

Spectral kinetic method and its applications in the evaluation of gabapentin

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Abstract

Context: A new and highly sensitive method for the determination of gabapentin (GBP), this method is of high importance in the assessment of GBP and other pharmaceutical preparations. GBP is a widely used antibiotic. There is a big challenge of analysis of anti-epilepsy drugs due to their instability and sensitivity to various conditions. The simple, sensitive, precise, and kinetic spectroscopy method was used to measure GBP in some pharmaceuticals developed and validated. **Objective:** The objective of the study was to develop a simple, sensitive, accurate, and kinetic spectroscopy method for the measurement of GBP in a pharmaceutical product. **Materials and Methods:** The current method was based on the spectral kinetic examination of epileptics (GBP) with potassium permanganate in alkaline medium at room temperature. Absorption of the stained manganese ions of the product was absorbed at 605 nm. **Results:** The concentration of GBP was calculated using the calibration equation for the time method and the initial rate method. The above method is used to determine GBP from 2.0 to 20 µg/mL. The BER Act was applied to roads within the range of concentrations used for analysis. The limit of quantification and limit of detection, equal to 0.640 and 1.940, were calculated, respectively. The relative standard deviation values was found to be 0.345% and Recovery values were 99.38 and 0.50%, respectively. **Conclusion:** The proposed and developed method is sensitive, accurate, and tolerable and can be used for the routine analysis of GBP in various pharmaceuticals. The proposed method was successfully applied to the determination of the drug gabapentin in the pharmaceuticals and the validation of the statistical data. The results were compared to the reference method showed good compatibility.

Key words: Anticonvulsant, anti-epileptic drugs, gabapentin drug, spectral kinetic method

INTRODUCTION

The drug gabapentin (GBP) has a chemical formula of $C_9H_{17}NO_2$. The molecular mass of 171.237 g/mol is known chemically as aminomethyl cyclohexane acetic acid; the trade names are Garrex, Neuroplex, Neurontin, Neurona, captain, and Conventin.^[1] GBP as an anticonvulsant, it can be used to treat seizures and strokes. It can be used as a barrier to blood in the brain. This can be used to treat seizures and strokes.^[2-4] GBP is a complementary tool for other anti-epileptic drugs in adult patients who do not have sufficient control over the effects of narcotic drugs in cases of molecular seizures and stroke.^[5] The treatment helps to prevent seizures or seizures in the brain and helps control them, so it is used (as a single treatment or with other treatments) to control certain types of seizures or epileptic seizures. It also regulates the work of a number of neurotransmitters responsible for the delivery

of pain, leading to its use in the treatment of some types of neuropathic pain. Treatment does not cure epilepsy but helps control seizures in terms of reducing recurrence, so it is not allowed to discontinue treatment without consulting the doctor once the patient has improved. The seizures may recur after discontinuation of treatment.^[6] GBP has a structural analogy of the amino acid (Butyric) and the inhibitory DNA (gamma-aminobutyric acid 1). Spectrophotometric measurements, high-performance liquid chromatography, serial injection measurements, and automated spectrum measurements were performed to determine the drug's GBP.^[7] The interaction of potassium permanganate ($KMnO_4$) as a potent oxidative

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agent with alginate in the alkaline medium was performed. The spectral method was used at the maximum absorption spectra of 605 nm. The GBP was shown with the oxidative factor of green color in the visible and ultraviolet region of the spectrum.^[8]

The Objective of the Study

The objective of the study was to study the development of a new spectral method of high and simple selectivity for the determination of GBP in pharmaceutical drugs.

EXPERIMENTAL

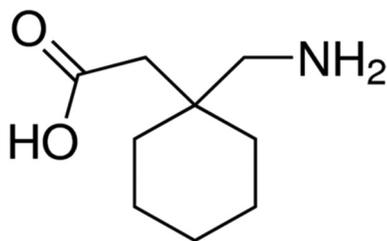
All spectral absorption values were performed using a German-made high-sensitivity spectrometer operating in the two visible areas of the spectrum and ultraviolet (A Jena Model 1100).

MATERIALS AND METHODS

Materials

- GBP pharmaceutical grade 99.5% from Sun Pharmaceuticals, Mumbai, India.
- 100 mg Gaba Plus capsules purchased from Platinum Pharma (Pvt.) Ltd.
- Karachi, (Pakistan) and Gabapin-300 (300 mg GBP per capsule) from Intas Pharmaceuticals, Dehradun, India.
- Neurontin capsules (Labeled to found 300 mg GBP) were product from Godecke AG/Germany.
- Potassium permanganate (KMnO_4) (Merck, Germany).
- Sodium hydroxide (NaOH) from (Merck, Germany).
- Hydrochloric acid (HCl) from (Merck, Germany).

Molecular Formula of GBP



Methods

Preparation of reagent and standard solutions

All the solvents and reagents used for the experiment were 99.9% pure. Deionized water was also used with a high purity of $0.055 \mu\text{S}/\text{cm}$.^[9] A standard solution of 100 ml of 250 mg/L

of standard pharmaceuticals was prepared in distilled water. A concentration of 0.158 KMnO_4 was prepared in 100 ml of distilled water. 0.5 m of sodium hydroxide was prepared by dissolving 2 g of NaOH in 100 ml distilled water and calibrating sodium hydroxide solution with standard hydrochloric acid.^[10]

Procedure of analysis standard material and pharmaceuticals

The working solution was prepared with a combination of GBP concentrations (2.0–20 mg/L) and the transfer of these concentrations, respectively, to 25 ml of volumetric flasks, plus 2 ml of KMnO_4 solution (0.1 m) and 1.5 ml of sodium hydroxide solution. Then complete the volume with deionized water. After 15 min, absorption was measured at a 605 nm wavelength and compared with a detector set at the same time. The calibration curve of the absorption values was plotted against the final concentration of the mg/L unit^[11,12]

A range of sample concentrations (1–1000) mg/L were prepared by dissolving 27 mg GBP in deionized water and taking 25 ml of each concentration for analysis. From the range of selected concentrations the standard curve was drawn.

RESULTS

The absorption spectrum at the maximum value (λ_{max}) for GBP was recorded at 200 nm using deionized water as a solvent. GBP was mixed and mixed with potassium permanganate at 25°C , as shown in Figures 1. The absorption spectra of the green mix solution (maximum absorption at 605 nm) were recorded against an blank.

Gapapentin was estimated in two methods. The first was the reaction of GBP with potassium permanganate at the concentration of $0.8 \times 10^{-2} \text{ m}$. The absorbance of the reaction mixture was measured at a maximum wavelength of 605 nm, and the other comparison method was made using GBP with

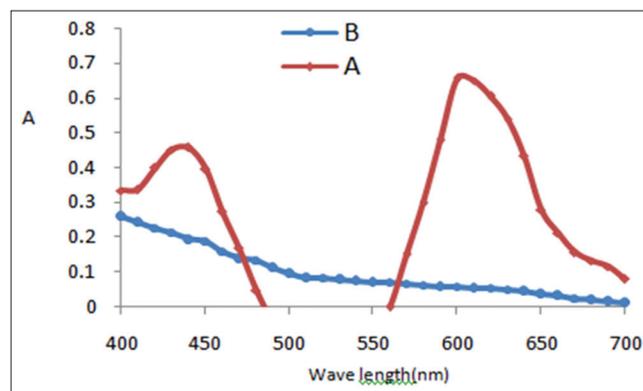


Figure 1: (A) Absorption spectrum of gabapentin (GBP) with potassium permanganate ($0.8 \times 10^{-2} \text{ m}$). (B) Absorption spectrum of GBP ($0.6 \times 10^{-4} \text{ m}$) against water

potassium permanganate at 0.6×10^{-4} m concentration at the same maximum wavelength. Two types of curves were obtained according to Figure 1a and b, which shows the effect of different concentrations of potassium permanganate as a potent oxidative agent on the kinetics of interaction with GBP. The effectiveness of GBP toward oxidizing agents such as potassium permanganate explains its uses extensively to relieve pain, especially nerve pain, and epilepsy of all kinds.

DISCUSSION

Reliability of Interaction Variables

The effect of different parameters on the development of single-color amygdala solutions was studied separately, and all factors studied and confirmed for subsequent studies were observed. These variables include KMnO_4 concentration effect, sodium hydroxide concentration effect, temperature, and time. GBP was found to interact with KMnO_4 in the center of alkali to produce a green solution with a peak of 605 nm [Figure 1]. The various experimental factors that influence the evolution and stability of the reaction output at this wavelength have been carefully studied, and several studies have been conducted for the purpose of improving them.^[12-14]

Effect of Potassium Permanganate Concentrations

The KMnO_4 concentration effect was studied on the absorbance in the range (0.2×10^{-2} – 1.6×10^{-2} m) by GBP concentration constant at 0.6×10^{-4} m. The absorbance was increased with increasing the potassium permanganate concentration [Figure 2]. 2 ml of (0.8×10^{-2} m) KMnO_4 solution was used to obtain the maximum absorbance value in 15 min.^[15]

Effect of Sodium Hydroxide Concentrations

The effect of sodium hydroxide concentrations was studied by taking a constant concentration of GBP (0.6×10^{-4} m) plus 2.0 ml of potassium permanganate solution at 0.1 m concentration and different volumes of sodium hydroxide at 0.5 m concentration within a range of volumes (0.5–4.0) ml. As shown in Figure 3, the highest absorption value was obtained when adding 1.5 ml of 0.5 M (3×10^{-2} m) sodium hydroxide solution, the increase in the volume of sodium hydroxide added to the low spectral absorption values.^[16,17]

Effect of Time Required for Reactance

The effect of the time needed for interaction between GBP and KMnO_4 was studied in the basal medium [Figure 4]. The oxidation reaction was performed for periods of 2–35 min.

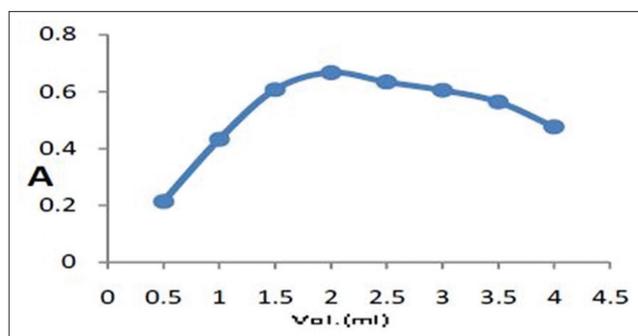


Figure 2: Effect of KMnO_4 volume on absorbance

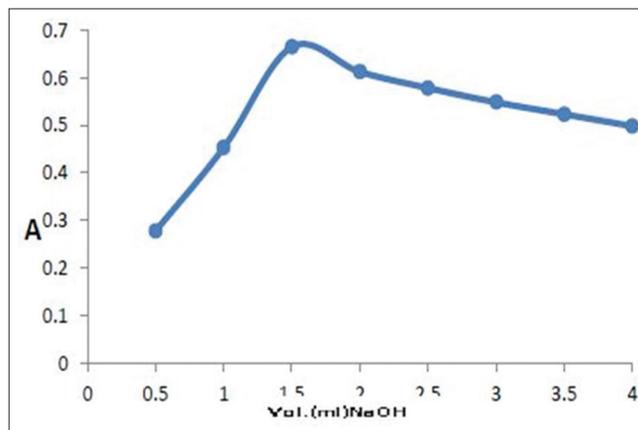


Figure 3: Effect of sodium hydroxide volume on absorbance intensity

The oxidation reaction was achieved within 15 min, and the maximum wavelength was obtained at 605 nm. The solutions turned into sour solutions after 50–60 min. Absorption values increase over time.^[18]

Effect of Temperature Required for Reactance

At 25°C, GBP reaction with potassium permanganate was observed. The reaction rate was significantly increased with the increase in the color of the mixture, but avoiding work at high temperatures caused the release of MnO_2 from the oxidation reaction.^[19]

Study of Kinetics of Materials Reactant

$$\text{Rate} = K[\text{Drug}]^n[\text{KMnO}_4]^m$$

The gradual changes in color intensity over time were due to differences in energy kinetics of the reaction of GBP with potassium permanganate in the basal medium as shown in Figure 5. Where the concentrations of potassium permanganate were within the linear range of the reaction (0.8×10^{-2} m), the equation of kinetics of reaction can be written as follows:

$$\text{Rate} = K'[\text{Drug}]^n$$

K' is the constant of the ratio of the reaction order and n represents the order of the interaction. The above equation can be considered the logarithmic form of the reaction as follows:

$$\text{Log rate} = \log K' + n \log [\text{Drug}]$$

At a range of GBP concentrations, initial reaction rates at 605 nm were determined by measuring the value of the initial contact tangent of the time curves during the first 35 min of the reaction as shown in Figure 5.

When plot the logarithm rate versus logarithm [Drug] the linear equation can be represented as the following:

$$\text{Log rate} = 1.135 \log [\text{Drug}] + 3.663$$

With correlation coefficient equal to $R^2 = 0.9049$. The value of n in the former equation shows that the reaction is first order.

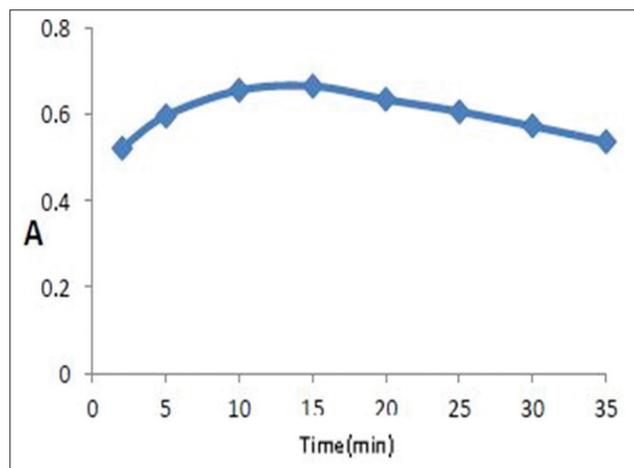


Figure 4: Effect of time on absorbance

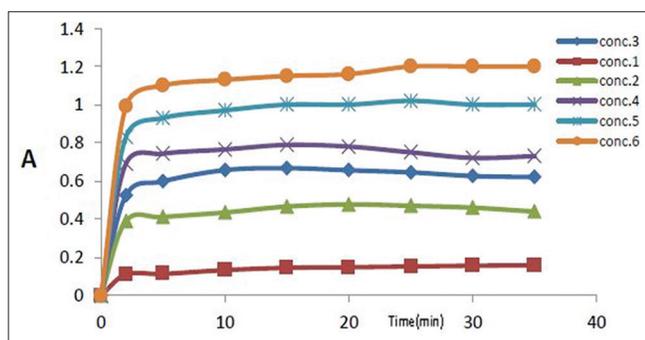


Figure 5: At varying concentration of gabapentin drug absorbance-time curves for the initial rate of the reaction (conc.1 = 1.25×10^{-5} m), (conc.2 = 3.7×10^{-5} m), (conc.3 = 5.024×10^{-5} m), (conce.4 = 6.280×10^{-5} m), (conce.5 = 11.304×10^{-5} m, and conc.6 = 12.560×10^{-5} m) keeping $[\text{KMnO}_4] = 0.8 \times 10^{-2}$ m and $[\text{NaOH}] = 0.3$ m

The Credibility of the Kinetic Method

To determine the ranges of GBP concentrations, several experimental tests were performed using the relationship between fixed absorption values and time values.

$1/t = 0.027 [\text{Drug}] + 3 \times 10^{-5}$ with correlation coefficient equal to $R^2 = 0.989$

Absorbance Method

GBP reaction rate data were recorded within the range (2.0–20.0 mg/L). The selective absorption period was determined as shown in Table 1 and time was measured in seconds.^[20] The standard calibration equation was also obtained by the time-frame (1/t) versus the initial concentration of the GBP drug [Table 2].

When the calibration graphs were plot at 15 min, the most acceptable linearity was obtained as shown in Table 3. The calibration graph was on the linearity range of 2.0–20.0 mg/L. The equation of the analysis data represented as the following:

$$A = 0.067C + 0.021$$

With correlation coefficient (R^2) equal to 0.9990. Where A represented the absorbance and C represented the concentration of GBP drug.^[21]

Table 1: Values of (1/t) at different concentrations of GBP drug

t (s)	1/t	[Drug]
1200	0.83×10^{-4}	0.5×10^{-4}
900	1.11×10^{-3}	0.6×10^{-4}
600	1.66×10^{-3}	0.8×10^{-4}
300	3.33×10^{-3}	1.2×10^{-4}

GBP: Gabapentin

Table 2: Analytical parameters for determination of GBP with KMnO_4

Time (s)	Calibration equation	Correlation coefficient (R^2)
300	$y = 0.058x + 0.024$	$R^2 = 0.995$
600	$y = 0.061x + 0.034$	$R^2 = 0.995$
900	$y = 0.067x + 0.021$	$R^2 = 0.999$
1200	$y = 0.063x + 0.038$	$R^2 = 0.995$
1500	$y = 0.064x + 0.030$	$R^2 = 0.997$
1800	$y = 0.065x + 0.027$	$R^2 = 0.998$
2100	$y = 0.068x + 0.025$	$R^2 = 0.998$

GBP: Gabapentin

Verification of the Credibility of the Analytical Method

The analytical method was validated by linear values, accuracy, sensitivity, precision, and recovery.^[22]

The Linearity and Sensitivity^[23]

The relationship between absorption values and GBP concentration values was determined within the range 2.0–20.0 mg/L at 605 nm at optimal conditions. It was observed that the relationship was linear for all values of GBP concentrations, as shown in Figure 6.

The calibration graph can be described by the following equation: $y = 0.067x + 0.021$

($R^2 = 0.9990$, $n = 6$) where Y is represented the absorption, and X equal to the concentration of GBP in concentration with mg/L.

The analytical parameters such as correlation coefficient, molar absorptivity, Sandell's sensitivity, limit of detection (LOD), and limit of quantification (LOQ) are calculated and

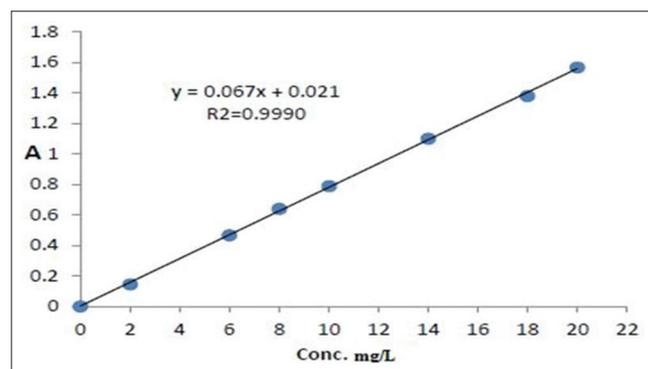


Figure 6: Gabapentin drug calibration curve

Table 3: Analytical parameters for determination of GBP with KMnO_4

Parameter	Value
Wavelength	605 nm
Beer's law limits ($\mu\text{g/ml}$)	2–20
Sandell's sensitivity ($\mu\text{g cm}^{-2}$)	0.0149
SD of intercepts	0.013
LOD ($\mu\text{g/mL}$)	0.640
LOQ ($\mu\text{g/mL}$)	1.940
Slope, b	0.067
Intercept, a	0.021
Correlation coefficient	0.9990
Regression equation $Y = a + bx$	$y = 0.067x + 0.021$

LOD: Limit of detection, LOQ: Limit of quantification, SD: Standard deviation, GBP: Gabapentin

listed in Table 3. The correlation coefficient, intercept and slope for the calibration data are summarized in Table 3. The below formula was used to calculate (LOD) and (LOQ):

$$\text{LOQ} = 10s/b$$

$$\text{LOD} = 3.3s/b$$

Whereas s is equal to the standard deviation of the intercept, and b represented the slope of the calibration curve.^[24]

The Precision and Accuracy^[25]

The precision and accuracy of the spectral study showed four levels of GBP concentration using five concentrations per sample.

Table 2 shows the high repeatability and precision of the current method by relying on the relative standard deviation values for results that did not exceed 2%. The analysis values obtained for GBP in pharmaceuticals were appropriate due to the high reproduction and accuracy of the method used. The percentage of heights obtained in the range of 99.38–100.50%. Using a standardized and internationally accepted method, the value of t -test and F-test was calculated. The result indicates that the t -test and the F-test values were obtained below the allowable range, which improved the precision and accuracy of the proposed method [Table 4].

The Applications of Method

The current method of analysis has been used successfully in the estimation of GBP in pharmaceutical preparations. The results of the method used indicate the precision and accuracy of the good evaluation of the drug GBP. Table 5 shows the results of application of the current method where the recovery values ranged from 103.020 to 97.470%. The current method is also free of interferences.

CONCLUSION

The results obtained from the measurement of the GBP interaction variables indicate that the proposed method is simple, fast, and high-sensitivity and can be easily applied to determine GBP in its pure form as standard and pharmaceutical preparations at a maximum absorption of 605 nm. A range of temperatures can be controlled during the interaction of GBP with potassium permanganate. The current spectral measurement method can be used in quality control laboratories for GBP in pharmaceuticals and biological samples.

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Table 4: Accuracy and precision studies of GBP

Amount taken ($\mu\text{g/ml}$)	Amount found ($\mu\text{g/ml}$)	% Recovery*	RSD %	Proposed method mean \pm SD	Ref method (20) mean \pm SD	t-test (**)	F-test (**)
6	6.03	100.50	0.3459	99.912 \pm 0.3456	100.80 \pm 0.84	t=1.88	F=1.49
8	7.95	99.38					
12	12.04	100.33					
16	15.91	99.44					

*Mean value of five determinations, **The t-value at the 95% confidence level is 2.78; and F-value at the 95% confidence level is 6.39, RSD: Relative standard deviation, GBP: Gabapentin, SD: Standard deviation

Table 5: GBP pharmaceutical method of preparation

Pharmaceutical preparations	Concentration ($\mu\text{g/ml}$)		Recovery %	RSD %
	Taken	Found*		
Neurontin	4	3.899	97.470	0.932
	8	8.034	100.420	0.995
	16	16.055	100.340	1.131
Gabapin	4	4.121	103.020	0.965
	8	7.984	99.800	0.643
	16	16.152	100.950	1.128
Gaba Plus	4	3.921	98.020	1.338
	8	8.212	102.650	0.998
	16	16.099	100.610	0.699

*Average of three determinations, RSD: Relative standard deviation, GBP: Gabapentin

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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