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A Review Article on Various Reported Analytical Methods for the Efonidipine Hydrochloride Ethanolate

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Abstract: ***Efonidipine hydrochloride ethanolate is a calcium channel blocker principally employed in the treatment of hypertension and angina pectoris. A thorough assessment of the reported analytical methods for its measurement in diverse matrices is necessary due to its therapeutic importance. This page consolidates current information, emphasising chromatographic techniques like High Performance Liquid Chromatography (HPLC) and Gas Chromatography (GC), which are widely utilised for their accuracy and dependability. Furthermore, spectroscopic techniques such as UV Vis spectroscopy and Mass Spectrometry have garnered interest for their capacity to deliver swift analysis with minimal sample preparation. The evaluation delineates the merits and drawbacks of each method, underscoring aspects such as sensitivity, specificity, and reproducibility. Furthermore, it examines emerging developments in analytical chemistry that could improve the detection capabilities for efonidipine hydrochloride ethanolate. This review is a great resource for researchers aiming to enhance analytical procedures for efonidipine hydrochloride ethanolate. By integrating existing information, it seeks to promote additional progress in pharmaceutical analysis and quality control methodologies.***

Keywords: ***Efonidipine hydrochloride ethanolate, HighPerforma nce Liquid Chromatography (HPLC) and Gas Chromatography (GC), Mass Spectrometry.***

I. INTRODUCTION

Efonidipine, a drug approved by the Drug Controller General of India (DCGI) in 2017, as a treatment for hypertension (1). It was initially launched under the brand name Landel and was later rebranded as Efnocar by Zuventus Healthcare Ltd. The drug's pharmacological profile is influenced by the dominant phosphorous moiety at the C5 position of the dihydropyridine ring (Figure 1). The treatment is expected to benefit between 10 and 25% of the population, depending on the blood pressure cutoff and age group (2, 3). Essential hypertension, which is less than 95% of cases, is more common in Black people of the African region, who are at higher risk of stroke and renal failure. The molecular formula for efonidipine is $C_{34}H_{38}N_3O_7P$ and its molecular weight is 631.7 g/mol (4).

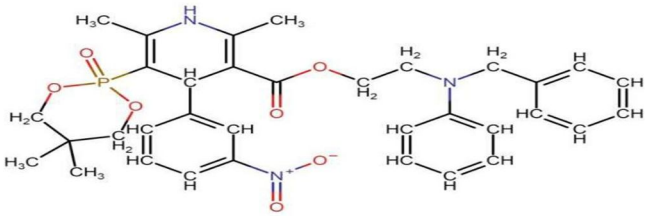


Figure 1: Structure of Efonidipine

II. MECHANISM OF ACTION

Efonidipine is a new agegroup dihydropyridine calc ium channel blocker that inhibits both L and Ttype calcium channels. It is highly lipophili c and easily penetrates the phospholipidrich cell membrane, leading to vasodilation and decreased heart automation (5). Efonidipine also increases coronary blood flow by blocking calcium channels and attenuating myocardial ischemia. It reduces aldosterone synthesis and secretion, preventing hypertrophy and remodeling of cardiac myocytes. It increases glomerular filtration rate without increasing intraglomerular pressure and filtration fraction, preventing hypertensioninduced renal damage (6). It increases sodium excretion from the kidneys by suppressing aldosterone synthesis and secretion from the adrenal glands. Efonidipine also lowers blood pressure in cerebral resistance vessels and stops hypertensioninduced brain damage (7).

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III. PHARMACOKINETICS OF EFONIDIPINE

Originally used mostly for the treatment of hypertension, efonidipine is a new dihydropyridine calcium channel blocker with different pharmacokinetic characteristics that increase its therapeutic value. Efonidipine indicates fast absorption after oral treatment; peak plasma concentrations are usually reached 1 to 2 hours (8). Food intake clearly influences bioavailability; simultaneous meals can increase absorption by means of extended gastrointestinal transit time. The notable amount of efonidipine dispersion points to strong binding to tissues. Mostly binding to plasma proteins, this drug influences its free concentration and general effectiveness. Cytochrome P450 enzymes in the liver breaks efonidipine into active metabolites that improve its antihypertensive action (9). The halflife of elimination is between five and ten hours, which helps clinical practice to provide oncedaily doses easily. Improving treatment regimens and ensuring patient safety depend on an awareness of these pharmacokinetic factors (10).

IV. PREVIOUSLY VALIDATED ANALYTICAL METHODS THAT WERE DEVELOPED FOR THE ESTIMATION OF EFONIDIPINE

Clinically as well as in pharmaceutical research depend on these approaches. Because of its sensitivity and accuracy in measuring efonidipine in various matrices, including plasma and tablet formulations, highperformance liquid chroma tography (HPLC) has become among the most often used methodologies. Apart from HPLC, spectrophotometric techniques have been developed utilising efonidipine's special absorbance properties. Especially in resource constrained environments, these methods provide a reasonably affordable substitute for standard analysis. Moreover, developments in mass spectrometry have made it possible to more fully profile efonidipine metabolites, therefore improving our knowledge of its pharmacokinetics. The constant development of these analytical methods emphasises the need of thorough quality control in medications (11). These approaches will probably be polished more as research advances to guarantee regulatory compliance and lower analysis time while improving detection limits.

Kumar et al. report a validated reverse phase high performance liquid chromatography technique for efonidipine estimation (EFD). We performed the separation using a 250 x 4.6 mm C18 column. Mobile phase consisted of acetonitrile and water (85:15 v/v), set at a flow rate of 0.8 mL/min. UVVisible detector was used for the study at 254 nm. EFD showed a linear response within a 20–140 g/mL (R2 = 0.9994) concentration r ange. Observed was a limit of quantification of 2.06 g/mL; the limit of detectio n was 681.83 ng/mL. The coefficient of variation for intraassay and interassay precision was less than or equal to 1.5%; the accuracy was 104.0 to 105.0% (12).

Rajput AS et al., developed a RPHPLC method to qua ntify Efonidipine hydrochloride (EFO) in solid dispersions using Eudragit EPO. The method was validated for system suitability, linearity, accuracy, precision, and robustness. The method showed excellent linearity and accurate results with a %RSD value less than 2% for EFO. The enhanced drug dissolution from Eudragit EPO carrier with 10% Citric Acid was attributed to the conversion of the drug from crystalline to amorphous form and the microenvironmental acidic pH provided by CA (13).

Liu M et al., studied Efonidipine hydrochloride, a new generation calcium channel blocker, has been determined in human plasma using a simple and robust LCMS/MS method. The method extracts efonidipine from plasma using an LLE procedure, separates it by LC, and detects it using MS/MS in positive mode ESI. The method was validated for selectivity, carryover, sensitivity, extraction recovery, matrix effects, linearity, accuracy, precision, dilution integrity, and stability studies. The calibration curves were linear over 0.100–20.0 ng/mL, and the lower limit of quantification was established at 0.100 ng/mL. The method showed acceptable matrix effect and reproducible extraction recovery. Efonidipine was stable under the investigated conditions, and the method was applied to the pharmacokinetics of efonidipine in human subjects (14).

Liu M et al., developed and validated an enantioselective and sensitive LC–MS/MS method for determining efonidipine enantiomers in human plasma. Plasma samples were processed using liquidliquid extraction, optimized for chiral sepa ration on a CHIRALPAK® ID column, and detected using MS in multiple reaction monitoring mode. The calibration curves were linear over 0.100–20.0 ng/mL for each enantiomer, and the lower limit of quantification was established at 0.100 ng/mL. The method had intra and interday pr ecisions of less than 12.1% for each enantiomer, and accuracies between 5.0% and 5.0% f or each enantiomer. No chiral inversion was observed during sample storage, preparation, and analysis. The validated method was successfully applied to a stereoselective pharmacokinetic study of efonidipine in healthy subjects after oral administration of 40 mg (20 mg × 2) efonidipine hydrochloride tablets (15).

Solanki KH et al., reported a highperformance thin layer chromatographic method has been developed to determine efonidipine hydrochloride (EFD) and telmisartan (TEL) in tablet dosage form for hypertension treatment. The method uses aluminum plates coated with silica gel 60 F254 as a stationary phase and nbutanol: toluen e: acetic acid as a mobile phase for separation.

Compact spots of TEL and EFD were obtained at Rf 0.73 and 0.37, respectively. Densitometric detection was carried out at 299 nm in UV, showing linear responses over the 200–1200 ng/band range for both drugs. The method was validated according to ICH guidelines and successfully applied for estimating both drugs in tablet formulations. The method was found to be greener with a greenness score of 0.69 using AGREE software (16).

Patel BD et al., developed a central composite designbased RPHPLC method was optimized for synchronized analysis of Efonidipine Hydrochloride Ethanolate (EFE) and Chlorthalidone (CHL) in tablets. The separation was performed using an Inertsil ODS C18 column and PDA detector with a 0.05 M KH2PO4 Buffer: Acetonitrile mobile phase. The optimum conditions were selected based on retention time, resolution, and tailing factor. The optimized HPLC condition was validated and met ICH acceptance criteria. The linear calibration curve was within the range of 6.2518.75 and 2060 g/ml, and the as say was 100.94 and 100.06% for CHL and EFE, making it suitable for routine tablet analysis (17).

Solanki KH et al., aimed to estimate the combined efonidipine hydrochloride and telmisartan in marketed formulations for hypertension treatment. The method was validated using an accurate isocratic RPHPLC method, using a Symmetry® C18 col umn as a stationary phase and acetonitrile: 0.05 M Potassium dihydrogen phosphate buffer as a mobile phase. The method was linear in the concentration range of 0.215 µg/ml f or both drugs, with a correlation coefficient of 0.998 for efonidipine and 0.996 for telmisartan. The method was validated according to the ICH Q 2 (R1) guideline. A forced degradation study was conducted to determine the instrinsic stability of both drugs. Efonidipine was found to be susceptible to base hydrolysis and oxidative stress degradation, while telmisartan was stable in acidbase hydrolysis, oxidative stress, dry heat, and photo stability testing conditions. The method's good recovery in tablet dosage form demonstrates its applicability for drug combination analysis (18).

Darji H et al., focuses on determining the drug combination in tablet dosage form using RP HPLC and Simultaneous equation UV methods. Greenness assessment tools were used to evaluate the ecological impact of the new UV spectrophotometric method and HPLC method. The HPLC chromatography was performed using a gradient technique on a reversedphase C18 column with mobile phase based on the polarity of the molecules. The Simultaneous equation UV method was developed and validated at 220 nm and 250 nm in methanol: distilled water (20:80, v/v). The results showed that the RPHPLC m ethod achieved chromatographic separation over the linearity of 3.0–60.0 g/mL and 10.0 200 .0 g/mL for Chlorthalidone (CLT) and Efonidipine (EFD), respectively. The method was found to be precise, accurate, and environmentally friendly in terms of solvent usage, chemical compounds, energy consumption, and trash creation. In conclusion, the analytical method validation parameters were found to be as per acceptance criteria, and statistical testing using an analysis of variance test did not find significant differences between the two methods. A reliable assessment of the health and environmental risk associated with chemical use is essential for evaluating the greenness and whiteness of an analytical method (19).

Rao MR et al., explores the use of nanosponges, prepared by crosslinking βcyclodextrin with diphenyl carbonate in a 1:4 ratio, to improve the solubility of Efonidipine. The nanosponges were characterized by particle size, phase solubility studies, and solution state interaction studies. The study also conducted solubility, in vitro dissolution, and molecular modeling studies. Phase solubility studies revealed a 1:2 complexation between the drug and carriers, while saturation solubility studies showed a significant increase with both beta CD and nanosponges. The study also confirmed the amorphization of the drug in the complexes, indicating that the solubility enhancement of EFD could be attributed to complexation and amorphization. Molecular modeling studies revealed the mode of entrapment of efonidipine in the carriers. The versatility of nanosponges in encapsulating both hydrophilic and hydrophobic drug molecules holds great promise for personalized medicine and targeted therapy, ultimately improving patient outcomes. The study also introduces spray drying as a scalable and practical approach to maximize the solubilityenhancing benefits of nanosponges (20).

V. CONCLUSIONS

According to the literature research, several analytical approaches are accessible to estimate efonidipine. Nevertheless, no method accessible for estimation by means of HPTLC, which might provide better experimental parameters, based on scientific approach employing design of experiment is known. These fast and significantly more inexpensive chromatographic techniques are For the researchers, the given data is quite helpful.

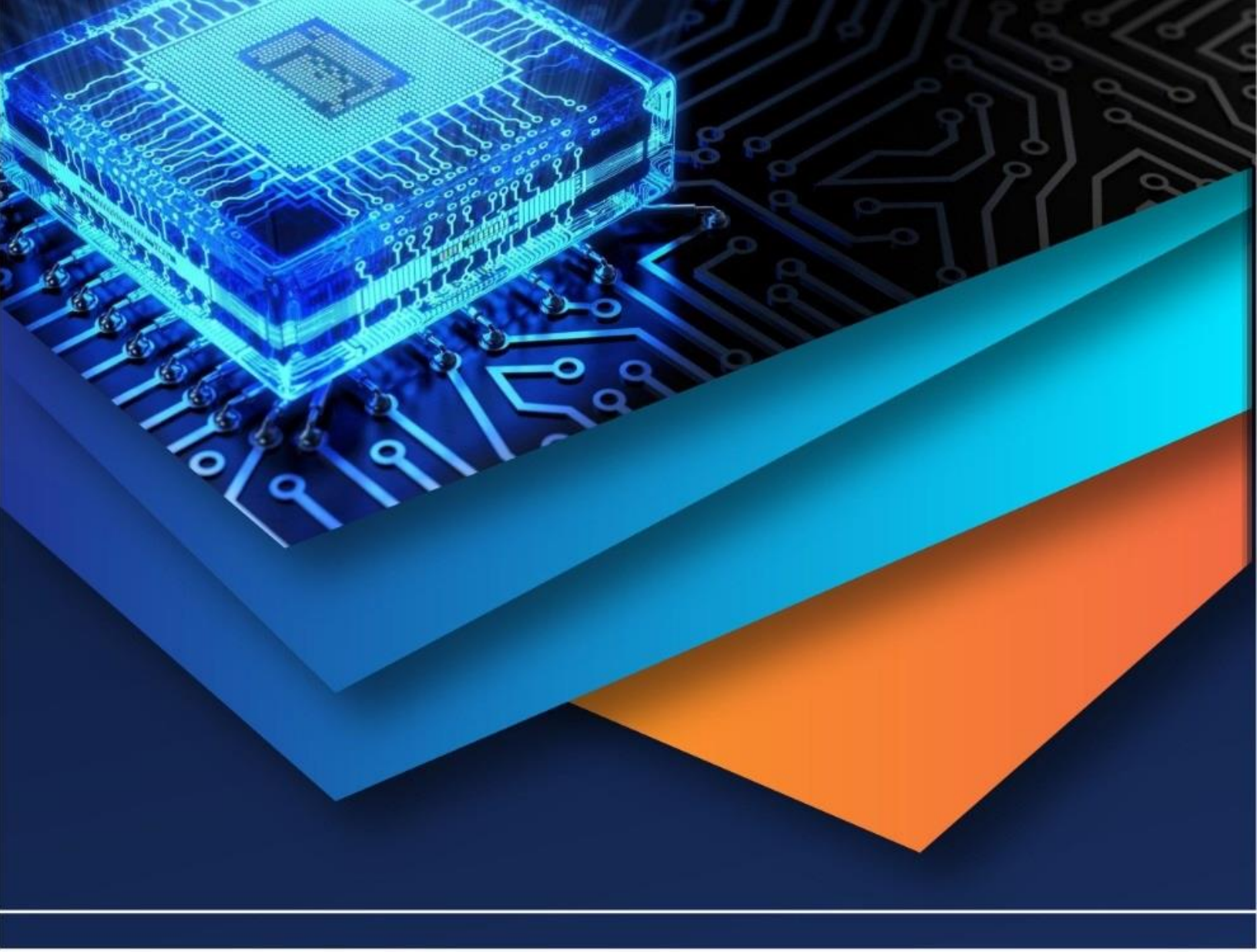
VI. CONFLICT OF INTEREST

None

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