International Journal of Biological & Pharmaceutical Research

e- ISSN 0976 - 3651
Print ISSN 2229 - 7480

www.ijbpr.com

Research Article

METHOD DEVELOPMENT AND VALIDATION OF NOVEL ANALYTICAL METHODS FOR TOPIRAMATE IN BULK AND PHARMACEUTICAL FORMULATIONS USING UPLC TECHNIQUE

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ABSTRACT

A simple and selective UPLC method is described for the determination of Topiramate. Chromatographic separation was achieved on a Cortecs Phenyl (100 x 2.0mm) 1.5µm C_{18} column using mobile phase consisting of a mixture of 60 volumes of Ammonium phosphate Buffer, 40 volumes of Methanol with detection of 260 nm. Linearity was observed in the range 50-150 µg /ml for Topiramate (r^2 =0.999) estimated by the proposed method was in good agreement with the label claim. The proposed methods were validated. The accuracy of the methods was assessed by recovery studies at three different levels. Recovery experiments indicated the absence of interference from commonly encountered pharmaceutical additives. The method was found to be precise as indicated by the repeatability analysis, showing %RSD less than 2. All statistical data proves validity of the methods and can be used for routine analysis of pharmaceutical dosage form.

Key Words: Topiramate, Cortecs Phenyl C_{18} column, UPLC

Access this article online		
Home page: http://ijbpr.com/ DOI: http://dx.doi.org/10.21276/ijbpr.2018.9.3.2		Quick Response code
Received:05.06.18	**Revised**:12.06.18	**Accepted**:25.06.18

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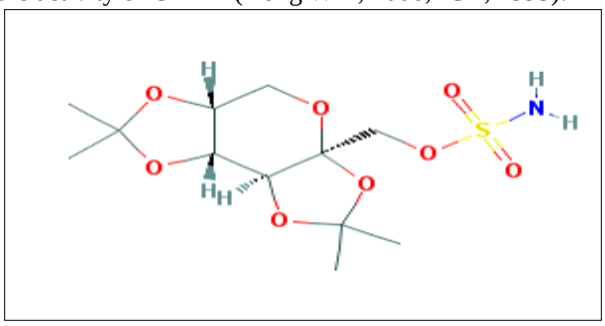
INTRODUCTION

Ultra Performance Liquid Chromatography (UPLC) which is based upon small, porous particles (sub 2 micron particles). Van Deemter equation is the principle behind this evolution which correlates the connection between linear velocity and plate height. The small particles require a high pressure to work with UPLC i.e., 6000 psi which is typically the upper limit of conventional HPLCs (Swartz ME and Ira Krull S, 2009; Satinder A and Dong MW, 2005). It was observed that when the particle size is decreased below 2.5 µm, there is a remarkable increase in the effectiveness and this effectiveness does not lessen on increasing the linear speed or rate of flow. This method reduces the mobile phase volume consumption by at least 80% compared to HPLC with a shorter runtime of about 1.5 min. The smaller sized particles increase the pressure up to 1000 bars or more which can alone increase the retention factor of the separation. Lower injection volume is required for UPLC which results in higher efficiency and increase in resolution (Chatwal RG and Anand KS, 2010). The higher column temperature reduces the mobile phase viscosity resulting in the high diffusion coefficient and flow rate without significant loss in

efficiency and increase in column back pressure (Sharma BK, 2005; Snyder RL *et al.*, 1997).

Drug Profile

The precise mechanism of action of topiramate is not known. However, studies have shown that topiramate blocks the action potentials elicited repetitively by a sustained depolarization of the neurons in a time-dependent manner, suggesting a state-dependent sodium channel blocking action. Topiramate also augments the activity of the neurotransmitter gamma-amino butyrate (GABA) at some subtypes of the $GABA_A$ receptor (controls an integral chloride channel), indicating a possible mechanism through potentiating of the activity of GABA (Dong WM, 2006; ICH, 1995).



Structure for Topiramate

Review of Literature

Mahadev B Kshirsagar, Moreshwar P. Mahajan, Sanjay D. Sawant. Method Development and Validation by RP-HPLC for Estimation of Topiramate in Bulk and Pharmaceutical Dosage form Gummadi Sridhar Babu, PS. Malathi Analytical Method development and validation for the estimation of Topiraate by RP-HPLC Method (https://www.drugbank.ca/drugs/DB00273)

MATERIALS & METHODS

Instrumentation

UV-Visible	Nicolet evolution 100
UV-Visible	Vision Pro
UPLC	Open lab EZ chrome
UPLC	Agilent Technologies
Ultra sonicator	Citizen, Digital
pH meter	Global digital
Electronic balance	Mettler Toledo
Syringe	Hamilton

Reagents And Chemicals

Water	HPLC Grade
Methanol	HPLC Grade
Ammonium phosphate	HPLC Grade
Orthophosphoric acid	HPLC Grade

Working/Reference Standards

Topiramate Gift samples obtained from Chandra Labs, Hyderabad.

MATERIALS & METHODS

Preparation of Standard Solution of Topiramate

Weigh accurately 10 mg of Topiramate in 100 ml of volumetric flask and dissolve in 60ml of mobile phase and make up the volume with mobile phase. From above stock solution 50 µg/ml of Topiramate is prepared by diluting 5ml to 10ml with mobile phase. This solution is used for recording chromatogram.

Preparation of Sample Solution of Topiramate

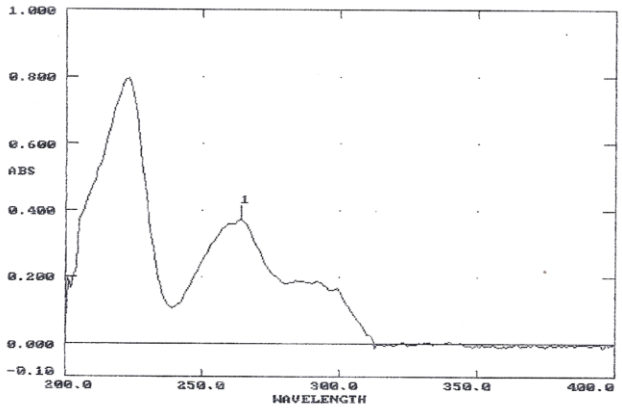
Sample preparation: (Brand Name:(Topamac-25 mg)) Weigh about 100mg Equivalent weight of Topiramate Crushed tablets and transferred in to 100 ml of volumetric flask and dissolve in 60ml of mobile phase and make up the volume with mobile phase. Sonicated for 30min and centrifuged for 10min.From above stock solution 100 µg/ml of Topiramate is prepared by diluting 5ml to 50ml with mobile phase. This solution is used for recording chromatogram.

Table 1. Optimized Chromatographic Conditions

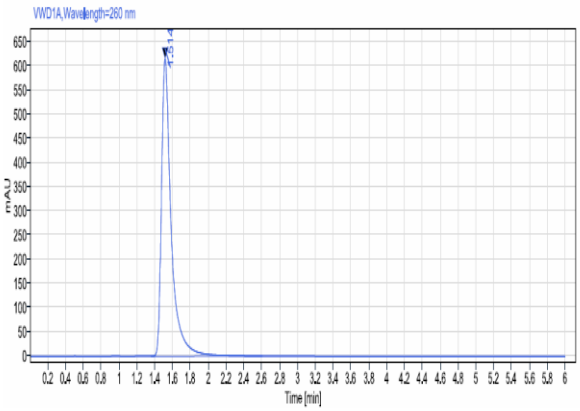
Mobile phase	Ammonium phosphate Buffer(pH:3.2): Methanol
Ratio	60:40
Column	Cortecs Phenyl(100x2.0mm) 1.5µm
Flow rate	0.5 ml/min
Column temperature	25°C
Wavelength	260
Injection volume	20 µl
Run time	6 min
Retention time	About 1.314min for Topiramate

RESULT AND DISCUSSION

UV – Vis Spectrum for Topiramate (260nm):



Chromatogram for Optimized Concentration



S.No.	Name	Rt (min)	Peak Area	Theoritical Plates	Tailing Factor	Resolution
1	TOPIRAMATE	1.514	29366622	8847	1.2	-

System Suitability

Results for system suitability of TOPIRAMATE.

Injection	RT	Peak area	Theoretical plates (TP)	Tailing factor (TF)
1	1.275	128775	3695	1.24
2	1.289	111985	3624	1.25
3	1.276	108527	3687	1.23
4	1.278	133128	3696	1.27
5	1.276	152688	3674	1.26
Mean	1.28	27020.	-	-
SD	0.0058	7799.41	-	-
%RSD	0.45	0.20	-	-

Accuracy

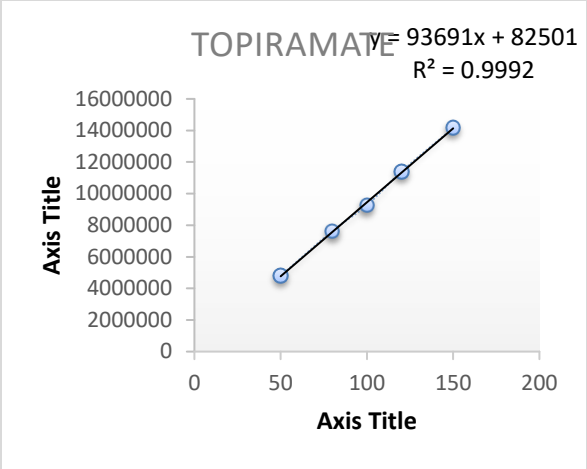
TOPIRAMATE						
Name of the Sample	Standard Weight in mg	Area	Conc Added (µg/ml)	Conc Recovered (µg/ml)	%Recovery	Average
50% Recovery_01	50	4591	50	49.9	99.8	9.7
50% Recovery_02	50	4585471	50	49.79	99.6	
50% Recovery_03	50	4587541	50	49.81	99.6	
100% Recovery_01	100	9265841	100	100.61	100.6	
100% Recovery_02	100	9274512	100	100.70	100.7	
100% Recovery_03	100	9265841	100	100.61	100.6	
150% Recovery_01	150	13662041	150	148.34	98.9	
150% Recovery_02	150	13669857	150	148.43	99.0	
150% Recovery_03	150	13655412	150	148.27	98.8	

Method Precision

Method precision results for TOPIRAMATE

S.No.	Area	%Assay
1	9231182	101.5
2	9241228	101.6
3	9231190	101.4
4	9231135	101.5
5	9241195	101.6
6	9231147	101.4
AVG		101.5
SD		0.10
%RSD		0.1

Linearity



Graph for Linearity of TOPIRAMATE

Ruggedness

Ruggedness Results of TOPIRAMATE

Topiramate	%Assay
Analyst 01	99.75
Analyst 02	101.5
%RSD	0.27

Robustness

Result of robustness study

Chromatographic changes		Rt(min)	Tailing Factor	Theoretical Plates	%RSD
Flow rate (mL/min)	0.	1.712	1.25	3654	0.12
	0.6	1.030	1.27	3694	0.11
Temperature	25	1.282	1.27	3622	0.22
	35	1.285	1.22	3614	0.19

DISCUSSION

Accuracy

The percentage mean recovery of Topiramate is 99.7%.

System Suitability

The plate count and tailing factor results were found to be within the limits and the % RSD was found to be 1.2 so system is suitable and giving precise results.

Linearity

The correlation coefficient for linear curve obtained between concentrations vs. Area for standard preparation 0.9992.

METHOD PRECISION

The %RSD of Assay for 6 Samples determinations of TOPIRAMATE found to be within the acceptance criteria (less than 2.0%). %Assay Also within the limits (95.0 to 105.0) hence method is precise.

Robustness

The tailing factor was found to be within the limits on small variation of flow rate and wavelength so method is Robust.

Ruggedness

From the above results % Assay and %RSD obtained acceptance criteria so method is rugged.

CONCLUSION

From the above experimental results and parameters it was concluded that, this newly developed method for the estimation of TOPIRAMATE was found to be simple, precise, accurate and high resolution and shorter retention time makes this method more acceptable and cost effective and it can be effectively applied for routine analysis in research institutions, quality control department in meant in industries, approved testing laboratories studies in near future.

ACKNOWLEDGEMENT

Nil

CONFLICT OF INTEREST

No interest

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Cite this article

Mohammed Yusuf S, Purushothaman M. Method Development and Validation of Novel Analytical Methods for Topiramate in Bulk and Pharmaceutical Formulations Using UPLC Technique. *International Journal of Biological & Pharmaceutical Research*. 2018; 9(3):69-73. DOI: **http://dx.doi.org/10.21276/ijbpr.2018.9.3.2**