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A NEW METHOD DEVELOPMENT AND VALIDATION OF TOPIRAMATE IN PHARMACEUTICAL DOSAGE FORM USING UPLC

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ABSTRACT

A simple and selective UPLC method is described for the determination of Topiramate Chromatographic separation was achieved on a c_{18} column using mobile phase consisting of a mixture of 80 volumes of Methanol and 20 volumes of Water with detection of 276 nm. Linearity was observed in the range 50-150 µg /ml for Topiramate (r^2 =0.998) for the amount of drugs estimated by the proposed methods 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: UPLC method, Topiramate

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INTRODUCTION

Chromatography is a non-destructive procedure for resolving a multi-component mixture of traces, minor or constituents in to individual fractions. It is a method of separating a mixture of components in to individual components through a porous medium under the influence of solvent. For many years, researchers have looked at “fast LC” as a way to speed up analyses. The need for speed, the availability Of affordable and easy to use mass spectrometers. Smaller columns and faster flow rates (amongst other parameters) have been used. Elevated temperature, having the dual advantages of lowering viscosity, and increasing mass transfer by increasing the diffusivity of the analytes, has also been investigated. However, using conventional particle sizes and pressures, limitations are soon reached and compromises must be made, sacrificing resolution. HPLC technology simply doesn’t have the capability to take full advantages of sub-2µm particles. UPLC can be regarded as new invention for liquid chromatography. UPLC refers to Ultra Performance Liquid Chromatography. UPLC brings dramatic improvements in sensitivity, resolution and speed of analysis can be calculated.

It has instrumentation that operates at high pressure than that used in HPLC & in this system uses fine particles(less than 2.5µm) & mobile phases at high linear velocities decreases the length of column, reduces solvent consumption & saves time. According to the van Deemter equation, as the particle size decreases to less than2.5 µm, there is a significant gain in efficiency, while the efficiency does not diminish at increased flow rates or linear velocities. Therefore by using smaller particles, speed and peak capacity (number of peaks resolved per unit time in gradient separations) can be extended to new limits, termed Ultra Performance Liquid Chromatography, or UPLC

The technology takes full advantage of chromatographic principles to run separations Using columns packed with smaller particles(less than2.5µm) and/or higher flow rates for increased speed, this gives superior resolution and sensitivity (1-6).

Quality investigation plays a very important role in quality specification establishment of chemical drugs. The number of drugs introduced into the market every year .very often there is a time lag from the date of introduction of a drug into the market to the date of its inclusion in pharmacopoeias. Hence, standards and analytical procedures for these drugs may not be available in the pharmacopoeias. It becomes necessary, therefore to develop newer analytical methods for such drugs. Analytical method development provides the support to track the quality of the product from batch to batch. Method development involves considerable trial and error procedures. The most difficult problem usually is where to start, what type of column is worth trying with what kind of mobile phase.

MATERIALS AND METHODS

Determination of Working Wavelength (λmax) (7-9)

Preparation of standard stock solution of Topiramate

10 mg of Topiramate was weighed and transferred in to 100ml volumetric flask and dissolved in methanol and then make up to the mark with methanol and prepare 10 µg /ml of solution by diluting 1ml to 10ml with methanol.

Assay of Topiramate

Preparation of samples for Assay

Preparation of mixed standard solution

Weigh accurately 10 mg of Topiramate in 25 ml of volumetric flask and dissolve in 25ml of mobile phase and make up the volume with mobile phase. From above stock solution 20 µg/ml of Topiramate is prepared by diluting 0.5ml to 10ml with mobile phase. This solution is used for recording chromatogram.

Sample preparation

Weigh accurately 10 Tablets **(Topiramate -25 mg)** weigh accurately 10 mg of Topiramate in 25 ml of volumetric flask and dissolve in 25ml of mobile phase and make up the volume with mobile phase. From above stock solution 20 µg/ml of Topiramate is prepared by diluting 0.5ml to 10ml with mobile phase. This solution is used for recording chromatogram.

Validation

To verify that the analytical system is working properly and can give accurate and precise results were evaluated by 20µg/mL of TOPIRAMATE was injected five times and the chromatograms were recorded for the same.

Method precision was determined by injecting sample solutions of concentration TOPIRAMATE (20µg/mL) for six timesare prepared separately.

RESULTS AND DISCUSSION

The wavelength of maximum absorption (λ_{max}) of the drug, 10 µg/ml solution of the drug in methanol were scanned using UV-Visible spectrophotometer within the wavelength region of 200–400 nm against methanol as blank.
The resulting spectra are shown in the Fig-1 and The absorption curve shows characteristic absorption maxima at 276nm for Topiramate, selected as detector wavelength for the UPLC chromatographic method.
The amount of Topiramate present in the taken dosage form was found to be 101.55 % respectively (Table-1).

Table-1 Assay Results

Topiramate		
	Standard Area	**Sample Area**
Injection-1	9111785	9245257
Injection-2	9128795	9272110
Injection-3	9123101	9282820
Injection-4	9101117	9257988
Injection-5	9140105	9252085
Average Area	9120980.60	9262052
Standard deviation	15086.63	
%RSD	0.2	
Assay(%purity)	101.55	

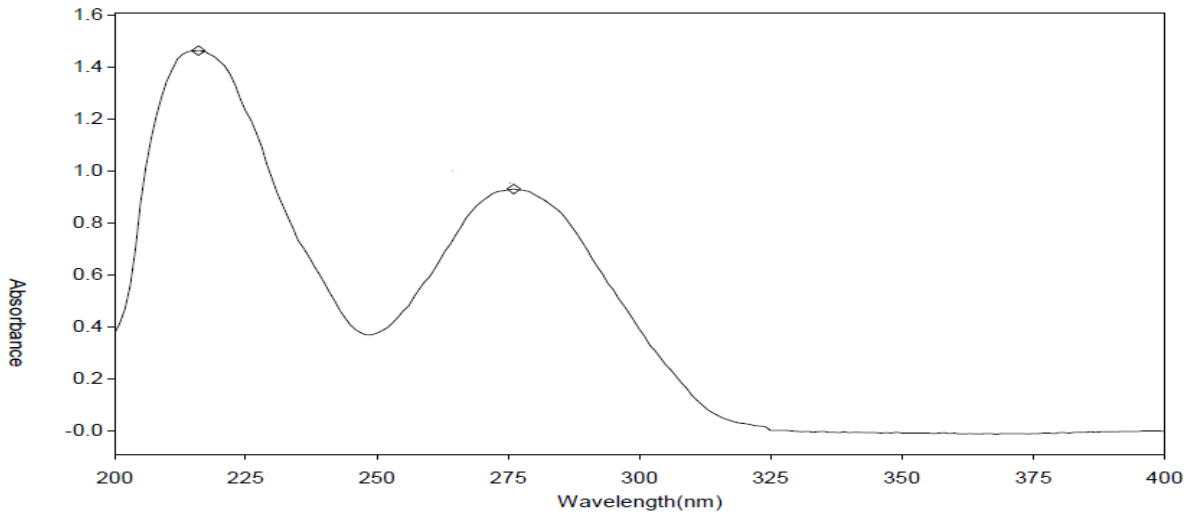

Fig-1 UV-VIS spectrum of Topiramate at 276nm

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. 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 (Fig-2-6).The LOD for this method was found to be 1.11µg/ml Topiramate. The LOQ for this method was found to be 3.37µg/ml Topiramate. From the above results % Assay and %RSD obtained acceptance criteria so method is rugged.

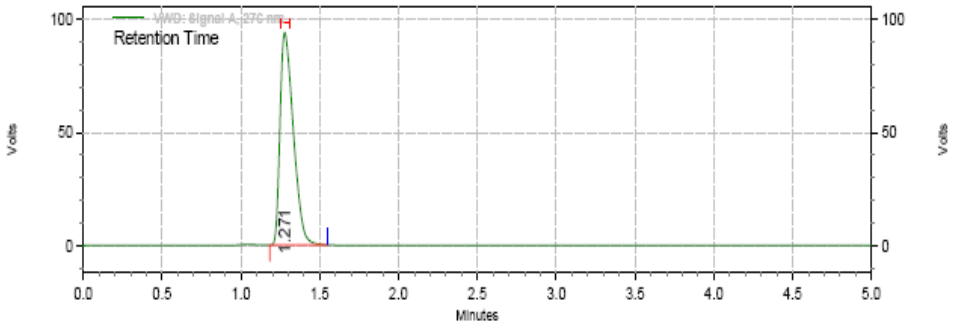

Fig-2 Chromatogram of Method Precision-01

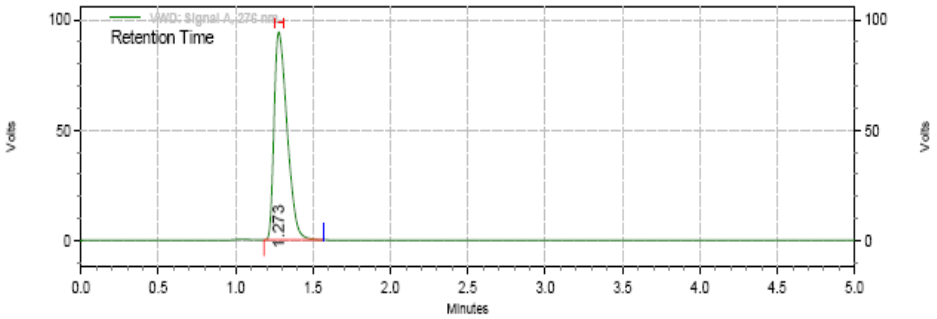

Fig-3 Chromatogram of Method Precision-02

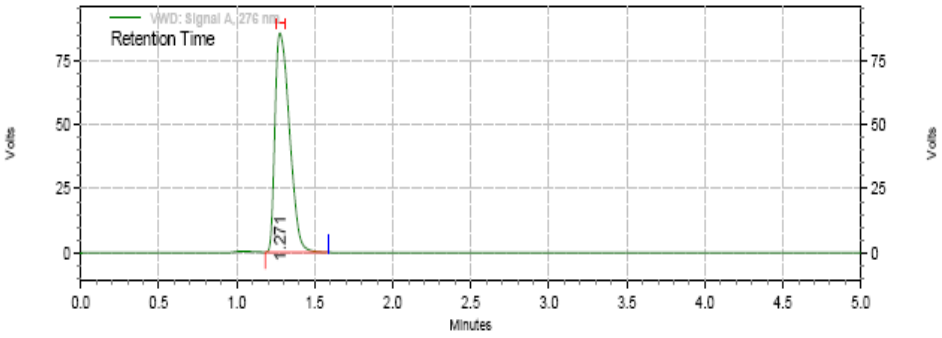

Fig-4Chromatogram of Method Precision-03

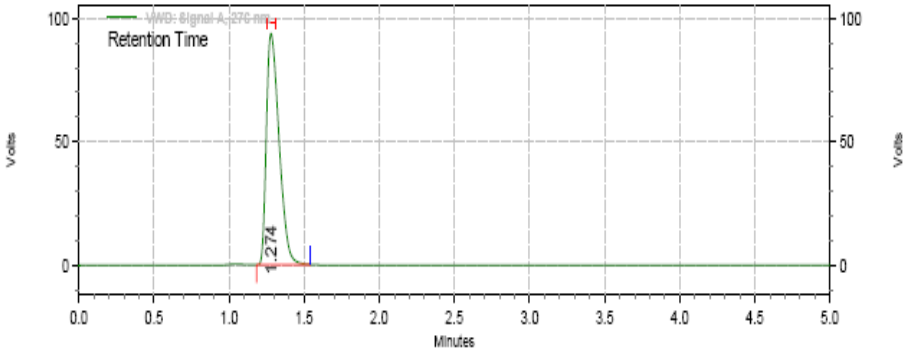

Fig-5 Chromatogram of Method Precision-04

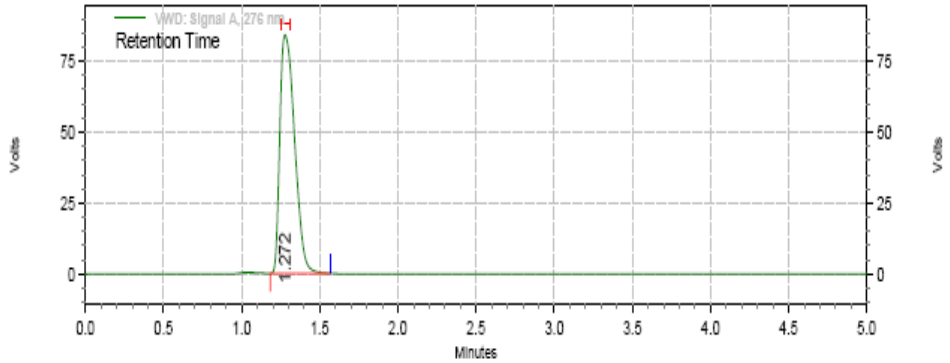

Fig-6 Chromatogram of Method Precision-05

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.

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