

Spectrophotometric Studies of Lamotrigine Charge Transfer Complexes: Synthesis and Characterization

Najma Sultana^{1*}, Saeed Arayne M² and Saeeda Nadir Ali²

¹Research Institute of Pharmaceutical Sciences, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan

²Department of Chemistry, University of Karachi, Karachi-75270, Pakistan

Abstract

Charge transfer complexes of lamotrigine with 7,7,8,8-tetracyanoquinodimethane, bromothymol blue and picric acid have been investigated by spectrophotometric method. Optimum conditions for the reactions and validation data is reported. Resulting complexes absorb at 394, 404 and 374 nm in the Beer's law range of 0.15-15, 0.25-10 and 3.0-18 $\mu\text{g mL}^{-1}$ with correlation coefficient greater than 0.998 in each case and detection limits 45, 47 and 57 $\mu\text{g mL}^{-1}$ respectively. The data are discussed in terms of molar absorptivity, association constant and Gibb's free energy. Spectral characteristics including oscillator's strength, dipole moment, ionization potential, energy of complexes and resonance energy have been determined. Benesi-Hildebrand plots for each complex have been constructed. The proposed method was applied successfully for the determination of lamotrigine in pharmaceutical formulations. Satisfactory recovery values suggested that the method is reliable for the determination of lamotrigine in pharmaceutical formulations without interference of excipients. Further, solid charge transfer complexes were synthesized and characterized by IR and ¹H NMR spectroscopy.

Keywords: Charge transfer complexes; Lamotrigine; π acceptors; Dye stuffs; Benesi-Hildebrand plot

Introduction

Lamotrigine (LAM) is an anticonvulsant drug; belong to drug class of phenyltriazine. It is used to treat epilepsy, bipolar disorder and neurological lesions and also act as a tranquilizer [1,2]. Like other anticonvulsant, it also behaves as an effective mood stabilizer. Chemically it is 6-(2,3-dichlorophenyl)-1,2,4-triazine-3,5-diamine and its structural formula is given in Figure 1.

Many of the methods have been reported for the determination of LAM including HPLC and GC [3], capillary electrophoresis [4], titrimetry [5] and voltammetry [6]. Literature survey revealed a number of spectrophotometric methods for the determination of LAM [7] in acidic medium [8], in basic medium [9], through CT and ion pair complexes with bromophenol blue [10], bromocresol green [11], bromocresol purple [12], chlorophenol red [13], *p*-chloranilic acid [14], through oxidation of LAM [15].

Analysis of drugs employing spectrophotometric method is being carried out in our laboratory for few years. Methods for the determination of verapamil [16], gabapentin [17], quinolone

antibiotics [18], metformin [19], ascorbic acid [20] and montelukast [21] have been developed spectrophotometrically by our research fellows. Currently, we are working on charge transfer complexes of gabapentin, ibuprofen, omeprazole and few other bulk drugs. In continuation of our work, this paper describes sensitive and rapid spectrophotometric method for the determination of LAM through charge transfer complexes with TCNQ, BTB and PA utilizing low cost easily available solvent. The method is simple and reports many of spectral characteristics including oscillator's strength, dipole moment, ionization potential, energy of complexes, resonance energy and also the thermodynamic parameters i.e. association constant and Gibb's free energy changes which have never been determined in previously reported methods. Benesi-Hildebrand plots for each complex have been constructed. Further, solid CT complexes of LAM were synthesized and characterized by IR and ¹H NMR spectroscopy. Moreover, the developed methods have been successfully applied for the determination of LAM in pharmaceutical formulation without interference of excipients.

Experimental

Materials and reagents

LAM was obtained from Searle Pakistan Ltd and Lamnet[®] 25 mg was purchased from the local pharmacy. TCNQ and BTB were purchased from Merck (Darmstadt, Germany) and PA was purchased from Sigma

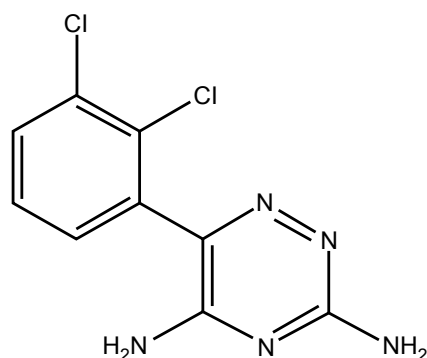


Figure 1: Structure of LAM.

***Corresponding author:** Najma Sultana, Research Institute of Pharmaceutical Sciences, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan, E-mail: araynezs@gmail.com

Received May 10, 2013; Accepted July 08, 2013; Published July 26, 2013

Citation: Sultana N, Saeed Arayne M, Ali SN (2013) Spectrophotometric Studies of Lamotrigine Charge Transfer Complexes: Synthesis and Characterization. Pharm Anal Acta 4: 260. doi:10.4172/2153-2435.1000260

Copyright: © 2013 Sultana N, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Aldrich Chemie GmbH. All the solvents used were of analytical grade and double distilled de-ionized water was used throughout the analysis.

Apparatus

Electronic spectra of LAM and its complex were recorded in the region 200-800 nm using Shimadzu 1800 double beam UV-visible spectrophotometer version 3.9 software with quartz cells of 1.0 cm path length. The IR spectra were obtained from KBr discs using Shimadzu Prestige-21200VEC version 1.2 software and ^1H NMR spectra were measured on Bruker AMX 500MHz spectrophotometer using TMS as internal standard and MeOD as solvent.

Standard stock solutions

- 0.39×10^{-2} M LAM in methanol
- 0.49×10^{-2} TCNQ in methanol
- 0.16×10^{-2} M BTB in double distilled deionized water
- 0.43×10^{-2} M PA in methanol
- Phthalate buffer of pH ranging from 2.2-4.0 was prepared by dissolving 20.4 g potassium hydrogen phthalate in 1.0 L distilled water and pH of solution was maintained by adding 0.1M HCl.

General Procedure

Method for TCNQ and PA

Aliquots of stock standard solution of LAM in the concentration range of 0.15-15 and 3.0-18 $\mu\text{g mL}^{-1}$ were transferred into two separate series of 10 ml volumetric flasks; to each flask 1 mL of TCNQ and 1mL of PA were added in the respective series. These solutions were allowed to react at room temperature for 15 min. The volume was made up to the mark with methanol and the absorbance was measured against reagent blank treated similarly.

Method for BTB

LAM solution in the concentration range of 12-96 $\mu\text{g mL}^{-1}$ was transferred in to 10 mL volumetric flasks, to this 3.0 mL buffer of pH 3.4 and 2.5 mL BTB solution was added and the volume was completed with distilled water. The mixture was then transferred into 50 mL separating funnel and extracted with 20 mL chloroform in two portions. The absorbance of extracted organic layer was measured against reagent blank treated similarly. The standard calibration graph was prepared by plotting absorbance vs. concentration of LAM.

Pharmaceuticals formulation

Twenty tablets of 25 mg Lamnet[®] were finely triturated. The powder equivalent to 100 mg of LAM was dissolved in methanol and shaken well for proper mixing. This solution was allowed to stand for 30 min and then sonicated for complete solubilization of drugs. Then the contents were filtered to separate the insoluble excipients and volume was completed with same solvent to get the final concentration of 1000 $\mu\text{g mL}^{-1}$. The procedure was continued as described under the procedure for pure LAM.

Synthesis of solid CT Complexes

Solid CT complexes were synthesized by refluxing the LAM with each of the complexing agent separately for 2 hrs in the ratio of 1:1 as found through the stoichiometric study by applying Job's method. The resulting product in each case was filtered off and washed with

minimum amount of methanol. The excess solvent was evaporated to dryness. The solid CT complexes were characterized by UV-visible, IR and ^1H NMR spectroscopy.

Results and Discussion

LAM, being a nitrogenous drug is present in the positively charged protonated form. It is reported to form CT complexes with many of compounds. In the present study, efforts have been made to develop the complexes of LAM with TCNQ, BTB and PA. It was observed that LAM interact with all of these agents in the stoichiometric ratio of 1:1 as determined by applying Job's method of continuous variation [22] leading to the formation of bluish green, yellow and dark yellow CT complexes. In all resulting product, LAM is in positively charged protonated form, whereas TCNQ forms radical anion and sulfonephthalein group of BTB and hydroxyl group of PA form anion. The newly formed complexes show intense absorption bands at 394, 404 and 374 nm respectively. The electronic absorption spectra of these complexes are given in Figure 2.

Different parameters influencing the intensity of absorption bands were investigated to establish the optimum experimental conditions for the assay. It was observed that the complete complexation occurs instantaneously for TCNQ and PA and absorbance remains constant for 24 hrs. The optimum reaction time for LAM-BTB complex was determined by investigating the absorbance of complex at every minute while shaking the reaction mixture. It is apparent from the Figure 3 that complete interaction occurs after proper shaking of mixture for 2 min and it also found to be stable for 24 hr. The effect of reagent concentration was examined by adding different volumes of 0.49×10^{-2} M TCNQ, 0.16×10^{-2} M BTB and 0.43×10^{-2} M PA in to a fixed amount of LAM. The 1 mL TCNQ and PA and 2.6 mL BTB were found to be appropriate for complete complexation. For BTB method, buffer of suitable pH was selected by testing them in the range of 2.0-4.0 and the maximum absorbance was obtained at pH 3.4. For proper extraction of complex, solvents like benzene, carbon tetra chloride, dichloromethane and chloroform were tested. Double extraction with chloroform was supposed to be adequate for maximum recovery.

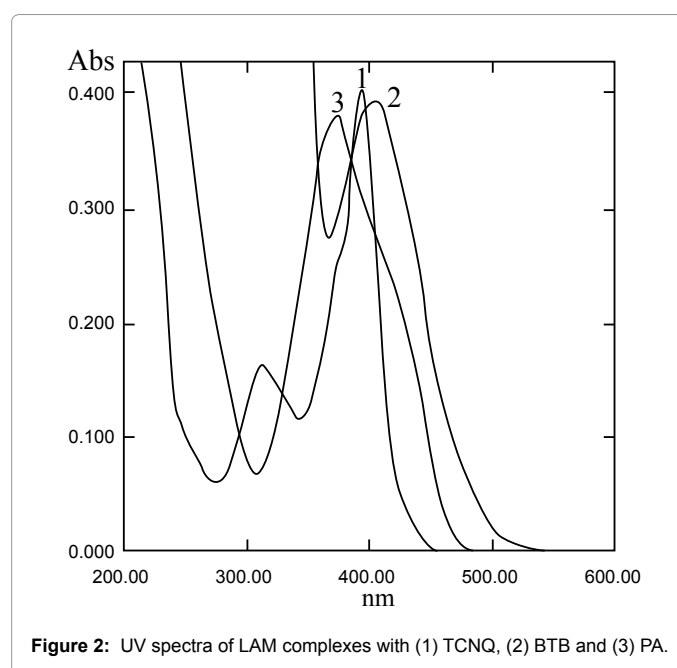


Figure 2: UV spectra of LAM complexes with (1) TCNQ, (2) BTB and (3) PA.

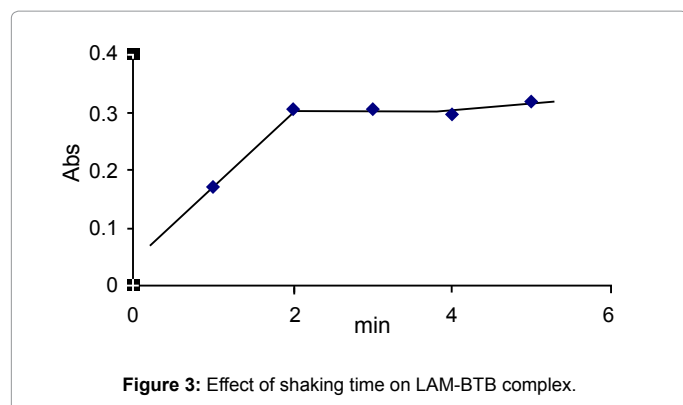


Figure 3: Effect of shaking time on LAM-BTB complex.

Analytical data

At the established experimental conditions, standard calibration curves for LAM with TCNQ, BTB and PA were constructed by plotting absorbance versus concentration. The linear regression curves were obtained in the Beer's law range of 0.15-15, 0.25-10 and 3.0-18 $\mu\text{g mL}^{-1}$ with correlation coefficient greater than 0.998 in each case respectively. Regression characteristics including slope, intercept, correlation coefficient and also the molar absorptivity values for each proposed method are given in Table 1. Limit of detection and quantitation were determined to establish the sensitivity of method. The LOD values were calculated to be 45, 47 and 57 ng mL^{-1} respectively (Table 1). Reproducibility of the method was measured for a series of six determinations at six concentration level. The data of percent relative standard deviation obtained for each method are reported in Table 2. The %RSD values in the range of 0.02-1.72, 0.05-0.45 and 0.31-1.28 confirm the sensitivity of method.

Pharmaceutical formulation

The proposed method was successfully applied for the determination of LAM in its dosage formulation. Six determinations were made at three concentration levels. The results obtained are shown in Table 3. Satisfactory recovery data was obtained in the range of 98.93-100.88%, 99.75-99.78% and 99.54-100.88% for TCNQ, BTB and PA. The low percent error indicated the reliability of method. The assay results were in good agreement with the label claim. Also, the effect of commonly found excipients was determined by scanning the blank solution of LAM and the placebo solutions. The percent recovery values given in Table 4 indicate that excipients of tablet did not found to interfere during the assay.

Spectral characteristics of CT complexes

The experimental oscillator strength (f) and transition dipole moment (μ) of newly formed CT complexes were determined by formulae given in equation (1) and (2) [23,24];

$$f = (4.319 \times 10^{-9}) \epsilon_{\text{max}} \nu_{1/2} \quad (1)$$

$$\mu = 0.0958 (\epsilon_{\text{max}} \nu_{1/2} / \nu_{\text{max}})^{1/2} \quad (2)$$

where ϵ_{max} is the molar extinction coefficient at maximum absorbance, $\nu_{1/2}$ is the band-width at half absorbance in cm^{-1} and ν_{max} is wave number in cm^{-1} . Relatively large values of oscillator strength indicate the strength of complexes. The ionization potential (I_p) of free donor was calculated by using the equation (3) [25],

$$I_p = 5.76 + 1.53 \times 10^{-4} \nu_{\text{CT}} \quad (3)$$

where ν_{CT} is the wave number in cm^{-1} corresponding to the CT band of

complex formed between donor and acceptor. The resonance energy of CT complex in the ground state was determined by Briegleb and Czekalla equation (4) given below [26]:

$$\epsilon_{\text{max}} = 7.7 \times 10^{-4} / [h\nu_{\text{CT}} / R_N - 3.5] \quad (4)$$

The energy of CT complexes was calculated by applying the relationship given in equation (5) [24]:

$$E_{\text{CT}} = 1243.667 / \lambda_{\text{CT}} \quad (5)$$

where λ_{CT} is the wavelength of CT band at maximum absorbance. All the spectral data including oscillator strength, dipole moment, ionization potential, resonance energy and energy of CT complexes are presented in Table 5.

The association constant was determined by employing Benesi-Hildebrand equation [27].

Parameters	LAM-TCNQ	LAM-BTB	LAM-PA
λ_{max} (nm)	394	404	374
Linearity range $\mu\text{g mL}^{-1}$	0.15-15	0.25-10	3.0-18
Molar absorptivity	12258	19643	7436
Slope	3.56E-02	4.90E-02	2.43E-02
Intercept	0.00633	0.2719	0.0857
Correlation coefficient	0.9985	0.9986	0.9986
LOD ng mL^{-1}	0.045882	0.047621	0.057616
LOQ $\mu\text{g mL}^{-1}$	0.139038	0.144308	0.174594

Table 1: Optimum conditions and analytical parameters.

LAM-TCNQ		LAM-BTB		LAM-PA	
Conc	%RSD	Conc	%RSD	Conc	%RSD
0.15	0.33	1	0.05	3	0.32
3	1.72	2	0.18	6	0.61
6	0.62	4	0.15	9	2.28
9	0.14	6	0.18	12	0.31
12	0.70	8	0.45	15	0.77
15	0.02	10	0.24	18	1.27

Table 2: Precision of method.

LAM-TCNQ			LAM-BTB			LAM-PA		
Conc	% Rec	% Err	Conc	% Rec	% Err	Conc	% Rec	% Err
3	100.47	0.46	2	99.75	-0.25	3	100.88	0.87
6	98.93	-1.08	4	99.78	-0.22	6	99.54	-0.46
9	100.88	0.87	6	99.75	-0.25	9	100.87	0.86

Table 3: Accuracy of method.

Excipients	LAM-TCNQ	LAM-BTB	LAM-PA
	% Recovery		
Pyrrolidone	99.13	99.76	99.86
Lactose	98.61	100.22	100.30
Talc	100.40	99.29	100.46
Magnesium stearate	100.17	99.68	98.97
Starch	99.58	101.42	100.89

Table 4: Recovery of lamotrigine in presence of different excipients.

Complex	f	μ	I_p	E_{CT}	R_N	$K_c \times 10^2$ (lit/mol)	ΔG° (KCal)
LAM-TCNQ	12.31	32.11	9.64	3.16	0.90	2.06	3.15
LAM-BTB	9.53	28.61	9.55	3.08	0.88	9.56	4.06
LAm-PA	3.45	16.57	9.85	3.33	0.95	3.26	3.42

Table 5: Spectrophotometric results.

$$[A_0]/A = 1/K [D_0], \epsilon + 1/\epsilon \quad (6)$$

where, K is the association constant, A is absorbance, ϵ is molar extinction coefficient and $[A_0]$ and $[D_0]$ are the initial concentrations of the acceptor and donor respectively. The values for Kc are given in Table 5. Further investigation was made by plotting the values of $1/D_0$ versus A_0/A , which showed linear curve in all the cases. Table 6 presents the values and the graphs are displayed in Figure 4.

The standard free energy changes (ΔG°) associated with GBP complexation reactions were calculated from the association constants by applying equation (2) [28]. The values of ΔG° for each complex are given in Table 5.

$$\Delta G^\circ = -2.303RT \log K_c \quad (7)$$

where, ΔG° is the free energy change of the complex in KJ mol^{-1} , R is the gas constant ($1.987 \text{ cal mol}^{-1} \text{ deg}^{-1}$), T is temperature in Kelvin and K_c is the association constant of drug-acceptor complexes.

Spectroscopic study

Spectroscopic studies of free donor and formed complexes were carried out to determine the structure of complexes. The IR spectra (Figure 5) were recorded using KBr discs and $^1\text{H NMR}$ spectra were measured at room temperature in MeOD. The IR spectra of LAM shows characteristic peak of $-\text{NH}_2$ at 3350 cm^{-1} which shift to $3450, 3448$ and 3215 cm^{-1} in LAM complexes with TCNQ, BTB and PA respectively, confirming that the interaction has occurred at $-\text{NH}_2$ site. The infrared frequencies and band assignments are given in Table 7 and the chemical shift values for the detected peaks are mentioned in Table 8. On the basis of spectroscopic data, the proposed chemical structure of LAM complexes with TCNQ, BTB and PA are given in Figure 6.

Advantages over reported methods

For the determination of LAM several techniques have been applied. A number of articles have been published for its determination in bulk drug, commercial formulations, biological and clinical samples. Recently, different reported spectrophotometric methods have been compared by vinay et al. [8] with their reported methods. Almost all of the previously reported methods are relatively less sensitive, time consuming or require the expensive reagents. In comparison, present study describe simple and more sensitive UV/ visible method based on the formation of charge transfer complexes of LAM with easily available reagents like TCNQ, BTB and PA. Simple methodology is

Complex	D (M) $\times 10^{-3}$	A (M) $\times 10^{-3}$	Abs	1/D $\times 10^5$	A/Abs $\times 10^2$
LAM-TCNQ	0.023	4.90	0.2867	0.43	1.71
	0.035	4.90	0.4033	0.28	1.22
	0.047	4.90	0.4886	0.21	1.00
	0.059	4.90	0.5868	0.17	0.84
	0.070	4.90	0.8619	0.14	0.57
LAM-BTB	0.008	1.60	0.3932	1.28	0.41
	0.016	1.60	0.4633	0.64	0.35
	0.023	1.60	0.5574	0.43	0.29
	0.031	1.60	0.6065	0.32	0.26
	0.039	1.60	0.7673	0.26	0.21
LAM-PA	0.012	3.06	0.298	0.85	1.03
	0.047	3.06	0.381	0.21	0.80
	0.070	3.06	0.466	0.14	0.66
	0.094	3.06	0.675	0.11	0.45
	0.117	3.06	0.771	0.09	0.40

Table 6: The values of $[A_0]/\text{Abs}$ and $1/[D_0]$ for lamotrigine complexes.

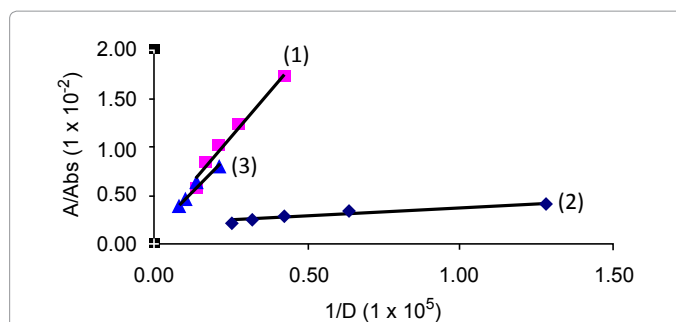


Figure 4: BH plot for LAM complexes with (1) TCNQ, (2) BTB and (3) PA.

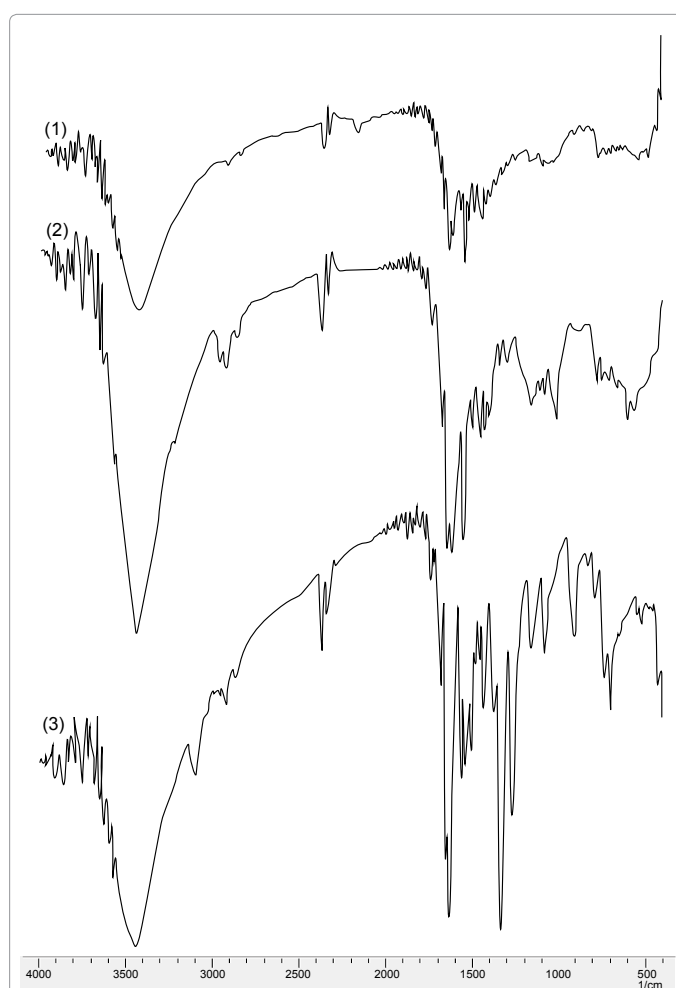


Figure 5: IR spectra of LAM complexes with (1) TCNQ, (2) BTB and (3) PA.

applied and results are calculated without employing any complicated equations. Moreover, none of the reported methods explicate the spectral characters of LAM and its complexes. Here, we reported the oscillator's strength, dipole moment, ionization potential, energy of complexes, resonance energy, association constant and Gibb's free energy changes and constructed the Benesi-Hildebrand plot in each case. The interday and intraday precision and percent recovery values were evaluated. Results of analysis were validated successfully. These methods were successfully applied for the determination of LAM in

LAM	LAM-TCNQ	LAM-BTB	LAM-PA	Assignment
3350	3450	3448	3215, 3856	v(N-H)
2954,2850	2924, 2858	2924	2924	v(C-H)
-	-	-	1653, 1683	v(NO ₂)
1560	1560	1558	1583	v(C=N)
1541	1541	1541	1546	v(C=C)
1502	-	1506	1506	v(N-H)
1440	1462, 1440	1460	1460	v(C-H) deformation
1327	1346	1300	1328	v(C-N)
1382	-	1342	1382	v(C-C)
-	1174	1172	1237	v(C-O)
1157	1163	1163	1159	v(C-H) in plane
-	-	-	1035	v(NO ₂)
-	-	1018	-	v(S=O)
846	842	853	846	$\delta_{rock} CH_2$
-	-	613	-	v(S-O)

Table 7: Infrared frequencies and their assignments.

Assignment	LAM	LAM-TCNQ	LAM-BTB	LAM-PA
(s, NH ₂)	δ 4.83	δ 4.56	δ 4.52	δ 4.56
(m, aryl)	δ 7.34-7.66	δ 7.40-7.73	δ 6.94-7.67	δ 7.34-7.71
(d, 4CH ₃)	-	-	δ 0.991	-
(s, CH ₃)	-	-	δ 1.99	-
(s, CH ₃)	-	-	δ 2.13	-
(m, 2CH)	-	-	δ 3.29	-

Table 8: ¹H NMR spectra.

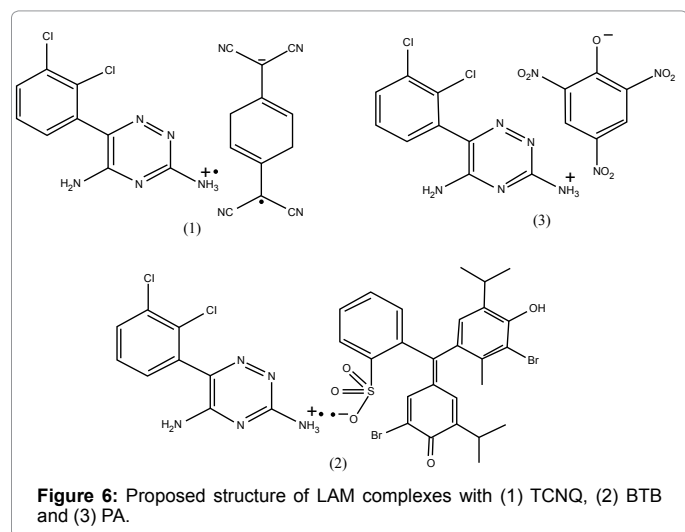


Figure 6: Proposed structure of LAM complexes with (1) TCNQ, (2) BTB and (3) PA.

pharmaceutical formulations. Commonly present excipients did not show interference during analysis. Solid charge transfer complexes were synthesized and characterized by IR and ¹H NMR spectroscopy.

Conclusion

The aim of present study was

- Development of charge transfer complexes of LAM with TCNQ, BTB and PA.
- Application of developed complexes for the UV-spectrophotometric determination of LAM in bulk and its formulation.

The investigation comprised the determination of its spectral characteristics including oscillator's strength, dipole moment,

ionization potential, energy of complexes, resonance energy, association constant and Gibb's free energy changes. Benesi-Hildebrand plots for each complex have been constructed. Also, the solid CT complexes were synthesized and characterized by IR and ¹H-NMR spectroscopy. Further, LAM was determined in bulk and its formulation by means of charge transfer complexes. Calibration graphs plotted between absorbance verses concentration of LAM were found to be linear within the limit of Beer's law with correlation coefficient greater than 0.998. The assay results were in good agreement with the label claim. Commonly present excipients did not found to interfere during the assay.

Acknowledgement

The author Mrs Saeeda Nadir Ali is grateful to Higher Education Commission, Pakistan for providing Indigenous Scholarship for this research work.

References

1. Goodman LS, Hardman JG, Limbird LE, Gilman AG (2001) Goodman and Gilman's-The Pharmacological Basis of Therapeutics. (10th edn), McGraw Hill, New York, USA.
2. Sweetman SC (2007) Martindale: The Complete Drug Reference. (4th edn), Pharmaceutical Press, London.
3. Greiner-Sosanko E, Giannoutsos S, Lower DR, Virji MA, Krasowski MD (2007) Drug monitoring: simultaneous analysis of lamotrigine, oxcarbazepine, 10-hydroxycarbazepine, and zonisamide by HPLC-UV and a rapid GC method using a nitrogen-phosphorus detector for levetiracetam. J Chromatographic sci 45: 616-622.
4. Theurillat R, Kuhn M, Thormann W (2002) Therapeutic drug monitoring of lamotrigine using capillary electrophoresis: Evaluation of assay performance and quality assurance over a 4-year period in the routine arena. J Chromatogr A 979: 353-368.
5. Rajendra Prasad N, Basavaiah K, Basavaiah Vinay K (2009) Determination of drug content of pharmaceuticals containing Lamotrigine by titrimetry in non-aqueous medium. Proc Indian Natl Sci Acad A Phys Sci 75: 131-136.
6. Domianquez-Renedo O, Calvo M, Arcos-Martinez MJ (2008) Determination of lamotrigine in pharmaceutical preparations by adsorptive stripping voltammetry using screen printed electrodes. Sensors 8: 4201-4212.
7. Talekar R, Dhake A, Sonaje D, Mourya V (2000) Spectrophotometric determination of lamotrigine. Indian J Pharm Sci 62: 51-52.
8. Vinay KB, Revanasiddappa HD, Rajendraprasad N, Ramesh PJ, Xavier CM, et al. (2012) Use of two sulfonphthalein dyes in the extraction-free spectrophotometric assay of tramadol in dosage forms and in spiked human urine based on ion-pair reaction. Drug Test Anal 4: 116-122.
9. Saini N, Saini K (2011) Quantitative determination of lamotrigine in bulk and dosage form by UV Spectrophotometry. J Appl Pharm Sci 1: 113-116.
10. Rajendraprasad N, Basavaiah K, Vinay KB (2010) Micro and nanogram determination of lamotrigine in pharmaceuticals by visible spectrophotometry using bromophenol blue. IJCT 17: 220-228.
11. Rajendraprasad N, Basavaiah K, Vinay KB (2010) Sensitive spectrophotometric determination of lamotrigine in bulk drug and pharmaceutical formulations using bromocresol green. Ecleica Quimica 35: 55-66.
12. Vinay KB, Revanasiddappa HD, Rajendraprasad N (2009) Development and validation of spectrophotometric methods for the sensitive and selective determination of lamotrigine in pharmaceuticals using bromocresol purple. J Food Drug Anal 17: 424-433.
13. Alizadeh N, Khakinahad R, Jabbari A (2008) Spectrophotometric determination of lamotrigine in pharmaceutical preparations and urine by charge-transfer complexation. Pharmazie 63: 791-795.
14. Youssef NF, Taha EA (2007) Development and validation of spectrophotometric, TLC and HPLC methods for the determination of lamotrigine in presence of its impurity. Chem Pharm Bull (Tokyo) 55: 541-545.
15. Revanasiddappa HD, Deepakumari HN, Mallegowda SM (2011) Development and validation of indirect spectrophotometric methods for lamotrigine in pure and the tablet dosage forms. Analele Universitatii Bucuresti: Chimie 20: 49-55.

16. Sultana N, Arayne MS, Waheed A (2011) Method Development and In vitro Interaction Studies of Verapamil in Presence, of Quinolones Using First Order Derivative UV Spectrophotometry and RP-HPLC Technique. *J Chil Chem Soc* 56: 848-855.
17. Siddiqui FA, Arayne MS, Sultana N, Qureshi F, Mirza AZ, et al. (2010) Spectrophotometric determination of gabapentin in pharmaceutical formulations using ninhydrin and pi-acceptors. *Eur J Med Chem* 45: 2761-2767.
18. Siddiqui FA, Arayne MS, Sultana N, Mirza AZ, Qureshi F, et al. (2009) Facile and Manifest Spectrophotometric Methods for the Determination of Six Quinolone Antibiotics in Pharmaceutical Formulations using Iron Salts. *Med Chem Res* 19: 1259-1272.
19. Arayne MS, Sultana N, Zuberi MH, Siddiqui FA (2009) Spectrophotometric Quantitation of Metformin in Bulk Drug and Pharmaceutical Formulations using Multivariate Technique. *Indian J Pharm Sci* 71: 331-335.
20. Arayne MS, Sultana N, Bibi Z (2009) Rapid and Specific Spectrophotometric and RP-HPLC Methods for the Determination of Ascorbic Acid in Fruit Juices and in Human Plasma. *J Chem Soc Pak* 31: 402-407.
21. Arayne MS, Sultana N, Hussain F (2009) Spectrophotometric Method for the Determination of Montelukast in Bulk, Pharmaceutical Formulations and Human serum. *J Anal Chem* 64: 690-695.
22. Tang PH, Miles MV, Glauser TA, DeGrauw T (1999) Automated microanalysis of gabapentin in human serum by high-performance liquid chromatography with fluorometric detection. *J Chromatogr B Biomed Sci Appl* 727: 125-129.
23. Rathore R, Lindeman SV, Kochi JK (1997) Charge-transfer probes for molecular recognition via steric hindrance in donor-acceptor pairs. *J Amer Chem Soc* 119: 9393-9404.
24. Refat MS, El-Hawary WF, Moussa MA (2011) IR, ¹H NMR, mass, XRD and TGA/DTA investigations on the ciprofloxacin/iodine charge-transfer complex. *Spectrochim Acta A Mol Biomol Spectrosc* 78: 1356-1363.
25. Aloisi GG, Pignataro S (1973) Molecular complexes of substituted thiophenes with s and p acceptors. Charge transfer spectra and ionization potentials of the donors. *J Chem Soc Faraday Trans* 1 69: 534-539.
26. Briegleb G, Czekalla J (1960) Intensity of electron transition bands in electron donor-acceptor complexes. *Z Physik Chem (Frankfurt)* 24: 37-54.
27. Benesi HA, Hildebrand JH (1949) A spectrometric investigation of the interaction of iodine with aromatic hydrocarbons. *J Am Chem Soc* 71: 2703-2707.
28. Martin AN, Swarbrick J, Cammarata A (1969) *Physical Pharmacy*, (3rd edn), Lee & Febiger, Philadelphia: 344.

Citation: Sultana N, Saeed Arayne M, Ali SN (2013) Spectrophotometric Studies of Lamotrigine Charge Transfer Complexes: Synthesis and Characterization. *Pharm Anal Acta* 4: 260. doi:[10.4172/2153-2435.1000260](https://doi.org/10.4172/2153-2435.1000260)

Submit your next manuscript and get advantages of OMICS Group submissions

Unique features:

- User friendly/feasible website-translation of your paper to 50 world's leading languages
- Audio Version of published paper
- Digital articles to share and explore

Special features:

- 250 Open Access Journals
- 20,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, EBSCO, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: <http://www.omicsonline.org/submission>

