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Overview of the Determination of Hydrochlorothiazide Levels in Pharmaceutical Preparations and Biological Matrices

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Abstract

Hydrochlorothiazide (HCT) is a diuretic drug that works to inhibit sodium and chloride reabsorption. Therefore, the determination of hydrochlorothiazide levels is essential for quality control, whether as raw material, in pharmaceutical preparations, biological fluids, or mixtures. Search information on the determination of hydrochlorothiazide content was carried out through Google Scholar with the keywords "hydrochlorothiazide," "determination," "pharmaceutical preparation," "biological matrix," "mixture." The results showed that the levels of hydrochlorothiazide as a raw material could be determined by high-performance liquid chromatography (HPLC), capillary zone electrophoretic (CZE), micellar electrokinetic capillary chromatography (MEKC), capillary electrophoresis, chemiluminescence, voltammetry, and quantitative point tests. Hydrochlorothiazide in a pharmaceutical dosage form can be determined by high-performance liquid chromatography, spectrophotometric, electroanalytic, thin layer chromatography (TLC) methods, voltammetry, and capillary zone electrophoresis. Hydrochlorothiazide in urine is determined by electrochemical method, and hydrochlorothiazide in human blood plasma is determined by liquid chromatography method. In contrast, the hydrochlorothiazide in mixtures with other substances can be determined using voltammetric methods and high-performance liquid chromatography.

Keywords: Hydrochlorothiazides, assay, pharmaceutical preparations, biological matrices, mixtures

1. Introduction

Hydrochlorothiazide (HCT) is the most frequently prescribed antihypertensive drug worldwide. Over 97% of all HCT prescriptions are 12.5 to 25 mg per day. The antihypertensive efficacy of HCT with outpatient blood pressure monitoring is less clear than inpatients. The antihypertensive efficacy of hydrochlorothiazide (HCT) in daily doses of 12.5 to 25 mg as measured in head-to-head studies with outpatient blood pressure measurements was consistently lower than all other drug classes. Because yield data at this dose are lacking, HCT is an unsuitable first-line drug for hypertension treatment [1].

Hydrochlorothiazide contains not less than 98.0% and not more than 102.0% $C_7H_8ClN_3O_4S_2$ calculated against the dry matter. Hydrochlorothiazide is a white or almost white powder, odorless. Its melting temperature ranges from 201 - 204 ºC. Hydrochlorothiazide is soluble in sodium hydroxide, n-butylamine, and dimethylformamide; it is relatively difficult to dissolve in methanol; it is difficult to dissolve in water;

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insoluble in ether, chloroform, and dilute mineral acids. The chemical name for hydrochlorothiazide is 6-Chloro-3,4-dihydro-2H-1,2,4-benzothiadiazole-7-sulfonamide 1,1-dioxide, molecular weight 297.74 and its structure, as shown in Figure 1 [2].

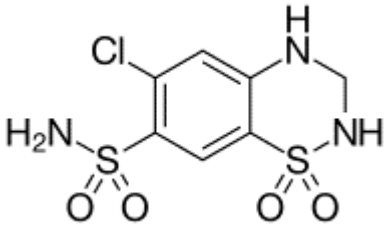

Figure 1: Structure of the hydrochlorothiazide

2. Method of collecting data

In preparing this article, the technique used is literature study by searching for sources or literature in official books and national and international journals for the last 20 years (2000-2020). The keywords used for the data search were "hydrochlorothiazide, raw materials, pharmaceutical preparations, biological matrices, mixtures." This review article's primary reference search was carried out through trusted websites such as Science Direct, NCBI, ResearchGate, Google Scholar, and other published and trustworthy journals.

3. Method of analysis of hydrochlorothiazide in pharmaceutical preparations

3.1 High-performance liquid chromatography (HPLC) method

A high-performance liquid chromatography method was developed, validated, and applied to determine hydrochlorothiazide in human plasma. The effects of mobile phase composition, buffer concentration, mobile phase pH and organic modifiers on hydrochlorothiazide retention and internal standards were investigated. This method involved solid-phase extraction on the RP-select B cartridge followed by isocratic reverse phase chromatography on the Hibar Lichrospher 100 RP-8 column with UV detection at 230 nm. Recovery, selectivity, linearity, precision, and method accuracy were evaluated from spiny human plasma samples. The quantification limit is ten ng/mL. This method has been applied to monitor hydrochlorothiazide levels in patient samples [3].

High-performance liquid chromatography (HPLC) is method stability for hydrochlorothiazide. Hydrochlorothiazide was well separated from the degradation product using a reverse phase (C-18) column and a mobile phase consisting of Methanol: Buffer pH-3.2 (60:40 v / v) and other HPLC parameters were flow rate of 1 mL/min, wavelength detection of 270 nm and injection volume of 20 µL. The method is validated for linearity, precision, accuracy, ruggedness, and durability. Results obtained after validation studies indicate that the single proposed method allows analysis of hydrochlorothiazide in the presence of degradation products formed under various stress conditions. The procedure developed is also applicable for determining hydrochlorothiazide's stability in commercial pharmaceutical dosage forms [8].

3.2 Capillary zone electrophoretic (CZE) and micellar electrokinetic capillary chromatography (MEKC) methods

Capillary zone electrophoretic (CZE) and micellar electrokinetic capillary chromatography (MEKC) methods were used to simultaneously separate hydrochlorothiazide and six angiotensin-II receptor antagonists (ARA-IIs): candesartan, eprosartan mesylate, irbesartan, losartan potassium, telmisartan, and valsartan. The CZE and MEKC methods are suitable for the qualitative and quantitative determination of HCT / ARA-II combined in pharmaceutical formulations. Depending on ARA-II, at least one of two methods can be used for each combination. Both methods have been validated in terms of response linearity, reproducibility, and accuracy [4].

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3.3 Capillary electrophoresis method

The capillary electrophoresis method was developed for the simultaneous determination of hydrochlorothiazide and several angiotensin-converting enzyme (ACE) inhibitors: enalapril, lisinopril, quinapril, fosinopril, ramipril, and cilazapril. The most critical parameter is the pH of the buffer that is running. The separation was carried out on fused silica capillaries (total length 52 cm x 75 µm ID) using sodium phosphate buffer (pH 7.25; 100 mM). This method is successfully applied to the quantitative determination of this compound in a suitable pharmaceutical formulation. This method was validated in terms of response linearity, reproducibility, and accuracy [5].

3.4 Chemiluminescence Method

A new chemiluminescence method for the determination of hydrochlorothiazide (HCT) has been developed based on the reaction between Ce (IV) in an acidic medium and this diuretic agent in the presence of rhodamine 6G as a sensitizer. The method described is based on recording the entire chemiluminescence intensity-versus-time profile, allowing other measured parameters such as total area proportional to the analyte concentration. The optimal chemical conditions for chemiluminescence emissions were investigated. Two defining approaches, intensity, and area, have been proposed. Linear calibration graph for the concentration range from 0.5 to 30 µg/mL. The detection limits were 0.34 and 0.16 µg/mL for intensity and area measurements, respectively. For the analysis of 7.5 and 20 µg/mL HCT, the relative error is less than 2% if the error propagation theory is assumed. This chemiluminescence procedure is applied to determine HCT in pharmaceutical formulations, with excellent recovery, because the determination is free from interference from common excipients and other drugs also present in the formulation [7].

3.5 Partial least squares method

This work develops and validates a new multivariate diffuse reflecting method near-infrared for the direct determination of hydrochlorothiazides in pharmaceutical powder samples. The best partial least squares (PLS) models were obtained in the spectral region from 1640 to 1780 nm, with centered-averaged data pre-processed by the first derivative and Savitzky-Golay refinement followed by vector normalization. This model was built with four latent variables and gave the root mean square prediction error of 1.7%. This method is validated according to the appropriate regulations in the range of 21.25 to 29.00 mg of hydrochlorothiazide per 150 mg of powder (average mass tablet), with an estimated number of benefits, such as accuracy, precision, linearity, analytical sensitivity, detectability, bias, and residual prediction deviation (RPD). The net analyte signal (NAS) concept was used to estimate multiple benefits figures and plot pseudo-univariate calibration curves. According to the official high-performance liquid chromatography (HPLC) method, tablets' determination is manufactured in powder form. Finally, the extrapolated method for determining whole tablets gave a prediction error of less than ± 9%. The developed method provides the advantage of about fifteen times faster than the reference HPLC method [14].

3.6 Method of anodic stripping voltammetry and cyclic voltammetry

The electrochemical oxidation behavior of hydrochlorothiazide (HCT) on glass carbon as a working electrode was investigated in the Britton-Robinson (B-R) pH 3 buffer, using anodic stripping voltammetry (ASV) and cyclic voltammetry (CV). This drug provides a clear voltammetric oxidation peak at + 1200 mV versus the Ag / AgCl reference electrode. The electrochemical oxidation process proved to be irreversible and diffusion controlled, with adsorption characteristics over the entire pH range. Optimized conditions, such as time and accumulation potential, scan rate, frequency, pulse amplitude, working electrode variation, and instrument parameters are studied. The calibration graph for HCT was obtained from 4 × 10−6 to 4 × 10−5 M (correlation coefficient = 0.997) using the developed electroanalytic method (ASV). The detection limit for this drug is 4.3 × 10-9 M. ASV, and CV techniques with sufficient precision and accuracy have been developed and applied for the direct determination of HCT in commercial tablets without separation or extraction procedures and biological fluids such as urine and plasma [9].

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The electrochemical preparation and characterization of nickel hydroxide-modified electrodes and their behavior as an electrocatalyst against hydrochlorothiazide oxidation (HCTZ) were investigated. The electrochemical behavior of the modified electrodes and the electrooxidation of HCTZ were explored using cyclic voltammetry. The modified electrode's voltammetric response in detecting HCTZ is based on the electrochemical oxidation of Ni (II) / Ni (III) and chemical redox processes. Analytical parameters for the electrooxidation of HCTZ by nickel hydroxide modified nickel electrodes were obtained in NaOH solution, where the linear voltammetry response was in the concentration range from 1.39×10^{-5} to 1.67×10^{-4} mol/L with a detection limit of 7, 92×10^{-6} mol/L and a sensitivity of 0.138 µA L/mmol. This analysis was used to explain the kinetics and oxidation mechanism of HCTZ with a modified electrode [11].

3.7 Quantitative point test analysis

The method of quantitative point test analysis for hydrochlorothiazide used diffuse reflectance spectroscopy. Reflectance measurements were carried out by analyzing colored compounds (λ = 585 nm) resulting from hydrochlorothiazide and p-dimethylaminocinnamaldehyde (PDAC) in an acidic medium. This reaction occurs on the filter paper after heating to 80ºC for 8 minutes. The factorial design allows for multiple reaction factors simultaneously to obtain the best reaction conditions. These factors include heating temperature, heating time, acid volume, and PDAC volume. Linearity was studied in the range 3.36 x 10^{-2} to 1.01 x 10^{-1} mol/L with a correlation coefficient of 0.998. The detection limit is estimated at 1.32 x 10^{-2} mol/L. Commercial samples were analyzed using the proposed method, and the results were better than those of the United States Pharmacopoeia, which suggests that quantitative point test analysis with diffuse reflectance can be used successfully to determine hydrochlorothiazide in drugs [10].

3.8 Differential pulse voltammetry (DPV) method

Carbon nanotube/silicon rubber multiwall composite electrodes (MWCNT/SR) have been used for the determination of hydrochlorothiazide (HCTZ) in pharmaceutical formulations by differential pulse voltammetry (DPV). The electrooxidation process was evaluated by cyclic voltammetry. It was observed that the HCTZ presented an irreversible oxidation peak at 0.82 V vs. the saturated calomel electrode (SCE) in the potential range 0.5 to 1.1 V, in the Britton-Robinson pH buffer of 7.0 at MWCNT/SR. HCTZ was determined by DPV using composite electrode MWCNT/SR 70% (MWCNT, m/m) after optimizing experimental parameters. The linear range was from 5.0 to 70.0 µmol/L, with a detection limit (LOD) of 2.6 µmol/L. According to Student's t-test, the HCTZ was determined in a pharmaceutical formulation using the proposed composite electrode, and the results were approved by the liquid chromatography high performance (HPLC) official method within a 95% confidence level t-test [13].

4. Method of analysis of hydrochlorothiazide in mixtures

4.1 Mixture of hydrochlorothiazide and enalapril

A high-performance liquid chromatography procedure is presented to determine hydrochlorothiazide (HCT) and enalapril maleate (EM) in pharmaceutical tablets. An aliquot of the sample was dissolved in 15% acetonitrile (ACN) containing theophylline as internal standard and chromatographed on the Supelcosil LC-8 column (5 mµ), (150 mm x 4.6 mm i.d.). The mobile phase is 3.0 mM tetrabutylammonium hydrogen sulfate (TBAHS) in ACN/water/triethylamine (TEA), (14, 85.6, 6.4 V/V) adjusted to pH 4.1 by glacial acetic acid. Detection was at 220 nm. The method was tested for linearity, accuracy, recovery, and specificity [14].

4.2 Mixture of hydrochlorothiazide and spironolactone

Hydrochlorothiazide (HCT) and spironolactone (SPR) are primarily formulated in antihypertensive formulations. Several methods have been developed and validated for their determination; these methods include spectrophotometric and chemometric-assisted spectrophotometry. The spectrophotometric methods developed are the isosbestic point method (ISO) and the ratio reduction method (RS). The absorbance values at 232.4 (λ_{iso1}) and 257.6 nm (λ_{iso2}) were used to determine the total mixture concentration, whereas HCT could be directly determined at 317.2 nm (λ_{max}) and a reduced SPR concentration could be obtained. Also, the SPR

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concentration can be calculated by the RS method using absorbance at 243.8 nm (λ_{max}). A wavelength selection method based on genetic algorithms (GAs) was developed and compared with the conventional partial least squares (PLS) method. In this method, several parameters are adjusted, and the optimal parameter settings are determined using an experimental design. The chemometric method developed has been successfully applied to determine HCT and SPR and determine impurity and degradation products. The proposed method was successfully applied to determine HCT and SPR in commercial tablets and statistically compared with each other and with the methods reported. No significant differences were found, giving accuracy and precision [15].

Methods for determining hydrochlorothiazide (HCT) and spironolactone (SPR) in their mixtures and the presence of impurities or their degradation products have been developed. The first method is based on thin-layer chromatography (TLC) combined with the discrete freckles' densitometric determination. The separation was achieved using TLC plates of silica gel 60 F254 and ethyl acetic acid-chloroform-formate-triethyl amine (7: 3: 0.1: 0.1, volume) as the expanding system. Good correlations were obtained between the studied drug's integrated peak area and the corresponding concentrations in different ranges. The second method is based on high-performance liquid chromatography with ultraviolet detection, in which the proposed components are separated on a reverse-phase C18 analytical column using a gradient elution system with deionized water-acetonitrile (97: 3, v / v) for 8 min. Then acetonitrile was increased successively to 35% in the next 2 minutes and kept constant in the next 10 minutes. Finally, 3% acetonitrile was recovered to stabilize the chromatography system. The flow rate was maintained at 2 mL/min and the detection wavelength at 230 nm. Linear regression was obtained in the range of 4.0-50 µg / mL and 5.0-50 µg/mL for HCT and SPR, respectively. Different parameters affecting the suggested method are optimized for maximum separation of the quoted components. The system suitability parameters of the two methods developed were also tested. According to ICH guidelines, the suggested methods were validated and were successfully applied to determine HCT and SPR in their commercial tablets. The two methods were also statistically compared and reported without any significant difference in performance [20].

4.3 Mixture of hydrochlorothiazide and triamteren

Hemodialysis is the most commonly used method for the treatment of chronic kidney disease. In this procedure, some patients use diuretics to control weight gain and blood pressure. In this work, a voltammetric sensor based on a glassy carbon electrode modified with carbon nanotubes (GCE/MWCNT) is described for the simultaneous determination of hydrochlorothiazide (HCT) and triamterene (TRT) diuretics. Diuretic oxidation on the GCE/MWCNT surface was observed at 1.01 and 1.17 V for HCT and TRT, respectively, allowing simultaneous determinations, which were not possible with unmodified glass carbon electrodes. The GCE/MWCNT electrodes provide a 6-fold and 10-fold gain in anode peak intensity for HCT and TRT, respectively, compared to the unmodified electrodes. After optimizing the conditions (pH, accumulation time, and accumulation potential), analytical curves are generated for the analyte range from 1.0×10^{-7} to 2.0×10^{-5} mol/L.The detection limits for HCT and TRT are 2.8×10^{-8} and 2.9×10^{-8} mol/L. A high-performance liquid chromatography method with diode array detection was also developed to determine HCT and TRT in hemodialysis samples compared to electroanalytic methods [16].

4.4 Mixture of hydrochlorothiazide and benazepril hydrochloride

Partial least squares regression (PLSR) and support vector regression (SVR) are two popular chemometric models subjected to comparative studies in the presented work. The comparison shows their characteristics through their application to analyze Hydrochlorothiazide (HCZ) and Benazepril hydrochloride (BZ) in the presence of HCZ impurities; Chlorothiazide (CT) and Salamide (DSA) as case studies. The analysis results proved valid for analyzing two active ingredients in raw materials and pharmaceutical dosage forms by handling UV spectral data in the range (220–350 nm). For precise analysis, the 4-factor 4-stage set experimental design resulted in a training set consisting of 16 mixtures containing different disturbing species ratios. A set of independent tests consisting of 8 mixtures was used to validate the suggested model's predictive ability. The results presented indicate the ability of the multivariate calibration model to analyze HCZ and BZ

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in the presence of HCZ CT and DSA impurities with high selectivity and average percentage gain accuracy (101.01 ± 0.80) and (100.01 ± 0.87) for HCZ and BZ using the PLSR model, respectively and (99.78 ± 0.80) and (99.85 ± 1.08) for HCZ and BZ using the SVR model, respectively. The dosage form analysis results were statistically compared with the reference HPLC method without significant accuracy and preciseness. The SVR model provides more accurate results than the PLSR model and shows high generalizability. However, PLSR still has the advantage of being fast in optimization and implementation [17].

4.5 Mixture of hydrochlorothiazide and telmisartan

Simple, sensitive, specific, and economical spectrophotometric methods were developed and validated simultaneously to estimate Hydrochlorothiazide and Telmisartan in the tablet dosage form. New methods based on the simultaneous estimation of drugs in binary mixtures without separation were previously developed. In the multiple wavelength method, Hydrochlorothiazide and Telmisartan are measured on the principle that the absorbance differing between two points on the spectrum of the mixture is directly proportional to the interest component's concentration is independent of component interference. Recovery studies statistically validated the accuracy and reproducibility of the proposed method. This method allows the simple, fast, and direct determination of Hydrochlorothiazide and Telmisartan in commercially available tablet dosage forms without prior separation and, therefore, can be used for routine analysis of both drugs in a quality control laboratory [18].

A simple, sensitive, specific, and economical spectrophotometric method was developed and validated for Hydrochlorothiazide and Telmisartan's simultaneous calculation in the tablet dosage form. New methods based on the simultaneous estimation of drugs in binary mixtures without prior separation were developed. In the simultaneous equation method, Hydrochlorothiazide and Telmisartan were measured using the absorptivity value at the selected wavelength, namely, 273 nm and 295 nm, respectively. Recovery studies statistically validated the accuracy and reproducibility of the proposed method. The simultaneous equation method allows simple, fast, and direct determination of Hydrochlorothiazide and Telmisartan in commercially available tablet dosage forms without prior separation and can therefore be used for routine analysis of both drugs in a quality control laboratory [19].

4.6 Mixture of hydrochlorothiazide and valsartan

This work deals with the simultaneous determination of hydrochlorothiazide (HCTZ) and valsartan (VAL) by square wave voltammetry using cathodically doped diamond electrodes. This method demonstrated a linear response to HCTZ and VAL in the concentration range of 1.97–88.1 μmol/L and 9.88–220 μmol/L, respectively, in a Britton-Robinson buffer solution (pH 5.0), with detection limits of 0.639 μmol/L and 0.935 μmol/L, respectively. The proposed method was successfully applied in the two antihypertensives' simultaneous determination in the combined dosage form, and the results were obtained using the high-performance liquid chromatography method [21].

4.7 Mixture of hydrochlorothiazide and losartan potassium

A combination of multi-syringe chromatographic analytical techniques with extraction disc sorbents for the pre-concentration and determination of hydrochlorothiazide and losartan potassium in shallow, groundwater, and outlet wastewater samples has been developed. The developed system has been proven to determine hydrochlorothiazide and losartan potassium in spiked water samples with yields ranging from 95 to 118%. This method involves online enrichment of the target analyte from a spiked water sample onto a Cation-SR absorbent material. The analyte is then eluted and transported to the monolithic column, RP-18e Chromolith Flash column (25 mm × 4.6 mm i.d.). The mobile phase used was 10 mM potassium dihydrogen phosphate (pH 3.0): acetonitrile: methanol (60:30:10 v / v / v), flow rate 0.8 mL/minutes. UV detection was carried out at 226 nm. Under optimized chemical and physical variables, the detection limits for hydrochlorothiazide and losartan potassium calculated as 3Syx/w were 0.07 and 0.09 mg/L, respectively, for a sample loading volume 1.0 mL [23].

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A new, precise, accurate gradient back phase high-performance liquid chromatography (RP-HPLC) method has been developed for the simultaneous determination of Hydrochlorothiazide (HCT) and Losartan potassium (LOS) in tablets. The stationary phase is the Microbondapak C18 column (10 µ, 300 mm × 3.9 mm ID). Gradient elution with a mobile phase of aqueous methanol (pH = 3) was used for separation. Detection was carried out at 270 nm using a UV detector. The flow rate was 1.0 mL/minute and the retention times were 7.89 minutes and 15.15 minutes for HCT and LOS, respectively. Linearity was obtained in a concentration range of 0.5 - 200 µg/mL for HCT and 2 - 800 µg/mL for LOS. The mean recovery percentages were 100.29% and 99.16% for HCT and LOS [24].

Simultaneous determination of hydrochlorothiazide (HCTZ) and losartan (LOS) in a pharmaceutical formulation using differential pulse voltammetry (DPV) was developed. Two magnificent reproducible peaks of HCTZ and LOS oxidation, with a separation of 0.23 V, were obtained in the Britton-Robinson (BR) buffer (pH 9.5) using an anodically treated boron-treated diamond electrode. Under optimal analytical, experimental conditions, the voltammetric method shows a linear response for the simultaneous determination of HCTZ and LOS in the concentration range of 3.0×10^{-6} to 7.4×10^{-5} mol/L for both compounds, with a detection limit of 1.2. $\times 10^{-6}$ mol/L and 9,5 $\times 10^{-7}$ mol/L, respectively. The proposed method was successfully applied in the simultaneous determination of LOS and HCTZ content in pharmaceutical formulations, the accuracy of which was evidenced by the excellent compatibility of the results (paired t-test at 95% confidence level) with those obtained using high-performance liquid chromatography (HPLC) [28].

4.8 Mixture of hydrochlorothiazide and rutin

Capillary zone electrophoresis by amperometric detection (CZE-AD) was first applied to the simultaneous determination of rutin (RT) and hydrochlorothiazide (HCT) in compound Chinese herbal medicines and human urine samples. Both analytes can be analyzed entirely within 12 minutes and show a significant current carbon electrode response under optimal conditions. It is known that the linear range of HCT is from 2.0×10^{-6} to 1.0×10^{-4} mol/L, and RT is from 1.0×10^{-6} to 1.0×10^{-4} mol/L. The sensitivity is determined by linear regression and calculated - 7.02×10^{4} and 2.17×10^{5} nA L/mol, respectively, and the detection limits are 5.0×10^{-7} and 2.0×10^{-7} mol/L, respectively (S/N = 3). The above results indicate that this method has high sensitivity, good repeatability, high selectivity and can be used to study drug metabolic kinetics. Excellent results were obtained when this method was used to simultaneously analyze the amounts of RT and HCT in one common compound of Chinese herbal medicine - Zhen Ju Jiang Ya Pian and human urine samples [25].

4.9 Mixture of hydrochlorothiazide and irbesartan

Three new analytical methods have conducted simultaneous determination of hydrochlorothiazide and irbesartan in binary mixtures without prior separation. The first method is presented for the spectrophotometric determination of the derivative of a binary mixture with overlapping spectra based on the compensation technique. The exact contribution of one of the components in a binary mixture can be measured and the amount quantified. The second method uses the first derivative of the radio spectrum. The ratio spectrum is obtained by dividing the absorption spectrum of a binary mixture using its components. Amplitudes in the first derivative of the ratio spectrum at 231, 266, 279, 238, and 248 nm were chosen to determine the hydrochlorothiazide and irbesartan in the binary mixture. The other components' concentrations were then determined from the respective calibration charts, which were treated similarly. With the third method, the absorbance ratio method, the determination of hydrochlorothiazide and irbesartan was carried out using absorbance readings at 272 nm, 241 nm, and 263 nm in the zero-order spectrum of the mixture. The absorbance ratio was also developed as a method of comparison. All three methods are simple, accurate, fast, and do not require an initial separation step and, therefore, can be used for routine analysis of both drugs in a quality control laboratory [26].

4.10 Mixture of hydrochlorothiazide and medoxomil olmesartan

A simple, specific, accurate, precise, and reproducible method has been developed and validated for the simultaneous estimation of hydrochlorothiazide and medoxomil olmesartan in the combined dosage form by

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the UV spectrophotometric method. The UV spectrophotometric method includes the simultaneous equation method (Method I) 271.5 nm and 257.0 nm λ_{max} of the two drugs selected, the absorbance ratio method (Method II) 261.5 nm, isoabsorptive wavelength, and 257.0 nm were selected for estimation. hydrochlorothiazide and olmesartan medoxomil respectively. In the three-wavelength method (Method III), the two wavelengths are chosen such that the hydrochlorothiazide provides the same absorbance (263.8 and 278.4 nm) at the two selected wavelengths while the third wavelength (316.5 nm) is such that olmesartan provides almost zero absorbance. Both drugs follow Beer's law in a concentration range of 5-25 µg/mL. The % recovery for both drugs was almost 100% representing the accuracy of the proposed method. According to the ICH guidelines, the proposed method's validation was carried out for accuracy, precision, specificity, and ruggedness. The proposed method can be successfully applied in routine work to determine hydrochlorothiazide and medoximil olmesartan in combined dosage forms [27].

5. Analysis of hydrochlorothiazide in biological matrices

5.1 Mixture of hydrochlorothiazide and folic acid in biological samples

Carbon paste electrode-based (CPE) sensors modified with benzoylferocene (BF) and NiO nanoparticles (NiO/NPs) are used for highly sensitive voltammetry and electro-catalytic measurements of hydrochlorothiazide (HCT) and folic acid (FA). The NiO/NP was synthesized via direct chemical deposition methods and characterized by X-ray diffraction (XRD) and scanning electron microscopy (SEM) techniques. Thus, the sensor represents an appropriate and robust electron-intermediate behavior and the oxidation peaks of HCT and FA, which are very well separated. The peak current is obtained from squared. The wave voltammetry technique (SWV) was linearly dependent on HCT and FA concentrations in the range 1.0–500.0 and 50.0–500.0 µmo/L with detection limits of 0.14 and 4.3 µmo/L, respectively. These mediator/nanoparticles modified electrodes are applied to detect and measure HCT and FA in pharmaceutical and biological samples [29].

5.2 Determination of hydrochlorothiazide in a urine sample

This work describes the development, optimization, and validation of an electrochemical method to determine hydrochlorothiazide (HCTZ) in the urine. This method allows the fast, inexpensive, and reliable determination of the current administration of diuretics used in doping control in sports. The sensor response is determined by differential pulse voltammetry (DPV). The glass carbon electrode has been modified with multiwall carbon nanotubes (MWCNT) and gold nanoparticles. The sensors are calibrated in a sample analyzed matrix by the cumulative standard summation method. Method validation is based on bottom-up evaluation Measurement uncertainty is a component combined using the Monte Carlo Method (MCM). It applies without limitation regarding the value of the component's uncertainty and the measurement function's linearity. The developed metrological model is implemented in an MS-Excel spreadsheet. The measurements' electrochemical adequacy was assessed by comparing their relative standard uncertainty with a target value of 20% and by evaluating the suitability of the measurements with the determinations made with the reference procedure. The tools developed for the construction and optimization of functioning electrodes can be applied to other analytes and matrices measurements. The standard cumulative summation method used and each measurement uncertainty model can be applied to any non-destructive chemical measurement of solutions. [30]

5.3 Determination of hydrochlorothiazide in human plasma

A fast and sensitive liquid chromatography/tandem mass spectrometry for hydrochlorothiazide determination in human plasma has been developed and validated. The analyte and irbesartan, used as internal standards, are precipitated and extracted from plasma using methanol. The analysis was carried out on the Phenomenex Kromasil C8 column with water and methanol (27:73, v/v) as the mobile phase. Linearity used to be assessed from 0.78 to 200 ng/mL in plasma. The analytical method proved to be applicable in pharmacokinetics after oral administration of 12 mg hydrochlorothiazide tablet to 20 healthy volunteers [6].

The sensitive, selective, and fast liquid chromatography/mass spectrometry method (LC-MS/MS) was developed and validated to determine hydrochlorothiazide (HCTZ) in human plasma. Plasma samples were

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prepared by solid-phase extraction using an Oasis HLB cartridge 30 mg/1CC. Chromatographic separation was performed on a Thermo Hypurity Advance column (50 mm x 4.6 mm i.d., 5 µm). The mobile phase consisted of HPLC grade acetonitrile: 2 mM ammonium acetate (90: 10 v/v) with a 0.5 mL/min flow rate. Detection of internal standard hydrochlorothiazides and zidovudine (IS) was achieved by electrospray ionization (ESI) MS/MS in negative ion mode. The total run time of chromatography was 2.5 minutes. The linear range of this method is from 2,036-203,621 ng/mL. The mass transition ion pairs are followed as m/z 296.10/205.00 for HCTZ and m/z 266.10/223.10 for zidovudine. The mean overall recovery for HCTZ was 66.40%, with a precision of 2.44%. The mean internal standard recovery (AZT) was 63.62%, with a precision ranging from 2.06% to 5.40%. This method was successfully applied to the pharmacokinetic evaluation of hydrochlorothiazide after a single oral dose of 25 mg hydrochlorothiazide in healthy volunteers [12].

The rapid and sensitive liquid chromatography-tandem mass spectrometry (LC-MS/MS) method has been developed and validated for the simultaneous estimation of hydrochlorothiazide, quinapril, and their quinaprylate metabolites in human plasma. After solid-phase extraction (SPE), the analyte and IS were chromatographed on a hypurity C8 column (100 mm x 2.1 mm i.d., particle size 5 µm) using an injection volume of 2 µL with a run time of 2.8 minutes. An isocratic mobile phase consisting of 0.5% (v / v) formic acid: acetonitrile (25:75, v / v) was used to separate these drugs. This medicinal product's precursors and ions are monitored on a triple quadrupole mass spectrometer, operating in dual reaction monitoring (MRM) mode without a polarity switch. The proposed method is validated in the range 5–500 ng / mL for the hydrochlorothiazide method and 5–1500 ng / mL for quinapril and quinaprylate. Inter-batch and intra-batch precision (coefficient of variation -% CV) across the five validations runs a lower quantitative limit (LLOQ), lower quality control (LQC), intermediate quality control (QMC), higher quality control (HQC), and the upper quantitation limit (ULOQ) is less than 15. The accuracy specified at this level is within ± 13% in terms of relative error percentage [22].

In this study, a rapid and sensitive liquid chromatography/tandem mass spectrometry method for determining hydrochlorothiazide in humans plasma is developed and validated. The analyte and irbesartan, used as internal standards, are precipitated and extracted from plasma using methanol. The analysis was carried out on the Phenomenex Kromasil C8 column with water and methanol (27:73, v/v) as the mobile phase. Linearity used to be assessed from 0.78 to 200 ng/mL in plasma. The analytical method proved to be applicable in pharmacokinetics after oral administration of 12 mg hydrochlorothiazide tablet to 20 healthy volunteers [31].

A specific, sensitive and rapid method based on high-performance liquid chromatography combined with tandem mass spectrometry (HPLC-MS/MS) was developed for the simultaneous determination of olmesartan (OLM) and hydrochlorothiazide (HCTZ) in human plasma and urine. Solid-phase extraction (SPE) was used to isolate the analyte from the biological matrix, followed by injecting the extract into column C18 by isocratic elution. The detection was carried out on a triple quadrupole tandem mass spectrometer in dual reaction monitoring (MRM) mode using negative electrospray ionization (ESI). Methods are validated in a concentration range of 1.00–1000 ng/mL and 5.00–5000 ng/mL for OLM in humans plasma and urine and 0.500–200 ng/mL and 25.0–25,000 ng/mL for HCTZ in human plasma and urine, respectively. The precision of inter-and intra-run OLM and HCTZ is less than 15%, and accuracy is within 85-115% for plasma and urine. The mean extraction recoveries were 96.6% and 92.7% for OLM, 87.2%, and 72.1% for HCTZ in human plasma and urine. Linearity, recovery, matrix effects, and stability were validated for OLM/HCTZ in human plasma and urine [32].

A rapid and sensitive liquid chromatography-tandem mass spectrometry method (LC-MS/MS) was developed and validated for the simultaneous estimation of hydrochlorothiazide, quinapril, and quinapril metabolites in human plasma. After solid-phase extraction (SPE), analyte and IS were taken chromatographically on a hypurity C8 column (100 mm × 2.1 mm i.d., particle size 5 µm) using a two µL volume injection with a run time of 2.8 minutes. The isocratic mobile phase consisting of 0.5% (v / v) formic acid: acetonitrile (25:75, v/v) was used to separate all of these drugs. This drug's precursors and productions are monitored with a three-quadrupole mass spectrometer, operating in a dual reaction monitoring mode (MRM) without a polarity switch. The proposed method is validated over the range from 5–500 ng/mL for the hydrochlorothiazide method and 5–1500 ng/mL for quinapril and quinaprilate. Interbatch and intra-batch precision (coefficient of variation -%

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CV) across five validation run lower limit of quantity (LLOQ), lower quality control (LQC), medium quality control (QMC), higher quality control (HQC), and upper limit of quantitation (ULOQ) less than 15. The accuracy specified at this level is within ± 13% in terms of relative error percentage [33].

A specific, sensitive and fast method based on high-performance liquid chromatography (HPLC) was developed for the simultaneous determination of telmisartan (TELM) and hydrochlorothiazide. (HCT) inhuman plasma using indapamide as an internal standard. The method utilizes protein deposition with acetonitrile only as sample preparation before RP-HPLC. The analyte was chromatographed on a shim-packaged cyanopropyl column in isocratic elution with methanol: 10 mM ammonium acetate solution (pH 6.0) (35:65 v/v) as the mobile phase at a flow rate of 1 mL/min and a detection wavelength of 270 nm. This method is validated in a concentration range of 1–10 µg/mL for TELM and 0.31–3.12 µg/mL for HCT in human plasma. The inter and intra-run precision of TELM and HCT is less than 3.60%, and the accuracy is less than 1.868%. Linearity, recovery, matrix effects, and stability were validated for TELM/HCT in human plasma [34].

A high-performance liquid chromatography method was developed, validated, and applied to determine hydrochlorothiazide in human plasma. The effects of mobile phase composition, buffer concentration, mobile phase pH, and organic converter concentration on hydrochlorothiazide retention and internal standards were investigated. His method involved solid-phase extraction on the RP-select B cartridge followed by isocratic reverse phase chromatography on the Hibar Lichrospher 100 Column RP-8 with UV detection at 230 nm. Recovery, selectivity, linearity, precision, and method accuracy were evaluated from spiny human plasma samples. The limit of quantification is 10 ng/mL. Methods have been applied to monitor hydrochlorothiazide levels in patient samples [35].

6. Conclusion

The analysis method of hydrochlorothiazide as a raw material can be determined by high-performance liquid chromatography (HPLC), capillary zone electrophoretic (CZE), micellar electrokinetic capillary chromatography (MEKC), capillary electrophoresis, chemiluminescence, voltammetry, and quantitative point tests. Hydrochlorothiazide in a pharmaceutical dosage form can be determined by high-performance liquid chromatography, spectrophotometric, electroanalytic, thin layer chromatography (TLC) methods, voltammetry, and capillary zone electrophoresis. The hydrochlorothiazide in mixtures with other substances can be determined using voltammetry and high-performance liquid chromatography methods. Electrochemical and liquid chromatography methods can determine hydrochlorothiazides in biological fluids such as human urine and plasma.

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A Brief Author Biography

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