Development And Validation Of UV Spectroscopic Method For The Estimation Of Levetiracetam In Tablet Dosage Form

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Abstract:

Simple, precise and accurate zero order derivative spectroscopic method has been developed and validated for the estimation of Levetiracetam in bulk and Pharmaceutical dosage form. The drug shows maximum absorption(λ_{max}) at 209nm in 0.01N sodium hydroxide solution and obeys Beer's law in the concentration range of 2-10 µg/ml. The linearity study carried and regression coefficient was found to be 0.9996 and it has showed good linearity, precision in this concentration range. The % recovery was found to be 99.97-100.78.TheLOD and LOQ were found to be 0.0328 and 0.0984µg/ml. The % relative standard deviation were found less than 2. The method has been validated according to ICH guidelines for linearity, precision, accuracy, robustness, ruggedness, LOD and LOQ. The developed and validated method can be successfully applied for reliable quantification of Levetiracetam in bulk form and pharmaceutical dosage form.

Keywords: *Levetiracetam, Zero order derivative spectroscopy, validation, pharmaceutical formulations.*

Introduction:

Levetiracetam is an anticonvulsant drug used to treat the epilepsy[1].Levetiracetam is a drug within the pyrrolidine class that is used to treat various types of seizures[2]. Chemically it is known as pyrrolidinone and acetamide derivative. Levetiracetam may selectively prevent hyper synchronization of epileptic form burst firing and propagation of seizure activity. It is also used to treat neuropathic pain[3]. The chemical name of Levetiracetam is (S)-2-(2-oxopyrrolidin-1-yl) butanamide with molecular formula of $C_8H_{14}N_2O_2$ and a molecular weight of 170.20g/ml.

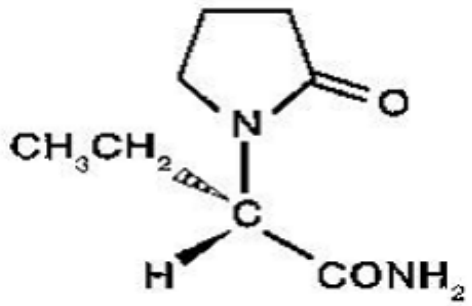

Fig.1: Chemical structure of Levetiracetam

Literature survey revealed that there were few analytical methods have been reported for the determination of Levetiracetam in pure drug and pharmaceutical dosage forms by using UV spectrophotometric[4-9], HPLC[10-16] and HPTLC[17] so far.

The aim of present work is to develop and validate a novel, rapid, simple, precise and specific Zero order derivative UV Spectrophotometric method for estimation of Levetiracetam in bulk and tablet dosage form.

Material and Method

Instrument:

UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software. All weights were taken on analytical balance.

Chemicals:

Levetiracetam pure drug was obtained as a gift sample from Mylan pharma industry and its pharmaceutical dosage form Levetiracetam 20 tablet labelled claim 500mg from local pharmacy manufactured by Mylan Ltd.

Solvent:

0.01N Sodium hydroxide (prepared by dissolving 0.4g in 1000ml of distilled water).

Selection of analytical wavelength:

Appropriate dilutions of Levetiracetam were prepared from standard stock solution and using spectrophotometer solution was scanned in the wavelength range 200-400nm. The absorption spectra obtained and shows maximum absorbance at 209nm. Which was selected as the wavelength for detection (Fig-2).

Preparation of standard stock solution:

100mg of Levetiracetam was weighed accurately and transferred in to 100ml volumetric flask and dilute in 0.01N Sodium hydroxide up to mark. From this solution was further diluted into 100µg/ml and from this solution pipette out 0.2,0.4,0.6,0.8 and 1ml into 10ml individual volumetric flask and dilute in 0.01N Sodium hydroxide up to mark, this gives 2,4,6,8 and 10µg/ml concentration.

Preparation of sample solution:

20 tablets of Levetiracetam marketed formulations were weighed and powdered. A quantity of tablet powder equivalent to 100mg of Levetiracetam was transferred into a 100ml of volumetric flask then it was diluted with 0.01N Sodium hydroxide and made up to the mark.

Method and validation:

The method was validated according to ICH guidelines.

Results and Discussion:

Method: Zero order derivative spectroscopy.

Linearity:

The linearity of an analytical method is its capacity to show the test results that are directly proportional to the concentration of the analyte in the sample within the range. The linearity was established in the range of 2-10µg/ml was measured at 209nm and absorbance values are shown in table-1. The calibration curve was prepared by plotting graph against the concentration and absorbance and the graph shown in Fig-3. Statistical parameter like slope, intercept, regression equation, correlation coefficient and sandell's sensitivity were determined. (table-2).

Precision:

The precision of an analytical method expresses the closeness of a series of individual analyte measurements obtained from multiple sampling of the same sample. Precision was determined by intra-day and inter-day study. Intra-day precision was determined by analyzing the same concentration for three times in a same day. Inter-day precision was determined by analyzing the same concentration daily for three days. (table-3).

Accuracy:

The accuracy of an analytical method say that closeness of test results obtained by that method to the true value. To assess the accuracy of the developed method, recovery studies were carried out at three different level as 80%, 100% and 120%. In which the formulation concentration kept constant and varied pure drug concentration.(table-4).

Ruggedness:

The ruggedness is defined as the reproducibility of results when the method is performed under the variation in conditions. This includes different analyst, laboratories, instruments, temperature etc. Ruggedness was determined between different analyst, the value of %RSD was found to be less than 2. (table-5).

Limit of detection and Limit of Quantitation:

The limit of detection is an individual analytical method is the smallest amount of analyte in a sample which can be reliably detected by the analytical method. The limit of quantization is an individual analytical procedure is the smallest amount of analyte in a sample which can be quantitatively determined. LOD and LOQ were calculated using formula.

LOD = 3.3(SD)/S and LOQ = 3(LOD)

LOD and LOQ value of Levetiracetam were found to be 0.0328 and 0.0984µg/ml.

Conclusion:

The present analytical method was validated as per ICH guidelines and met the acceptance criteria. It was concluded that the developed analytical method was simple, specific, accurate, economical and sensitive and can be used for routine analysis of Levetiracetam in bulk drug and in pharmaceutical dosage forms.

Acknowledgment:

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Tables:

Table 1: Results of calibration curve at 209nm by zero order spectroscopy

SL NO	Concentration in µg/ml	Absorbance ±Standard deviation*
1	0	0
2	2	0.075±0.00753
3	4	0.146±0.00160
4	6	0.216±0.00150

5	8	0.284±0.00344
6	10	0.351±0.00167

*Average of six determinations.

Table 2: Regression parameter for Levetiracetam by zero order spectroscopy

Regression parameter	Results
Range(µg/ml)	2-10
λ_{max}(nm)	209
Regression Equation	Y= 0.035x+0.0035
Slope(b)	0.035
Intercept(a)	0.0035
Correlation coefficient(r^2)	0.9996
Sandell'sequation	0.0277
Limit of detection(µg/ml)	0.0328
Limit of quantitation(µg/ml)	0.0984

Concentration (µg/ml)	Intra-day Absorbance ±Standard deviation*	%RSD**	Inter-day Absorbance ±Standard deviation*	%RSD**
2	0.075±0.001	1.333	0.076±0.001	1.315
4	0.145±0.00152	1.048	0.144±0.001155	0.802
6	0.215±0.001155	0.534	0.215±0.001528	0.710
8	0.281±0.001528	0.543	0.281±0.001528	0.543
10	0.352±0.001	0.284	0.351±0.001	0.284

Table 3: Determination of precision results for Levetiracetam at 209nm by zero order spectroscopy.

*****Average of six determinations, **percentage relative standard deviation.

Table 4: Determination of Accuracy results for Levetiracetam at 209nm by Zero order spectroscopy.

Spiked Levels	Amount of Sample (µg/ml)	Amount of Standard (µg/ml)	Amount recovered	% Recovery ±Standard deviation*	%RSD**
80	6	4.8	10.85	100.4 ±0.650	0.648
100	6	6	11.99	99.97 ±0.610	0.610
120	6	7.2	13.30	100.78 ±0.500	0.496

*****Average of three determinations, **percentage relative standard deviation.

Table 5: Determination of Ruggedness results for Levetiracetam at 209nm by Zero order spectroscopy.

Analysts	Analyst 1	Analyst 2
Mean absorbance	0.214	0.215
±Standard deviation*	0.001528	0.001528
%RSD	0.714	0.7106

*****Average of three determinations, **percentage relative standard deviation.

Figures:

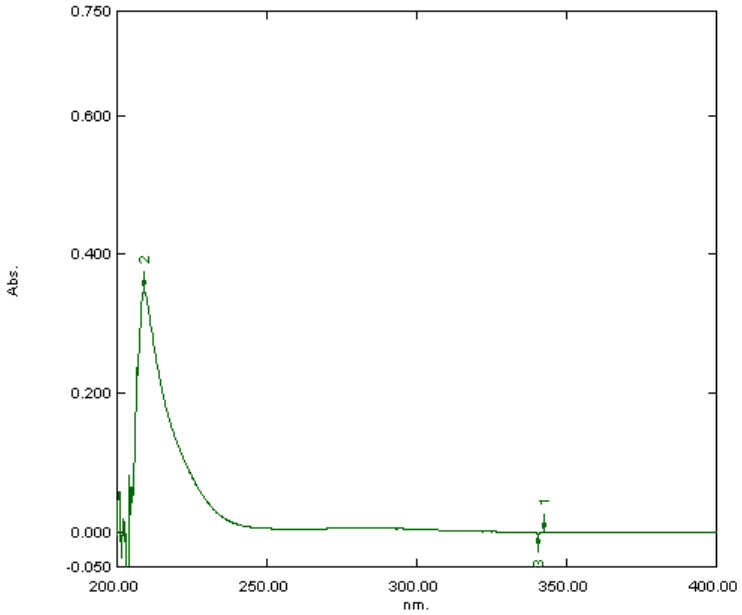

Fig.2: Zero order spectrum of Levetiracetam at 209nm

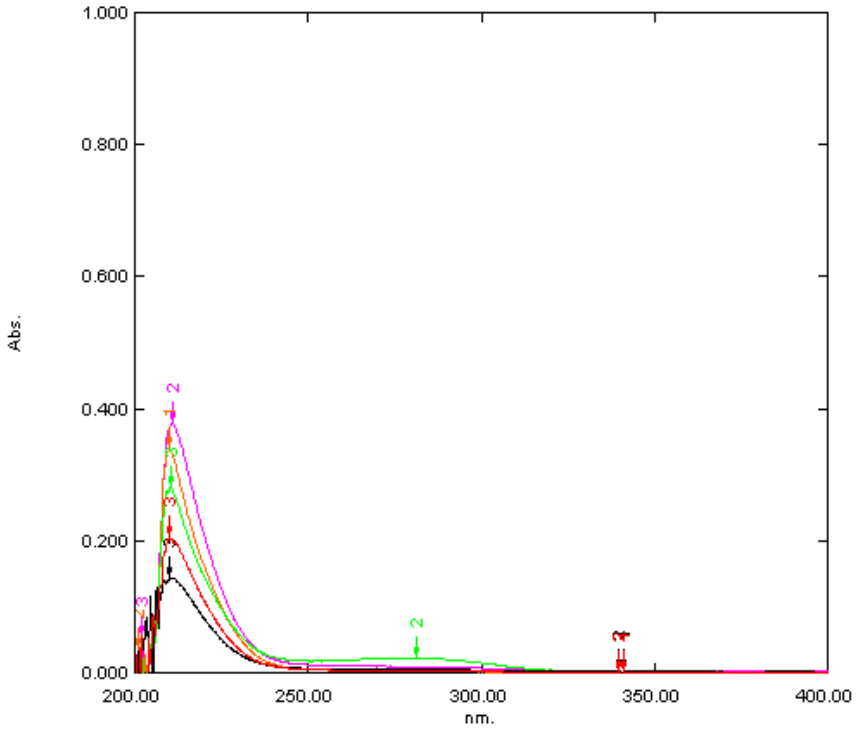

Fig.3: Zero order overlain spectra of Levetiracetam showing absorbance at 209nm

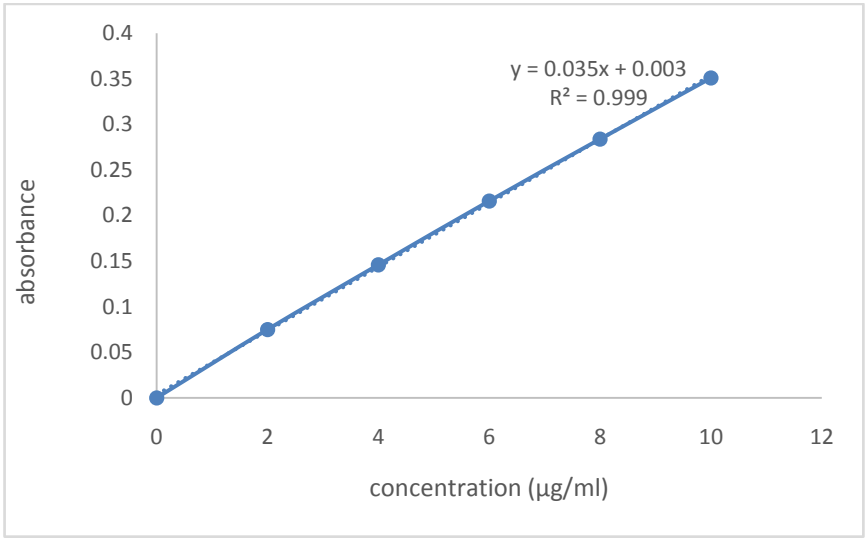

Fig.4: Calibration curve of Levetiracetam by zero order spectroscopy