Technical paper

Volumetric and Spectrophotometric Determination of Oxcarbazepine in Tablets

Nagaraju Rajendraprasad, Kanakapura Basavaiah* and Kanakapura Basavaiah Vinay

Department of Chemistry, Manasagangothri, University of Mysore, Mysore-570 006, India

** Corresponding author: E-mail: basavaiahk@yahoo.co.in; Mobile: +91 9448939105*

Received: 30-10-2010

Abstract

Two cerimetric procedures are described for the assay of oxcarbazepine (OXC) in bulk drug and in tablets. Titrimetry (method A) is based on the reaction of OXC by a measured excess cerium(IV) sulphate in sulphuric acid medium and the determination of the unreacted oxidant by titration with iron(II) solution using ferroin as indicator. Spectrophotometry (method B) is based on oxidation of OXC by cerium(IV) in perchloric acid ($HClO_4$) medium and the determination of the unreacted oxidant using a colour reaction with *p*-dimethylaminobenzaldehyde (*p*-DMAB) having an absorption maximum of 460 nm. The titrimetric method is applicable in the range of 2.0–20.0 mg OXC with a 1:2 reaction stoichiometry [OXC:Ce(IV)]. In the spectrophotometric method a rectilinear relationship is obtained over the concentration range of 0.3–6.0 μg mL^{-1} OXC. The linear regression equation of the calibration graph is A = 0.9820–0.1477 C with a regression coefficient (r) of –0.9967 (n = 6). The molar absorptivity is calculated to be 3.76×10^4 L mol^{-1} cm^{-1} and the Sandell sensitivity is 0.0067 μg cm^{-2}. The limits of detection (LOD) and quantification (LOQ) values are calculated according to ICH guidelines. The methods are successfully applied to the determination of OXC in tablets.

Keywords: oxcarbazepine; assay; titrimetry; spectrophotometry; tablets

1. Introduction

Oxcarbazepine (OXC), (chemically known as 10,11-dihydro-10-oxo-5H-dibenzo[b,f]azepine-5-carboxamide, (Figure 1) is an antiepileptic agent which belongs to the iminostilbene class and is effective against partial seizures and generalized tonic–clonic seizures[1] as well as bipolar affective disorders.[2]

OXC is not official in any Pharmacopoeia. High performance liquid chromatography,[3–6] high performance thin layer chromatography,[7] gas chromatography,[6] microemulsion electrokinetic chromatography,[8] capillary electrokinetic chromatography,[9] voltammetry,[10,11] capillary electrophoresis[12] and visible spectrophotometry[13–15] were found in the literature for the assay of OXC in pharmaceuticals.

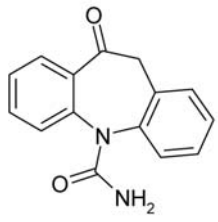


Figure 1. Chemical structure of OXC

No titrimetric method is reported for OXC. However, few spectrophotometric methods are found. Gandhimathi and Ravi[13] have reported two spectrophotometric methods for the determination of OXC. The first method involves addition of Folin-Ciocalteu's (F-C) reagent to OXC in alkaline medium, followed by measurement of absorbance at 760 nm, and the second method involves addition of a fixed volume of 3-methyl-2-benzothiazolinone hydrazine hydrochloride (MBTH) after treatment of OXC with iron(III) chloride and measurement of the absorbance at 456 nm. In another report,[14] OXC has been determined using iron(III) chloride and potassium hexacyanoferrate(III). The method is based on reduction of iron(III) ions to iron(II) ions by the drug,

Table 1: Comparison of performance characteristics of the proposed spectrophotometric method with reported spectrophotometric methods.

Sl No	Reagent(s)	Method	λ (nm)	Linear range (μg mL^{-1}) ε/LOD/LOQ*	Remarks	Reference
1	a) F-C reagent	Blue chromogen measured	760	5–30 8.06×10^3/1.6/5.0	Narrow linear dynamic range, less sensitive, methanol used as solvent	13
	b) MBTH-iron(III) chloride	Orange coloured product measured	456	10–50 3.13×10^3/3/10	Narrow linear dynamic range, less sensitive	
2	Iron(III) chloride-hexacyanoferrate(III)	Green chromogen measured	770	4–28 4.63×10^3	Narrow linear dynamic range, less sensitive, heating required	14
3	CH_3OH-KOH/DMSO	Yellow chromogen measured	430	1.0–7.02 1.21×10^4/0.027/0.082	Methanol used, less sensitive	15
4	**Cerium(IV)-*p*-DMAB/$HClO_4$**	**Orange chromogen measured**	**460**	**0.3–6.0 3.76×10^4/0.1/0.32**	Wide linear dynamic range, highly sensitive, no use of organic solvent, no heatingrequired	**Present work**

* ε in L mol^{-1} cm^{-1}; LOD and LOQ are in μg mL^{-1}

which in the presence of hexacyanoferrate(III) produces green-coloured chromogen measured at 770 nm. The yellow chromogen with an absorption maximum at 430 nm formed by the reaction of OXC with methanolic KOH in DMSO medium as the basis for the assay of OXC has been reported by Sathish and Nagendrappa.[15] All the reported methods have one or more disadvantages (Table 1) such as low sensitivity,[13–15] use of a toxic solvent (to dissolve OXC)[13] or preparation of reagents[15] and require heating on a boiling water bath.[14]

The present paper describes a titrimetric (method A) and a spectrophotometric (method B) procedure for the assay of OXC in the pure drug and in tablets using cerium(IV) as an oxidimetric reagent.

2. Experimental

2. 1. Apparatus

A Systronics model 106 digital spectrophotometer (Systronics Limited, Ahmedabad, India) with 1 cm path length and matched quartz cells was used to record the absorbance values. An Acculab (Sartorious Group, Germany) electronic analytical balance was used for weighing.

2. 2. Reagents and Standards

All chemicals used were of analytical reagent grade. Distilled water was used throughout the investigation.

Acetic acid (7 mol L^{-1}), sulphuric acid (H_2SO_4) (10 mol L^{-1}) and perchloric acid ($HClO_4$) (4 mol L^{-1}) were prepared by diluting appropriate volumes of their concentrated acids (99% glacial acetic acid, 98% H_2SO_4, 70% $HClO_4$ -all from Merck, Mumbai, India) with distilled water, and 10 mol L^{-1} H_2SO_4 was diluted further to obtain 0.5 mol L^{-1} and used in the preparation of the cerium(IV) solution. Two brands of tablets, viz. Trioptal-300 (Novartis India Ltd, Mumbai, India) and Oxetol-600 (Sun Pharmaceuticals, Sikkim) were purchased from local commercial sources.

2. 2. 1. Cerium(IV) Sulphate Solution (0.025 mol L^{-1})

A 0.025 mol L^{-1} solution was prepared by dissolving an accurately weighed quantity of ceric sulphate [$Ce(SO_4)_2.4H_2O$; assay 99%-from Loba Chemie Ltd, Mumbai, India] in 0.5 mol L^{-1} H_2SO_4 with the aid of heat. The solution was cooled to room temperature, and filtered using Whatman No. 42 filter paper. The solution was used for the assay in method A after standardization.[21] This solution, equivalent to ~3504 μg mL^{-1} Ce^{4+}, was diluted with 4 mol L^{-1} $HClO_4$ to get a working concentration of 300 μg mL^{-1} Ce^{4+}.

2. 2. 2. Ferrous Ammonium Sulphate [Fe(II)] Solution (0.025 mol L^{-1})

An accurately weighed amount of 9.804 g of $[NH_4]_2[Fe][SO_4]_2\cdot 6H_2O$ (Loba Chemie Ltd, Mumbai, India) was dissolved in 10 mL of 0.5 mol L^{-1} H_2SO_4 in a 1000-mL volumetric flask and the solution was brought up to the mark with water.

2. 2. 3. *p*-Dimethylaminobenzaldehyde (*p*-DMAB) (0.5%)

An accurately weighed amount of 1.25 g of *p*-DMAB (Merck, Mumbai, India) was transferred to a 250-mL volumetric flask, dissolved in 4 mol L^{-1} $HClO_4$ and the volume made up to the mark with the same solvent.

2. 2. 4. Stock OXC Solution

A stock standard solution containing 2 mg mL^{-1} OXC was prepared by dissolving 200 mg of pure OXC (Jubilant Life Sciences Ltd, Nanjangud, Mysore, India, purity 99.5%) in 40 mL of glacial acetic acid; the volume was brought to 100 mL with water in a volumetric flask and used for the assay in method A.

A 100 μg mL^{-1} OXC standard solution was also prepared by dissolving an accurately weighed amount of 10 mg of pure OXC with 4 mol L^{-1} $HClO_4$ in a 100-mL calibrated flask. A working solution with a concentration of 10 μg mL^{-1} OXC was used in method B.

2. 3. General Procedure

2. 3. 1. Titrimetry (Method A)

A 1–10 mL aliquot of pure drug solution (2 mg mL^{-1}) containing 2.0–20.0 mg of OXC was measured accurately and transferred to a 100-mL titration flask; the total volume was brought to 10 mL with 7 mol L^{-1} acetic acid. The solution was acidified by adding 5 mL of 10 mol L^{-1} H_2SO_4. Ten mL of 0.025 mol L^{-1} Ce(IV) standard solution was added by means of a micro burette and the content was mixed well. After 5 min, the unreacted Ce(IV) was back titrated with 0.025 mol L^{-1} Fe(II) solution using ferroin as an indicator. A blank titration was also performed in a similar fashion but in the absence of the drug.

The amount of the drug present in the measured aliquot was calculated by using the formula:

$$Amount(mg) = \frac{(VM)_{Ce(IV)reacted} \times M_w}{n}$$

where V is the volume of Ce(IV) reacted, M is the molar concentration (mol L^{-1}) of Ce(IV), M_w is the relative molecular mass of OXC and n is the number of moles of Ce(IV) reacting with each mole of OXC.

2. 3. 2. Spectrophotometry (Method B)

Different aliquots (0.3–6.0 mL) of 10 μg mL^{-1} OXC standard solution were transferred to 10-mL volumetric flasks using a microburette and the total volume in each flask was adjusted to 6 mL by adding 4 mol L^{-1} $HClO_4$. To each flask, 1 mL of 300 μg mL^{-1} Ce^{4+} solution was added, and the content was mixed well and kept aside for 15 min at room temperature. Finally, 1 mL of 0.5% *p*-DMAB was added to each flask and the volume was made up to mark with 4 mol L^{-1} $HClO_4$. After 15 min, the absorbance of the coloured product was measured at 460 nm against water.

A calibration graph was prepared by plotting absorbance against concentration and the unknown concentration was read from the graph or computed from the regression equation.

2. 4. Procedure for the Analysis of Tablets

Method A

Twenty tablets were weighed and finely powdered. The tablet powder equivalent to 200 mg OXC was transferred to a 100-mL volumetric flask, and about 40 mL of glacial acetic acid was added. The content of the flask was shaken for 10 min, 30 mL of water was added, and shaking continued for 10 more min before the flask was filled to the mark with water. The content was mixed well and filtered through a Whatman No. 42 filter paper. The first 10-mL portion of the filtrate was discarded and a suitable aliquot (say 5 mL) was then subjected to analysis by following the procedure described earlier.

Method B

A quantity of tablet powder containing 10 mg of OXC was transferred into a 100-mL volumetric flask. The content was shaken well with about 70 mL of 4 mol L^{-1} $HClO_4$ for 20 min. The mixture was diluted to the mark with the same solvent and filtered using Whatman No 42 filter paper. The first 10-mL portion of the filtrate was discarded and the resulting tablet extract (100 μg mL^{-1} in OXC) was diluted to 10 μg mL^{-1} with 4 mol L^{-1} $HClO_4$. A suitable aliquot was then subjected to analysis by following the general procedure.

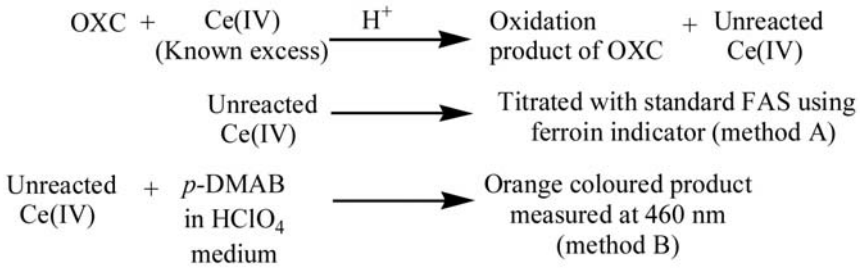
2. 5. Procedure for the Analysis of Placebo Blank and Synthetic Mixture

A placebo blank containing starch (10 mg), acacia (15 mg), hydroxyl cellulose (10 mg), sodium citrate (10 mg), talc (20 mg), magnesium stearate (15 mg) and sodium alginate (10 mg) was prepared by combining all components to form a homogeneous mixture. An amount of 5 mg of the placebo blank was accurately weighed and its solution was prepared as described under 'tablets', and then subjected to analysis by following the general procedure.

A synthetic mixture was prepared by adding an accurately weighed amount of 200 mg of OXC to the placebo mentioned above. The extraction procedure for tablets as described for method A and method B were applied separately by taking the required quantity of synthetic mixture to prepare 2 mg mL^{-1} and 10 μg mL^{-1} OXC solutions, respectively. Three different volumes of the resulting synthetic mixture solution (equivalent to 5, 10 and 15 mg OXC in method A; 2, 3 and 4 μg mL^{-1} in method B) were subjected to analysis by following the respective procedure.

3. Results and Discussions

The proposed methods are indirect and are based on the determination of unreacted cerium(IV) after the reaction between OXC and the oxidant is complete according to the following reactions:



The titrimetric method (method A) involves oxidation of OXC by a known excess of Ce(IV) sulphate in sulphuric acid medium and the unreacted oxidant was determined by back titrating with FAS. The reaction between OXC and Ce(IV) was found to occur in an 1:2 (drug:oxidant) stoichiometric ratio and all calculations are based on this fact. Using 0.025 mol L^{-1} Ce(IV), 2–20 mg of OXC was conveniently determined. In spectrophotometry (method B), the unreacted Ce^{4+} was treated with *p*-DMAB in $HClO_4$ medium to yield formic acid and *p*-dimethylaminophenol, which upon further oxidation gave the corresponding quinoimine derivative.[22]

4. Method Development

4. 1. Absorption Spectra (method B)

The addition of *p*-DMAB to Ce^{4+} resulted in the formation of orange coloured product (quinoimine derivative) that was measured at 460 nm. OXC and *p*-DMAB had no absorption at 460 nm. The decrease in the absorption intensity at 460 nm, caused by the presence of the drug, was directly proportional to the amount of drug reacted. Figure 2 illustrates the absorption spectra of the orange coloured product formed by the reaction between Ce^{4+} and *p*-DMAB for various OXC concentrations.

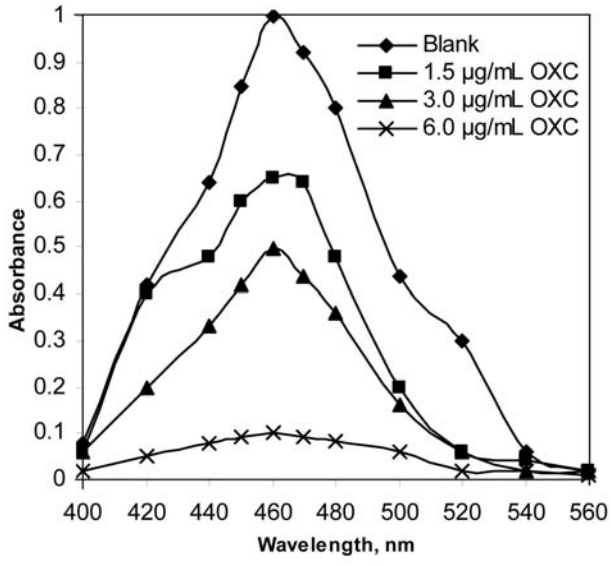


Figure 2. Absorption spectra of coloured product formed by the reaction between Ce^{4+} and *p*-DMAB in the presence of increasing concentrations of OXC and in the absence of OXC.

4. 2. Optimization of Reaction Variables

Method A

OXC is not soluble in any of the acids other than acetic acid. To prepare OXC stock solution, different volume ratios of acetic acid and water were tried, and the drug was found to be completely soluble in 7 mol L^{-1} acetic acid and OXC was found to be stable for more than a day at room temperature. This approach was followed to prepare the OXC solution throughout the investigation.

In order to obtain the optimum conditions necessary for the quantitative determination of OXC, a fixed amount of the drug was titrated under varying experimental conditions. The reaction was found to be quantitative and stoichiometric in H_2SO_4 medium. A constant reaction stoichiometry of 1:2 [OXC:Ce(IV)] was obtained when 4.0–6.0 mL of 10 mol L^{-1} H_2SO_4 was used in a total volume of 25 mL. Hence, a 5 mL of 10 mol L^{-1} H_2SO_4 was used as the optimum for the reaction between OXC and Ce(IV), giving an overall acidity of 2 mol L^{-1} with respect to H_2SO_4, and for the latter's titration with iron(II). The reaction time was studied by titrating the unreacted Ce(IV) with iron(II) at different time intervals after addition of oxidant to the acidic solution of OXC. It was found that the reaction yielded a constant stoichiometry in the time range from 5 to 10 min, and at a reaction time less than 5 min and more than 10 min, there was no constant and definite reaction stoichiometry. Hence, it is necessary to terminate the reaction at the end of the fifth min by titrating residual Ce(IV) with iron(II).

Method B

Selection of Reaction Medium

Perchloric acid (4 mol L^{-1}) medium was found necessary for rapid and quantitative reaction between OXC and Ce(IV), and to obtain maximum and constant absorbance values of the Ce^{4+}-*p*-DMAB reaction product at 460 nm. This may be attributed to the highest oxidation potential of Ce^{4+} in $HClO_4$ (E_o = 1.75 *V*) as compared to that of Ce(IV) in H_2SO_4 (E_o = 1.44 *V*), HNO_3 (E_o = 1.61 *V*) or HCl (E_o = 1.28 *V*)[23]. Therefore, all the solutions [OXC, Ce(IV) and *p*-DMAB] were prepared in 4 mol L^{-1}

$HClO_4$ throughout the investigation and the same was maintained as reaction medium.

Optimization of Ce^{4+}

To fix the optimum concentration of Ce^{4+}, different concentrations of oxidant were reacted with a fixed concentration of *p*-DMAB in $HClO_4$ medium and the absorbance measured at 460 nm. A constant and maximum absorbance resulted with 30 μg mL^{-1} Ce^{4+}; hence, different concentrations of OXC were treated with 1 mL of 300 μg mL^{-1} Ce^{4+} in $HClO_4$ medium before determining the residual Ce^{4+} by reacting with *p*-DMAB. This facilitated the optimization of the linear dynamic range over which the procedure could be applied for the assay of OXC.

Study of Reaction Time and Stability of the Coloured Species

Under the described experimental conditions, the reaction between OXC and Ce^{4+} was complete within 15 min (Figure 3) at room temperature (28 ± 2 °C). After the addition of *p*-DMAB, a reaction time of 15 min was necessary for the formation of the coloured product, and thereafter, the absorbance of the coloured product (quinoimine derivative) was stable for more than one hour.

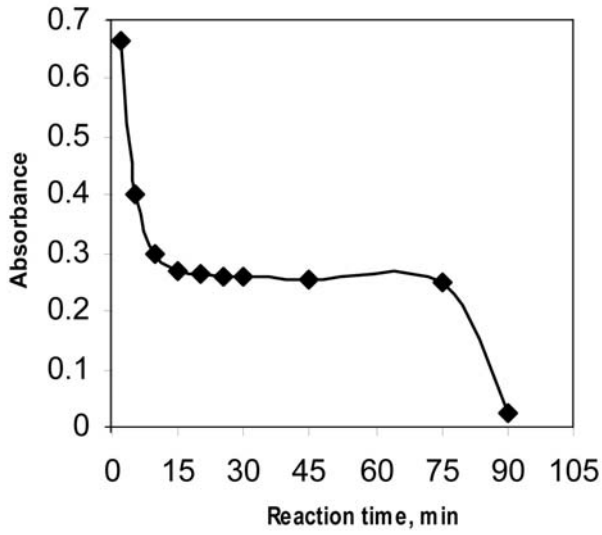


Figure 3. Effect of time on the reaction between Ce^{4+} and OXC (5.0 μg mL^{-1})

Effect of Diluent

In order to select the proper diluent different solvent were tried. The highest absorbance values were obtained when 4 mol L^{-1} $HClO_4$ was used as diluent. Substitution of 4 mol L^{-1} $HClO_4$ with other solvent (methanol, water and 6 mol L^{-1} $HClO_4$) resulted in a decrease in the absorbance values.

4. 3. Method Validation

4. 3. 1. Linearity and Sensitivity

Over the range investigated (2–20 mg), a fixed stoichiometry of 1:2 [OXC : Ce(IV)] was obtained in titrimetry which served as the basis for calculations. A rectilinear calibration graph was obtained for the range 0.3–6.0 μg mL^{-1} OXC; the measured absorbance values were plotted *versus* concentration. The least square calibration equation was A = 0.9820–0.1477 C (where the concentration C is measured in μg mL^{-1}) with a regression coefficient of –0.9967 (n = 6). The calculated molar absorptivity and Sandell sensitivity values are 3.76×10^4 L mol^{-1} cm^{-1} and 0.0067 μg cm^{-2}, respectively. The limits of detection (LOD) and quantification (LOQ) were calculated according to the ICH guidelines[24] using the formulae: LOD = 3.3 S/slope and LOQ = 10 S/slope, where S is the standard deviation of the absorbance of six blank readings. The calculated LOD and LOQ are 0.10 and 0.32 μg mL^{-1}, respectively.

4. 3. 2. Accuracy and Precision

The repeatability of the proposed methods was determined by performing replicate determinations. The intra-day and inter-day variations in the analysis of OXC were measured at three different levels by calculating percentage relative standard deviations (%RSD). Accuracy was evaluated as the bias (percentage relative error between the measured and reference value). The results of this study are compiled in Table 2 and show an excellent

Table 2: Intra-day and inter-day accuracy and precision.

Method*	OXC,	Intra-day accuracy and precision			Inter-day accuracy and precision		
	Reference	OXC found	RE %	RSD %	OXC found	RE %	RSD %
A	6.0	5.90	1.67	1.56	5.92	1.33	2.11
	12.0	11.85	1.25	1.11	11.80	1.67	1.89
	18.0	17.50	2.78	1.85	17.42	3.22	1.56
B	2.0	2.04	2.00	3.10	2.05	2.50	3.26
	4.0	4.04	1.00	1.13	4.08	2.00	1.56
	6.0	5.83	2.83	0.50	5.90	1.67	2.13

* In method A, OXC reference/found values are in mg and they are μg mL^{-1} in method B

intermediate precision (%RSD ≤ 3.26) and accuracy (%RE ≤ 3.22).

4. 3. 3. Selectivity

In the analysis of the placebo blank there was no measurable consumption of Ce(IV) (method A) and the same absorbance value as obtained for the reagent blank was recorded in method B, suggesting that the inactive ingredients added to prepare the placebo are interference-free.

In method A, 5 mL of the resulting solution prepared using the synthetic mixture was assayed titrimetrically (n = 3) yielded a recovery of 102.3 ± 0.62% OXC. In method B, a 3 mL aliquot of 10 μg mL^{-1} OXC subjected to analysis (n = 5) yielded a recovery of 101.7 ± 0.86% OXC. These results complement the findings of the placebo blank analysis with respect to selectivity.

4. 3. 4. Robustness and Ruggedness

To evaluate the robustness of the methods, reaction time and H_2SO_4 concentrations were slightly altered with reference to optimum values in titrimetry. However, in spectrophotometry, the reaction time and volume of *p*-DMAB were altered. To check the ruggedness, analysis was performed by four different analysts and using three different burettes (method A) or cuvettes (method B) by the same analyst. The robustness and the ruggedness were checked at three different drug levels. The intermediate precision, expressed as percent RSD, is a measure of the robustness and ruggedness and was within acceptable limits (0.72–3.74%, Table 3).

4. 3. 5. Application to Tablet Analysis

Commercial OXC tablets were analyzed by the developed methods and also by a reference published method.[13] The published method involves addition of Folin-Ciocalteu's (F-C) reagent to OXC in alkaline medium, followed by measurement of the absorbance at 760 nm. The results obtained were compared statistically by the Student's t-test and the variance-ratio F-test.[25] The calculated t- and F- values did not exceed the tabulated values [2.77 (t) and 6.39 (F) at the 95 % confidence level and for four degrees of freedom], indicating a close similarity between the proposed methods and the reference method with respect to accuracy and precision (see Table 4 for a summary).

4. 3. 6. Recovery Study

To further ascertain the accuracy and reliability of the methods, recovery experiments were performed *via* the method of standard additions. Pre-analyzed tablet powder was spiked with pure OXC at three different levels

Table 3: Robustness and ruggedness.

Method A					Method B				
	Robustness (RSD %)		Ruggedness (RSD %)			Robustness (RSD %)		Ruggedness (RSD %)	
OXC studied mg	Conditions altered* Volume of H_2SO_4 (n = 3)	Reaction time (n=3)	Inter-analysts (n = 4)	Inter-burettes (n = 4)	OXC studied μg mL^{-1}	Conditions altered* Volume of *p*-DMAB (n = 3)	Reaction time (n = 3)	Inter-analysts (n = 4)	Inter-instruments (n = 3)
6.0	1.56	2.26	1.65	2.01	2.0	1.58	2.67	1.56	3.74
12.0	1.38	1.84	0.72	1.85	4.0	2.11	1.54	2.38	1.94
18.0	1.74	1.47	1.41	1.56	6.0	1.99	3.14	1.85	2.48

* In method A, volumes of 10 mol L^{-1} H_2SO_4 varied were 5 ± 1 mL, and reaction times were 5 ± 0.5 min, In method B, volumes of *p*-DMAB varied were 1 ± 0.1 mL, and reaction times employed were 15 ± 1 min.

Table 4: Results of analysis of tablets by the proposed methods.

Tablets analysed	Label claim, mg/tablet	Found* (Percent label claim ±SD) Reference method	Method A	Method B
Trioptal 300	300	100.3 ± 1.22	98.5 ± 0.89 **t** = 2.69 **F** = 1.88	99.6 ± 1.28 **t** = 0.88 **F** = 1.10
Oxetol 600	600	99.58 ± 0.85	100.6 ± 1.10 **t** = 1.65 **F** = 1.67	101.2±1.56 **t** = 2.12 **F** = 3.37

* Mean value of five determinations.

Table 5: Accuracy assessment by recovery experiments.

	Method A				Method B			
Tablets studied	**OXC in tablet, mg**	**Pure OXC added, mg**	**Total found, mg**	**Pure OXC recovered*, Percent ± SD**	**OXC in tablet, μg mL^{-1}**	**Pure OXC added, μg mL^{-1}**	**Total found, μg mL^{-1}**	**Pure OXC recovered*, Percent ± SD**
Oxetol 600	8.05	4.0	12.13	102.0 ± 1.44	2.02	1.0	3.07	105.0 ± 1.56
	8.05	8.0	16.15	101.3 ± 0.89	2.02	2.0	4.10	104.0 ± 2.12
	8.05	12.0	19.74	97.42 ± 0.97	2.02	3.0	5.07	101.6 ± 1.48

* Mean value of three measurements

and the total was found by the proposed methods. Each determination was repeated three times. The percent recovery of pure OXC added (Table 5) was within the permissible limits indicating the absence of inactive ingredients in the assay.

5. Conclusion

A titrimetric and a spectrophotometric method was developed and validated for the determination of oxcarbazepine using cerium(IV) sulphate as the oxidimetric reagent. The methods have been demonstrated to be simple, rapid, economical and accurate and precise; they were successfully applied to the determination of OXC in tablets. Especially titrimetry is a simpler and faster technique for determination of oxcarbazepine than all other methods reported so far. It is applicable over a wide range (2–20 mg), requires inexpensive chemicals, and yet provides very accurate and precise results. The proposed spectrophotometric method has the advantages of high sensitivity, which permits the determination of a concentration of oxcarbazepine even down to 0.32 μg mL^{-1} with fair accuracy and precision. Compared to many existing instrumental methods for oxcarbazepine, the proposed spectrophotometric method has two additional advantages, viz. simplicity of operation and the use of generic laboratory instruments. Since the method requires easily available reagents [Ce(IV) and *p*-DMAB], it is certainly the most cost-effective of all the existing spectrophotometric methods.

6. Acknowledgements

The authors thank Jubilant Life Sciences Ltd., Nanjangud, Mysore, India, for gifting pure oxcarbazepine. The authors are grateful to the authorities of the University of Mysore, Mysore, for permission and facilities. One of the authors (N.R.P) thanks the University Grants Commission, New Delhi, India, for awarding a Meritorious Research Scholarship.

7. References

1. R. Sachdeo, A. Beydoun, S. Schatcher, B. Vazquez, N. Schaul, P. Mesenbrink, L. Kramer, J. D'Souza, *Neurology* **2001**, *57,* 854–871.
2. A. Musenga, M.A. Saracino, G. Sani, M. A. Raggi, *Curr. Med. Chem.* **2009,** *16,* 1463–1481.
3. J. M. Juenke, P. I. Brown, F. M. Urry, G. A. McMillin,; *J. Chromatogr. Sci.* **2006,** *44,* 45–48.
4. M. L. Qi, P. Wang, L. J. Wang, R. N. Fu, *J. Pharm. Biomed. Anal.* **2003,** *31*, 57–62.
5. K. S Rao, N. Belorkar, M.E.B. Rao, *Pharma. Anal. J. Young Pharm.* **2009,** *1,* 270–277.
6. E. Greiner-Sosanko, S. Giannoutsos, D. R. Lower, M. A. Virji, M. D. Krasowski, *J. Chromatogr. Sci.* **2007,** *45,* 616–622.
7. T. S. Reddy, P. S. Devi, *J. Planar Chromatogr.-Mod. TLC.* **2007,** *20,* 451–456.
8. M. Ivanova, E. Marziali, M. A. Raggi, E. Kenndler, *J. Sep. Sci.* **2002,** *25*, 863–871.
9. E. Marziali, M. A. Raggi, N. Komarova, E. Kenndler, *Electrophoresis* **2002,** *23,* 3020–3026.
10. M. Encarnación Burgoa Calvo, Olga Domínguez Renedo, M. Julia Arcos Martínez, **2007,** *43*, 1156–1160.
11. Domínguez-Renedo, Olga; Calvo, M. Encarnación Burgoa; Alonso-Lomillo, M. Asunción; Arcos-Martínez, M. Julia, **2010,** *8,* 268–272.
12. Beata Paw, Katarzyna Woœ, *J. Pre-Clin.Clin. Res.* **2008,** *2,* 157–159.
13. C. S. Ramaa, P. P. Chothe, A. A. Naik, V. J. Kadam, *Indian J. Pharm. Sci.* **2006,** *68,* 265–266.
14. M. Gandhimathi, T. K. Ravi, *Acta Pharm.* **2008,** *58,* 111–118.
15. M.A. Sathish, G. Nagendrappa, *Int. J. Pharm. Pharm. Sci.* **2010,** *2,* 93–98.
16. K. Basavaiah, V. Ramakrishna, U. R. Anil Kumar, *Ecl. Quim.* **2006,** *31,* 67–74.
17. K. Basavaiah, V. Ramakrishna, U. R. Anil Kumar, *Acta. Pharm.* **2007,** *57,* 211–220.
18. K. Basavaiah, P. Nagegowda, B. C. Somashekar, V. Ramakrishna *Science Asia* **2006,** *32,* 403–409.
19. K. Basavaiah, P. Nagegowda, *Anal. Chem. Indian J.* **2006,** *2,* 167–173.
20. N. Rajendraprasad, K. Basavaiah, *J. Anal. Chem.* **2010,** *65,* 482–488.

21. A. I. Vogel, A Quantitative Inorganic Analysis including Elementary Instrumental Analysis, 3rd ed., Longman Group Ltd, London, **1961,** p-319.
22. B. R. Dasgupta, D.A. Boroff, *Anal. Chem,* **1968,** *40,* 2061–2062.
23. G.D. Christian, Text Book of *"Analytical Chemistry",* 6th ed., Wiley and Sons (Asia), Pte Ltd, Singapore, **2007,** p. 430.
24. International Conference on Hormonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, ICH Harmonised Tripartite Guideline, Validation of Analytical Procedures: Text and Methodology Q2(R 1), Complementary Guideline on Methodology dated 06 November 1996, incorporated in November 2005, London.
25. J. Inczedy, T. Lengyel, A. M. Ure, *IUPAC Compendium of Analytical*

Povzetek

Opisana sta cerimetrična postopka za določevanje okskarbazepina (OXC) v farmacevtskih preparatih. Titrimetrična metoda (metoda A) temelji na reakciji OXC s presežkom cerijevega (IV) sulfata v žveplenokislem mediju in določitvijo nezreagiranega oksidanta s titracijo z raztopino Fe(II) z uporabo feroina kot indikatorja. Spektrofotometrična določitev (metoda B) temelji na oksidaciji OXC s Ce(IV) v perkloratnem ($HClO_4$) mediju in določitvijo nezreagiranega oksidanta z barvno reakcijo s p-dimetilaminobenzaldehidom (*p*-MAB) pri 460 nm. Titrimetrična metoda je primerna za območje od 2,0–20,0 mg OXC. Območje linearnosti je pri spektrofotometrični metodi med 0,3 in 6,0 μg mL^{-1} OXC s korelacijskim koeficientom (r) 0,9967 (n = 6). Po IHC metodologiji sta bili izračunani meji zaznave in kvantifikacije. Metoda je bila uspešno uporabljena za določevanje OFX v tabletah.