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Research Article

Spectrophotometric Estimation of Torsemide in Tablet Dosage Form Using Chemical Derivatization Technique

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ABSTRACT

A simple and cost effective spectrophotometric method is described for the determination of Torsemidein pure form and in pharmaceutical formulations. The method is based on the formation derivative when the drug reacts with picric acid solution. The colored derivative solution has an absorption maximum at 350 nm; also obeys Beer's law in the concentration range 5-25µg /mL. The absorbance was found to increase linearly with increasing concentration of torsemide, which is corroborated by the calculated correlation coefficient value of 0.997. The slope and intercept of the equation of the regression line are 0.035 and 0.002 respectively. The optimum experimental parameters for the reaction have been studied. The validity of the described procedure was assessed. Statistical analysis of the results has been carried out revealing high accuracy and good precision. The proposed method was successfully applied to the determination of Torsemide in pharmaceutical formulations.

Key words:
Torsemide, chemical derivatization, UV-Spectrophotometry

INTRODUCTION

Torsemide[1] is a loop diuretic and chemically known as 3-pyridine sulfonamide *N*-[[(1-methylethyl) amino] -carbonyl]-4-[(3-methylphenyl) amino]. It acts by inhibiting the $Na^{+}/ K^{+}/ 2Cl^{-}$ carrier system in the lumen of the thick ascending portion of the loop of Henle, resulting in the decrease in reabsorption of sodium and chloride. It is commonly used in cases of congestive heart failure and in kidney disease. Literature survey reveals that, few Spectroscopic methods[2] for estimation in formulation and chromatographic methods[3,] have been reported for the estimation of Torsemide in human plasma and urine[4]. To the best of our knowledge, there is no spectrophotometric in the literature reported using chemical derivatisation technique for torsemide. The objective of the present work is to develop simple and sensitive spectrophotometric method for the estimation of Torsemidein pure drug and in pharmaceutical formulations.

From Below graph it can be seen that Torsemide drug showed less absorbance at 284nm (λ_{max}) so derivatisation of Torsemide was done to improve absorbance of Torsemide.(Fig. No.01)

The method was validated as per standard ICH guidelines. [5, 6]

EXPERIMENTAL[7-14]

Instruments and Chemicals

UV-Visible Spectrophotometer (Perkin-Elmer, Lambda 25) was used for spectral measurements with spectral band width 1 nm; wavelength accuracy is 0.5 nm and 1 cm matched quartz cells.

All chemicals used were of analytical reagent grade and methanol was used throughout. Dytor and Tide are then commercial tablet formulations labeled to contain 10 mg of torsemide per tablet. Stock reference solution was freshly prepared from pure sample of torsemide derivative by dissolving 25mg in 25 mL of methanol.

Table1: Regression and Optical characteristics of derivative of Torsemide

Parameters	Value
Selected analytical wavelength	350 nm
Beer's law range	5-25 µg mL^{-1}
Coefficient of correlation	0.999
Slope	0.035
Intercept	0.002

Preparation of Picric Acid Derivative of Torsemide

0.5 mg of pure drug was dissolved in 5ml of hydrochloric acid and added about 5 ml of saturated solution of picric acid in water. This above mixture was then warmed for 5 minutes on the water bath and then allowed to cool to room temperature, for crystallization. The precipitate obtained above was then subjected to recrystalisation by using water or methanol as solvent. The yellow crystals obtained were
of ionic bond of picric acid with the drug. (Fig. No. 2)

Preparation of solutions

Accurately weighed 25 mg of Torsemide derivative transferred to 25mL volumetric flasks and the resultant solution was further diluted to get100ppm solution.

In to 10 mL measuring flasks, different aliquots of working standard solution (1.0- 5.0 mL) were transferred to provide final concentration range 5.0 – 25.0µ/g mL.

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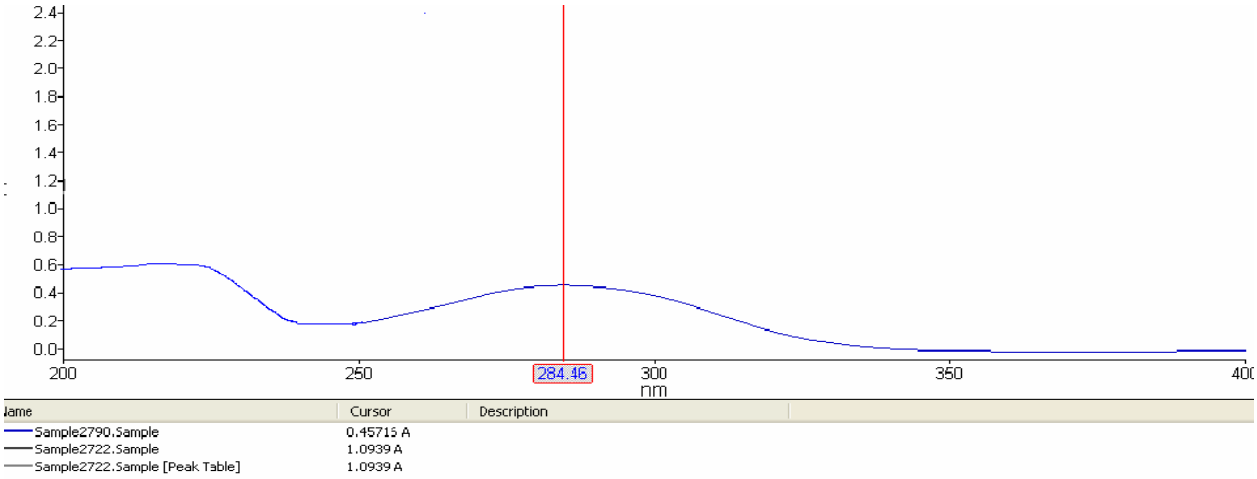
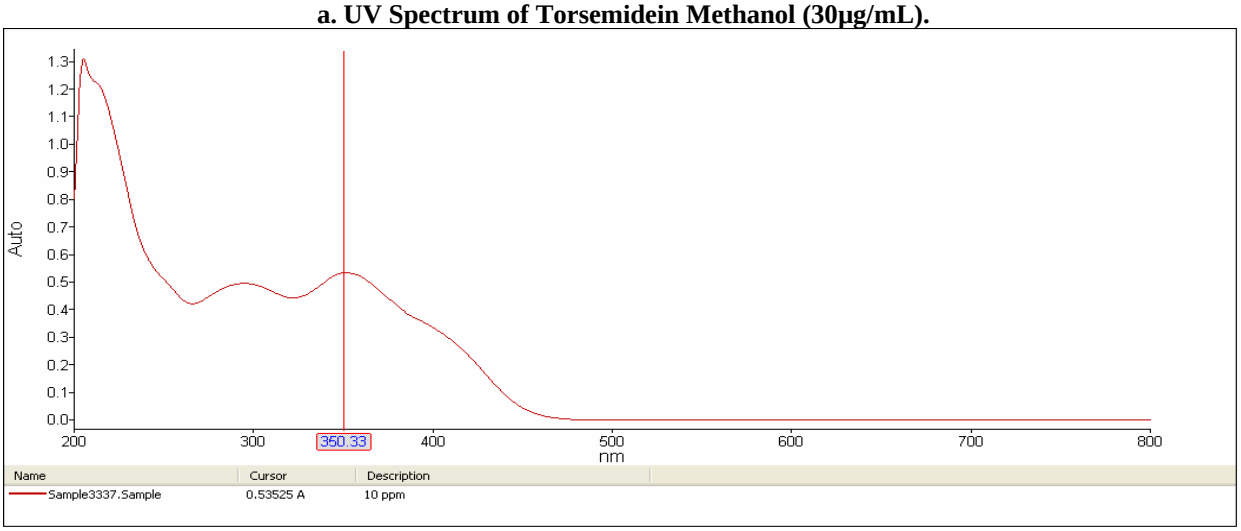


a. UV Spectrum of Torsemidein Methanol (30µg/mL).



b. UV Spectrum of derivative of Torsemidein methanol. (15µg/mL)

Fig.1: Difference between UV specrum of Torsemide derivative (b) and Torsemide (a).

Table 2: Results of analysis of tablet by dramatization

Pharmaceutical formulation	% Label Claim in mg	%Average	S.D.	%RSD
Tablet (Dytor)	10	99.22%	0.389	0.392
Tablet (Tide)	10	100.03%	0.209	0.209

The solutions were made up to volume with distilled water. The absorbance of each solution was measured at 350 nm against the reagent blank. The calibration graph was then prepared by plotting the absorbance versus concentration of the drug. (Fig. No.3)

Table 3: Results of Recovery Study

% Solution	% Recovery± SD	%RSD
For 80 %	99.16 ± 0.588%	0.590
For 100 %	99.87 ±1.59%	1.592
For 120 %	101.19 ± 0.392%	0.387
Ruggedness	101.07 ±0.301 %	0.297
Robustness	97.77 ±0.224%	0.224

Assay of tablet formulation

In order to see the feasibility of proposed method for estimation of Torsemide in marketed pharmaceutical formulations, for analysis of commercial formulation; twenty tablets were weighed, average weight determined and crushed into fine powder. A quantity of tablet powder equivalent to 10 mg of Torsemide was transferred into 100 ml glass volumetric flask containing 50 ml water, shaken manually for 10 min, volume was adjusted to mark with same solvent and filtered through whatmann filter paper no.1. The appropriate aliquots were transferred to 10 ml glass volumetric flask; volume was adjusted to the mark with same solvent to obtain concentration of 15 µg/mL. The absorbance of the solutions were recorded at 350nm and the concentration of the torsemide was determined. % label claim was then calculated; results are shown in Table No. 1**.**

Table 4: Results of Precision

Precision (as % Relative standard deviation)		
Parameter	**Avg±SD**	**%RSD**
Interday Precision	0.1881±0.185 %	0.188
Intraday Precision	0.2173±0.213%	0.217
Repeatability	0.5647±0.558%	0.567

Validation

The Proposed method was validated as per the USP

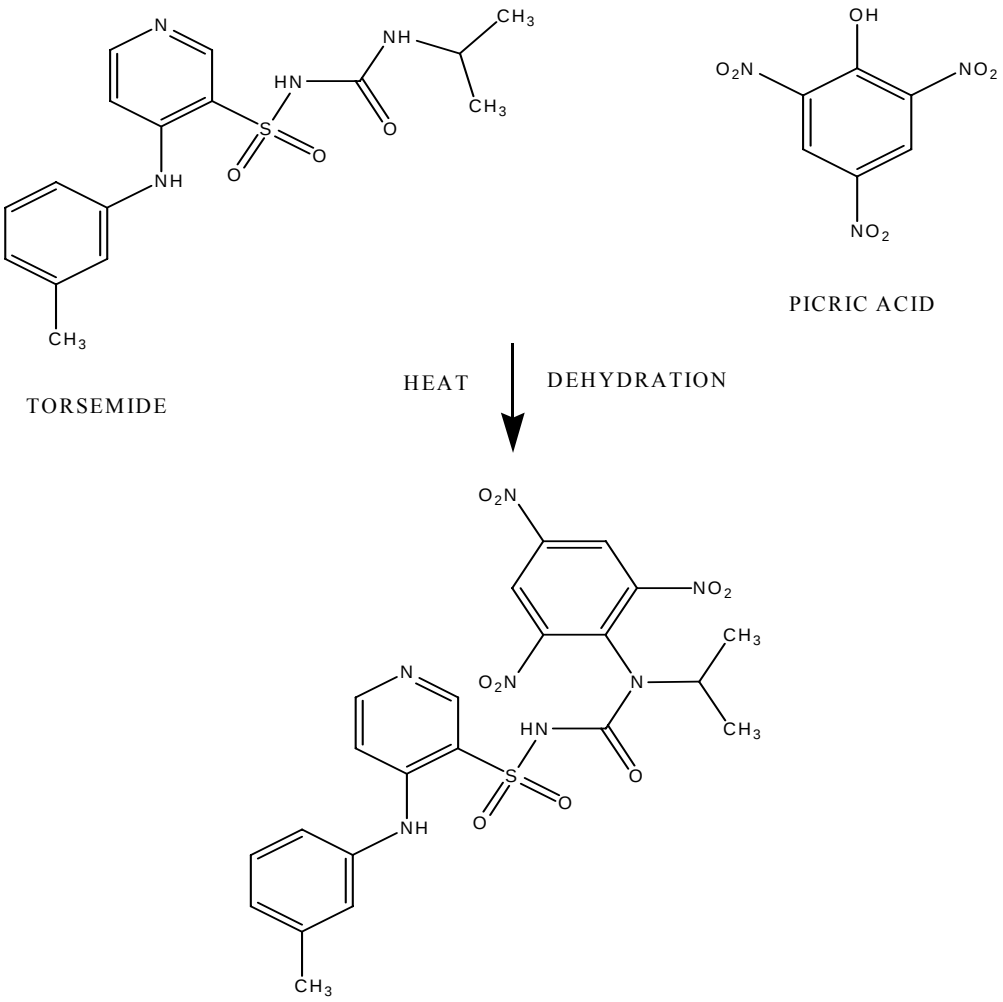


Figure 2: Formation of ionic bond with picric acid

guidelines for linearity and accuracy, precision

Recovery studies

To study the accuracy of the proposed methods and to check the interference from excipients present in the dosage form, recovery experiments were carried out by the standard addition method. Recovery studies were carried out by standard addition method at three different levels. A known amount of drug was added to preanalyzed capsule powder and percentage recoveries were calculated. The results of recovery studies were satisfactory and are presented in Table No.3

Table 5: Results of Specificity

Condition (24hrs)	Wt. taken In mg	% rug estimated	% Degradation
0.1N HCl	25.16	61.48	38.52
0.1N NaOH	24.80	37.70	62.30
3% H_2O_2	25.62	47.77	52.23
Heat(60^0C)	25.41	59.92	40.08
Nomal	25.09	97.43	96.56

Precision

Precision of the method is studied as repeatability, intra-day and inter-day precision. Repeatability was determined by analyzing Torsemide derivative (15µg/mL). For six times. Intra-day precision was determined by analyzing the 15 µg/mL of Torsemide derivative for three times in the same day. Inter-day precision was determined by analyzing the same concentration of the solutions daily for three days, results are reported in Table No.4**.**

Table No. 6: Results of Ruggedness and Robustness

Ruggedness	101.07 ±0.301 %	0.297
Robustness	97.77 ±0.224%	0.224

Specificity

The specificity study was performed for the proposed analytical method by the preparation of degradants such as 0.1N HCL, 0.1N NaOH, 3% H_2O_2, Heat and UV Light by subjecting the analyte to different degradation conditions for 24 hours and results were recorded and are depicted in Table No 5.

Ruggedness

The studies of ruggedness were carried out by using two different analysts.

a) Different analyst

The sample solutions were prepared by two different analysts and same procedure was followed as described earlier. The % label claim was calculated as done in marketed formulation estimation. Results and statistical data are shown in Table No.6.

Robustness

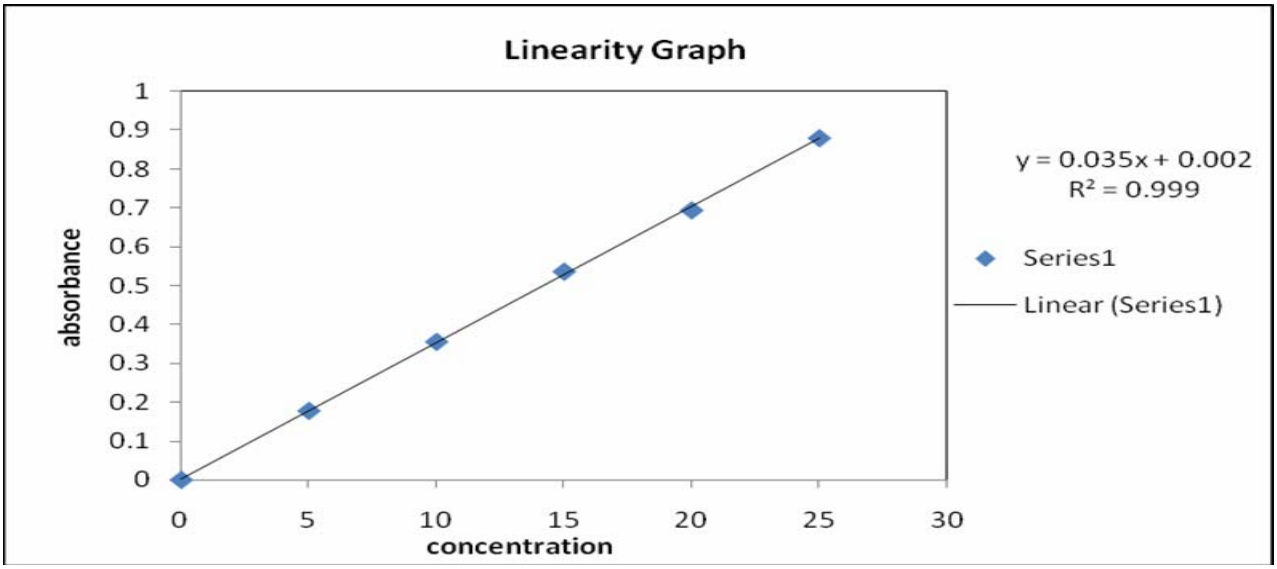


Figure 3: Calibration curve of Torsemide derivative

The robustness of an analytical procedure is studied by a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters. Robustness was studied by taking absorbance of 15 mcg/mL solution at lower wavelength for five times. Results and statistical data are shown in Table No.6.

RESULTS AND DISCUSSION

The method developed for spectrophotometric determination of Torsemide in tablet formulation was found to be simple and convenient for the routine analysis. Beer-Lambert law was obeyed in the concentration range of 5-25 mcg/ml. Co-efficient of variation was found to be 0.997. The percentage recoveries were found in the range of 100.25%. While the method was found to be precise with % relative standard deviation ± (0.1881 %) for interday precision and for intraday (0.2173%).

CONCLUSION

The proposed method is simple, rapid, precise and inexpensive, and hence can be used in routine analysis of Torsemide in bulk drug and in formulations. It can be easily conveniently applied for quality control analysis.

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