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Research Article

NOVEL SPECTROPHOTOMETRIC ESTIMATION OF OXCARBAZEPINE USING MIXED HYDROTROPIC TECHNIQUE

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ABSTRACT

There is no official method of estimation of oxcarbazepine. A novel, safe and sensitive method of spectrophotometric estimation in ultraviolet region has been developed for oxcarbazepine using 50%w/v optimized blend of urea, sodium acetate, sodium citrate as hydrotropic solubilising agent for quantitative determination of oxcarbazepine, a poorly water soluble drug. It shows maximum absorbance at 256 nm. Beers law was obeyed in the concentration range of 2-10 µg/ml. Commonly used tablet excipients and hydrotropes did not interfere in spectrophotometric estimation above 230 nm. The developed methods were validated according to ICH guidelines and result of accuracy, precision and other statistical analysis were found to be good in accordance with prescribed values. The proposed method utilizes solution of non-toxic, non-volatile materials. The objective of the present study is to explore the application of hydrotropy in spectrophotometric analysis of oxcarbazepine to replace the use of organic solvents which may be costlier, toxic and pollutant.

Keywords: Spectrophotometric, Hydrotropic solubilisation, Quantitative analysis, Oxcarbazepine.

INTRODUCTION

Oxcarbazepine is an anticonvulsant and mood stabilizing drug, used primarily in the treatment of epilepsy. It is also used to treat anxiety and mood disorders, and benign motor tics. Oxcarbazepine is marketed as Trileptal by Novartis and available in some countries as a generic drug.

Since oxcarbazepine and its formulations have not yet been listed in any of the pharmacopoieas, an analytical method needs to be developed for the quality control of the product. Several methods HPLC have been reported in the literature for the determination of OXC[1,2], spectrophotometric method based on the reduction of ferric ions in their salt form to ferrous ions by the drug[3], spectrophotometric method by dissolving drug in methanol and validation of the procedure[4]. The HPLC method is widely employed in the quality control assessment of drugs because of its sensitivity, repeatability and specificity. Spectroscopic technique is a promising simple, faster, direct and relatively lower cost alternative for the determination of active drug content. Hence we developed a method simple UV spectrophotometric method to determine OXC in dosage forms.

Increasing the aqueous solubility of insoluble and slightly soluble drugs is of major importance. Various techniques have been employed to enhance the aqueous solubility of poorly water soluble drugs. Hydrotropic solubilisation is one of them. The term hydrotropy has been used to designate the increase in solubility in water with controlled dilution[5] of various substances like acids, esters, alcohols and aldehydes etc., [6, 7] due to the presence of large amounts of additives. Urea, niacinamide, sodium citrate, sodium acetate, sodium salicylate, sodium benzoate etc are the most common examples of hydrotropic agents. Various organic solvents such as methanol, chloroform and dimethylformamide have been employed for solubilisation of poorly water soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents.

Maheswari etal has analyzed various poorly water soluble drugs using hydrotropic solubilisation phenomenon [8-10].

The objective of the present work is to develop new spectrophotometric method for its estimation in bulk and pharmaceutical formulations with good accuracy, simplicity, precision and economy. Urea, sodium acetate, sodium citrate have been employed to enhance the aqueous solubility of oxcarbazepine.

MATERIALS AND METHODS

Materials

Oxcarbazepine obtained as gift sample from Novartis, Mumbai. Urea(9.78%), sodium citrate(16.67%) and sodium acetate(24.44%) from s.d fine chem. Ltd. Commercial tablets of oxcarbazepine procured from local market (trioptal-150 mg) manufactured by Novartis and (oxetol-150 mg) manufactured by Sun pharma.

Validation of UV Spectrophotometric Method[11]

Estimation of λmax and preparation of calibration curve:

A stock solution of oxcarbazepine is prepared and by using UV spectrophotometric method it is scanned between 200-400 nm.

Preliminary solubility studies

Solubility of oxcarbazepine was determined in distilled water, other aqueous solvents and mixed blend of hydrotropic solution of urea, sodium acetate and tri-sodium citrate at 28° C±1 ° C.

Linearity: The calibration curve was obtained with five concentrations of the standard solution (2 -10 µg/ml). The solutions were prepared in triplicate. The linearity was evaluated by least squares linear regression analysis and correlation coefficients were calculated.

Selectivity: The method selectivity was assessed by comparing UV spectrum obtained from oxcarbazepine with those obtained from placebo formulations (excipients in water without OXC).

Precision: The precision of the assay method was determined by repeatability (intra-day) and intermediate precision (inter-day). The intraday precision was evaluated by analyzing three samples at 100% of the test concentration (n=3). The concentration of OXC was determined and the value of relative standard deviation (%RSD) of the assay method was calculated.

Accuracy: The concentration of OXC was determined by spiking known amounts of the analyte across specified range of analytical procedure. At each level solutions were prepared in triplicate and accuracy was evaluated in terms of percent recovery. Percent recovery was calculated from the formula

%Recovery= 100*Mean experimental concentration/ Theoretical concentration.

Robustness: Three sample solutions were prepared each containing 15mcg/ml and analyzed in two different spectrophotometers. The data was submitted to statistical analysis (student's t test) at significance level of 0.05.

Detection limit: Detection and quantification limits were based on standard deviation of the response (σ) and the slope (S) of the calibration curve of the analyte. The detection limit may be expressed as 3.3(σ/S) [12]

MATERIALS AND METHODS

Standard Calibration Curve

The Standard stock solution of oxcarbazepine (100µg/ml) was prepared in optimized blend of urea, sodium acetate and sodium citrate which is obtained from preliminary studies. This standard stock solution was diluted with distilled water to obtain various dilutions from 2 - 10 µg/ml. The solution containing 10µg/ml was scanned between 200-400 nm and the λmax was found at 256 nm.

The absorbance of other diluted solutions were measured and standard calibration graph was plotted against concentration as shown

Solubility studies

Excess amount of drug was added gradually to 5 ml of each of the solvent in 10ml volumetric flask. These are shaken using mechanical shaker for 12 h and kept aside for 12 h without disturbance to attain equilibrium solubility. The solutions were filtered through whatmann filter paper #41. Aliquots of the filtrate were suitably diluted and the dilutions were analyzed spectrophotometrically at 256 nm. The results are presented as in Table 2

Analysis of Oxcarbazepine tablets by the proposed method

Twenty tablets of oxcarbazepine were weighed and finely powdered. Powder equivalent to 10 mg of drug was taken in 100 ml volumetric flask and 50% of mixed hydrotropic solution blend of urea, sodium citrate, sodium acetate was added and the flask was shaken properly for 10 min to solubilize the drug and the volume was made up to mark with distilled water for spectrophotometric estimation against reagent blank to calculate drug content from the regression equation.

Validation of Proposed Method [13]

Accuracy

Accuracy of the method was determined by recovery studies in the tablet formulations. Recovery studies were carried out by addition of known quantities of standard drug to pre-analyzed sample at three different concentrations. The results of analysis of recovery studies are to be tabulated.

Precision

To evaluate precision at different parameters like repeatability, intermediate precision- 5 dilutions in three replicates were analyzed in same day, in two different days, by two analysts for day to day and analyst to analyst variation.

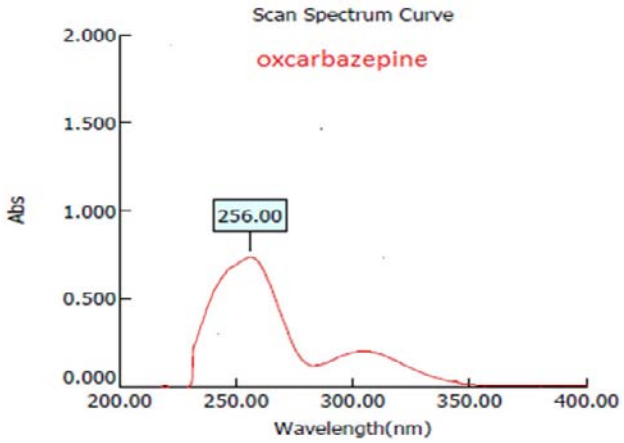

Fig. 1: Scan spectrum of Oxcarbazepine at 10µg/ml

The maximum absorbance spectra [fig.1]

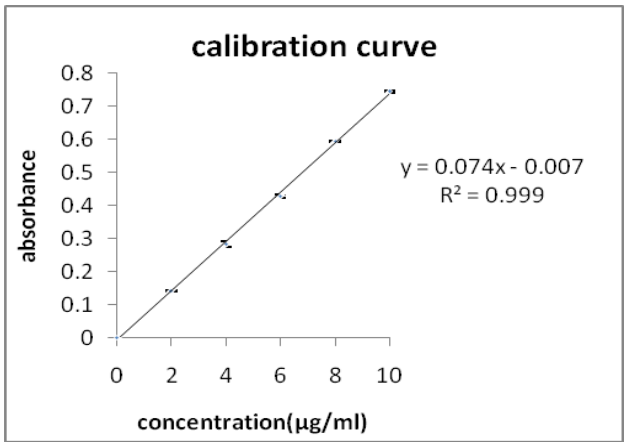

Fig. 2: calibration curve of oxcarbazepine for 2-10µg/ml

The standard curve of the drug [fig.2]

RESULTS AND DISCUSSION

Solubility Studies

Solubility is calculated from the regression equation of the respective solvents [table 1]

By preliminary solubility studies, it was found that the solubility of oxcarbazepine in hydrotropic blend was more satisfied compared to its solubility in other aqueous solvents and the results of solubility studies revealed that enhancement in solubility in a mixed hydrotropic solution of urea, sodium acetate and trisodium citrate (50% blend) was more than 10fold as compared with its solubility in distilled water. The λmax for pure oxcarbazepine was found at 256nm and optical parameters [table 2]

Drug content

We consider the commonly accepted limit of 92-108% of label claim (specified limit for carbamazepine).

It is evident from the [table 3] that the value of mean percent drug estimated by proposed spectrophotometric method for formulation 1 and 2 are 98.857 and 99.160 respectively. The amount of drug estimated by the proposed method for both the formulations are very close to 100 indicating the accuracy of the proposed method of analysis. Low values of standard deviation, percent coefficient of variation and standard error further validated the proposed method.

Accuracy and Precision

The percent recoveries were estimated with in the range from 98.177 to 101.663 [table 4]. The values are close to 100 indicating the accuracy of proposed method. The values of standard deviation, percent coefficient of variation and standard error are statistically low and thus validate the proposed method.

Linearity

The method demonstrated to be linear with a correlation coefficient of the standard curve greater than 0.999. The linear regression equation was Y=0.074X-0.007. Beers law is obeyed concentration range 2-10 µg/ml.

Selectivity

Placebo samples showed no interference in absorbance at 256 nm. These results demonstrate the good selectivity of the method.

Robustness

The mean absorbances measured using two different spectrophotometer models (Labindia 3000 and Shimadzu 160A) were 0.420 and 0.434. The experimental t value is indicating that there is no significant difference between the results from two spectrophotometers.

The overall validation parameters of OXC were as in [**table 5]** and are found to be satisfactory

Table 1: Solubilities of oxcarbazepine

Solvent	Solubility (µg/mL)
Water	83
0.1N HCl	102
4.6 Acetate buffer	98
5.8 Phosphate buffer	92
6.8 Phosphate buffer	83
50% blend	803

Table 2: Summary of optical parameters of oxcarbazepine

Parameters	Data
λ max	256nm
Linearity	2-10µg/ml
Regression equation	Y=0.074X-0.007
Correlation coefficient	0.999
Slope	0.074
Intercept	0.007
Std.deviation	0.142
LOD	6.33µg/ml

Table 3: Analysis data of oxcarbazepine tablet formulation with statistical evaluation (n=3).

Tablet formulation	Label claim (mg/tablet)	Percent drug estimated (Mean±SD)	Percent coefficient of variation	Standard error
Oxetol (F1)	150	98.857±0.586	0.006	0.338
Trioptol (F2)	150	99.160±0.892	0.009	0.515

Table 4: Recovery studies using proposed analytical method with statistical evaluation (n=3)

Drug present in preanalysed tablet powder (mg)	Spiked drug added (mg)	Percent recovery estimated (Mean±SD)		% coefficient of variation		Standard error	
		Intraday	Interday	Intra day	Inter day	Intra day	Inter day
50	5	100.08±1.068	98.21±0.840	0.011	0.007	0.616	0.386
50	10	98.177±0.95	100.073±1.426	0.010	0.013	0.549	0.762
50	15	100.04±0.214	101.057±1.061	0.002	0.014	0.123	0.800
50	5	99.393±0.920	98.98±0.668	0.009	0.009	0.531	0.485
50	10	101.663±1.334	98.38±1.319	0.013	0.014	0.770	0.823
50	15	101.383±1.588	98.673±1.385	0.026	0.020	1.494	1.190

Table 5: Validation parameters for UV method of analysis of OXC

Parameters		Acceptance criteria	F1	F2
Selectivity		Evaluated the ability of the proposed method to discriminate OXC from placebo formulations	-	-
Accuracy (% recovery)	Intraday	98-102%	100.813	99.58
	Interday		98.678	99.346
Precision	Intraday	*RSD<2%	1.238	0.566
	Interday	*RSD<2%	0.300	0.618

***RSD** – Relative standard deviation **R^2** – Correlation coefficient.

CONCLUSION

The UV Spectrophotometric method described in the present study has been shown to be accurate, sensitive, precise, rapid and easy to perform and can be successfully employed in routine analysis of oxcarbazepine in bulk drug and tablets without interference from excipients normally used in formulation. It is, thus, concluded that the proposed method is new, simple, environment friendly, accurate and reproducible.

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