*Asian Journal of Chemistry* Vol. 18, No. 1 (2006), 640–644

# Novel Application of Hydrotropic Solubilization in the Spectrophotometric Analysis of Tinidazole in Dosage Form

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In the present investigation, tinidazole has been selected as a poorly water-soluble model drug. There was more than 60, 70 and 105 fold enhancement in aqueous solubility of tinidazole by 1.25 M sodium citrate, 4 M sodium acetate and 8 M urea solutions (as compared to aqueous solubility), respectively. These hydrotropic agents were employed to solubilize the drug from the fine powder of tablet formulations. The selected $\lambda_{max}$ for spectrophotometric estimation was 318 nm. The hydrotropic agents and the additives used in the manufacture of tablets did not interfere in the analysis. Proposed method is new, rapid, simple, accurate and reproducible. Statistical data proved the accuracy, reproducibility and the precision of the proposed method.

**Key Words: Hydrotropy, Tinidazole, Sodium acetate, Sodium citrate, Urea.**

## INTRODUCTION

In hydrotropic solubilization phenomenon, addition of large amount of a second solute results in an increase in the aqueous solubility of another solute. Concentrated aqueous solutions of a large number of hydrotropic agents have been employed to enhance the aqueous solubility of many poorly water-soluble drugs[1-11]. Sodium benzoate, sodium salicylate, sodium acetate, sodium ascorbate, nicotinamide, sodium citrate and urea are most popular examples of hydrotropic agents. Maheshwari[1] has analyzed poorly water-soluble frusemide by titrimetric analysis using 2 M sodium benzoate solution as solubilizing agent.

Recently, Maheshwari *et al.*[2] have used 2 M sodium benzoate solution as solubilizing agent to solubilize poorly water-soluble ofloxacin from fine powder of tablet formulatons for its spectrophotometric determination. Tinidazole (1-[2-(ethylsulphonyl) ethyl]-2-methyl-5-nitroimidazole) is an antiprotozoal drug. There was tremendous increase in the solubility of tinidazole in 1.25 M sodium citrate, 4 M sodium acetate and 8 M urea solutions. Thus, it was thought worthwhile to employ these hydrotropic solutions to solubilize tinidazole from fine powder of its tablets for spectrophotometric analysis. Hydrotropic agents did not interfere in the analysis.

## EXPERIMENTAL

Tinidazole was a generous gift by Alkem Lab. Ltd., Mumbai (India). All chemicals used were of analytical grade. A Shimadzu UV-Visible recording spectrophotometer (Model-UV 160 A) with 1 cm matched silica cells was used for spectrophotometric analysis. Commercial tablets of tinidazole were procured from the market.

**Calibration Curve:** The standard solution (200 μg/mL) of tinidazole was prepared in distilled water. The standard solution was diluted with distilled water to obtain various dilutions (5, 10, 15, 20, 25 and 30 μg/mL). A linear relationship was observed over the range of 0 to 25 μg/mL for tinidazole ($\lambda_{max}$ 318 nm).

**Preliminary solubility studies of drug:** Solubility of tinidazole was determined in distilled water and different concentrated solutions of hydrotropic agents at 27 ± 1°C. Enhancement in the solubilities of tinidazole in 1.25 M sodium citrate, 4 M sodium acetate and 8 M urea solutions were more than 60, 70 and 105 fold, respectively (as compared to its solubility in distilled water).

**Analysis of tablet formulations of tinidazole by the proposed method using 8 M urea solution:** Twenty tablets of tinidazole (formulation-I) were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 100 mg of tinidazole was transferred to a 50 mL volumetric flask containing 20 mL of 8 M urea solution. The flask was shaken for about 5 min to solubilize the drug and the volume was made up to the mark with distilled water. The solution was filtered through Whatman filter paper No. 41. The filtrate was divided into two parts A and B. Part A was kept at room temperature for 48 h to check its chemical stability and precipitation, if any. Part B was diluted sufficiently with distilled water and was analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated (Table-1). After 48 h, Part A solution was analyzed in the same may as Part B solution. Same procedure was followed for formulation-II and formulation-III.

**Analysis of tablet formulations of tinidazole by the proposed method using 1.25 M sodium citrate solution:** Tablet powder (formulation-I) equivalent to 100 mg tinidazole was transferred to a 50 mL volumetric flask containing 40 mL of 1.25 M sodium citrate solution. Remaining procedure was exactly same as mentioned in the proposed method using 8 M urea solution. Drug contents estimated are shown in Table-1.

**Analysis of tablet formulations of tinidazole by the proposed method using 4 M sodium acetate solution:** Tablet powder (formulation-I) equivalent to 100 mg tinidazole was transferred to a 50 mL volumetric flask containing 40 mL of 4 M sodium acetate solution. Remaining procedure was exactly same as mentioned in the proposed method using 8 M urea solution and the drug contents estimated are shown in Table-1.

**Recovery studies**

For recovery studies 10 and 20 mg of tinidazole pure drug was added to tablet powder equivalent to 100 mg tinidazole. Procedure of analysis was same using 8 M urea, 1.25 M sodium citrate and 4 M sodium acetate solutions. The drug contents were calculated and reported in Table-2.

TABLE-1
RESULTS OF ANALYSIS OF COMMERCIAL TABLET FORMULATIONS WITH STATISTICAL EVALUATION

| Tablet formulation | Label claim (mg) | Method | Per cent label claim estimated[a] (mean ± S.D.) | Per cent coeff. of variation | Standard error |
|---|---|---|---|---|---|
| I | 300 | U[b] | 98.73 ± 0.863 | 0.874 | 0.498 |
| | 300 | SC[c] | 99.03 ± 1.302 | 1.315 | 0.752 |
| | 300 | SA[d] | 100.88 ± 0.628 | 0.622 | 0.362 |
| II | 300 | U[b] | 101.32 ± 1.123 | 1.108 | 0.640 |
| | 300 | SC[c] | 98.68 ± 1.022 | 1.036 | 0.590 |
| | 300 | SA[d] | 98.35 ± 0.734 | 0.746 | 0.424 |
| III | 300 | U[b] | 98.33 ± 0.992 | 1.009 | 0.573 |
| | 300 | SC[c] | 100.81 ± 0.833 | 0.826 | 0.481 |
| | 300 | SA[d] | 99.36 ± 1.121 | 1.128 | 0.647 |

[a]Average of three determinations, [b]Proposed method using 8 M urea,
[c]Proposed method using 1.25 M sodium citrate, [d]Proposed method using 4 M sodium acetate.

TABLE-2
RECOVERY STUDY FOR SPIKED CONCENTRATION OF TINIDAZOLE ADDED TO THE PREANALYZED DOSAGE FORM

| Tablet formulation | Amount of drug (mg) | Pure tinidazole added (mg) | Method | Percent recovery estimated[a] (mean ± S.D.) | % Coeff. of variation | Standard error |
|---|---|---|---|---|---|---|
| I | 100 | 10 | U[b] | 98.88 ± 1.317 | 1.332 | 0.760 |
| | 100 | 20 | U[b] | 100.44 ± 0.683 | 0.680 | 0.394 |
| | 100 | 10 | SC[c] | 99.39 ± 1.086 | 1.093 | 0.627 |
| | 100 | 20 | SC[c] | 101.45 ± 0.928 | 0.915 | 0.536 |
| | 100 | 10 | SA[d] | 97.98 ± 0.681 | 0.695 | 0.393 |
| | 100 | 20 | SA[d] | 101.83 ± 1.223 | 1.201 | 0.706 |
| II | 100 | 10 | U[b] | 98.67 ± 0.876 | 0.888 | 0.506 |
| | 100 | 20 | U[b] | 99.04 ± 1.323 | 1.336 | 0.764 |
| | 100 | 10 | SC[c] | 99.38 ± 1.108 | 1.115 | 0.640 |
| | 100 | 20 | SC[c] | 100.89 ± 0.831 | 0.824 | 0.480 |
| | 100 | 10 | SA[d] | 100.35 ± 1.228 | 1.224 | 0.709 |
| | 100 | 20 | SA[d] | 98.71 ± 0.992 | 1.005 | 0.573 |
| III | 100 | 10 | U[b] | 98.08 ± 1.185 | 1.208 | 0.684 |
| | 100 | 20 | U[b] | 99.38 ± 0.628 | 0.632 | 0.362 |
| | 100 | 10 | SC[c] | 98.68 ± 1.113 | 1.128 | 0.643 |
| | 100 | 20 | SC[c] | 99.54 ± 0.645 | 0.648 | 0.372 |
| | 100 | 10 | SA[d] | 101.38 ± 0.613 | 0.874 | 0.506 |
| | 100 | 20 | SA[d] | 98.88 ± 1.317 | 0.605 | 0.354 |

[a]Average of three determinations. [b]Proposed method using 8 M urea, [c]Proposed method using 1.25 M sodium citrate, [d]Proposed method using 4 M sodium acetate.

## RESULTS AND DICUSSION

Results of solubility studies indicated that enhancement in aqueous solubilities of tinidazole in 1.25 M sodium citrate, 4 M sodium acetate and 8 M urea solutions were more than 60, 70 and 105 fold, respectively, as compared to solubility in distilled water. Therefore, these solutions were empolyed to extract tinidazole from fine powder of tablet formulation. It is evident from Table-1 that per cent label claims ranged from 98.33 ± 0.992 to 101.32 ± 1.123, 98.68 ± 1.022 to 100.81 ± 0.833 and 98.35 ± 0.734 to 100.88 ± 0.628 in cases of proposed methods employing 8 M urea, 1.25 M sodium citrate and 4 M sodium acetate solutions, respectively. Per cent label claims are very close to 100 with low values of standard deviation, per cent coefficient of variation and standard error, showing the accuracy of the proposed methods.

Accuracy, reproducibility and precision of the proposed methods were further confirmed by per cent recovery values. As evident from Table-2, per cent recovery values ranged from 98.08 ± 1.185 to 100.44 ± 0.683, 98.68 ± 1.113 to 101.45 ± 0.928 and 97.98 ± 0.681 to 101.83 ± 1.223 in cases of proposed methods employing 8 M urea, 1.25 M sodium citrate and 4 M sodium acetate solutions, respectively. Per cent recovery values were close to 100 with low values of standard deviation, per cent coefficient of variation and standard error. These results validated the proposed methods.

The drug contents in extracts of all three hydrotropic solutions were same during 48 h and also there was no precipitation in 48 h. This indicates that extracts can be analyzed within 48 h at least, with sufficient accuracy.

### Conclusions

Ethanol, methanol, acetonitrile, hexane, cyclohexane, diethyl ether, chloroform, carbon tetrachloride, toluene and acetone have been employed for solubilization of poorly water-soluble drugs for their spectrophotometric analyses. Most of the organic solvents are toxic, costlier and are responsible for pollution. Inaccuracy due to volatility is another drawback of organic solvents. Using poorly water-soluble tinidazole as a model drug, the author wants to emphasize on the use of hydrotropic solutions as solubilizing agents. Sodium acetate, sodium citrate and urea do not interfere in the spectrophotometric estimations of drugs having $\lambda_{max}$ above 250 nm. Thus, other poorly water-soluble drugs can be checked for their solubilities in these hydrotropic solutions. If they have good solubilities they can be easily estimated by the use of such hydrotropic agents excluding the use of organic solvents provided their $\lambda_{max}$ is above 250 nm. It is concluded that the proposed method is new, simple, cost-effective, accurate, safe, free from pollution and precise and can be successfully employed in the routine analysis of tinidazole tablets.

## ACKNOWLEDGEMENT

The author is thankful to Alkem Lab. Ltd., Mumbai for providing gift sample of tinidazole.

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(*Received*: 30 April 2005; *Accepted*: 27 October 2005) AJC-4451