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## Review on cyclic voltammetric and spectrophotometric approaches for the analysis of drugs (antihypertensive) using different electrodes and wavelength

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### ABSTRACT

Hypertension is the most prevalent cardiovascular disease in the developed as well as developing countries, affecting about 20 – 30% of the adult population. It is an independent risk factor for cardiovascular disease and is associated with an increased incidence of stroke and coronary heart disease. To control the risk factors several types of antihypertensive drugs are used in the world. Therefore, pharmacodynamic and pharmacokinetic studies are utmost important for the quality control. The advent of electronics has allowed to develop more sensitive, reliable and less expensive instrumentations which have significant contribution in the field of drug development and analysis. The use of various types of modified electrodes in the voltammetric techniques and spectrophotometric method play an important role due to its advantages over other sophisticated instruments in terms of low cost, simplicity and portability.

**Keywords:** cardiovascular disease; antihypertensive drugs; spectrophotometry; voltammetry.

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### INTRODUCTION

Antihypertensive drugs play a very crucial role in the treatment and lifesaving of cardiac patients. In spite of their crucial role, they create specifically desired effect as administered by the most desired route at minimal dosage and dosing frequency. Almost all the drugs are harmful or even poisonous at high dose levels. Therefore it is utmost important to determine the activity of drug and their pharmacokinetic and pharmacodynamics studies in pharmaceutical formulations. The analysis of drug is an integral part of overall drug development process. It involves the determination of not only for active components but also impurities, excipients, stability of active components (degradation intermediates or end-products) and other parameters such as content uniformity, solubility and dissolution rate.

Keeping these points in consideration, various analytical methods, including gas chromatography (GC) [1, 2] high-performance liquid chromatography (HPLC) [3, 4] liquid chromatography mass spectrometry (LC-MS, LC-MS-MS) [5, 6], cyclic voltammetric and spectrophotometric method have been developed for the determination of antihypertensive drugs in commercial dosage forms. All these analytical techniques are well established and recommended as good and validated methods for the analysis. However, our concern is to review the development of cyclic voltammetric (electrochemical method) and spectrophotometric approach for the analysis of antihypertensive drugs because of its wide range of applications, sensitivity, selectivity, accuracy, precision, rapid analysis time, large linear dynamic range, low cost instrumentation, portability and instrument simplicity. Moreover, electrochemical techniques are useful tools for the study of adsorption and crystallization phenomena at electrode surfaces [7-11]. It has been also used as a complementary technique to spectrophotometry due to its high sensitivity, speed of analysis, reduction in solvent and sample consumption [8-12]. The principal advantages of these electrochemical techniques such as linear sweep, cyclic, differential pulse, square wave etc. are that the excipients

do not interfere and generally the separation and extraction procedures are not necessary. Therefore, the utility of these techniques increased in pharmaceutical industries.

Among instrumental analytical techniques, spectrophotometry occupies a unique position because of its simplicity, speed, precision, accuracy and economical compared to other methods such as chromatography and electrophoresis [13]. These methods are widely used for the determination of organic substances, drugs in pharmaceutical formulations, biological fluids, blood serum, ointment and urine samples [14-18]. Various review papers are available for the drug analysis by different electroanalytical and spectrophotometric techniques [19-30]. But to the best of our knowledge, a review especially focused on the analysis of antihypertensive drugs using cyclic voltammetry and spectrophotometry is not available. Therefore, the main objective of this review is to present the advantages and use of cyclic voltammetric and spectrophotometric techniques for the analysis of antihypertensive drugs.

## MATERIALS AND METHODS

Electrochemical methods have worldwide reputation for the analysis of drugs and pharmaceuticals due to their high sensitivity, versatile, low detection limits and inexpensive instrumentations [31]. These modalities involve the direct conversion of chemical information into signals in terms of current, potential and charge. Electrochemical methods are highly capable for assaying the concentration of electroactive analyte at trace level and supply useful information concerning its physical and chemical properties such as oxidation potential, diffusion coefficients, electron transfer rates and electron transfer number. Besides, their analytical advantages, these techniques play an important role in the study of pharmacologically active compounds and metabolites produced by different metabolic pathways involving redox reactions [32]. Consequently, electrochemical data develop the relationship between the biological activity and electrodic processes of the drugs, which help to provide the hints about the action mechanism of the specific drug and correlate to the molecular structure and pharmacological activity. Moreover, the interaction of drug with metals, proteins and the degradation of photo or pH sensitive drugs were also studied by using electrochemical techniques [33].

### **Voltammetry**

Voltammetry is in fact a set of analytical methods used to determine the properties of an analyte by measuring the reactivity of analyte to an electrical charge while the potential of the current is varied [34]. This technique based on the continuous variation of the potential applied across the electrode-solution interface, being the resulting current recorded. The resulting voltammogram is analogous to a conventional spectrum in the sense that it conveys information as a function of energy scan. Voltammetric methods can also be used to perform solubility and stability studies to understand the interaction among drugs and living cells [35, 36]. Nowadays, voltammetric techniques associated to flowing or convective systems have intensely been employed for the analysis of a variety of samples (although in reduced extension) even for drug analysis [37-41]. Voltammetric techniques have been extremely useful in measuring blood levels, metabolites and urinary excretion of drugs following low doses, especially when coupled with chromatographic methods. In many cases, modern electro-analytical techniques like square wave voltammetry (SWV) are also available alternative to more frequently used spectrometric or separation methods [42,43]. Voltammetric measurements can also be applied directly to the colored and suspended colloidal systems. Although biological or complex environmental samples required pretreatment, but this process is faster, cheaper and easier as compared to the pretreatment of samples analyzed for chromatographic techniques [44]. In this modality solid or mercury based electrodes are served as working electrode where the reaction of interest occurs. The field of modified solid electrodes has become very popular and applied in industries, quality control of drugs and foods, determination in pharmaceutical formulations and environmental monitoring [45-47]. Various scientists used different voltammetric techniques such as potential step, linear sweep, differential pulse, square wave, stripping and cyclic voltammetry for the analysis of drugs in dosage forms [48-56]. These techniques have been successfully applied for trace measurement of important pharmaceutically active compounds due to its high sensitivity and selectivity.

### *Cyclic Voltammetry*

Cyclic voltammetry is often the first experiment performed in an electrochemical study based on potential control and most widely used for acquiring qualitative information about electrochemical reactions [57-61]. It is widely applicable in the study of redox reactions, detection of reaction intermediate and the observation of follow up reaction of products formed at the electrode and most versatile electroanalytical tool for the analysis of pharmaceuticals and biologically active compounds [62-65].

*Cyclic Voltammetric analysis of some miscellaneous drugs*

Acuna et al. studied the kinetics of the hydrolytic decomposition of droxicam and established the pharmacological action of the drug in the organism of the human body [66]. Bollo et al. carried out the experiment for the formation and stability of the radical anion from PA-824 and compared with metronidazole [67]. Wang et al. discussed the cyclic voltammetry study along with bulk electrolysis and deduced the redox reaction mechanism of nicotinic acid and nicotinamide in which it was rationalized by the formation/disappearance of the new nitrogen-oxygen bonds in pyridine rings [68]. The determination of acetaminophen in paracetamol tablets was performed by using cyclic voltammetry in phosphate buffer with good linearity and precision range [69]. Topal et al. investigated the electrochemical oxidation of loracarbef by using cyclic, linear sweep, differential pulse and square-wave voltammetric techniques. The results obtained from this study indicated that the oxidation process of loracarbef is irreversible and diffusion controlled on glassy carbon electrodes and the quantitative determination of loracarbef was in the range of  $6 \times 10^{-6}$  to  $2 \times 10^{-4}$  M. This method was also proposed for the determination of loracarbef in pharmaceutical dosage forms [70]. Liu et al. studied the electrochemical behavior of isorhamnetin at glassy carbon electrode and a linear dependence on the concentration of isorhamnetin in the range of  $1 \times 10^{-7}$  to  $4 \times 10^{-6}$  M and  $1 \times 10^{-6}$  to  $1 \times 10^{-5}$  M were obtained [71]. Norouzi et al. developed the method for the determination of rantidine in pharmaceutical formulations with the detection limit  $24 \text{ pg ml}^{-1}$  [72]. The relevant analytical data based on the cyclic voltammetric study of some antihypertensive drugs is given in Table 1 [61, 73-94].

**Table 1: Use of cyclic voltammetry in the analysis of antihypertensive drugs**

| Name of drug        | Working electrode      | Detection limit  | References |
|---------------------|------------------------|--|------------|
| Amlodipine          | GCE                    | --   | [73]       |
| Captopril           | MCPE                   | $1.1 \times 10^{-6}$ M                                       | [74]       |
| Carvedilol          | GCE                    | $0.10 \text{ } \mu\text{g ml}^{-1}$                          | [75]       |
| Diosmin             | GCE                    | $3.5 \times 10^{-8}$ M                                       | [76]       |
| Dipyridamole        | Pt, Pd, Au, Carbon     | --   | [77]       |
| Dopamine            | Mod. GCE               | $5 \times 10^{-6}$ M   | [78]       |
| Hydrochlorothiazide | GCE                    | $0.10 \text{ } \mu\text{g ml}^{-1}$                          | [79]       |
| Imipramine          | Au microelectrode      | $4.55 \text{ pg ml}^{-1}/14\text{-}22400 \text{ pg ml}^{-1}$ | [80]       |
| Indapamide          | MCPE                   | 5 nM   | [81]       |
| Irbesartan          | HMDE                   | $5.33 \times 10^{-6}$ – $1 \times 10^{-4}$ M                 | [82]       |
|                     | GCE                    | $5.33 \times 10^{-7}$ M                                      | [83]       |
| Lercanidipine       | Mod. GCE               | $0.02$ – $3 \text{ } \mu\text{g ml}^{-1}$                    | [84]       |
| Losartan            | Au microelectrode      | --   | [61]       |
| Nifedipine          | GCE                    | $2 \times 10^{-5}$ M   | [85]       |
| Nimodipine          | HMDE                   | $7.11 \text{ ng ml}^{-1}$                                    | [86]       |
|                     | Mod. GCE               | $0.025$ – $3 \text{ } \mu\text{g ml}^{-1}$                   | [84]       |
| Ramipril            | DME, Pt. electrode     | $4.8 \times 10^{-8}$ M                                       | [87]       |
| Rutin               | HMDE                   | $4.9 \times 10^{-9}$ M                                       | [88]       |
| Terazosin           | GCE                    | $6 \times 10^{-7}$ M   | [89]       |
| Timolol             | Au microelectrode      | $1.58 \text{ ng ml}^{-1}$                                    | [90]       |
|                     | SMDE                   | 2.5 ppb  | [91]       |
| Tramadol            | Au disk microelectrode | $0.32 \text{ pg ml}^{-1}$                                    | [92]       |
| Trimetazidine HCl   | GCE                    | $2 \times 10^{-8}$ M   | [93]       |
| Verapamil           | DME,PCE                | $5 \times 10^{-10}$ M  | [94]       |

**Abbreviations:**

GCE = glassy carbon electrode,

DME= dropping mercury electrode

HMDE = hanging mercury drop electrode

SMDE = static mercury drop electrode

MCPE = modified carbon paste electrode

CPE= carbon paste electrode

PCE= platinum counter electrode

**SPECTROPHOTOMETRIC METHOD**

Analytical methods based on measurements of ultraviolet or visible (UV-Visible) light absorption belongs to the most popular and most often used laboratory practices. UV-Visible spectrophotometry can be regarded as one of the most suitable and economical method in the laboratories of research, hospitals and pharmaceutical industries due to its low cost, portability and inherent simplicity [95, 96]. Moreover, its coupling with other modalities increases the application of spectrophotometry. However, direct spectrophotometric methods are not suitable for simultaneous determination of drugs due to their spectral overlapping. To overcome this problem derivative spectrophotometric approach is widely applicable to enhance the sensitivity and specificity by using the information from overlapping bands of the analytes and interferences [97, 98]. It also has been commonly used for the analysis of several

antihypertensive drugs and reviewed by various scientists [99-101]. Salem et al. developed the method for the determination of domperidone maleate and cinnarizine in a binary mixture by using derivative ratio spectrophotometry [102].

Interferences from active substances were eliminated by applying derivative spectrophotometry for determination of irbesartan and hydrochlorothiazide in CoAprovel 150/12.5 [103], hydrochlorothiazide and losartan in Losazid and Neo Lotan Plus [104], candesartan and hydrochlorothiazide [105]. Perindopril and indapamide were also determined in Pretrax using derivative spectrophotometry and liquid chromatographic method, as a reference one [105]. This approach is able to eliminate the interferences from degradation products, co-formulated drugs and also excipients, however their uses in highly complex samples such as biological fluids are limited. The use of UV spectrophotometry as detector in flow injection analysis (FIA) systems for drug analysis is another important application of this technique [106]. Several drugs and metals have been determined using UV-FIA in dosage forms [107-108]. A second generation of flow analysis designated as sequential injection analysis was proposed by Ruzicka and Marshal in 1990, which provides a powerful and versatile instrument for the automation of diverse analytical procedures [109]. This technique has been associated with a large number of detectors including UV-Visible spectrophotometry and has been applied in chemistry areas as diverse as pharmaceutical, environmental, food and beverage radiochemical kinetic studies of chemical reactions [110, 111]. Representative examples of spectrophotometric method for the analysis of antihypertensive drugs have been published are summarized in Table 2 [112-255].

**Table 2: Use of spectrophotometric methods for the analysis of antihypertensive drugs**

| Name of drug       | Reagents/Method                                  | Absorption maxima<br>$\lambda_{\text{max}}$ (nm) | References |
|--------------------|--|--|------------|
| Ramipril           | Cu (II) and eosin                                | 535  | [112]      |
|                    | Fe (III) + ammonium thiocyanate                  |  | [113]      |
|                    | 7,7,8,8-tetracyanoquinodimethane                 | 840  | [114]      |
|                    | <i>p</i> -chloranilic acid                       | 520  | [114]      |
|                    | 2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone |  | [114]      |
|                    | <i>p</i> -chloranilic acid                       | 524  | [115]      |
|                    | Picric acid                                      | 370  | [115]      |
|                    | Bromocresol green                                | 412  | [115]      |
|                    | Alkaline KMnO <sub>4</sub>                       | 610  | [116]      |
|                    | 7-fluoro-4-nitrobenzo-2-oxo-1,3-diazole          | 460  | [117]      |
|                    | KIO <sub>3</sub> and KI                          | 352  | [118]      |
|                    | 1-chloro-2,4-dinitrobenzene                      | 420  | [119]      |
|                    | Excess Ce (IV)+ amaranth dye                     | 523  | [120]      |
|                    | UV   | 210  | [121]      |
|                    | Tropaeolin 000                                   | 489  | [122]      |
|                    | Sodium nitroprusside acetaldehyde                | 560  | [123]      |
|                    | UV   | 250  | [124]      |
|                    | Molybdenum (V) thiocyanate                       | 517  | [125]      |
|                    | Benzalkonium chloride                            | 545  | [125]      |
|                    | Brucine + Sodium metaperiodate                   | 525.6  | [126]      |
| UV                 | 200-350  | [127]  |            |
| UV                 | 201-270  | [128]  |            |
| Perindopril        | Bromothymol blue                                 | --   | [129]      |
|                    | FeCl <sub>3</sub> in the presence of KSCN        | --   | [129]      |
|                    | 2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone | 588  | [130]      |
|                    | 7,7,8,8-tetracyanoquinodimethane                 | 843  | [130]      |
|                    | Tetracyanoethylene                               | 419  | [130]      |
|                    | Chloranil  | 550  | [130]      |
|                    | <i>p</i> -chloranilic acid                       | 520  | [130]      |
|                    | 1-chloro-2,4-dinitrobenzene                      | 420  | [131]      |
|                    | Zn (II) and eosin                                | 510  | [132]      |
|                    | Iodine   | 365  | [132]      |
|                    | Cu (II) and eosin                                | 535  | [112]      |
|                    | UV   | 215  | [133]      |
|                    | UV   | 213  | [134]      |
|                    | KMnO <sub>4</sub> in alkaline medium             | 603  | [135]      |
|                    | 2, 4 dinitrofluorobenzene                        | 410  | [136]      |
|                    | Sanranin - O                                     | 520  | [137]      |
|                    | Bromothymol blue                                 | 410  | [137]      |
|                    | KMnO <sub>4</sub>                                | 605  | [137]      |
| Ammonium molybdate | 750  | [137]  |            |
| Enalapril maleate  | 2,4-dinitrofluorobenzene                         | 356,420  | [138]      |
|                    | KMnO <sub>4</sub> with acidic dyes               | 510, 521,484                                     | [139]      |
|                    | KIO <sub>3</sub> and KI                          | 352  | [140]      |

|  |   |                |       |
|--|---|----------------|-------|
|  | <i>p</i> -chloranilic acid  | 510            | [140] |
|  | 2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone                        | 565            | [140] |
|  | Iodine  | 365            | [140] |
|  | <i>p</i> -chloranilic acid  | 534            | [115] |
|  | Picric acid   | 370            | [115] |
|  | Bromocresol green.  | 412            | [115] |
|  | UV  | 200-400        | [141] |
|  | Molybdenum (V) thiocyanate  | 517            | [125] |
|  | Benzalkonium chloride   | 545            | [125] |
| Captopril  | KIO <sub>3</sub> in acidic medium                                       | 510            | [142] |
|  | KMnO <sub>4</sub> + methylene blue                                      | 660            | [143] |
|  | KMnO <sub>4</sub> + Acid blue 74  | 610            | [143] |
|  | KMnO <sub>4</sub> + Acid red 73   | 510            | [143] |
|  | KMnO <sub>4</sub> + Amarnath dye  | 520            | [143] |
|  | KMnO <sub>4</sub> + Acid Orange 7                                       | 458            | [143] |
|  | Hexacyanoferrate (III)  | 510            | [144] |
|  | Dichlone  | 347            | [145] |
|  | Excess KIO <sub>3</sub> in acidic medium                                | 606            | [146] |
|  | Excess Ce (IV) + Methyl Orange  | 510            | [147] |
|  | Fe (III) + Hexacyanoferrate (III)                                       | 700            | [148] |
|  | Bromine + indigo carmine  | 610            | [149] |
|  | Bromine + Fe (II) + 1,10 phenanthroline                                 | 510            | [149] |
|  | Bromine + Fe(II) + thiocyanate  | 478            | [149] |
|  | KBrO <sub>3</sub> + Celestine blue                                      | 540            | [150] |
|  | NaNO <sub>2</sub> + HCl   | 555            | [151] |
|  | 2,2- diphenyl 1-picryl-hydrazyl   | --             | [152] |
|  | PdCl <sub>2</sub>   | 380            | [153] |
|  | N-bromophthalimide in 50% H <sub>3</sub> PO <sub>4</sub>                | 516            | [154] |
|  | Molybdophosphoric acid  | 685            | [154] |
|  | Cr (VI) + Diphenylcarbazide   | 540            | [155] |
|  | Excess Fe (II) + Pot. Ferricyanide                                      | 730            | [156] |
|  | FeCl <sub>3</sub> + bipyridyl or I <sub>2</sub>                         | 523,351, 620   | [157] |
|  | Cu (II) + neocuproine   | 448            | [158] |
|  | Sodium azide and I <sub>2</sub>   | 348            | [159] |
|  | AgNO <sub>3</sub> +methyl orange  | 520            | [160] |
|  | AgNO <sub>3</sub> + eosin + 1,10 phenanthroline                         | 550            | [160] |
|  | Excess bromide + methyl orange  | 510            | [161] |
|  | Excess Chloramine T + metol + sulphanillic acid                         | 520            | [162] |
|  | Chloramine T  | 610            | [163] |
|  | 2,6- dichloroquinone-4 chlorimide                                       | 443            | [164] |
|  | KIO <sub>3</sub> +2',7'-dichlorofluorescein                             | 520            | [165] |
| • Fluorescein natrium(C <sub>20</sub> H <sub>10</sub> Na <sub>2</sub> O <sub>5</sub> ) | 436   | [166]          |       |
| Lisinopril   | 2,4-dinitrofluorobenzene  | 400, 365       | [138] |
|  | 7,7,8,8,tetracyanoquinodimethane  | 743            | [167] |
|  | <i>p</i> -chloranilic acid  | 525            | [167] |
|  | N-bromosuccinimide  | 353            | [168] |
|  | KMnO <sub>4</sub> with acidic dyes                                      | 509, 521, 485  | [139] |
|  | Sodium 1,2-Naphthoquinone-4-sulphonate                                  | 481            | [169] |
|  | Fluorescein   | 228            | [170] |
|  | Ninhydrin in the presence of bicarbonate                                | 420            | [171] |
|  | Chloranil   | 346            | [172] |
|  | Dichlone  | 580            | [172] |
|  | Acetyacetone and formaldehyde   | 356            | [172] |
|  | 1-fluoro-2, 4-dinitrobenzene  | 356.5 or 405.5 | [173] |
|  | Sodium hypochlorite and phenyl hydrazine                                | 362            | [174] |
|  | Ninhydrin and ascorbic acid   | 420, 530       | [175] |
|  | Ninhydrin   | 600            | [176] |
|  | Ninhydrin   | 410            | [177] |
|  | Ninhydrin   | 420            | [178] |
|  | UV  | 220, 340       | [179] |
|  | Cu(II) +Nile Blue A with H <sub>2</sub> O <sub>2</sub> in Borate buffer | 635            | [180] |
|  | Ninhydrin + Sodium molybdate  | 570            | [181] |
| Methyldopa   | 2,6-dichloroquinone-4-chlorimide  | 400            | [182] |
|  | Ammonium molybdate  | 410            | [183] |
|  | FeCl <sub>3</sub>   | 423            | [184] |
|  | Fe(III)- <i>o</i> -phenanthroline                                       | 510            | [185] |
|  | Fe(III) in acidic medium  | 510            | [186] |
|  | Isoniazid in presence of <i>N</i> -Bromosuccinamide                     | 480-490        | [187] |
|  | Sodium nitroprusside + hydroxylamine hydrochloride                      | 635-660        | [187] |
|  | Diazotised sulphanilamide + molybdate ions                              | 500            | [188] |
| Barbituric acid  | 540   | [189]          |       |

|                    |  |               |       |
|--------------------|--|---------------|-------|
|                    | Semicarbazide hydrochloride + potassium persulfate         | 460-470       | [190] |
|                    | p-Chloranil  | 535           | [191] |
|                    | Polyphenol oxidase enzyme                                  | 480           | [192] |
|                    | Neotetrazolium chloride                                    | --            | [193] |
|                    | Bromate – bromide mixture                                  | 670           | [194] |
|                    | Fe(III) +Salicylic acid +HCl                               | 525           | [195] |
|                    | Fe(III) chloride and nitroso-R-salt                        | 708           | [196] |
| Prazosin           | 2,3,-dichloro-5,6-dicyano- <i>p</i> benzoquinone           | 460           | [197] |
|                    | Bromophenol blue   | 410           | [197] |
|                    | <i>p</i> - <i>N</i> -methyl aminophenol sulphate           | 520           | [198] |
|                    | 3-methyl-2-benzothiazolinone hydrazone hydrochloride       | 620           | [198] |
|                    | Orange-II  | 490           | [198] |
|                    | Alizarin violet 3B   | 570           | [198] |
|                    | UV   | 356,346       | [199] |
|                    | Britton–Robinson buffer (pH 1.8)                           | 246 and 329   | [200] |
| Doxazosin          | 1,2-naphthoquinone-4- sulphonic acid sodium                | 400           | [201] |
|                    | Bromocresol purple   | 403           | [202] |
|                    | Bromophenol blue   | 410           | [202] |
|                    | 2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone           | 457           | [202] |
|                    | 7,7,8,8,tetracyanoquinodimethane                           | 838           | [202] |
|                    | Bromocresol green  | 418           | [203] |
|                    | Bromothymol blue   | 414           | [203] |
|                    | Methyl orange  | 425           | [203] |
| Indapamide         | Alizarin red- S  | 426           | [203] |
|                    | Ammonium molybdate   | 710           | [204] |
| Terazosin          | p-dimethyl amino cinnamaldehyde                            | 450           | [205] |
|                    | 3-methyl-2-benzothiazolinone hydrazone                     | 641           | [205] |
|                    | 3-methyl-2-benzothiazolinone hydrazone + FeCl <sub>3</sub> | 660           | [206] |
|                    | UV   | 250           | [206] |
|                    | p-dimethyl amino cinnamaldehyde                            | 410           | [207] |
|                    | Bromocresol purple   | 420           | [207] |
|                    | Chloranil  | 340           | [208] |
|                    | Mercurochrome  | 543           | [208] |
|                    | Bromocresol purple   | 412           | [208] |
|                    | Bromocresol green  | 419           | [203] |
|                    | Bromothymol blue   | 415           | [203] |
|                    | Methyl Orange  | 425           | [203] |
|                    | Alizarin Red- S  | 428           | [203] |
|                    | NaNO <sub>2</sub> + HCl + 1-Naphthol                       | 560           | [209] |
| Losartan Potassium | KMnO <sub>4</sub> in alkaline medium                       | 603           | [210] |
|                    | UV   | 234           | [211] |
|                    | UV   | 220,320,232.5 | [212] |
|                    | Bromocresol purple   | 415           | [213] |
|                    | Cresol- red  | 435           | [213] |
|                    | UV   | 240.8         | [214] |
|                    | Iodine   | 365           | [215] |
|                    | 7,7,8,8,tetracyanoquinodimethane                           | 842           | [215] |
|                    | 2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone           | 460           | [215] |
|                    | 1,3,5- trinitrobenzene                                     | 438           | [215] |
|                    | <i>p</i> -Chloranilic acid                                 | 520           | [215] |
|                    | Tetracyanoethylene   | 414           | [215] |
|                    | Bromanil   | 500           | [215] |
|                    | Chloranil  | 463           | [215] |
|                    | 2,4,7-trinitro-9-fluorenone                                | 413           | [215] |
|                    | Bromocresol green  | 612.4         | [216] |
|                    | Bromophenol blue   | 607           | [216] |
| Irbesartan         | Bromocresol purple   | 415           | [213] |
|                    | Cresol- red  | 435           | [213] |
|                    | KIO <sub>3</sub> + KI                                      | 352           | [217] |
|                    | UV   | 263           | [218] |
|                    | Picric acid  | 416           | [219] |
|                    | Bromocresol red  | 410           | [219] |
|                    | Bromothymol blue   | 415           | [219] |
|                    | Cobalt thiocyanate   | 625           | [219] |
|                    | Molybdenum(V) thiocyanate                                  | 475           | [220] |
|                    | Tropaeoline 000  | 484           | [220] |
|                    | Alizarin red-S   | 420           | [220] |
|                    | UV   | 200-300       | [221] |
|                    | UV   | 230.1         | [222] |
|                    | Bromophenol blue   | 420           | [223] |
| Bromocresol purple | 420  | [223]         |       |



|               |   |                       |       |
|---------------|---|-----------------------|-------|
|               | Bromothymol blue                                      | 420                   | [223] |
|               | Naphthol blue black                                   | 625                   | [223] |
| Dihydralazine | 2-hydroxy-1-naphthaldehyde                            | 420                   | [224] |
|               | 2-hydroxy-1-naphthaldehyde                            | 408                   | [225] |
| Hydralazine   | UV  | 314-316               | [226] |
|               | Folin Ciocalteu reagent                               | 640                   | [227] |
|               | Fe (III)  | 720                   | [227] |
|               | Vanillin  | 390                   | [228] |
|               | p-dimethylaminobenzaldehyde                           | 470                   | [229] |
| Reserpine     | Fe(II) + 1,10 phenanthroline                          | 510                   | [230] |
|               | 4-carboxyl-2,6-dinitrobenzene diazonium ion           | 470                   | [231] |
|               | Iodine  | 369                   | [232] |
| Clonidine     | Bromocresol green                                     | ---                   | [233] |
|               | UV  | 228.4                 | [234] |
| Benazepril    | UV  | 240, 244              | [235] |
|               | Bromocresol green                                     | 412                   | [235] |
|               | 3-methylbenzothialozone hydrazone                     | 593                   | [235] |
|               | UV- derivative methods                                | 214.8                 | [236] |
|               | Second order derivative method                        | 241.2                 | [236] |
|               | Ratio spectra derivative method                       | 217.7                 | [237] |
|               | Safranin-O  | 525                   | [238] |
| Cilazapril    | UV  | 238.1                 | [237] |
| Valsartan     | UV  | 205.6,221.6,<br>231.2 | [239] |
|               | UV  | 200-400               | [142] |
|               | UV  | 250                   | [240] |
|               | Safranin-O  | 525                   | [240] |
|               | Ratio derivative UV                                   | 231.5,260.5           | [241] |
| Telmisartan   | Alizarin in presence of thionyl chloride              | 427                   | [242] |
|               | Phenol red  | --                    | [243] |
|               | Cresol red  | --                    | [244] |
| Larcanidipine | Vanillin  | 600                   | [245] |
|               | Citric acid/acetic anhydride                          | 555                   | [245] |
|               | Chloranil-acetaldehyde                                | 585                   | [245] |
|               | Diazotization with nitrous acid + $\beta$ -Naphthol   | 553                   | [246] |
|               | UV (D <sub>0</sub> , D <sub>2</sub> ,D <sub>3</sub> ) | 236,238,<br>234       | [247] |
| Milrinone     | 2,3,-dichloro-5,6-dicyano-p-benzoquinone              | 356                   | [248] |
|               | p-chloranilic acid                                    | 519                   | [248] |
| Fosinopril    | Molybdenum (V) thiocyanate                            | 517                   | [125] |
|               | Benzalkonium chloride                                 | 545                   | [125] |
| Disopyramide  | Picric acid   | 416                   | [219] |
|               | Bromocresol red                                       | 410                   | [219] |
|               | Bromothymol blue                                      | 415                   | [219] |
|               | Cobalt thiocyanate                                    | 625                   | [219] |
|               | Molybdenum(V) thiocyanate                             | 475                   | [219] |
| Candesartan   | UV  | 254                   | [249] |
| Lacidipine    | Dimethylaminobenzaldehyde                             | 615.7                 | [250] |
|               | UV  | 240,230               | [251] |
|               | UV  | 218                   | [252] |
|               | p-dimethylaminobenzaldehyde                           | 415                   | [253] |
|               | p-dimethyl amino cinnamaldehyde                       | 420                   | [253] |
|               | Vanillin  | 520                   | [253] |
|               | FeCl <sub>3</sub> + potassium ferricyanide + HCl      | 740                   | [254] |
|               | Tropaeolin 000  | 420                   | [255] |
|               | Bromocresol green                                     | 500                   | [255] |
|               | Azocarmine G  | 540                   | [255] |

Furthermore, interactions of an antihypertensive drug with anti-inflammatory drugs were also investigated to monitor their pharmacokinetic studies using UV-Visible spectrophotometry and cyclic voltammetry [256].

## CONCLUSION

This review is aimed at focusing the role of cyclic voltammetric and spectrophotometric methods in the assay of pharmaceuticals and giving a thorough literature survey of these two methods involved in pharmaceutical analysis. In recent decade the electrochemical and spectrophotometric techniques are well established and fast growing areas with a number of possible research applications in the area of pharmaceutical analysis. Of course, various sensitive, fast, and advanced analytical methods are developing in the field of clinical and analytical sciences but the demand and usability of these modalities cannot be replaced as it has a lot of significant features such as easily available,

cost effective, accurate, sensitive and user friendly. Moreover, the use of various types of modified electrodes enhances the electroanalytical properties of the voltammetric techniques. On the other hand spectrophotometry plays a very important role due to its advantages over other sophisticated instruments in terms of low cost, simplicity and portability. Many people are now a days suffering from cardiovascular diseases. Hence, the continuous research and attention to the analysis of antihypertensive drugs by the analytical chemistry community and scientists will eradicate this life threatening diseases.

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