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Review Article on Various Comparative Analytical Study Approach for Antihypertensive Drug Category

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ABSTRACT

A chronic medical condition characterized by elevated blood pressure, hypertension is still a major global health concern. Because of its complexity, it is important to have a thorough understanding of the various antihypertensive drug categories that are available for managing hypertension. It includes the medications taken for the hypertension. Analytical procedures such as spectrometry and chromatography are used in the pharmaceutical industry to determine the qualitative and quantitative properties of medicines, APIs, raw materials, and biological samples. Validation plays role in demonstrating that any procedure, process, method, equipment, material, activity as expected under a given set of circumstances. The process by which it's developed, by laboratory studies that the performance specifications of the process connect the need for the deliberated analytical application. It includes a general study of some antihypertensive drugs assessed by HPLC technology.

Keywords: Antihypertensive drugs, Pharmaceutical preparations, Analytical methods, Validation

INTRODUCTION

A chronic medical condition characterized by elevated blood pressure; hypertension is still a major global health concern. Because of its complexity, it is important to have a thorough understanding of the various antihypertensive drug categories that are available for managing hypertension. Because researchers are always coming up with new ways to treat hypertension, there is a pressing need for a thorough review that methodically compares and analyses the various approaches used in the field of antihypertensive drug development. The objective of this review article is to present a comprehensive analysis of the changing antihypertensive medication landscape, with a particular emphasis on the various classes and their comparative analytical studies. This study aims to provide a thorough overview of the present status of antihypertensive medication development by exploring the most recent research findings, clinical trials, and new trends. An essential component of this analysis is the comparative analytical technique, which allows for a detailed assessment of the safety, effectiveness, and distinctive qualities of various antihypertensive medication classes. The research emphasizes how crucial it is to choose the right medication class in order to achieve proper blood pressure control with minimal adverse effects. They also stress the importance of exercising extra vigilance when keeping an eye on adherence and any side effects from these drugs. Additionally, a systematic review and meta-analysis have examined the timing of antihypertensive medication therapy, focusing on the importance of night-time blood pressure in predicting mortality in hypertension patients. New analytical technologies are constantly being created and applied where it makes sense to create stability-indicating techniques. The unidentified contamination, which is noted throughout the examination, pharmaceutical growth stress analyses, and formal stability assessments of the drug substances and drug product. It is possible to separate the drug ingredients and drug product and examined with a range of chromatographic methods. [1]

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Table 1. Explains the medications taken for the hypertension [2]

YEAR	HYPERTENSION DRUGS
1950	Reserpine, ganglionic blockers, guanethidine, thiazide diuretics, and hydralazine
1960	Spironolactone, beta blockers, and alpha 2 adrenergic receptor agonists
1970	Alpha 1 adrenergic receptor antagonists, ECA inhibitors, agonists and serotonin antagonists
1980	Calcium antagonists, imidazonline agonists, and potassium channel openers
1990	Antagonist of endothelin receptors, ARBs, crosslink breakers of the end products of advanced glycation, aminopeptidase inhibitors,
2000	Oubain antagonist, Urotensin II antagonists, vascular NAD(P) H oxidase inhibitors, modulators of the endocannabinoid, vasopeptidase inhibitors, renin imhibitors, renal sympathetic denervation, vaccines, and Rheos system
2010	Dual inhibitors of endothelin converting enzyme and neutral endopeptidase, NO releasing drugs with dual action: NO releasing sartans, NO releasing statins, angiotensin II blockers, and dual inhibitors of neutral endopeptidase
2020	Newer classes of antihypertensive drugs, such as endothelin A receptors antagonists and dual antagonists of angiotensin II, are being researched and developed.

ANALYTICAL METHOD DEVELOPMENT

Analytical procedures such as spectrometry and chromatography are used in the pharmaceutical industry to determine the qualitative and quantitative properties of medicines, APIs, raw materials, and biological samples. These approaches are used to assure the identity, purity, potency, and efficacy of pharmaceuticals. Analytical method development is critical to pharmaceutical development and manufacturing. [3]

There are several steps included in method development:

- Physiochemical properties of drugs
- Extraction of analyte
- Set up instrumental conditions
- Sample preparation
- Method optimization
- Validation of the developed method

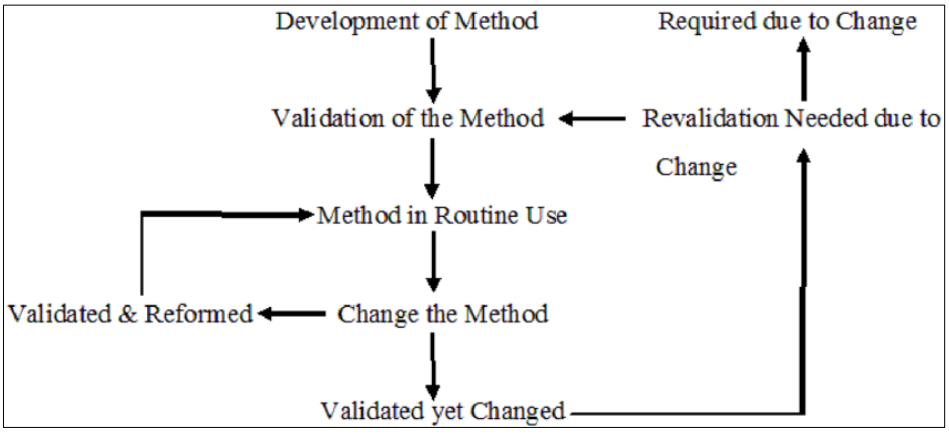

Fig.1 Life cycle of the analytical method [4]

VALIDATION OF ANALYTICAL METHOD

Validation plays role in demonstrating that any procedure, process, method, equipment, material, activity as expected under a given set of circumstances. The process by which it's developed, by laboratory studies that the performance specifications of the process connect the need for the deliberated analytical application. Analytical procedure mentions that how to perform the analysis. It gives

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details about every step to conduct all analytical tests. The purpose of validation is that an analytical procedure is to demonstrate that is suitable for its intended use [5]. There is main four types of procedure to be validated are identification test, quantitative test, limit test and qualitative test. According to ICH Q2 (R1) guidelines analytical method was developed and validated by using various parameters. Method development is a moderate and very difficult procedure. For method development labs require estimating a combination of mobile phase, temperature, pH, column and gradient to produce precise and accurate separation for all activity.

The characteristics of analytical method validation are:

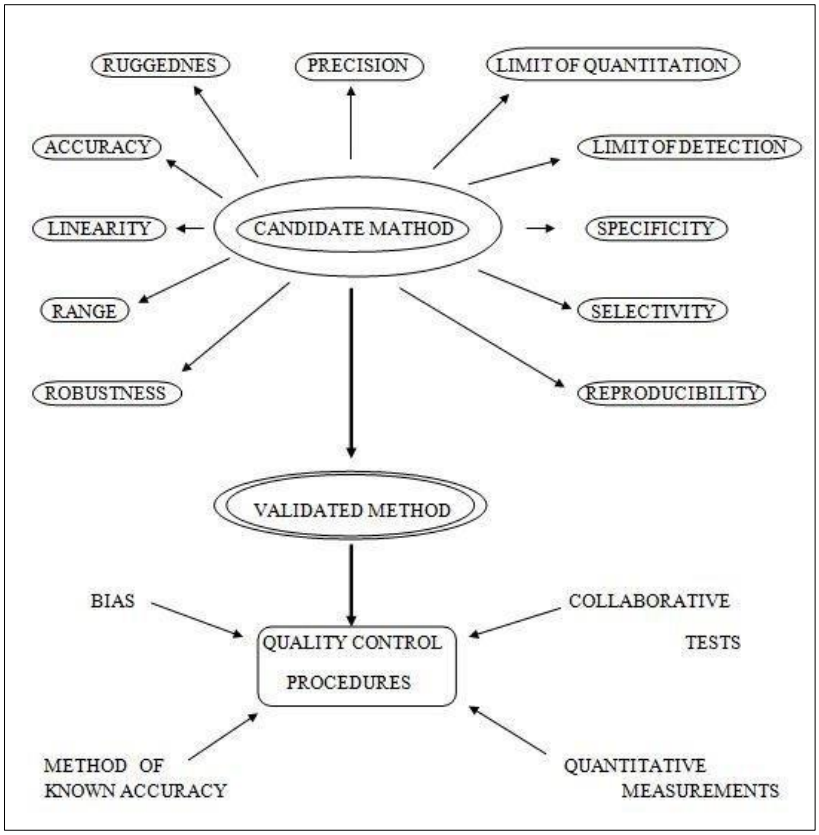

Fig. 2 Flow chart of analytical method development [6]

METHODS

Table 2. Methods of analysis used in pharmaceutical preparations:

Method	Description	Example
UV-Visible Spectrophotometric Method	It determines the transmittance, reflectance, and absorbance of a material by measuring the quantity of visible and UV light absorbed by it [7]. It is frequently used to measure active ingredients in pharmaceutical analyses.	Drugs can be directly tested using UV-Visible spectrophotometry, which is an easy and affordable method of drug testing without requiring a derivative reaction. However, for drugs with overlapping spectrum derivative spectrometry [8].
Fluorimetric methods	It measures the fluorescence emitted by a sample when triggered with a given wavelength of light. On the basis of phenomena of fluorescence, these approaches are highly sensitive and selective, in which it absorbs light at one	Fluorimetric methods have been widely used to measure a variety of active pharmaceutical substances, including hypertension drugs such as Valsartan, Irbesartan, Candesartan, Losartan and Telmisartan [10]. These techniques

	wavelength and emits at a longer wavelength [9].	are particularly sensitive and selective, which can be useful for compounds with low detection limits.
Titrimetric methods	Titration is a technique that uses a known concentration solution (known as a titrant) to calculate the concentration of an unknown solution. It is a quantitative analysis technique that determines an analyte's concentration by measuring its stoichiometric reaction with a reagent [11]. Titrimetric methods have various advantages, including the ease with which the measures sensitivity may be changed.	Titration is commonly utilized in pharmaceutical research for many reasons 1. Drug titration: In the pharmaceutical industry titration is commonly used to adjust the dosage of a medication to get the desired therapeutic effect. 2. Precipitation reaction Precipitation reactions are used to prepare pharmaceutical goods and analyze the content and purity of drugs. Titrimetric method used in a range of industries, including water tesing and pharmaceuticals [12].
Electroanalytical methods	Electroanalytical techniques encompass a wide range of quite diverse methods. Some of these methods are selective such as potentiometry while others are almost completely non-specific e.g. conductometry. Similar variations in other performance characteristics such as dynamic range or detection limit are found. For some methods a signal that is linear with the logarithm of the concentrations, or the activity, is obtained while others show the more usual direct relationship with analyte concentrations. In many instances the electrochemical methods provide a unique means for analysis, while in others they are a alternative to spectroscopic or chromatographic methods [13].	These methods can be categorized into several types based on the aspects of the cell that are controlled and measured. The main categories include potentiometry, amperometry, voltammetry, coulometry, and conductometry. Electroanalytical techniques have various advantages, including as sensitivity, selectivity, cheap cost, and flexibility. They are widely employed in a variety of applications, such as environmental monitoring, clinical analysis, and food testing. The development of new electroanalytical techniques continues to improve the possibilities of chemical analysis in many areas of human activity [14].
Capillary electrophoresis	A useful technique for separating big and tiny molecules, capillary electrophoresis is applied in many fields, such as pharmaceutical measurement [15]. This technique provides low sample and solvent consumption, quick method fabrication, excellent separation efficiency, automated and simple equipment, and a short analysis time.	Capillary electrophoresis has been utilized in the pharmaceutical sector to quantify lercanidipine enantiomers in industrial formulations, measure l- and d-carnitine in formulations, and identify parabens in food samples and human milk [16]. Researchers looked into the use of new electrochemiluminescence sensors in capillary electrophoresis in 2018 for the real-time measurement of quinapril hydrochloride in human plasma.
Vibrational Spectroscopies	For the non-destructive identification and characterization	It has been used in many different domains, such as environmental

	of materials based on their vibrational energy, vibrational energy, vibrational spectroscopy is a potent tool. Raman, near-infrared, and infrared spectroscopies are covered [17]. Every chemical bond has a unique vibrational frequency that can be used as fingerprint to identify different compound structures. The masses, geometric configuration, and strength of the chemical connections between atoms determine the frequency of molecular structure.	monitoring, material characterization, and biomedical study. The digitalization of vibrational spectra and the creation of algorithms for biomedical informatics and AI-assisted analysis have been made possible by recent advances in artificial intelligence. These developments have opened up new possibilities for clinical analyses, histopathological inspectionsm and quick in vivo diagnostics [18].

Table 3. Chromatographic methods:

Method	Description	Example
Thin Layer Chromatography	A potent analytical method for chromatographic information of complex mixtures of pharmaceuticals, natural products, clinical samples, and foodstuffs is high-performance thin layer chromatography (HPTLC), an advanced version of thin-layer chromatography (TLC) that offers improved resolution and automation. The purity and effectiveness of numerous pharmacological formulations and dosage forms are also examined using HPTLC [19].	TLC particulary HPTLC continues to be a useful method for qualitative and quantitative investigation in a range of settings, including the manufacture of pharmaceuticals [20].
Gas Chromatography	A popular analytical method for isolating and examining substances that evaporate without breaking down is gas chromatography (GC). It is very helpful for studying composite mixtures, which includes tablet and pharmaceutical preparation analysis, and is widely employed in the evaluation of pharmaceutical concerns. Gas chromatography mass spectrometry (GC-MS) is a widely used analytical tool in the pharmaceutical industry that is sensitive, accurate, repeatable, quantitative, and robust. It is well-suited for the analysis of complicated mixtures [21].	Antihypertensive medications such as bisoprolol, atenolol, metoprolol, enalpril, propranolol, and nifedipine have been identified using GC-MS. Furthermore, a sensitive and efficient method for detecting atenolol in human urine was established using GC-MS [22].
High Performance Liquid Chromatography	The most recent advancements are designed to optimize the delivery of accurate findings for industrial, food, and pharmaceutical laboratories. Furthermore, there have been developments in HPLC	For example, a quick HPLC technique has been created to enhance formulation quality control research, making it possible to regularly analyse bioequivalency and

	techniques, such as the creation of a quick HPLC approach that can enhance formulation quality control investigations [23]. The creation of robust analytical HPLC separation techniques tailored for different phases of drug research and production, such as pharmacokinetics, early drug exploration, drug metabolism, process analysis, formulation and preformulation, has been greatly impacted by the most recent developments in HPLC technology. These developments have made HPLC useful in a variety of pharmaceutical research fields.	pharmaceutical formulations. Furthermore, HPLC has been used to map the pharmacokinetics and tissue distribution of large triterpenoids following the administration of rhizome alismatis extract to mice, isolate angiotensin I-converting enzyme (ACE) inhibitory peptides from wakame hydrolysates, and investigate the impact of inadvertent digestion of sweet potato protein on blood pressure [24].
Ultra High Performance Liquid Chromatography	The use of Ultra High Performance Liquid Chromatography (UHPLC) has become commonplace in many fields, such as clinical, biotech, pharmaceutical, and environmental research. Complex mixture separation is now possible with improved performance, speed and resolution by recent developments in UHPLC technology [25].	Peak capacity is increased and faster results can be obtained with multidimensional separations. Utilizing UHPLC for the characterization and quality assurance of recombinant protein therapies is another recent advancement [26]. UHPLC enables the characterization and quality control of protein-based therapies by offering insightful information about their structure and function. Furthermore, because UHPLC can separate complicated combinations with high performance, high speed, and high resolution, it is being used more and more in the pharmaceutical business.

A general study of some antihypertensive drugs assessed by HPLC technology:

Telmisartan

Pharmacological formulations have had the concentration of Telmisartan measured using a variety of chromatographic techniques. High-Performance Liquid Chromatography (HPLC) is one technique that has been utilized to ascertain the concentration of hydrochlorothiazide and telmisartan in medicinal products. To separate the medicines chromatographically, the technique uses a mobile phase, an analytical column, and a detection wavelength. The robustness, detection limit, quantification limit, linearity, accuracy, and precision of the method have all been verified. Another technique that has been employed to study the synchronized isolation and quantitative measurement of Telmisartan in the presence of hydrochlorothiazide is the isocratic RP-HPLC method. An ACE 5 C18 25-cm analytical column and a buffer with 50 mM ammonium acetate in double distilled water are used in this procedure as the mobile phase. The robustness, detection limit, quantification limit, linearity, accuracy, and precision of the method have all been verified [26].

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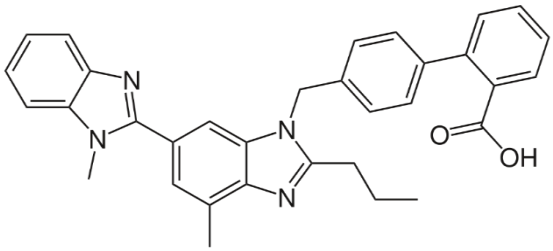

Fig. 3 Shows chemical structure of Telmisartan

Irbesartan

An antihypertensive medication called Irbesartan is used to treat hypertension. For its determination, a number of analytical techniques have been developed, such as voltammetric, spectroflourimetric, spectrophotometric, and RP-HPLC techniques. According to recent studies, an easy to use and quick HPLC technique that makes use of fluoresnce detection has been created to measure the amount of Irbesartan in human plasma. Furthermore, a quick and easy liquid chromatographic technique for determining hydrochlorothiazide and Irbesartan simultaneously has been devised. Liquid chromatography tandem has also been used to construct a straightforward, quick, and reliable high-throughput test for the quantitative measurement of Irbesartan has been accomplished through the description and validation of a stability-indicating RP-HPLC technique. Ultimately, a chemometric approach has helped to establish an enhanced HPLC method for the simultaneous measurement of Hydrochlorothiazide and Irbesartan [27].

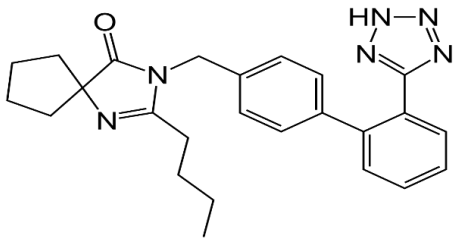

Fig. 4 Shows chemical structure of Irbesartan

Losartan

One of the main drugs used to treat hypertension is losartan potassium, which is an angiotensin II receptor antagonist. Numerous analytical techniques, most notably high-performance liquid chromatography (HPLC), have been used to examine Losartan potassium in medication formulations. Although there are multiple HPLC techniques available for the simultaneous measurement of Losartan potassium, the flammability, reactivity, and toxicity of conventional mobile phases such as methyl alcohol and acetonitrile raise safety concerns. By employing safer substitutes in mobile phases, recent developments in HPLC techniques have addressed these problems and ensured accuracy and safety in pharmaceutical analysis [28].

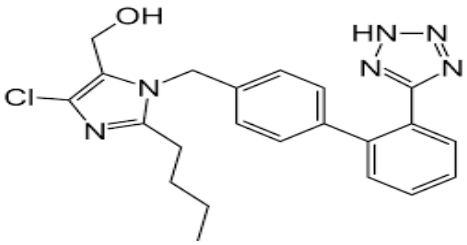

Fig. 5 Shows chemical structure of Losartan

Valsartan

Valsartan is an angiotensin II receptor antagonist that is used to treat disorders such as post-myocardial infarction, excessive blood pressure, and congestive heart failure, Its molecular formula is C24H29N5O3. It lowers blood pressure, enhances blood circulation,

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and inhibits angiotensin's activity. There are not many HPLC based techniques available in the literature for Valsartan individual assessment. Using derivative spectroscopy and high pressure liquid chromatography, researchers have examined Valsartan in human plasma and medication combinations. There are not many technologies available for simultaneously estimating valsartan in pharmaceutical goods. Furthermore, for the purpose of identifying combined medication formulations of Valsartan, a stability-indicating high pressure liquid chromatographic technique has been refined and validated. Furthermore, by adjusting the mobile phase, analytical parameters, temperature, and pressure effects, a unique supercritical fluid chromatography method has been tailored to evaluate four antihypertensive medication combinations, including Valsartan [29].

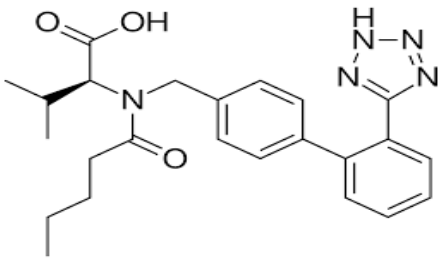

Fig. 6 Shows chemical structure of Valsartan

Methyldopa

An antihypertensive medication called methyldopa (MLD) is used to treat mild to severe hypertension. It is sold under the brand name Aldomet and is frequently measured with spectrophotometers and chromatography (HPLC). With the use of solid-phase extraction and mixed-mode liquid chromatography for sample preparation, recent research has produced sensitive and environmentally benign techniques for determining the presence of methyldopa in human serum and plasma [30].

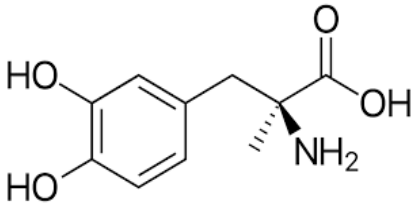

Fig. 7 Shows chemical structure of Methyldopa

Carvedilol

Antioxidant-producing and non-selective beta-receptor antagonist, carvedilol is a vasodilator. It has been demonstrated to exhibit greater antioxidant action than other commonly used beta-blockers. In addition, it has been found to have additional advantageous effects, including the inhibition of apoptosis and the improvement of cardiac healing following a MI. Carvedilol has also been shown to possess anticancer effects in recent studies. Spectrophotometry, flurometry, chemiluminescence, electrochemical techniques, gas chromatography, and capillary electrophoresis are further analytical methods for determining the amount of carvedilol. However, because of their sensitivity, repeatability, and capacity to separate and quantify carvedilol in complex matrices, high performance liquid chromatography preparation and biological fluids [31].

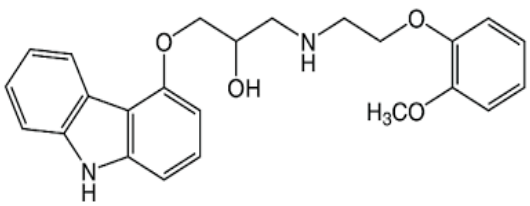

Fig. 8 Shows chemical structure of Carvedilol

CONCLUSION

The development and validation of analytical techniques for tertiary combinations of antihypertensive medications is the main topic of the review paper. The writers stress the use of analytical techniques in medication development, production, and quality assurance, as well as the necessity of developing and validating these techniques in accordance with International Conference on Harmonization (ICH) Q2 (R1) criteria. The article covers a variety of analytical methods for determining antihypertensive medications, such as ultraviolet spectrophotometry, fluorimetry, titrimetry, electroanalytical methods, capillary electrophoresis, and vibrational spectroscopies. Chromatographic methods such as TLC, gas chromatography, HPLC, UHPLC etc. It covers analytical procedures such as spectrometry and chromatography are used in the pharmaceutical industry to determine the qualitative and quantitiative properties of medicines, APIs, raw materials, and biological samples. The use of antihypertensive drugs, such as alpha-blockers, hydralazine, clonidine, potassium-sparing diuretics, and loop diuretics, in the treatement of hypertension is included. The main analytical methods used in pharmaceutical preparations are essential for ensuring the quality, safety and stability of pharmaceutical products throughout their development and production. Antihypertensive medicines are commonly evaluated using HPLC technology to determine quantities in pharmaceutical formulations and biological materials. Several studies have been undertaken to develop and validate HPLC methods for the quantification of various antihypertensive medications. One study conducted a comparative analysis of analytical methodologies for evaluating several antihypertensive medications in pharmaceutical manufacture. The review sought to examine current quantitative analytical approaches for calculating antihypertensive medications. The researchers discovered that HPLC is the most common analytical technology utilitzed in pharmaceutical analysis for quality control operations.

CONFLICTS OF INTEREST

There are no conflicts of declare.

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Conflict of Interest Statement: All authors have nothing else to disclose.