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A Simple Spectrophotometric Method for the Estimation of Oxcarbazipine in Pharmaceutical Formulation

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ABSTRACT

A simple, sensitive, rapid and accurate spectrophotometric method has been developed for the estimation of oxcarbazepine in bulk and pharmaceutical dosage forms. The method is based on the reaction of oxcarbazepine with 2, 3-dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) to form a red colored charge-transfer complex which shows maximum absorbance in 465nm. The red colored solution is used to determine the oxcarbazepine spectrophotometrically.

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INTRODUCTION

Oxcarbazepine chemically designation as 5-oxo-6*H*-benzo[b][1]benzazepine-11-carboxamide. Oxcarbazepine is a dibenzazepine carboxamide derivative with an anticonvulsant property. As a prodrug, oxcarbazepine is converted to its active metabolite, 10-monohydroxy. Although the mechanism of action has not been fully elucidated, electrophysiological studies indicate this agent blocks voltage-gated sodium channels, thereby stabilizing hyper-excited neural membranes, inhibiting repetitive neuronal firing, and decreasing the propagation of synaptic impulses. Oxcarbazepine is a keto analogue of carbamazepine and, like the parent drug, is a potent anticonvulsant used alone or in combination with other agents in the therapy of poartial seizures. Oxcarbazepine has been linked to rare instances of clinically apparent acute drug induced liver injury which resembles carbamazepine hepatotoxicity. Several analytical methods have been reported for assay of Oxcarbazipine including spectrophotometric method[1-12], RPLC method[13], RHPLC method[14]and LC method [15]. Molecular formula is $C_{15}H_{12}N_2O_2$. Molecular weight is 252.268 g/mol. Slightly soluble in chloroform, dichloromethane, acetone, and methanol and practically insoluble in ethanol, ether, and water. Oxcarbazepine has the following fig.1.

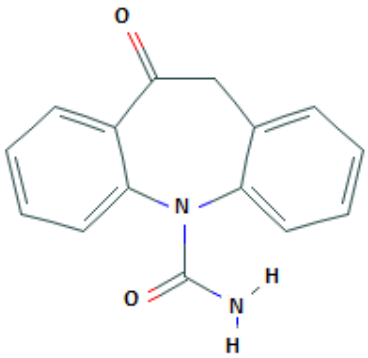

Figure No. 1: Structure of Oxcarbazepine

The method is based on the reaction of oxcarbazepine with 2, 3-dichloro-5, 6-dicyano-1, 4-benzquinone (DDQ) to form an orange red colour charge-transfer complex. The orange red colour solution is used to determine the oxcarbazepine spectrophotometrically.

EXPERIMENTAL

MATERIALS AND METHOD

Instrument:

All measurement were done on Milton Roy 1001spectrophotometer by using 10 mm matched quartz cuvettes.

Preparation of reagents and solutions:

DDQ (100µg/ml):

DDQ (2,3-dichloro 5,6-dicyano-p-benzoquinone) (Loba Chem., India) is prepared by dissolving 80 mg of DDQ in 100 ml of methanol and 5 ml of this stock solution is dissolved in 40 ml methanol.

Assay of Oxcarbazepine with DDQ:

Oxcarbazepine, (chemically known as 10,11-dihydro-10-oxo-5H-dibenzo[b,f] azepine-5-carboxamide), is a novel antiepileptic drug, which was developed as a second generation and a follow-up compound to carbamazepine. Clinically, it has been used to treat several types of epilepsy [1–3] and bipolar disorders. The method is based on the reaction of oxcarbazepine with 2, 3-dichloro-5, 6-dicyano-1, 4-benzquinone (DDQ) to form an orange red colour charge-transfer complex. The orange red colour solution is used to determine the oxcarbazepine spectrophotometrically.

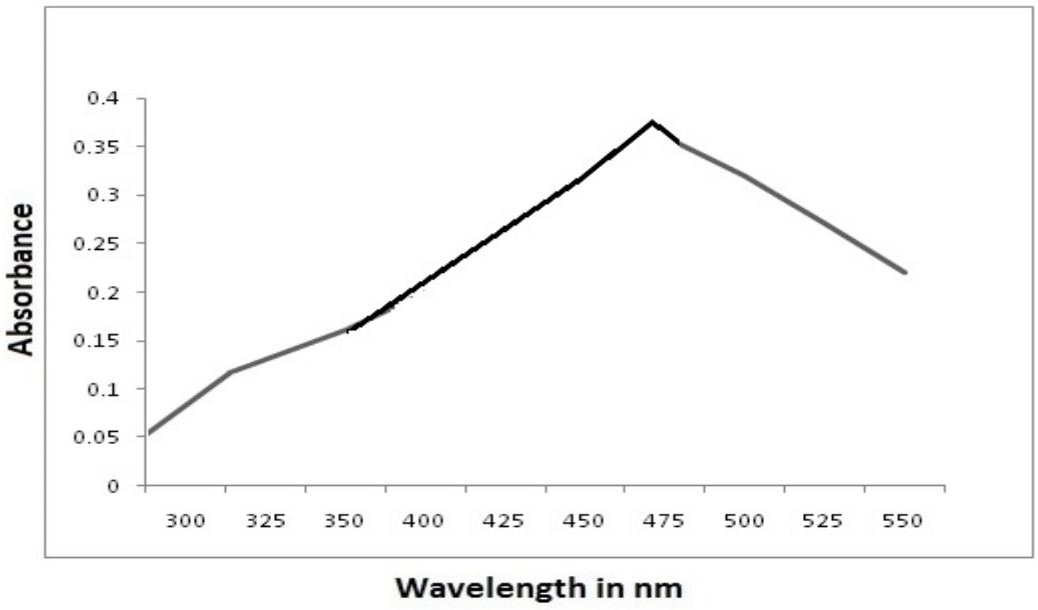

Figure No. 2: Spectrum of oxcarbazepine treated with DDQ

The wavelength of maximum absorbance of the oxcarbazepine drug treated with DDQ solution is ascertained by the following procedure.

1ml of oxcarbazepine solution (50µg/ml) is transferred into a standard flask. To this solution, 1.0 ml of DDQ reagent is added to form an orange red colour solution. The final volume is brought to 10 ml with methanol. The resultant solution is well mixed and allowed to stand for 5 min for complete the reaction. The reaction scheme between DDQ and oxcarbazepine is shown in fig.3.

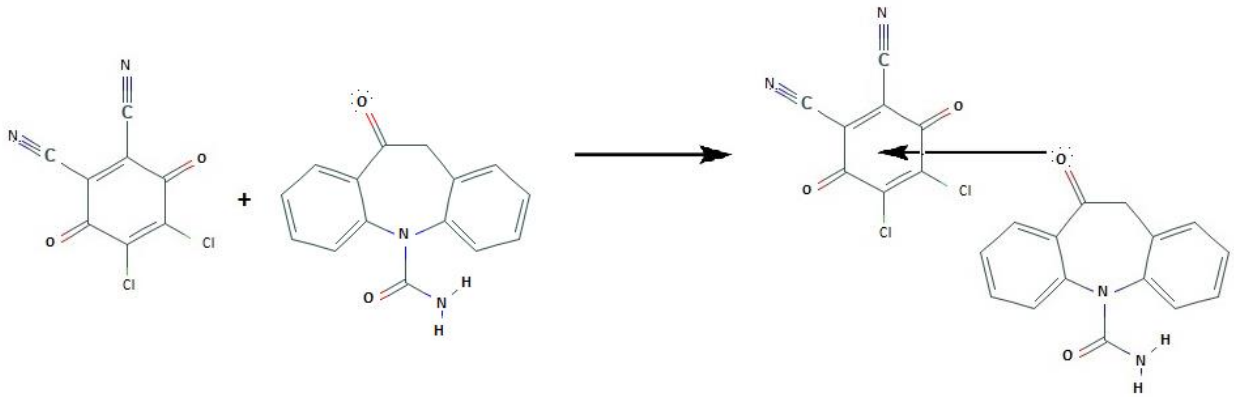

Figure No. 3: Reaction between oxcarbazepine and DDQ forming charge-transfer complex

The absorbance of the orange red colour solution is measured in the wavelength range of 300 to 550 nm, against the reagent blank. The spectrum is given in fig.2.

From fig .2, it is clear that the oxcarbazepine drug treated with DDQ solution has maximum absorbance at 465 nm. Hence, all further studies are made at 465 nm.

The optimal conditions for the determination of oxcarbazepine are arrived at by the following steps.

Effect of concentration of DDQ **solution on the absorbance of Charge transfer complex is studied by the following procedure.**

In a series of standard flask, 1.0 ml of oxcarbazepine are taken and varying amounts of DDQ solution are added. The contents are made up to the mark with methanol. Reaction mixture was shaken gently for 5 min and allowed to stand for 5 min to complete the reaction. The absorbance of the resultant solutions is measured at 465 nm and the data are presented in table.1.

Table No. 1: Effect of concentration of DDQ solution

Volume of DDQ solution (ml)	Absorbance at 465 nm.
0.5	0.242
1.0	0.314
1.5	0.312
2.0	0.312
2.5	0.311

The data in table. 1 indicates that 1.0 ml of DDQ is necessary for achieving maximum absorbance and hence maintained throughout the experimental studies.

Assay Procedure:

Various aliquots of the standard oxcarbazepine solution ranging from 0.2-1.0 ml are transferred into a series of standard flasks. To each flask, 1.0 ml of DDQ solution is added to produce an orange red colour. The final volume is brought to 10 ml with methanol. The reaction mixture in each flask is well shaken and allowed to stand for 5 min to complete the

reaction. The absorbance of the orange red colour solution is measured at 465 nm, against the reagent blank prepared in similar manner omitting drug solution. Calibration graph is obtained by plotting absorbance values against the concentration of oxcarbazepine solution. The calibration curve is found to be linear over a concentration range of 20 to 100 µg/ml of oxcarbazepine. The amount of oxcarbazepine present in the sample is read from the calibration graph. The results are presented in fig.4.

Assay of oxcarbazepine in pharmaceutical formulations:

The method is then applied to the determination of the drug from the marketed tablet formulations. Tablets are weighed and contents are powdered and well mixed. The powder equivalent to 50 mg of oxcarbazepine is dissolved in methanol, filtered, residue is washed with distilled water and the volume is made up to 50 ml with methanol. Further dilution is made as described in the preparation of standard solution of oxcarbazepine. Further analysis is carried out as per procedure described above and results are summarized in Table.3. The amount of drug present in the sample is estimated from calibration graph.

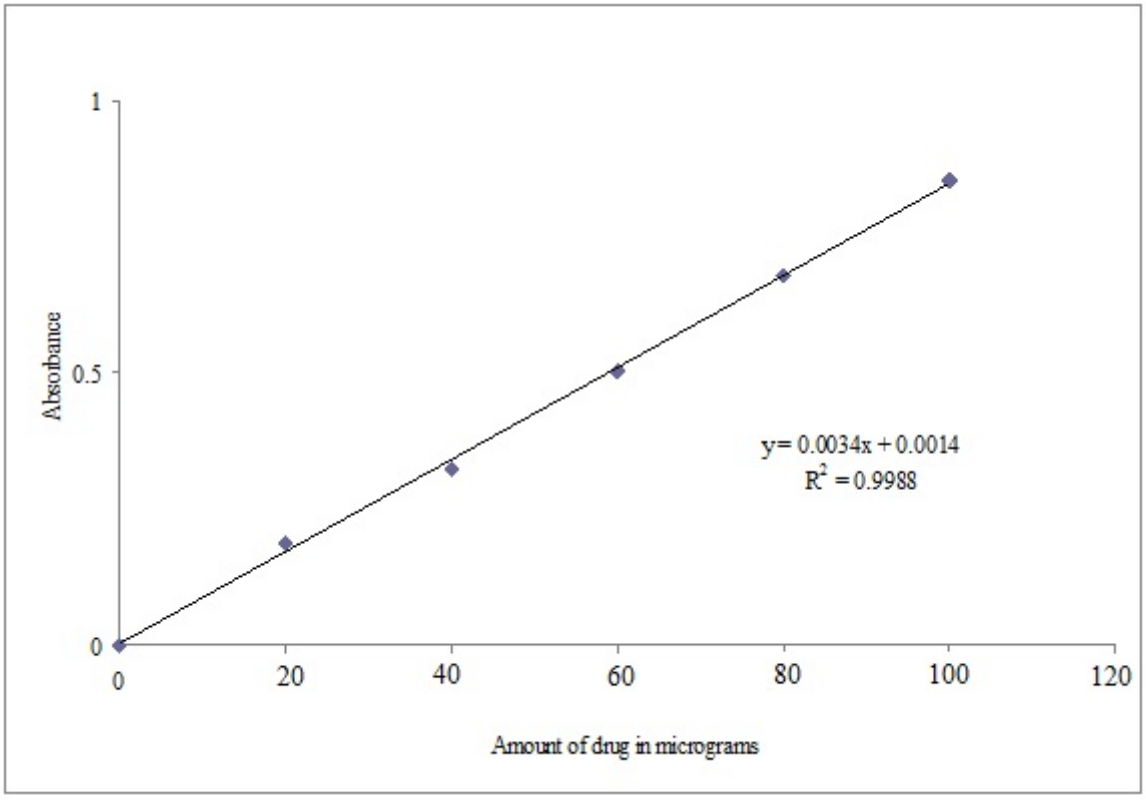

Figure No. 4: Calibration curve of oxcarbazepine

RESULTS AND DISCUSSION

In this method, the drug react with DDQ solution to form an orange red charge complex. The orange red coloured charge complex solution formed is measured at 365 nm against reagent blank. The amount of drug read from calibration curve. The calibration curve is linear over the range of 20-100 µg/ml of oxcarbazepine. The optical characteristics of the proposed method such as absorption maxima, Beer´s law limits, molar absorptivity and Sandell´s sensitivity are presented in Table .2. The molar absorptivity and Sandell´s sensitivity values show sensitivity of the method. The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and results are summarized in Table 2. The value of correlation coefficient (r) was 0.999, which indicated the good linearity of calibration lines. The percent relative standard deviation calculated from the five measurements of oxcarbazepine shown in Table 3. The % RSD is less than 2, which indicates that the method has good reproducibility. The values of standard deviation values are low, indicates high accuracy and reproducibility of the method. The 't' calculated values are compares well with the theoretical value of 2.78 thereby indicating that the precision of the method. There is no effect of additives and excipients such starch, calcium lactose and glucose in the concentrations those present in general pharmaceutical preparations.

The proposed method is found to be simple, precise, accurate and time saving, reproducible and can be conveniently adopted for routine analysis of estimation of oxcarbazepine in bulk drugs samples and pharmaceutical formulations.

Table 2: Optical characteristics of the proposed methods

parameters	Proposed method
λmax (nm)	465
Beer's law limit (µg/ml)	20-100
Molar absorptivity (l mole-^{1} cm-^{1})	6.574x10^{3}
Sandell's sensitivity(µg cm-2 / 0.001 absorbance unit)	0.03837
Regression equation (Y = a + bC)	Y=0.0034X+0.0017
Slope (b)	0.0034
Intercept (a)	0.0017
correlation coefficient (r)	0.9988

*Y = a+bx, where Y is the absorbance and x concentration in 50 µg/ml

Table 3: Assay of oxcarbazepine in tablet formulations

Tablets	Labeled amount(mg)	*Amount found (mg)±S.D*	% label claim	%RSD*	*t value
Tablet 1	300	299.98±0.46	99.99	0.1534	0.0971
Tablet 2	300	300.02±0.69	100.006	0.2313	0.0644
Tablet 3	300	300.04±0.47	100.01	0.1592	0.1872

*Average of five determination based on label claim.

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