IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Novel Analytical Method Development and Validation of Carbamazepine Bulk drug and Pharmaceutical Dosage Form: Review

PRATHAP S K*, PRAJWAL S. J, MOHITH GOWDA C V, NIVEDHYA K, ASWIN JOE FRANCIS,

Department of Pharmaceutical Analysis, Bharathi College of Pharmacy, BharathiNagara, K.M.Doddi, Maddur Taluk, Mandya District, Karnataka, India – 571 422

*Corresponding adress : prathapsk94@gmail.com Ph no : 09900537241.

*Corresponding adress : mohithgowda886@gmail.com Ph no : 08951553655.

Abstract: Analytical method development and validation are the continuous and inter dependent task associated with the research and development, quality control and quality assurance departments. Analytical procedures play a critical role in equivalence and risk assessment, management. It helps in establishment of product specific acceptance criteria and stability of results. Validation should demonstrate that the analytical procedure is suitable for its intended purpose. Designs of experiment are a powerful tool for the method characterization and optimize the analytical method. An effective analytical method development and its validation can provide significant improvement in precision and a reduction in bias errors. It can further help to avoid costly and time consuming exercises. Literature survey reveals the information about the different analytical methods for the determination of Carbamazepine. The published methods were validated for various parameters as per ICH guidelines. Statistical analysis proved that the published methods were reproducible and selective for the estimation of the Carbamazepine in Bulk and pharmaceutical dosage form.

Key words: Carbamazepine, Literature Survey, Validation, ICH Guidelines.

Introduction:

Carbamazepine, sold under the brand name Tegretol among others, is an anticonvulsant medication used in the treatment of epilepsy and neuropathic pain. It is used as an adjunctive treatment in schizophrenia along with other medications and as a second-line agent in bipolar disorder. Carbamazepine appears to work as well as phenytoin and valproate for focal and generalized seizures. It is not effective for absence or myoclonic seizures.

Carbamazepine was discovered in 1953 by Swiss chemist Walter Schindler. It was first marketed in 1962. It is available as a generic medication. It is on the World Health Organization's List of Essential Medicines. In 2020, it was the 185th most commonly prescribed medication in the United States, with more than 2 million prescriptions.

Photo switchable analogues of carbamazepine have been developed to control its pharmacological activity locally and on demand using light, with the purpose to reduce adverse systemic effects. One of these compounds (carbadiazocine, based on a bridged azobenzene) has been shown to produce analgesia with noninvasive illumination in a rat model of neuropathic pain.

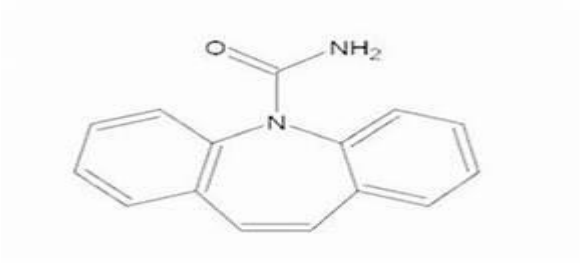

Figure 1: Chemical Structure of carbamazepine.

LITERATURE SURVEY:

1. Nityanand zadbuke *et al.*, To develop and validate simple, accurate, rapid, precise, reproducible and cost effective spectrophotometric method for the quantitative estimation of carbamazepine in a pharmaceutical formulation: The developed UV spectrophotometric method for the quantitative estimation of carbamazepine is based on measurement of absorption at maximum wavelength 284 nm using methanol as a solvent. The stock solution of carbamazepine was prepared, and subsequent suitable dilution was prepared in distilled water to obtained standard curve. The standard solution of carbamazepine shows absorption maxima at 284 nm. The drug obeyed beer lambert's law in the concentration range of 2-14 µg/ml with regression 0.9997 at 284 nm. The overall % recovery was found to be 99.99% which reflects that the method was free from the interference of the impurities and other excipients used in the formulation. The low value of % RSD was indicative of accuracy and reproducibility of the method the % RSD for inter-day and intra-day precision was found to be 0.1568 and 0.1746 respectively.

2. Rashmin B. Patel, [4] *et al.*, A new, simple, and rapid high-performance thin-layer chromatographic method was developed and validated for quantitative determination of Carbamazepine. Carbamazepine was chromatographed on silica gel 60 F254 TLC plate using ethyl acetate-toluenemethanol (5.0 + 4.0 + 1.0 v/v/v) as mobile phase. Carbamazepine was quantified by densitometric analysis at 285 nm. The method was found to

give compact spots for the drug (Rf = 0.47 ± 0.01). The linear regression analysis data for the calibration plots showed good linear relationship with r2 = .9995 in the concentration range 100–600 ng/spot. The method was validated for precision, recovery, repeatability, and robustness as per the International Conference on Harmonization guidelines. The minimum detectable amount was found to be 16.7 ng/spot, whereas the limit of quantitation was found to be 50.44 ng/spot. Statistical analysis of the data showed that the method is precise, accurate, reproducible, and selective for the analysis of Carbamazepine. The method was successfully employed for the estimation of equilibrium solubility, quantification of Carbamazepine as a bulk drug, in commercially available preparation, and in-house developed mucoadhesive micro emulsion formulations and solution.

3. FARAAT ALI [5] *et al.,* A simple, precise, fast, accurate and sensitive UV-visible first order derivative spectrophotometric method was developed and validated for amitriptyline and chlordiazepoxide estimation in pure and tablet dosage form. The method involved determination of amitriptyline and chlordiazepoxide using first derivative spectrophotometric technique at 219 nm and 239 nm over the concentration ranges of 5-17 µg/mL and 1-7 µg/mL. Mean recoveries were found to be about 98.33 ± 0.45 % w/w for amitriptyline and 99.75 ± 1.16 % w/w for chlordiazepoxide. The coefficient (r2) was 0.9998 for amitriptyline and 0.9997 for chlordiazepoxide, respectively. The limit of detection and limit of quantification were found to be 131 and 398 ng/mL, respectively for amitriptyline and 26 and 79 ng/mL, respectively for chlordiazepoxide. The assay percentage of the marketed formulation calculated were 99.87 ± 0.03 % w/w for amitriptyline and 98.81 ± 1.04 % w/w for chlordiazepoxide, respectively. This study provides a validated UV spectrophotometric method by using a first order derivative method. This validated method was carried out with respect to the parameters such as linearity, specificity, stability, accuracy, and precision, limit of quantification and limit of detection in the light of internationally accepted ICH guidelines.

4. Sevgi Tatar ULU [6] *et al.,* A sensitive e re erased phase high-performance liquid chromatographic (HPLC) and second deli ati e spectrophotometric methods for determination of carbama3epine in tablets ha e been developed. In the HPLC method, carbama3epine was separated using Phenomenex C18 column and acetonitrile: water (75:25,) the mobile phase system; the speed of the mobile phase flowing was 1mh/min and the detection was actuali3ed at 285 nm. Enalapril was used as an internal standard. For the second-deri ate e spectrophotometric method; carbamazepine was determined by applying the technique of the "peak to peak amplitudes". The assay was linear o er the concentration range of 0.2-2.0 µg/mh for HPLC and 4.0-10.0 µg/mh for second deri ati e spectrophotometric method. The detection limits of carbama3epine were 0.055 and 1.25 µg/mh for HPLC and deri ati e spectrophotometric methods, respect ely. The reco ery (mean±RSD) in HPhC was 99.22±0.25% and in the deri ati e spectrophotometry 99.05±0.25%. The proposed methods were successfully applied to the determination of carbama3epine in tablets: the reco ery was of high percentage, the accuracy and presicion were good.

5. Dural, E [7] *et al.,* Carbamazepine (CBZ) is an antiepileptic drug, which is prescribed as a first-line drug for the treatment of partial and generalized tonic–clonic epileptic seizures. The aim of this study was to develop and validate a simple, fast and reliable HPLC method for the determination of carbamazepine in human plasma. Methods: Chlorpromazine (CPR) was used as an internal standard. The separation was conducted with a C18 reverse-phase column (150x3.9 mm, 5 µm) at 30°C, using a mobile phase prepared with 20 mM KH2PO4, acetonitrile and methanol (6:3:1, v/v/v) by isocratic elution. The method was linear between 0.5 and 40 µg/mL, determined by 10 individual calibration points. Total run time was ≤ 5 mins. Accuracy (RE %) values were determined between (-5.6) and 3.6%, and precision was determined at ≤4.2%. Limit of detection (LOD) was 0.04 µg/mL. The robustness test results of the method showed good values. Plasma CBZ of (n=30) those receiving CBZ quantities ranging from 0.2 to 1.2 g/day were measured with this method, and following analyses of their concentrations were found to be between 0.1 and 11.4 µg/mL (6.2±2.4 µg/mL). While all plasma sample analyses were applied properly, it was observed that 16 (53.3%) of the plasma samples had CBZ lower than the recommended range. In addition to that, female patient plasma-CBZ levels were found significantly higher than male plasma contents ($p<0.05$).

6. Essam Ezzeldin [8] et al., A simple method for the determination of carbamazepine using high performance liquid chromatography (HPLC) with ultraviolet absorbance detection (UV) was developed. The method involves two steps (protein precipitation and liquid–liquid extraction). Diclofenac sodium was used as the internal standard (is). The separation was carried out using an analytical Thermo C8 (250 x 4.6 mm), 5 µm column with mobile phase consisted of acetonitrile: isopropyl alcohol: phosphate buffer pH: 3 (36:15:49). The flow rate was 1.2 mL/min. The eluent was monitored at 220 nm with a sensitivity setting at 0.05 absorbance units. Linear detection response was obtained for concentrations ranging from 0.1 to 8.0 µg mL−1. The limit of quantification (LOQ) was 0.1 µg mL−1. The method was validated successfully for the determination of carbamazepine and, the proposed HPLC method is simple, rapid and highly sensitive, and it could be reliable for pharmacokinetic studies in humans.

7. Ibrahim Bulduk1 *et al.,* Carbamazepine is a first-line drug used in the treatment of epilepsy. High performance liquid chromatographic and spectrophotometric methods have been developed for the determination of carbamazepine in tablet dosage forms. UV spectrums were recorded in the wavelength range of 200-800 nm using methanol solvent, and the wavelength for determining carbamazepine was selected as 286 nm. LC analysis was performed using Agilent Extend-C18 column and mobile phase composed of KH2PO4 solution (pH: 3.5) and acetonitrile (40:60 v/v) at a flow rate of 1.2 mlmin-1.These analytical methods were validated in agreement with the International Conference on Harmonization (ICH) guidelines using the following analytical parameters: specificity, linearity, precision, accuracy, detection and quantification limits, and robustnes. Analytical methods showed wonderful linearity (r2 >0.999) in the concentration range of 5-25 µg mL-1 for both methods.

8. REEM EMAL *et al.,*.A simple, rapid and accurate method of High-Performance Liquid Chromatography (HPLC) with UV detector was used for determination of Carbamazepine (CBZ). The mobile phase was a mixture of 55% of water contains (1 ml triethylamine per 1 liter) and 45% acetonitrile, the pH was adjusted with phosphoric acid, BDS hypersil C18 column (5µmx150mmx4.6mm) equipped with UV detection at 285 nm with flow rate of 1.0ml/min, using 15µl injection volume and 10°C auto-sampler temperature. Metronidazole benzoate was used as internal standard; the method was precise, and accurate. Beverages were given in drinking water to the rats before giving CBZ dose (10mg/kg). Plasma level of CBZ alone (group 1) was compared to CBZ with tamarind (group 2), mango (group 3), sugarcane (group 4), and red bull (group 5). Maximum plasma concentrations (Cmax) were 2222.7 ng/ml, 1006.3 ng/ml, 2090.4 ng/ml, 4446.3 ng/ml, and 4523.6 ng/ml respectively for the five groups, group 2 was significantly decreased in Cmax (p-value 0.05). The times for reaching the peak of concentration (Tmax) were significantly increased in all comparison to drug alone (p-value).

9. A. Padma *et al.,* The aim of the present research was broadly focused on the estimation of carbamazepine in bulk and pharmaceutical dosage form by using two UV –Spectrophotometric methods namely, Zero order UV spectrophotometry (Method -1) and Area under the curve UV spectrophotometry (Method -2). The Zero order UV Spectrophotometric method was based on the measurement drug absorbance at wave length of 284 nm, which was its wavelength of maximum absorbance .The Area under the curve method, was based on the calculation of area occupied by the UV absorbance curve between 278-290 nm. The solvent employed for both methods was 50% v/v ethanol. In the estimation of Carbamazepine, both the methods showed linearity in the range of 2-12µg/ml. The correlation co-efficient was ≥ 0.999. The precision for both the methods was ≤2% RSD. The accuracy was performed by using percentage recovery studies of standard drug spiked at 50,100 and 150% of the test concentration and the values obtained were within the limits. The developed methods were applied for the assay of the drug in its respective dosage forms. The assay of pharmaceuticals dosage form was found to be within limits. All the results were satisfactory, the developed methods can be routinely used for the analysis of the drugs in both bulk and dosage forms.

10. Sarmad B *et al.,* The study aimed to recommend a new spectrophotometric-kinetic method for determination of carbamazepine (CABZ) in its pure form and pharmaceutical forms. The proposed procedure based on the coupling of CABZ with diazotized sulfanilic acid in basic medium to yield a colored azo dye. Factors affecting the reaction yield were studied and the conditions were optimized. The colored product was followed spectrophotometrically via monitoring its absorbance at 396 nm. Under the optimized conditions, two method (the initial rate and fixed time (10 minute)) were applied for constructing the calibration graphs. The graphs were linear in concentration ranges 2.0 to 18.0 µg.mL-1 for both methods. The proposed was applied successfully in the determination of CABZ in its commercial formulations.

Conclusion:

Literature survey suggested that various Spectrophotometric, UV methods were developed and reported. The published methods were validated for various parameters according to ICH guidelines. Statistical analysis proved that the published methods were reproducible and selective. Thus it can be concluded that the reported and published methods can be successfully applied for the Novel analytical method Development and Validation of Carbamozepine in bulk drug and pharmaceutical dosage form.

References:

1. www.en.wikipedia.org/wiki/ Carbamozepine.
2. https://pub chem.ncbi.nlm .nih .gov/compound/ Carbamozepine.
3. NITYANAND ZADBUKE1*, SADHANA SHAHI2, AJIT JADHAV2, SANTOSH DEVELOPMENT AND VALIDATION OF UV-VISIBLE SPECTROSCOPIC METHOD FOR ESTIMATION OF CARBAMAZEPINE IN BULK AND TABLET DOSAGE FORM. Vol 8, Issue 2, 2016, ISSN- 0975-1491
4. Rashmin B. Patel,1 Mrunali R. Patel,2 Kashyap K. Bhatt,2 and Bharat G. Patel1Development and Validation of HPTLC Method for Estimation of Carbamazepine in Formulations and Its In Vitro Release Study. Volume 2011, Article ID 684369, 8 pages, doi:10.4061/2011/684369.
5. FARAAT ALI* , UTPAL NANDI, RAVENDRA VERMA, RAMJI RATHOD, P.L. SAHU, ROBIN KUMAR, ANUJ PRAKASH and G.N. SINGH, UV-Visible First Order Derivative Spectrophotometric Method Development and Validation for Simultaneous Estimation of Amitriptyline Hydrochloride and Chlordiazepoxide in Tablet Dosage Form.
6. Essam Ezzeldin1 Abdelaaty A. Shahat2 and Omer A. Basudan2, Development and Validation of an HPLC Method for the Determination of Carbamazepine in Human Plasma.
7. Ibrahim Bulduk1* and Serdar Gungor2, Spectrophotometric and High Performance Liquid Chromatographic Determination of Carbamazepine in Tablets Dosage Form.
8. REEM EMADA , EYAD MALLAHA*, FATIMA SHAHINA , FERAS DARWISH EL-HAJJI B , WAEL ABU DAYYIHA*, NASIR IDKAIDEKA , LUAY ABU-QATOUSEH A*, DA'SAN M. M. JARADATC , TAWFIQ ARAFAT , Determination of carbamazepine in rat plasma by using high performance liquid chromatography (HPLC) in presence of some traditional beverages (tamarind, mango, sugarcane, red bull) and its pharmacokinetic applications.
9. ICH, Q2A Text on Validation of Analytical Procedures; 1994.
10. ICH, Q2B Validation of Analytical Methodology; 1996.
11. ICH, Q2 (R1) Validation of Analytical Procedures: text and methodology; 2005.
12. Beckett AH, Stenlake JB. Pharmaceutical Chemistry. 4th ed. Part two. New Delhi: CBS; 1997. 293-299..