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Original article

Spectrophotometric determination of gabapentin in pharmaceutical formulations using ninhydrin and π-acceptors

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ABSTRACT

Simple, rapid and sensitive spectrophotometric procedures are developed for the analysis of gabapentin in pure form as well as in their pharmaceutical formulations. The methods are based on the reaction of gabapentin as n-electron donor with ninhydrin and pi-acceptors namely, 2,3,5,6-tetrachloro-1,4-benzoquinone, chloranilic acid, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, tetracyanoethylene and 7,7,8,8-tetracyanoquinodimethane. The obtained complexes were measured at 568, 230, 314, 304, 335 and 439 nm for ninhydrin, chloranil, Chloranilic acid, DDQ, TCNE and TCNQ respectively. The proposed procedures could be successfully applied to the determination of gabepentin with good recovery; percent ranged from 99.3 to 100.7 The association constants and free energy changes using Benesi–Hildebrand plots are also studied.

1. Introduction

The anti-convulsant drug gabapentin (1-(aminomethyl)cyclohexaneacetic acid) is an analogue of γ-aminobutyric acid (GABA) and its action is attributed to the irreversible inhibition of the enzyme GABA-transaminase, thus preventing the physiological degradation of GABA in the brain [1,2]. Gabapentin is not included in either United States' or British Pharmacopoeia. The reported analytical methods for its determination includes high-performance liquid chromatography (HPLC) [3–8], spectrofluorimetry [9,10], gas chromatography–mass spectrometry (GC–MS) [11,12], capillary electrophoresis [13] and spectrophotometry applying Hantzsch reaction [14]. Only some methods reported in literature to determination of gabapentin by colorimetric technique, a method reported by Hisham et al. [1], method is based on the reaction of the primary amino group of gabapentin with ninhydrin reagent in N,N-dimethylformamide medium producing a colored product which absorbs maximally at 569 nm. Beer's law is obeyed in the concentration range 40–280 μg mL^{-1} of gabepentin, but in our work it can be analyse up to 2 μg mL^{-1} so our work has an advantage on this previously reported work, Belal et al. [9] reported Spectrofluorimetric determination of gabapentin in urine and dosage forms through derivatization with fluorescamine, but we used some different derivitizating agents for the quantification of gabapentin. The literature is still starving for such analytical procedures which could analyse gabapentin by colorimetric method.

Present study describes more simple, direct, sensitive and precise spectrophotometric methods than the existing UV and HPLC methods that are free from such experimental variables as extraction step, for the determination of gabapentin via formation of charge-transfer complexes with ninhydrin (NIN) and pi-acceptors; 2,3,5,6-tetrachloro-1,4-benzoquinone [(chloranil) (CH)], chloranilic acid (CHA), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), tetracyanoethylene (TCNE) and 7,7,8,8-tetracyanoquinodimethane (TCNQ) in pharmaceutical formulations.

No interference was observed in the assay of gabapentin from common excipients in levels found in pharmaceutical formulations. These methods rely on the use of simple and inexpensive chemicals and techniques but give out sensitivity analogous to that procured by sophisticated and expensive techniques such as HPLC, and are validated as per ICH recommendations [15]. The reaction conditions and application of the methods for determination of gabapentin in pharmaceutical formulations have been established, in addition, the association constant, stoichiometric ratio of reactants and the standard free energy changes (ΔG°) were determined.

The molecular interactions between electron donors and acceptors are generally associated with the formation of intensely

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colored charge-transfer complexes, which absorb in the visible region [16]. The photometric methods based on molecular interactions are classically simple and suitable since they result in the rapid formation of the complexes. Gabapentin is good n-electron donors and will form charge-transfer complexes with sigma or π-acceptors.

Ninhydrin (NIN) and π-acceptors such as CH, ChA, DDQ, TCNE and TCNQ are known to result in charge-transfer (CT) complexes and radical anions with a variety of electron donors [16–18].

Our present study suggests simple and sensitive spectrophotometric procedures for the determination of gabapentin in pharmaceutical formulations. The methods are based on the reaction of primary amino group of gabapentin with ninhydrin and π-acceptors cited above.

2. Experimental

2.1. Apparatus

Shimadzu 1601 double beam UV–visible spectrophotometer possessing a fixed slit width (2 nm) with quartz cells of 10 mm path length connected to a P IV computer loaded with Shimadzu UVPC version 3.9 software were used to record the absorption spectra.

2.2. Materials and reagents

All reagents were of analytical grade. Gabapentin pure drug was obtained from Godecke AG, Darmstadt, Germany under license of Park-Davis (Pvt.) Ltd., Karachi, Pakistan. Gabix® capsules 100 mg (Getz Pharmaceuticals (Pvt.) Ltd., Karachi, Pakistan), Gabaplus® capsules 100 mg (Platinum Pharma (Pvt.) Ltd., Karachi, Pakistan) and Engaba® tablets 100 mg (English Pharma (Pvt.) Ltd., Karachi, Pakistan) were purchased from the market.

NIN, CH, CHA, DDQ, TCNE and TCNQ were purchased from Merck Schuchardt OHG, Darmstadt, Germany.

2.3. General procedure

2.3.1. Preparation of standard stock solutions

Solution of 0.1 mg mL^{-1} gabapentin was prepared in acetonitrile (ACN) and stored in a cool (<25 °C) and dark place. CH was 3 mg mL^{-1} in ACN, prepared fresh daily. ChA, DDQ and TCNE were 1 mg mL^{-1} in ACN and prepared fresh daily. TCNQ was 1 mg mL^{-1} in ACN, the solution was found to be stable for at least 1 week at 5 °C. Ninhydrin reagent was 2 mg mL^{-1} in methanol and was prepared fresh daily.

2.3.2. Method 1 (with ninhydrin)

Different aliquots of drug solution were transferred into test tubes. To each test tube 2 mL of ninhydrin reagent in methanol was added and 10 mL of de-ionized water was added, then test tubes were heated on a water-bath at 70 ± 5 °C for 15 min. These solutions were transferred to volumetric flasks after cooling and the volume was made up to the mark with de-ionized water to provide final concentration range of 2–30 μg mL^{-1}. The absorbance of the solution was measured against a reagent blank at 568 nm. The calibration graph was prepared by plotting absorbance vs concentration of gabapentin.

2.3.3. Method 2 (with π-acceptors)

Into different measuring flasks, 1 mL of π-acceptor was added and then different aliquots of drug solution were transferred to provide final concentration ranges for different reagents (16–70 μg mL^{-1} for CH, 6–30 μg mL^{-1} for ChA, 2–40 μg mL^{-1} for DDQ, 6–30 μg mL^{-1} for TCNE and 4–30 μg mL^{-1} for TCNQ) along with 10 mL of ACN and set aside at room temperature (see Table 1 for reaction times). The volume was made up to the mark with acetonitrile and the absorbance was measured against a reagent blank at respective λ_{max} (568 nm for ninhydrin, 230 nm for chloranil, 314 for Chloranilic acid, 304 for DDQ, 335 for TCNE and at 439 nm for TCNQ). The calibration graph was prepared by plotting absorbance vs concentration of gabapentin.

2.3.4. Procedures for pharmaceuticals formulation

Twenty tablets/capsules of each formulation were weighed and powdered. The powder equivalent to 10 mg of gabapentin was dissolved in 100 mL of acetonitrile. The procedure was continued as described under general procedures.

2.4. Stoichiometric study

Job's method of continuous variation was employed. Master equimolar solutions of gabapentin and π-acceptors were prepared in acetonitrile whereas ninhydrin was prepared in methanol and made up to volume with the same solvent. A series of 10 mL portions of master solution of gabapentin with the respective acceptor was made up comprising different complementary proportions (0:10, 1:9, 2:8……9:1) in 10-mL calibrated flasks. The absorbance of the resulting solutions were measured at the wavelength of maximum absorption after the appropriate time (Table 1) against reagent blanks treated similarly.

2.5. Interference from excipients

Samples were prepared by mixing 50 mg of gabapentin with various amounts of common excipients such as glucose, lactose, talc powder, magnesium stearate, pyrrolidone, HPMC (hydroxypropylmethylcellulose) and starch. The procedure was continued as described under general procedures.

3. Results and discussion

Gabapentin exhibits a very low UV absorption, with $A^{1\%}_{1\ cm}$ at 276 nm = 6.5 and as a result poor sensitivity will be achieved by conventional UV spectrophotometric methods [1].

3.1. Reaction with ninhydrin (NIN)

Ninhydrin reagent is used for the determination of an aliphatic primary amine [19–21]. The reaction is usually carried out by heating for a short time in a mixture of water and an organic solvent and the reaction product is measured at 568 nm depending on the reaction condition [22].

Gabapentin interacts with ninhydrin reagent in methanol medium via oxidative deamination of the primary amino group followed by the condensation of the reduced ninhydrin to form the purple colored reaction complex with λ_{max} at 568 nm (Fig. 1 & Scheme 1).

Gabapentin was found to be competent of reacting with ninhydrin only at higher temperatures. Maximum color was obtained by heating on a water bath at 70 ± 5 °C for 15 min. Prolonged heating decreased the chromogenic intensity, so the

Table 1
Optimum reaction conditions with NIN and π-acceptor

Parameters	NIN	CH	ChA	DDQ	TCNE	TCNQ
Time	20	30	instant	instant	15	15
Wavelength	568	230	314	304	335	439

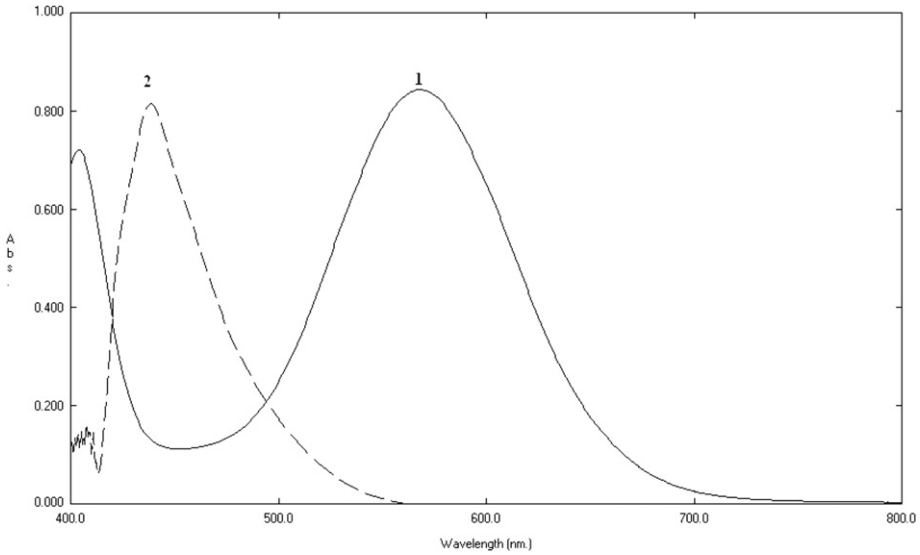


Fig. 1. Absorption spectra of the reaction products of gabapentin with each of NIN(1) and TCNQ(2).

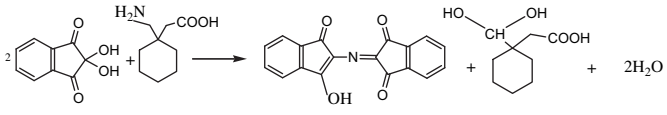
reaction time should be controlled. Different solvents such as water, ethanol, methanol, isopropanol, acetone, dioxane and acetonitrile have been tried, but the best results were obtained with methanol.

3.2. Reaction with π-acceptors

When the solution of gabapentin (Lewis base) was mixed with solution of π-acceptors (Lewis acid) in acetonitrile at room temperature, intense coloration was developed, reddish brown for gaba-CH, intense violet in case of gaba-ChA, dark red for gaba-DDQ, yellowish green for gaba-TCNE and bluish green for gaba-TCNQ showing broad bands in the region of 230–450 nm, 230 nm for CH, 314 nm for ChA, 304 nm for DDQ, 335 nm for TCNE (Fig. 2) and 439 nm for TCNQ (Fig. 1), which indicates the formation of CT complex. The colors developed were not associated with any of the reactants, hence, confirming formation of CT complex. The newly formed bands were accredited to an electron transfer complexation reaction between gabapentin (lone pair-donor) and electron deficient π-acceptors followed by formation of radical ions. The intensity of these bands increased with increased concentration of gabapentin. The proposed mechanisms with respect to each π-acceptor are illustrated in Scheme 2.

The reaction mixture (donor + acceptor) was essential to achieve reproducible results. The period of time allows the complete change of the molecular complex (outer complex) into the inner complex having radical ions formation, which is responsible for the observed wavelength.

In order to optimize the conditions, we have investigated a number of parameters such as temperature, time, reagent concentration and solvent. The optimum conditions were established by changing one variable and observing its effect on the absorbance of the colored product. A representing spectra is exposed in Fig. 3, which shows the pure gabapentein spectra and different concentration of gabapentein with unvarying concentration of



Scheme 1. Suggested reaction pathway between gabapentin and NIN.

chloranilic acid (80 μg mL^{-1}) it is very understandable that how spectra is changed with chronalic acid.

3.3. Reagent concentration

We found that 1 mL is the optimum volume for carrying the assays of gabapentin stock solution with the polyhaloquinone and polycyanoquinone π-acceptors while 2 mL of ninhydrin was used. It can be concluded that the elevated concentrations of the reagents used may be useful for rapid attainment of equilibrium, thus reducing the time required for formation of CT complex.

3.4. Reaction time

Following the absorbance of the developed color at different time intervals at ambient temperature (25 ± 5 °C) for all the reagents except ninhydrin (70 °C), the reaction time was determined. Complete color development was attained either instantaneously or after 10–30 min with all investigated reagents (Table 1).

3.5. Association constants and standard free energy changes

The association constants were determined for the interaction of each drug with NIN, CH, ChA, DDQ, TCNE or TCNQ complex using Benesi–Hildebrand equation [23].

$$\frac{Ca}{A} = \frac{1}{\varepsilon} + \frac{1}{Kc_x\varepsilon} \times \frac{1}{Cb}$$

Where Ca and Cb are the concentrations of the acceptor and donor respectively, A is the absorbance of the complex, ε is the molar absorptivity of the complex and K_c is the association constant of the complex.

From the aforementioned equation, on plotting the values of Ca vs A, straight lines were obtained as shown in Table 2. The standard free energy changes of complexation (ΔG°) were calculated from the association constants by the following equation [24].

$$\Delta G^\circ = -2.303RT\log K_C$$

Where ΔG° is the free energy change of the complex (kJ mol^{-1}), R the gas constant (0.001987 K cal mol^{-1} deg^{-1}), *T* the temperature in

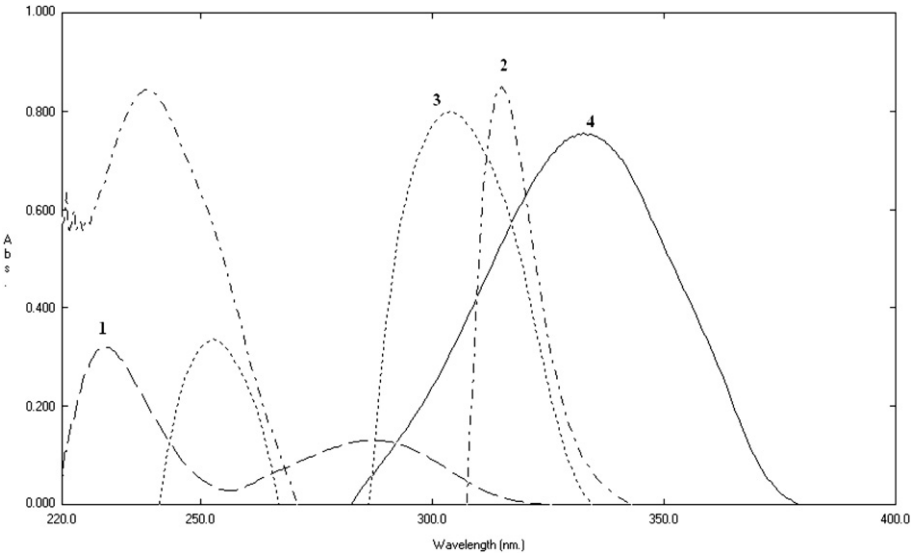
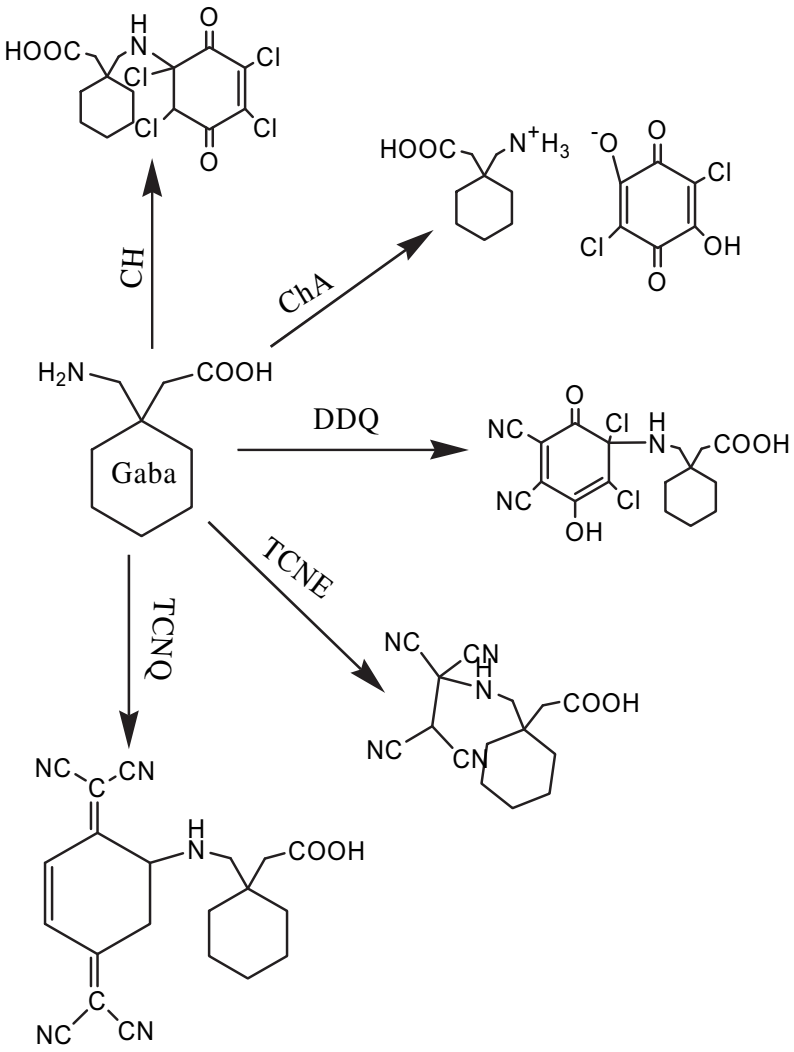


Fig. 2. Absorption spectra of the reaction products of gabapentin with each of CH[(1)], ChA[(2)], DDQ[(3)] and TCNE[(4)].



Scheme 2. Suggested reaction pathway between gabapentin and CH, ChA, DDQ, TCNE and TCNQ.

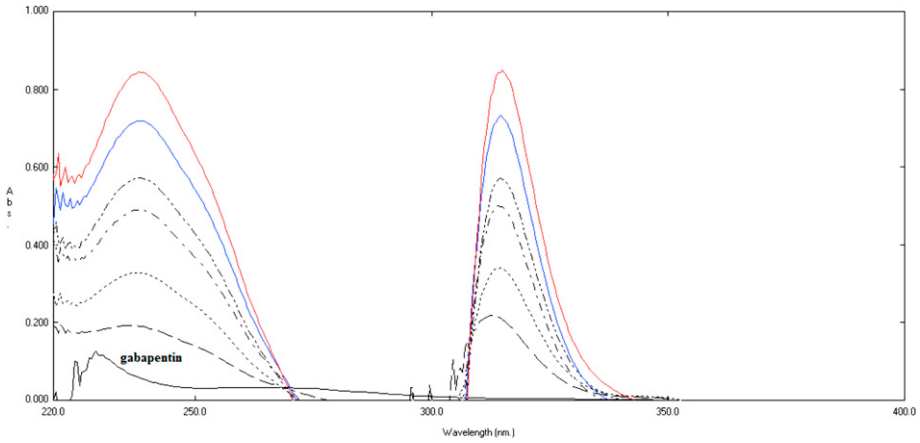


Fig. 3. Representative spectra of gabapentin and gaba + Chloranilic Acid complex (different concentration of gabapentein6, 10, 16, 20, 26 and 30 μg mL^{-1} with constant concentration of Chloranilic acid 80 μg mL^{-1}).

Kelvin (273+°C) and K_c is the association constant of drug–acceptor complexes (1 mol^{-1}) given in Table 3.

3.6. Stoichiometry of the reaction

On observing the molar ratio of the gabapentin with NIN, CH, ChA, DDQ, TCNE and TCNQ using Job's method of continuous variation [25], it was found to be 1:1 for all reagent except with NIN which was found to be 1:2.

3.7. Quantification

3.7.1. Linearity, accuracy and precision

To establish the linearity, accuracy and precision, a series of calibration standards were prepared four linearity curves containing seven non-zero concentration were analyzed. Linear regression equations were attained for the proposed procedures. The calibration curve showed linear dependence of the absorbance over Beer's law range given in Table 2. The table also shows the results of the statistical analysis of the experimental data, such as the slopes, the intercepts, the Square of correlation coefficients obtained by the linear least-squares treatment of the results.

In order to determine the accuracy and precision of the methods, solution containing different concentrations of gabapentin were prepared and analyzed in five replicates. The analytical results obtained from this investigation are summarized in Table 4. The relative standard deviation (RSD) and the standard deviation (SD) obtained were very satisfactory.

With current experimental conditions, the intensity of absorption at the specified wavelength was found to be a function of the concentration of the gabapentin. In all cases studied, Beer's law plots were linear with very small intercept values (−0.268 to 0.0543). Slopes ranged from (0.0053–0.076) in the general concentration ranges presented in Table 2. The regression equations for the proposed procedures were derived using the least-square method and the correlation coefficient ranged from 0.9923 to 0.9999.

3.7.2. Specificity

Before dealing with the analysis of the pharmaceutical preparations, the effect of common additives, adjutants and excipients on the proposed method was experimentally studied.

Pertaining to the interference of the excipients and additives generally presented in pharmaceutical formulations and interference due to the degradation products of gabapentin, the energy of the charge transfer (E_{CT}) depends on the ionization potential (IP) of the donor and the electron affinity of the acceptor (E_A); hence the λ_{max} values of other p-donors mostly vary from those of the investigated acceptors if they are able to form charge-transfer (CT) complexes. This specificity of the charge-transfer reaction for gabapentin was accredited to its basic character, which allows the charge transfer, rather than the degradation products of gabapentin, which does not have enough basicity to achieve charge transfer. Potential interference by the excipients in the dosage forms was also considered. The good percentage recoveries (Table 5) revealed that no interference was observed from any of these excipients in the proposed methods.

3.7.3. Limit of detection (LOD) and limit of quantification (LOQ)

The LOD and LOQ were calculated for gabapentin with NIN and each π-acceptor. The theoretically determined values of LOD and LOQ were cross checked by actual analysis of these concentrations using proposed methods. LOD of gabapentin with NIN, CH, ChA, DDQ, TCNE and TCNQ were 0.15, 0.44, 0.09, 0.08, 0.2 and 0.04 μg mL^{-1} respectively while LOQ were 0.454, 1.33, 0.3, 0.25, 0.06 and 0.13 μg mL^{-1} respectively.

Table 2
Quantitative parameters for the reaction of the studied gabapentin with NIN, CH, ChA, DDQ, TCNE and TCNQ

Acceptor	Linearity μg mL^{-1}	Intercept	Slope		Molar absorptivity
		A	B	r2	
NIN	2–30	0.032	0.028	0.9999	12 500
CH	16–70	0.117	0.009	0.999	61 578
ChA	6–30	0.074	0.025	0.9994	57 399
DDQ	2–40	−0.023	0.053	0.9923	87 452
TCNE	6–30	−0.113	0.076	0.9969	106 426
TCNQ	4–30	−0.268	0.043	0.9977	67 743

Table 3
Association constants (K_c), correlation coefficients and standard free energy changes (ΔG°) of gabapentin complexes obtained from Benesi–Hildebrand plots

Acceptor	ΔG°	%RSD	K_c 10^3	%RSD	r
NIN	−4.297	1.05	1.418	1.34	0.999
CH	−3.241	0.79	0.2381	0.49	0.998
ChA	−4.07	1.35	0.965	1.08	0.999
DDQ	−4.215	1.28	1.232	1.26	0.998
TCNE	−4.167	0.96	1.137	1.96	0.998
TCNQ	−3.879	1.71	0.699	0.88	0.999

Table 4
Evaluation of the accuracy and precision of the proposed methods

Added μg mL^{-1}	Found	% rec[a]	SD	RSD	Added μg mL^{-1}	Found	% rec[a]	SD	RSD
NIN					DDQ				
30	30.63	102.10	0.398	0.388	40	39.77	99.42	0.692	0.688
20	20.22	101.10	0.598	0.629	30	29.96	99.86	0.714	0.712
18	18.11	100.63	0.534	0.526	26	25.98	99.92	0.778	0.769
14	13.96	99.75	0.667	0.661	16	20.02	100.11	0.524	0.522
10	10.00	100.00	0.941	0.936	12	15.98	99.86	0.559	0.552
6	6.11	101.82	0.882	0.865	10	10.01	100.14	0.635	0.631
2	1.94	97.12	0.692	0.684	4	4.02	100.52	0.735	0.732
					2	2	100	0.296	0.288
CH					TCNE				
70	70.44	100.6	0.751	0.745	30	30.1	100.34	0.492	0.49
60	60.11	100.2	0.628	0.619	20	20.09	100.46	0.741	0.74
50	50.54	101.1	0.528	0.523	16	16.02	100.11	0.825	0.82
40	39.54	98.8	0.695	0.692	14	14.02	100.11	0.399	0.398
30	29.55	98.5	0.581	0.58	12	12.03	100.24	0.415	0.413
26	26.19	100.7	0.558	0.551	10	9.97	99.73	0.662	0.66
20	19.88	99.4	0.954	0.953	6	6.01	100.15	0.743	0.741
16	15.82	98.9	0.824	0.82					
ChA					TCNQ				
30	30.07	99.6	0.586	0.578	30	30.16	100.53	0.336	0.335
26	25.91	100.4	0.547	0.542	26	26.12	100.46	0.429	0.42
20	20.11	100.5	0.664	0.791	20	20.02	100.11	0.394	0.9
16	16.12	100.7	0.487	0.485	16	15.89	99.31	0.524	0.522
10	10.11	101.1	0.336	0.332	12	12.02	100.2	0.41	0.4
6	5.89	98.22	0.518	0.512	10	10.04	100.4	0.552	0.55
					4	4.04	100.88	0.621	0.62

[a] = recovery.

3.7.4. Analysis of pharmaceutical dosage forms

The proposed charge-transfer spectrophotometric methods were applied to the determination of gabapentin in pharmaceuticals formulations together with the reference method [1]. These determinations were carried out on the same samples.

In the *t* and *F* tests, no considerable variation was found between the calculated and theoretical values (95% confidence) of the proposed and official methods. This indicates similar precision and accuracy. Data of Table 6 suggests that the present procedures can be applied to the assay of these drugs in their single dosage forms without interference. Frequently encountered common ingredients of formulations were found not to interfere. Percentage recoveries ranged from 99.3 to 100.7 for the applied acceptors.

3.8. Spectroscopic studies

In order to have an idea of mechanism of these reactions and to propose structures of the complexes, the complexes were isolated, purified and subjected to spectroscopic studies. The reaction (Schemes 1,2) is suggested on the basis of results mentioned below.

3.8.1. Infrared spectra

The IR spectra of gabapentin showed the expected doublet of primary NH_2 at 2857 and 2927 cm^{-1}, C–N stretch at 1165 cm^{-1} and the carbonyl stretch of COOH near at 1615 cm^{-1}. Primary amines are reported to give Ruhemann's Purple complex with NIN [18]. The formation of the complex was evidenced by comparing the spectra of complex with gabapentin and NIN. NIN exhibited two broad bands at 3300 and 3250 cm^{-1} owing to two OH groups and 1061 cm^{-1} because of secondary alcohol C–O stretch. The carbonyl gave two peaks in the region 1660–1760 cm^{-1}. Aromatic resonance was recorded at 750 cm^{-1} [26,27].

Table 5
Recovery of Gabapentin in presence of different excipient

Ingredient	Recovery (%)					
	NIN	CH	CHA	DDQ	TCNE	TCNQ
Pyrrolidone	99.46	99.34	99.69	99.46	101.22	101.24
Lactose	99.07	99.37	98.68	100.26	99.28	98.94
Talc	99.62	100.24	100.92	101.45	99.28	100.42
Magnesium stearate	100.52	100.34	100.3	101.34	100.24	99.65
Starch	100.77	99.38	100.28	98.96	99.96	99.29
HPMC	100.69	101.08	100.36	100.25	99.51.6	99.84

Table 6
Determination of the gabapentin in commercial pharmaceutical preparations by the proposed method and official methods [25]

	Mean % rec[a]	STDEV	RSD	*T*-test	*F*-test
Gabix®					
Reference	99.3	1.03	1.03		
NIN	99.6	0.92	0.92	0.33	1.11
CH	99.6	1.21	1.22	0.08	1.18
ChA	100.1	1.20	1.20	0.92	1.17
DDQ	99.6	1.06	1.06	0.36	1.06
TCNE	99.5	0.91	0.91	0.08	1.12
TCNQ	100.6	0.98	0.98	0.21	1.04
Gabaplus®					
Reference	99.8	1.32	1.35		
NIN	99.8	0.70	0.70	0.086	1.88
CH	99.7	1.08	1.08	0.11	1.22
ChA	99.3	1.12	1.12	0.52	1.19
DDQ	99.7	0.60	0.60	0.05	2.22
TCNE	99.8	0.87	0.88	0.03	1.51
TCNQ	100.1	1.17	1.17	0.41	1.14
Engaba®					
Reference	100.7	1.12	1.09		
NIN	100.5	0.75	0.75	0.33	1.25
CH	99.8	0.70	0.70	1.11	1.56
ChA	100.1	0.46	0.46	0.87	2.38
DDQ	99.6	0.95	0.96	1.37	1.16
TCNE	99.8	0.66	0.67	1.21	1.66
TCNQ	99.5	0.75	0.75	1.6	1.47

[a] = recovery.

Many of the functionalities of NIN and gabapentin were found absent which confirms the formation of complex. The twin peak of NH_2 in gabapentin disappeared indicating that the primary amine has been changed to tertiary. The doublet of carbonyl in NIN changed significantly into one single sharp peak at 1680 cm^{-1} and the broad band of O–H shifted to 3400 cm^{-1}.

CH exhibited a ketonic carbonyl stretch at 1691 cm^{-1} and aryl chloride bends at 1141 and 1245 cm^{-1}. This also corresponded with the reported IR of CH [27]. When the infrared spectra of gaba-CH complex was compared with that of gabapentin and CH, it was found that the twin peaks of NH_2 changed into a singlet, showing that the primary amine may be converted to secondary, the C–N stretch also shifted to the higher frequency. While the aryl chloride bends were found absent, only one aryl chloride bend was observed lower then 1000 cm^{-1}.

The IR spectra of ChA reports to give OH peak at 3243 cm^{-1}, C=O stretch at 1664 and 1632 cm^{-1} and C–O stretch at 1369 cm^{-1} which also coincides with the reported IR of ChA [27,28]. The IR spectra of gaba-ChA complex, however, shows multiple peaks in the region 2500–3000 cm^{-1} that can be attributed to ammonium ion ($^{+}NH_3$) [29] along with $^{+}NH_3$ bending at 1550 cm^{-1} as observed in amino acids [29] Peak of C–O was missing due to $^{-}ON^{+}H_3$ [27].

The IR spectra of DDQ showed C=O stretch at 1679 cm^{-1} and C–O stretch at 1173 cm^{-1} as also reported [27]. The IR spectra of gaba-DDQ complex showed that the doublet of primary amine in gabapentin changed to a singlet indicating conversion into secondary amine. Also in the spectra of complex, a broad stretch appeared at 3400 cm^{-1} and a C–O stretch at 1280 cm^{-1} showing that one of the C=O of DDQ has been converted to –OH function.

In the reported spectra of TCNE [27] and in our studies as well, the peak of $-C\equiv N$ appeared at 2209 cm^{-1} and the weak C=C stretch was observed in the region 1644–1631 cm^{-1}. In the IR spectra of gaba-TCNE complex, it was observed that the C=C stretch diminished and the double peak of –NH2 of gabapentin changed into a single peak suggesting conversion into secondary amine and the C–N stretching absorption shifted from 1165 to 1247 cm^{-1}. While C=C stretch of TCNE disappeared.

The IR spectra of TCNQ reported a $-C\equiv N$ stretch at 2223 cm^{-1} and C=C stretching at 1619 cm^{-1} [27]. The IR of the gaba-TCNQ complex, the peak of nitrile shifted to 2349 cm^{-1} and the double peak of –NH2 of gabapentin changed into a single peak suggesting conversion into secondary amine, the C–N stretching absorption changed from a medium to weak intensity bend.

3.8.2. Nuclear magnetic resonance spectra

The ^1H NMR spectra of gabapentin showed the likely peak of NH_2 at δ 3.303 ppm as a triplet and the $-CH_2$ attached to NH_2 gave a triplet at δ 2.873 ppm while the cyclohexyl protons appeared in the region of δ 1.365–1.585 ppm.

By studying the ^1H NMR spectrum of the gaba-NIN complex it was found that the NH_2 protons completely diminished and the broad multiplet appearing between δ 7.42 and δ 8.163 ppm showing eight aromatic CH protons. A singlet at δ 4.803 ppm represents the enolic OH proton.

By studying the ^1H NMR spectrum of the gaba-CH complex it was found that the NH_2 protons shifted to δ 2.91 ppm while that of $-CH_2$ shifted to δ 2.51 ppm and appeared as a doublet which shows that NH_2 has been changed to NH.

The ^1H NMR spectra of gaba-ChA complex shows that the NH_2 protons shifted to δ 6.87 ppm may be because of salt formation at amino group [30] and $-CH_2$ protons shifted to δ 2.97 ppm appearing as a broad peak.

The ^1H NMR spectra of gaba-DDQ complex show similar results as that of gaba-CH complex, that is, the NH_2 protons shifted to δ 2.94 ppm while that of $-CH_2$ shifted to δ 3.96 ppm and appeared as a doublet showing that NH_2 has been changed to NH.

The above results were found in accord with UV and IR spectra, confirming the proposed structure.

4. Conclusion

The proposed methods are simple, rapid, accurate, precise and economical for the routine analysis of gabapentin in pharmaceutical quality control laboratories. With these methods, one can do the analysis with pace at low cost without losing accuracy. The proposed methods have been successfully applied to the determination of gabapentin in pharmaceutical formulations as well. Although all six reagent used gave suitable results for quantitative analysis of gabapentin, a comparative study based on the validation data recommended that ChA and DDQ are the reagent of first choice as the complex form instantly with lowest LOD and LOQ values, ninhydrin as well is a suitable reagent as it is known for derivatization and gave most reliable statistical data in our experiment.

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