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Analytical Methods for Determination of Certain Sartans and Diuretics

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Abstract

Hypertension is a progressive cardiovascular syndrome with a variety of causes, including cardiovascular risk factors that can lead to changes in heart and blood vessels function and structure. Hypertension is a chronic disease that has negative effects on human health and is the main cause of cardiovascular-disease related deaths. The main objective of the treatment of hypertension is to reduce the overall risk of long-term cardiovascular disease and cardiovascular disease-related mortality, which is closely related to the degree of blood pressure lowering. Antihypertensive drugs describe several classes of compounds with the therapeutic action of preventing, controlling, or treating hypertension. Antihypertensive drug classes differ both structurally and functionally.

Introduction

In this literature review, we will introduce all reported methods that have been developed for determination of certain antihypertensive drugs such as valsartan, losartan, spironolactone, and xipamide in their pure form, combined form with other drugs, combined form with degradation products, and in biological samples. We also will shed the light on the most important combination of drugs that are used for treatment of hypertension.

Valsartan

Chemical name: 3-Methyl-2-(pentanoyl{[2'-(1H-tetrazol-5-yl)-4-biphenyl]methyl}amino) butanoic acid.

Molecular formula: $C_{24}H_{29}N_5O_3$.

Molecular weight: 572.855 g/mol.

Description: White fine powder, soluble in organic solvents such as methanol and acetonitrile.

Melting point: 117 °C.

Pharmacological action and uses: Valsartan is an orally active nonpeptidetetrazole derivative and selectively inhibits angiotensin II receptor type 1 which causes reduction in blood pressure and is used in treatment of hypertension [1].

Method of analysis

Official method

Valsartan is an official drug in BP 2017. The method depends on dissolving 0.170 gm in 70 mL of 2-propanol, then titrating with [0.01 M] tetrabutyl ammonium hydroxide [1].

Chromatographic methods

Valsartan was estimated with hydrochlorothiazide in combined dosage form and in tablets by RP-HPLC. The separation was achieved using a Diamonsil C_{18} column (200 × 4.6 mm, 5 μm) in isocratic mode with a mobile phase containing methanol: acetonitrile: water: isopropylalcohol (22:18:68:2, v/v/v/v) adjusted to pH 8.0 using triethylamine. The flow rate was 1.0 mL/min and effluent was monitored at 270 nm [2].

Valsartan was also estimated in pure and pharmaceutical formulation by two methods, first by RP-HPLC using 0.01 M $NH_4H_2PO_4$ (pH 3.5) buffer: methanol [50:50] as the mobile phase with detection at 210 nm and a flow rate of 1 mL/min and retention time of 11.041 min [3]. The second was performed using Thermo-hypersil column (150 × 4.6 mm, 5 μm) with a mobile phase comprised of water: acetonitrile: glacial acetic acid (50:50:01). The flow rate was set at 1.0 mL/min and effluent was detected at

273nm [4].

Moreover, valsartan was determined in combination with nebivolol hydrochloride using a HIQ sil C_{18} column (250 × 4.6 mm, 5 µm) with UV detection at 289 nm and flow rate of 1 mL/min. The mobile phase consisting of methanol: water (80:20, v/v) with addition of 0.1 percent 1-hexanesulfonic acid monohydrate sodium salt as an ion-pairing reagent was selected [5].

Valsartan was estimated in human plasma using octadecylsilica column (50 × 4 mm, 5 µm). The mobile phase consisted of acetonitrile: 15 mMdihydrogen potassium phosphate, pH 2.0 (45:55, v/v). The run time was 2.8 min and the fluorimetric detector was operated at 234/374 nm [6].

Simultaneous estimation of valsartan and amlodipine was carried out by two HPLC methods. The first method was achieved on a Kromasil KR-C_{18} column (250 x 4.6 mm) using potassium dihydrogen orthophosphate buffer (50 mM, pH 3.7) with 0.2% triethylamine as the modifier and acetonitrile in the ratio of 56:44 (v/v) as the mobile phase with flow rate 1mL/min [7]. The second method of separation was achieved using a xTerra C_{18} column and methanol: acetonitrile: water: 0.05% triethylamine in a ratio of 40:20:30:10 by volume as mobile phase (pH was adjusted to 3 ± 0.1 with o-phosphoric acid). The flow rate was 1.2 mL/min [8].

Valsartan and its degradation products were determined by using isocratic RP-HPLC using C_{18} column (250 × 4.6, 5 µm) for both major degradants of valsartan by acid hydrolysis and by oxidation. The flow rate was adjusted to 1.2 mL/min and detection was performed at 250 nm using a UV detector in both assays [9].

Spectrophotometric methods

Valsartan was estimated with hydrochlorothiazide by first derivative UV spectrophotometry. The derivative procedure was based on the linear relationship between the drug concentration and the first derivative amplitudes at 270.6 and 335 nm for valsartan and hydrochlorothiazide, respectively [10,11]. Also, determination of valsartan and hydrochlorothiazide was performed using second derivative UV spectrophotometry at 205.6 nm [12] .

Two spectrophotometric methods were developed for the simultaneous estimation of valsartan and hydrochlorothiazide, the first method measures absorbances at a pair of wavelengths, 216 and 228 nm [13] ,also both drugs were determined simultaneously by using radio derivative and different derivative spectrometry [14].

Simultaneous estimation of valsartan, amlodipine and hydrochlorothiazide was carried out by three spectrophotometric methods. The first method was determined by measuring the absorbance of the prepared mixtures at 365 nm, 315 nm and 250 nm for valsartan, amlodipine and hydrochlorothiazide, respectively [15]. The second method was estimated in tablet at 250 and 238 nm for valsartan and amlodipine, respectively [16], while the third method was estimated using methanolic solution at 360.5 nm by first derivative of ratio spectra [17].

Spectroflourimetric methods

Valsartan was determined spectroflourimetrically in combination with amlodipine besylate. The method involved measurement of the native fluorescence at 455 nm (λ_{Ex} 360 nm) and 378 nm (λ_{Ex} 245 nm) for amlodipine and valsartan respectively [18]. Valsartan was also estimated spectroflourimetrically with losartan in human urine [19].

Voltammetric method

Stripping voltammetric determination of valsartan using a hanging mercury drop electrode (HMDE) was described. The method was based on adsorptive accumulation of the species at HMDE, followed by first harmonic alternating current AC stripping sweep at pH 6 [20].

Losartan

Chemical name: [2-butyl-5-chloro-3-[[4-[2-(2H-tetrazol-5-yl) phenyl]phenyl]methyl]imidazol-4-yl]methanol.

Molecular formula: C22H23ClN6O.

Molecular weight: 422.917 g/mol.

Description: White to off-white powder, freely soluble in water, slightly soluble in acetonitrile, soluble in iso-propyl alcohol.

Melting point: 183-184°C.

Pharmacological action and uses: Losartan potassium is an orally active, nonpeptide angiotensin II (AII) receptor antagonist. It is used in the treatment of hypertension .This agent binds competitively and selectively to the AII sub type 1 (AT_1) receptor, thereby blocking AII-induced physiological effects [21].

Method of analysis

Official method

Losartan is an official in BP 2017. The method depends on dissolving in anhydrous acetic acid and titration with 0.1 M perchloric acid, where the end point is detected potentiometrically [1].

Chromatographic methods

HPLC methods

Losartan was estimated with hydrochlorothiazide in combined dosage form in tablets by four methods. The first method was carried out using reversed-phase Erbasil columns. Separations were performed at room temperature. The mobile phase consisted of a mixture of acetonitrile: phosphate buffer (pH 4.0; 0.1 M)(35:65, v/v). The mobile phase was prepared daily, sonicated before use and delivered at a flow rate of 1.0 mL /min. Column eluant was monitored at 230 nm [22]. The second method was carried out using 0.01 M sodium dihydrogenphosphate: methanol: acetonitrile (8:2:1, v/v/v) mobile phase, adjusted to pH 5.5 with phosphoric acid. The analytical column was RP-YMC pack ODS A A-132 C_{18} (5 μm, 15 cm, 6.0 mm) column. All analysis were done under isocratic conditions at a flow rate of 1.0 mL/ min and at room temperature [23]. The third method was carried out using buffer solution of KH_2PO_4 and Na_2HPO_4 (pH 7.0, 0.02 M). This buffer solution was then mixed with acetonitrile in ratios of 85:15 (v/v) and 93:7 (v/v) buffer–acetonitrile. The mobile phase flow rate was 1.0 mL/min with ambient column temperature, 10 mL injection volume, and UV detection at 250 nm [24]. The fourth method was performed in human plasma using C_{18} reversed-phase column and a mixture of 0.01 M KH_2PO_4: acetonitrile (65:35; v/v) adjusted to pH 3.1 with H_3PO_4 at a flow rate 1.0 mL/min. Detection was realized at 232 nm using a UV detector [25].

Losartan was also estimated in tablets combined with amlodipine besylate using RP C_{18} Column (Microsorb-MV 100-5, 250 x 4.6 mm) and a mobile phase of 0.02% triethylamine in water: acetonitrile (60:40), pH adjusted to 2.5 with o-phosphoric acid at a flow rate of 1.0 mL/min and the detection wavelength was 226 nm [26].

Losartan was determined by RP-LC with ramipril and hydrochlorothiazide in pharmaceutical preparation using 150 mm × 4.6 mm., 5 μm, Cosmosil C_{18} column. The mobile phase was 0.025 m sodium perchlorate: acetonitrile, (62:38, v/v), containing 0.1% heptane sulphonic acid, pH adjusted to 2.85 with orthophosphoric acid, at a flow rate of 1.0 mL min^{-1}. UV detection was performed at 215 nm [27].

Losartan was estimated by HPLC with its metabolite E-3174 in human plasma, urine and dialysate using a gradient mobile phase consisting of 25 mM potassium phosphate and acetonitrile pH 2.2 with a phenyl analytical column and fluorescence detection for plasma and an isocratic mobile phase consisting of 25 mM potassium phosphate and acetonitrile (60:40, v/v) pH 2.2 was used for urine and dialysate [28].

Losartan was also estimated in human plasma by three methods. The First method depends on using a monolithic column, the separation was carried out in reversed-phase conditions using a Chromolith Performance (RP-18e, 100 × 4.6 mm) column with an isocratic mobile phase consisting of 0.01 mol/L disodium hydrogen phosphate buffer-acetonitrile (60:40, v/v) adjusted to pH 3.5. The wavelength was set at 254 nm [29].

The second method was operated using solid phase extraction, using C_{18} reversed phase column, a UV detector set at 254 nm, and an integrator. The mobile phase was a mixture of 0.01 M ammonium phosphate: acetonitrile: methanol (6:3:1) containing 0.02% sodium azide and 0.04% TEA, with pH adjusted to 3.2. The system was operated isocratically at ambient temperature and at a flow rate of 0.3 mL/min [30].

Mahmoud Sebaiy *et al*, [31] described a gradient HPLC method for rapid simultaneous separation and determination of eight drugs of sartan and statin classes in their pure and dosage forms within 15 minutes: irbesartan, losartan, valsartan, olmesartan, rosuvastatin, atorvastatin, lovastatin and simvastatin. Separation was carried out on a Kinetex C_{18} 100A column (2.60 m, 4.60 mm × 100 mm) using a gradiant binary mobile phase of 0.05M potassium dihydrogen phosphate buffer (pH 3.50 adjusted by ortho-phosphoric acid) and acetonitrile at room temperature. The flow rate was 1.00 mL/min and maximum absorption was measured using a DAD detector at 280 nm.

Losartan also was estimated with perindopril erbumine in tablet formulation by RP-HPLC. Chromatography was performed on a ODS Hypersil C_{18} (250 mm x 4.6 mm., 5 μm) column with mobile phase containing acetonitrile: acidic water pH 3.4 (50:50). The flow rate was 1.5 mL/min and the eluent was monitored at 218 nm [32].

HPTLC methods

HPTLC technique was used for determination of losartan in presence of amlodipine besylate and hydrochlorothiazide [33].

Spectrophotometric methods

Losartan potassium was simultaneously estimated spectrophotometrically by four methods. The first method was based on its physicochemical interaction with cationic surfactant [34]. The second method using first derivative spectrum recorded between 220 and 320 nm, and a zero-crossing technique for first derivative measurement at 232.5 nm was selected [35]. The third method based on measuring absorbance at 234nm [36]. The fourth method using bromothymol blue as a chromogen and phosphate buffer solution (pH 3-4) as a diluting agent was developed. The developed color shows maximum absorbance at 620nm [37].

Losartan was estimated with hydrochlorothiazide in tablets by measuring absorbance at 206.6 nm and 270.6 nm [38] and by using UV derivative method, losartan uses the signal around 280–290 nm while hydrochlorothiazide uses the peak around 330–340 nm [39].

Losartan was determined colorimetrically, where the method was based on the formation of an orange-red and orange ion-pair complex due to the action of Calmagite (CT) and Orange-II (O-II) on losartan potassium in acidic medium (pH 1.2) [40].

Chemometric method was carried out to determine losartan potassium, amlodipine besilate and hydrochlorothiazide in pharmaceuticals by measuring absorbance at range of 230.5-350.4 nm in their zero order spectra [41].

Losartan was estimated with amlodipine spectrophotometrically by dissolving in methanol at 208 and 237.5 nm, respectively [42].

Spectroflourimetric methods

Losartan was determined spectroflourimetrically with irbersartan, valsartan, and candesartan. The relative fluorescence intensity (RFI) was measured at 1ex/1em equal to 260/390 nm, 262/410 nm, 258/430 nm and 260/389 nm for losartan, irbersartan, valsartan and candesartan, respectively [43].

Voltammetric methods

Voltammetric methods for determination of losartan in pharmaceutical formulation were reported. Losartan was determined alone using hanging mercury drop electrode HMDE [44], with hydrochlorothiazide using differential-pulse voltammetry [45], and in pharmaceutical compounds and urine with triametrine using cathodic adsorptive stripping voltammetry [46].

Spironolactone

Chemical name: 17-Hydroxy-7a-mercapto-3-oxo-17a-pregn-4-ene-21-carboxylic acid g-lactone acetate.

Molecular formula: $C_{24}H_{32}O_4S$.

Molecular weight: 416.576 g/mol.

Description: Light cream-colored to light tan, crystalline powder, poorly soluble in water, soluble in ethanol and ethyl acetate, slightly soluble in methanol.

Melting point: 134-135 °C.

Pharmacological action and uses: Spironolactone is an aldosterone antagonist used as a diuretic in patients with cirrhosis or edema secondary to heart insufficiency [47].

Method of analysis

Official method

Spironolactone is official by BP 2017. The method was determined by liquid chromatography through dissolving 50 mg of spironolactone to be examined in 2.5 mL tetrahydrofuran and diluted to 25 mL with acetonitrile [1].

Chromatographic methods

Spironolactone was simultaneously estimated in human plasma with its metabolites using HPLC by four methods. The first method was performed using a Waters Symmetry® C_{18} (150 × 4.6 mm, 5 μm) analytical column fitted with a Waters Symmetry® C_{18} (20 ×3.9 , 5 μm) Sentry guard column, both maintained at 28 °C. UV detection was carried out at two wavelengths, 238 nm for spironolactone, 7-thiomethylspirolactone and 17-methyltestosterone, and 280 nm for canrenone. The mobile phase was consisting of methanol: water (60:40, v/v) [48]. The second method was carried out using a reversed-phase C_{18} column with a mobile phase of methanol: water (57:43, v/v) [49]. The third method was performed for simultaneous determination of spironolactone and its metabolite using S5 ODS2 (500 × 4.6) column. The mobile phase was a mixture of acetonitrile: aqueous orthophosphoric acid (pH 3.4). Chromatographic separations were performed at 5°C [50]. The fourth method was carried out for determination of spironolactone and its metabolites in human biological fluids after solid-phase extraction [51].

Spironolactone was simultaneously estimated with furosemide , and separation was performed on an SGE 150 × 4.6 mm SS Wakosil II 5C8RS 5 μm column using a mobile phase of acetonitrile: ammonium acetate buffer (50:50, v/v) at a flow rate of 1.0 mL/min. The detection was carried out at 254 nm using a photodiode array detector [52]. Also, spironolactone was estimated with hydrochlorothiaze by HPLC-photolysis-electrochemical detection [53].

Simultaneous determination of spironolactone, carnenone, furosemide, saluamine, terbinafine, *N*-desmethylcarboxyterbinafine and vancomycin in human plasma and urine was carried out using Rapid UHPLC Method [54].

Spectrophotometric methods

Spironolactone was estimated spectrophotometrically with hydrochlorothiazide in tablets by two methods. The first chemometric analysis methods [55] and the second, colorimetric method were depending on the reaction of spironolactone with isoniazid forming a coloured hydrazine [56], and with furosemide in capsule formulation [57], and with canrenone in urine using partial least-squares regression [58].

Spectroflourimetric method

Spironolactone was determined spectroflourimetrically with carnenone in urine. The method was based on the different rates at which the two analytes react with hot sulfuric acid to form a trienone [59].

Xipamide

Chemical name: 4-Chloro-2,6-dimethyl-5-sulfamoylsalicylanilide.

Molecular formula: $C_{15}H_{15}ClN_2O_4S$.

Molecular weight: 354.805 g/mol.

Description: Off white solid, poorly soluble in water, soluble in methanol or di-methyl sulfoxide.

Melting point: 255-256 °C.

Pharmacological action and uses: Xipamide is a sulphonamide-type diuretic used in the treatment of hypertension alone or in combination with other drugs [60]. Xipamide acts on the kidneys to reduce sodium reabsorption in the distal convoluted tubules.

Method of analysis

Official method

It is not official in any pharmacopeia but few methods were reported as follow.

Chromatographic methods

Xipamide was determined by HPLC in human plasma. The method involved extraction of the drug and an internal standard, mephenesin, into diethyl ether: isopropanol (19 : 1), evaporation of the organic phase and analysis of the reconstituted residue on a C_8 reversed-phase column, which was eluted with acetonitrile: acetate buffer pH 6.7 (25:75). The drug and internal standard were detected by ultraviolet absorption at 225 nm [60].

Another HPLC method with amperometric detection has been developed for the determination of xipamide using a µ-Bondapak C_{18} column. The mobile phase consisted of a mixture of water: acetonitrile (50:50), in 5 mM KH_2PO_4/K_2HPO_4, pH 4.3. The compound was monitored at +1325 mV with an amperometric detector equipped with a glassy carbon working electrode. A liquid-liquid or solid-liquid extraction prior to chromatographic analysis was done to avoid the interferences found in urine matrix [61].

Another HPLC method has been developed for determination of xipamide, triamterene and hydrochlorothiazide in bulk drug samples. Chromatographic separation was carried out in less than two minutes. The separation was performed on a RP C_{18} stationary phase with an isocratic elution system consisting of 0.03 mol/L orthophosphoric acid (pH 2.3) and acetonitrile (ACN) as the mobile phase in the ratio of 50:50 at 2.0 mL /min flow rate at room temperature. Detection was performed at 220 nm [62].

Xipamide was also estimated in combination with clopamide in pharmaceuticals by HPLC, mobile phase methanol: H_2O: acetic acid (69:30:1), C_{18} column was used [63].

Spectrophotometric methods

Xipamide was determined spectrophotometrically in combination with triamterene in pure form and in pharmaceutical formulation. This method depends on quantitative densitometric separation of thin layer chromatogram of triamterene and xipamide at 254 nm [64].

Xipamide was also determined in pure and dosage forms by complexation with Fe(III), Cu(II), La(III), UO2(II), Th(IV) and ZrO(II) ions. The formed complexes had maximum absorbance at 500, 390, 335, 445, 325 and 333 nm for Fe(III), Cu(II), La(III), UO2(II), Th(IV) and ZrO(II), respectively [65].

Spectroflourimetric method

Xipamide was determined by stability-indicating spectroflourimetric method in combination with metolazone in their tablets. The proposed method was based on the measurement of the native fluorescence of metolazone in methanol at 437 nm after excitation at 238 nm and xipamide in alkaline methanolic solution at 400 nm after excitation at 255nm [66].

Voltammetric method

Xipamide was determined by voltammetry at pH 2.5 (phosphate buffer) and 0.4 M KNO_3. The peak current showed a linear relationship with concentration in the range 4.65×10^{-7} - 2.88×10^{-5} M with detection limits of 6.76×10^{-8} M (24 ppb) by differential pulse voltammetry and 3.94×10^{-7} M (140 ppb) by linear scan voltammetry [67].

Conclusion

This literature review represents an up to date survey about all reported methods that have been developed for determination of valsartan, losartan, spironolactone, and xipamide in their pure form, combined form with other drugs, combined form with degradation products, and in biological samples such as liquid chromatography, spectrophotometry, spectroflourimetry, voltammetry, etc...

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