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ORIGINAL ARTICLE **OPEN ACCESS**

A Development and Validation of By Using UV-Spectroscopic Methods for A Carbamazepine in Bulk Dosage Form

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ABSTRACT
The Carbamazepine is sold under the name of anticonvulsant medication which is used for primary treatment of epilepsy and neuropathic pain. It is not effective for absence or myoclonic seizures. It is often considered to be one of the most vital drugs for the relief of pain associated with trigeminal neuralgia. Carbamazepine is related chemically to the tricyclic antidepressants. Aim of the Study was to develop and validate a simplified accurate, rapid, precise, reproducible and cost-effective Spectroscopic method for the quantitatively analysis estimation of carbamazepine in a pharmaceutical formulation.
Keywords: *Carbamazepine, UV Spectrophotometry, Method development, Validation, Antiepileptic, Methanol.*

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INTRODUCTION

The Carbamazepine, sold under the anticonvulsant medication used primary treatment of epilepsy and neuropathic pain. (fig.1) it is not effective for absence or myoclonic seizures. considered to be one of the most vital drugs for the relief of pain associated with trigeminal neuralgia [1-2] carbamazepine are related chemically to the tricyclic antidepressants. It is a derived of 5H-Dibenzo[b,f]azepine with a carbamoyl phosphate group of 5 positions this moiety is essential for potent antiseizure activity [3-4] it is white or almost white crystalline powder practically insoluble in the water freely soluble in methylene chloride sparingly soluble in acetone and alcohol practically insoluble ether. It shows polymorphism. carbamazepine is official in IP, BP, USP, etc [5-7] As per investigation of literature the UV spectrophotometric analytical method were developed on different wavelength for analysis of carbamazepine in plasma fluids human serum plasma and pharmaceutical tablet dosage form or bulk drug samples[8-11] the rationale of this work to develop a simple accurate rapid precise reproducible and cost-effective Spectrophotometric method for the direct quantitative determination of carbamazepine in this method for determination carbamazepine in bulk drug sample and tablet dosage form and validation as per international conference on Harmonization (ICH)guidelines [12].

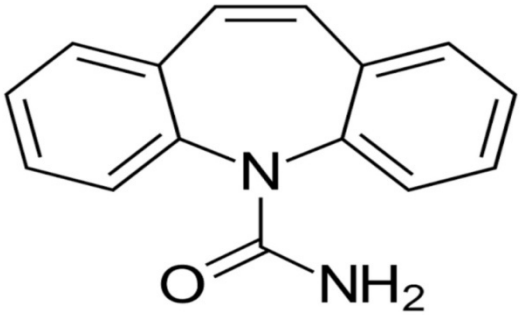

Fig.1: Chemical structure of Carbamazepine

MATERIAL AND METHODS

The Developments UV-spectrophotometer methods for a quantitatively analysis simultaneous Estimation methods for a carbamazepine 10,11 epoxide a based on measurement of absorption at maxima wavelengths 284nm by using methanol as a solvents the stock diluted of carbamazepine was preparations and substance suitability dilution a prepared methanol to a obtain standardization curve the standard solvent of carbamazepine show absorption maximum at 284nm

MATERIALS

A UV Visible double beam spectrophotometer (Shimadzu model UV 1800) attached to computer UV probe 2.33 with a spectral width of 2 nm, wavelength accuracy 0.5 nm and pair of 1 cm matched quartz cell was employed. Kindly gifted reference standard of Carbamazepine (Glen mark pharmaceutical) was used for the study.

METHOD DEVELOPMENT

Preparation of standard stock solution

An accurately weighed quantity of about 25mg of carbamazepine was taken in a 25 ml volumetric flask dissolved in a sufficient quantity of methanol then solicited for 15 min and diluted to 100 ml with the same solvent to get the concentration of 100 µm/ml.

Selection of wavelength for analysis of carbamazepine:

Accurately measured 1ml of standard stock solution was transferred into 10ml volumetric flask and diluted to 10 ml to give a concentration of 10 µg/ml and it was used for initial spectral scan in the UV range 200-400nm to detect the maximum wavelength and further dilution for linearity were prepared to form the stock solution by allegation method.

Preparation of serial dilutions:

The serial dilution was prepared to form the standard stock solution to get a respective concentration of 2,4,6,8 up to 10 µg/ml.

Method Validation

The proposed method was validated for various parameters such as linearity, and range, accuracy, precision, the limit of detection (LOD), the limit of quantitation (LOQ), robustness, ruggedness, sensitivity, and specificity accordingly to ICH Q9 guideline and USP guidelines [15-16].

Linearity and range

The linearity of a analysis preparations is a ability within a given ranges to obtained test result which a directed proportion to a concentrations of a Analysis in a samples the ranges of a analyticals preparations is a intervals distance the upper and lower concentrated of a Analytical in a sampled for a which has been a demonstrated that a analyticals procedures was a suitable level of precision, accuracy, and linearity the linearity of the analytical method was demonstrated over the concentration range investigated by triplicate analysis (n=3) at a concentration range of 2 - 10µg/ml.

Accuracy

The accuracy of a analyticals preparation express the closeness's of agreements between a value which a accepted eitherlly as a conventionally true value or a accepted references values and a value found .this is sometimes termed trueness the accuracy of the proposed method was determined based on recovery study.

Precision

The precisely of a analytics' procedure expresses of a closely of a agreement (degree of scatterings) between seriously a measurements obtains from a multiply sampled of a homogenously samples under was prescribed condition the precisions of a methods was a demonstrated by a intraday and inter-days variations study in the intraday precision study, three different solutions of the same concentration were prepared and analyzed in the same day (morning, noon and evening), all study was performed in triplicates .the result was indicated by calculating %RSD.

Limit of detection (LOD)

The detections of a limited individuals analysis procedures is a lowest amounted of Analytical in a samples that can be detected but not necessarily quantitatively as a exacted values.

The detection of limited (LOD) was determined by preparations solvents is differenced concentrations from a [2-10µg/ml].

LOD=3.3 s/S

Where, S = standard deviation, S=slope

Limit of quantification (LOQ)

The detection limit is the lowest amount of Analyte in a sample which can be detected but not quantitated the LOQ was calculated using the formula involving the standard deviation of responses and a slopes of the calibrations curved.

LOD=10 s/S

Where s=standard deviation

s=slope

Specificity

Specificity is a ability to assess the Analytical unequivocally in a presences of compounds which may be expected to be presents Typically these might a impurities degrading matrix, etc. the three different concentrations at three levels 80%, 100%, 120% respectively of standard carbamazepine.

RESULT AND DISCUSSION

Selection of wavelength

The spectra carbamazepine in methanol showed absorption at 284nm shown in fig.2. Which is complying with reported lax. Hence it was selected as lax of carbamazepine in methanol distilled water for further use.

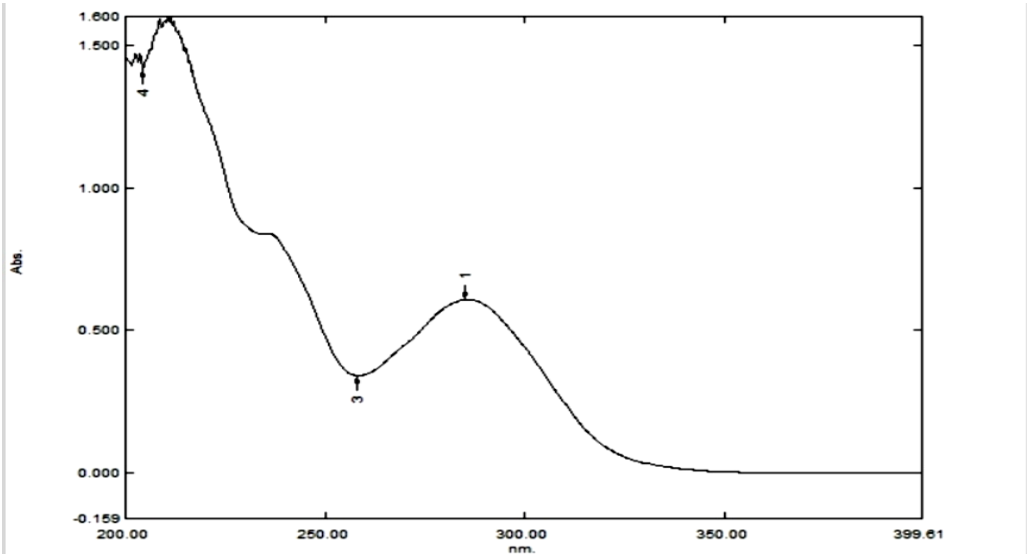

Fig.2: UV Spectrum of carbamazepine

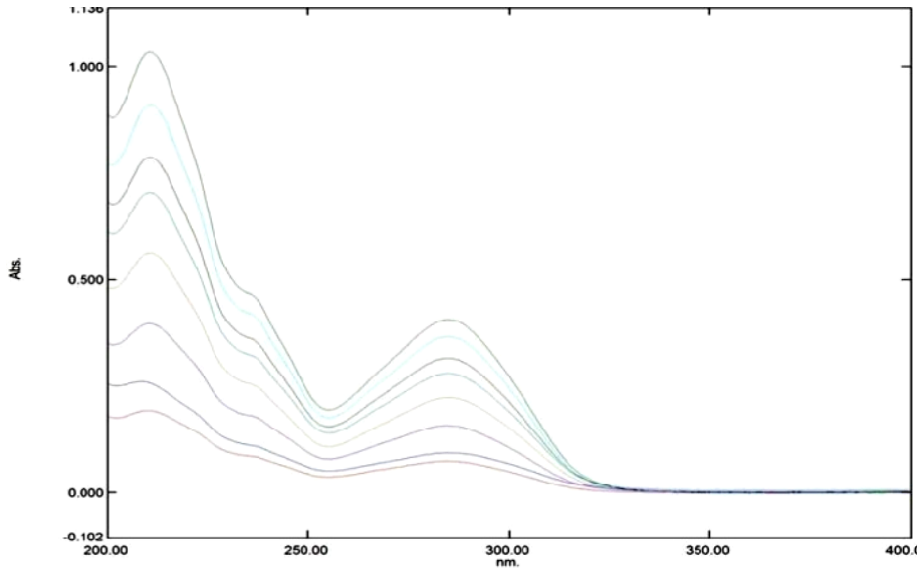

Fig.3: Overlay spectra of carbamazepine at 284nm

Linearity and range

The linearity for the developed method was investigated by replicate analysis (n=3) at seven concentration levels (2-10µg/ml) of reference standard carbamazepine .the absorbance obtained at

respective concentration was recorded and the graph was plotted shows good linear correlation coefficient from the UV probe software the linearity was shown in table 1 and fig .

Table 1: Calibration curve data of carbamazepine

Concentration. µg/ml	Absorbance
2	0.122
4	0.132
6	0.139
8	0.149
10	0.161

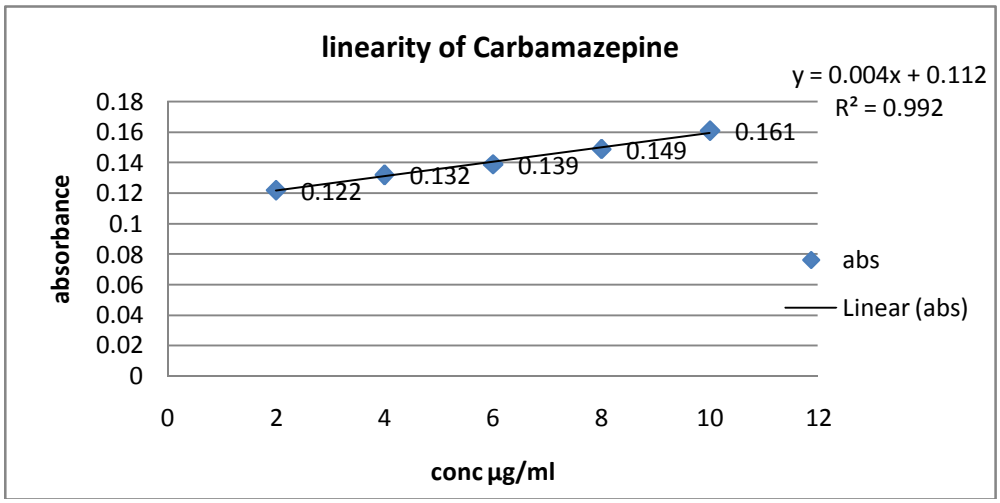

Fig.4: Calibration curve of carbamazepine

Method precision

The precision of the proposed method was determined by Intra-day and Inter-day precision and it was expressed in terms of percent relative standard deviation (%RSD). For Inter-day %RSD were found in the range of 0.1568 and o.1746repectively as shown in table 3

Accuracy

The accuracy was a determines in a triplicate by a analysis the %recovery of a carbamazepine by a standards additions of a methodology the percents recovery obtained indicates non- interferences from the recipients used in a formulations the result shown in table 2.

Table 2: Accuracy results of carbamazepine

Level of standard formulation total addition % recovery							
(%)	(µg/ml)	(µg/ml)	(µg/ml)	(µg/ml)	Mean	±SD	%RSD
80	5	4	9	8.987	99.8555	99.9148±0.513	0.0513
	5	4	9	8.987	99.9444		
100	5	4	9	8.995	99.9444	100.1733±0.06420	0.641
	5	5	10	10.022	100.22		
120	5	5	10	10.01	100.01	99.9090±8847	0.8855
	5	5	10	10.02	100.02		
	5	6	11	10.926	99.3227		

Table 3: Inter-day Precision

Mean absorbance	Mean SD ±	%RSD	Mean %RSD
0.8256 0.8231 0.8246	0.8244±0.0016	0.1526	
0.8256 0.8251 0.8229	0.8245±0.0014	0.1742	0.1568
0.8245 0.8225 0.8246	0.8238±0.0011	0.1437	

Table 4: Intra-day precision

Mean absorbance	Mean±SD	%RSD	Mean %RSD
0.8255 0.8231 0.8246	0.8244±0.0016	0.2058	
0.8251 0.8256 0.8229	0.8245±0.0014	0.1742	0.1746
0.8245 0.8225 0.8246	0.8238±0.0011	0.1437	

Table 5: specificity study

Level of standard aerosol table				Absorbance	% recovery		Mean % recovery
Addition API	(µg/ml)	(µg/ml)	(µg/ml)		(µg/ml)		
80	5	4	9	0.2958	5.00	100.00	100.00
	5	4	9	0.2958	5.00	100.00	
	5	4	9	0.2959	5.001	100.033	
100	5	5	10	0.2958	5.00	100.00	99.9887
	5	5	10	0.296	5.0033	100.067	
	5	5	10	0.2955	4.9949	99.8985	
120	5	6	11	0.2959	5.0016	100.033	100.0
	5	6	11	0.2956	4.9966	99.9323	
	5	6	11	0.2959	5.0016	100.0338	

Table 6: Assay of tablet Dosage form

Brand name	Sample solution Concentration (µg/ml)	Amount of mean ±SD found (%)	%RSD
Tegretal®CR200	10	100.23	0.1470
Mg Novartis	10	100.24	
India Ltd.	10	99.98	
Tegretal®200	10	100.1	0.1204
Mg. Novartis	10	99.96	
India Ltd.	10	100.2	
Vegetal® 100mg Chewable India Ltd.	10 10 10	100.59 100.20 99.89	0.3499

Table 7: Result of Validation Parameters

Parameters	Results
λ_{max}(nm)	284
Linearity range (µg/ml)	2-10
Regression equation	y=0.0583x+0.0033
The correlation coefficient (r^2)	0.9997
Precision	0.1568
Inter-day precision (%RSD)	0.1746
Intra-day precision (%RSD)	0.1746
LOD (µg/ml)	0.4439
LOQ (µg/ml)	1.267
Ruggedness (%RSD)	0.4429-0.4452
Robustness (%RSD)	0.0768-0.0887
Molar absorptivity	15471L/mol
Sandell's sensitivity	0.0152µg/cm^2
Accuracy (%)	99.99
Specificity (%RSD)	0.0195-0.0850
Assay of marketed formulation (%)	100.15

Assay of a marketed tablet formulation

Twenty tablets was a accurately weighed and a average weights a calculated they are crushed to fines powder a powder equivalent to a 25mg carbamazepine was a dissolved in 15ml methanol with a help of sonication and volume was made up using methanol up to the mark of 25ml volumetric flask. The

observed assay for commercially available tablets Tegretal®CR200mg, Tegretal®CR200mg, and Tegretal®chewable 100mg and validation parameters were summarized in table 8 and 9 respectively.

CONCLUSION

The simple rapid precise and economical Spectrophotometric method has been developed for the quantitative estimation of carbamazepine in bulk and pharmaceutical formulation the method is validated as per ICH and USP Guidelines is a founds that developed methods is a robust and sensitive's hence this a methods can be successfully and suitable acquired for a routine quality controls analysis of a carbamazepine in a bulk and pharmaceutical dosage form.

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CONFLICT OF INTREST

Authors do not have any conflict of interest.

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