistically and by recovery studies. The results of analysis obtained by the proposed method were comparable with the results of analysis obtained by the Indian Pharmacopoeial method.

Key words: *Hydrotropy, lignocaine hydrochloride, tinidazole, spectrophotometry*

INTRODUCTION

Increasing the aqueous solubility of insoluble and slightly soluble drug is of major importance. Hydrotropy refers to the ability of a concentrated solution of a chemical compound to increase the aqueous solubility of another compound (usually a poorly water-soluble compound). Compounds that have this property are called "hydrotropes." Maheshwari *et al*. have nicely applied the use of hydrotropy in titrimetric and spectrophotometric estimation of a large number of poorly water-soluble drugs, discouraging the use of organic solvents.[1-17] Sodium benzoate, sodium salicylate, sodium ascorbate, sodium glycinate, niacinamide, sodium citrate and urea are the most popular examples of hydrotropic agents that have been used to solubilize a large number of poorly water-soluble compounds.[1-22] Hydrotropic solution of lignocaine hydrochloride was employed as a solubilizing agent to analyze a sparingly water-soluble drug, tinidazole, by spectrophotometric estimation.

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DOI: 10.4103/0973-8398.59951

There was tremendous increase in solubility of tinidazole (a widely used antiprotozoal agent) in 1M lignocaine hydrochloride solution. Therefore, it was thought worthwhile to solubilize the drug with the help of lignocaine hydrochloride solution to carry out the estimation.

Analysis of tinidazole tablet formulation by the Indian Pharmacopoeial (IP) method is performed by spectrophotometry. Besides this, various methods for the analysis of tinidazole have been reported, among which are gas-liquid chromatography (GLC) and spectrophotometric and absorptrometric assay,[23-25] thin layer chromatography, high pressure liquid chromatography[26] and the electrochemical method based on single-wall carbon nanotubes,[27] direct current (DC) polarography[28] and differential pulse (DP) polarography.[29] British Pharmacopoeia describes potentiometric and nonaqueous titration methods using perchloric acid as a titrant.[30]

MATERIALS AND METHODS

Tinidazole bulk drug sample was supplied as a gift sample by Alkem Laboratories, Mumbai, India. Tini-300 (tablet formulation I of tinidazole; Kopran Pharmaceuticals Ltd., Mumbai, India) and Tiniba-300 (Tablet formulation II of tinidazole; Cadila Healthcare Ltd., Ahmedabad, India)

were procured from the local market. All other chemicals and solvents used were of analytical grade. A spectrophotometer (Model UV-160A) (Shimadzu, Kyoto, Japan) with 1 cm matched silica cells was used for spectrophotometric analysis.

Preparation of the calibration curve of tinidazole

Fifty milligrams of tinidazole standard drug was accurately weighed and transferred to a 25 ml volumetric flask. To this, 20 ml of 1M lignocaine hydrochloride solution was added and the flask was shaken to solubilize the drug. The volume was made up to the mark with distilled water. This stock solution (2000 μg/ml) was further diluted with distilled water to obtain various dilutions containing 5, 10, 15, 20 and 25 μg/ml of drug. The Beer's law range was 5-25 μg/ml for tinidazole. Absorbance was noted at 318 nm against reagent blanks to get the calibration curve. The equation for the calibration curve of tinidazole was obtained as $y = 0.0339 x + 0.0075$.

Preliminary solubility studies of tinidazole

Solubility of tinidazole was determined in distilled water and 1M lignocaine hydrochloride solution at 27 ± 1°C. Solubility was found to be increased by more than six-fold in 1M lignocaine hydrochloride solution as compared with the solubility in distilled water.

Analysis of tinidazole tablet formulations by the Indian pharmacopoeial (1996) method[31]

Twenty tablets of tinidazole (formulation I) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 0.15 g of tinidazole was transferred to a 100 ml volumetric flask. Twenty milliliters of methanol was added, the flask was shaken for about 10 min to dissolve the drug and the volume was made up to the mark with methanol. Ten milliliters of the solution was diluted to 100 ml with methanol. Further, 10 ml of this solution was diluted with 100 ml of methanol. The absorbance of the resulting solution was measured at a maximum at 310 nm. The drug content of the tablet formulation was then calculated [Table 1]. The same procedure was followed for formulation II [Table 1].

Analysis of tinidazole tablet formulations by the proposed method

An accurately weighed tablet powder sample equivalent to 50 mg of tinidazole was transferred to a 25 ml volumetric flask. Twenty milliliters of 1M lignocaine hydrochloride solution was added to this and the flask was shaken for about 10 min to dissolve the drug. The volume was made up to the mark with distilled water. The solution was filtered through Whatmann filter paper no. 41. The filtrate was diluted appropriately with distilled water and was analyzed using a UV spectrophotometer. Absorbance was noted at 318 nm against a reagent blank. The drug content of the tablet formulation was then calculated [Table 1]. The same procedure was followed for formulation II [Table 1].

Recovery studies

To evaluate the validity and reproducibility of the proposed method, recovery experiments were carried out. For recovery studies, in preanalyzed tablet powder equivalent to 50 mg tinidazole, bulk drug samples 15 and 30 mg were added as spiked concentrations and drug contents were determined by the proposed analytical method. The results of analysis of recovery studies are presented in Table 2.

RESULTS AND DISCUSSION

Results of solubility studies of tinidazole revealed that enhancement in solubility in 1M lignocaine hydrochloride solution was more than six-fold as compared with its solubility in distilled water.

It is evident from Table 1 that the values of mean percent drug (tinidazole) estimated by IP and the proposed method are 99.88 and 100.54, respectively, for formulation I and the values of mean percent drug (tinidazole) estimated by IP and

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

Tablet formulation	Label claim per tablet (mg)	Method of analysis	Percent drug estimated (mean ± SD)	% coefficient of variation	Standard error
I	300	PM	100.54 ± 1.227	1.220	0.708
I	300	IPM	99.88 ± 0.932	0.933	0.57
II	300	PM	99.22 ± 1.070	1.078	0.618
II	300	IPM	100.66 ± 1.339	1.390	0.818

PM - Proposed method; IPM - Indian pharmacopoeial method

Table 2: Recovery studies using the proposed analytical method with statistical evaluation (n = 3)

Tablet formulation	Drug present in pre-analyzed tablet	Pure drug added (spiked) powder (mg)	Percent recovery estimated (mean ± SD)	% coefficient of variation	Standard error
I	50	15	98.80 ± 1.831	1.853	1.057
I	50	30	100.73 ± 0.740	0.734	0.427
II	50	15	100.31 ± 0.804	0.801	0.464
II	50	30	99.45 ± 1.287	1.294	0.743

proposed method are 100.66 and 99.22, respectively, for formulation II. The results of the analysis by the proposed method are comparable to the results obtained from the IP method. The amounts of drug estimated by the IP and the proposed methods [Table 1] are very close to each other and are very close to 100.0, indicating the accuracy of the proposed method of analysis. Low values of standard deviation, percent coefficient of variation and standard error [Table 1] further validated the proposed method.

The percent recoveries estimated ranged from 98.80 to 100.73 for formulation I and from 100.31 to 99.45 for formulation II. The values that are close to 100 indicated the accuracy of the proposed method. The values of standard deviation, percent coefficient of variation and standard error are statistically low and thus validate the proposed method [Table 2].

CONCLUSION

It was thus concluded that the proposed method is new, simple, cost-effective, accurate, safe and precise and can be successfully employed in the routine analysis of tinidazole in tablet formulations. No organic solvent was employed. There is good scope for other poorly water-soluble drugs (provided absorbance is measured above 280 nm), which may be analyzed for solubility in 1M lignocaine hydrochloride solution (as hydrotropic agent) to carry out their analysis, excluding the use of costlier and unsafe organic solvents. The proposed method is worth adopting in the respective pharmacopoeia.

ACKNOWLEDGEMENTS

The authors are thankful to Alkem Laboratories, Mumbai, India, for the gift sample of bulk drug (tinidazole).

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Source of Support: Nil, **Conflict of Interest:** None declared.