Available online on 15.09.2016 at http://jddtonline.info
Journal of Drug Delivery and Therapeutics
An International Peer Reviewed Journal
Open access to Pharmaceutical and Medical research

RESEARCH ARTICLE

COLORIMETRIC METHODS FOR THE ESTIMATION OF TOPIRAMATE IN TABLETS

** Sunitha PG, Deattu N, Dhanalakshmi R, Gangatharan A, Kavi Bharathi A, Murali Shankar G, Sathya M*

Department of Pharmaceutical Chemistry, College of Pharmacy, Madras Medical College, Chennai-600 003, Tamil Nadu, India

**Corresponding Author's E-mail: sunitha.srm@gmail.com*

Received 21 July 2016; Review Completed 16 Aug 2016; Accepted 16 Aug 2016, Available online 15 Sep 2016
DOI: http://dx.doi.org/10.22270/jddt.v6i5.1308
URI: http://jddtonline.info/index.php/jddt/article/view/1308

ABSTRACT

Two simple sensitive and precise colorimetric methods A and B were developed for the estimation of topiramate in bulk drug as well as in pharmaceutical dosage form. Methods A is based on the formation of yellow colored chromogen by condensation reaction of topiramate with Ehrlich's reagent (p - dimethyl amino benzaldehyde) which has absorption maximum at 547nm. Method B is based on the formation of an orange colored complex by oxidation reaction of topiramate with 2, 2'- bipyridyl in the presence of ferric chloride which has absorption maximum at 519nm. The proposed methods are statistically validated and found to be useful for the routine determination of topiramate in tablets.

Keywords: Topiramate, Colorimetry, Tablets, Validation

INTRODUCTION

Topiramate (TPM) is an anticonvulsant indicated in the treatment of epilepsy and migraine.[1,2] TPM acts by enhancing the prolongation of Na^+ channel inactivation.[3,4] Chemically it is 2,3:4,5-Bis-o-(1-methyl ethylidene)-beta-d-fructo pyranose sulfamate.[5] The available methods for analysis of the drug in biological fluids and pharmaceutical products are gas chromatography coupled with flame ionization or nitrogen phosphorous detection[6], fluorescence polarization immunoassay[7] and HPLC method including ionic chromatography.[8] The present wok deals with the estimation of TPM in tablets by visible spectrophotometric methods. In Method A, TPM is first condensed with Ehrlich's (p-dimethylamino benzaldehyde) reagent to form a yellow chromogen, which absorbs intensively at 547nm. In method B, TPM forms colored complex with 2, 2'- bipyridyl and ferric chloride which exhibited λ_{max} at 519 nm. The method is alternative and comparable in specificity and accuracy to chromatography methods, which although highly specific and accurate, are more time consuming, performed in several steps and are rather expensive.

MATERIALS AND METHODS

Instrumentation: All spectral and absorbance measurements were made on Shimadzu UV-Vis Spectrophotometer – 1650PC.

Reagents:

Ehrlich's reagent (0.5% w/v), Concentrated hydrochloric acid, Ethanol (95% w/v), 2, 2'Bipyridyl (0.1% w/v), Ferric choride (5% w/v) are used in this study. All reagents were used of analytical grade.

Preparation of standard solution:

A 1 mg/ml stock solution of TPM was prepared by dissolving 100 mg of drug in 100 ml of ethanol.

Sample preparation:

Twenty tablets were weighed and powdered. A quantity equivalent to 25 mg of TPM was weighed accurately, transferred to a beaker, dissolved in ethanol, filtered through whatmann filter paper No. 1 into a 25 ml volumetric flask and made up to volume with ethanol to get a concentration of 1mg/ml.

Assay:

Method A:

Appropriate aliquots of TPM were pipetted out into a series of 25 ml volumetric flasks. To each flask 2 ml of Ehrlich's reagent (p-dimethylamino benzaldehyde) was added, mixed thoroughly and made up to volume with ethanol. The λ_{max} of the yellow coloured chromogen was found to be 547nm (Figure-1).The absorbance of the yellow coloured chromogen was measured at 547 nm against the reagent blank. The yellow chromogen was stable for more than 3 hours. The analytical curve

was constructed by plotting concentration versus absorbance.

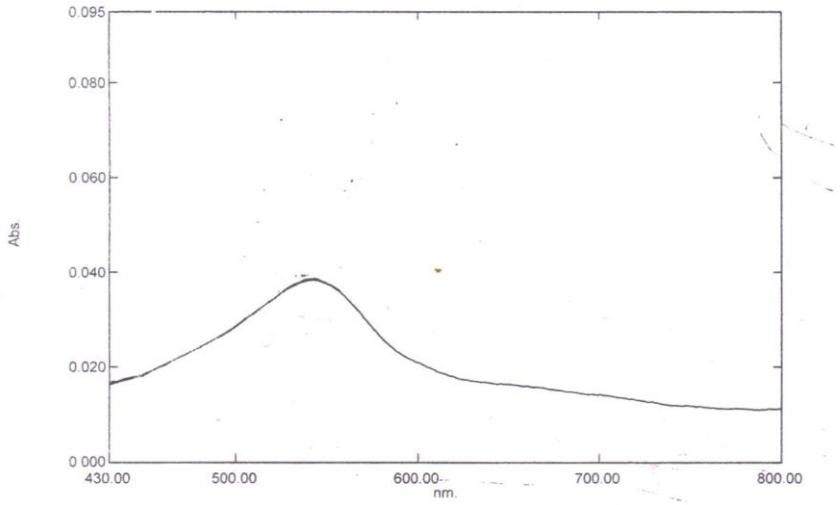

Figure 1: λ_{max} of the yellow chromogen by Method A

Method B:

Appropriate aliquots of TPM were pipetted out into a series of 25 ml volumetric flasks. To each flask 1 ml of ferric chloride (1% w/v) and 3 ml of 2,2'bipyridyl (0.1% w/v) were added, heated on a boiling water bath for 15 minutes, cooled and then made up to volume with ethanol. The λ_{max} of the orange colored chromogen was found to be 519nm (Figure-2). The absorbance of the orange colored chromogen was measured at 519 nm against the reagent blank. The amount of TPM was computed from the calibration curve obtained by plotting concentration versus absorbance.

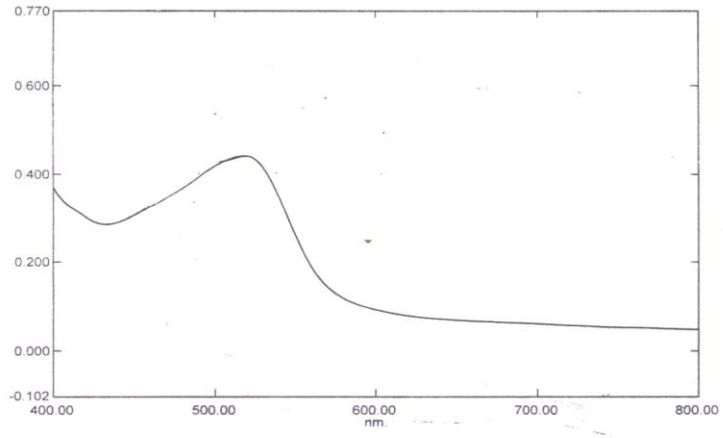

Figure 2: λ_{max} of the orange chromogen by Method B

Sample Analysis:

Pharmaceutical formulation of TPM was successfully analyzed by the proposed methods. Appropriate aliquots were subjected to the above methods and the amount of the TPM was determined from the calibration curves. The results of sample analysis are furnished in table- 2.

RESULTS AND DISCUSSION:

The optical characteristics such as absorption maxima, Beer's law limits, Molar absorptivity and Sandell's sensitivity are furnished in table-1. The regression characteristics like slope (b), intercept(a), correlation coefficient(r), percent relative standard deviation (%RSD) and standard error (SE) obtained from different concentrations were calculated and the results are summarized in table-1.

To study the accuracy and reproducibility of the proposed methods, recovery experiments were carried out by adding a known amount of drug to pre-analyzed sample and the percentage recovery was calculated. The results are furnished in table-2.The results indicate that there is no interference of other ingredients present in the formulation. Thus, the proposed methods are simple, sensitive, precise, accurate and reproducible and useful for the routine determination of TPM in bulk drug and its pharmaceutical dosage form.

 ISSN: 2250-1177 CODEN (USA): JDDTAO

Table 1: Optical characteristics, Precision and Accuracy of the proposed methods

Parameter	Method A	Method B
λ_{max} (nm)	547	519
Beer's law limit(µg/ml)	100-600	200-1200
Molar absorptivity ($Lmol^{-1}cm^{-1}$)	4.4376×10^2	2.2536×10^2
Sandell's sensitivity (µg/cm²/0.001 absorbance unit)	0.0930	0.1643
Regression equation(*y)		
Slope(b)	0.0094	0.002
Intercept(a)	0.111	0.0938
Correlation co-efficient (r)	1.088	1.037
% RSD	0.5827	0.5498
Standard error(SE)	0.4462	0.5498

*y = a+bc where c is the concentration of TPM in µg/ml.

Table 2: Assay and recovery of TPM in the dosage form (tablets)

Method	Labelled amount (mg)	Amount obtained (mg)*	Percentage recovery**
A	100 mg	99.63	99.97
B	100 mg	99.92	100.02

*Average of six determinations ** Average of three determinations*

ACKNOWLEDGEMENTS:

We are thankful to the Department of Pharmaceutical Chemistry, Madras Medical College, Chennai-03, for providing the instrumentation and laboratory facilities.

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Cite this article as:

Sunitha PG, Deattu N, Dhanalakshmi R, Gangatharan A, Kavi Bharathi A, Murali Shankar G, Sathya M, Colorimetric methods for the estimation of topiramate in tablets, Journal of Drug Delivery & Therapeutics. 2016; 6(5):11-13. DOI: http://dx.doi.org/10.22270/jddt.v6i5.1308

