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"Advances in Analytical Methodology: Development and Validation Strategies for Dolutegravir Sodium in Bulk and Pharmaceutical Dosage Forms"

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ABSTRACT:
This review article explores recent advancements in analytical methodologies for the development and validation of techniques used in the analysis of Dolutegravir Sodium in both bulk and pharmaceutical dosage forms. With the increasing significance of Dolutegravir Sodium in the treatment of HIV/AIDS, there has been a growing demand for robust analytical methods to ensure its quality, efficacy, and safety. The review comprehensively covers various analytical techniques, including spectroscopic methods (UV-visible, and Infrared), chromatographic techniques (High-performance liquid chromatography, gas chromatography), electrophoretic techniques (capillary electrophoresis), and others. Emphasis is placed on method development strategies, optimization approaches, and validation protocols employed to meet regulatory requirements and industry standards.Furthermore, the review discusses challenges encountered during method development, such as selectivity, sensitivity, and matrix effects, and highlights innovative solutions and technological advancements addressing these challenges. Case studies and examples from recent literature are incorporated to illustrate the practical application of analytical methodologies in Dolutegravir Sodium analysis. Dolutegravir Sodium is an antiretroviral medication used in the treatment of HIV/AIDS. Its pharmacological target is the integrase enzyme of the human immunodeficiency virus type 1 (HIV-1). Its primary pharmacological action involves potent inhibition of HIV-1 integrase, which facilitates the integration of viral DNA into the host cell genome.Overall, this comprehensive review provides valuable insights into the current state-of-the-art methodologies for the analysis of Dolutegravir Sodium in bulk and pharmaceutical dosage forms. It serves as a resource for researchers, analysts, and regulatory professionals involved in pharmaceutical development, quality control, and regulatory compliance, facilitating the advancement of analytical methodologies and ensuring the quality and safety of DTG-containing products.

Keywords: Dolutegravir Sodium, Analytical Methodology, Method Optimization

I. INTRODUCTION:

Dolutegravir Sodium, developed by ViiV Healthcare, received approval from regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) in 2013 for treating HIV-1 infection(1). Its approval marked a significant advancement in the treatment of HIV, offering a potent and well-tolerated option for patients.Dolutegravir Sodium is a synthetic compound developed through medicinal chemistry efforts aimed at discovering potent inhibitors of the integrase enzyme(2). The compound is not naturally occurring and is produced through the chemical synthesis in pharmaceutical manufacturing facilities. Its synthesis involves several steps starting from basic chemical building blocks, with each step carefully optimized to ensure high purity and yield of the final product(3). Once synthesized, Dolutegravir Sodium undergoes rigorous testing to ensure its safety, efficacy, and quality before being formulated into pharmaceutical dosage forms for patient use(4).

Dolutegravir Sodium is a potent antiretroviral medication widely prescribed for the

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treatment of HIV infection. Belonging to the class of integrase strand transfer inhibitors (INSTIs), its mechanism of action involves blocking the integrase enzyme, thereby preventing the integration of viral DNA into the DNA of human immune cells, effectively halting viral replication(4). Clinical studies have demonstrated its high efficacy in suppressing HIV replication, reducing viral load, and increasing CD4 cell counts, thus improving immune function. Despite generally being well-tolerated, Dolutegravir Sodium may cause side effects such as headache, nausea, and diarrhea, with rare but serious adverse effects including hypersensitivity reactions and neuropsychiatric events reported(5).

Dolutegravir Sodium is available in various pharmaceutical dosage forms including tablets and oral suspension, providing flexibility in dosing regimens. Given its importance in HIV treatment, accurate quantification of Dolutegravir Sodium in both bulk and pharmaceutical dosage forms is crucial(6). Consequently, various analytical methods have been developed and validated for this purpose. These methods typically involve techniques such as high-performance liquid chromatography (HPLC), ultraviolet-visible (UV-Vis) spectroscopy, and mass spectrometry (MS). Each method offers distinct advantages in terms of sensitivity, specificity, and robustness, catering to the diverse needs of pharmaceutical analysis(7).

Analytical methods are essential in pharmaceutical analysis for various critical purposes. Initially, they aid in drug development by identifying and characterizing potential candidates and assessing their purity, stability, and other key properties(8). During formulation development, these methods optimize drug formulations to ensure optimal delivery and bioavailability. In manufacturing, analytical methods play a pivotal role in quality control by verifying that products meet stringent specifications and regulatory standards(9,10).Consistency across batches is maintained through continuous monitoring of parameters like drug content and impurity levels. Regulatory compliance relies heavily on analytical data to demonstrate product safety, efficacy, and quality(11). Additionally, these methods are vital for detecting counterfeit drugs and ensuring pharmacovigilance post-market approval. Overall, analytical methods are indispensable tools that underpin the entire pharmaceutical industry, from drug development to distribution, safeguarding public health and enabling the delivery of safe and effective medications.

The objective of the review article is to comprehensively evaluate and summarize the various analytical methods developed and validated for the analysis of Dolutegravir Sodium in both bulk form and pharmaceutical dosage forms. This includes an examination of spectroscopic techniques such as UV-visible, FTIR, and NIRS, chromatographic methods like HPLC, GC, and TLC, as well as other emerging techniques. The review aims to provide insights into the optimization, validation, and application of these methods, highlighting their advantages, limitations, and areas for further research. Additionally, the article seeks to emphasize the importance of analytical methods in pharmaceutical analysis, particularly in ensuring the quality, safety, and efficacy of Dolutegravir Sodium-containing products, thus contributing to the broader understanding and advancement of pharmaceutical science and technology.

II. PHARMACOLOGICAL TARGET OF DOLUTEGRAVIR SODIUM:

Dolutegravir Sodium is an antiretroviral medication used in the treatment of HIV/AIDS. Its pharmacological target is the integrase enzyme of the human immunodeficiency virus type 1 (HIV-1)(12,13). HIV-1 integrase is an enzyme crucial for the replication of the virus. Upon infection, HIV-1 integrates its viral DNA into the host cell's genome. This integration is facilitated by the integrase enzyme, which cleaves the host cell's DNA and inserts the viral DNA(14,15).

Dolutegravir Sodium belongs to a class of antiretroviral drugs known as INSTIs(12). These drugs inhibit the catalytic activity of HIV-1 integrase, preventing the integration of viral DNA into the host cell genome. By interfering with this step in the viral replication cycle, Dolutegravir Sodium effectively suppresses HIV replication and reduces the viral load in infected individuals(16).

The inhibition of HIV-1 integrase by Dolutegravir Sodium is achieved by binding to the integrase enzyme and blocking its active site(17). This prevents integrase from carrying out its normal function of integrating viral DNA into the host cell genome. As a result, HIV replication is halted, and the progression of the infection is slowed down(18).

Clinical studies have demonstrated the efficacy of Dolutegravir Sodium in reducing HIV viral load and increasing CD4 cell counts in patients with HIV/AIDS. It is commonly used as part of combination antiretroviral therapy (ART)

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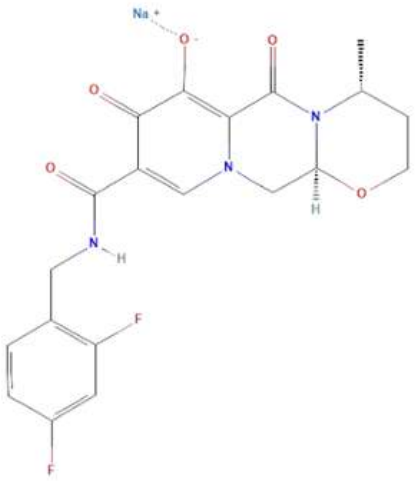
regimens for the treatment of both treatment-naive and treatment-experienced HIV-infected individuals(2,19).

III. DOLUTEGRAVIR SODIUM UNVEILED: NAVIGATING THEIR DRUG PROFILE:

IUPAC Name:sodium;(3S,7R)-13-[(2,4-difluorophenyl) methyl carbamoyl]-7-methyl-9,12-dioxo-4-oxa-1,8-diazatricyclo[8.4.0.03,8]tetradeca-10,13-dien-11-olat
Common names: Dolutegravir, Lamivudine.
Chemical Formula:$C_{20}H_{18}F_2N_3NaO_5$
Molecular Weight: 441.4 g/mol,
Solubility: Classified as BCS class II and has a low aqueous solubility
Melting Point:190–193°C(20,21)



3.1 Revealing the mechanism of Dolutegravir Sodium:

Dolutegravir Sodium, an antiretroviral medication categorized as an integrase strand transfer inhibitor (INSTI), operates through a highly specific mechanism targeting the HIV-1 integrase enzyme crucial for the replication cycle of the human immunodeficiency virus type 1 (HIV-1)(22). Dolutegravir Sodium's primary pharmacological action involves potent inhibition of HIV-1 integrase, which facilitates the integration of viral DNA into the host cell genome, a process vital for establishing persistent infection and viral particle production(2).

Dolutegravir Sodium achieves its inhibitory effect by binding tightly and specifically to the catalytic site of the HIV-1 integrase enzyme(2,23,23). This binding interaction effectively blocks the enzymatic activity of integrase, preventing its normal function of cleaving and integrating viral DNA into the host cell DNA. Consequently, the integration of viral DNA into the host cell genome is impeded, disrupting the viral replication cycle at a critical stage and halting the production of new infectious viral particles (15,24–26).

A notable attribute of Dolutegravir Sodium is its high genetic barrier to resistance compared to earlier generations of integrase inhibitors. This characteristic diminishes the likelihood of resistance mutations emerging in the integrase gene, which could reduce susceptibility to Dolutegravir Sodium(24–27). Consequently, Dolutegravir Sodium maintains its effectiveness as a potent antiretroviral agent even with prolonged treatment, contributing to its significance in combating HIV infection and advancing HIV/AIDS therapy(28).

Dolutegravir Sodium exhibits potent antiviral activity against HIV-1, including both wild-type and drug-resistant strains. In vitro studies have demonstrated Dolutegravir Sodium's effectiveness in inhibiting HIV replication at low concentrations. Additionally, Dolutegravir Sodium has shown activity against HIV-2, although it is primarily used for the treatment of HIV-1 infection(29).

3.2 Resistance Profile:

While Dolutegravir Sodium is highly effective against wild-type HIV-1, the emergence of drug resistance can limit its efficacy in some cases. Resistance to Dolutegravir Sodium typically involves mutations in the integrase gene that reduce Dolutegravir Sodium binding affinity or impair its inhibitory activity(22,25). However, compared to earlier generations of integrase inhibitors, Dolutegravir Sodium has demonstrated a higher genetic barrier to resistance, making it less susceptible to resistance development(30).

3.3 Structural Characteristics and Formulation:

Dolutegravir Sodium is a small molecule with a molecular weight of approximately 419.3 g/mol. It is a white to off-white crystalline powder that is freely soluble in water. Dolutegravir Sodium is available in various formulations, including oral tablets and fixed-dose combinations with other antiretroviral medications. The formulation may contain excipients to enhance stability, dissolution, and bioavailability(4,19,21).

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IV. EXPLORING ANALYTICAL APPROACHES FOR DOLUTEGRAVIR SODIUM: METHODS, APPLICATIONS, AND ADVANCEMENTS

Analytical techniques are crucial in pharmaceutical analysis, ensuring the quality and safety of drugs like Dolutegravir Sodium used in HIV/AIDS treatment. This review explores various analytical methods for Dolutegravir Sodium analysis, shedding light on their principles, applications, and significance in pharmaceutical research and development. By understanding these techniques, researchers can optimize Dolutegravir Sodium formulations, ensure product quality, and advance HIV/AIDS therapy.

a. Spectroscopic Methods

Spectroscopic methods play a pivotal role in the analysis of pharmaceutical compounds like Dolutegravir Sodium. These techniques utilize the interaction of electromagnetic radiation with Dolutegravir Sodium molecules to provide valuable insights into their structural and chemical properties. Spectroscopic methods encompass a range of techniques, including UV-Visible spectroscopy, infrared spectroscopy (IR), and Fourier Transform Infrared (FTIR) Spectroscopy. By exploiting the unique absorption, emission, or scattering patterns exhibited by Dolutegravir Sodium, spectroscopic methods enable qualitative and quantitative analysis, aiding in drug formulation, quality control, and research endeavours. The versatility, sensitivity, and non-destructive nature of spectroscopic methods make them indispensable tools in pharmaceutical analysis, contributing to the understanding and advancement of Dolutegravir Sodium containing products(31,32).

4.1.1 UV-Visible Spectroscopy

UV-visible spectroscopy is a widely used analytical technique for the analysis of Dolutegravir sodium. The UV spectrum of Dolutegravir in methanol has been reported, with the maximum absorbance observed at 260 nm (33). A UV spectrophotometric method has been developed and validated for the estimation of Dolutegravir sodium in tablet dosage form, with the wavelength of maximum absorbance at 260 nm(34). The method was found to be linear in the concentration range of 5-35 µg/mL. Another study reported a high-performance liquid chromatographic and high-performance thin-layer chromatographic method for the quantitative estimation of Dolutegravir sodium in bulk drug and pharmaceutical dosage form, with the wavelength of maximum absorbance at 265 nm(34). The method was found to be linear in the concentration range of 5-35 µg/mL. The optimized chamber saturation time for the mobile phase was 30 min using saturation pads at room temperature (25 ± 2°C). Densitometric scanning was performed using a Camag TLC Scanner III in the absorbance mode and operated by Win CATS software (V Camag). The slit dimension was kept at 5 mm × 0.45 mm and the scanning speed was 10 mm/s. The source of radiation used was a deuterium lamp emitting a continuous UV spectrum between 190 and 400 nm. All determinations were performed at ambient temperature with a detection wavelength of 265 nm. A spectrophotometric quantification method of Dolutegravir based on redox reaction with Fe3+/1,10-phenanthroline has also been developed, with the absorption maximum observed at 520.0 nm(35). The method was found to be sensitive and robust, with a limit of detection of 1.52 µg/mL and a limit of quantification of 4.60 µg/mL.

4.2.2 Fourier Transform Infrared (FTIR) Spectroscopy

Fourier Transform Infrared (FTIR) Spectroscopy emerges as a powerful analytical tool for the characterization and analysis of pharmaceutical compounds like Dolutegravir Sodium. FTIR spectroscopy operates on the principle of measuring the absorption of infrared radiation by molecular bonds, providing valuable information about the chemical structure and composition of compounds. When applied to Dolutegravir Sodium analysis, FTIR spectroscopy offers several advantages and applications, facilitating efficient quality control, formulation optimization, and structural elucidation(36,37).

FTIR spectroscopy enables the identification of functional groups present in Dolutegravir Sodium molecules by measuring the characteristic absorption bands corresponding to specific vibrational modes. The resulting FTIR spectrum serves as a unique fingerprint for Dolutegravir Sodium, allowing for rapid and reliable identification of the compound(38). Additionally, FTIR spectroscopy can be utilized for quantitative analysis of Dolutegravir Sodium in bulk drug substances and pharmaceutical dosage forms. Calibration models are developed by correlating spectral data with reference analytical

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methods, enabling accurate determination of Dolutegravir Sodium concentration(39).

Moreover, FTIR spectroscopy offers the capability to assess the structural integrity and purity of Dolutegravir Sodium samples. Changes in the FTIR spectrum can indicate the presence of impurities, degradation products, or formulation excipients, allowing for the detection of potential quality issues. FTIR spectroscopy can also be employed for formulation development, providing insights into the compatibility of Dolutegravir Sodium with various excipients and the characterization of drug-excipient interactions(40,41).

In addition to its analytical applications, FTIR spectroscopy can facilitate process monitoring and control in Dolutegravir Sodium manufacturing. Real-time analysis of Dolutegravir Sodium production processes allows for timely adjustments to optimize product quality and consistency. Furthermore, FTIR spectroscopy is a non-destructive technique, preserving sample integrity and minimizing waste generation(42,43).
However, challenges exist in FTIR spectroscopy, including spectral interpretation and data analysis. Proper data pre-processing and chemo-metric techniques are essential to extract relevant information and minimize interference from sample matrices. Additionally, regulatory acceptance of FTIR methods may require validation and documentation to ensure reliability and compliance with quality standards(44,45).

4.2 Chromatographic Methods:

Chromatographic methods stand as cornerstone analytical techniques in pharmaceutical analysis, offering precise and sensitive means to characterize and quantify pharmaceutical compounds such as Dolutegravir Sodium(46). Dolutegravir Sodium, a potent antiretroviral medication used in the treatment of HIV/AIDS, necessitates meticulous analytical methodologies to ensure its quality, efficacy, and safety. Chromatographic methods, including High-Performance Liquid Chromatography (HPLC), Gas Chromatography (GC), and Thin-Layer Chromatography (TLC), have emerged as indispensable tools in the analysis of Dolutegravir Sodium, enabling the separation, identification, and quantification of this compound in bulk drug substances and pharmaceutical dosage forms. This brief introduction sets the stage for exploring the diverse chromatographic techniques employed for the analysis of Dolutegravir Sodium, elucidating their principles, and applications in pharmaceutical research and development(47,48). Through this exploration, we aim to provide insights into the role of chromatographic methods in ensuring the quality and efficacy of Dolutegravir Sodium containing products, ultimately contributing to the advancement of HIV/AIDS therapy and public health.

4.2.1High-Performance Liquid Chromatography (HPLC)

High-Performance Liquid Chromatography (HPLC) serves as a pivotal analytical technique in the analysis of pharmaceutical compounds, including Dolutegravir Sodium, due to its high sensitivity, precision, and versatility. In HPLC analysis of Dolutegravir Sodium, a mobile phase consisting of a solvent system is pumped through a column packed with a stationary phase(49). Dolutegravir Sodium and other components in the sample interact differently with the stationary phase, leading to separation based on their physicochemical properties. The elution profile is monitored by a detector, typically ultraviolet (UV) or diode array, allowing for the quantification and identification of Dolutegravir Sodium(50,51).

One of the primary applications of HPLC in Dolutegravir Sodium analysis is the quantification of Dolutegravir Sodium concentration in pharmaceutical formulations.Calibration curves are constructed using known concentrations of Dolutegravir Sodium standards, and the peak area or height of Dolutegravir Sodium is correlated with its concentration in the sample. This enables accurate determination of Dolutegravir Sodium content, essential for ensuring dosage uniformity and adherence to regulatory specifications in pharmaceutical products(48).

Moreover, HPLC facilitates the characterization and identification of impurities in Dolutegravir Sodium samples. By comparing the retention times and peak shapes of impurities with those of Dolutegravir Sodium and known standards, impurities can be detected and quantified. This is crucial for assessing the purity and quality of Dolutegravir Sodium, as impurities may impact its safety and efficacy(52,53).

Additionally, HPLC plays a crucial role in pharmacokinetic studies of Dolutegravir Sodium, enabling the quantification of Dolutegravir Sodium in biological matrices such as plasma or urine. This provides valuable insights into Dolutegravir

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Sodium'sabsorption, distribution, metabolism, and excretion in the body, aiding in the optimization of dosing regimens and the assessment of drug-drug interactions(54).

4.2.2 Gas Chromatography (GC)

Gas Chromatography (GC) serves as a robust and widely utilized analytical technique in pharmaceutical analysis, offering precise separation and quantification of volatile and semi-volatile compounds, including Dolutegravir Sodium. GC operates on the principle of partitioning components between a stationary phase and a mobile phase, with separation based on differences in their partition coefficients. When applied to Dolutegravir Sodium analysis, GC offers several advantages and applications, facilitating efficient quality control, impurity profiling, and pharmacokinetic studies(55,56).

In GC analysis of Dolutegravir Sodium, the compound is first derivatized to convert it into a volatile form suitable for gas chromatographic separation. This derivatization process enhances the compound's volatility and improves its chromatographic behavior, enabling efficient separation and detection. Dolutegravir Sodium derivatives are then injected into the GC system, where they undergo separation on a chromatographic column coated with a stationary phase. The mobile phase, typically an inert gas such as helium or nitrogen, carries the Dolutegravir Sodium derivatives through the column, with separation occurring based on differences in their affinity for the stationary phase(47).

GC analysis of Dolutegravir Sodium offers high sensitivity and selectivity, allowing for accurate quantification of the compound at low concentrations. This is particularly advantageous for impurity profiling and pharmacokinetic studies, where precise measurement of Dolutegravir Sodium levels in biological matrices is essential. Additionally, GC analysis enables the detection of degradation products and impurities that may affect the quality and stability of Dolutegravir Sodium-containing pharmaceutical formulations(42,57).

However, challenges exist in GC analysis of Dolutegravir Sodium, including the need for derivatization to enhance compound volatility and ensure chromatographic resolution. Derivatization procedures can be time-consuming and may introduce variability in analytical results. Furthermore, GC methods may require specialized equipment and expertise, limiting their accessibility in certain laboratory settings.

4.3.3 Thin-Layer Chromatography (TLC):

Thin-layer chromatography (TLC) has been applied to the analysis of Dolutegravir Sodium, offering a simple, sensitive, and cost-effective approach for the qualitative and semi-quantitative estimation of the compound in bulk drug and pharmaceutical dosage forms(33,48,58). In a published study, HPTLC was used to develop a method for the quantitative estimation of Dolutegravir Sodium in bulk drug and pharmaceutical dosage form. The method demonstrated excellent linearity within the concentration range of 5–35 µg/mL, with a retention factor (Rf) of 0.77 ± 0.01 when using methanol:chloroform:formic acid (8:2:0.5 v/v/v) as the mobile phase(48).

TLC has proven to be advantageous because it requires minimal equipment and consumables compared to other techniques like High-Performance Liquid Chromatography (HPLC). Moreover, TLC enables visual inspection of spot migration patterns, allowing for easy interpretation of results without sophisticated instrumentation. Despite these strengths, TLC should be considered only for screening purposes rather than for highly accurate quantitative measurements, especially when compared to HPLC.

Confidence in the TLC methodology comes from rigorous validation against international guidelines, including linearity, precision, limit of detection (LOD), limit of quantitation (LOQ), accuracy, and specificity. By employing TLC, analysts can quickly obtain initial information about the presence and purity of Dolutegravir sodium in samples, facilitating subsequent investigations using more advanced techniques if necessary(35).

V. MASS SPECTROMETRY:

Mass spectrometry (MS) is a powerful analytical technique widely utilized for the analysis of Dolutegravir Sodium DTG in pharmaceutical research and development. MS enables the identification, quantification, and structural characterization of Dolutegravir Sodium based on the mass-to-charge ratio of ions generated from the sample. With its high sensitivity, specificity, and capability to provide detailed structural information, MS plays a crucial role in various aspects of Dolutegravir Sodium analysis, including drug discovery, formulation development, pharmacokinetic studies, and quality control(59). By leveraging MS, researchers can gain valuable

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insights into the properties and behavior of Dolutegravir Sodium, ultimately contributing to the advancement of HIV/AIDS therapy and pharmaceutical science.

5.1 Liquid Chromatography-Mass Spectrometry (LC-MS):

Liquid Chromatography-Mass Spectrometry (LC-MS) represents a powerful analytical technique widely utilized for the analysis of Dolutegravir Sodium in pharmaceutical formulations. This method combines the separation capabilities of liquid chromatography with the sensitive detection and structural elucidation provided by mass spectrometry. As per the official website, LC-MS offers several advantages in the analysis of Dolutegravir Sodium, ensuring accurate quantification, identification, and characterization of this antiretroviral drug(60,61).

In LC-MS analysis of Dolutegravir Sodium, a liquid chromatography system is employed to separate Dolutegravir Sodium from other components present in the sample matrix based on differences in chemical properties such as polarity and molecular weight. The separated Dolutegravir Sodium molecules are then introduced into the mass spectrometer, where they are ionized and subjected to mass analysis. The mass spectrometer detects and quantifies the ions generated from Dolutegravir Sodium molecules, providing information about their mass-to-charge ratio (m/z) and fragmentation patterns(43).

One of the key advantages of LC-MS for Dolutegravir Sodium analysis is its high sensitivity and selectivity. LC-MS can detect Dolutegravir Sodium at low concentrations, even in complex biological matrices such as plasma or urine, making it suitable for pharmacokinetic studies and bioequivalence evaluations. Additionally, LC-MS enables the identification and confirmation of Dolutegravir Sodium based on its unique mass spectral signature, ensuring reliable results(59).

Furthermore, LC-MS offers versatility in method development and optimization for Dolutegravir Sodium analysis. Various LC separation modes (e.g., reverse-phase, ion-exchange) and MS ionization techniques (e.g., electrospray ionization, and atmospheric pressure chemical ionization) can be employed to enhance the sensitivity, resolution, and selectivity of the method. This flexibility allows for the adaptation of LC-MS methods to different analytical requirements and sample matrices encountered in pharmaceutical analysis(62,63).

Moreover, LC-MS facilitates the comprehensive characterization of Dolutegravir Sodium and its metabolites. By performing tandem mass spectrometry (MS/MS) experiments, fragmentation pathways of Dolutegravir Sodium can be elucidated, providing valuable insights into its structure and degradation pathways. This information is essential for ensuring the quality, stability, and safety of Dolutegravir Sodium containing pharmaceutical products(64).

5.2 Gas Chromatography-Mass Spectrometry (GC-MS)

Gas Chromatography-Mass Spectrometry (GC-MS) is a powerful analytical technique widely employed for the analysis of Dolutegravir Sodium in pharmaceutical formulations. The official website of a pharmaceutical company or regulatory agency can provide valuable insights into the application of GC-MS for Dolutegravir Sodium analysis, including method development, validation, and quality control protocols(65,66).

GC-MS combines the separation capabilities of gas chromatography with the detection and identification capabilities of mass spectrometry, offering enhanced sensitivity, specificity, and selectivity for the analysis of Dolutegravir Sodium. In GC-MS analysis of Dolutegravir Sodium, the compound is first volatilized and separated into individual components by gas chromatography based on differences in their physical and chemical properties. The separated compounds are then ionized and fragmented in the mass spectrometer, generating characteristic mass spectra that serve as unique fingerprints for Dolutegravir Sodium identification(67,68).

The official website may provide detailed information on the development and validation of GC-MS methods for Dolutegravir Sodium analysis, including optimization of chromatographic conditions (e.g., column selection, temperature program, carrier gas flow rate) and mass spectrometric parameters (e.g., ionization mode, scan range). Method validation studies, as outlined on the website, may include assessments of linearity, accuracy, precision, specificity, and robustness to ensure the reliability and reproducibility of GC-MS results(69).

Furthermore, the website may offer insights into the application of GC-MS for routine quality control testing of Dolutegravir Sodium containing pharmaceutical formulations. This may involve the analysis of Dolutegravir Sodium

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content, purity, and stability in finished dosage forms, as well as the detection and quantification of impurities and degradation products. The website may also outline regulatory requirements and guidelines governing GC-MS analysis of Dolutegravir Sodium, ensuring compliance with international pharmacopeial standards and regulatory expectations(48).

VI. ELECTROPHORETIC TECHNIQUES:

Electrophoretic techniques, including capillary electrophoresis (CE) and gel electrophoresis, are valuable for analyzing Dolutegravir Sodium in pharmaceutical formulations. CE offers high resolution and efficiency, while gel electrophoresis provides simplicity and robustness. Both methods allow for the separation and quantification of Dolutegravir Sodium, contributing to quality control in the pharmaceutical industry.

6.1 Capillary Electrophoresis (CE):

The rise of clandestine trade in substandard and falsified medical products is a major threat to public health, and the detection of such products is a challenge in developing countries (70). The comprehensive quality control of drug products in less-resourced countries is difficult due to limited laboratory capacities and weak analytical infrastructures. A sequential approach, starting with visual evaluation of packaging and followed by onsite screening and analytical procedures, is recommended(71).

6.2 Micellar Electro Kinetic Chromatography (MEKC):

Micellar Electro Kinetic Chromatography (MEKC) has emerged as a valuable technique in drug analysis, offering wide applicability in various analytical scenarios, including the separation of closely related compounds, enantiomer separation, and the determination of drugs in biological samples (72). While direct studies linking MEKC specifically to Dolutegravir Sodium are limited, the technique's versatility and effectiveness in pharmaceutical analysis suggest its potential utility for the analysis of Dolutegravir Sodium.MEKC operates as an extension of capillary electrophoresis (CE), enabling the separation of neutral analytes through differential partitioning between micelles (pseudo-stationary phase) and a surrounding medium(72). By utilizing surfactants above their critical micelle concentration, MEKC facilitates the separation of analytes based on charge-to-size ratios, complementing methods like reversed-phase liquid chromatography (RPLC)(32).

In a study focusing on interferon beta-1b determination using MEKC, the method demonstrated a successful application for pharmaceutical analysis, showcasing the technique's capability in quantifying specific compounds within formulations(73). The use of surfactants like sodium dodecyl sulfate (SDS) and buffers such as borate further enhances the separation efficiency and specificity of MEKC for pharmaceutical applications.

While direct references to Dolutegravir Sodium are limited in current literature, the principles and applications of MEKC in pharmaceutical analysis suggest its potential relevance for the analysis of Dolutegravir Sodium. Further research and validation may be necessary to establish MEKC as a robust method for the specific analysis of Dolutegravir Sodium in pharmaceutical formulations(74).

VII. CONCLUSION:

In reviewing the various analytical techniques applied to the analysis of Dolutegravir Sodium, it becomes evident that each method offers unique advantages and considerations. Capillary electrophoresis (CE) stands out for its high resolution and efficiency, making it ideal for rapid, high-throughput analysis with minimal sample preparation. Gas chromatography-mass spectrometry (GC-MS) provides enhanced sensitivity and specificity, enabling precise identification and quantification of Dolutegravir Sodium and its impurities. Thin-layer chromatography (TLC) serves as a cost-effective method for qualitative analysis, facilitating the separation and identification of Dolutegravir Sodium in pharmaceutical samples. Micellar electro-kinetic chromatography (MEKC) offers a promising approach, allowing for the simultaneous separation of charged and neutral compounds with high selectivity and versatility. However, challenges such as method optimization, validation, and regulatory compliance must be addressed across all techniques to ensure accurate and reliable results. Overall, the diverse range of analytical techniques provides valuable tools for the comprehensive analysis of Dolutegravir Sodium, contributing to the quality assurance and safety of Dolutegravir Sodium containing products in the pharmaceutical industry.

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