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COLORIMETRIC METHOD DEVELOPMENT AND VALIDATION OF GABAPENTIN IN BULK AND SOLID DOSAGE FORM

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ABSTRACT

A simple, accurate, precise and economic spectrophotometric method for the determination of gabapentin is described. The method is based on the formation of brown coloured chromogen with 1,2-naphthoquinone 4-sulphonic acid reagent by gabapentin in alkaline medium. The coloured species has an absorption maximum at 454 nm with 0.1 N sodium hydroxide. Beer's law obeys over the concentration range of 10-60 µg mL-1 with regression coefficient of 0.998. The limit of detection and quantification value are 3.145 and 9.531 µg mL-1 respectively. Accuracy and precision of the developed methods have been tested in addition recovery studies have been carried out in order to confirm their accuracy. The method successfully applied to the determination of gabapentin in pharmaceutical formulation.

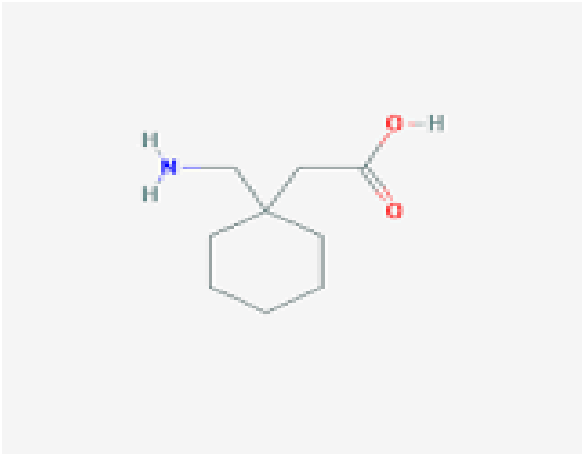
KEYWORDS: Gabapentin, 1,2- naphthoquinone 4-sulphonic acid reagent, Colorimetry, Pharmaceutical preparations.

INTRODUCTION

Uv-Visible Spectrophotometry[1]

UV-visible spectrometers can be used to measure the absorbance of ultra violet or visible light by a sample, either at a single wavelength or perform a scan over a range in the spectrum. The UV region ranges from 190 to 400nm and the visible region from 400 to 800nm. The technique can be used both quantitatively and qualitatively.

The light source (a combination of tungsten/halogen and deuterium lamps) provides the visible and near ultraviolet radiation covering the 200 to 800nm.



Gabapentin (1(amino methyl) cyclohexane acetic acid) is an antiepileptic drug. It is soluble in water, Sparingly soluble in ethanol, Dimethyl sulfoxide, Dimethyl farmamide. It is currently used for treatment of neuropathic pain. It is also commonly prescribed for many off label uses, such as treatment of anxiety disorders, insomnia and bipolar disorder.

Literature review revealed different methods for the determination of gabapentin in bulk and pharmaceutical dosage forms. The Present work aims to develop accurate, precise, specific, linear, simple and rapid method for the estimation of Gabapentin in its tablet dosage form by Colorimetry.

EXPERIMENTAL INSTRUMENTS AND REAGENTS

(Shimadzu instruction manual) Model: shimadzu, UV-1700, pharmaspec, cuvetts:1 cm matched quartz cells was used. The chemicals used for the study were distilled water, Sodium hydroxide, 1, 2-Napthoquinone-4-sulphonic acid.

Preparation of standard stock solution

100mg of Gabapentin raw material was weighed and transferred in to 100 ml of volumetric flask and dissolved in a distilled water and made up to the volume with water and further diluted to get 10µg/ml.

Selection of wavelengths and Optimisation of Reage.nts

The selections of wavelengths for the estimation of Gabapentin a suitable diluted stock solution contain 10µg/ml.

Optimisation of Reagents

The reagents Methyl-2-benzothiazolinone hydrazine hydrochloride (MBTH), 1,2- naphthaquinone -4-sulfonate sodium (NQS), Bratton Marshal (BM) and β-naphthol were studied for the colour complex development.

Among the reagents used**, 2-Naphthaquinone -4-sulfonate sodium (NQS),** was found to form most stable coloured complex. The other reagents used were not able to produce colour complexes with good stability. The reagent sodium1, 2-naphthoquinone-4-sulfonate (NQS) has been widely used for the determination of many Pharmaceutical compounds.

1,2-Naphthoquinone-4-sulfonic acid sodium salt NQS reagent (β-naphthoquinone-4- sulfonatesodium salt) (0.5%w/v)

500 mg of NQS reagent was dissolved in distilled water and made up to 100ml with distilled water. The solution was freshly prepared and protected from light when not in use.

Determination of Absorption spectra

From the standard stock solution, further diluted to get 10 µg/mL was added with 2 mL NQS reagent, 1mL of 0.1M Sodium hydroxide in a 10mL volumetric flask. After 15 min, the volume was made up to the mark with water and the content was mixed thoroughly. A blank solution was prepared in the same way. This solution was scanned in the range of 400-800 nm against the reagent blank. Maximum absorption was observed **at 454 nm** and was fixed as analytical wavelength.

Linearity Construction of calibration graph

Different aliquots (1, 2, 3, 4, 5, 6 mL) of a standard GBP (10µg/mL) solution were accurately transferred into a series of 10mL standard flasks to get 10-60µg/mL. To each flask, 2 mL of NQS reagent and 1mL of 0.1M NaOH was added. The reaction was allowed to proceed at room temperature (27 ± 2°C) for15 min, and the volume was made up to 10 mL with water. The resulting colored solution was measured at 454 nm against a reagent blank prepared in the same manner without drug solution.

Quantification of formulation

Twenty tablets of formulation (GABASTONE-100) were weighed accurately. The average weight of tablets was found and powdered. The powder equivalent to 50 mg of Gabapentin was weighed and transferred into 50 mL volumetric flask, added minimum quantity of distilled water to dissolve the substance by using ultra sonication for 15 minutes and made up to the volume with the same (1000µg/mL). The content was filtered through Whatmann filter paper no.41. From the clear solution, further dilutions were made in a volumetric flask to obtain 30µg/ml of Gabapentin. Then added 2mL of NQS reagent and 1mL of 0.1M NaOH and made up to the volume with distilled water. The absorbance measurements were made 6 times for the formulation at 454nm. From the Absorptivity values of Gabapentin at 454 nm the Amount of Gabapentin was determined by using Colorimetric method.

Recovery studies

The Recovery studies were done by adding known concentration of Gabapentin raw material to the 50% pre analysed formulation. Standard Gabapentin in the range of 80%, 100% and120% to the 50% pre analysed formulation into a series of 10mL volumetric flasks. Then added 2mL of NQS reagent and 1mL of 0.1M NaOH and made up to the volume with distilled water. The absorbances of the resulting solutions were measured at the selected wavelength for determination of Gabapentin. The amount of each drug recovered from the formulation was calculated. The procedure was repeated for three times for each percentage recovery.

RESULTS AND DISCUSSION

Gabapentin has an amino group, hence it was planned to treat with different reagents like Methyl-2-benzothiazolinone hydrazine hydrochloride (MBTH), 1,2-naphthaquinone -4-sulfonate sodium (NQS), Bratton Marshal (BM) and β-naphthol were studied for the colour complex development.

Among the reagents used**, 1,2-Naphthaquinone -4-sulfonate sodium (NQS),** was found to form most stable brown colour.

The stability of the coloured solution was found to be stable up to 3 hours and there is no change in absorbance.

Gabapentin was found to yield a brown coloured product with NQS reagent and 0.1M sodium hydroxide and has absorbance maximum of 454 nm. Therefore studies were carried out to establish the mostly favourable condition for the formation of these coloured products.

The influence of the concentration with constant volumes of the reagent on the reaction has been studied. After optimisation of reagent concentration, 1mL of 0.1M sodium hydroxide, 2mL of NQS reagent was added to produce the color complex.

Gabapentin was dissolved in distilled water, and made upto the volume with distilled water to get a concentration of 1000µg/mL. Then prepared 100µg/mL solution using distilled water, from which a linearity of 10-60µg/mL was made and measured the absorbance at 454nm.

The optical characteristics of gabapentin are correlation coefficient, regression equation, slope, intercept, limit of detection, limit of quantification, sandell's sensitivity and standard error of mean were calculated.

Correlation coefficient was found to be 0.9981 close to 1, intimate that it has good linearity and obey's Beer's Lambert's law. The limit of detection, limit of quantification were found from the linearity analysis by using average of slope and intercept values.

Assay of commercial formulation involved using 30µg/mL solution. The amount of drug present in the marketed formulation was determined by average values of slope and intercept and the average percentage label claim was found to be 98.06.

To determine the accuracy of the method by using recovery analysis, known amount of pure drug (80, 100 and 120% of quantification concentration) were added to the previously analyzed solutions. The absorbance of the recovery solutions were measured at 454 nm. The percentage recovery was found to 99.69%.

The precision studies were carried out by intraday and interday repeatability studies for assay. The results of quantification for intraday and interday 99.1% and 100.32% respectively.

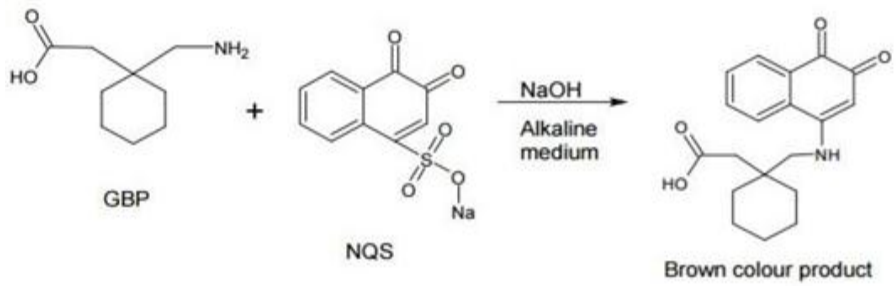


Figure 1: Ir Spectrum of Gabapentin.

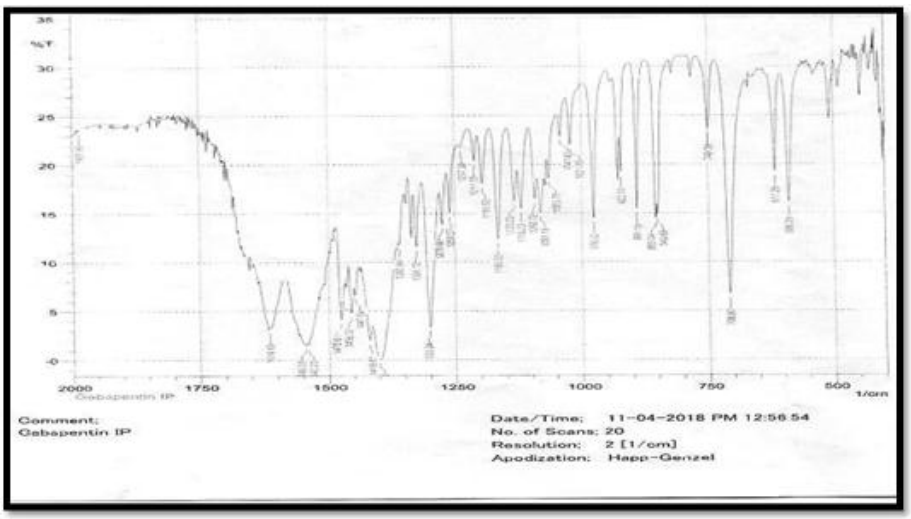


Figure 2: Visible Spectrum of Gabapentin At 454nm.

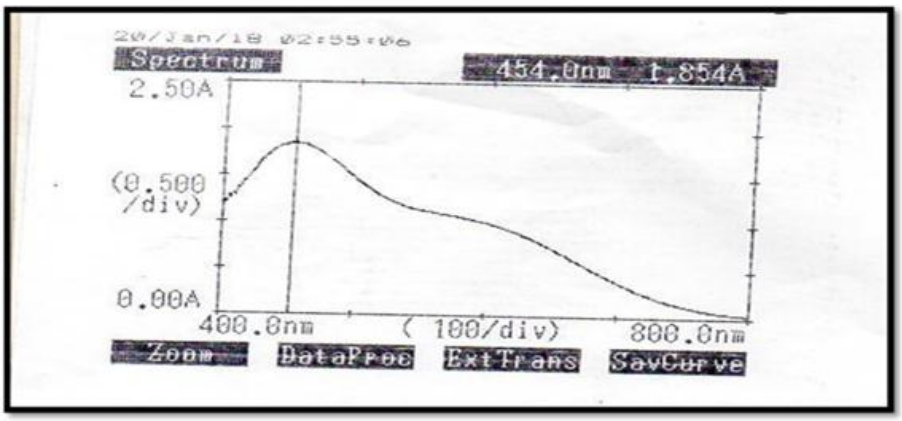


Figure 3: Calibration graph of Gabapentin by colorimetric method by NQS method.

Table 1: Optical Characteristics of Gabapentin.

PARAMETERS	GABAPENTIN* At 454 nm
Beers law limit (µg/mL)	10-60
Molar absorptivity (L mol^{-1} $cm^{-1)}$	0.1952
Sandell's Sensitivity (µg/cm^2/0.001 A.U.)	0.0914
Correlation Coefficient (r)	0.9981
Regression Equation (y=mx+c)	Y=0.0109X+0.0149
Slope (m)	0.0109
Intercept (c)	0.0149
LOD (µg/mL)	3.145
LOQ (µg/mL)	9.531
Standard Error	0.0124

*Mean of six observations

Table 2: Quantification Of Gabapentin Formulation.

S.NO	Labelled amount (mg tab^{-1})	Amount found(mg)	% Obtained	Average *	S.D	%RSD	SE
1.	100	96.96	96.96	98.06	1.264	1.289	0.035
2.	100	98.16	98.16				
3.	100	96.33	96.33				
4.	100	99.7	99.7				
5.	100	99.1	99.1				
6.	100	98.16	98.16				

*Mean of six observations

Table 3: Intraday Analysis of Gabapentin Formulation.

Drug	Sample No	Labeled amount (mg/tab)	Amount found (mg/tab)*	% Obtained*	Average (%)	S.D	% R.S.D	S.E
GBP	1	100	99.1	99.1	99.1	0.6788	0.6866	0.0424
	2	100	99.7	99.7				
	3	100	98.5	98.5				

*Mean of three observations

Table 4: Interday Analysis of Gabapentin Formulation.

Drug	Sample No	Labeled amount (mg/tab)	Amount found (mg/tab)*	% Obtained*	Average (%)	S.D	% R.S.D	S.E
GBP	1	100	102.17	102.17	100.32	1.7081	1.7026	0.1897
	2	100	98.8	98.8				
	3	100	100	100				

*Mean of three observations

Table 5: Recovery Analysis of Gabapentin Formulation.

Drug	%	Amount present (µg/mL)	Amount added (µg/mL)	Amount estimated (µg/mL)*	Amount recovered (µg/mL)*	% Recovery	Average (%)	S.D	% R.S.D	S.E
GBP	80	29.36	24	53.31	23.95	99.79	99.69	0.095	0.0953	0.010
	100	29.36	30	59.27	29.91	99.7				
	120	29.36	36	65.23	35.87	99.6				

*Mean of three observations

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