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Spectrophotometric estimation of gabapentin in bulk and capsule formulation

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ABSTRACT

A simple sensitive, rapid spectrophotometric method for the determination of gabapentin(GBP) in bulk and formulation is described. The method is based based on reaction of drug with ferric chloride in presence of potassium ferricyanide. The bluish green coloured chromogen formed has absorption maxima at 746nm. Beer's law was followed in the concentration range of 2 to 16µg/ml. The proposed method is useful, accurate, reproducible for the routine estimation of GBP in bulk and capsule.

KEYWORDS

Spectrophotometry;
Gabapentin;
Ferric chloride;
Potassium ferricyanide.

INTRODUCTION

Gabapentin [1-(amino methyl) cyclohexane acetic acid] is a new generation antiepileptic drug (Figure 1). It is structurally related to γ aminobutyric acid (GABA). It is official in United State Pharmacopoeia. It produces its action by irreversible inhibition of enzyme GABA transaminase, thus preventing the physiological degradation of GABA in the brain[1]. Various methods like GCMS[2], HPLC[3,4] are reported in literature for determination of GBP in bulk drug and formulations. Only one spectrophotometric method is available for determination of GBP in bulk and formulations[5]. The present paper gives a simple spectrophotometric method for the determination of GBP in bulk drug and formulation.

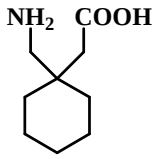

Figure 1: Chemical structure of gabapentin

EXPERIMENTAL

Apparatus and reagents

A Shimadzu model 1601 double beam UV Visible spectrophotometer with a pair of 1mm matched quartz cell was used to measure absorbance of the resulting solutions. A Shimadzu analytical balance, gabapentin standard, sulfuric acid, potassium ferricyanide were also used in the study.

Preparation of standard solutions

Gabapentin standard stock solution (1mg/ml) was prepared in distilled water. From this stock solution working standard solutions of 100µg/ml was prepared by appropriate dilution. Sulphuric acid(0.1N), ferric chloride(0.1%w/v), were prepared in distilled water. Potassium ferricyanide solution (0.2% w/v) was prepared in 0.1 N H_2SO_4.

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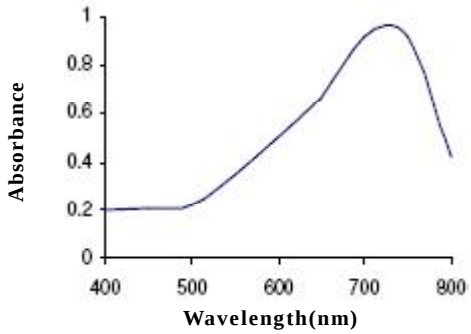

Figure 2: Absorption spectra of Gabapentin

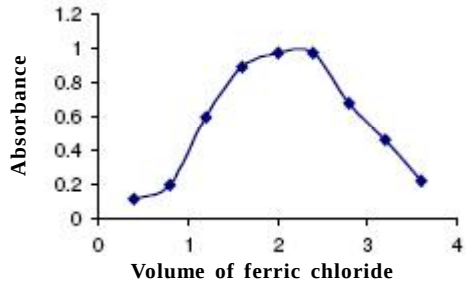

Figure 3: Effect of concentration of ferric chloride on absorption maximum

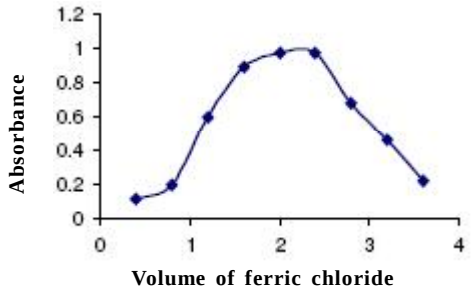

Figure 4: Effect of potassium ferricyanide concentration on maximum absrbance

General procedure for assay

Aliquots of the working standard solution of gabapentin(2 to 16µg/ml, i.e.0.2 to 1.6ml) were transferred in a series of 10ml volumetric flask. These drug solutions were mixed with 2ml of ferric chloride solution, followed by 1ml of potassium ferricyanide. Final volume was adjusted with distilled water. After thoroughly shaking, The flasks were kept aside for 20 minutes for colour development. Absorbance of the resulting bluish green coloured solution was measured at 746 nm and the calibration curve was plotted.

Procedure for assay of gabapentin in capsule formulation

The content of ten capsules was emptied out as completely as possible. An accurately weighed amount of powder equivalent to 10mg of drug was dissolved in 100ml of distilled water. The procedure was continued as described under general procedure.

RESULTS AND DISCUSSION

Determination of absorption maximum

Gabapentin when treated with ferric chloride followed by potassium ferricyanide bluish green coloured solution is formed. To determine absorption maximum, 10µg/ml solution of drug was reacted with ferric chloride followed by potassium ferricyanide. After 20min. absorption spectra was recorded against reagent blank (Figure 2). Absorption maximum wavelength was found to be at 746 nm.

Optimization of variables

To study the effect of concentration of ferric chloride and potassium ferricyanide on maximum absorbance a number of preliminary experiments were carried out. In a series of 10ml volumetric flask containing 10µg/ml of the drug solution, keeping concentration of one reagent constant the concentration of other reagent was varied and the mixture was diluted up to mark with distilled water. After 20 minutes absorbance of each solution was measured at 746nm. It was found that 0.1% solution of ferric chloride in the range of 1.75-2.25 ml and 0.2% solution of potassium ferricyanide in the range of 1-1.5ml of were necessary to achieve maximum colour intensity. Therefore 2ml of ferric chloride and 1ml of potassium ferricyanide were recommended for all measurements. Results obtained for optimization of variables are presented in figure 3 and figure 4 .

The effect of time on maximum absorbance was also tested by measuring the absorbance of solutions at regular interval and it was found that solution show maximum absorbance after 20min. and was stable for further 3 hrs.

Optical characteristics and validation of the method

Optical characteristics such as Beer's law limit, molar absorptivity and Sandell's sensitivity for the proposed method is given in TABLE 1.The accuracy and precision of the method were checked by analyzing 6 replicate samples within Beer's law range containing same amount of drug. Values of RSD were below 0.9%. Lower values of RSD indicate good precision and re-

TABLE 1: Optical characteristics of the proposed method

Parameter	Values
λ max (nm)	746
Beer's law limit(μg/ml)	2-16
Stability	3 hrs
Molar absorptivity($mol^{-1}cm^{-1}$)	2.97×10^{4}
Sandell's sensitivity ($\mu g/cm^2$/0.001 A)	2.34×10^{-2}
Correlation coefficient (r)	0.9952
Regression equation	
Slope	0.089
Intercept	0.011

TABLE 2: Determination of GBP in the presence of excipients[a]

Excipients	Amount taken (mg/ml^{-1})	% Recovery ± % RSD[b]
Glucose	45	98.6±0.56
Lactose	40	98.95±0.12
Dextrose	50	99.34±0.56
Sodium alginate	25	99.34±0.45
Talc	25	98.4± 0.84
Mg. Stearate	35	99.4 ± 0.29

[a]10μg mL^{-1} of Gabapentin was used; [b]Average of 6 replicate analyses

TABLE 3: Analysis of gabapentin in capsule formulations

Formulation	Label claim (mg)	% of label claim* ± S.D.	Amount % added (in mg)	recovery* ±S. D	t value
G_1	300	299.18±0.176	300	98.79±0.152	0.645
G_2	300	298.92±0.322	300	99.44±0.749	0.398

Where, G_1 and G_2 are two different brands of capsule formulation; *denotes n = 6, average of six readings

producibility of the method.

Interference studies

To study the potential interference problems from commonly used excipients and other additives such as glucose, dextrose, lactose, sodium alginate, talc, magnesium stearate, recovery studies were carried out. Under the experimental condition employed, to a known amount of drug (10μ/ml), excipients in different concentration were added and analysed. Results of the recovery analysis are presented in TABLE 2. Excipients up to the concentration shown in table do not interfere with the assay. In addition recoveries in most cases were 100% and the lower values of the RSD indicate the good precision of the method.

Applicability of the method

The applicability of the proposed spectrophotometric procedure was tested analyzing various available commercial formulations. The result of analysis is presented in TABLE 3. The result shows that the data are consistent with label claim of the formulations. The calibration curves shows linear response over the range of concentration used in the assay procedure. RSD values are in the range of 0.152-0.398 which shows that the method is precise and accurate. The precision and accuracy of the method was further compared stastically using students't' test. The calculated t values do not exceed the tabulated values. The low S.D shows that the excipients in formulation do not interfere in analysis.

Mechanism of colour reaction

There are many methods reported for estimation of drugs using ferricchloride[6,7]. The proposed method is based on reduction of Fe^{+++} to Fe^{++} which on reaction with divalent potassium ferricyanide gives bluish green colored complex.

CONCLUSIONS

The proposed spectrophotometric method for determination of gabapentin is simple, sensitive, accurate, precise and reproducible. Colour reaction neither requires any stringent condition nor any specific reagent or buffers. This method can be successfully applied for routine estimation of gabapentin in bulk and pharmaceutical dosage forms.

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