Journal for ReAttach Therapy and Developmental Diversities
eISSN: 2589-7799
2022 December; 5 (2s): 239-248

A New Spectra Method for Estimation and Evaluation of the Gabapentin Drug in Antiepileptic Pharmaceuticals

Ali K. Mohammed[1], Khawla Salman Abd-Alrassol[2], Qutaiba A. Qasim[3], *H. N. K. AL-Salman[4]

[1,2,4]Department of Pharmaceutical Chemistry, College of Pharmacy, University of Basrah, Iraq.
[3] College of Pharmacy, Al-Ayen University, Thi-Qar, Iraq.
hussein.khalf@uobasrah.edu.iq

Received: 12-September-2022
Revised: 19-November-2022
Accepted: 11-December-2022

Abstract

Gabapentin in bulk powder and prescription dose form can now be measured using a brand-new spectrophotometric method, which was just created. It's easy to use, accurate, and cheap. The method was tested and a variety of dosage forms were examined. It is Fe(II) that oxidises Gabapentin at pH 4.0 when it comes into contact with iron ions (acetate buffer). 355 nm is the maximum absorption wavelength of the colouredeques medium. At optimal concentrations, Beer's law and the concentration range of 2.0-12.0 g mL^{-1} had a significant relationship coefficient (0.9998). The detection limit was found to be 1.22 ng mL^{-1}, while the detection limit was discovered to be 3.40 ng mL^{-1}. Sandell's sensitivity of 0.3889 x 10^{-11} g/cm^2 and the molar absorption coefficient of 1.182608 x 10^4 $Lmol^{-1}$/cm-1 combine to give us a value of 0.3889 x 10-11 g/cm^2. The International Conference on Harmonization's recommendations were followed when evaluating the procedure's validity. To ensure that the method is suitable for routine gabapentin analysis, it was successfully used to estimate drug concentrations in pharmaceutical dose forms without influence from additives.

Keywords: Gabapentin, antiepileptic drug,UV-Vis, spectrophotometric determination, hydrogen peroxide, acetate buffer.

INTRODUCTION

Gabapentin has a pKa1 of 3.7 and a pKa2 of 10.7, giving it a crystalline appearance. It comes in a variety of colours ranging from white to off-white. It has a significant impact on epilepsy and a variety of other neurological illnesses (1). Powdered crystalline GBP is white to practically white in colour and nearly insoluble in methylene chloride (98 percent). Water, ethanol, and methylene chloride are all soluble in GBP. GBP is a glycol-derived polymer. When the pH is 7.4 and N-octanol/0.05M phosphate buffer is used, it has a partition coefficient of 1.25. Gabapentin, sold as Neurontin, was designed to treat epilepsy but is now used to treat a variety of other disorders (2,3). Gabapentin is a well-known medication for neuropathic pain in humans. This medication is generally viewed as safe, with minimal adverse effects, and is well tolerated by those who use it." (4). After reviewing the literature, it was discovered that a variety of analytical approaches, including high-performance liquid chromatography (HPLC), have been employed to analyse two drugs at the same time (5-10). $C_9H_{17}NO_2$ is one of the chemical names for gabapentin (GBP); its molecular formula is $C_9H_{17}NO_2$(11) (shown in Figure 1). (12).

It is easily dissolved in dilutions of acids and hydroxide solutions. The pH of the water solution decreases from 6.5 to 7.4 as the concentration of GBP increases (13)

Despite its initial development as an epilepsy medication, no one knows exactly how gamma-aminobutyric acid structural analogue GBP exerts its antiepileptic and analgesic characteristics. This chemical, contrary to popular opinion, was the first of its kind (14).

GBP is used to treat secondary generalisation in patients with complex partial seizures. This medicine could be used to treat both post-operative acute pain and neuropathic pain (15).

Several methods have previously been published for the evaluation of GBP in dosage forms, including spectrophotometery (16–20), spectrofluorometery (21,22), capillary electrophoresis (33) and potentiometry (24)

as well as HPLC (25–28) and high-performance thin-layer chromatography (HPTLC) with ninhydrinderivatization (29).

In natural aquatic systems, as well as in environmental remediation technologies and biological systems, hydrogen peroxide plays an important role as a reactant. Hydroxyl radicals (s OH) and hydrogen peroxide (H_2O_2) are examples of reactive oxygen species that can be found in rain and surface waters. (31) Radiolysis (32), pyrite oxidation (33), and photochemical oxidation (34), all of which take place in aquatic conditions, all include reactive oxygen species. Hydrogen peroxide is introduced to wastewaters with the specific goal of increasing in situ oxidation processes. This is done by taking use of the high level of reactivity that radicals have toward organic contaminants. When microbiological techniques of degrading contaminants are not sufficient, it is possible to eliminate contaminants by breaking down H_2O_2 and creating OH in its place. During the processes of metabolism and the immune system, humans and other creatures like them produce ROS. The reactivity of H_2O_2 is drastically reduced when compared to that of H_2O. When FeSII is present, the reactivity potential of H_2O_2 is significantly increased (34) When reactive oxygen species (ROS) concentrations are elevated to levels significantly higher than usual over an extended length of time, oxidative stress may develop. There is mounting evidence to support the idea that oxidative stress plays a significant part in the development or progression of a wide variety of diseases.In the course of this research, methods for analysing gabapentin in tablet dosage form were developed and shown to be in accordance with ICH criteria. The overarching goal of this work was to establish a method that is economical (35).

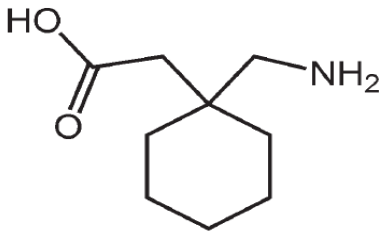

Figure 1. Chemical structure of Gabapentin

EXPERIMENTAL

Apparatus

High-sensitivity spectrometers developed in Germany and capable of operating in both the visible and ultraviolet parts of the electromagnetic spectrum were used to determine all absorption values (A Jena Model 1100).

Reagents and Chemicals

We made sure that the chemicals and reagents we utilised were of an analytical grade, and we made sure that all of our solutions used water that had been distilled twice.After cleaning all of the glassware with aqueous HCl at a ratio of 1:1, it was given a thorough washing with running distilled water, and then it was given a washing with deionized water.

The Indian company Sun Pharmaceuticals, with headquarters in Mumbai, supplied pharmaceutical grade gabapentin (GBP) and claimed that its purity was 99 percent. The following formulations of commercially available medications were investigated for this study: Getz pharma in Karachi, Pakistan, and Al-Debeiky pharmaceutical goods in Egypt are the two different pharmaceutical companies that produce Gabapentin capsules with a dosage of one hundred milligrammes of GAB each. Each GABATREX capsule contains a total of 100 milligrammes of gabapentin (HIKMA).

Stock solutionof Gabapentin($1000\ \mu g ml^{-1}$)

Gabapentin stock solution was prepared using deionized water and gabapentin powder (certified purity: 99.92 percent). Temperatures were then kept constant at 4 degrees Celsius throughout the experiment. All of the solutions were created using analytical reagent grade chemicals and deionized water.

One hundred milligrammes of pure medication were dissolved in two millilitres of ethanol, and a thousand millilitres of calibrated flask were filled with deionized water until the mark was attained. Working concentrations of 100 gmL1 GBP were prepared using diluted stock standard solution for application in the current procedure.

The stock solution of ferrous sulphate ($FeSO_4$. $7H_2O$) dissolved in water contained 1 x 10^{-4}mol L^{-1} of ferrous ion.

Acetate buffer solutions

After adding sodium acetate of varying concentrations to a volumetric flask of 1,000 ml, having it weighed and transferred, dissolving it in distilled water, and continuing to add acetic acid solution 2 M in increasing volumes until the volume reached 1,000 ml, the procedure was considered complete. The reaction mixture was buffered with a standard acetate solution in order to keep the pH stable throughout the process. (36)

Hydrogen peroxide solution (0.2moll^{-1}) wasarranged from the 34 % Hydrogen peroxide H_2O_2 reagent.

Procedure for determination of GBP in pharmaceutical formulations

The 300 mg of gabapentin in one capsule was properly metered out and pulverised. A 50-gram sample of the powder was dissolved in 20 mL of distilled water, followed by two more extractions, each requiring 10 mL of distilled water. A 0.45 millilitre particle filter and distilled water were used to reduce the solution's concentration to roughly 100 grammes per millilitre. It was further diluted if necessary, and the results were analysed in accordance with the suggested strategy. There were two methods used to determine the capsule's contents: the calibration graphs mentioned earlier or a regression equation.

General procedure

The GBP solution that had been previously analysed was carefully transferred into 10 ml calibrated flasks, and the total volume was brought up to 2.0 ml by adding an appropriate amount of water to each flask using a microburette. The flasks were then stored at room temperature until the next step. The acetate buffer solution was added to each flask, as well as the combination itself, at a volume of one millilitre. In order to raise the total volume of the solution up to 10 millilitres, one millilitre (0.75 percent) hydrogen peroxide (0.2M) and one millilitre (0.75 percent) water were each added to the solution. After waiting for ten minutes, the absorbance of each solution was measured at 335 nm, and the results were compared to the absorbance of a reagent blank.

RESULTS

In the absorption spectra of the coloured product, an absorption band at 335 nm can be seen in the aqueous solution of gabapentin. At this wavelength, the reagent blank creates no absorption band, as seen in figure (2).

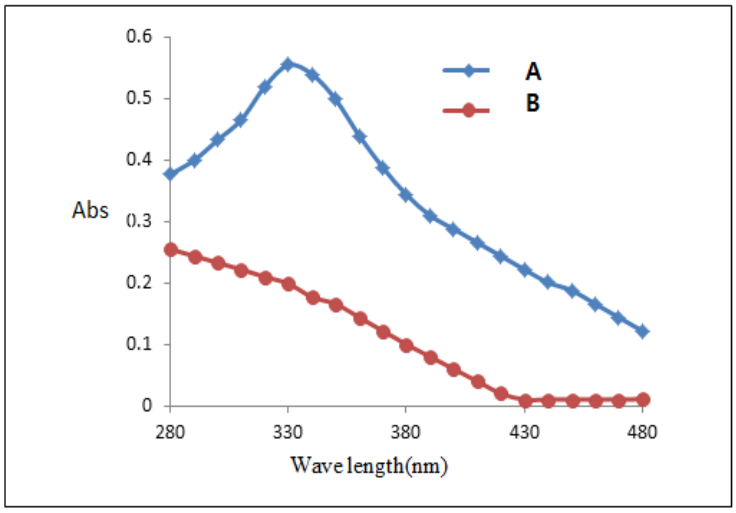

Figure 2: Absorption spectra of A=Gab with Fe , B= Blank

Optimization of reaction conditions

By altering the reaction circumstances one variable at a time while holding the others constant, the variables that affect the reaction conditions were investigated.

The PH acetate buffer

Examining the process's pH dependence in an acetate buffer throughout a range of 3.0–4.5 while holding all of the other experimental variables constant was the objective of this study. At a pH of 4.0, it was discovered that one millilitre of acetate buffer is the ideal volume to use (mL). Figure 3 demonstrates absorbance in addition to pH values (see below).

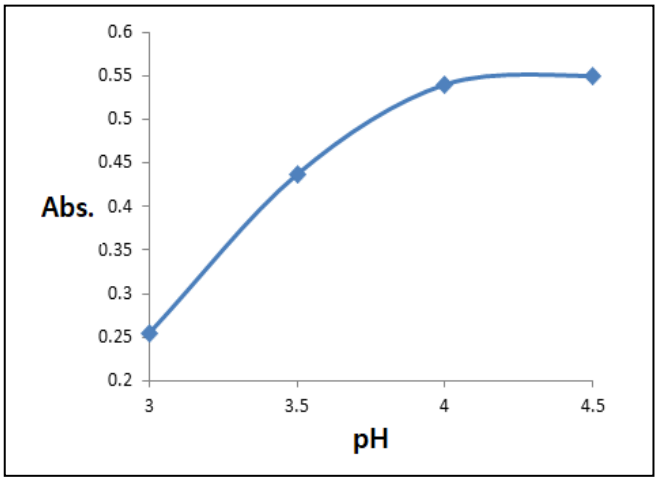

Figure 3: The effect of PH on the Abs.

The effected of ferrous sulfate concentration

The effect of reaction rates on Fe(II) concentrations was explored over the course of this inquiry (0.6 $x10^{-5}$ - 1.4x 10^{-5}mol L^{-1}). Future study will benefit from the discovery that a concentration of Fe(II) of 1 x 10^{-5}mol l^{-1} is ideal. At a pH of 4, the gabapentin concentration was found to be 8.0100 gml^{-1} and the hydrogen peroxide concentration was found to be 1.5x10^{-2} $mol.l^{-1}$. Figure 4 depicts these numbers in more detail..

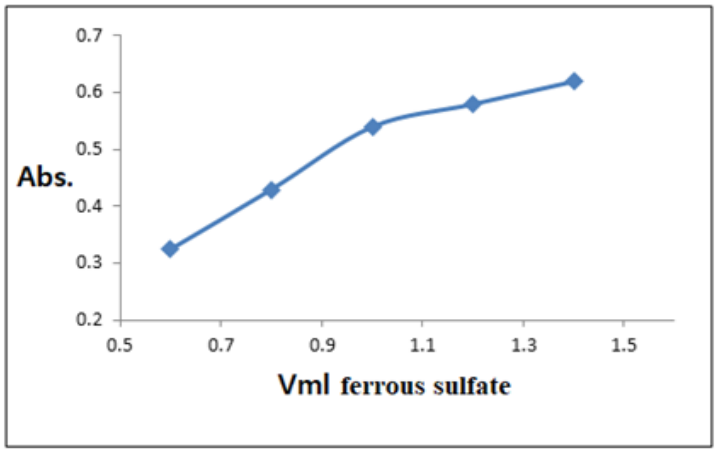

Figure 4. The dependence of reaction on Fe(II) volume

Effect of hydrogen peroxide concentration

It was determined that a concentration of hydrogen peroxide with a value of 1.5 x $10^{-2}$$moll^{-1}$ was suitable. The relationship between the concentration of hydrogen peroxide and the absorbance of hydrogen peroxide at that concentration is broken down in Figure 5. The quantities of hydrogen peroxide that were investigated ranged from 0.5 to 2.5 times 10^{-2} $mol.l^{-1}$.

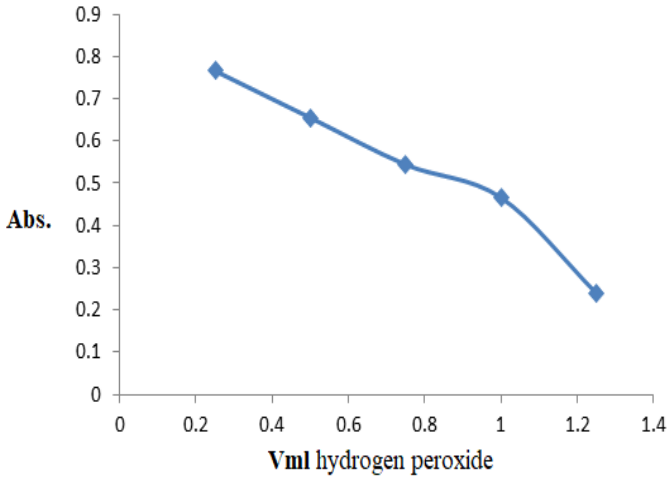

Figure 5: The effect of H_2O_2 concentration .On the optimal reaction conditions were: pH = 4.0 (acetate buffer), Fe(II)concentration = 1 $x10^{-5}moll^{1-}$, H_2O_2 concentration= $1.5x10^{-2}$ $mo.l^{-1}$at λ=335nm.

Validation studies

In order to verify the validity of the developed analytical method, it was subjected to numerous tests, including those for linearity, precision, accuracy, and limit of quantification (LOQ) (37)

calibration curve

When the conditions of the experiment were as good as they could be, the standard solutions were used to generate the calibration graphs. Each volumetric flask of 10 millilitres has been filled with a gabapentin solution that has been diluted. The concentration of the solution ranges from 2.0 to 12.0 grammes per millilitre (millilitres). After 10 minutes of hydrogen peroxide infusion into volumetric bath cells using 1 cm bath cells, absorbance at 335 nm was measured and compared to the corresponding blank solution using 1.5 mg/ml of acetate buffer solution. This measurement was done against the corresponding blank solution (0.75 percent). For purposes of comparison, blank reagents were utilised. Because sufficient water was added, the capacity was raised to 2.0 millilitres.

Beer Lambert's law, often known as linearity, was seen to be true across the range of 2.0 to 12.0 g/mL, with regression graphs yielding an R^2 value of 0.9998. Figure 6 provides a visual representation of the typical progression of events. Analysis of performance data and statistical characteristics revealed that the proposed method was highly linear in terms of linear regressions, correlation coefficients, and Sandell's sensitivity. These findings were supported by the findings of the study, which showed that the method had a high degree of linearity (38). Table 1 presents the validation data that was gathered for the method that was proposed for recognising gabapentin.

Table 1: Optimal conditions for the spectroscopic method

Validation parameter	Results
Absorption maximum	335nm
Regression equation	y = 0.0673x –0.0005
Slope	0.0673
Intercept	0.0005
Beer's law limit	2.0-12.0µg mL^{-1}
Molar Absorptivity ($L/mol^{-1}/cm^{-1}$)	11826.08
Sandell's sensitivity (µg/cm^2)	$0.3889x10^{-11}$
Coefficient of correlation	R^2 = 0.9998
Limit of detection (LOD) µg mL^{-1}	1.22 µg mL^{-1}
limit of quantitation (LOQ) µg mL^{-1}	3.400µg mL^{-1}

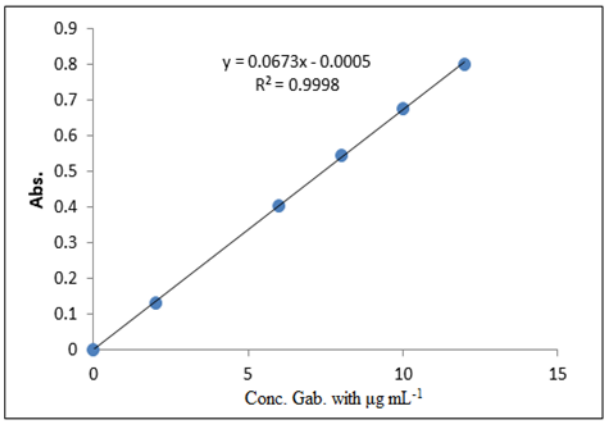

Figure 6: Calibration curve for Gabapentin

Calibration standards were used to determine the method's LOD and LOQ (Table 1). Figures for LOD and LOQ were calculated to show that the recommendations of ICH were adhered to (39)
It has been determined that the analytical limits of detection (LOD) are 3.33 s0/m and the analytical limits of quantification (LOQ) are 10.

Accuracy
The procedure's accuracy might be defined as the degree to which the measured value matches the sample's true value. In order to assess the efficacy of the proposed process, several concentrations of the drug were prepared from separate stock solutions and tested.
To test the recommended procedure's precision and accuracy, it was performed five times with Gabapentin present at low, medium, and high concentrations. Table 2 shows the results of the study.

Table 2: Accuracy and precision of the proposed method

Proposed method	Gabapentinconc. µg/ml		%RSD	%RE**	%Recovery
	Taken	found±SD*			
Intra day	4.00	4.02±0.010	1.249	0.50	100.50
	8.00	8.05±0.025	1.311	0.625	100.62
	10.00	9.98±0.011	1.028	0.20	99.80
Inter day	4.00	3.97±0.016	1.403	0.75	99.25
	8.00	7.99±0.005	1.625	0.521	99.88
	10.00	10.03±0.015	1.150	0.300	100.3

*Mean for 5 independent analyses; **%Relative error

For the tests to determine the precision within a single day, there were a total of five samples used, each of which contained a different concentration of gabapentin (4.0, 8.0, and 10.0 g/ml). In order to evaluate the precision between days, five days' worth of pure drug samples were analysed using the same concentration levels as those used for precision within a day. This was done so that the results could be compared. Table 2 contains a summary of these tests, which can be viewed in its entirety by clicking on the link provided below. As can be seen in Table 2, the suggested analytical method appears to have a very high degree of accuracy due to its good mean recovery percentages, which range from 100.62 to 99.8 percent, and its low SD values (0.025). The outcomes of an intraday precision analysis are summarised in Table 2, which may be found below. When

using RSD figures that are less than one percent, it is quite evident that the method that is being provided is very repeatable. The findings of the investigation into the precision between days are presented in Table 4 below. The proposed method exhibits a high degree of precision, as is seen from the RSD values that were derived from the analysis (less than 1.62 percent).

Interference studies

Standard gabapentin was analysed in order to determine the selectivity of the proposed method. This was done in the presence of a number of excipients and ions, including talc, glucose, fructose, and lactose, starch, magnesium stearate, and microcrystalline cellulose. It was discovered that the excipients do not have any effect on the proposed approach (39).

Applicability of the proposed method

Gabapentin levels in a variety of pharmaceutical items were analysed using the approach proposed. In a statistical analysis, it was shown that the proposed strategy outperforms the more conventional way The F and t-values were determined to be lower than theoretical values with a 95% level of confidence, showing that there are no significant differences in the ability to recognise a signal between the proposed and current approaches (35). Because of this, the method provided can be used to determine the amount of gabapentin in a drug.

Table 3: determination of Gabapentin in pharmaceutical preparations.

Pharmaceutical preparation	**Taken µg/ml**	**Found µg/ml Proposed method**	***Recovery%**	**RSD%**	**Found µg/ml satandared method**	***Recovery%**	**RSD%**	**F-test**	**T-test**
Gabtin capsules-	4.0	4.03	100.75	2.140	4.05	101.25	2.774	3.523	1.538
	8.0	8.08	101.00	1.750	8.10	101.25	1.952		
	10.0	10.05	100.50	1.112	9.87	98.70	1.823		
Gabix capsules	4.0	4.01	100.25	1.246	4.04	101.00	2.475	4.606	1.847
	8.0	7.99	99.88	0.625	8.03	100.38	1.245		
	10.0	10.03	100.30	0.863	10.05	100.50	0.862		
GABATREX capsules	4.0	4.04	101.00	2.475	4.07	101.75	3.250	3.050	1.775
	8.0	7.97	99.66	1.087	8.05	100.63	1.389		
	10.0	9.99	99.90	0.501	9.59	95.90	3.338		

*Data are based on the mean of five determinations; *theoretical F-value)and t-value at 95 % confidencelevel are 6.39 and 2.306, respectively.

CONCLUSION

In order to generate hydroxyl radicals, it is required to first combine gabapentin with hydrogen peroxide, and after that, it is necessary to add an acetate buffer to the mixture (II). For the purpose of monitoring the reaction, spectrophotometric analysis was used to detect the absorbance of the product at 335 nm. The ideal conditions for the reaction were a concentration of H_2O_2 of 1.5 x 10^{-2} mol.l^{-1} at a wave length of 335 nm and a pH of 4 in an acetate buffer. The correlation coefficient for this particular range of gabapentin concentration was determined to be 0.9998. Both the detection and quantification limits were set at 1.22 g mL^{-1}, with 3.400 g mL^{-1} being the upper limit for the latter. During testing, it was discovered that the majority of the ions and excipients did not have any discernible effect. A comparison of the statistics was performed in order to determine which strategy—the new one or the old one—was more successful. According to the findings of an investigation that

was carried out with a degree of confidence equal to or greater than ninety-five percent, there were no noteworthy differences in the F-values or t-values produced by the suggested and standard methodologies. Therefore, the approach that has been discussed here can be utilised to assess the amount of gabapentin that is contained within medications.

ACKNOWLEDGEMENT

In recognition of the assistance they provided me in finishing this article, I would like to thank the Department of Pharmaceutical Chemistry in the College of Pharmacy at the University of Basra.

REFERENCES

[1]. Napoleon, A.A., 2006. Pharmaceutical titrimetricanalysis theory andpractical1 Edn, kalaimani publishers and distributors, kanchipuram, 1.1-1.4.

[2]. Chatwal, G.R and K.S. Anand, 1998. Instrumental methods of chemical analysis, 5th Ed.,Himalayapublishing House, 1: 2-1.5.

[3]. Beckett, A.H. and J.B. Stenlake, 1988. Text book of pharmaceutical chemistry 4thEd. part 2CBS publishers and Distributors, New Delhi, pp: 157.

[4]. UdaykumarRao, B., F. Maqdoomb and Anna PratimaNikaljea, 2009. Determination of gabapentin in bulk drug and in pharmaceutical dosage form by hplc method, J. Chil. Chem. Soc., 54(4): 2009.

[5]. Abdulrahman A. Al-Majed, 2005. A Derivatization Reagent for Vigabatrin and Gabapentin in HPLC with Fluorescence Detection, Journal of Liquid Chromatography & Related Technologiesw, 28: 3119-3129.

[6]. Varsha R. Galande, K.G. Baheti and M.H. Dehghan, 2010. UV-VIS spectrophotometric method For estimation of gabapentin and methylcobalamin in bulk and tablet, International Journal of ChemTech Research, CODEN (USA): IJCRGG 2(1): 695-699.

[7]. Singh gujral, R., S. Manirulhaque and R.P. Shanker, 2009. Asensitive UV Spectrophotometric Method for the Determination of Gabapentin, E,Journal of Chemistry, http://www.e-journals.net, 6(S1): S163-S170.

[8]. Brijesh Patel, Japan Patel, Hardeep Singh and Bhagirath Patel, 2011. Extractive Spectrophotometric Methods for the Determination of Gabapentin in PharmaceuticalDosage Forms, International Journal of Pharmaceutical Sciences and Drug Research, 3(3): 197-201 197.

[9]. Visible Spectrophotometric Methods for Determination of Gabapentin in Pharmaceutical Tablet and Capsule Dosage Forms, Asian Journal of Pharmacy and Life Science, 1(3), July-Sept, 2011

[10]. ICH, 1996. Q2B Validation of Analytical Procedures Methodology. Consensus Guidelines, ICH Harmonized Tripartite Guidelines

[11]. Adegbolagun OM, Thomas OE, Aiyenale EO, Adegoke OA. A new spectrophotometric method for the determination of gabapentin using chromotropic acid. Acta Pharm Sci, 2018; 56(3):93–110.

[12]. Adegoke OA, Adegbolagun OM, Aiyenale EO, Thomas OE. New spectrophotometric method for the determination of gabapentin in bulk and dosage forms using p-dimethylaminobenzaldehyde. J TaibahUnivSci, 2018; 12(6):754–64.

[13]. Ambala PS, Patel NJ. Visible spectrophotometric methods for determination of gabapentin in pharmaceutical tablet and capsule dosage forms. Asian J Pharmacy Life Sci, 2011; 1(3):223–33.

[14]. Behnam B, Semnani V, Saghafi N, Ghorbani R, Shori MD, Choobmasjedi SG. Gabapentin effect on pain associated with heroin withdrawal in Iranian crack: a randomized double-blind clinical trial. Iran J Pharm Res, 2012; 11:979–83.

[15]. Mohammed T.O and Elbashir A.A, 2015.Spectrophotometric Method for Determination of Gabapentin in Pharmaceutical Formulation by Derivatization with 4-Chloro-7-Nitrobenzo2-Oxa1,3-Diazole (NBD-Cl), International Journal of Drug Development and Research, Volume 7(4): 001-004 -01 ISSN: 0975-9344. 3.

[16]. Sara, MA, Hosny MM, Abdellatef HE, et al. Spectrscopic and conductometric analysis of gabapentin. E-J Chem. 2011;8:1784–1796.

[17]. Khawla S. Rassol, H. N. K. AL-Salman, Hussein H. Hussein ,Spectral kinetic method and its applications in the evaluation of gabapentin International Journal of Green Pharmacy • Oct-Dec 2018 • 12 (4) | 303

[18]. Siddiqui FA, Sher N, Shafi N, et al. Kinetic and thermodynamic spectrophotometric technique to estimate gabapentin in pharmaceutical formulations using ninhydrin .J Anal Sci Technol. 2013;4: 1–8.

[19]. Hashem EY, Saleh MS, Youssef AK, et al. A novel spectrophotometric method for determination of gabapentin in pharmaceutical formulations using 2,5-dihydroxy benzaldehyde. Comput Chem. 2014;2:22–30.

[20]. Khawla S. Alrassol, Mazin N., Estimation and Evaluation of Gabapentin and Pregabaline Anti-Epileptic Drugs in Bulk and Pharmaceutical Preparations by Eco-Friendly Bromate-Bromide Reagent ,Eurasian Journal of Analytical Chemistry ISSN: 1306-3057 , 2019 14 (2): 10-20

[21]. Prasad MKC, Sagar GV, Sudhakar P. Spectrofluorimetric method of analysis for gabapentin in spiked human plasma and formulations. Int J ChemTech Res. 2013;5: 2732–2746.

[22]. Belal F, Abdine H, Al-Majed A, et al. Spectrofluorimetric determination of vigabatrin and gabapentin in urine and dosage forms through derivatization with fluorescamine. J Pharm Biomed Anal. 2002;27:253–260.

[23]. Sekar R, Azhaguvel S. Indirect photometric assay determination of gabapentin in bulk drug and capsules by capillary electrophoresis. J Pharm Biomed Anal. 2004;36:663–667.

[24]. Basavaiah K, Abdulrahman SAM. Non-aqueous titrimetric assay of gabapentin in capsules using perchloric acid as titrant. ChemIndChemEng Q. 2011;17:173–178.

[25]. Ulu ST, Kel E. Highly sensitive determination and validation of gabapentin in pharmaceutical preparations by HPLC with 4-fluoro-7-nitrobenzofurazan derivatization and fluorescence detection. J Chromatographic Sci. 2011;49:417–421.

[26]. Lakshmi B. RP-HPLC method development for the quantification of gabapentin in formulations. Int J Sci Technol. 2012;2:84–92.

[27]. Uboh CE, Liu Y, Soma LR, et al. Analysis of gabapentin in equine plasma with measurement uncertainty estimation by liquid chromatography–tandem mass spectrometry,J Anal Toxicol. 2011;35:75–84.

[28]. Sandhya SM, Jyothisree G, Babu G. Analysis of gabapentin by HPTLC with densitometric measurement after derivatization. Int J Pharm Pharm Sci. 2014;6:707–710.

[29]. Sharma, S. and M.C. Sharma, 2011. UVSpectrophotometric Method for the Perindopril Erbumine in Pharmaceutical Formulations Using Indigo Carmine,American-Eurasian Journal of Scientific Research, 6(st 4): 210-216, IDOSI Publications 2011.

[30]. V. M Miljkovic, D. A Kostic, Z. Z Bojanic1, B. M.Kalicanin1,G.M Kocic,Development and Application of Kinetic Spectrophotometric Method for the Determination of Metronidazole, Trop J Pharm Res;13(3): 417(2014)

[31]. H. Lee a , H.Lee a , D. L. Sedlak b , Ch. Lee a,pH-Dependent reactivity of oxidants formed by iron and copper-catalyzed decomposition of hydrogen peroxide, / Chemosphere 92 (2013) 652–658

[32]. Pignatello, J.J., Oliveros, E., MacKay, A.: Advanced Oxidation Processes for Organic Contaminant Destruction Based on the Fenton Reaction and Related Chemistry. Crit. Rev. Environ. Sci. Technol. 36, 1-84 (2006)

[33]. Shari F.H., Almiahi A., Abduljabbar A.S., Salahuddin A., AL-Salman H. N. K., Optimization of a micro-high-performance liquid chromatography method for determination of metronidazole benzoate in their standard powder and in dosage pharmaceuticals. International Journal of Green Pharmacy, 13 (1) 48-59(2019).

[34]. Abd-Alrassol1 K.S., Qasim Q.A., shari F.H., AL-Salman H.N.K., Hussein H.H., The Spectrophotometric Determination of Antiepileptic Drug in Standard and Pharmaceutical Formulations by Diazotization Coupling Reaction and Some Metals Complexes. Sys Rev Pharm, 11(3), 247 260(2020).

[35]. ICH, Validation of Analytical Procedures; Text and Methodology; Q2 (R1), International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, 2005.

[36]. United States Pharmacopeia, USP. NF 27. Monograph of gabapentin. 32nd edition, Asian Edition, United States Pharmacopeial Convention, Inc., Rockville, MD, 2009

[37]. Khawla S. Alrassol1 , Q. A. Qasim , G.S.Ahmed , H. N. K. ALsaman ,A Modified and Credible Methods to Estimate Nitrofurantoin In the Standard of Substances and Pharmaceutical Dosage, ,International Journal of Pharmaceutical Research | Oct - Dec 2019 | Vol 11 | Issue 4

[38]. Khawla S. Alrassol1 , Q. A. Qasim , M. A.Rikabi , H. N. K. AL-Salman ,The development of analytical methods to determine metoclopramide-hydrochloric acid in the standard raw and it compared with pharmaceuticals, Int. J. Res. Pharm. Sci., 10(4), 1-14

[39]. Khawla Salman Abd-Alrassol b , Qutaiba A. Qasim a , Hussein H. Hussein b , H.N.K. AL-Salman Spectrophotometric determination of folic acid using 1,10- phenanthroline materials with ninhydrin reagent Mazin A.A. Najm a,⇑ Materials Today

[40]. ICH Topic Q2 (R1). Validation of analytical procedures: text and methodology (CPMP/ICH/281/95). [May,2016].