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A REVIEW ON THE ANALYTICAL METHODS FOR ESTIMATION OF FIMASARTAN IN BULK AND PHARMACEUTICAL DOSAGEFORM

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ABSTRACT

Fimasartan, an angiotensin II receptor blocker (ARB), is widely used for managing hypertension and cardiovascular disorders due to its high selectivity for the AT1 receptor. Ensuring its efficacy, safety, and regulatory compliance necessitates robust analytical methods for its quantification in bulk drugs and pharmaceutical formulations. High performance liquid chromatography (HPLC), Ultra performance liquid chromatography (UPLC), High performance thin layer chromatography (HPTLC), and Liquid Chromatography-Tandem mass spectrometry (LC-MS/MS) are some of the analytical methods used for Fimasartan that are examined in this review. These methods provide high sensitivity and accuracy, making them essential for stability testing, impurity profile and pharmacokinetic assessment. Additionally, UV-Visible spectrometry has been utilized for qualitative and quantitative analysis due to its simplicity and cost – effectiveness. Stability indicating methods are emphasized for detecting degradation products under stress conditions, ensuring regulatory compliance. Validation parameters set by the International Council for Harmonization (ICH), including accuracy, precision, robustness, and specificity, is discussed. Despite the effective ness of current techniques, challenges such as high cost and labor-intensive procedures persist. Future trends focus on automation, green chemistry practices, and IA-driven method optimization, improving efficiency and sustainability in Fimasartan analysis.

INTRODUCTION

Fimasartan, an angiotensin II receptor blocker (ARB), was developed by Boryung Pharmaceutical in South Korea and approved in 2010 for hypertension. Research began in the early 2000s, with clinical trials confirming its safety and benefits. It is now used in monotherapy and combination therapies for managing hypertension and related cardiovascular conditions. Its chemical structure, (2-butyl-4-chloro-1-{[2′ (1H-tetrazol-5-yl)-1, 1′-biphenyl-4-yl] methyl}imidazole-5-carboxylic acid), exhibits a high binding affinity. Fimasartan selectively inhibits AT1R, which is key in regulating blood pressure and fluid balance.3 By blocking this receptor, Fimasartan prevents angiotensin II from causing vasoconstriction and aldosterone secretion. This leads to vasodilation, reduced blood pressure, and improved cardiovascular

outcomes. Robust analytical methods are essential for ensuring pharmaceutical compounds' efficacy, safety, and quality. Fimasartan is generally well tolerated, with adverse effects such as dizziness or mild hypotension occurring infrequently. In addition to therapeutic studies, considerable research has focused on analytical methods and instrumentation used to evaluate Fimasartan in bulk drug, formulations, and biological samples. High-Performance Liquid Chromatography (HPLC) and Ultra-Performance Liquid Chromatography (UPLC) are widely employed for quantitative determination, often coupled with UV detection or tandem mass spectrometry (LC–MS/MS) for high sensitivity. These methods are crucial for bioequivalence studies, pharmacokinetic profiling, and stability testing.

MECHANISM OF ACTION: Fimasartan selectively blocks AT1R, reducing vascular resistance, aldosterone secretion, and fluid retention. This leads to vasodilation and lowered blood pressure. Unlike non-selective ARBs, Fimasartan minimizes adverse effects linked to angiotensin II type 2 receptor stimulation, such as hyperkalemia and renal dysfunction. Renin–angiotensin–aldosterone system (RAAS), normally binds to AT_1 receptors present in vascular smooth muscle, the myocardium, kidney, and adrenal cortex. Activation of these receptors promotes vasoconstriction, aldosterone secretion, sodium and water retention, increased sympathetic drive, and vascular remodeling, all of which contribute to the development and progression of hypertension and related cardiovascular disease. By selectively antagonizing AT_1 receptors, vasodilation, decreased peripheral vascular resistance, reduced afterload, and a subsequent fall in systemic blood pressure.

PHARMACOKINETICS OF FIMASARTIN: After oral administration, Fimasartan is quickly absorbed, reaching peak plasma concentrations (Cmax) in 0.5 to 3 hours. Its absorption is influenced by factors such as food intake, which can slightly delay Tmax without affecting the overall bioavailability. Fimasartan exhibits dose-proportional pharmacokinetics within the therapeutic range. Once absorbed, Fimasartan binds extensively (over 99%) to plasma proteins, primarily albumin. This high protein-binding affinity aids in its sustained therapeutic effect by ensuring a stable concentration in the bloodstream. The apparent volume of distribution indicates limited penetration into tissues outside the systemic circulation.

PHARMACODYNAMICS OF FIMASARTIN: The liver metabolizes Fimasartan predominantly via oxidative pathways and glucuronidation. Cytochrome P450 enzymes play a minimal role, reducing the likelihood of significant drug-drug interactions. Fimasartan is primarily excreted unchanged in feces (about 80%), with a smaller fraction eliminated via urine. Its elimination half-life ranges from 5 to 16 hours, depending on the dose and individual patient factors, allowing for once-daily dosing in most clinical scenarios. Fimasartan is primarily indicated for essential hypertension.

ANALYTICAL METHODS FOR FIMASARTIN: The analytical methods used to evaluate Fimasartan, providing an over view of chromatography and spectroscopic methods and emphasizing their application in pharmaceutical analysis.

1. Chromatographic Methods: Chromatographic methods are laboratory techniques that uses a mobile phase (a liquid or gas) and a stationary phase (a solid or liquid) to separate, identify, and purify the components of a mixture. Separation occurs because components distribute themselves between the two phases based on their differencing affinities. This differential movements allows for the physical separation of components for qualitative and quantitative analysis. Chromatographic techniques are vital for the analytical assessment of Fimasartan, allowing for its separation, identification, and quantification in various matrices. Below are the primary techniques used:

PHYSICAL AND CHEMICAL PROPERTIES:

Table no.1 physical and chemical properties of fimasartin:

Chemical name	2-(1-((2-(2H-Tetrazol-5-yl)-[1,1-biphenyl]-4-yl)methyl)-2-butyl-4-methyl-6-oxo-1,6-dihydropyrimidin-5-yl)-N,N-dimethylethanethioamide
CAS Number	247257-48-3
Molecular formula	C27H31N7OS
Molecular weight	501.65mg/mol
Half life	9-16hrs
Solubility	Very solubility in water, but its solubility is significantly higher in organic solvent like DMSO and ethanol
Category	Angiotensin II receptor antagonist (ARB)
BCS	Class II

CHEMICAL STRUCTURE OF FIMASARTIN: 2-(1-((2-(2H-Tetrazol-5-yl)-[1,1-biphenyl]-4-yl)methyl)-2-butyl-4-methyl-6-oxo-1,6-dihydropyrimidin-5-yl)-N,N-dimethylethanethioamide

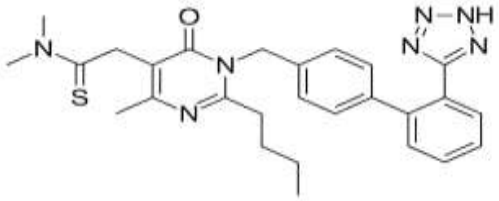

Figure 1: Structure of Fimasartin

Table 2 Representative chromatographic and MS methods for Fimasartan

Techniques	Sample matrix	Column(type)	Mobile phase	Detector	Linearity	Remarks
LC-MS/MS	Human plasma	Reversed phase(UPLC/C18)	Gradient LC with aqueous buffer	MS/MS	1-500mg/ml	Validate for pk and DDI studies
UPLC-MS/MS	Human plasma	UPLC C 18	Optimized gradient for speed	MS/MS	Reported validated sensitive assay for plasma pk	Faast UPLC condition for high through put.
RP-HPLC	Tablet	Symmetry c18	Methanol	DAD@240nm	Validated for assay	Robust
HPLC+UV	Tablet	C18	Isocratic	DAD	Validate for simultaneous estimation	Useful for simultaneous estimation

Table 3: Representative spectroscopic and fluorometric methods

Technique	Sample matrix	Principle	Remarks
Spectrofluorimetric	Plasma	Native fluorescence or derivative reaction, ecofriendly solvents	Ecofriendly solvents (water or ethanol)
Spectrofluorimetric / probe-based	Plasma (spiked)	Enhanced sensitivity using probes or derivatization	Emerging green protocols
UV-Visible	Tablet	Ratio spectra, dual-wavelength techniques	Low cost, suitable for routine qc

1.1 High-Performance Liquid Chromatography (HPLC): A widely

employed method for quantifying Fimasartan in bulk drug substances and pharmaceutical formulations due to its precision, reproducibility, and adaptability. HPLC utilizes a stationary phase and a liquid mobile phase to effectively separate components, enabling accurate determination of drug content and impurities.

1.2 Ultra-Performance Liquid Chromatography (UPLC): Operating at higher pressures compared to HPLC, UPLC enables faster analysis and higher resolution, making it particularly advantageous for stability studies where quick and precise detection of degradation products is necessary.

1.3 Reverse-Phase Liquid Chromatography (RP-HPLC): RP-HPLC, a widely used analytical method for estimating Fimasartan in pharmaceutical formulations and bulk, uses a polar mobile phase and a non-polar stationary phase to achieve effective separation. This method offers high sensitivity, selectivity, and robustness, making it suitable for routine quality control and stability studies.

1.4 High-Performance Thin Liquid Chromatography (HPTLC): A sophisticated chromatographic method for both qualitative and quantitative compound analysis is High-Performance Thin Layer Chromatography (HPTLC). It offers high resolution, automation, and reproducibility compared to conventional TLC. HPTLC is widely used in pharmaceutical, food, and environmental analysis for identifying and quantifying complex mixtures efficiently.

1.5 Liquid Chromatography-Tandem Mass Spectrometry (LCMS-MS): A potent analytical method that combines mass spectrometry for detection and liquid chromatography for separation is called Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). It provides high sensitivity, specificity, and accuracy, making it ideal for pharmaceutical, forensic, environmental, and biological analyses, including drug quantification, metabolite profiling, and biomarker identification.

2. SPECTROSCOPIC METHODS: Spectroscopic methods study the interaction of matter with electromagnetic radiation, providing valuable insights into the chemical structure and molecular behavior of substances like Fimasartan.Below are some standard spectroscopic methods:

2.1 UV-visible spectroscopy: This method provides information about a substance's electronic transitions by measuring how much ultraviolet and visible light it absorbs. UV-Visible spectroscopy is widely used to quantitatively estimate compounds like Fimasartan in bulk and pharmaceutical dosage forms. It is simple, cost-effective, and efficient for routine analysis, although it requires compounds to absorb in the UV or visible range.

3. Fluorimetry: Fluorimetry is an analytical technique that involves exciting the substance with ultra violet light, causing it to emit visible light through a process called fluorescence.

ANALYTICAL METHOD DEVELOPMENT:

Analytical method development ensures accurate, precise, and reproducible drug analysis. It involves selecting suitable techniques like HPLC, UV spectrophotometry, or LC-MS based on drug properties. Key steps include method selection, optimization, validation (specificity, accuracy, precision, robustness), and regulatory compliance. A well-developed method ensures drug quality, stability, and efficacy, which are essential for pharmaceutical formulation, regulatory approval, and routine quality control in research and industry.

VALIDATION: In analytical chemistry, method validation is a crucial procedure that guarantees a method's accuracy and dependability. Strict guidelines for validating analytical methods are provided by regulatory agencies like the U.S. Food and Drug Administration (FDA) and the International Council for Harmonisation (ICH). These guidelines emphasize elements such as system suitability, assessing whether the system is operating correctly before

starting an analysis, and method robustness, which tests the method's ability to perform consistently under slight variations in experimental conditions.

CONCLUSION:

This review underscores the significant role of analytical methods in evaluating Fimasartan, an angiotensin II receptor blocker used in managing hypertension and cardiovascular disorders. The various chromatographic, spectroscopic, and hyphenated techniques, including HPLC, UPLC, UV-VIS spectroscopy, and LC-MS/MS, have proven invaluable in ensuring the quality, stability, and pharmacokinetic profiling of Fimasartan in bulk drugs and pharmaceutical formulations. However, challenges persist regarding some analytical processes' high costs, complexity, and time-intensive nature. Future trends indicate a promising shift toward automation and green chemistry practices to enhance efficiency, reduce environmental impact, and provide more accessible solutions for Fimasartan analysis. As emerging technologies such as nanotechnology and machine learning-assisted analysis continue to evolve, they hold the potential to revolutionize analytical practices by offering cost-effective, rapid, and highly sensitive methods. Continued research and innovation in these areas will be crucial for addressing current limitations and further advancing pharmaceutical analysis, ensuring Fimasartan safe and effective use in clinical settings.

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