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(Review)

Review on different analytical techniques for analysis of atenolol alone or in combination with other antihypertensive drugs in different matrices

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ABSTRACT

Several analytical techniques were reported for the analysis of atenolol (antihypertensive) either in pharmaceutical dosage forms or in biological samples by various analytical techniques including HPLC, spectrophotometry, fluorimetry, and electrochemical methods. This article includes important information about the cited drug involving physical and chemical characteristics in addition to its pharmacological actions. Atenolol is a β-adrenoreceptor blocker that is used for hypertension, myocardial infarction, and angina. It works via inhibition of renin release, angiotensin -II, and aldosterone production. Atenolol is combined with several antihypertensive agents like losartan, amlodipine, and nifedipine. This review is concerned with different analytical methods of atenolol either alone or with others. The most common method that is used for the analysis of the studied drug is the chromatographic technique then spectroscopy. Fluorimetric and electrochemical methods were used mostly for the determination of atenolol in biological fluids. All methods were validated according to ICH.

Keywords: Atenolol; Analytical methods; antihypertensive.

1. Introduction

Atenolol is a β-adrenoreceptor blocker used for hypertension, myocardial infarction (MI), and angina. It works via inhibition of the release of the renin, angiotensin –II [1].

Atenolol **Figure 1** is 2-[4-{(2RS)-2- hydroxy-3-[(1-methyl ethyl) amino] propoxy} phenyl] acetamide. A white powder, soluble in water, acetonitrile, and acetic acid, sparingly soluble in ethanol, acetone, dioxane, dichloromethane, and chloroform [1]. Physically it was found as a white to slightly yellow crystalline powder and has good solubility in water, practically insoluble in chloroform, methyl alcohol, and benzene. Solutions are stable at pH 2.5 - 4.5 and stored in airtight containers [1, 2].

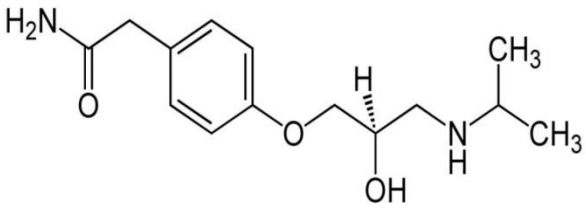

Fig.1. Chemical structure of Atenolol

This article was developed to discuss various analytical techniques that were reported for the analysis of atenolol. These techniques included spectrophotometric, spectrofluorimetric, electrochemical, and chromatographic methods.

2. Analytical methods

Several methods have been reported for the determination of atenolol in pure samples, pharmaceuticals, and biological fluids.

2.1. Titrimetric methods:

- Atenolol is titrated in glacial acetic acid with acetous perchloric acid using crystal violet as an indicator of the visual endpoint [3].
- A titrimetric method involving the oxidation of atenolol by a measured excess of chloramine-T in an acid medium followed by the determination of the residual oxidant by iodometric back titration had been reported for the determination of bumadizone [4].

- Another titrimetric method for the determination of atenolol was reported based on back titration with a bromate-bromide mixture in a hydrochloric acid medium, and the unreacted bromine was determined iodometrically [5].
- Another titrimetric method based on the treatment of atenolol with a measured excess of cerium (IV) sulfate in sulphuric acid medium followed by determination of the residual oxidant by back titration with ammonium ferrous sulfate using a ferroin indicator had been developed for the determination of atenolol [6].

2.2. UV-Visible spectrophotometric methods:

There are many reports on the UV-spectrophotometric determination of atenolol in dosage forms when present in combination with other drugs including:

- Atenolol with amlodipine has been estimated by using different methods including:

- Vierodt's Method: Atenolol and amlodipine were measured at 224.6 nm and 239.6 nm respectively [7].
- Vierodt's Method: The λ_{max} values for amlodipine and atenolol in the solvent medium were found to be 238.4 nm and 273.4 nm respectively [8].
- Vierodt's Method: Then spectra of amlodipine and atenolol exhibit λ_{max} of 239 nm and 228 nm respectively [9].
- Simultaneous equation and Q analysis method: based on measuring the absorptivity at 224.4 nm and iso-absorptive point at 232.2 nm [10].
- Dual wavelength method: Two wavelengths 209 and 244.5 nm were chosen for atenolol the absorbance difference was found to be almost zero [11].
- Another dual wavelength method at which the wavelengths selected for the determination of atenolol were 230 nm and 242 nm, whereas, the wavelengths selected for the determination of amlodipine were 263nm and 277nm [12].
- Derivative spectrophotometric method: The obtained spectra were derivatized to obtain third-order derivative spectra [13].

- Zero crossing technique: Atenolol has absorbance maxima at 223 nm and amlodipine has absorbance maxima at 238nm. The interference of amlodipine at 228nm (wavelength for estimation of atenolol) was removed by using absorbance at 245nm; whereas estimation of amlodipine was done directly from its absorbance at 377 nm at which atenolol showed no absorbance [14].
- Absorbance ratio method: The quantitation of amlodipine and atenolol was done at wavelengths, 240 nm (λ max for Amlodipine) and 231 nm, (an isosbestic point) [15].
- Derivative spectroscopy: Involves the conversion of a normal spectrum (fundamental, zero-order, or D spectrum) to its first, second, or higher derivative spectrum by differentiating absorbance of a sample concerning wavelength λ for higher accuracy [15].
- Area under the curve: This method also utilizes two wavelength ranges. From the overlain spectra of both drugs, the area under the curve is determined at both the selected analytical wavelength ranges [15].
- Absorption factor method: The scanned spectra of amlodipine were measured at 226 nm and 360 nm [16].
- Ratio difference method: The stored spectra of atenolol were divided by the spectrum of 24 µg/mL amlodipine. Calibration curves of Atenolol were constructed by plotting the difference between the amplitudes of ratio spectra at 210 and 226 nm, versus its corresponding concentrations and the regression equation was computed [16].
- Mean centering of the ratio spectra: The scanned spectra were exported to Matlab® for subsequent calculation, then the spectra of atenolol were divided by the absorption spectrum of the standard solution of amlodipine, and the obtained ratio spectra were mean-centered. The calibration curve for atenolol was constructed, by plotting the mean-centered values at 284 nm versus corresponding concentrations and the regression equation was computed [16].

Atenolol in combination with other drugs has been determined by several methods.

➢ With Losartan:

- Absorption ratio method (Q-Analysis) zero crossing method with losartan potassium at 275 nm for atenolol and 282 nm for losartan. [17].

- Artificial neural networks: Several concentrations of atenolol and losartan potassium were measured in the wavelength range (215-275) nm, interval 1 nm, to be used in computing the composition of the calibration mixture [18].
- Vierodt's simultaneous equation method: The maximum absorbance of atenolol and losartan potassium was found to be 223.6 nm & 205 nm respectively [19].
- Extractive spectrophotometric method: The method was based on the formation of colored complexes with reagents like ferroin solution and methyl orange. The ion-pair complex formed was extracted using chloroform and the absorbances of the organic layers were measured at 571 nm and 426 nm for losartan potassium and atenolol respectively [20].

➢ With hydrochlorothiazide:

- First-order derivative spectroscopy, using 214 nm (zero cross for atenolol) and 241 nm (zero cross for hydrochlorothiazide) [21].
- The area under the curve method involved the measurement of areas between 221 to 231 nm and 265 to 275 nm for the estimation of atenolol and hydrochlorothiazide respectively [22].
- Second-order derivative spectrophotometry, which involved measuring the amplitude values at 226 nm and 270 nm of the second derivative spectrum [22].
- With losartan and hydrochlorothiazide separately: by solving simultaneous equations using (251.6 nm and 224.2 nm) for losartan potassium and atenolol, (224.2 and 271.6) for atenolol and hydrochlorothiazide [23].

➢ With atorvastatin:

The method was based on the determination of atenolol and atorvastatin at their λ max 225 nm and 241 nm, respectively [24].

➢ With lercanidipine:

- Ratio derivative: 266.98 nm and 386.97 nm wavelength were selected to determine atenolol and lercanidipine respectively [25].

- Dual wavelength: two wavelengths were chosen for each drug, at wavelengths 234.01 nm and 238.66 nm lercanidipine had equal absorbance therefore these two wavelengths were used to determine atenolol and at 253.33 nm and 286.07 nm were chosen to determine lercanidipine in their combined mixture [25].
- Q Analysis: Employs 261 nm as λ1 (Isosbestic point) and 273 nm as λ2 (λ max of atenolol) for formation of equations [26].
- Simultaneous equation method: where the absorbances of these drugs were maximum. So λ max for lercanidipine hydrochloride and atenolol was 242 and 273 nm respectively [26].

➢ With Chlorthalidone:

- The first method depends on the first derivative of the ratio spectra by measurement of the amplitudes at 235 nm for atenolol and (236,249 nm) for chlorthalidone [27].
- The second method is the factorized absorptivity method at which both drugs are determined at more than one isosbestic point at (265, 284.5 nm) [27].
- The third method involved the application of the bivariate calibration algorithm for spectrophotometric simultaneous determination of the mixture [27].
- Partial least square chemometric method [28].
- UV-Spectrophotometry: The λmax of atenolol and chlorthalidone were found to be 225 nm and 284 nm respectively [29].

➢ With nifedipine:

- Partial least squares (PLS) and principal component regression (PCR) chemometric methods. [30].
- Simultaneous equation method: The λmax was found to be 341.2 nm for nifedipine and 273.8 nm for atenolol [31].
- Absorption correction method: Atenolol and nifedipine had λmax at 276.5 nm and 328.5 nm respectively [32].

- First-order derivative zero-crossing method: Atenolol showed a zero-crossing point at 226.5 nm while nifedipine showed a zero-crossing point at 235 nm [32].

➢ With indapamide:

- Simultaneous equation: The signals were measured at 225 nm and 240 nm corresponding to absorbance maxima of atenolol and indapamide respectively [33].
- Simultaneous equation: The signals were measured at 246.4 nm and 266 nm for atenolol and indapamide [34].
- Dual wavelength method: Atenolol was measured at 266 nm and 270.2 nm [34].
- Ratio subtraction method: A calibration curve was constructed relating the absorbance of zero-order spectra of atenolol at λmax 225 nm [35].
- Bivariate method: The absorbance was measured at 220 and 240 nm [35].
- Area under the curve method: The area under the curve for the wavelength ranges selected for the determination of atenolol and indapamide was 220-230 nm (λ1-λ2) and 235-245 nm (λ3-λ4) [35].

➢ There are many reports on the UV-spectrophotometric determination of atenolol alone in dosage forms including:

- Using Bromate-Bromide mixture as an eco-friendly brominating agent: The methods were based on the bromination of atenolol by the bromine followed by the determination of unreacted bromine by reacting with either meta-cresol purple or erioglaucine and measuring the absorbance at 540 nm, 630 nm respectively [36].
- Via hydroxamic acid formation: forms a reddish violet colored complex with Iron (III) in an acidic medium having maximum absorbance at 510 nm [37].
- Application of bromate-bromide mixture as a green brominating agent: The methods were based on the bromination reaction of atenolol with a known excess of the bromate-bromide mixture in acid medium followed by the determination of unreacted bromine. The residual bromine was determined by its reaction with excess iodide and the liberated iodine was either

measured at 360 nm (method A) or reacted with starch followed by the measurement of the starch-iodine chromogen at 570 nm (method B) [38].

- Using sodium nitroprusside reagent: Based on the determination of atenolol in basic media followed by the addition of sodium nitroprusside to generate a colored complex that absorbed at 495 nm [39].
- A spectrophotometric method: This assay involved the absorbance measurement of atenolol solution in 0.1 N sodium hydroxide at 273nm [40].
- Via complex formation: The methods were based on the formation of a colored complex between the drug and metal ions like Fe (III) chloride and Cr (III) sulfate. The maximum absorption wavelength was 454 nm for the Fe(III)-Atenolol complex and 594 nm for Cr(III)-Atenolol complex [41].
- Via charge transfer complex formation reaction: The methods were based on the charge transfer complexation reaction of atenolol as an n-electron donor with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), 2,4-dinitrophenol (DNP) and 2,4,6-trinitrophenol (picric acid; PA) as π-acceptors to give highly colored radical anion species. The colored products were quantified spectrophotometrically at 590 nm with DDQ and at 420 nm with both DNP and PA [42].
- A spectrophotometric method: Atenolol reacts with phenol red and the resulting yellow-colored product was measured at 430 nm [43].
- Kinetic method: Based on the oxidation of atenolol by a known excess of permanganate in an alkaline medium and unreacted permanganate was measured at 526 nm by rate-constant, constant-concentration and constant-time methods [44].
- Spectrophotometric methods: involve the addition of an excess of Ce4+ and the determination of the amount of unreacted oxidant by reacting with ferroin or methyl orange, and measuring the increase in absorbance at 510 nm or 520 nm respectively [45].
- Another charge-transfer complex formation method: In this method 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) was utilized for the determination of atenolol forming charge transfer complex with maximum absorbance at λ max 405 nm [46].
- UV- Spectrophotometry: Atenolol exhibited maximum absorbance at 273.2 nm in ammonium acetate solution [47].

- Two derivative spectrophotometric methods were described for the determination of atenolol. In first derivative spectrophotometry, absorbance values were measured at 273, 276, and 285 nm [48]. In second derivative spectrophotometry, absorbance values were measured at 276, 279, 282, and 287 nm [48].
- UV- Spectrophotometry: Based on the oxidation of atenolol with excess quantities of oxidants, N-bromosuccinimide (NBS) and nitrous acid. The excess NBS was determined using a dye celestine blue (CB) at λmax 540 nm, while the excess nitrous acid was determined using a dye cresyl fast violet acetate CFVA at λmax 555nm [49].
- UV- Spectrophotometry: The method was based on the measurement of the absorbance of atenolol solution in (10% methanol:90% phosphate buffer pH 6.8) at 224 nm [50].
- Derivatization of atenolol with 1,2-naphthoquinone-4-sulfonic (NQS) and the formed color measured at 454 nm [51].
- By using a hydrotropic solubilizing agent, the primary objective of the addition of this agent was to employ these hydrotropic solutions to improve the solubility of the poorly soluble drug, without the use of costlier organic solvents. The selected wavelength for atenolol was 275 nm [52].
- Another charge-transfer method based on the oxidization of the drug by a known excess of chloramine-T followed by the determination of the unreacted oxidant by a charge-transfer complexation reaction involving metal and sulphanilic acid was reported. The reacted oxidant amount corresponds to the drug content. The colored species exhibits maximum absorbance at 520 nm [53].
- Via ion pair formation method: The method was based on the formation of ion-pair between atenolol and bromothymol blue measured at 414 nm [54].
- Another ion-pair formation method: The method depends on the interaction of the drugs with 0.1% chloroform solutions of acidic sulphophthalein dyes to form stable, yellow-colored, ion-pair complexes measured at 415 nm [55].

2.3. spectrofluorimetric methods:

- A Spectrofluorimetric method based on a native fluorescence of atenolol was developed for the determination of atenolol in pure and pharmaceutical preparation. λex 276 nm and λem 296 nm [56].

- Another reported spectrofluorimetric method was based on the reaction of atenolol with 0.1 N sodium hydroxide, which shows strong fluorescence. λex at 278 nm and λem at 302 nm [57].
- Spectrofluorimetric method for the determination of atenolol was reported based on a native fluorescence of atenolol in human urine and the λex was at 277 nm and λ em was at 300 nm [58].
- A spectrofluorimetric method was based on the reaction of atenolol as n-electron donors with the fluorogenic reagent 9,10-dimethoxy-2-anthracene sulfonate (DMAS) as an π-acceptor in an acidic medium. The obtained ion pairs were extracted into chloroform. λex at 385 nm and λem at 452 nm [59].
- Multivariate calibration method (partial least squares) combined with second-order data obtained from excitation-emission fluorescence matrices to determine atenolol in urine [60].
- A micellar-stabilized room-temperature phosphorescence (MS-RTP) method: maximum phosphorescence signal was completely developed in 10 min and the intensity was measured at λex at 272 nm and λex at 412 nm [61].

2.4. Electrochemical methods:

- Voltammetric method: Determination of atenolol at multi-walled carbon nanotubes modified glassy carbon electrode [62].
- Voltammetric oxidation: Determination of atenolol using a carbon paste electrode [63].
- Voltammetric method: Determination of atenolol at C-60 modified glassy carbon electrodes [64].
- Using graphite-polyurethane composite electrode as an amperometric flow detector in the determination of atenolol [65].
- Voltammetric method: Using nanogold-modified carbon paste electrode (GN-CPE) for the determination of atenolol in pharmaceutical formulations and urine [66].
- By graphite-polyurethane composite electrode: bare graphite-polyurethane composite was evaluated as an alternative electrode in the determination of atenolol in pharmaceutical formulations [67].

- Square-wave voltammetric determination of atenolol in pharmaceuticals using a boron-doped diamond electrode [68].
- Differential pulse voltammetric determination of atenolol in pharmaceutical formulations and urine using nanogold-modified indium tin oxide electrode [69].
- Electrochemical sensor based on gold nanoparticles/multiwall carbon nanotubes-modified glassy carbon electrode for selective determination of traces of atenolol was reported [70].
- Atenolol with propranolol was determined electrochemically using a platinum nanoparticle-doped multi-walled carbon-nanotube-modified glassy carbon electrode as a sensor [71].
- Atenolol with acetaminophen was determined electrochemically using a gold nanoparticle-modified carbon paste electrode as a sensor [72].
- Voltammetric method: Nanogold-modified carbon paste electrode for the determination of atenolol in pharmaceutical formulations and urine [73].
- Application of N-4,4'-azodianiline (ferrocenyl Schiff base): For electrocatalytic determination of atenolol on modified carbon paste electrode [74].

2.5. Chromatographic methods:

2.5.1. Capillary electrophoresis (CE) methods:

➢ Atenolol in Combination with:

- Chlorthalidone: The Capillary electrophoresis using the following conditions: capillary temperature, 25°C; applied voltage, 25 kV; 20 mM H3PO4-NaOH running buffer (pH 9.0); and detection at 198 nm [75].
- Amiloride: Capillary electrophoresis coupled with a capacitive coupled contactless conductivity detector (CE-C(4)D. The separation was carried out in normal polarity mode at 28 °C, 25 kV, and using hydrodynamic injection (25 s) [76].
- Other complementary anti-hypertensive agents in urine: The electrophoretic separation was performed using a 78-cm x 75-micron-i.d. (70-cm effective length) fused-silica capillary. A borate buffer (pH 9) was used as a running electrolyte. The sample was hydrostatically introduced for 20 s, and the running voltage was 25 kV at the injector end of the capillary [77].

- In tertiary mixture with amiloride and chlorthalidone: The separation was carried out in normal polarity mode at 25 degrees C, 25 kV, and using hydrodynamic injection (10 s). The separation was done in an uncoated fused-silica capillary (75µm i.d. x 52 cm) and a background electrolyte of 25 mm H3PO4 adjusted with 1 M NaOH solution (pH 9.0) and detection at 198 nm. Using phenobarbital as an internal standard, the analytes were all separated in less than 4 min [78].

➢ Atenolol alone By CE methods:

- Determination of atenolol in the presence of its related substances in bulk and tablet dosage form [79].
- The electrophoretic separation was performed using a 78 cm × 75 µm I.D. fused silica capillary. The electrolyte consisted of a buffer Na2HPO4 (25 mM)-Na2B4O7 (25 mM) (50-50) v/v, pH 9.7. The introduction of the sample was made hydrostatically for 25 s and the running voltage was 20 KV at the injector end of the capillary. Photometric detection was used and a wavelength of 214 nm [80].
- The capillary zone electrophoretic method was optimized for the determination of atenolol in plasma. Separation was performed in an uncoated silica capillary of 58.5 cm (effective length 50 cm x 75 micron I.D.,) and detection was at 194 nm [81].

2.5.2. Thin layer chromatographic methods:

- Densitometric evaluation of thin layer chromatograms of atenolol in tertiary mixture with amlodipine and hydrochlorothiazide: The chromatographic separation of the drugs was performed on aluminum plates pre-coated with silica gel 60 F254 as the stationary phase and the solvent system consisted of chloroform: methanol: acetic acid (8: 2: 0.2) by volume. The scanning was done at 232 nm [82].
- Densitometric evaluation of thin layer chromatograms of atenolol in a binary mixture with aspirin: using mobile phase n-butanol: water: acetic acid (8: 2: 0.2) by volume [83].
- Thin layer chromatographic separation of atenolol in a binary mixture with nitrendipine: the mobile phase was chloroform: methanol: toluene: 25% ammonia (2:2.5:5.5:0.1) by volume [84].

- Using HPTLC for separation of atenolol in binary mixture with losartan: The chromatographic separation was done using a Camag HPTLC system consisting of Camag Linomat V automatic sample applicator, Camag syringe, Camag TLC scanner 3, Camag WinCats software and Camag twin trough chamber, with pre-coated Silica Gel 60 F-254 aluminum sheets as stationary phase and ethyl acetate: methanol: 1,4 dioxane: ammonia (10: 2: 1: 2) by volume as the mobile phase. The scanning was done at 225nm [85].
- Densitometric method of atenolol in a binary mixture with lercanidipine using toluene: methanol: triethylamine (3.5: 1.5: 0.1) by volume as mobile phase. Detection was performed at 275 nm [86].
- Thin layer chromatographic separation of atenolol in a binary mixture with chlorthalidone and their degradation products using silica gel plates and chloroform: methanol: ethyl acetate: ammonia solution (75: 28: 2: 1.6) by volume at 227 nm [87].

2.5.3. Gas chromatographic (GC) methods:

- Atenolol was determined in human urine by gas chromatography-mass spectrometry (GC-MS): atenolol and metoprolol (internal standard, IS) were extracted from human urine with a mixture of chloroform and butanol at basic pH with liquid-liquid extraction. The extracts were derivatized with N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) and analyzed by GC-MS using a capillary column [88].
- Atenolol in whole blood, serum, tissue, and urine was reported to be determined by gas chromatography: The method involves the extraction of the free base from the prepared biological sample into an organic solvent mixture [89].
- Another method describes the validation of gas chromatography with flame ionization (FID) and mass spectrometric (MS) detection after derivatization with N-Methyl-N-(trimethylsilyl) trifluoroacetamide (MSTFA) for the determination of atenolol with an internal standard (Metoprolol) in pharmaceutical preparations [90].

2.5.4. HPLC methods:

Several HPLC methods have been reported for the analysis of atenolol, as maintained in Table (1).

Table (1): HPLC methods reported for the determination of Atenolol:

Matrix	Column	Mobile phase	Detection	Ref No.
Atenolol alone				
Pharmaceutical preparations	Inertsil ODS C_{18}	Phosphate buffer: acetonitrile (53:47) v/v	UV-230 nm.	[91]
Pharmaceutical preparations	Waters µbondapak C_{18}	Acetonitrile: sodium phosphate monobasic pH 3.0 (10:90) v/v.	UV-284 nm.	[92]
Plasma and urine	Ultrasphere ODS C_{18}	(29/80 Acetonitrile/H20, 1% acetic acid, 5 mM heptane sulfonic acid, 2.5 mM triethylamine).	Fluorescence λ_{ex} = 222.	[93]
Pharmaceutical preparations	Purospher RP-C_{18}	Ammonium acetate buffer (pH 7.0) and acetonitrile (80:20) v/v.	UV- 226 nm.	[94]
Human plasma	Ace C_{18} reverse-phase	Methanol-water containing 0.1% trifluoroacetic acid (50:50) v/v.	Fluorescence λ_{ex} = 276 nm. λ_{em} = 296 nm.	[95]
Pharmaceutical preparations	Hibar 100 RP- C_8	Acetonitrile : methanol: 0.02 M phosphate buffer, pH 5 (20:20:60) by volume.	UV - 226 nm.	[96]
Pharmaceutical preparations	hypersil RP-C_{18}	Acetonitrile: methanol: KH_2PO_4 (250:250:500) by volume.	UV - 237 nm.	[97]
Human plasma	Kromasil KR100-5sil	5% Acetonitrile and 95% formate buffer.	Tandem mass spectrometry.	[98]
Pharmaceutical preparations	Atlantis d RP- C_{18}	Ammonium acetate: methanol (60:40) v/v.	UV - 225 nm.	[99]
Pharmaceutical preparations	Purospher start C_{18}	Methanol: water (80:20) v/v.	UV - 224 nm.	[100]

In vitro studies	Phenomenex C_{18} – RP	Ammonium acetate: methanol (75:25) v/v.	UV - 225 nm.	[101]
Human plasma	ODS-3 C_{18} inertsil	Dichloromethane: 2-propanol (75:25) v/v.	Fluorescence λ_{ex} = 228 nm. λ_{em} = 298 nm	[102]
Pharmaceutical preparations	Chiralcel AGP C_{18}	Sodium phosphate buffer : methanol (95:5) v/v.	UV - 225 nm.	[103]
Human plasma	A Brownlee cartridge spheri-5 cyano analytical column	Aqueous solution containing 5 mM triethylamine, 10 mM phosphoric acid and 7 mM 1-octanesulfonic acid sodium salt with: acetonitrile (60/40) v/v.	(DAD).	[104]
Pharmaceutical preparations	Inertsil ODS C_{18}	Water and acetonitrile (50:50v/v).	UV - 228 nm.	[105]
Whole blood	Nucleosil C_{18}	Acetonitrile, methanol in 0.05 M phosphate-triethylamine buffer, pH 3.3.	Fluorescence detection.	[106]
		Atenolol in combination with amlodipine		
Pharmaceutical preparations	Shim-pack CLC, ODS C_{18}	Ammonium acetate buffer, acetonitrile, and methanol (35: 30: 35) by volume.	UV - 237 nm.	[107]
Pharmaceutical preparations	BDS C_{18}	K_2HPO_4 pH 5: methanol: acetonitrile (40:30:30) by volume.	UV - 213 nm.	[108]
Pharmaceutical preparations	Hypersil, BDS	Potassium dihydrogenate phosphate : acetonitrile (62:38) v/v.	UV - 238 nm.	[109]

Pharmaceutical preparations	Welchrom RP-C_{18}	Phosphate buffer (pH 3.0): acetonitrile (50:50, v/v).	UV - 235 nm.	[110]
Pharmaceutical preparations	Waters, USA C_{18}	Methanol: acetonitrile: buffer (55:10:35) by volume.	UV - 237 nm.	[111]
Pharmaceutical preparations	RP- stainless steel ODS C_{18}	Potassium buffer: acetonitrile (50:50) v/v.	UV - 237 nm.	[112]
Pharmaceutical preparations	Thermo-hypersil keystone C_{18}	0.05 M of Potassium dihydrogen orthophosphate in water.	UV - 230 nm.	[113]
		Atenolol with amlodipine and aspirin		
Pharmaceutical preparations	Cosmosil C_{18}-MS-II	Acetonitrile: ammonium acetate buffer pH 4.6 (80:20) v/v.	UV - 233 nm.	[114]
Pharmaceutical preparations	Thermo hypersil BDS-C_{18}	Methanol: 10 mM phosphate buffer with pH 7.0 adjusted with orthophosphoric acid (70: 30) v/v.	UV - 235 nm.	[115]
		Atenolol with losartan		
Pharmaceutical preparations	Symmetry C_{18}	Phosphate buffer: methanol: Acetonitrile (30:20:50) by volume.	UV - 234 nm.	[116]
Pharmaceutical preparations	Develosil C_{18}	1%TEA: acetonitrile (60:40) v/v.	UV - 237 nm.	[117]
Pharmaceutical preparations	Supelcosil ODS C_{18}	Acetonitrile : KH_2PO_4 (45:55) v/v.	UV - 227 nm.	[118]
		Atenolol in combinations with losartan and hydrochlorothiazide		

Pharmaceutical preparations	Phenomenex luna 5 µ CN 100 R	Acetonitrile: 0.2% of phosphate buffer pH 2.8 (50:50) v/v.	UV - 230 nm.	[119]
Pharmaceutical preparations	Phenomenex C_{18}	Acetonitrile: KH_2PO_4 (pH 3.5) (50:50) v/v.	UV - 270 nm.	[120]
Pharmaceutical preparations	Luna C_{18} phenomenex	(A) Acetonitrile: methanol (65:35) and (B)10 mM sodium dihydrogen phosphate monohydrate buffer with 0.4% v/v triethylamine and mixture of A:B (60:40) v/v.	UV - 230 nm.	[121]
Pharmaceutical preparations	C_{18}	0.035 M potassium dihydrogen orthophosphate, acetonitrile.	UV - 225 nm.	[122]
Pharmaceutical preparations	Hypersil gold	Methanol: water (95:5) v/v.	UV - 225 nm.	[123]
		Atenolol with losartan and atorvastatin		
Pharmaceutical preparations and plasma	KYA TECH HiQ Sil C_{18} HS	Acetonitrile: 0.02 M KH_2PO_4 buffer (70:30) v/v pH 3.4 .	UV - 236 nm.	[124]
		Atenolol with hydrochlorothiazide and chlorthalidone		
Pharmaceutical preparations	Supelcosil LC-$_8$-DB	Ammonium acetate and octane sulfonic acid sodium salt in acetonitrile : water (25 : 75) v/v.	UV - 232 nm.	[125]
		Atenolol with hydrochlorothiazide		
Pharmaceutical preparations	Zorbax SB-CN	Water: buffer: methanol (50:35:15) by volume.	UV - 286 nm.	[126]

		Atenolol with chlorthalidone		
Spiked human plasma	Shim-pack cyanopropyl	KH_2PO_4 (pH 6.0) : methanol (70:30) v/v.	UV - 225 nm.	[127]
Pharmaceutical preparations	Xterra RP_8	KH_2PO_4: methanol (50:50) v/v.	UV - 240 nm.	[128]
Human breast milk.	Luna CN phenomenex	Acetonitrile : water (35:65) v/v.	UV - 225 nm.	[129]
Pharmaceutical preparations	Comosil	Methanol: water (60: 40) v/v.	UV - 226 nm.	[130]
Human plasma	ODS	Sodium dodecyl (pH 5.8): n-propanol (95:5) v/v.	UV for Chlorthalidone , fluorometric for atenolol.	[131]
		Atenolol with lercanidipine		
Pharmaceutical preparations	Phenomenx gemini C_{18}	Methanol: water (95:5) v/v.	UV - 235 nm.	[132]
Pharmaceutical preparations	Phenomenex Gemini C_{18}	Acetonitrile: KH_2PO_4 buffer (55:45) v/v.	UV - 235 nm.	[133]
Pharmaceutical preparations	Luna C_{18}	Acetonitrile: phosphate buffer pH 3.6 (60:40) v/v.	UV - 235 nm.	[134]
Pharmaceutical preparations	X-terra RP-C_{18}	Acetonitrile: methanol : KH_2PO_4 buffer (50:10:40) by volume.	UV - 226 nm.	[135]
Pharmaceutical preparations	Inertsil 3V ODS	Ammonium acetate: THF: acetonitrile (35:10:55).	UV - 221 nm.	[136]
		Atenolol with nifedipine		

Pharmaceutical preparations	Agilent ODS C_{18}	Methanol : acetonitrile : phosphate buffer (60:20:20) by volume.	UV - 235 nm.	[137]
Pharmaceutical preparations	PhenomenexODS 3	Methanol : water : phosphate buffer : suitable quantity of sodium heptane sulfonate (65:35:3:0.13) v/v/v/w.	UV - 240 nm.	[138]
Pharmaceutical preparations	ODS - C_{18} metaphase	Phosphate buffer : methanol pH 4.0 (50:50) v/v.	UV - 237 nm.	[139]
		Atenolol with indapamide		
Pharmaceutical preparations	Waters C_{18}	Methanol : water (80:20) v/v.	UV - 230 nm.	[140]
Pharmaceutical preparations	Gemini C_{18}	Acetonitrile : 0.02M KH_2PO_4 (50: 50) v/v.	UV - 241 nm.	[141]
Pharmaceutical preparations	Xterra® C_{18}	Octane sulphonic acid, sodium salt : methanol (55:45) v/v.	UV - 235 nm.	[142]
Pharmaceutical preparations	Intelligent C_{18}	Methanol : water : diethylamine : glacial acetic acid (70 : 30 : 0.12 : 0.08) by volume.	UV - 240 nm.	[143]
Pharmaceutical preparations	Symmetry X-Terra C_8	KH_2PO_4: acetonitrile (40: 60) v/v.	UV - 240 nm.	[144]

3. Conclusion:

This review includes the majority of analytical methods used for the quantification of atenolol in different matrices so; it will help every analyst to be aware of all the analytical methods used for the analysis of the studied drug. The most used analytical technique is the chromatographic technique, which has different advantages such as good resolution and can

separate different compounds at the same time. For determination in biological fluids, fluorimetric and electrochemical methods were used giving excellent sensitivity.

Conflict of interest

All authors declare no conflict of interest

4. References:

1. The Merck Index 14th Ed. Published by Merck and CO. INC., Rahway, USA., (2006).
2. Sweetman S. Martindale: the complete drug reference. 36th ed. London: The Pharmaceutical Press; 2009.
3. Prashanth KN, Basavaiah K, Raghu MS and Vinay KB. "Determination of Atenolol and its preparations by Acid-Base Titration in Non-aqueous Medium". Der Pharmacia Lettre, 2012, 4 (5),1534-1540 .
4. Basavaiah K, Chandrashekar U And Nagegowda P. "Sensitive determination of atenolol in tablets using chloramine T and two dyes". Indian J. Chem. Technol. 2004, 11(2), 769-776.
5. Basavaiah K, Chandrashekar U And Nagegowda P. "Titrimetric, spectrophotometric and kinetic methods for the assay of atenolol using bromate–bromide and methyl orange". J. Serb. Chem. Soc. 2006, 71 (5), 553-563.
6. Basavaiah K, Chandrashekar U And Nagegowda P. "Titrimetric and spectrophotometric determination of atenolol using cerium(IV) sulphate". Bulg. Chem. Comm. 2003, 35(3), 174-182.
7. Girdhari J, Prabhakara P, Pankaj K and Annu K. "Simultaneous Estimation Of Atenolol And Amlodipine Besylate In Tablets Formulations By Vierodt's Method Using U.V.Spectrophotometry". Int. Res. J. pharmacy. 2012, 3(2), 248-250.
8. Rathee P ,Rathee S, Thakur S and Kumar V. "Simultaneous Estimation Of Amlodipine Besylate And Atenolol As A.P.I. And In Tablet Dosage Forms By Vierodt's Method Using U.V. Spectrophotometry". Int J ChemTech Res. 2010, 2(1), 62-68.

9. Pawar PY, Mane BY, Auti SM and Trivedi VV. “Simultaneous estimation of amlodipine besylate and atenolol in combined dosage form by Vierodt’s method using U.V. spectroscopy”. Der Pharma Chemica, 2013,5(2), 97-102 .
10. Mali SL, Dhabale PN, Gonjari ID, Deshmukh V and Chanekar PD. “Simultaneous UV Spectrophotometric Methods For Estimation Of Atenolol And Amlodipine Besylate In Combined Tablet Dosage Form”. Int. J. Pharmacy Pharm. Sci, 2010, 2(3), 71-74.
11. Suresh P, Babu BH and Chakravarthy IE. “UV-absorbance difference method for simultaneous estimation of atenolol and amlodipine besylate in combined dosage forms”. Der Pharmacia Lettre, 2015,7(1), 280-284.
12. Avula S, Madhu S and Ummaraspaty UR. “A new method development and validation of dual wavelength UV Spectrophotometric method for Simultaneous estimation of Atenolol and Amlodipine besylate in combined dosage form”. J. Compr. Phar, 2015, 2(3), 98-104.
13. Kasture AV and Ramteke M. “Simultaneous UV-spectrophotometric method for the estimation of atenolol and amlodipine besylate in combined dosage form”. Ind. J. Pharm. Sci, 2006, 68(3), 394-396.
14. Bhatia NM, Mohite AS and Bhatia MS. “Simultaneous spectrophotometric estimation of atenolol and amlodipine besylate by multi-wavelength method”. The Indian Pharmacist, 59(6), 59-62 (2007).
15. Kamoda AC, Sawant RL and Mogal SA. “Spectrophotometric Methods for Estimation of Atenolol and Amlodipine besylate in Combined Tablet Dosage Form”. Anal. Chem. Lett, 2013, 3(3), 191-189.
16. Lamei NT. “Spectrophotometric Methods for Simultaneous Determination of Binary Mixture of Amlodipine Besylate and Atenolol Based on Dual Wavelength”. Spectrochim. Acta. A Mol Biomol Spectrosc, 2015, 149(5),201-207.
17. Lalitha KV, Kiranjyothi R and Padma B. “Uv Spectrophotometric Method Development and Validation For The Determination Of Atenolol And Losartan Potassium By Q-Analysis”. Int. Bull. Drug Res., 2013, 3(4), 54-62.
18. Satyanarayana D, Kannan K and Manavalan R. “Artificial Neural Network Calibration Models for Simultaneous Spectrophotometric Determination of Atenolol and Losartan Potassium in Tablets”. Chem. Anal. (Warsaw),2006, 51, 771-776.

19. Singh S and Koland M. “Spectrophotometric Quantitative Estimation Of Atenolol And Losartan Potassium In Bulk Drugs And Pharmaceutical Dosage Form”. Wor. J. Pharmacy Pharm. Sci., 2014, 3(7), 1026-1033.
20. Patel ND and Captain AD. “Extractive Spectrophotometric Method For Simultaneous Determination Of Losartan Potassium And Atenolol In Bulk And In Pharmaceutical Dosage Form”. Int. J. Pharm. Tech. Res., 2013, 2(5), 629-640.
21. Behera AK. “Simultaneous Spectrophotometric Estimation of Atenolol and Hydrochlorothiazide in Tablet Dosage Forms”. Int. J. Chem. Tech. Res.,2010, 2(4) 1901-1906.
22. Ahmed M , Jamadar N and Shetty AS. “Simultaneous Estimation Of Atenolol And Hydrochlorothiazide In Combined Dosage Form By UV-Spectrophotometric Methods”. Acta. Chim. Pharm. Indica,2012, 2(3), 134-142.
23. Bari S, Sathe S, Jain P and Surana S. “Spectrophotometric method for simultaneous estimation of atenolol in combination with losartan potassium and hydrochlorothiazide in bulk and tablet formulation”. J. Pharm. Bioapp. Sci. 2010, 2(4), 372–375.
24. Dey S, Sarkar S , Malakar J , Ghosh A, Gangopadhyay A and Mazumder B. “Spectrophotometric method for simultaneous determination of atenolol and atorvastatin in tablet dosage forms”. Int J Pharm Biomed Res.,2012, 3(1), 40-43.
25. Choudhari VP, Suryawanshi VM, Mahabal RH, Deshchougule SG, Bhalerao KP and Kuchekar BS. “Simultaneous Spectrophotometric Estimation Of Atenolol And Lercanidipine Hydrochloride In Combined Dosage Form By Ratio Derivative And Dual Wavelength Method”. Int. J. Pharm. Sci. Rev. Res., 2010, 3(1), 73-76.
26. Jain N, Jain R and Thakur N. “Simultaneous Spectrophotometric Estimation of Lercanidipine Hydrochloride and Atenolol in Tablet Dosage Form”. Eurasian J. Anal. Chem., 2011, 6(2), 84-90 .
27. Abou-elkheir A, Saleh HM, El-henawee MM and Ghareeb BE, “Derivative Ratio, Isosbestic Point, Factorized Absorptivity And Bivariate Spectrophotometric Determination Of Atenolol And Chlorthalidone”. Int. J. Pharm. Chem. Bio. Sci., 2015, 5(1), 19-33.

28. Ferraro MC, Castellano PM and Kaufman TS. "Chemometrics-assisted simultaneous determination of atenolol and chlorthalidone in synthetic binary mixtures and pharmaceutical dosage forms". Anal. Bioanal. Chem. 2003, 377(7-8) 1159-1164.

29. Haque MA, Nivedita G, Kumar KP, Kumar TP, Amrohi. SH and Diwan PV. "Simultaneous Estimation of Atenolol and Chlorthalidone as Bulk and In Tablet Dosage Form Using Uv-Spectrophotometry". J. Pharm. Bio. Sci.,2012, 4(1), 20-23.

30. Abdallah I, Ibrahim A, Ibrahim N, Rizk M and Tawakkol S. "Simultaneous Determination of Atenolol and Nifedipine by Using Spectrophotometric Method with Multivariate Calibration and HPLC Method Implementing" "Design of Experiment". Pharm Anal Acta, 2015, 6, 384-390.

31. Ghadge NN, Shinde AG, Hole MB, Kadam SS and Gaikwad DD. " Uv-Spectrophotometric Method For The Simultaneous Determination Of Atenolol And Nifedipine In Solid Dosage Forms". Inventi J. Pvt. Ltd. 2013, 13(2), 637-642.

32. Kasture AV and Ramteke M. "Simultaneous UV-Spectrophotometric Methods For The Estimation Of Atenolol And Nifedipine In Solid Dosage Forms". Ind. J. Pharm. Sci., 2005, 67(6), 752-754.

33. Pawar PV, Gaikwad PD, Bankar VH and Pawar SP. "Development And Validation Of Uv-Spectrophotometric Method For Simultaneous Estimation Of Atenolol And Indapamide In Bulk And Tablet Dosage Form". Int. J. Pharm. Tech., 2010, 2(4) 676-685.

34. Fernandes N , Nimdeo MS , Choudhari VP , Kulkarni RR , Pande VV and Nikalje AG. "Dual Wavelength And Simultaneous Equation Spectrophotometric Methods For Estimation Of Atenolol And Indapamide In Their Combined Dosage Form". Int. J. Chem. Sci., 2008, 6(1), 29-35.

35. Attia KA, El-Abasawi NM and Ramzy Sh. "Ratio Subtraction, Bivariate And Area Under Curve Spectrophotometric Methods For Determination Of Atenolol In Binary Mixture With Indapamide". Euro. J. Biomed. Pharm. Sci., 2015, 2(4) 48-60.

36. Prashanth KN and Basavaiah K. "Sensitive Spectrophotometric Determination of Atenolol in Pharmaceutical Formulations Using Bromate-Bromide Mixture as an Eco-Friendly Brominating Agent". J Anal Methods Chem.2012, 2012, 1-12.

37. Agrawala YK, Raman MK, Rajputa MS and Mrs SK. "Spectrophotometry Determination of Atenolol via Hydroxamic acid Formation". Anal. Lett. 1992, 25(8) 1503-1510.

38. Prashanth KN, Basavaiah K, Sameer AM and Nagaraju A. "Application Of Bromate–Bromide Mixture As a Green Brominating Agent For The Spectrophotometric Determination Of Atenolol In Pharmaceuticals". Chem. Indust. Chem. Eng. Quarterly, 2012, 18 (1), 43-52 .

39. Bashir N, Shah SWH, Bangesh M and Rizkullah. "A novel spectrophotometric determination of atenolol using sodium nitroprusside". J. Sci. Indust. Res., 2011,70, 51-54 .

40. Prashanth KN and Swamy N. "UV- Spectrophotometric Assay of Atenolol in Pharmaceuticals and Study of its Forced Degradation". Asian. J. Biochem. Pharm. Res, 2014, 1(4), 240-253 .

41. Divya K and Narayana B. "New Visible Spectrophotometric Methods For The Determination Of Atenolol In Pure And Dosage Forms Via Complex Formation". Indo American J. Pharm. Res., 2014,4(1), 194-203.

42. Prashanth KN And Basavaiah K. Simple, "Sensitive And Selective Spectrophotometric Methods For The Determination Of Atenolol In Pharmaceuticals Through Charge Transfer Complex Formation Reaction". Acta Poloniae Pharm. Drug Res., 2012, 69(2), 213-223.

43. Basavaiah K, Chandrashekar U, Somashekar BC and Ramakrishna V. "Development and validation of neutralization reaction based analytical methods for the assay of atenolol in pharmaceuticals". National Academy of Sciences, India, Section A: Physical Sciences, 2005, 75(4), 233-238.

44. Hiremath GC, Mulla RM and Nandibewoor ST. "Kinetic Methods of Determination of Atenolol in Pure Compound and in Pharmaceutical Formulations". Chem. Anal. (Warsaw), 2005, 50, 449-455 .

45. Basavaiah K, Chandrashekar U and Nagegowda P. "Titrimetric and spectrophotometric determination of atenolol using cerium(IV) sulphate". Bulg. Chem. Comm., 2003, 35(3), 174-182 .

46. Nagaraja SK and Chakravarthi IE. "A UV-Visible Spectrophotometric Determination of atenolol in Pharmaceutical Formulations". Int. J. Sci. Res., 2013, 2(3), 31-32 .

47. Lalithag , Salomi P and Ravindra RK. “Development Of An Analytical Method And Its Validation For The Analysis Of Atenolol In Tablet Dosage Form By Uv-Spectrophotometry”. Int. J. Pharmacy Pharm. Sci, 2013, 5(2), 197-199 .
48. Yelmaz B. “Determination of Atenolol in Pharmaceutical Preparation by Zero-, First-, Second- and Third Order Derivative Spectrophotometric Methods”. J. Pharm. Sci., 2008,33, 119–129.
49. Prasad UV, Rao GV and Sastry CSP. “New spectrophotometric analysis of atenolol in pure and pharmaceutical formulations”. Ind. J. Pharm. Sci,. 2002, 64(4), 129-132 .
50. Gite1 SS, Shinkar DM and Saudagar RB. “UV Spectrophotometric Method for the Estimation of Atenolol In Bulk and Pharmaceutical Formulations”. Am. J. Pharm. Tech Res. 2013, 3(6), 708-714 .
51. Ali AAA and Elbashira AA. “A new spectrophotometric method for the determination of cardiovascular drugs in dosage forms”.Am. Acad. Schol. Res. J., 2013, 5(1), 106-121 .
52. Aher BO, Dr.Jain NP, Shinde GS, GaykeAmol, Jadhav VK and Bankar KA. “Novel spectrophotometric estimation of atenolol using hydrotropic solublizing agent”. Int. J. Adv. Res. Biol.Sci. 2015, 2(4), 151-156.
53. Basavaiah K. Chandrashekar U and Nagegowda P. “Determination of atenolol by spectrophotometry based on charge-transfer complex formation reaction”. Acta Ciencia Indica, Chemistry, 2004, 30 (1), 75-79 .
54. Sungur S and Yurdakul G. “Spectrophotometric Determination Of Atenolol By Ion-Pair Extraction Technique”. J. Pharm. Univ. Mar., 1991,7(1), 63-68.
55. Al-Ghannam SM. “A simple spectrophotometric method for the determination of β-blockers in dosage forms”. J. Pharm. Biomed. Anal., 2006, 40(1) 151-156 .
56. Yilmaz B and Meral K. “Validated Spectrofluorimetric Method For Determination Of Atenolol In Pharmaceutical Preparations”. Asian. J. Pharm. Res. HC., 2(2), 170-176 (2010).
57. Patel SA, Pate CN, Rathod IS, Suhagia BN and Patel MM. “Spectrofluorimetric Method For The Determination Of Atenolol In Tablet Dosage Forms”. Ind. J. Pharm. Sci., 67(2), 224-226 (2005).
58. Basan H and Yarımkaya S. “A novel solid-phase extraction-spectrofluorimetric method for the direct determination of atenolol in human urine”. Luminescence, 29(3), 225-229 (2013).

59. Abdine H, Sultan MA, Hefnawy MM and Belal F. "Spectrofluorometric determination of some β-blockers in tablets and human plasma using 9,10-dimethoxyanthracene-2-sodium sulfonate". Int. J. Pharm. Sci., 60(4), 265-268 (2005).

60. Damiani PC. "Determination of atenolol in human urine by emission-excitation fluorescence matrices and unfolded partial least-squares with residual bilinearization". Talanta, 85(3), 1526-1534 (2011).

61. Castillo M, Ongaro L, Polizzi G, Andreetta HA and Bruzzone L. "Determination of atenolol by the micelle-stabilized room-temperature phosphorescence methodology". Luminescence, 22(6), 527-533 (2007).

62. Hegde RN, Chandra P and Nandibewoor ST. "Sensitive Voltammetric Determination of Atenolol at Multi-walled Carbon Nanotubes Modified Glassy Carbon Electrode". Res. J. Nanosci. Nanotech., 1, 75-86 (2011).

63. Patil RH, Hegde RN and Nandibewoor ST. "Voltammetric Oxidation and Determination of Atenolol Using a Carbon Paste Electrode". Ind. Eng. Chem. Res., 48(23), 10206-10210 (2009).

64. Goyal RN and Singh SP. "Voltammetric determination of atenolol at C-60-modified glassy carbon electrodes". Talanta, 69(4), 932-937 (2005).

65. Cervinia P and Cavalheiroa ETG. "Graphite-Polyurethane Composite Electrode as an Amperometric Flow Detector in the Determination of Atenolol". Anal. Lett., 41(10), 1867-1877 (2008).

66. Behpour M. Honarmand E and Ghoreishi SM. "Nanogold-modified Carbon Paste Electrode for the Determination of Atenolol in Pharmaceutical Formulations and Urine by Voltammetric Methods". Bull. Kor. Chem. Soc. 31(4), 845-849 (2010).

67. Cervini P, Ramos LA and Cavalheir ETG. "Determination of atenolol at a graphite–polyurethane composite electrode". Talanta, 72(1), 206-209 (2007).

68. Sartori ER, Medeiros RA, Romeu C, Rocha-Filho RC and Fatibello-Filho O. "Square-wave voltammetric determination of propranolol and atenolol in pharmaceuticals using a boron-doped diamond electrode". Talanta, 81(4-5), 1418-1424 (2010).

69. Goyal RN, Gupta VK , Oyama M and Bachheti N. "Differential pulse voltammetric determination of atenolol in pharmaceutical formulations and urine using nanogold modified indium tin oxide electrode". Electrochem. Comm., 8(1), 65-70 (2006).

70. Shamsipur M, Saberb R and Emamic M. "A highly sensitive electrochemical sensor based on gold nanoparticles/multiwall carbon nanotubes-modified glassy carbon electrode for selective determination of traces of atenolol ". Anal. Methods. 6, 7038-7045 (2014).

71. Kun Z, Hongtao C, Yue Y, Fangzheng L and Sanming L. "Platinum nanoparticle-doped multiwalled carbon-nanotube-modified glassy carbon electrode as a sensor for simultaneous determination of atenolol and propranolol in neutral solution". Ionics, 21(4), 1129-1140 (2014).

72. Behpour M, Ghoreishi SM and Honarmand E. "A Gold Nanoparticle-Modified Carbon Paste Electrode as a Sensor for Simultaneous Determination of Acetaminophen and Atenolol". Int. J. Electrochem. Sci., 5, 1922 - 1933 (2010).

73. Behpour M. Honarmand E and Ghoreishi SM. "Nanogold-modified Carbon Paste Electrode for the Determination of Atenolol in Pharmaceutical Formulations and Urine by Voltammetric MethodsBull". Kor. Chem. Soc., 31(4),845-849 (2010).

74. Taei M, Hasanpour F and Shavakhi M. "Application of N-4,4'-azodianiline (ferrocenyl Schiff base) for electrocatalytic determination of atenolol on modified carbon paste electrode". Iran. Chem. Commun, 3, 19-31 (2015).

75. Al-Azzam K, Elbashir AA, Elbashir MA, Bahruddin S and Shafida A. "Simultaneous determination of atenolol and chlorthalidone in pharmaceutical preparations by capillary-zone electrophoresis". Anal. lett, 42(10), 1458-1470 (2009).

76. AL Azzam KM, Hassan Y and Aboul-Enein HY. "Simultaneous Determination of Atenolol and Amiloride by Capillary Electrophoresis with Capacitively Coupled Contactless Conductivity Detection (C4D)". Methods in Molecular Biology, 919, 67-78 (2012).

77. Maguregui MI, Jimenez RM and Alonso RM. "Simultaneous Determination of the β-Blocker Atenolol and Several Complementary Antihypertensive Agents in Pharmaceutical Formulations and Urine by Capillary Zone Electrophoresis". J. Chrom. Sci., 36, 516-522 (1998).

78. Al Azzam KM, Saad B and Aboul-Enein HY. "Simultaneous determination of atenolol, chlorthalidone and amiloride in pharmaceutical preparations by capillary zone electrophoresis with ultraviolet detection". Biomed. Chromatogr, 24(9), 977-981(2010).

79. Shafaati A and Clark BJ. "Development and validation of a capillary zone electrophoretic method for the determination of atenolol in presence of its related substances in bulk and tablet dosage form". J. Pharm. Biomed. Anal., 14(8), 1547-1554 (1996).

80. Magureguia MI, Alonsoa RM and Jiméneza RM. "Capillary Zone Electrophoretic Method for the Quantitative Determination of the β-Blocker Atenolol in Human Urine". J. Liq. Chrom. Relat. Tech., 20(20), 3377-3387 (1997).

81. Arias R, Jiménez RM, Alonso RM, Télez M, Arrieta I and Flores P. "Determination of the β-blocker atenolol in plasma by capillary zone electrophoresis". J. Chrom. A, 916(1-2), 297-304 (2001).

82. Bhusari VK and Dhaneshwar SR. "Validated HPTLC Method for Simultaneous Estimation of Atenolol, Hydrochlorothiazide and Amlodipine Besylate in Bulk Drug and Formulation". Int. J. Anal. Biomed. Chem., 1(3), 70-76 (2011).

83. Bhusari VK and Dhaneshwar SR. "Validated HPTLC Method for Simultaneous Estimation of Atenolol and Aspirin in Bulk Drug and Formulation". Int. Schol. Res. Net., 2012, 1-5 (2012).

84. Sawant JG and Argekar A. "Simultaneous determination of atenolol and nitrendipine in pharmaceutical dosage forms by HPTLC". J. Liq. Chrom. Related Tech., 22(10), 1571-1578 (2006).

85. Keny SM, Nazareth C and Sawaikar L. "Development and validation of a new sensitive method for the quantitative analysis of Atenolol-Losartan potassium in a Tablet dosage form by using HPTLC". Sch. Acad. J. Pharm., 2(6), 464-467 (2013).

86. Deore PV, Shirkhedkar AA, Surana SJ. "Simultaneous TLC-densitometric analysis of atenolol and lercanidipine hydrochloride in tablets". Acta chromatographica, 2008, 20(3), 463-473.

87. Abdelwahab NS. "Determination of atenolol, chlorthalidone and their degradation products by TLC-densitometric and chemometric methods with application of model updating". Anal. Methods, 2010, 2, 1994-2001 .

88. Yilmaz B and Arslan S. “Determination of atenolol in human urine by gas chromatography-mass spectrometry method ”. J Chromatogr Sci., 2011,49(5), 365-369 .

89. Scales B and Copsey PB. “The gas chromatographic determination of atenolol in biological samples”. J. Pharm. Pharmac., 1975, 27, 430-433 .

90. Yilmaz B. “Determination of Atenolol in pharmaceutical preparations by gas chromatography with flame ionization and mass spectrometric detection”. Anal. Letter, 2010, 43(15), 2311-2317.

91. Kumar N, Verma N, Songh O, Joshi N and Singh KG. “Estimation of Atenolol by Reverse Phase High Performance Liquid Chromatography”. E-Journal of Chemistry. 2010, 7(3), 962-966.

92. Ceresole R, Moyano MA, Pizzorno MT and Segall A. “Validated Reversed-Phase HPLC Method for the Determination of Atenolol in the Presence of Its Major Degradation Product”. J. Liq. Chrom. Related Tech., 2006, 29(20), 3009-3019.

93. Gillilan RB and Mason WD. “Revised HPLC Determination of Atenolol in Plasma and Urine”. Anal. Lett., 1983, 16(12), 941-949 .

94. Weich A, De-Oliveira DC, De-Melo J, Goebel K and Rolim CMB. “Validation of UV Spectrophotometric and HPLC Methods for Quantitative Determination of Atenolol in Pharmaceutical Preparations”. Lat. Am. J. Pharm. 2007, 26 (5), 765-70 .

95. Yilmaz B, Arslan S and Asci A. “HPLC Method for Determination of Atenolol in Human Plasma and Application to a Pharmacokinetic Study in Turkey”. J. Chrom. Sci., 2012, 1, 1-6.

96. Belal F, Sharaf El-Din M, Aly F, Hefnawy M and El-Awady M. “Stability-indicating HPLC Method for the Determination of Atenolol in Pharmaceutical Preparations”. J Chromat Separation Techniq.,2013, 4(1), 164-170 .

97. Sharma A, Tailang M, Khare S and Shukla T. “RP-HPLC Determination of Atenolol in Its Pharmaceutical Dosage Forms”. Asian. J. Res. Chem., 2009, 2(4), 485-487.

98. Dong L and Huang J. “Determination of Atenolol in Human Plasma by Pseudo Reversed Phase Liquid Chromatography-Tandem Mass Spectrometry”. Chromatographia. 2006, 64(9), 583-586.

99. Bhaskara, BL, Anil-Kumar S and Anil-Kumar UR. “A facile and rapid HPLC method for the determination of atenolol in pharmaceutical formulations”. Asian J. Applied Sci., 2011,4 (3), 306-313.

100. Sultana N, Arayne MS, Iftikhar B and Nawaz M. “A new RP-HPLC method for monitoring of atenolol : Application to atenolol metal interaction studies”. J. Chem. Soc, Pak., 2008,30(1), 113-118.

101. Firdose S, Anusha VS, Bramhini RS, Madhavi S and Nalluri BN. “Analysis Of Atenolol In In-Vitro Transdermal Permeation Studies By RP-HPLC-PDA Method”. Indo American J. Pharm. Res., 2013, 3(9), 7573-7579 .

102. Hussein AA. “Determination of Atenolol in Human Plasma by New HPLC Method with Fluorescence Detection for Pharmacokinetics Studies”. Kerbala J. Pharm. Sci., 2014,7, 238-261 .

103. Eaga CM, Somagoni JM, Maddi SR, Reddy S and Yamsani MR. “New Chiral Reverse Phase HPLC Method For Determination Of Atenolol Enantiomers in Pharmaceutical Formulations”. Int. J. Pharm. Sci. Rev. Res., 2010,4(1), 22-26.

104. Spanakis M and Niopas I. “Determination of Atenolol in Human Plasma by HPLC with Fluorescence Detection: Validation and Application in a Pharmacokinetic Study”. J. Chrom. Sci., 2013, 5, 128-132 .

105. Sunitha P, Satyavathi K, Lavanya K and Anil Kumar A. “Method Development And Validation For The Estimation Of Atenolol In Tablet Dosage Form By Rp-HPLC Method”. Int. Res. J. Pharm., 2012, 3(11), 87-89 .

106. Miller RP. “A validated high-performance liquid chromatographic method for the determination of atenolol in whole blood”. J. Pharm. Biomed. Anal., 2015, 9(10-12), 849-853 .

107. Barman RK, Islam MA, Ahmed M, Ibne Wahed MI, Islam R, Khan A, Hossain MB and Rahman BM. “Simultaneous High-performance liquid chromatographic determination of atenolol and amlodipine in pharmaceutical-dosage form”. Pak J Pharm Sci., 2007, 20(4), 274-279.

108. Naikini P, Akula A, Ajitha A and Maheswara Rao. "VU. RP-HPLC Method Development And Validation For The Simultaneous Estimation Of Amlodipine And Atenolol In Bulk And Tablet Dosage Forms". Int J Pharm Pharm Sci., 2014,6(1), 390-394.

109. Akki S, Sujitha H and Swathi M. "Development and Validation of RP-HPLC Method for Simultaneous Estimation of Atenolol and Amlodipine in Bulk and Tablet Dosage Form". Int. J. Pharm., 2014, 4(1), 265-269 .

110. Ravisankar P, Chaitanya MK, Devadasu Ch, Babu PS and Rao GD. "Validated RP-HPLC Method for Simultaneous Separation and Estimation of Atenolol and Amlodipine in Combination Tablet Dosage Form". Int. J. Adv. Pharm. Sci., 2013, 4(5), 834-848 .

111. Ahsanul-Haque MD, Naznin A, Hamidul-Kabir ANM, Hossain K and Ashraful-Islam SM. "Development and Validation of RP-HPLC Method for the Simultaneous Estimation of Atenolol and Amlodipine in Tablet Dosage Form". Dhaka Univ. J. Pharm. Sci., 2010, 9(2), 131-138.

112. Ubale M, Husain S and Chaudhri V. "Stability Indicating RP-HPLC Method for Determination of Atenolol and Amlodipine Besylate in Tablets". J. Chem. Bio. Phys. Sci., 2013, 4(1), 63-69.

113. Farooqui M, Ahmed RZ, Zaheer Z and Sangshetti JN. "Development and Validation of RP-HPLC Method for Simultaneous Determination of Amlodipine Besylate and Atenolol in Tablet Dosage Form". J. Med. Chem. Drug Dis., 2015,1, 685-698 .

114. Kumaraswamy G, Ravindra N and Jyothsna B. "Development and Validation of a Reversed-Phase HPLC Method for Simultaneous Determination of Aspirin, Atenolol and Amlodipine in Capsules Dosage Forms". Asian J. Pharm. Ana., 2014, 4(3), 116-120.

115. Bhusari VK and Dhaneshwar SR. "Validated HPLC Method for Simultaneous Quantitation of Amlodipine Besylate, Atenolol and Aspirin in Bulk Drug and Formulation". J. Pharm. Biomed. Sci., 2012, 17(9), 1-6 .

116. Rajesh K, Ganesh T, Kavita B and Reddy GN. "Simultaneous Estimation of Atenolol and Losartan by HPLC". Int. J. Chem. Nat. Sci., 2013, 1(1), 41-44 .

117. Ashwini G, Lavanya R and Ramarao T. "Development and Validation of Analytical Method for the Simultaneous Estimation of Atenolol and Losartan by Using RP-HPLC Method". Int. J. Med. Nanotech., 2014, 1(2), 33-39 .

118. Sivakumar T, Venkatesan P, Manavalan R and Valliappan K. “Development of a HPLC method for the simultaneous determination of losartan potassium and atenolol in tablets”. Ind. J. Pharm. Sci., 2007, 69(1), 154-157 .

119. Tengli AR and Gurupadayya BM. “Method Development and Validation of Tablet Dosage form Containing Losartan, Atenolol and Hydrochlorthiazide Using Internal Standard by RP-HPLC”. J Chromat. Separation Techniq. 2013, 4(5), 1-5 .

120. Kavitha J and Muralidharan S. “Development and Validation of New Method for Atenolol, Hydrochlorothiazide and Losartan potassium by RP-HPLC: Its Application to Routine Quality Control Analysis”. Int. J. ChemTech Res., 2010,2(2), 880-884 .

121. Sharma R, Khanna S and Mishra GP. “RP-HPLC Method for Simultaneous Estimation of Atenolol, Hydrochlorothiazide and Losarton in Tablet Dosage form”. Chem Sci Trans., 2013, 2(1), S1-S6 .

122. Thomas AB, Chavan UB, Nanda RK, Kothapalli LP, Jagdale SN, Dighe SB and Deshpande AD. “Simultaneous RP-HPLC Analysis of Atenolol, Hydrochlorothiazide, and Losartan Potassium in a Tablet Formulation”. Acta Chromatographica, 2010, 22(2), 219-226.

123. Yadav SS and Rao JR. “Simultaneous Estimation of Losartan, Hydrochlorothiazide and Atenolol from Solid Dosage Form by RP-HPLC”. Int. J. Pharm. Pharmaceutical. Sci., 2014, 6(1), 283-288.

124. Bhatia NM, Gurav SB, Jadhav SD, and Bhatia MS. “RP-HPLC Method for Simultaneous Estimation of Atorvastatin Calcium, Losartan Potassium, Atenolol, and Aspirin from Tablet Dosage Form and Plasma”. J. Liq. Chrom. Related Tech., 2012, 35(3), 428-443 .

125. Sa'sa' SI, Jalal IM and Khalil. “Determination of Atenolol Combinations with Hydrochlorothiazide and Chlorthalidone in Tablet Formulations by Reverse-Phase HPLC”. J. Liq. Chromatogr., 1988, 11(8), 1673-1696 .

126. Zaveri M and Khandharb A. “Development And Validation Of A Rp-Hplc For The Simultaneous Estimation Of Atenolol And Hydrochlorothiazide In Pharmaceutical Dosage Forms”. Asi. J. Pharm. Res. Health Care, 2010,2(3), 248-252.

127. Elgawish MS, Mostafa SM and Elshanawane AA. “Simple and rapid HPLC method for simultaneous determination of atenolol and chlorthalidone in spiked human plasma”. Saudi Pharm J. 2011, 19(1), 43-49.

128. Kumar GS, Ramya V, Mondal S and Kumar SP. "Development and Validation of RP-HPLC Method for Simultaneous Estimation of Atenolol and Chlorthalidone from Pharmaceutical Formulation". Int. Res. J. Pharm., 2012, 3(10), 215-219.

129. El-Gindy AE, Sallam S and Abdel-Salam RA. "HPLC method for the simultaneous determination of atenolol and chlorthalidone in human breast milk". J. Sep. Sci. 2008, 31(4), 677-682.

130. Charde MS, Welankiwar AS and Chakole RD. "Development of validated RP-HPLC method for the simultaneous estimation of atenolol and chlorthalidone in combine tablet dosage form". Int. J. Adv. Sci., 2014, 3(1), 6-18 .

131. Giachetti C, Tenconi A, Canali S and Zanolo G. "Simultaneous determination of atenolol and chlorthalidone in plasma by high-performance liquid chromatography. Application to pharmacokinetic studies in man". J. Chromatogr-B Biomed. Sci. Appl. 1997, 698(1-2), 187-194 .

132. Pansode PS. "Development and Validation of Lercanidipine Hydrochloride and Atenolol by Using RP-HPLC and UV Spectroscopy". Ind. J. Pharm. Pharmacology, 2014,1(1), 37-41.

133. Kaila HO, Ambasana MA, Thakkar RS, Saravaia HT, and Shah AK. "Stability-indicating High Performance Liquid Chromatographic Assay for the Simultaneous Determination of Atenolol and Lercanidipine Hydrochloride in Tablets". Indian J Pharm Sci., 2011,73(4), 376-380 .

134. Jain DK, Patel P, Khan AS and Jain N. "Development and Validation of a RP-HPLC method for the simultaneous estimation of Atenolol and Lercanidipine hydrochloride in Pharmaceutical dosage forms". Int. J, Chemtech. Res., 2011, 3(2), 766-771 .

135. Gade BR, Bandhakavi SR and Ramanaiah G. "Method Development and Validation of Stability Indicating RP-HPLC Method for Simultaneous Estimation of Atenolol and Lercanidipine in Bulk and its Pharmaceutical Formulations". American J. Adv. Drug Delivery, 2014, 2(6), 752-766 .

136. S. Shirisha S, Chiranjeevi G, Prahalad R and Thirupathi R. "Method Development and Validation for the Simultaneous Estimation of Atenolol and Lercanidipine in a Pharmaceutical Formulation by RP-HPLC Method". Int. J. Res. Pahrm. Nanosci. 2013, 2(4), 402-416.

137. Vidyadhara S. Sasidhar RLC. Kumar BP, Ramarao NT and Sriharita N. “Method Development and Validation for Simultaneous Estimation of Atenolol and Nifedipine in Pharmaceutical Dosage Forms by RP-HPLC”. Oriental J. Chem., 2012, 28(4), 1691-1696 .

138. Bing LI, De-fu HU and Fei LIU. “HPLC Determination of Atenolol and Nifedipine in Compound Atenolol Tablets”. Chin. J. Pharm. Anal.,2004, 24(5), 485-486.

139. Asirvatham S and Kamble NS. “Reversed-Phase Liquid Chromatographic Method for Simultaneous Determination of Atenolol and Nifedipine in a Capsule Formulation”. World J. Pharm. Res., 3(9), 1466-1475 (2014).

140. Rani GT, Shankar DG, Kadgapathi P and Satyanarayana B. “A Validated RP-HPLC Method for Simultaneous Estimation of Atenolol and Indapamide in Pharmaceutical Formulations”. E-Journal Chem., 2011,8(3), 1238-1245.

141. Kher GJ, Ram VR, Dodiya BL and Joshi HS. “HPLC Method Development and Validation of Combined Dosage Form of atenolol and Indapamide in Tablets”. Int. J. Pharm. Tech., 2011, 3(3), 3277-3298 .

142. Baheti KG. Shah N and Shaikh S. “Ion-Pairing Reverse-Phase High Performance Liquid Chromatography Method for Simultaneous Estimation of Atenolol and Indapamide in Bulk and Combined Dosage Form”. Ind. J. Pharm. Sci. 2011, 74(3), 271-274 .

143. Vasant pp, Damuanna GP, Himmatrao BV and Pandit PS. “Development and validation of RP-HPLC method for simultaneous estimation of atenolol and indapamide in pharmaceutical dosage form”. Int. J. Res. Ayurveda Pharm., 2011,2(3), 918-923.

144. Harika B, Deepti K and Madhavi K, “RP-HPLC method development and validation for the simultaneous estimation of atenolol and indapamide in pharmaceutical tablet dosage form”. Int. J. Pharm. Anal. Res., 2014, 3(1), 109-117.