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Method Development and Validation of Gabapentin and Estimation of Gabapentin Tablets by Uv Spectroscopy

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Abstract: A simple, accurate, precise and economic spectrophotometric method has beendeveloped for the determination of Gabapentin in their bulk powder and pharmaceutical dosage form. Gabapentin showed maximum absorbance at 217 nm with 0.1 N sodiumhydroxide as solvent. Beer's law was obeyed in the concentration range 1.5-9 µg/ml with regression coefficient of 0.998. The concentration of active component were then determined from the calibration curve obtained by measuring the amplitude at 217 nm for gabapentin. Accuracy and precision of the developed methods have been tested in addition recovery studies have been carried out in order to confirm their accuracy. Themethod was validatedintermsoflinearity, precision, accuracy (98.03–101.45%w/w) and specificity. This method is simple, precise, accurate, sensitive and reproducible and can be used for the routine quality control testing of the marketed formulations.

Key words: Spectrophotometry · Gabapentin · 0.1N NaoH

INTRODUCTION

Spectroscopy Methods [1, 2]: It is the branch of science dealing with the study of interaction between Electromagnetic radiation and matter. It is a most powerful tool available for the study of atomic and molecular structures and is used in the analysis of wide range of samples. Optical spectroscopy includes the region on electromagnetic spectrum between 100 Å and 400 nm. The regions of electromagnetic spectrum are shown in Table 1.

Ultraviolet-Visible Spectrophotometry [3]: UV-Visible spectrophotometry is one of the most frequently employed technique in pharmaceutical analysis. It involves measuring the amount of ultraviolet or visible radiation absorbed by a substance in solution. Instrument which measure the ratio, or function of ratio, of the intensity of two beams of light in the U.V-Visible region are called Ultraviolet-Visible spectrophotometers.

The active ingredient in NEURONTIN capsules, tablets and oral solution is gabapentin, which has the chemical name 1-(Amino methyl)cyclohexaneacetic acid. The molecular formula of gabapentin is $C_9H_{17}NO_2$ and the molecular weight is 171.24. The structural formula of Gabapentin is:

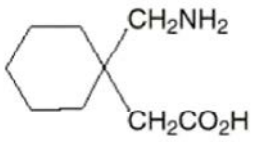

Table 1: Accuracy

Spike level (%)	Absorbance	Average mg added (API)	mg Found	Avg. mg Found	% Recovery
80	0.240	2.57	2.5	2.6	99.3
	0.242	2.6			
	0.242	2.6			
100	0.412	4.92	5.2	5.2	98.9
	0.410	5.2			
	0.412	5.1			
120	0.614	7.58	7.5	7.8	98.7
	0.612	7.6			
	0.612	7.6			

Gabapentin is a white to off-white crystalline solid with a pKa1 of 3.7 and a pKa2 of 10.7. It is freely soluble in water and both basic and acidic aqueous solutions. The log of the partition coefficient (n-octanol/0.05M phosphate buffer) at pH 7.4 is 1.25. Gabapentin (Brand name Neurontin) is a medication originally developed for the treatment of epilepsy. Presently, gabapentin is widely used to relieve pain, especially neuropathic pain.

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Gabapentin is well tolerated in most patients, has a relatively mild side-effect profile and passes through the body unmetabolized [4].

Literature survey revealed that various analytical methods such as HPLC [5-10] have been reported for the simultaneous estimation of both the drugs. The aim of the present investigation is to develop a simple, sensitive and reproducible UV Spectrophotometric method for analysis of Gabapentin in tablet dosage form and hence an economical method was developed and validated according to the ICH guidelines [11].

Instrumentation and Reagents: Perkin Elmer UV-visible spectrophotometer equipped with a matched quartz cells ultrasonic bath was used to carry out the assay. The solvent used for the assay was 0.1N NaoH. Gabapentin working standard was supplied by Aurabindopharma Ltd. Marketed sample for the analysis which bought from local pharmacies Neurontin (300mg/tablet) was manufactured by Aurobindo Pharmaceutical Ltd. All other chemicals used in the analysis were AR grade.

Preparation of 0.1N NaoH: 1g of NaoHas weighed**,** transferred into 250ml volumetric flask and dissolved by using distilled water and made up the volume.

Preparation of Stock Solution: 0.1g of Gabapentin was made up with 0.1N NaoH to 100ml, sonicated for 15 minutes.

Preparation of Standard Solution: From the stock solution consecutive dilutions are made and the final concentration was 1µg/ml to 7.5µg/ml were prepared.

Preparation of Sample Solution: Ten tablets of gabapentin (300mg gabapentin) were weighed and powdered. Weighed the tablet powder equivalent to average weight of the tablet and transferred into 100ml volumetric flask and 100ml 0.1N NaoH was added and sonicated for 15 min and diluted to volume with mobile phase. The solution was filtered through whatmann filter paper.

Methods

Accuracy and Recovery Studies: To check the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels according to ICH guidelines. A series of solutions of Gabapentin at 80%, 100% and 120% of the standard preparation in the ratio of the formulation were prepared and checked for accuracy by determining the absorbance values at ëmax of 217nm respectively. To a fixed concentration of the formulation, varying concentrations of pure drug solutions were added and percentage recoveries calculated. The result of the analysis is given in Table 1

Table 2: Precision

Sample No.	Abs	%Assay
1.	0.492	100.2
2.	0.490	100.6
3.	0.488	100.5
4.	0.494	100.1
5.	0.490	100.8
6.	0.488	100.5
Average	100.4	
Standard Deviation	0.25	
% RSD	0.25	

Table 3: Linearity

S No.	Concentration (ppm)	Absorbance
1.	1.5	0.114
2.	3	0.252
3.	4.5	0.379
4.	6	0.502
5.	7.5	0.601
Slope	0.081	
Intercept	0.001	
Correlation Coefficient	0.998	

Precision: Precision of the analytical method is ascertained by carrying out the analysis as per the procedure and as per normal weight taken for analysis. Repeat the analysis six times. Calculate the% assay, mean assay,% Deviation and% relative standard deviation and%RSD.

The developed method was found to be precise as the%RSD values for the repeatability and intermediate precision studies were 0.25 respectively in (Table2)

Linearity: Six points calibration curve were obtained in a concentration range from 0-150 ppm for Gabapentin. The response of the drug was found to be linear in the investigation concentration range and the linear regression equation was y = 0.081x+0.001 with correlation coefficient 0.998 (Table 3, Figure 1)

Solution Stability Study: Table shows the results obtain in the solution stability study at different time intervals for test preparation. It was concluded that the test preparation solution was found stable up to 8 hrs at room temperature, as during this time the result was not decrease below the minimum percentage.

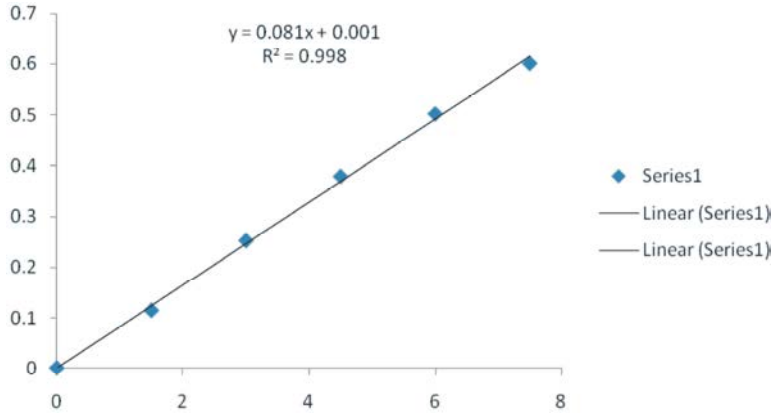

Fig. 1: Linearity for Gabapentin

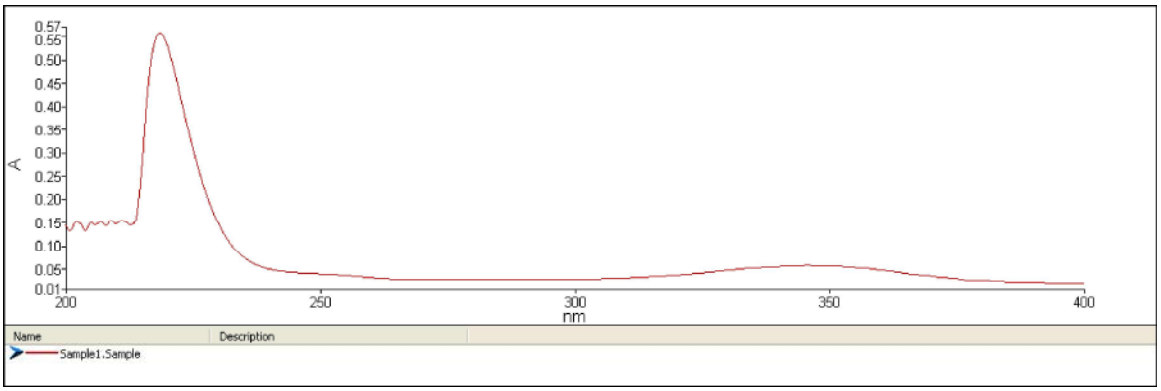

Fig. 2: UV spectrum of Gabapentin in sample solution

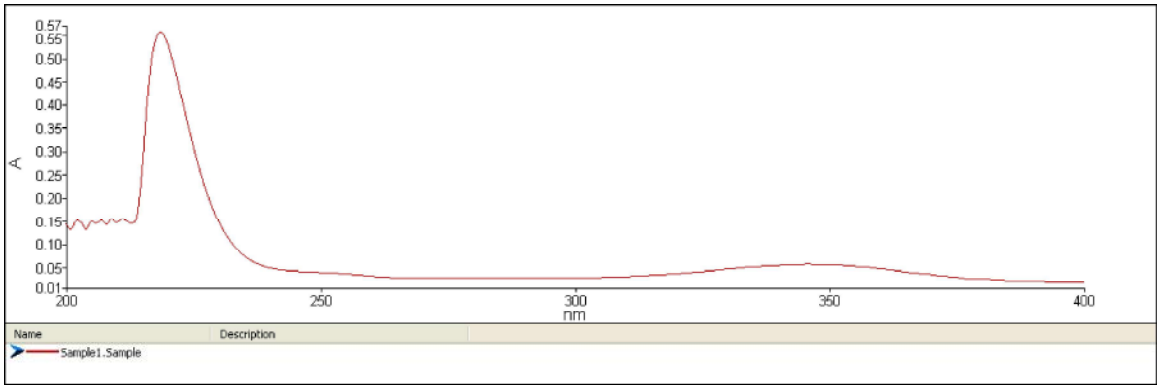

Fig. 3: UV spectrum of Gabapentin in standard solution

System Suitability: A system suitability test of the spectrophotometric system was performed before each validation run. Six replicate reading of standard preparation were taken and%RSD of standard reading were taken for same. Acceptance criteria for system suitability,% RSD of standard reading not more than 2.0%, were full fill during all validation parameter (Table 4).

Robustness: The evaluation of robustness should be considered during the development phase and depends on the type of procedure conditions, assay value of the test preparation solution was not affected and it was in accordance with that of actual. System suitability parameters were also found satisfactory; hence the analytical method would be concluded as robust.

Direct comparison method:
Formula:

$$\text{Amount present} = \frac{\text{sample absorbance}}{\text{Standard absorbance}} X \frac{\text{standard weight}}{\text{standard dilution}} X \frac{\text{sample dilution}}{\text{sample weight}} X \frac{\text{potency}}{100} X \text{ avgwt}$$

$$= 1.053 \times 1 \times 0.5 \times 0.6779 \times 2 \times 0.99 \times 590$$

$$= 416.94$$

$$\text{Percentage purity} = \frac{\text{Amount present}}{\text{Label claim}} X 100$$

$$= \frac{416.94 \times 100}{400}$$

$$= 104.23\%$$

Table 4: System suitability study

Sample no	Absorbance
1	0.379
2	0.379
3	0.379
4	0.378
5	0.379
6	0.379
Average	0.378
SD	0.000373
RSD	0.098

Table 5: Robustness study

SI no	217	218	219
1	0.252	0.254	0.256
2	0.251	0.254	0.256
3	0.252	0.255	0.257
4	0.252	0.254	0.256
5	0.251	0.254	0.256
6	0.252	0.254	0.256
Average	0.251667	0.254167	0.25617
SD	0.0005164	0.00044721	0.00040825
RSD	0.205	0.175	0.188

Table 6: Analytical and regression parameters

Parameters	Gabapentin
Linearity	1.5-7.5µg/ml
Coefficient correlation	0.9981
Slope	0.081
Intercept	0.001
Regression equation	0.081x+0.001
Detection wavelength	217nm

RESULTS AND DISCUSSION

The proposed methods were validated as per ICH Guidelines and the absorbance vs concentration of Gabapentin was plotted.

The linearity for spectrophotometric methods was established in the concentration 1.5-7.5µg/ml for the drug absorbance at 217nm for Gabapentin standard and tablets. Calibration curve were plotted using concentration vs absorbance. A slope, intercept and correlation coefficient value was found to be 0.081, 0.001 and 0.9981 respectively (Fig 1).

Precision studies were performed by preparing the standard 5 concentrations and measuring the absorbance of drugs at?$_{max}$217nm.Low% RSD shows that the method has good precision (Table 2).

In order to ensure the suitability and reliability of proposed method, recovery studies were carried out. To an equivalent quantity of formulation powders a known quantity of standard Gabapentin was added and contents were analysed by the proposed method.

The percentage recovery and percentage RSD were calculated and it was found to be less than 2

The developed spectrophotometric method was validated by using linearity, range, accuracy and precision and the estimation was done by direct comparison method. The RSD for all parameters were found to less than 2, which indicates validity of method and assay results obtained by this method are in fair agreement. The developed method can be used for routine quantitative simultaneous estimation of Gabapentin in multi component analysis.

The proposed methods were found to be simple, precision & sensitive for the routine determination in capsule formulation. To study the validity and reproducibility of proposed methods, recovery studies were carried out (Table 1) the methods were validated in terms of linearity accuracy, precision specificity and reproducibility. The proposed method can be successfully used for estimation of gabapentin in combined dosage form.

Interference studies, accurate, precision, linearity interference studies revealed that the common excipients used in the dosage form do not interference with the estimation of gabapentin using the proposal method the

check the recovery using the proposing method known amount of pure drug was added and used in the pharmaceutical preparation of gabapentin and the mixture were analyzed by the prepared method.

CONCLUSION

The proposed spectrophotometric method was accurate, precise and reliable for the measurement of Gabapentin. The developed spectrophotometric method was validated by using linearity, range, accuracy and precision and the estimation was done by direct comparison method. The RSD for all parameters were found to less than 2, which indicates validity of method and assay results obtained by this method are in fair agreement. The developed method can be used for routine quantitative simultaneous estimation of Gabapentin in multi component analysis.

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