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Development and validation of a UV spectrophotometric method for the estimation of torsemide in bulk and in tablet dosage form

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ABSTRACT

A simple and cost effective spectrophotometric method described is based on use of 0.1N sodium hydroxide solution in which the drug is completely soluble, is used as a solvent. The drug has an absorption maximum at 290 nm and obeys Beer's Lambert law in the concentration range 1–25μg $ml^{-1.}$ The absorbance was found to increase linearly with increasing concentration of torsemide, which is corroborated by the calculated correlation coefficient value of 0.9999(n=6). The apparent molar absorptivity is1.896x10^{3} L $mol^{-1}cm^{-1}$. The slope and intercept of the equation of the regression line are 3.4 ×10^{-2} and 11.2x10^{-2} 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.

Keywords*:* Torsemide, spectrophotometry,

INTRODUCTION

Torsemide (TSM) is loop diuretic and is chemically known as 3-pyridine sulfonamide *N*-{[(1-methylethyl) amino] - carbonyl]-4-[(3-methylphenyl) amino] (Fig.1).

It acts by inhibiting the Na^{+} / K^{+} / $2Cl^{-}$ carrier system (via interference of the chloride binding site) in the lumen of the thick ascending portion of the loop of Henley, resulting in the decrease

in reabsorption of sodium and chloride [1-5]. Literature survey reveals that few chromatographic methods have been reported for the estimation of torsemide in human plasma and urine [6]. To the best of our knowledge, there is single work in the literature reported about the visible spectrophotometric method for the analysis of torsemide in either biological fluids or pharmaceutical formulations [7]. The purpose of this investigation was to develop a simple and sensitive ultra violet spectrophotometric method for the quantization of torsemide in pure drug and in pharmaceutical formulations. Literature reports that torsemide is insoluble in water and ether, but slightly soluble in acetone and chloroform. However it is soluble in alcohol, 0.1N NaOH, 0.1N HCl. The method is based on use of 0.1N sodium hydroxide solution in which the drug is completely soluble, is used as a solvent. The drug has an absorption maximum at 290nm [8](Fig. 3) and obeys Beer's lambert law in the concentration range 1– 25µg mL^{-1}.

MATERIALS AND METHODS

Instrument:

SHIMADZU double beam UV-visible spectrophotometer (model 1700) with 1 cm matched quartz cuvettes were used for all absorbance measurements. Shimadzu AUX220 balance was used for weighing the samples**.** All the chemicals used were of AR grade. Double distilled water and Whatmann filter paper (no.41) were used throughout the experimental work.

Material:

Torsemide working standard was obtained as a gift sample from MSN laboratories Medak district, India. Tablets containing torsemide drug was purchased from local pharmacy. Sodium hydroxide was purchased from Merck limited Mumbai. Double distilled water was used for making solvent.

Preparation of standard stock solutions:

A stock solution of torsemide (1mg/ml) was prepared by accurately weighing approximately 25mg of torsemide and dissolved in 25ml of 0.1N sodium hydroxide. Aliquots of the standard stock solutions were transferred using A-grade bulb pipettes into 100ml volumetric flasks and solutions were made up to volume with solvent to give a final concentrations of 1-25µg/ml. The absorbance of each solution was measured at 290nm in UV spectrophotometer (Table 1). The standard graph (Fig.2) was then prepared by plotting the absorbance versus concentration of the drug.

Estimation of torsemide from pharmaceutical dosage forms:

To determine the content of torsemide in tablets (Label claim: 20mg torsemide), 10 tablets were weighed and crushed. An aliquot of powder equivalent to 25mg was accurately weighed and transferred to 25ml volumetric flask and was dissolved in 0.1N sodium hydroxide and made up to the volume. The solution was stirred continuously for 30minutes to affect complete dissolution. The solution was filtered. Suitable aliquots of filtered solution was added to 100ml volumetric flask and made up to the volume with solvent to yield concentrations of 10, 15 and 20µg/ml. The absorbance for these drug solutions were measured in UV spectrophotometer at 290nm and concentrations in the sample were determined by comparing the standard curve (Table 3).

Table 1: Observations of standard solution

CONCENTRATION(in µg/ml)	ABSORBANCE
1	0.146
5	0.282
10	0.451
15	0.624
20	0.793
25	0.962

Table 2: Method validation parameters

Parameter	Value
LINEARITY RANGE	1-25µg/ml
REGRESSION COEFFICIENT (R^2)	0 .9997
CORRELATION COEFFICIENT = $N\Sigma XY - (\Sigma X)(\Sigma Y)/sqrt[N\Sigma X^2 - (\Sigma X)^2][N\Sigma Y^2 - (\Sigma Y)^2]$	0.9999(N=6)
REGRESSION EQUATION	
SLOPE(m)	0.034
INTERCEPT(c)	0.1119
LINE EQUATION	Y = 0.034*X + 0.1119
MOLAR ABSORPTIVITY	1.896x103 L $mol^{-1}cm^{-}$

Fig.1 Chemical structure of torsemide

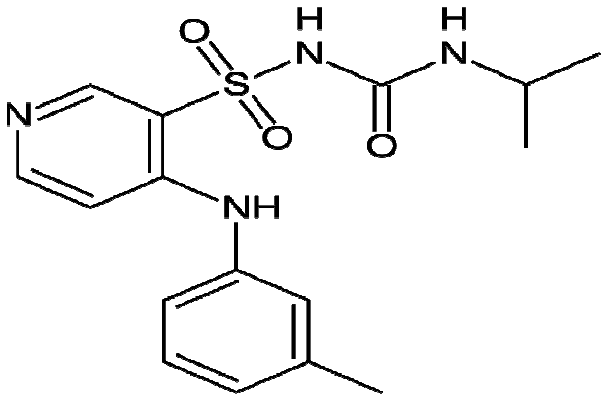


Fig.2 Standard curve of torsemide

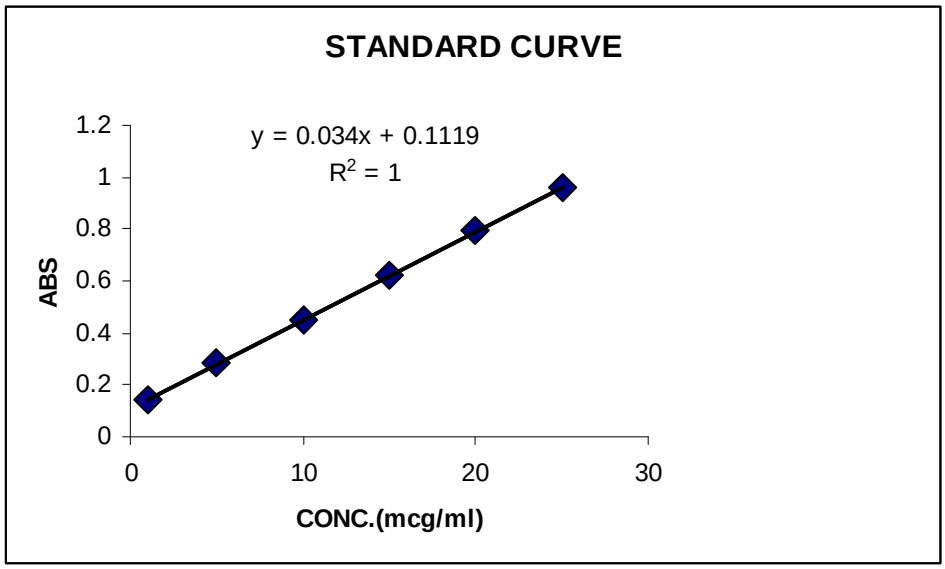
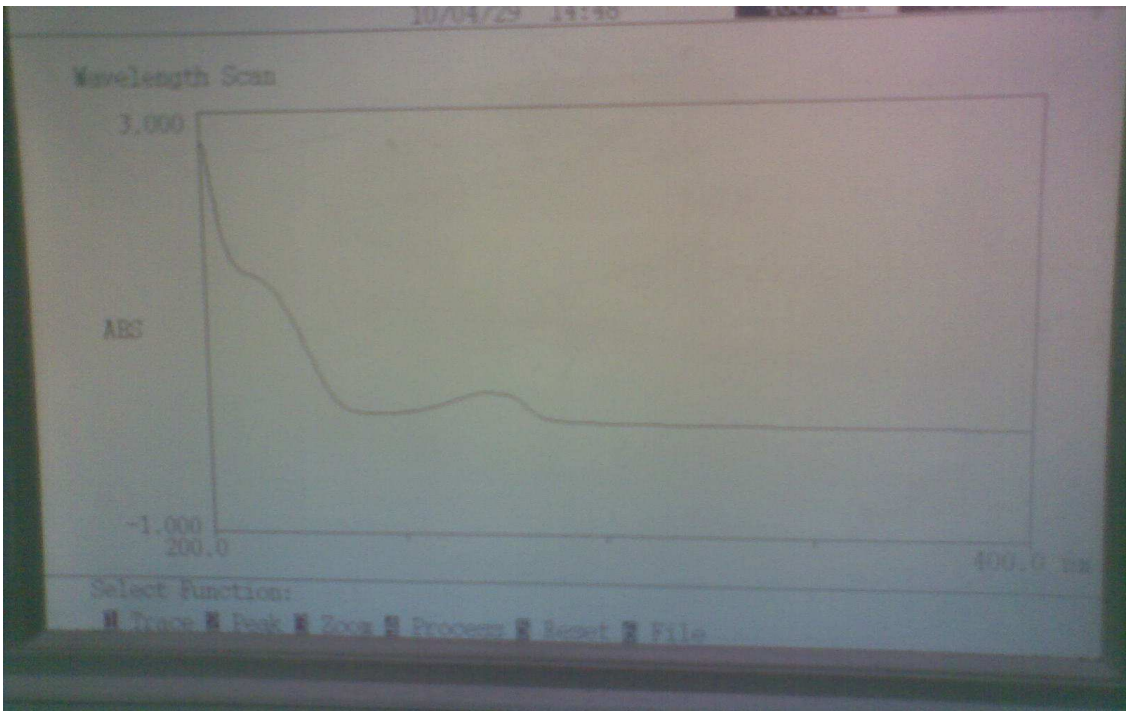


Table 3: Observations of marketed formulations

CONCENTRATION (in µg/ml)	ABSORBANCE
10	0.448
15	0.622
20	0.790

Fig .3: UV-spectra of torsemide



RESULTS AND DISCUSSION

Various solvents were screened. The drug was found to be soluble in alcohol, strong base and acid. Sodium hydroxide was selected as solvent system as it is easily available and it is not volatile compared to alcohol. Linearity range was studied by preparing standard solutions of torsemide at different concentrations level. The linearity was found in range of 1-25µg/ml. The standard curve obtained was generated using regression analysis with Microsoft Excel. The assay judged to be linear as correlation coefficient was found to be 0.9999 (Table 2).The proposed procedure was applied to the determination of torsemide in commercially available tablets. The same samples were analyzed, simultaneously by the UV reference method and the proposed method. The results obtained from the two sets of analyses were compared statistically. The observation indicates no significant difference between the methods in so far as accuracy and precision are concerned.

CONCLUSION

A simple, accurate, fast and precise UV spectrophotometric method has been developed for the determination of torsemide in bulk and tablet dosage form. This method stood validated at the laboratory level. This method can be of use and value for the quality control department division of pharmaceutical companies manufacturing these formulations.

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