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Review Article of Eslicarbazepine Acetate by RP-HPLC

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ABSTRACT

Determining the qualitative and quantitative composition of pharmacological mixes relies heavily on logical chemistry. High-Performance Liquid Chromatography (HPLC), among other logical ways, has surfaced as a reliable and precise system for separating, relating, and quantifying chemicals, particularly in pharmaceutical phrasings. Due to its remedial significance, Eslicarbazepine acetate a third- generation antiepileptic drug chemically related to carbamazepine and oxcarbazepine is vastly analyzed using HPLC. The primary mechanisms of action for this medicine include the inhibition of excitatory neurotransmitters and the block ADE of voltage-gated sodium channels. various validated HPLC and Ultra- Performance Liquid Chromatography (UPLC) ways have been developed for its analysis, incorporating different column types, mobile phases, flux rates, and discovery wavelengths, thereby offering versatility in different logical surrounds. These ways are essential for stability studies, remedial drug monitoring, and icing the effectiveness and safety of the medicine. This study outlines several logical styles for the effective evaluation of Eslicarbazepine acetate and underscores the significance of system development and evidence in the field of logical chemistry.

Keywords: Eslicarbazepine acetate, RP- HPLC, ICH guidelines, Method validation.

1. INTRODUCTION

Both the qualitative and quantitative composition of the object under study are ascertained using analytical chemistry. For a thorough comprehension of the sample content, both elements are necessary. Analytical chemistry is divided into two subfields: qualitative and quantitative analysis. By identifying the presence or absence of particular features, qualitative analysis offers insight into the sample's characteristics. In contrast, quantitative analysis expresses the relative amounts of one or more components numerically. Various analytical techniques are commonly employed to analyze biological fluids, pharmaceutical formulations, and bulk drug samples. In non-instrumental analysis, the sample is evaluated based on conventional and physicochemical properties. Instrumental methods of analysis rely on instruments to measure the physical characteristics of a substance[1].

In contemporary chemistry, high-performance liquid chromatography (HPLC) is a powerful analytical tool. It excels at determining, quantifying, and separating the components of liquid-dissolved materials. HPLC is widely employed in the analysis of pharmaceutical products and is highly regarded for its accuracy in both quantitative and qualitative assessments, significantly advancing the field of analytical chemistry. A sample solution—also known as the stationary phase—is injected into a porous column during HPLC. Subsequently, a high-pressure liquid, known as the mobile phase, is pumped through the column. The components of the sample migrate across the column at varying speeds as they are separated into the stationary and mobile phases. Elution occurs at different times, which enables separation. The delicate behaviours of components during partitioning provide High-Performance Liquid Chromatography (HPLC) with its precision, which makes it a dependable method for examining a range of samples in industries such as analytical chemistry and pharmaceuticals.

A compound with a lower affinity for the stationary phase moves more quickly and travels a greater distance in high-performance liquid chromatography (HPLC), while a molecule with a higher affinity moves more slowly and covers a shorter distance. Effective sample component separation and analysis are made possible by this differential migration. HPLC is particularly advantageous in pharmaceutical analysis, as it efficiently separates and quantifies critical drugs, reaction contaminants, synthesis intermediates, and degradation products. As a leading analytical technology, HPLC excels in detecting, quantifying, and separating various liquid-soluble sample components. Its precision is vital for evaluating the stability of drug products and is essential for both quantitative and qualitative assessments of these products.

Pharmaceutical discovery, development, and manufacturing heavily depend on the creation and validation of analytical methods. These techniques are employed to ensure the efficacy, identification, purity, and performance of pharmaceutical products. When developing these methods, several factors must be considered. To determine the most suitable detection method for analysis, particularly in the case of UV detection, researchers first gather data on the physicochemical properties of the analyte, including pKa, log P, and solubility. The bulk of the analytical development work is focused on validating a stability-indicating HPLC technique. The main active ingredient, any reaction contaminants, all accessible synthetic intermediates, and any degradants are all intended to be separated and quantified using the method[2].

There are many steps involve in method development which are:

- Physicochemical properties of drug.
- Set up HPLC conditions.
- Sample preparation.
- Method optimization.
- Validation of developed method.

2. INTRODUCTION TO DRUG PROFILE OF ESLICARBAZEPINE ACETATE

Eslicarbazepine acetate (ESL) is a medication used to treat epilepsy, a chronic condition that necessitates ongoing care. The World Health Organization (WHO) estimates that 50 million individuals globally, or around 1% of the world's population, suffer with epilepsy at any given moment. One of the most commonly prescribed classes of medications for this condition is antiepileptic drugs (AEDs)[3]. A recent study conducted in Denmark, which included 471,873 participants, found that 5,426 individuals were receiving AEDs, indicating a prevalence rate of 1.1%. As people age, their use of these drugs tends to rise. In a U.S. study involving 10,168 senior citizens residing in nursing homes, 1,132 (11.1%) were prescribed an AED, with 19% of these prescriptions being for indications unrelated to epilepsy or seizures. In addition to epilepsy, AEDs are frequently utilized to treat a variety of other conditions, including anxiety, bipolar disorder, neuropathic pain, migraines, and more[4].

Eslicarbazepine acetate [(S)-10-Acetoxy-10, 11-dihydro-5H-dibenz [b,f]azepine-5-carboxamide] is a broad-spectrum antiepileptic drug that is chemically different from other anticonvulsants[5]. In addition to blocking voltage-dependent sodium channels, Eslicarbazepine acetate inhibits the release of excitatory neurotransmitters such as glutamate and aspartate. When used alone or in combination with other antiepileptic medications, Eslicarbazepine acetate effectively treats partial and generalized tonic-clonic seizures[6].

One of the most well-known and often prescribed anticonvulsants for the treatment of tonic-clonic seizures, carbamazepine (CBZ), is oxidized to carbamazepine-10,11-epoxide (CBZ-E) by inducible hepatic cytochrome P-450-dependent enzymes. The adverse side effects associated with to CBZ are mostly caused by this metabolite, which also has antiepileptic qualities. Further conversion of CBZ-E leads to the formation of the inactive metabolite 10,11-trans-dihydroxy-10,11-dihydrocarbamazepine (trans-diol). Therapeutic drug monitoring (TDM) of CBZ is particularly prevalent in clinical practice due to its complex pharmacokinetics and narrow therapeutic range (4–12 µg/mL). Additionally, monitoring plasma levels of CBZ-E can enhance the effectiveness of individual treatment regimens[7].

A keto group was added to the tenth position of the azepine ring in carbamazepine (CBZ) to create oxcarbazepine (OXC) and prevent the formation of CBZ-E. This modification resulted in significant changes to the metabolic and tolerability profiles of both medications; however, it did not affect CBZ's mechanism of action or its range of anticonvulsant activity. In fact, only 13% of OXC in humans remains as the parent drug, while the majority (79%) is rapidly and extensively converted into licarbazepine (Lic), its primary pharmacologically active metabolite, which appears in plasma as a 4:1 mixture of S-licarbazepine (S-Lic) and R-licarbazepine (R-Lic)[8].

The newest antiepileptic drug (AED), Eslicarbazepine (ESL), shares structural similarities with carbamazepine (CBZ) and oxcarbazepine (OXC). It is rapidly and nearly completely metabolized to S-licarbazepine (about 95%) and, to a lesser extent, to R-licarbazepine and OXC. The plasma concentrations of these substances can be useful in assessing patient compliance and managing treatment in specific physiological or pathological conditions, even though the necessity for therapeutic drug monitoring (TDM) of ESL or its primary metabolite has not been definitively established, given that ESL is a relatively new medication. Undoubtedly, TDM is an effective strategy essential for optimizing clinical outcomes and facilitating individualized dose adjustments.

Consequently, the successful implementation of TDM in clinical practice and the advancement of pharmacokinetic studies rely on the availability of straightforward, accurate, and reliable analytical techniques[9].

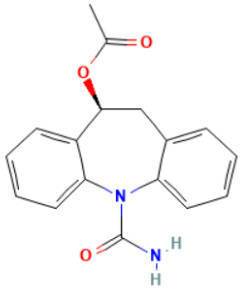

Fig no:- 1 Chemical Structure of Eslicarbazepine acetate

Mechanism of action:

Eslicarbazepine, an active metabolite with anticonvulsant properties, is produced from Eslicarbazepine acetate. Although the exact mechanism of action remains unclear, it is believed to involve the blockade of voltage-gated sodium channels. In vitro electrophysiological investigations have demonstrated that Eslicarbazepine suppresses recurrent neuronal activity by maintaining these channels in their inactivated state and preventing their return to the activated state. Additionally, Eslicarbazepine has been found to inhibit T-type calcium channels in laboratory experiments, which likely contributes to its anticonvulsant effects.

3. SUMMARY OF ANALYTICAL METHODS

Table no:- 1 Results of all the research paper of Eslicarbazepine Acetate

SL No	Drug	Method	Brief Description	Results
1	Eslicarbazepine Acetate	RP-HPLC	Column:C8, 5µ (4.6 x 150 mm) Mobile Phase: Acetonitrile – Tris (hydroxyl –methyl) amino methane solution (40:60 v/v) Detected Wavelength: 240nm Flow rate: 1.0 ml/min	Retention time: 3.23 min Linearity: 4-24 precision intra day: 0.3292 inter day: 0.2751 accuracy 80% : 99.90 100% : 99.91 120% : 100.11 Robustness data Flow rate: 0.9mL/min :3.273, 1.1mL/min :3.2800 Detection wavelength: 245nm: 3.253, 235nm: 3.297 LOD : 0.427 LOQ : 1.423
2	Eslicarbazepine Acetate	RP-HPLC	Column: Inertsil ODS 3V 150 x 4.6 mm, 5mm Mobile Phase: 0.1% orthophosphoric acid buffer, methanol and acetonitrile (500:250:250) Detected Wavelength: 210 nm Flow rate: 1.5 mL/min	Retention time: 4.233 min precision intra day: 0.3292 inter day: 0.2751 accuracy 50% : 98.45 100% : 99.65 150% : 9878 LOD : 2.40 LOQ : 7.29
3	Eslicarbazepine Acetate	RP-HPLC	Column: Finepak SIL C18T-5 (250 mm× 4.6 mm, 5µm	Retention time: 6.8 min linearity: 80-160

			Mobile Phase: Orthophosphoric acid was used to modify the pH of water to 2.5 (65:35) Detected Wavelength: 218nm Flow rate: 0.8 ml/min Retention time: 6.8 min	precision intra day: 0.7395 inter day: 01.0513 accuracy 80% : 100.13 100% : 100.29 120% : 98.34 LOD : 2.5 LOQ : 7.6
4	Eslicarbazepine Acetate	RP-HPLC	Column: C18, 5µm Waters column (150 mm × 4.6 mm) Mobile Phase: Methanol - Potassium dihydrogen phosphate solution (60:40, v/v) Detected Wavelength: 230nm Flow rate: 1.0 ml/min	Retention time: 8 min linearity: 0.9984 precision intra day: 0.017 inter day: 0.068 accuracy 80% : 98.0 100% : 98.9 120% : 98.4 LOD : 1.63 LOQ : 5.4362
5	Eslicarbazepine Acetate	RP-HPLC	Column: Inertsil ODS-2, (150 x 4.6mm), 5µm Mobile Phase: Buffer: Methanol: 50: 50 Detected Wavelength: 230nm Flow rate: 1ml/min	Retention time: 5.208 min linearity: 0.9996 precision intra day: 0.61 inter day: 0.21 accuracy 80% : 99.46 100% : 98.42 120% : 99.10
6	Eslicarbazepine Acetate	UPLC	Column: Waters Acquity BEH 150 x 2.1 mm, 1.7 mm, C18 column Mobile Phase: Potassium dihydrogen orthophosphate and acetonitrile (90:10, V/V) Detected Wavelength: 215nm Flow rate: 0.2 mL/min	Retention time: 2.63 min Linearity: 10-50 precision intra day: 0.635 inter day: 0.5208
7	Eslicarbazepine Acetate	RP-HPLC	Column: Dionex C18 column (250×4.6 mm, 5 µm Mobile Phase: Methanol and ammonium acetate 70:30 v/v. Detected Wavelength: 230nm Flow rate: 1.0 ml/min Retention time: 4.9 min	Retention time: 4.9 min precision intra day: 0.64 inter day: 0.10 accuracy 80% : 98.0 100% : 98.9 120% : 98.4 Robustness Flow rate : 4.87 Temperature: 4.90 LOD : 3.144 LOQ : 9.52
8	Eslicarbazepine Acetate	RP-HPLC	Column: LiChroCART Purospher Star (C18, 3 µm,55 mm×4 mm) Mobile Phase: water–methanol–acetonitrile (64:30:6, v/v/v)	Retention time: 9 min

			Detected Wavelength: 235nm Flow rate: 1.0 ml/min	

4. CONCLUSION

In the study of Eslicarbazepine acetate, several reverse-phase high-performance liquid chromatography (RP-HPLC) and ultra-performance liquid chromatography (UPLC) techniques have been developed. These techniques differ in terms of column type, mobile phase composition, detection wavelength, flow rate, and retention time. Most methods utilize C18 columns with mobile phases consisting of phosphate or acid-based buffers, organic solvents (such as methanol and acetonitrile), and water. The retention times vary widely, ranging from 2.63 to 9 minutes, indicating differences in efficiency and resolution based on the specific parameters employed. While RP-HPLC methods offer flexibility in mobile phase selection, the UPLC method (Entry 6) demonstrates the shortest retention time of 2.63 minutes with commendable efficiency, making it suitable for rapid analysis. Therefore, the selection of the appropriate technique can be optimized based on the required sensitivity, speed, and resolution.

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