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A Comparative Review of Methods for Estimation of Some Antihypertensive Drugs in Pharmaceutical Production

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Abstract

This review aim was to study and analyze some of the existing quantitative analytical methods for estimating some antihypertensive drugs in pharmaceutical planning. Several methods (such as capillary electrophoresis, high-performance liquid chromatography, spectrometry, chromatography methods, and titrimetric methods) for quantitative study of antihypertensive medications have been used. For the advancement in technology and implementation, fast response, high precision, low cost, and user-friendly drug analysis approaches have become critical. HPLC approaches are commonly used because of their precision, sensitivity, low cost, and ability to perform on-site analyses of a variety of substances. Methods such as ZIC-HILIC (Zwitterion stationary phase-Hydrophilic Interaction Chromatography) are extremely capable of assaying drug concentrations and providing outstanding knowledge of its physical and chemical properties. The advancement of the ZIC-HILIC column has enabled the development of more accurate, responsive, and cost-effective instrumentation, which has made a major contribution to biomolecule analysis and drug development. The study used previous literature to test antihypertensive drugs and compare it to the new ZIC-HILIC form. They are preferred for a variety of applications such as environmental surveillance, food quality management, clinical diagnosis, biomolecule, and drug detection due to their ease of usage, portability, and low expense.

Key words: Pharmaceutical preparation, Antihypertensive drugs, ZIC-HILIC, HILIC.

1. Introduction

Hypertension, well-defined as a steady blood **p**ressure of 140\90 mmHg or higher, affects coarsely a quarter of the grown-up populace in many countries, especially in Western populations. Vascular disease is the main reason of decease, accounting for about one-third of all deaths worldwide [1]. Hypertension screening and management is an essential part of preventing cardiovascular disease (CVD). Hypertension is a leading reason of stroke, heart failure, coronary heart disease, and related disability, and it is particularly prevalent in the elderly[2,3]. Antihypertensive therapy helps to reduce complications associated with increased blood pressure, such as myocardial infarction and stroke [4]. Because of the resulting morbidity, death, and economic effects on population, hypertension remains a major public health concern. It's a major contributor to coronary, cerebrovascular, and renal disorders. It is projected that 1.56 billion people would have hypertension by 2025 [5]. Long-term hypertension can cause heart enlargement and eventually heart failure, before the detrimental symptoms of hypertension are noticed, this condition is normally asymptomatic, As a result, hypertension is dubbed the "silent murderer"[6]. COVID-19 has a bad result when hypertension is present. Unique antihypertensive medications have been suggested as a possible cause of this connection[7[8]. Antihypertensive are divided into several categories, each of which lowers blood pressure in a particular way. Beta blockers, or angiotensin-converting enzyme inhibitors (ACEIs), angiotensin 2 receptor blockers (ARBs) calcium channel blockers, and thiazide diuretics are among the most effective and commonly used drugs[8,9]. Table.1. Explain historic evolution in antihypertensive therapeutics of period between 1950 to 2010 [10, 11].

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Table 1. Explains the medicines used for high blood pressure for the period (1950-2010)

Year	Hypertension drugs
1950	Reserpine, ganglionic blockers, guanethidine, thiazide diuretics, hydralazine
1960	Spironolactone, β blockers, α 2 adrenergic receptor agonists
1970	α 1 adrenergic receptor antagonists, ECA inhibitors, agonists & serotonin antagonists
1980	Calcium antagonists, imidazoline agonists, potassium channells openers
1990	Antagonist of endothelin receptors, ARBs, crosslink breakers of the end products of advanced glycation, aminopeptidase A inhibitors, Rho kinase inhibitors
2000	"Ouabain antagonists, urotensin II antagonists, vascular NAD(P)H oxidase "Inhibitors, modulators of the endocannabinoid, vasopeptidase" "inhibitors, renin inhibitors, renal sympathetic denervation, vaccines, 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 Endothelin A receptors and dual antagonist of angiotensin II

2. Analytical Methods for pharmaceutical preparations:

2.1. UV-VIS spectrophotometric methods:

To quantify pharmaceutical active ingredients, a variety of spectrophotometric UV/VIS measurements have been developed. Due to the presence of chromophore groups in most pharmaceuticals, they can be tested directly in the ultraviolet range without the need for a derivative reaction. Spectrophotometric methods remain appealing due to their widespread availability of instrumentation, ease of procedures, speed, economy, accuracy, and precision[13]. The direct UV/VIS spectrophotometric method, on the other hand, is ineffective for determining drugs with spectral overlap at the same time [14]. Derivative spectrophotometry is an alternative approach for improving precision and accuracy in the analysis of mixtures for this purpose. This method has also been used to extract knowledge from interference and simultaneous analytic bands. Cagigal *et al* used spectrofluorimetry to determine the acid-base balance constants of angiotensin 2 receptor antagonists such as Valsartan, Irbesartan, Candesartan, Losartan and Telmisartan, a novel class of antihypertensive drugs [15]. For evaluating olmesartan medoxomil in pharmaceutical formulations, Chintan and colleagues validated reverse phase high pressure chromatography (RP-HPLC) methods and spectrophotometric [16]. Gadkariem and colleagues devised a novel spectrophotometric method for determining methyldopa in pharmaceutical products. The combination of methyldopa with 2,6-dichloroquinone-4-chlorimide was the basis for the process [17]. The researcher Nada was able to use Spectrophotometric methods to determine Carvedilol in combined dosage type[18]. For the instantaneous assessment of ramipril and celecoxib in pharmaceutical mixes containing amlodipine, Ankush Parmar and Shweta investigated Smart UV spectrophotometric techniques established on simple accurate separation[19].

2.2. Fluorimetric methods

Luminescence spectroscopy is a particularly sensitive analytical method that has been commonly applied to problems with poor detection limits[20]. As a result, luminescence intensity measurements have allowed the quantification of a broad variety of active pharmaceutical ingredients in a selective and sensitive manner. Despite all of the advantages of luminescent techniques, native luminescence happens in just a few classes of compounds as a result of molecule deactivation processes. Furthermore, as opposed to other analytical techniques like chromatography and UV/visible spectrophotometry, the effects of absorption and scattering make luminescent approaches more difficult to use[21]. In luminescence spectroscopy, three different techniques can be used: phosphorescence, fluorescence, and chemiluminescence. On the other hand, fluorimetry is the most frequently used luminescence technique in pharmaceutical science. In 2012 Guerrero *et al*, studied Improvement of validated RP-HPLC method with fluorescence exposure for seventeen flavonoids belonging to 5 structural subtypes were assessed in vitro for their capacity to inhibit ACE in order to found the mechanical basis of their bioactivity[22]. In the following year Takayasu *et al*, considered chemical library showing for WNK (with-no-lysine kinases) signalling inhibitors using fluorescence correlation spectroscopy [23]. In 2018 Xie *et al*, studied Improvement of practiced RP-HPLC method with fluorescence finding for immediate quantification of valsartan "from rat plasma[24] .

2.3. Titrimetric methods

Despite the fact that titrimetry has been widely used in the previous, a literature review shows that there are few modern approaches that

use this procedure for pharmaceutical research. Titrimetry has a number of benefits, including a quick turnaround period and low equipment costs. However, as opposed to modern separation approaches such as HPLC or capillary electrophoresis, titrimetric methods display a lack of selectivity, which is likely why they are no longer used[25]. In 2015 Rini *et al*, studied analyses of exposure, clinical response and blood pressure from a randomised stage two study in renal metastatic cell carcinoma [26]. In 2016 Tokunaga et al studied rapid and high-dose titration of epoprostenol improves pulmonary clinical outcomes and hemodynamics in patients with genetic pulmonic idiopathic and major hypertension [27]. In 2018 molecular docking analysis, antihypertensive results, and isothermal titration calorimetric analyze of angiotensin 1 transforming enzyme inhibitory peptides from chlorella vulgaris were investigated[24]. Monahan *et al*, in 2019 studied cost-effectiveness of telemonitoring of blood pressure and self-monitoring for antihypertensive titration in primary care (TASMINH4)[28].

2.4. Electro analytical Methods

Electrochemical methods are well-known for their low detection limits and high sensitivity, as well as their low instrumentation costs and ease of use [28]. Conductometry, electrogravimetry, coulometry, polarography, potentiometry, amperometry, and voltammetry are electrochemical techniques for drug identification of dose formulations. Voltammetric approaches, on the other hand, are by far the most commonly used electrochemical procedures, with several studies of their use in dosage formulation material analysis in the literature[29]. In 2016, Moraes *et al*, used a cathodically pretreated boron doped diamond electrode to study synchronized voltammetric estimation of some antihypertensive drugs in pharmaceutical preparation[30].

2.5. Capillary electrophoresis

For both large and small molecules, capillary electrophoresis is an effective separation process. Pharmaceutical quantification is one of the many applications that must be used. This method has a high separation efficiency that allows for difficult separations, a short analysis time, fast method production, low sample and solvent usage, and automatic and easy instrumentation [31]. Sánchez and colleagues developed a method for determining l- and d-carnitine in pharmaceutical formulations using capillary electrophoresis electrospray ionization tandem mass spectrometry[32]. In 2015, Lourenço *et al* used capillary electrophoresis to quantify lercanidipine enantiomers in industrial formulations[33]. In the same year, Alshana *et al*, used capillary electrophoresis to determine parabens in food samples and human milk after back extraction with dispersive liquid–liquid micro extraction[34]. In 2018, Sun *et al* investigated the use of capillary electrophoresis with novel electro chemiluminescence sensors in combination for the instantaneous purpose of quinapril hydrochloride in human plasma[35].

2.6. Vibrational spectroscopies

Raman, Infrared, near infrared, and, more lately, terahertz pulsed spectroscopy have become communal for solid state examination because they are non-destructive and quick allowing solid state variations to be surveyed at the molecular level [36]. In the pharmaceutical industry, vibrational spectroscopy techniques based on Raman spectrophotometers and infrared (IR) are becoming standard practice in both quality management and production in laboratory [37]. In 2018, Mazivila *et al*, investigated the use of chemometrics in conjunction with spectroscopic imaging and vibrational spectroscopy to analyze solid-phase pharmaceutical drugs [38]. As opposed to other analytical techniques, the usefulness of vibrational spectroscopy methods is largely due to their low cost and rapidity.

3. Chromatographic methods:

3.1. Thin layer chromatography

For analyzing pharmaceutical preparations, thin layer chromatography (TLC) is a simple, moderately sensitive, inexpensive technique, and quick. Thin layer chromatography has been exposed to provide exceptional qualitative and quantitative study of a wide range of organic and metal organic compounds in several publications[39]. Thin layer chromatography, on the other hand, is widely regarded as an antiquated form of impurity detection. Furthermore, advances in sorbent layers and instrumentation have improved the efficiency of quantitative planar chromatography, rendering it a cost-effective alternative to HPLC[40]. In 1998, Mccarthy *et al*, used RP-HPLC thin-layer chromatography to determine losartan and its degradates in COZAAR® capsules[41]. In 2000, Argekar and Powar used high performance TLC to assess the simultaneous prevalence of atenolol and amlodipine in drugs[42].

3.2. Gas chromatography:

Gas chromatography (GC), more specifically gas chromatography mass spectrometry (GC-MS), is a sensitive, precise, repeatable, quantitative, and robust instrument ideally improved for the study of composite mixtures, and it is extensively used in the examination of tablets and

pharmaceutical matters[43]. The authors present a general approach for analyzing guanido-containing drugs used to treat hypertension[44]. GC-MS was used to establish a sensitive and effective process for determining atenolol in human urine [45]. GC united with mass spectrometry is used to detect antihypertensive drugs such as bisoprolol, atenolol, metoprolol, enalapril, propranolol, and nifedipine[46].

3.3. High performance liquid chromatography

In today's pharmaceutical industry, high pressure liquid chromatography (HPLC) is a vital analytical system used in all stages of drug discovery, development, and manufacturing. The two most important roles in the creation of novel chemical entities are drug discovery and manufacturing. In this drug research and production model, rugged analytical HPLC separation methods are built and customized for each development culture (i.e., pharmokinetics, early drug exploration, drug metabolism, process analysis, formulation, and preformulation) [47,48]. The terms "high quality" "fast speed," "high pressure," and "high performance" have all been used to define the core characteristics of this "new" liquid chromatography (HPLC). Using 3 step high-pressure liquid chromatography (HPLC) on a RP column, the protease Amano was used to isolate 7 forms of angiotensin I-converting enzyme (ACE) inhibitory peptides from wakame hydrolysates [49]. The influence of accidental digestion of sweet potato protein on blood pressure was calculated in 2012 by purifying the angiotensin converting enzyme in hypertensive mice with peptides substitute as inhibitors [50]. Wen and colleagues used HPLC tandem mass spectrometry to map the pharmacokinetics and tissue distribution of 5 large triterpenoids after giving mice rhizoma alismatis extract [51]. Serum metabolism was researched in 2018 based on antihypertensive effects and LC-MS of naturally occurring ankarya Rats of high blood pressure [51-53].

3.3.1. Hydrophilic Interaction Liquid Chromatography (HILIC)

The technique of hydrophilic contact liquid chromatography (HILIC) is useful for separating polar compounds [54]. HILIC has been defined as a variant of normal phase liquid chromatography (NP-LC) for historical reasons, but the estimation method used in HILIC is more difficult than that used in normal phase liquid chromatography [55]. Alpert proposed the acronym HILIC for the first time in 1990 [56]. In comparison to conventional adsorption chromatography on normal phase(NP) compounds, chromatography of carbohydrates on HILIC stationary phases(SP) has been shown to require a partitioning process [57]. Analytes can interact with strongly polar (hydrophilic) stationary phases including amine, bare silica particles, amide-bonded, hydroxy, and zwitterionic (ZIC-HILIC) columns using HILIC [58]. Since other processes besides hydrophilic partitioning may occur, the features of the hydrophilic stationary phase may affect and, in some cases, ion density, limit the mobile phase configuration, and buffer pH value choices obtainable [59]. The retaining of mixtures in HILIC, which is from time to time also called (NP-LC), is usually due to 3 mechanisms separating of analyzes between water layer and organic rich mobile phase adsorbed on polar and stationary phase, ion exchange interactions [60]. (HILIC)-mass spectrometry has lately exposed to be an effective technique for separating and characterizing complete protein glycoforms [58]. Takahiro and colleagues used the ZIC-cHILIC method to isolated eight catechol mixtures (epinephrine, dopamine, 3,4-di hydroxy phenyl alanine, nor-epinephrine, 3,4 di hydroxy phenyl glycol, 3,4 di hydroxy phenyl acetic acid, and internal standard 3,4 di hydroxy benzamine) within fifteen minutes [62]. Hydrophilic interaction liquid chromatography(HILIC) is gaining a lot of attention right now because it solves a lot of issues with previously problematic separations [63].

3.3.2. Zwitterionic Iion Chromatography Hydrophilic Interaction Liquid Chromatography (ZIC-HILIC) :

Zwitterionic ion chromatography (ZIC) is an alternate form of ion chromatography (IC), which uses zwitterionic ion chromatography columns for anion and cation separations [64]. Alpert introduced an HILIC separation process based on the separation of a water-enriched layer on the stationary phase surface from a largely organic mobile phase. Zwitterionic stationary phases can be used as strongly hydrophilic aids with significant surface water enrichment [63]. Hydrophilic liquid chromatography has been advanced in latest years to separate and retain hydrophilic and polar molecules in the suitable chromatographic mode (HILIC) [65]. Graft polymerization of a series of sulfobetaine precursors onto the surface of porous PS/DVB particles produced zwitterionic stationary phases with nearly equal capacities. The various spacer lengths are used to examine specifically malonic, carboxylic acid retention actions, glutaric, succinic, and maleic acid retention [٦٥]. Two zwitterion stationary phases with largely substantiated capabilities were achieved by attachment sulfobetaine monomers ($H_2C{=}CHC_6H_4CH_2N^+(CH_3)_2\text{-}(CH_2)_5\text{-}SO_3^-$ and $H_2C{=}CHC_6H_4CH_2N^+(CH_3)_2\text{-}CH_2\text{-}SO_3^-$) onto a PS\DVB particles were examined for chromatographic separation of ranitidine hydrochloride [66]. In 2020 Karabat and his

colleagues developed a new technique for assessing quercetin without processing the sample using ZIC-HILIC method [67].

4. A general study of some antihypertensive drugs assessed by HPLC technology

4.1. Telmisartan (TEL) $C_{33}H_{30}N_4O_2$:

Telmisartan reduces blood pressure by blocking the activity of angiotensin II by inhibiting the angiotensin II receptor [68]. A thorough review of the literature on Telmisartan revealed many approaches for determining its concentration in plasma, urine, and pharmaceutical formulations, including HPLC and electrochemical methods [69]. In 2012 a high pressure liquid chromatography (RP-HPLC) indicating determination technique was advanced and validated for simultaneous identification of trace level impurities of telmisartan in their tablets [70]. Ravisankar *et al*, used isocratic RP-HPLC to investigate the synchronized isolation and quantitative determination of telmisartan in the presence of hydrochlorothiazide [71]. In same year it was prepared analytical technique development and validation for the determination of telmisartan in multi-component tablet amount form and in bio relevant media by RP-HPLC methods [72]. A new, precise, accurate simple, and rapid (RP-HPLC) technique was advanced for the immediate estimate of telmisartan in pharmaceutical construction. Figure 1 show the chemical structure of telmisartan. Table 2: Explain an overview determination of telmisartan in some pharmaceuticals preparation using chromatography methods[73].

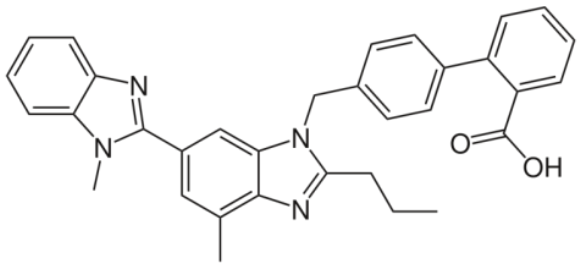

Fig. 1. show chemical structure of Telmisartan

4.2. Captopril (CAP) $C_9H_{15}NO_3S$:

Captopril, also known as Capoten, is an angiotensin translating enzyme inhibitor that is usage to treatment some forms of hypertension and heart failure [74]. HPLC was used to compare captopril to other medicines in prescription formulations and biological fluids. HPLC was used to perform stability suggesting assays for captopril. The United States Pharmacopoeia (USP) and the British Pharmacopoeia (BP) use high-performance liquid chromatography (HPLC) to assess captopril and related substances in prescription dosage types [75]. Many approaches obtainable for the estimation of captopril are including high pressure liquid chromatography, titrimetry, spectrophotometry, voltammetry, and capillary electrophoresis [76]. Figure 2, show the chemical structure of Captopril. Table 3: Explain an overview determination of Captopril in some pharmaceuticals preparation using chromatography methods.

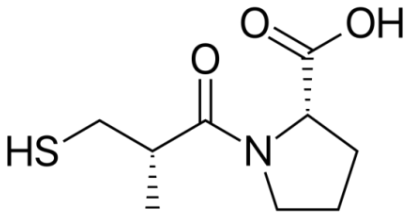

Fig. 2. show chemical structure of Captopril[77].

4.3. Irbesartan (IRB) $C_{25}H_{28}N_6O$:

Irbesartan is a drug that is used to control elevated blood pressure, diabetic kidney disease, and heart failure. It is marketed under the trade names Avapro and others [78]. An analysis of the literature revealed that several analytical methods for quantifying IRB in biomatrices have been published, the majority of which are focused on liquid chromatography [79]. Analytical methods for calculating IRB were discovered in a literature review of experiments on quantitative study of these drugs such as HPLC method [80]. Various chromatographic methods for estimating IRB in pharmaceutical dosage types and biological fluids have been published [81]. Figure 3, show the chemical structure of Irbesartan [82]. Table 4: Explain an overview determination of Irbesartan in some pharmaceuticals preparation using chromatography methods.

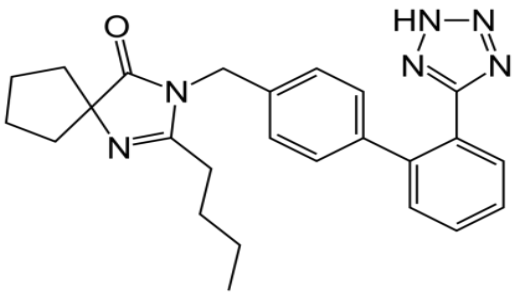

Fig. 3. Show chemical structure of Irbesartan

4.4. Losartan potassium (LOP) $C_{22}H_{22}ClKN_6O$:

Losartan potassium was the first of a new breed of other well potent angiotensin Receptor antagonists used to treat hypertension [83]. Numerous analytical approaches have been practical

to the examination of Losartan potassium in drug products that make use of high performance liquid chromatography(HPLC) [84]. For the simultaneous determination of LOP several HPLC methods have been identified. However, the traditional mobile phases used in these trials, such as methyl alcohol, acetonitrile, are flammable, reactive, and poisonous [85]. Figure 4, shows the chemical structure of Losartan potassium [85]. Table 5: Explain an overview determination of Losartan potassium in some pharmaceuticals preparation using chromatography methods.

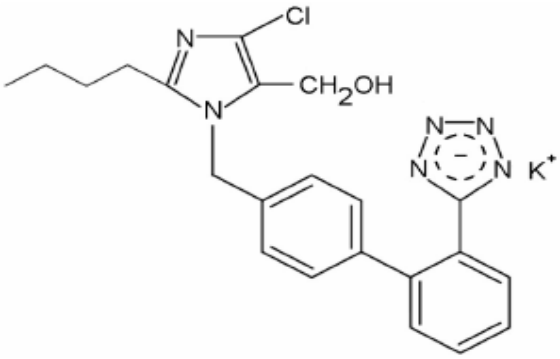

Fig. 4. show chemical structure of Losartan potassium

4.5. Valsartan $C_{24}H_{29}N_5O_3$ (VAL):

Valsartan is an angiotensin 2 receptor antagonist that is used to treat congestive heart failure, elevated blood pressure, and post myocardial infarction. Valsartan works by blocking angiotensin's activity, circulation of the blood, and lowers blood pressure [86]. There are only a few HPLC-based approaches for evaluating Valsartan individually in the literature. There has been some calculation of analyze assays in human plasma using liquid chromatography, as well as some drug combinations using derivative spectroscopy and high pressure liquid chromatography [87]. Few systems were described for the simultaneous estimation of Valsartan in pharmaceutical products. There are only a few approaches in the literature for evaluating VAL individually using HPLC [88]. For the determination of combined drug formulations of valsartan, a constancy designating high pressure liquid chromatographic system was validated and advanced [89]. Using a customized procedure, a novel supercritical fluid chromatography approach is defined to evaluate four antihypertensive drug combinations that include a diuretic (olmesartan, amlodipine, telmisartan, and valsartan). The mobile process, analytical panel, temperature, and pressure effects were all properly optimized [90]. Figure 5, Shows the chemical structure of Valsartan. Table 6: Explain an overview determination of Valsartan in some pharmaceuticals preparation using chromatography methods.

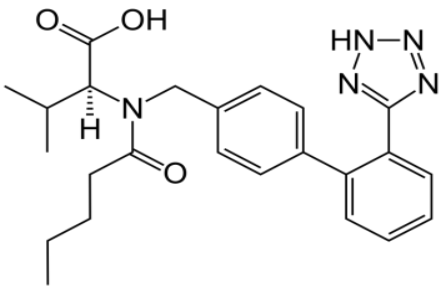

Fig. 5. shows the chemical structure of valsartan [90].

4.6. Methyldopa (MLD) $C_{10}H_{13}NO_4$:

Methyldopa (l-methyl-3,4-dihydrophenylal:anine) is an antihypertensive drug that has been used for a long time and is used to treat mild to severe hypertension. A drug for high blood pressure is marketed under the brand name Aldomet, among other names [91]. The most commonly used methods for quantifying methyldopa are chromatography and spectrophotometry[92]. Several analytical methods have been used to analyze methyldopa, according to the literature. Spectrophotometry, high pressure liquid chromatography, and electro examination are among the most commonly employed methods[93]. Figure(6) shows the chemical structure of Methyldopa[94]. Table 7: Explain an overview determination of Methyldopa in some pharmaceuticals preparation using chromatography methods.

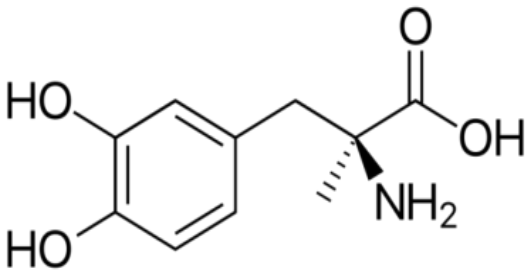

Fig. 6. shows the chemical structure of Methyldopa[94].

4.7. Carvedilol (CRV) $C_{24}H_{26}N_2O_4$:

Carvedilol is a non-selective beta-receptor antagonist and vasodilator that also has antioxidant effects [95]. Carvedilol has been shown to have much more antioxidant activity than other widely used beta-blockers [96]. This medication is also a potent antioxidant and oxygen radical neutralizer, as well as having other beneficial effects including inhibiting apoptosis and improving myocardial postinfarction recovery [97]. CAR has been found to have anti-cancer properties in recent research [98]. In order to rapidly evaluate and isolate, candesartan, carvedilol, and hydrochlorothiazide in

pure and tablet drugs, an isocratic HPLC method was advanced [99]. Figure 7, show the chemical structure of carvedilol [100].

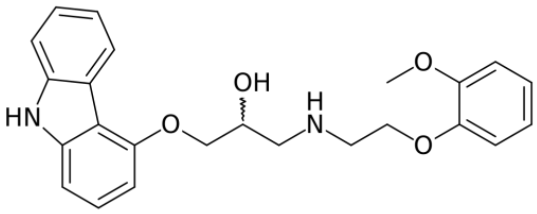

Fig. 7. show the chemical structure of Carvedilol [100].

In this review, an analytical study of some antihypertensive drugs using HPLC technique is presented in this review compared to other conventional methods. Table 8: Explain an overview determination of Carvedilol in some pharmaceuticals preparation using chromatography methods.

5. Conclusion

This review analyzed new methods approaches for quantitative study antihypertensive drugs in pharmaceutical preparations. Some of the techniques used include fluorimetry, titrimetry, electro analytical, and UV\VIS spectrophotometry techniques, chromatographic approaches (HPLC, GC, and TLC), and vibrational analytical, with a movement toward faster techniques that save cost and reduce solvent usage. As a result of this work, there is a trend to use technologies such as high-performance liquid chromatography and ZIC-HILIC methods. Liquid chromatography, hydrophilic reaction (HILIC) is a high-performance liquid chromatography technique that separates compounds of high polarity and ionic compounds such as amino acids, enzymes, peptides and other compounds, as this technique has shown high efficiency in separation compared to previous methods of analysis that were mentioned in the review. The development of HILIC stationary phases, which are considered the heart of chromatographic science, is critical for increasing chromatographic separation selectivity and efficiency, as well as influencing the growth and generalizability of HILIC. The synthesis of silica based HILIC stationary phases, comprising original silica, cyano, amide, amino, saccharides, succinimide, and zwitterionic-based stationary phases, is reviewed in this article allowing to the functional groups of chromatographic supplies.

Table 2: Explain an overview determination of Telmisartan in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	t_R min	Application	Ref.
"C18 column (75 mm x4.6 mm; 3.5 µ)"	"ammonium acetate buffer (10 mM; pH 4.0) and acetonitrile in a ratio 40:60 v/v"	(UV) 210	1-16 µgmL^{-1} R^2 = 0.999 % Rec = 99.91 %RSD = 0.15 LOD = 0.189 µgmL^{-1} LOQ = 0.8µgmL^{-}	3.21	Tablet	[73]
"Shiseido C18 (250 x 4.6 mm, 5µm)"	"0.5% orthophosphoricacid (A), combination of acetonitrile: methanol (70:30, v/v) (B). A: B in the ratio of (50:50, v/v)"	(UV) 220	40-120 µgmL^{-1} R^2 = 0,99 % Rec = 99.93 %RSD = 1.63 LOD = 0.01µgmL^{-1} LOQ = 0.603µgmL^{-1}	3.5	Pharmaceutical Dosage	[101]
"C_{18} (4.6 × 100 mm i. d., 3.7 µm particle"	"40:60 (v/v) 20 mM potassium dihydrogen orthophosphate buffer: methanol"	(UV) 248	20-320 µgmL^{-1} R^2 = 0,999 % Rec = 100.17 %RSD = 0.44 LOD = 0.012 µgmL^{-1} LOQ = 0.041 µgmL^{-}	4.19	Tablet	[72]
"C18 column (4.6 X 250 mm, 5 µm)"	"phosphate buffer pH-3.3 and acetonitrile in the portion of 50:50 v/v"	(UV) 232	8- 40 µgmL^{-1-} R^2 = 0,9987 % Rec = 100.09 %RSD = 0.71 LOD = 0.298 µgmL^{-1} LOQ = 0.980 µgmL^{-}	3.77	drugs	[71]
"Phenomenex C18 column (150 x 4.6 mm, 5 µm) particle size"	"0.05M sodium dihydrogen phosphate buffer (60:40) adjusted pH= 6"	(UV) 254	5-30 µgmL^{-1} R^2 = 0,9993 % Rec = 99.55 %RSD = 0.54 LOD = 2 µgmL^{-1} LOQ = 4 µgmL^{-1}	8.2	pharmaceutical dosage	[102]
" C18 250 × 4.6 mm, 5 µm column"	"0.1% Formic acid buffer (pH 3.2): Acetonitrile (60:40 v/v)"	(UV) 245	40–160 µgmL^{-1} R^2 = 0.9990 % Rec = 96.68 %RSD = 0.66 LOD = 0.01 µgmL^{-1} LOQ = 0.06 µgmL^{-1}	3.90	Tablet	[103]
"Cosmosil PAQ (150 mm × 4.6 mm) 5 µm"	"0.05 M sodium dihydrogen phosphate buffer and acetonitrile"	(UV) 220	2-150 µgmL^{-1} R^2 = 0.9998 % Rec = 96.4 %RSD = 0.38	10.2	Drug Products	[104]

Table 3: Explain an overview determination of Captopril in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	Application	tR min	Ref.
"Purospher Start C18 (250 mm x 4.6 mm, 5 µm)"	"methanol: water (70:30 v/v) pH 3.0"	(UV) 225	5-25 µgmL $^{-1}$ R^2 = 0.999 % Rec = 101.11 %RSD = 0.0073 LOD = 0.4 µgmL^{-1} LOQ = 2.3 µgmL^{-1}	Pharmaceutical Dosage Forms and Human Serum	3.3	[105]
"C18 column (100mm×4.6mm,3µm i.d.)"	"phosphate buffer adjusted to pH 3.0 (45:55, v/v) pH 3.0"	(UV) 270	0.5–100 µgmL $^{-1}$ R^2 = 0.999 % Rec = 98.9 %RSD = 0.72 LOD = 1.2 µgmL^{-1} µgmL^{-1}٤,٠LOQ =	Drugs	4.3	[106]
"Phenomenex® Luna 5µm (C18) column"	"Phosphate buffer (adjusted to pH 3.0): acetonitrile in a ratio of 70:30 (v/v)"	(UV) 270	2–70 µgmL $^{-1}$ R^2 = 0.9993 % Rec = 99.47 %RSD = 2.27 LOD = 0.6 µgmL^{-1} LOQ = 2.27 µgmL^{-1}	Tablet	3.08	[107]
"C18 (5 µm, 250×0.46 cm) column"	methanol: water (60:40 v/v) were used as the mobile phase, pH 3.0	(UV) 225	9.37 –150 µgmL $^{-1}$ R^2 = 0.978 % Rec = 101.6 %RSD = 0.02 LOD = 1.75 µgmL^{-1} LOQ = 5.3 µgmL^{-1}	Drugs	5.2	[77]
"ODS C18 (150×4.6mm, 5micron) columns"	"(methanol-water 50:50(v/v) pH 3.0"	(UV) 225	1.25-50 µgmL $^{-1}$ R^2 = 0.999 % Rec = 99.64 %RSD = 0.98 LOD = 2 ngmL^{-1} LOQ = 8 ngmL^{-1}	Pharmaceutical Dosage Forms and Human Serum	2	[108]
":Purospher Star RP-18 endcapped (250 mm x 4.6 mm id)"	"methanol–water as mobile phase 50:50 (v/v) and 60:40 (v/v) as diluent pH 3.0"	(UV) 218	2.5–250µgmL $^{-1}$ R^2 = 0.9998 % Rec = 98.63 %RSD = 0.02 LOD = 0.145µgmL^{-1} LOQ = 0.441 µgmL^{-1}	dosage formulations and in human serum	4.78	[109]
"C18 (150×4.6mm, 5micron) columns"	"methanol (75%, v/v) and phosphate buffer (25%, pH = 8, 0.01 M)"	(UV) 290	3–2000 ngmL $^{-1}$ R^2 = 0.995 % Rec = 101.5 %RSD = 0.45 LOD = 1ngmL^{-1} LOQ = 3 ngmL^{-1}	Pharmaceutical Dosage Forms and Human Serum	7.2	[110]

Table 4: Explain an overview determination of Irbesartan in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	Application	tR min	Ref.
"C18 column (2.1 mm × 50 mm,1.7 µm particle size) and inline 0.2 µm"	"(0.1% formicacid in water) and solvent B (acetonitrile) as follows: 35–35%B (0–0.5 min), 35–80%"	(UV) 250	5–3000 ngmL^{-1} R^2 = 1.000 % Rec = 90.7 %RSD = 4.3 LOD = 5 ngmL^{-1} LOQ =15 ngmL $^{-1}$	human plasma	9.2	[111]
"C18 column (50 mm x_ 2.1 mm, i.d. 1.7 µm"	"acetonitrile: methanol: 10 mM ammonium acetate (70: 15: 15 v/v/v)"	MS analyzer	2-500ngmL^{-1} R^2 = 0.995 % Rec = 90.7 %RSD = 4.3 LOD = 2 ngmL $^{-1}$ LOQ =6 ngmL $^{-1}$	human plasma	5.8	[79]
"(C18) analytical column"	"50 mM potassium di-hydrogen orthophosphate:acetonitrile (55:45, *V/V*) buffer" (pH 2.5)	(UV) 210	10-100 µgmL^{-1} R^2 = 0,999 % Rec = 98.89 %RSD = 1.00 LOD = 1.33 µgmL^{-1} LOQ =4.0 µgmL^{-1}	Bulk and Pharmaceutical Dosage Form	5.2	[80]
"Hypersil Gold C18 column (4.6mm×250 mm, 5 µm)"	"0.5% ortho-phosphoric acid (pH 3.0) and ethanol (65:35 v/v) under isocratic elution"	(UV) 225	0.2-10 µgmL^{-1} R^2 = 0.9974 % Rec = 99.89 %RSD = 1.27	Rat plasma	4.8	[81]
"Kinetex C18 100A column (2.60 µm, 4.60 mm × 100 mm)"	"0.05M potassium dihydrogen phosphate buffer (pH 3.50 adjusted by ortho-phosphoric acid) and acetonitrile"	(UV) 280	10-250 µgmL^{-1} R^2 = 0,9999 % Rec = 99.69 %RSD = 1.6 LOD = 2.01µgmL^{-1} LOQ =6.11 µgmL^{-1}	Dosage Forms	4.72	[82]
"Phenomenex C18 column (150 x 4.6 mm, 5 µm) particle size"	"0.1% Formic acid buffer (pH 3.2): Acetonitrile (60:40 v/v)"	(UV) 220	1.5-120 µgmL^{-1} R2 = 0,999 % Rec = 96.68 %RSD = 0.72 LOD = 0.04 µgmL^{-1} LOQ = 0.13 µgmL^{-1}	Tablet dosage	2.22	[112]

Table 5: Explain an overview determination of Losartan potassium in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	Application	tR min	Ref.
"Zorbax C8 column (150 x 4.6 mm, 5 µm)"	"methanol–acetonitrile–acetate buffer 45:20:35 v/v/v, pH" 4.8	(UV) 240	0.01–0.5 µgmL^{-1} R^2 = 0.9952 % Rec = 99.89 %RSD = 0.45 LOD = 0.08µgmL^{-1} LOQ = 0.24µgmL^{-1}	Dosage Forms	15.6	[110]
"C18 column (250 mm × 4.6 mm, 5 µm)"	"0.01 M ammonium acetate buffer (pH 5.5): acetonitrile"	(UV) 240	10-60µgmL^{-1} R^2 = 0.9998 % Rec = 100.79 %RSD = 0.59 LOD = 0.18µgmL^{-1} LOQ = 0.54µgmL^{-1}	Drugs	5.5	[114]
"ACCHROM ODS-C18 (250 mm×4.6 mm, 5 µm) column"	"The mobile phase was composed of 0.1% phosphoric acid (A) and acetonitrile (B)"	(UV) 220	50-750 µgmL^{-} R^2 = 0.9995 % Rec = 97.00 %RSD = 2.00 LOD = 2.90µgmL^{-1} LOQ = 10.00µgmL^{-1}	Tablets	7.31	[84]
"Hypersil®-Gold C18 (150 x 4.6 mm, 5 µm, Thermo Fisher Scientific, USA)"	"(v/v/v) was water (containing 0.25 ml/L triethylamine), methanol and acetonitrile" (60:38:30, pH adjusted to 2.7±0.1)	(UV) 271	2-48 µgmL^{-1} R^2 = 0.99996 % Rec = 99.6 %RSD = 1.09 LOD = 0.138µgmL^{-1} LOQ = 0.418µgmL^{-1}	pharmaceutical formulations		[115]
"C18 (150 mm× 4.6 mmID, 5 µm particle size)"	"95% (v/v) of 3.0% (w/w) SDS, 6.0% (w/w) n-butanol, 0.8% (w/w) n-octane, 90.2% (w/w) water and 5% (v/v) acetonitrile" (pH 5	(UV) 265	10-60 µgmL^{-1} R^2 = 0.999 % Rec = 101 %RSD = 1.4 LOD = 40 ng mL^{-1} LOQ = 150 ng mL^{-1}	Osmotic Pump Tablets	3.59	[85]
"Thermo C_{18} column (4.6 x 250mm, 5µ particle size)"	"Methanol: Acetonitrile (10:90v/v)" pH 6.4	(UV) 286	5-25 µgmL^{-1} R^2 = 0.9998 % Rec = 99.8 %RSD = 0.26	Marketed Formulation	3.30	[116]

Table 6: Explain an overview determination of Valsartan in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	Application	t_R min	Ref.
"C18 column (250 mm x 4.6 mm id, 5 µm",	"20 mM ammonium formate and acetonitrile in the 57:43"	(UV) 250	25-50 µgmL^{-1} R^2 = 0,998 % Rec = 98.57 54.٠%RSD = LOD = 14.8 ngmL^{-1} LOQ =44.6 ngmL^{-1}	Nanoparticles	10.1	[117]
"C18 column [Xterra, 250 x 4.6 mm, 5µ]"	"acetonitrile, methanol and potassium dihydrogen phosphate, pH 3.8 in the ratio of 30: 50:20 v/v"	(UV) 263	20-160 µgmL^{-1} R^2 = 0,998 % Rec = 98.54 %RSD = 0.27 LOD = 2.80 µgmL^{-1} LOQ =8.50µgmL^{-1}	Tablet formulation	4.22	[89]
"Zorbax Eclipse C18 Cyano column (150 mm, 4.6 mm, 5 µm)"	"ammonium acetate buffer (0.02 M, adjusted to pH 4 with acetic acid): acetonitrile (55:45, v/v)"	(UV) ٥٤2	4–30 µgmL^{-1} R^2 = 0,999 % Rec = 98.9 %RSD = 0.46 LOD = 0.29µgmL^{-1} LOQ =0.99µgmL^{-1}	Experimental design	4.22	[118]
"(Luna C8 150*4.6, 3 µm) C8 column"	"0.1%v/v Trifluoroacetic acid in water: Methanol (25:75)"	(UV) 267	48.5 -145.5µgmL^{-1} R^2 = 0,9999 % Rec = 99.9 %RSD = 0.5	Drug product	3.04	[119]
"C18 column (250 × 4.6 mm, 3 µm",	"water, acetonitrile, and acetic acid (100) (500: 500: 1)"	(UV) 235	0.011–7.4µgmL^{-1} R^2 = 0,999 % Rec = 99.9 %RSD = 0.01 LOD = 0.0085µgmL^{-1} LOQ =0.0285µgmL^{-1}	Drug substance and its products	7.5	[120]
"C18 column (4.6 mm i.d. 250 mm, 5 µm)"	acetonitrile-acetate buffer 0.1M(pH = 4.0) (40:60, v/v)	(UV) 254	5–2000 µgmL^{-1} R^2 = 0.9997 % Rec = 99.99 %RSD = 0.54 LOD = 1.5 µgmL^{-1} LOQ =4.9 µgmL^{-1}	drugs	7.8	[121]
"DCPak P4VP (250 × 4.6 mm, 5 µm)"	"CO2 and 0.1% formic acid in methanol by gradient elution"	230 and 250 nm using a photo diode array detector	5–200 µgmL^{-1} R^2 = 0,9996 % Rec = 96.9 %RSD = 1.2 LOD = 1.5 µgmL^{-1} LOQ =3.925 µgmL^{-1}	drugs	3.42	[90]

Table 7: Explain an overview determination of Methyldopa in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	Application	t_R min	Ref.
"C-18 column (300x3.9 mm i.d)"	"water–methanol (75:25) and pH 3.60"	(UV) 286	9.0–90 µgmL $^{-1}$ R^2 = 0.9998 % Rec = 100.0 %RSD = 0.77 LOD = 4.5 µgmL^{-1} LOQ = 9.00 µgmL^{-1}	tablets		[122]
"ODS packing material and protected by a Shim-pack G-ODS guard column (10mm×4.0mm I.D"	"triethylamine (100_l/l, v/v; pH 2.3) and methanol (92:8, v/v)" pH2.3	fluorescence detector270 and 320	9.0–90 µgmL $^{-1}$ R^2 = 0.9998 % Rec = 100.0 %RSD = 0.77 LOD = 6.5 µgmL^{-1} LOQ = 20 µgmL^{-1}	Application to a bioequivalence study	2.4	[91]
"Hypersil BDS C8 column (250 mm x 4.6 mm; 5µ)"	"phosphate buffer 5.5 and acetonitrile in a ratio of 50:50 v/v"	(UV) 287	62.5-375.0µgmL $^{-1}$ R^2 = 1.0 % Rec = 99.83 %RSD = 0.16 LOD = 5.756 µgmL^{-1} LOQ = 17.44 µgmL^{-1}	tablet dosage form	3.56	[123]
"ODS-80 TM analytical column (50 3 4.0 mm i.d., 5 mm)"	acetate buffer (0.1 M, pH 2.4)	(UV) 270	0.1–30µgmL $^{-1}$ R^2 = 0.9996 % Rec = 99.97 %RSD = 0.43 LOD = 0.027 µgmL^{-1} LOQ = 17.44 µgmL^{-1}	serum	3.5	[124]
"C8 column (dimensions: 150 × 4.6 mm; particle size: 5 µm)"	water and acetonitrile:methanol (90:10 v/v)	-HPLC–MS/MS	0.1–30 ngmL $^{-1}$ R^2 = 0.9994 % Rec = 98.97 %RSD = 11.3 LOD = 1.5 ngmL^{-1} LOQ = 10 ngmL^{-1}	human plasma	٢,٠٣	[125]
"Hypersil ODS analytical columns (100mmx4.0mm i.d., 5 µm)"	acetate buffer (0.1M, pH 2.4)	(UV) 270	0.1–40µgmL $^{-1}$ R^2 = 0.9997 % Rec = 99.47 %RSD = 0.895 LOD = 0.029µgmL^{-1} LOQ = 0.089µgmL^{-1}	human urine	5.8	[126]
"Hypersil-ODS analytical column (125mm×4.0mm, 5 µm"	methanol/0.002 mol L^{-1} KH_2PO_4 (pH 5) solution (25:75, v/v)	(UV) 280	0–7.00 µgmL $^{-1}$ R^2 = 0.9989 % Rec = 104.2 %RSD = 2.6 LOD = 0.244µgmL^{-1} LOQ = 0.080µgmL^{-1}	human plasma	3.46	[127]

Table 8: Explain an overview determination of Carvedilol in some pharmaceuticals preparation using chromatography methods.

Stationary phase	Mobile phase	Detection	Statistical data analysis	Application	t_R min	Ref.
"Chromolit RP8e, 100x 4.6 mm"	"Acetonitrile/water (50:45, v/v) (pH 2.5)"	(UV) 280	0.5–1.1µgmL^{-1} R^2 = 0.999 % Rec = 101.58 %RSD = 1.02 LOD = 0.007µgmL^{-1} LOQ = 0.026µgmL^{-1}	bulk drug	3.4	[128]
"RP-18e, 100mm×4.6 mm) column"	"0.01M disodium hydrogen phosphate buffer–acetonitrile (40:60, v/v) (pH 3.5")"	(UV) 240	1–80 ng ml^{-1} R^2 = 0.999 % Rec = 99.71 %RSD = 1.394 LOD = ٠,٠٠١µgmL^{-1} LOQ = 0.008µgmL^{-1}	human plasma	2.7	[129]
"C8, Kromasil KR 100 ,C8 column"	"acetonitrile, 15 mM orthophosphoric acid (37:63), and 0.25% v/v of triethylamine' (pH 2.5)	(UV) 238	5–500 ng ml^{-1} R^2 = 0.9979 % Rec = 99.3 %RSD = 0.0620 LOD = 1–80 ng mL^{-1} LOQ = 1 ngmL^{-1}	human serum	6.1	[130]
"C18 column"	"0.05 M potassium dihydrogen phosphate and acetonitrile" (60:40, v/v) (pH 2.5)	(UV) 245	10-200 µgmL^{-1} R^2 = 0.9998 % Rec = 101.58 %RSD = 0.72 LOD = 1.29µgmL^{-1} LOQ = 3.92µg mL^{-1}	Pharmaceutical Formulations	4.2	[95]
"Phenomenex Lux-cellulose–4 (250 mm × 4.6 mm; 5 µ particle size)"	"Isopropanol and n-Heptane" (v/v) ٦٠:٤٠ (pH 3)	(UV) 254	5-50 ngmL^{-1} R^2 = 0.999 % Rec = 99.18 %RSD = 0.18 LOD = 1.08 ngmL^{-1} LOQ = 3.29 ngmL^{-1}	Active Pharmaceutical Ingredient (API) and marketed tablet formulation of racemic Carvedilo	9.3	[131]
"C18 column (3 mm, 4.6 mm i.d. _ 250 mm"	methanol/acetate buffer (pH 4.0; 0.1 M) (70:30, v/v)	(UV) 285	4-16 µgmL^{-1} R^2 = 0.995 % Rec = 102 %RSD = 0.18 LOD = 8 µgmL^{-1} LOQ = 25µgmL^{-1}	Pharmaceutical Dosages		[132]

Conflicts of interest

There are no conflicts to declare.

Formatting of funding sources

There are no formatting sources.

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