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Acta Pharm. Sci. Vol 56 No: 3. 2018
DOI: 10.23893/1307-2080.APS.05621

A new spectrophotometric method for the determination of gabapentin using chromotropic acid

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ABSTRACT

The purpose was to develop a colorimetric method for determining gabapentin.

The method was based on the diazo coupling reaction between diazotized gabapentin and chromotropic acid. The method was validated using ICH guidelines before its application to generic brands of gabapentin.

Coupling reaction generated an orange azo adduct whose absorbance was linearly correlated with concentration in the range of 1-6 µg/mL at 470 nm. The method was accurate and precise with recovery range of 97.6-103.1%; intra- and inter-day precisions (%RSD) were less than 0.65% and showed no statistical difference when compared with reference method in the analysis of the dosage forms. The 3D optimization of the adduct revealed an E-type configuration around the azo linkage which would contribute to its stability.

The new method can serve as a reliable alternative to the official method for the routine analysis of gabapentin in bulk and dosage forms.

Keywords: Gabapentin, colorimetric analysis, chromotropic acid, diazo coupling reaction.

INTRODUCTION

Epilepsy is a neurological disorder that is associated with a deficiency in gamma-aminobutyric acid (GABA) receptors in the microgyric cortex of the brain[1]. With an estimated 4 to 10 persons per 1000 people in the general population with active epilepsy i.e. continuing seizures or need for treatment, epilepsy is the fourth most common neurological disorder after migraine, stroke and Alzheimer's disease [2, 3]. Of this world-wide incidence, 80% of those with the disorder live in low- and middle-income countries where the incidence is prob-

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(Received 22 May 2018, accepted 08 June 2018)

ably closer to 7 to 14 per 1000 persons[3]. Epilepsy is characterised by recurrent unprovoked seizures which are either generalized or partial. The latter type can occur with or without alteration of consciousness also known as complete or simple partial seizures respectively[4]. While brain surgery and nervus vagus stimulation and, strict ketogenic diet are useful management options, drug therapy remains the mainstay of epilepsy treatment[5-6]. Unfortunately, adequate seizure control might not be achievable in 20-25% of patients being managed on conventional medicinal agents which include carbamazepine, ethosuximide, phenobarbital, phenytoin, and valproate[7]. Consequently, management of these patients with uncontrolled seizures often involves the inclusion of the newer atypical antiepileptics including gabapentin, lamotrigine, topiramate, levetiracetam[4]. Gabapentin which chemically is 1- (amino methyl) cyclohexane acetic acid and a derivative of endogenous GABA is licensed for use in both adult and paediatric populations and has since emerged as the most frequently included medication in the adjunct treatment of epilepsy. Gabapentin is soluble in water, acidic and alkaline media as the molecule in solution can exist in the cationic, zwitterionic or anionic form at low, physiological and high pH respectively[8-9].

A review of the existing methods of analysis of gabapentin reveal a number of procedures that involve derivatization, a step which is necessitated by the minimal presence of chromophores in the analyte. These methods include derivatization prior to colorimetry[10-12], fluorimetry[13,14], planar chromatographic quantification[15] as well as post column derivatization in chromatographic analysis[16]. In a study comparing the direct spectroscopic methods of analysis of gabapentin with those involving derivatization, the latter consistently yielded the highest sensitivity, lowest limits of detection and quantification[17]. Other previously reported methods are non-aqueous titration[18] and capillary electrophoresis[19]. Due to the lack of extensive chromophores in gabapentin molecule, several chromatographic and electrophoretic methods have been developed and reported for the analysis of the drug in bulk samples, dosage forms and particularly in biological samples. These methods include HPLC[20-25], LC-MS[26] and GC-MS[27-28]. However, a few drawbacks are noticeable in a number of these methods. Majority of the previously reported assay procedures that are based on ion pair complexation and liquid chromatography involve an additional step of solvent extraction and strict control of pH respectively. Some of the UV methods also allow determination only at the UV region which is often fraught with interference leading to decreased selectivity. The objective of this study was therefore to develop a visible spectrophotometric method which offers comparative advantage over the previously reported methods and is sufficiently accurate to serve as an alternative to reference methods.

METHODOLOGY

Chemicals and reagents

Methanol (BDH UK), ethanol, ethyl acetate, sulphuric acid, hydrochloric acid, sodium nitrite (BDH-Poole, England), lactose, magnesium stearate, talc, starch, gelatin, distilled water, Chromotropic acid (Sigma Aldrich USA), gabapentin chemical reference substance.

Instrumentation

Lambda 25 digital UV/VIS spectrometer (Perkin Elmer Inc., Singapore) with 1 cm path length and matched quartz cells, thermostatic water bath (Langford UK), vortex mixer, analytical balance (Mettler PC 400).

Preparation of solutions

Preparation of 0.3%w/v chromotropic acid solution

A 0.075g quantity of chromotropic acid (CTA) was dissolved in about 15.0 mL of water in a 25.0 mL volumetric flask and then made up to volume with distilled water.

Preparation of diazonium solution

A 0.01604 g quantity of gabapentin was transferred into a mixture of 2.0 mL distilled water and 0.12 mL of 2.0 M HCl contained in a beaker with a means of agitation and maintained at 0°C using an ice bath. An aliquot (5.0 mL) of 0.3 M sodium nitrite solution was then added to the mixture and stirred for an additional 20 mins. Thereafter the volume of the diazonium solution was made up to 10.0 mL in a volumetric flask with ice-cold distilled water.

Evidence of coupling reaction

Coupling reaction between the diazotized drug and chromotropic acid was established using spot test and thin layer chromatographic analysis.

Spot test

A 0.5 mL aliquot of the diazonium was added to an equal volume of the chromotropic acid solution in a test tube and vortex-mixed. The colour of the resultant azo adducts after 5 mins and 20 mins following incubation at 30 °C were noted. The procedure was repeated at 70 °C.

Thin layer chromatography

TLC analysis of the diazonium, chromotropic and adduct solutions were carried out by spotting freshly prepared solutions on pre-coated TLC (GF254 0.2 mm, Merck Germany) and then developed using the several mobile phases.

Effect of dilution solvents

The suitability of methanol, ethanol, 1-propanol, ethyl acetate and water to serve as the dilution solvent for UV absorbance measurements was investigated by using each of the solvent in turn to make up the volume of the adduct.

Selection of analytical wavelength

An aliquot (0.5 mL) of the diazonium solution was added to an equal volume of chromotropic acid solution in a test tube. The reaction mixture was vortex mixed and then incubated at 30 °C for 10 mins after which the solution was made up to 5.0 mL with methanol. The UV-vis spectrum, between 190 - 900 nm, of the azo adduct was then acquired using methanol as blank. The UV-vis spectra of 0.5 mL aliquots of chromotropic acid and gabapentin stock solutions in methanol were also acquired.

Optimization of critical response parameters

For the optimization steps, the concentration of diazotized gabapentin utilized was 1.604 µg/mL of gabapentin

Optimization of sodium nitrite concentration for diazotization

Different batches of the diazonium solution were prepared using 5 mL of 0.05, 0.1, 0.2, 0.3, 0.4 and 0.5 M solutions of sodium nitrite as described in 2.3.2. A 0.5 mL aliquot of each of the diazonium solutions was used in turn to generate the adduct with 0.5 mL chromotropic solution. Following incubation at 30 °C for 10 mins, the reaction mixture was made up to 5 mL volume with methanol and the absorbance determined at 470 nm. Each determination was done in duplicates.

Optimization of hydrochloric acid concentration for diazotization

The effect of varying the concentration of the HCl used in the diazotization was investigated by using equal volumes of 0.5, 1.0, 2.0, 2.5 and 3.0 M HCl solutions in turn to prepare different batches of the diazonium solutions. Each diazonium solution was then used to generate the azo adduct and the absorbance determined at 470 nm. Each determination was done in duplicates.

Optimization of volume of hydrochloric acid for diazotization

The effect of varying the volume of the optimized concentration of HCl obtained from section on the optimization of hydrochloric acid concentration for diazotization was investigated by using 0.12, 0.25, 0.5, 1.0 and 2.0 mL of the acid solution in the diazotization procedure. Each diazonium solution was then used to generate the azo adduct and the absorbance determined at 470 nm. Each determination was done in duplicates.

Effect of chromotropic acid concentration on coupling reaction

The effect of varying the concentration of the coupling agent was investigated by using different CTA solutions corresponding to 0.1, 0.2, 0.3, 0.4, 0.5, 1.0, 2.0 and 3.0% w/v to obtain the adduct with the diazonium. The absorbance at 470 nm of each methanolic solution of the adduct was determined.

Optimization of coupling temperature

Optimization of temperature and time was done using the method of steepest ascent[29]. Equal volumes (0.5 mL) of the diazonium and CTA solutions were vortex mixed in test tubes and then incubated at 30°C for 5 and 20 mins. The entire procedure was repeated at 50, 60 and 70°C. After each time interval, the reaction was terminated by cooling in an ice-bath and the volume of each reaction mixture made up to 5 mL with methanol. The absorbance was determined at 470 nm using methanol as blank. Each determination was carried out in duplicates.

Optimization of coupling time

The effect of coupling time was investigated by varying the incubation times 0, 2, 5, 10, 15, 20, 25 and 30 mins of the azo adduct at the optimized temperature. After each time interval, the reaction was terminated by cooling in an ice-bath and the volume of each reaction mixture made up to 5.0 mL with methanol. The absorbance was determined at 470 nm using methanol as blank. Each determination was carried out in duplicates.

Determination of stoichiometric ratio

The Job's method of continuous variation was employed to determine the stoichiometric ratio that was optimal for colour development[30]. Into nine test tubes containing 0, 0.2, 0.25, 0.33, 0.5, 0.67, 0.75, 0.8 and 1.0 mL of the diazonium, appropriate quantities of CTA were added to make the volume 1.0 mL. Each reaction mixture was then incubated at 30 °C for 10 mins after which the reaction was terminated by cooling in ice and diluting to 5.0 mL with methanol. The absorbance of each of the solutions was determined at 470 nm using methanol as blank. Each determination was done in duplicates.

Validation studies

The calibration line was obtained from the 3-day average curves using volumes of the diazonium solution equivalent to 0.0, 1.0, 2.0, 3.0, 4.0, 5.0 and 6.0 µg/mL of the drug. To each of the test tube, 0.5 mL CTA solution was added, mixed and then incubated at 30 °C for 10 mins. After this, the reaction was terminated

by cooling in ice and dilution to 5.0 mL with methanol before the absorbance was determined at 470 nm using methanol as blank. Each determination was done in triplicates. Model recoveries and repeatability of the new method was carried out on three successive days as stipulated by USP[31]. The percent recoveries of the method as well as the intra- and inter-day precision were determined at three different concentrations equivalent to 2.0, 3.4 and 5.0 µg/mL of the diazotized drug. The current ICH guidelines were employed to determine the limits of detection and quantification as the ratio of the 3.3 and 10 standard deviation of the blank signal (n=6) respectively, divided by the slope of the calibration line.

Method selectivity

The interference liabilities of the new method were demonstrated by the determination of the recoveries of spiked amounts of the analyte in the presence of commonly pharmaceutical aids including starch, lactose, talc, magnesium stearate, gelatin and a mixture of all. Four replicate analyses were carried out with each excipient.

Analytical signal stability

Methanolic solutions of the azo adduct equivalent to 3.4 µg/mL gabapentin were divided into one of either two groups: those exposed to diffuse light or those protected with aluminum foil coverings. The absorbance of the solutions was determined at 30-minute intervals for 3 hours, and after these at twenty-four and seventy hours.

Dosage form analysis

The new method was applied to the active pharmaceutical ingredient content of three brands of gabapentin. The weight uniformity test was determined on twenty capsules and the amount of the powder equivalent to 50 mg of gabapentin transferred to a 10.0 mL volumetric flask. Enough water was added to make up the volume and the mixture filtered after adequate equilibration. A portion of the filtrate (2.0 mL) was then employed for the diazotization procedure as described in section 2.3.2. An aliquot of 0.017 mL of the diazonium (equivalent to 3.4 µg/mL gabapentin) was added to 0.5 mL CTA and then mixed for 10 seconds. The reaction mixture was incubated at 30 °C for 10 mins after which the reaction was terminated by cooling in an ice-bath and dilution with methanol. The absorbance was determined at 470 nm with methanol as the blank.

Non-aqueous titrimetric assay of gabapentin using 0.01 M perchloric acid with 0.2% crystal violet as indicator was used as the reference method. Six replicate analyses of each of the brand were carried out using both methods.

Infra-Red analysis of the isolated adduct

Spectroscopic characterisation of the isolated azo adduct was carried out by the acquisition of the infra-red data of the KBr disc.

2.13 Statistical analysis

The data obtained from the analysis of gabapentin in dosage forms using the new method described in this work and the reference method were compared statistically using Student t-test and F-ratio test. A p value of less than 0.05 was considered to show a statistically significant result.

RESULTS AND DISCUSSION

Evidence of coupling reaction

Diazotised gabapentin reacted instantly with chromotropic acid solution to give an intense orange adduct that was quite distinct from the colourless diazonium and pale-yellow CTA solutions. Similar results were obtained following incubation at higher temperature and prolonged time. The colour was stable for more than forty-eight hours as monitored by the absorbance. The TLC analysis also revealed that the R_f values of the adduct using the mobile phases were different from those of the diazonium and CTA solutions. TLC examination also confirmed the formation of a mono product as only a single spot was observed in the chromatogram.

Selection of analytical wavelength

The overlaid spectra of the drug, the diazonium, CTA and adduct solutions are presented in figure 1. The increase in the conjugation associated with the conversion of the free amino group of the drug to the diazonium functional group was evident in the bathochromic shift of the diazonium which absorbed at 235 and 360 nm when compared with the almost insignificant absorption of the drug at 225 nm. On coupling with CTA, the spectra of the azo adduct also showed extensive bathochromic shift with absorption peaks at 435 nm. The analytical wavelength was therefore selected at 470 nm at which both the diazonium and CTA showed minimal absorptivities.

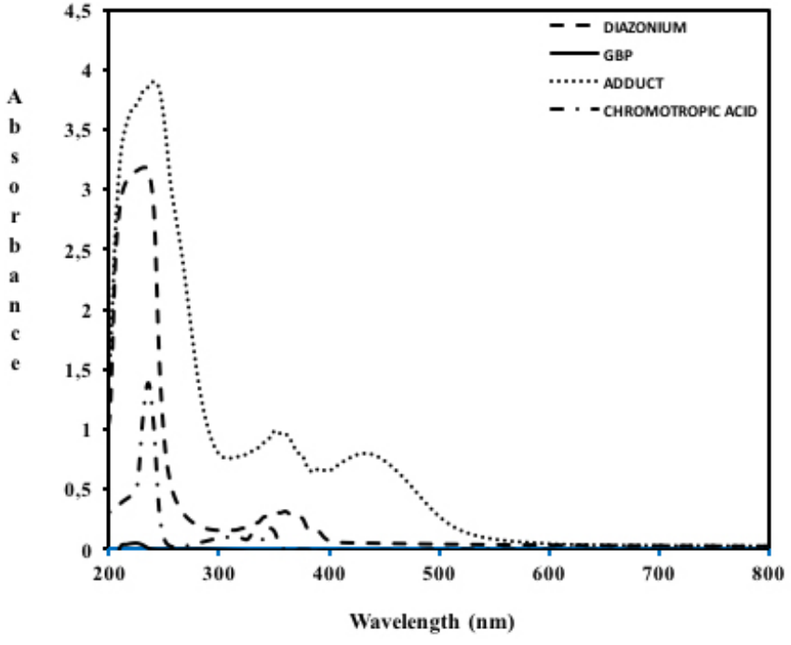


Figure 1. Overlaid spectra of gabapentin, the diazonium, CTA and adduct solutions

Optimization of critical response parameters

The optimization of diazotization conditions for gabapentin is necessitated by the fact that being an aliphatic amine, gabapentin lacks aromatic π electrons that can stabilize, via delocalisation, the resultant positive charge on its diazonium. The conversion of the free amino group in the drug to the diazonium was therefore monitored by absorbance changes with increasing concentrations of sodium nitrite as shown in figure 2. The plateau in the absorbance observable at 0.3 M and beyond of sodium nitrite concentration as well as the presence of free nitrous acid after the optimal diazotization time of 20 mins is indicative of the completion of the diazotization process. The results of the variation of acidity on the diazotization process also revealed optimal volume and concentration of 0.1 mL and 2.0 M HCl respectively. Further increase in the volume of the acid solution resulted in a decrease in absorbance as shown in figure 3. Increasing acidity beyond a critical point will be expected to impair diazotization because of the decreased solubility of the amino carboxylic acid drug as well as the permanent ionization of the amino functional group. The effect of CTA concentrations on the colour intensity of the azo adduct is depicted in figure 4. The results show that the optimal concentration is 0.3%w/v and this was adopted for subsequent work. Further increase in the concentration led to a decline in absorptivity.

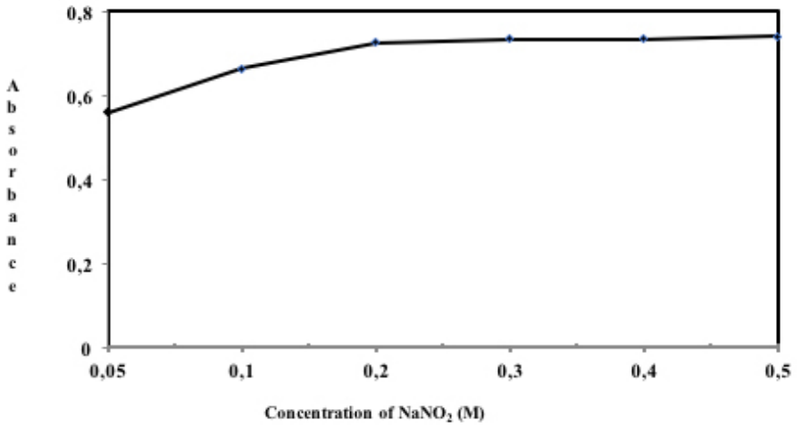


Figure 2. Variation in absorbance with concentration of sodium nitrite solution (1.604 µg/mL of gabapentin)

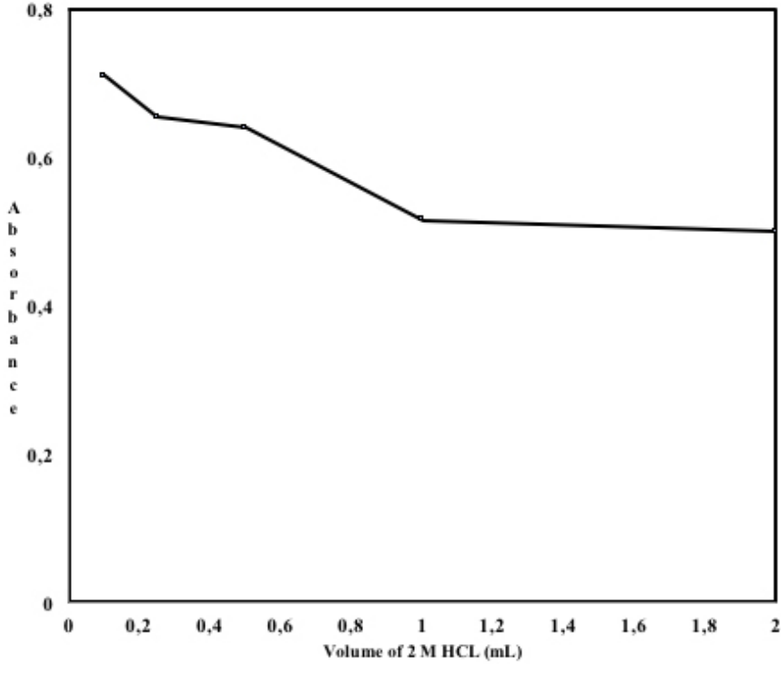


Figure 3. Optimisation of HCl concentration in the diazotization process (1.604 µg/mL of gabapentin)

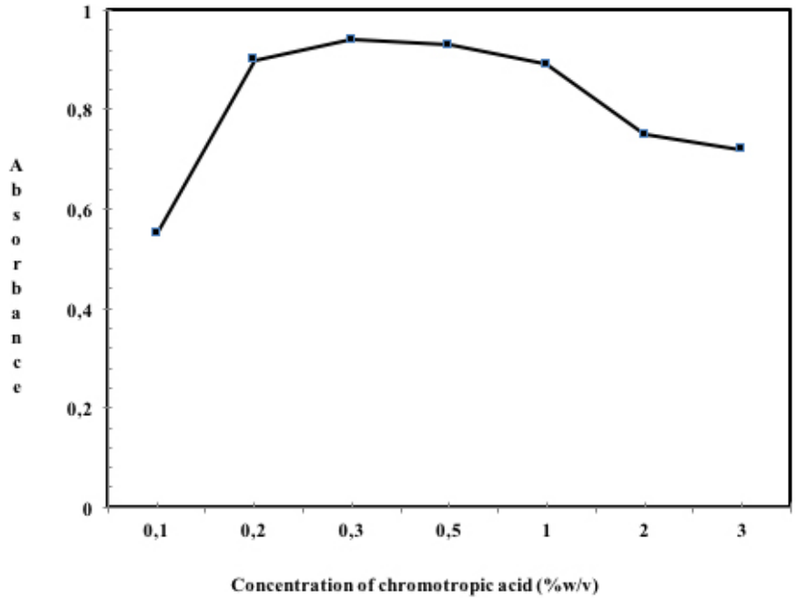


Figure 4. Effect of CTA concentration on the absorbance of adduct (1.604 µg/mL of gabapentin)

The method of steepest ascent was employed in establishing the optimal coupling temperature and time. The effect of temperature allowed for coupling reaction to take place as a function of time was carried out at temperature levels of 30, 50, 60 and 70°C. The results as depicted in figure 5 reveal that at 5 min reaction times, there is a gradual increase in the absorbance values as the temperature increased but, at 20 mins a decrease in absorbance was observed with temperature rise. This is most likely due to the thermal decomposition of the azo adduct. While an increase in temperature usually increases the rate of diazo coupling, it will also hasten the spontaneous breakdown of the less stable aliphatic diazonium leading to the formation of the azotate form which lack electrophilic character and therefore cannot couple. A decrease in the thermal stability of the adduct formed by an aliphatic diazonium, as is the case with gabapentin, is also expected. An optimal temperature of 30 °C was therefore selected for subsequent work. The optimal reaction time for the adduct formation was found to be 10 mins as no higher absorbance values were obtained with longer coupling times as shown in figure 6. The completion of the coupling reaction within 10 mins and at 30 °C also attests to the avidity of the reaction between the diazonium and the strongly activated CTA which contains two hydroxyl groups.

Amongst the compounds investigated for their suitability as dilution solvents, methanol gave the highest absorbance values and best correlation at the selected analytical wavelength as shown in figure 7. The suitability of methanol may be due to its ability to mop up excess water in the medium which may otherwise promote hydrolytic degradation of the azo adduct.

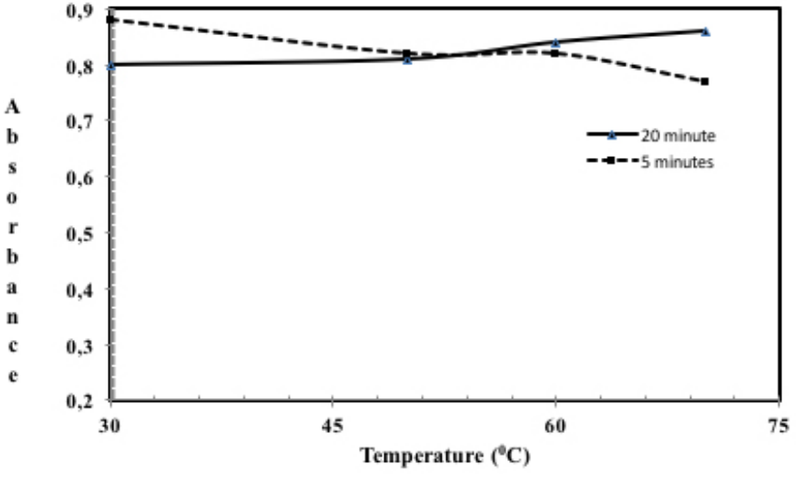


Figure 5. Optimisation of coupling temperature (1.604 µg/mL of gabapentin)

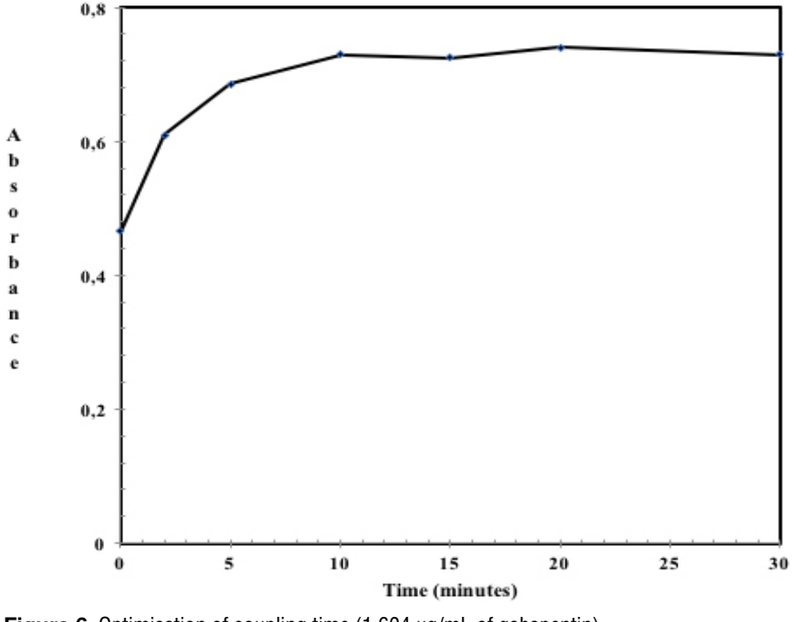


Figure 6. Optimisation of coupling time (1.604 µg/mL of gabapentin)

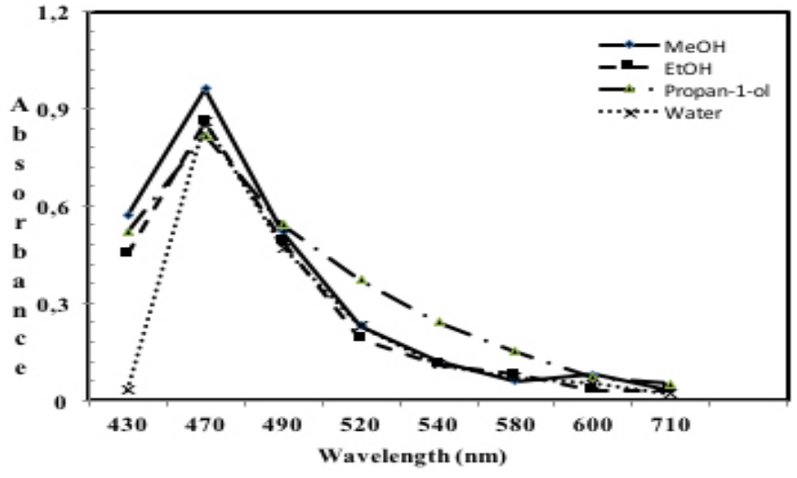


Figure 7. Optimisation of diluting solvents

Stoichiometric ratio and mechanism of reaction

The variation of the absorbance values with the mole ratio of the coupling agent is depicted in figure 8. Maximum absorbance value was obtained when the diazonium and CTA combined in 1:1 ratio indicating the presence of only one diazotizable group in gabapentin as well as one accessible point of electrophilic attack on the coupling agent. This was also consistent with the observation that only one spot was obtained in the TLC analysis of the azo adduct. Similar 1:1 ratios and mono azo products were reported in a number of studies in which chromotropic acid was employed as coupling agent with diazotizable drugs[32-33].

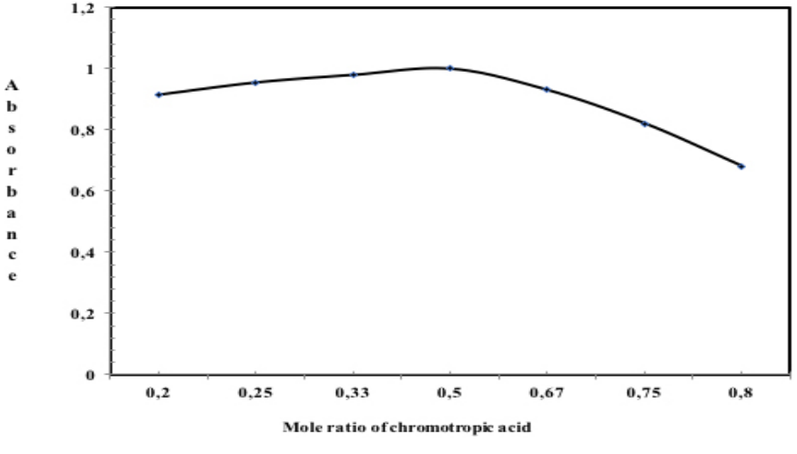
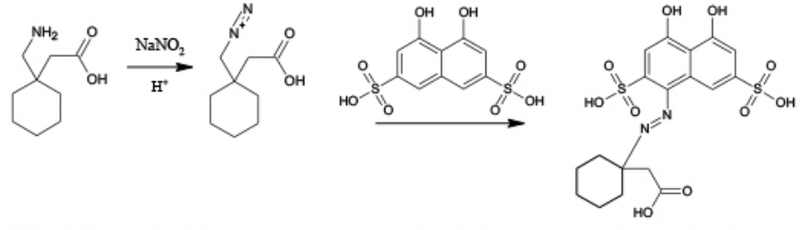


Figure 8. Variation of absorbance of adduct with mole fraction of chromotropic acid

However, unlike these reports that suggest that the point of electrophilic attack of the diazonium on CTA is on the carbon sandwiched between the sulphonic and the hydroxyl groups (in which case the stoichiometric ratio should be 2:1 as there are two of such chemically equivalent positions with little or no possibility of steric interference from each other), we propose that the electrophilic attack will be driven by the strongly activating effect of the hydroxyl group present on chromotropic acid and thus occur at its *para* position as depicted in scheme 1. The new azo substituent will sterically hinder the approach and attack of another diazonium ion on the *para* position of the *peri* (second) hydroxyl group. This mechanism is also in conformity with the well-documented observation that hydroxyl group on naphthyl rings are *ortho* and *para* directing when present at position 1 and 2 respectively and that substitution in between groups that are *meta* to each other (as is the case with the sulphonic and hydroxyl groups in CTA) is less probable due to steric effects[34]. Thus, a 1:1 ratio is observed.



Scheme 1: Proposed coupling reaction pattern between diazotised gabapentin and chromotropic acid

The 3D optimization of the azo adduct is presented in figure 9 and it shows that the highly staggered arrangement of the chair conformational isomer of the alicyclic residue which would contribute to the stability of the azo adduct. The configurational arrangement of substituents around the azo linkage is also of the E-type which precludes steric interference between the t

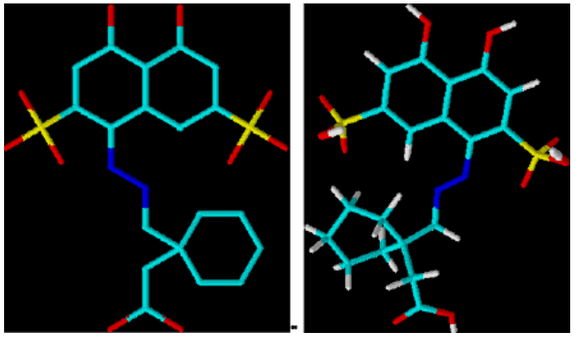


Figure 9. 3D optimization of the proposed azo adduct

Spectroscopic characterization of the azo adduct

A comparison of the IR spectra of gabapentin and the coupling product reveal the formation of a new chemical entity. IR data of gabapentin revealed the presence of twin absorption bands at 2857.14 and 2925.36 cm^{-1} which is characteristic of a primary amino functional group as well as well-defined bands at 3298.33 and 1662.91 cm^{-1} due to the stretching vibrations of the hydroxyl group and the carbonyl functional groups respectively. The most diagnostic feature of the formation of a new chemical entity is the disappearance of the bands of the amino group and the appearance of a new strong absorption band at 1600.00 cm^{-1} that can be attributed to the azo linkage. The broadening of the band previously at 3298.33 cm^{-1} which can now be observed at 3355.0 cm^{-1} in the new azo adduct confirms that the carboxylic acid group is now present in the azo adduct bringing about the OH_{str}.

Validation studies

The 3-day calibration revealed that absorbance increased linearly with concentration over the ranges 1.0 – 6.0 µg/mL at 470 nm with a correlation coefficient of 0.997. Other analytical and validation parameters are presented in Table 1.

Table 1. Analytical and validation parameters for the proposed method

Performance parameter	Value
Beer's law limit (µg/mL)	1.0-6.0
Limit of detection (µg/mL)	0.2864
Limit of quantification (µg/mL)	0.8679
Molar absorptivity (L mol^{-1} cm^{-1})	$6.232x10^3$
Sandell's sensitivity (µg cm-2)	27.48
Slope ± 95% CI	0.0595±0.0312
Intercept ± SD	0.0386±0.0038
Coefficient of determination	0.9982
Standard deviation of slope	$1.42x10^{(-3)}$
Standard deviation of intercept	$3.42x10^{(-3)}$
Interference liabilities (% gabapentin)	95.9±0.01 – 100.0±0.03

Accuracy, which is a measure of the closeness of the test results obtained by the method to the true value, was determined as the difference between the estimated and the reference values and expressed as percent recovery. The mean recoveries of the new method with replicate sample matrices spiked with the analyte are therefore indicated in table 2. The intra-day and inter-day variations at three different concentrations of the analyte were also determined using percentage relative standard deviation.

Table 2. Accuracy and repeatability assessment of the new method

Concentration (µg/mL)	Day 1a		Day 2 a		Day 3 a		Inter-day statistics b	
	Mean recovery (%)	RSD	Mean recovery	RSD	Mean recovery	RSD	Mean recovery	RSD
2	97.6±0.005	(%)	(%)	(%)	(%)	(%)	(%)	(%)
3.4	103.1±0.00	0.25	97.6±0.013	0.65	99.5±0.00	0	98.26±0.007	0.35
5	100.6±0.005	0.00	99.4±0.005	0.15	100.8±0.01	0.29	99.4±0.008	0.24
		0.10	100.4± 0.01	0	102.1 ±0.01	0.12	102.5±0.007	0.14

[a] *n=4;* [b] *n=12*

The proposed method competes favourably with previously reported visible spectrophotometric methods for the assay of gabapentin in bulk and dosage forms.

As shown in table 2, the intra-day mean recovery of the method is 98.26–102.5% indicating good accuracy while the percentage relative standard deviation for the intra-day precision did not exceed 0.35% indicating excellent repeatability. For inter-day accuracy, the mean recovery was determined as 96.0–101.47% while the percentage relative standard deviation was 0.14–0.35%, indicating good reproducibility. The new method therefore showed greater accuracy and reproducibility when compared with the intra-day percent recovery values of 102.13-102.8% and the inter-day percent RSD values of 1.42-2.11% obtained using picric acid in the derivatization of gabapentin[10]. The new method also allowed determination at a wavelength longer than those obtained with the use of vanillin[12], 2,3-dichloro-5,6-dicyano-1,4-benzoquinone[35] or 7,7,8,8-tetracyanoquinodimethane[36] as chromogenic agents.

Method selectivity

The mean recoveries of the analyte in the presence of excipients varied from 95.9±0.01 to 100±0.03% showing the selectivity of the method (table 1), except with gelatin for which it returned abnormally high absorbance and recovery values. This is probably due to the acid and/or thermal catalysed degradation of the polypeptide into amino acids which causes dispersion in the reaction mixture.

Analytical signal stability

Over the entire test period of seventy hours, the responses obtained from the two groups of samples were relatively constant corroborating the sufficient stability of the azo adduct to permit accurate and convenient quantification of the analyte.

Application to dosage form analysis

The mean recoveries of the analyte from three commercial brands of gabapentin using the new method and a reference titrimetric method were carried out and are depicted in table 3. A statistical comparison between the mean recoveries using the Student t test did not reveal any significant difference in the mean recoveries obtained with the two methods. Similarly, there was no statistical difference in their variances as estimated by the F test. This establishes that the new method can therefore serve as a suitable alternative as there are no statistical differences in their accuracy and precision. In addition, the new method in comparison to majority of previously reported methods is simple, fast and employs readily available non-toxic reagents. The LOD and LOQ are low and would permit the determination of the analyte when present in minute amounts in sample matrices. The derivatization and signal acquisition did not require prior solvent extraction or the strict control of pH with the use of buffers.

Table 3. Comparative mean recoveries of analyte using the new and reference methods

Drug Formulation	New Method[a]		Reference Method[a]		Statistics (p-values)[c]	
	%Recovery ± SD b	RSD (%)	%Recovery ± SD	RSD (%)	F-test	T-test
TEVA	100.7 ± 0.01	0.24	102.0 ± 2.83	2.77	0.61	0.76
Biopentin	100.8 ± 1.08	0.24	102.0 ± 2.83	2.77	0.62	0.69
Akobal-G	99.5 ± 0.001	0.18	98.83 ± 0.41	0.41	0.53	0.75

[a] *Mean value, n = 6. % Content of gabapentin stated by USP Pharmacopoeia ranges from 90% to 110%*

[b] *% recovery calculated as a function of amount of sample utilized*

[c] *Statistical analyses done between the results obtained from the proposed method and the Reference method*

CONCLUSION

A new visible spectrophotometric method for the assay of gabapentin in bulk and dosage forms has been developed. The new method offers the advantages of being fast, reliable, sensitive and sufficiently accurate to serve as a suitable alternative to reference methods.

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