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Novel Spectrophotometric Quantitative Estimation of Torsemide in Tablets Using Mixed Hydrotropic Agent

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Abstract

A novel, safe, accurate and sensitive spectrophotometric method was developed using containing mixture of 2 M sodium acetate and 8 M Urea in the ration of 50:50% V/V solution as hydrotropic solubilizing agent for the quantitative determination of poorly water-soluble mixed hydrotropic solution torsemide , a very slightly water soluble ($5.96X10^{-02}$ mg/ml) diuretic drug in tablet dosage form. There were more than 86 fold enhancements in the solubility of torsemide increases in mixed hydrotropic solution as compared to solubility in distilled water precluding the use of organic solvents. Torsemide shows maximum absorbance at 288 nm. Sodium acetate, urea and other commonly used tablet excipients did not show any absorbance above 240 nm, and thus no interference in the estimation was seen. Torsemide is obeyed Beer's law in the concentration range of 10 to 50µg/ml (r^2= 0.9996) in mixed hydrotropic solution with mean recovery ranging from 99.23 to 99.64%. The present investigation is new, simple, economic, safe, rapid, accurate and reproducible. The developed methods were validated according to ICH guidelines and result of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values.

Keywords: Torsemide, hydrotropic, sodium acetate, urea, spectrophotometry

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INTRODUCTION

Torsemide[1, 2], chemically 3-[4-[(3-methylphenyl) amino] pyridin-3-yl]sulfonyl-1-propan-2-ylurea (Fig.1), is a loop diuretic mainly used in the management of edema associated with congestive heart failure. It is also used at low doses for the management of hypertension [3, 4]. Hydrotropy phenomenon is considered as a unique technique by which solubility for sparingly soluble solute under normal conditions increase in the several folds.

Various techniques have been employed to enhance the aqueous solubility. Sodium salicylate, sodium benzoate, urea, nicotinamide, sodium citrate and sodium acetate are the most common

examples of hydrotropic agents utilized to increase the water solubility. Maheshwari has analyzed various poorly water-soluble drugs using hydrotropic solubilization phenomenon [5-18]. Various organic solvents have been employed for solubilization of poorly water-soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents. Literature survey reveals that some chromatographic methods [19-26] have been reported for the estimation of TSM in human plasma and urine. In the preliminary solubility studies there were more than 86 fold enhancements in the solubility of TSM in mixed hydrotropic solution. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the drug from fine powder of tablets to carry out spectrophotometric estimation.

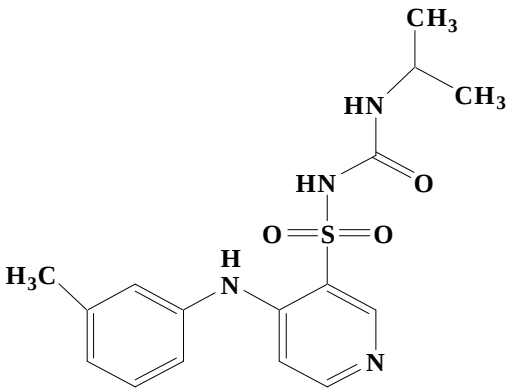


Fig-1 Chemical structure of TSM

MATERIALS AND METHODS

Apparatus

The proposed work was carried out on a shimadzu UV-visible spectrophotometer (model uv-1700 series), which possesses a double beam double detector configuration with a 1 cm quartz matched cell.

Reagents and Standards

Reference standard of TSM was a generous gift from Macleodes Ltd, Mumbai, sodium acetate and urea obtained from Merck Chemical Division, Mumbai. Commercial tablets of TSM, Dyamide (Macleodes Ltd) and Dytor (Cipla Ltd) were procured from the local drug market. Tablet contains 20 mg of TSM.

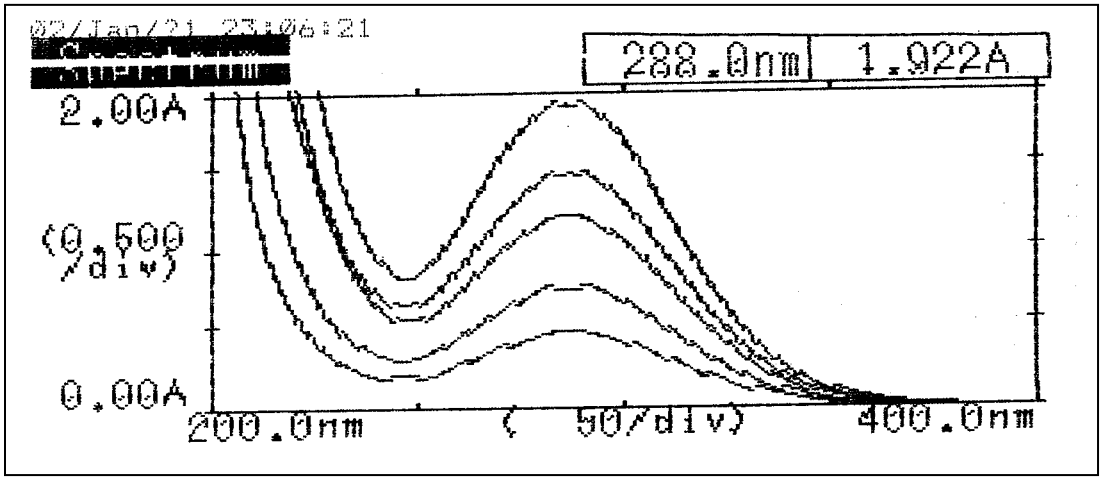
Preliminary Solubility Studies

Solubility of TSM was determined at 28±1°C. An excess amount of drug was added to screw capped 30 ml glass vials containing different aqueous systems viz. distilled water, 8 M urea and 2 M sodium acetate solution and mixture of 2 M sodium acetate and 8 M Urea (50:50% V/V) solution. There was more than 86 fold solubility enhanced in missed hydrotropic solution as compare with distilled water. Solubility was enhanced due to the hydrotropic solubilization phenomenon.

Preparation of calibration curve

Accurately weighed 100 mg of the TSM drug sample were transferred in to 100 ml volumetric flask containing 80 ml of mixture of 2 M sodium acetate and 8 M Urea (50:50% V/V) solution and diluted up to 100 ml with mixed hydrotropic solution. The standard solution (1000 µg/ml) was further diluted with distilled water to obtain 10, 20, 30, 40 and 50 µg /ml. Detection

wavelength was selected for TSM was 288nm. Absorbances were noted against distilled water as blank. Calibration curve was plotted between concentration verses wavelength. Spectra of TSM were shown in Fig.2.



Analysis of Tablet Formulation

Two marketed formulation Dyamide (Macleodes Ltd) and Dytor (Cipla Ltd) were selected for tablet analysis. Twenty tablets of each formulation were weighed and ground to a fine powder. An accurately weighed powder sample equivalent to 20 mg of TSM was transferred to 100 ml of volumetric flask containing mixed hydrotropic solution. The flask was sonicated for about 10 min to solubilize the drug and the volume was made up to mark. The solution was filtered through Whatmann filter paper No 41. The filtrate was diluted appropriately with distilled water and was analyzed on UV spectrophotometer against distilled water as blank. Drug content of tablet formulation were calculated using calibration curve and value are reported in Table-1 and Table-2.

Recovery studies

To evaluate the recovery studies, to pre-analyzed tablet solution, a definite amount of drug was added and then its recovery was studied. These studies were performed, in pre-analyzed tablet solution ranging from 10-50 µg /ml, bulk drug samples 10 µg /ml was added as spiked concentrations and drug contents were determined by the proposed analytical method. Result of recovery studies are presented in Table -3.

Precision studies

To evaluate precision at different parameter like repeatability, intermediate precision, five dilutions in three replicates were analyzed in same day, in two different days and by two analysts for day to day and analyst to analyst variation and results were shown in Table- 4.

RESULT AND DISCUSSION

Based on the solubility and stability and spectral characteristics of the drug, mixed hydrotropic solution containing 2 M sodium acetate and 8 M urea (50:50%v/v) were selected as hydrotropic agent. TSM after solubilized in the selected hydrotropic agent was scanned in spectrum mode and 288nm was selected as wavelength for estimation. The developed method was found to be linear in the range of 10-50µg/ml with correlation coefficient (r^2) of 0.9996. The mean Percent label claims of tablets of TSM in formulation-I and formulation-II estimated by the proposed method were found to be 99.13±1.2 and 100.59±0.38 respectively. These values are close to 100,

indicating the accuracy of the proposed analytical method. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method Table-1 and Table-2. The values of mean percent recoveries were also found ranging from 99.23 to 99.64% Table-3. Result of precision at different level were found be within acceptable limits (RSD ‹ 2) Table-4. Presence of hydrotropic agent do not shows any significant interference in the spectrophotometric assay thus further confirming the applicability and reproducibility of the developed method

Table 1: Result of Tablet Analysis

Amount of drug claimed (mg) in tablet	Tablet Analysis Using Mixed Hydrotropic Solution As Hydrotropic Agent							
	Amount of drug found (mg) in tablet				Percentage estimated in formulation			
	Dyamide		Dytor		Dyamide		Dytor	
	R-I	R-II	R-I	R-II	R-I	R-II	R-I	R-II
20	20.06	20.11	20.2	19.86	100.3	100.55	101	99.3
20	19.98	19.62	20.19	20.14	99.9	98.1	100.95	100.7
20	19.99	19.19	20.13	20.19	99.95	95.95	100.65	100.95

R-I and R-II are the replicates

Table 2: Statistical Evaluation of Analysis of Tablet

Parameter	Marketed Tablets	
	Dyamide	Dytor
Mean % estimated	99.13	100.59
Standard deviation	1.24	0.38
% Coefficient of variation	1.25	0.38
*Standard error	0.51	0.1562

*n=3 in 2 replicates

Table 3: Result of recovery studies of tablet formulation with statically evaluation

Theoretical conc. (µg/ml)	Amount added (µg/ml)	Percentage recovery Mean ± S.D. (n=6)	Percentage coefficient of variation	*Standard error
10	10	99.49±0.80	0.80	0.32
20	10	99.54±0.63	0.64	0.26
30	10	99.64±0.42	0.42	0.17
40	10	99.62±0.54	0.54	0.22
50	10	99.23±0.93	0.94	0.38

* Mean of thirty determinations (6 replicates at 5 concentration level)

Table 4: Result of Precision of TSM

Validation Parameter	Percentage Mean ± S.D*. (n=6)	Percentage RSD*
Repeatability	100.12±0.26	0.26
Intermediate precision		
Day to Day	99.42±1.05	1.05
Analyst to Analyst	98.98±0.24	0.24

* Mean of thirty determinations (6 replicates at 5 concentration level)

CONCLUSION

It was, thus, concluded that the proposed method is new, simple, cost effective, accurately, precise and safe free from pollution and can be successfully employed in the routine analysis of TSM in bulk drug and tablet dosage forms.

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