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Brief review on analysis of Prazosin Hydrochloride

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Abstract

Prazosin is one of the alphaone adrenoreceptor blocker used in hypertension, benign prostatic hyperplasia, prostate cancer etc. The alpha blockers are relatively inexpensive and exert their effects quickly and Prazosin is the most commonly used alpha blocker. This review highlights various analytical methods for the determination of Prazosin hydrochloride in different matrices. Analytical methods reported are classified into four categories viz; spectrophotometry, chromatography, pharmacopoeial and other methods. The methods were described in terms of sensitivity (LOD & LOQ), linear range, principle and its applicability. This review also briefly highlights pharmacology of prazosin. This review is helpful for the researchers and scientists studying Prazosin hydrochloride in its analytical and pharmacological aspect.

Keywords: Prazosin, Hypertension, Benign Prostatic Hyperplasia, Analytical methods, Spectrophotometry, Chromatography.

1. Introduction

Prazosin Hydrochloride [CAS number 19237-84-4], [4-(4-Amino-6,7-dimethoxy-2-quinazolinyl)-1-piperazinyl]-2-furanylmethanone, 1-(4-amino-6,7-dimethoxy-2-quinazolinyl)-4-(2-furanylcarbonyl) piperazine and 2-[4-(2-furoyl)piperazin-1-yl]-4-amino-6,7-dimethoxy quinazoline furazosin [1] a quinazoline derivative, is a peripheral vasodilator used in the treatment of arterial hypertension and congestive heart failure (CHF). Prazosin is extensively metabolised by the liver and has high first-pass metabolism and low oral bioavailability. In normal healthy volunteers, the time of peak concentration occurs between 1 and 3 hours after oral administration, with wide interindividual variations. The extent of oral absorption seems to be similar for different pharmaceutical forms and is not influenced by the presence of food in the digestive tract. Oral bioavailability of prazosin ranges from 43.5 to 69.3% (mean 56.9%). Prazosin is highly (92 to 97%) bound to human plasma proteins (albumin and alpha 1-acid glycoprotein) and the extent of binding is independent of the plasma concentration of the drug in the range of 20 to 150 ng/ml [2].

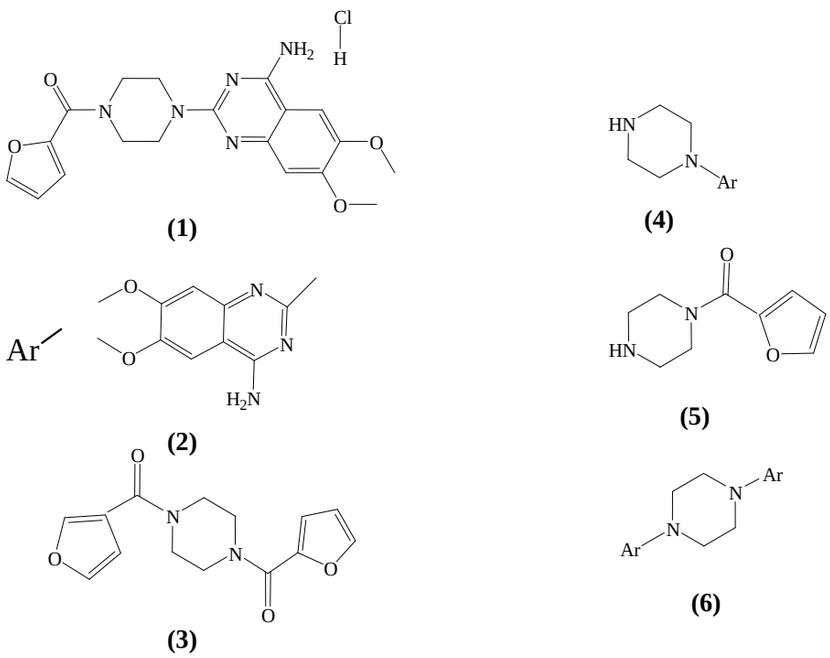

Figure 1: Structure of Prazosin Hydrochloride and impurities: (1) Prazosin Hydrochloride (2) Ar: 2-chloro-6,7-dimethoxyquinazolin-4-amine, (3) 1,4-bis(furan-2-ylcarbonyl)piperazine, (4) 6,7-dimethoxy-2-(piperazin-1-yl)quinazolin-4-amine, (5) 1-(furan-2-ylcarbonyl)piperazine, (6) 2,2′-(piperazin-1,4-diyl)bis(6,7-dimethoxyquinazolin-4-amine)

Selective α_1-blockers (Prazosin and doxazosin) causes vasodilation. They are also used for benign prostatic hyperplasia (relaxation of urinary tract smooth muscle), congestive heart failure and Raynaud's disease. All α-blockers should be titrated carefully as first-dose hypotension can be severe. They have additional favourable metabolic effects on lipid and glucose metabolism [3].

The quinazoline-based α_1-blockers have been shown to have antitumor efficacy against prostate cancer cells via their potency to induce apoptosis and anoikis via an α_1-adrenoceptor- independent mechanism [4]. Prazosin is a potential anticancer agent that induces apoptotic signaling cascades in a sequential manner [5].

Prazosin was the next selective (after Phenoxybenzamine) alpha-1-blocker used to manage benign prostatic

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hyperplasia (BPH), at which time it was already being used for treating hypertension. Prazosin must be given three times per day to be effective for BPH. The prostatic-specific subtype is alpha-a, an adrenergic receptor that constitutes 70% of all prostatic alpha-1 receptors. Since alpha-1 receptors are also present at various nonprostatic smooth muscles, they are not entirely uroselective. Blockade of these receptors causes few additional unwanted systemic side effects [6]. The first-dose effect (profound postural hypotension and reflex tachycardia) is a well-recognized complication of the first dose of prazosin and related agents. This phenomenon is dose-related and can usually be avoided by using a low initial dosage taken at bedtime [7]. It has been suggested that the high affinity for the α_1-adrenoceptor is due to 2,4-diamino-6,7-dimethoxyquinazolinium nucleus [8].

In recent review article, Prazosin was suggested as well-tolerated generically available medication that has a small but positive evidence base for the treatment of posttraumatic stress disorder associated nightmares [9].

Prazosin is synthesized from 2-amino-4,5-dimethoxybenzoic acid, which upon reaction with sodium cyanate undergoes heterocyclation into 2,4-dihydroxy-6,7-dimethoxyquinazoline. Substituting hydroxyl groups of this compound with chlorine atoms by reaction with thionyl chloride, or a mixture of phosphorous oxychloride with phosphorous pentachloride gives 2,4-dichloro-6,7-dimethoxyquinazoline. Upon subsequent reaction with ammonia, the chlorine atom at C4 of the pyrimidine ring is replaced with an amino group, which leads to the formation of 4-amino-2-chloro-6,7-dimethoxyquinazoline. Introducing this into a reaction with 1-(2-furoyl)piperazine gives prazosin [10].

Prazosin are usually prepared as solid-state forms of prazosin hydrochloride, five crystalline polymorphic modifications of which are claimed, namely, forms α, β, γ, δ, and ε [11]. The alpha form is reproducibly manufactured and has valuable advantages over the other polymorphic forms due to ease of handling, storage, stability and formulating. This alpha form was used in clinical trials to khow efficacy of the drug. Prazosin hydrochloride is a white to off-white, crystalline, odorless powder [12]. Its chemical formula is $C_{19}H_{21}N_5O_4$, molecular weight is 383.41 and melting point is 278-280 ℃ [1].

2. Analytical methods

2.1 Spectrophotometry methods

Spectrophotometry methods are among the oldest methods of analytical chemistry. Spectrophotometric methods of identification and determination of substances are based on the existence of relationship between the position and the intensity of absorption bands of electromagnetic radiations, on the one hand, and the molecular structure on the other [13].

In this paper, twenty one different spectrophotometry methods are described. The summary of these methods are presented under Table 1. Methods available in the current literature are described in terms of principle, linear range, limit of detection (LOD), limit of quantitation (LOQ) and applicability. It is clear from Table 1 that spectrofluorimetry methods are more sensitive methods as compared to direct and simple spectrophotometry methods. Flow injection analysis by using spectrofluorimetry has additional advantage over other methods of determining many samples in a short period of time.

Table 1: Summary of various spectrophotometry methods for Prazosin HCl determination

Principle	Wavelength	Linear Range	LOD	LOQ	Application	Ref.
Ion pair formation with bromocresol purple	410 nm	2-10 µg/ml	-	-	Tablets	14
Reaction with mercurochrome	542 nm	5-10 µg/ml	-	-	Tablets	
Fluoremetry: with mercurochrome in aqueous neutral buffered solution.	λ_{ex} = 295, λ_{em} = 530	0.05-0.2µg/ml	-	-	Tablets	
Dissolved in Britton–Robinson buffer at pH 1.8.	317, 329 and 341 nm.	1.0×10^{-7} and 5.0×10^{-5} M	0.9×10^{-7} M	1×10^{-7} M	Tablets	15
Coloured derivative between the drug and 1,2-naphthoquinone-4- sulphonic acid sodium salt (NQS). The reaction proceeds quantitatively at pH 4.5 and 70°C for 40 min and extracted with chloroform: n-butanol (3:1).	400 nm	6-30 µg /mL	-	40 µg/ml	Tablets	16
Second-derivative in 0.2 N methanolic hydrochloric acid	Positive peak at 356 nm, negative peak at 346 nm	l-20 µg /mL	-	-	Polythiazide/prazosin mixtures in tablets	17
Reaction with 2,3,-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) in acetonitrile.	460 nm	5–60 µg /mL	-	-	Tablets	18
Reaction with bromophenol blue (BPB) in $CHCl_3$	410 nm	2–18 µg /mL	-	-	Tablets	
Treating with excess *N*-bromosuccinimide (NBS) and determining the unconsumed NBS with *p*-,*N*-methyl aminoophenol sulphate (meto])-sulphanilamide (SA) reagent	520 nm	1- 10.0 µg /mL			Tablets	19
Treating with 3-methyl-2-benzothiazolinone hydrazone hydrochloride (MBTH) in the presence of ceric ammonium sulphate (CAS)	620 nm	2.5-25 µg /mL			Tablets	
Treating with acidic dyes such as orange-II (O-11) and alizarin violet 3B	490 and 570 nm	1- 17.5 and 2.5-30.0 µg /mL resp.			Tablets	
Dilutions prepared in methanol	246nm	5-80 µg /mL	1 µg /mL	2.2 µg /mL	API and tablet	20
Diazotization with sodium nitrite and hydrochloric acid and reaction with *β* naphthol	480 nm	40-225 µg /mL	1.23 µg /mL	4.1 µg /mL	Tablets	21
Complex with rose Bengal (RB)	572 nm	2.5 - 25 µg /mL	0.89 µg /mL	0.5-8 µg /mL	Tablets	22
Fluorimetry: Dilutions prepared with Clark and Lubs buffer solution pH 5.5	λ_{em} 388 nm using λ_{ex} 340 nm.	0.05– 1.4 µg /mL	0.019 µg /mL	0.182 µg /mL	Tablets	
Fluorimetry: Dilutions prepared with Clark and Lubs buffer solution pH 5.5. The difference in the fluorescence intensity (ΔF) was plotted vs. the final concentration of the drug (µg/mL) to get the calibration curve	577 nm after excitation at 483 nm.	0.5 –8 µg /mL	0.006 µg /mL	0.55 µg /mL	Tablets	
Drug extracted from blood by ethyl acetate after alkalinization of the plasma with NaOH and then extracted back from the ethyl acetate into 0.1 N HC1 and estimated by spectrofluorimetry.	λ_{eex} 330 nm, λ_{eem} 390 nm	-	-	-	plasma prazosin levels	23

Fluorimetry: Bovine serum albumin (BSA) and Tris-HCl buffer (pH 7.4) used to prepare dilution	λ_{ex} 280 nm with λ_{em} recorded between 300–520nm.	0 to 1.58×10^{-7} mol L^{-1}	-	-	Interaction studies with BSA	24
Spectrofluorimetry	λ_{ex} = 244 nm ($\lambda_{em} \geq$ 389 nm)	0.02–2.43 mg l^{-1}	0.007 mg l^{-1}	-	Tablets	25
Spectrofluorimetry, Flow injection analysis enhancement of the native fluorescence in the presence of sodium dodecyl sulfate (SDS)	λ_{ex} = 250 and λ_{em} = 390	20–400 ng ml^{-1}	326.5 ng ml^{-1}	13.8 ng ml^{-1}	Pure and Tablets	26
Reaction with 1,2-naphthoquinone-4-sulfonic acid sodium salt (NQS). The reaction proceeds quantitatively at pH = 4.5 and 70 °C in 40 min. After the extraction of the derivative with chloroform: *n*-butanol (3:1).	400 nm	40-200 µg/mL	-	-	Tablets	27

2.2 Chromatography methods

High-performance liquid chromatography (HPLC) was introduced to pharmaceutical analysis not long after its discovery in the late 1960s. By now it has developed into a generally applicable analytical method providing rapid and versatile separation possibilities that meet the increasing requirements for purity testing of bulk pharmaceuticals and pharmaceutical products [28].

The summary of chromatography methods for the determination of Prazosin is provided under Table 2. Different official methods are described in Table 3. HPLC coupled with different types of detectors such as UV, MS, RLS, Fluorosence and Electrochemical detectors were used for analysis of prazosin in different matrices.

The modern HPTLC technique, combined with automated sample application and densitometric scanning, is sensitive and completely reliable, suitable for use in qualitative and quantitative analysis. HPTLC is a valuable tool for reliable identification because it can provide chromatographic fingerprints that can be visualized and stored as electronic images [28]. Three different methods are also described under Table 2.

Table 2: Summary of different chromatography methods for the determination of Prazosin HCl in different matrices

Method	Chromatographic condition	Linear range	LOD	LOQ	Application	Ref.
HPLC-F	*µ*Bondapak CN particle size 10 µm, 30 cm × 3-9 mm column. Mobile phase: acetonitrile-water:acetic acid (50:47:3) flow-rate 2.2 ml/min, λ_{ex} = 248 nm, λ_{em} 389.	1-15 ng/ml	-	-	Human Plasma	29
HPLC-Electrochemical Detection	ODS Hypersil HPLC column (150 x 4.6 mm). Mobile phase consisting of 0.05 M $NazHPO_4$-acetonitrile (60:40), pH 8.4. Flow rate 1.0 ml/min. Potential of channel 2 was kept at + 0.00 mV and the guard cell had a potential of + 300 mV.	5 ng/ml to 250 ng/ml	2.5 ng/ml	-	Serum samples	30
HPLC-F	Column: 10mm × 25cm, Partisil 10-SCX cation-exchanger. Mobile phase: 14.7% acetonitrile, 83.4% deionized water, 0.5% diethylamine and 1.3% orthophosphoric acid. The flow rate was 2 ml/min. λex = 246 nm, λem = 370 nm.	Prazosin: 1-60 ng/ml, metabolite 1-120 ng/ml	0.1-0.2 ng/ml for both	-	prazosin and its metabolite in serum, urine and saliva	31
HPLC-F	Varian Micro-Pak MCH-10 (monomeric C_{18} bonded) reversed phase column (25 cm x 2.0 mm I.D.). One pump contained a 0.01 M pentane sodium sulfate in water adjusted to pH 3.4 with glacial acetic acid (solvent A). The other pump contained the same concentrations of pentane sodium sulfate and acetic acid as solvent A in methanol (solvent B). An isocratic mixture of 49 % solvent B and 51% solvent A was used with daily minor adjustments in solvent composition (1-2 %) to maintain optimum baseline separation of prazosin and the internal standard. The flow-rate = 40 ml/h. λ_{em} = 390 nm, λ_{ex} = 246 nm	0.2 ng to 50 ng/ml	0.2 ng/ml in whole blood and 0.5 ng/ml in plasma	-	Pharmacokinetic studies	32
HPLC-F	Column: *µ*Bondapak C_{18} reversed-phase column (30 cm × 3.9 mm ID, 10 µm particle size), λ_{ex} = 340 nm, λ_{em} = 384 nm	l-164 ng/ml.	0.1 ng/ml in plasma, urine and whole blood.	-	Pharmacokinetic studies	33
HPLC-F	ODS column (25 cm x 4.6 mm i.d.) of 5µm particle size (Finepak SIL C18-5; Jasco). The ODS guard column had dimensions 5cmx4.6 mm i.d. (Finepak SIL C18-5). Mobile phase: methanol-water- PIC B-5 (456:24:1,v/v). Flow rate of 1.0 ml min. λ_{ex} 340 and λ_{em} 405 nm.	0.1 to 30 pmol/ml	0.2 pmol/ml	0.4 pmol $m1^{-1}$	Plasma determination	34
HPLC-UV	Nuclosil 100-10, C-18 column (250×4.6mm, 10 micron) using methanol:water:acetonitrile (60:45:5 v/v, pH 3.83) as the mobile phase at a flow rate of 1mL min-1 effluents λ = 240 nm.	2.5 to 50 µg ml^{-1}	0.0315 µg ml^{-1} (Bulk) 0.0174 (Serum)	0.0953 µg ml^{-1} (Bulk) 0.0527 (Serum)	Human Serum	35
HPLC-UV	Column: Nuclosil, C_{18} (250×4.6 mm, 10 µm), mobile phase 75:25 v/v acetonitrile:water having pH 3.20 adjusted with glacial acetic acid. Flow rate of 1.5 ml min^{-1} using gradient elution through prepacked. λ = 250 nm.	1.0-10 µg ml^{-1}	3.3 ng ml^{-1} (Bulk) 9.8 ng ml^{-1} (Serum)	2.2 ng ml^{-1} (Bulk) and 6.1 ng ml (Serum)	Pharmaceutical formulation, human serum, Drug–metal interaction studies	36
(LC‑ESI‑TOF/MS	Thermo Scientific C_{18} (250 mm × 2.1 mm, i.d.: 5 µm) column. Dilutions of this mixture were prepared in 0.1% formic acid in (Methanol-water (10:90, v/v)). Mobile phase: (A) 0.1% FA in water and (B) Acetonitrile-Methanol (3:1, v/v) at 0.3 ml min^{-1}. The elution started at 5% B and was then linearly increased to 60% B over 3 min, further increased to 97% B over 3 min and then kept isocratic for 5 min.	1.5-150 μgl^{-1}	-	33 ng/ml	Analysis in Tangkas River-Malaysia	37
HPLC-F	Cosmosil column, $5C_{18}$-MS II (150 × 4.6 mm, 5 µm i.d.). Security guard cartridge (C18) (4 mm × 3 mm, i.d.) was	0.5-20 ng ml^{-1}	0.16-0.71 ng ml^{-1}	0.53-2.14 ng ml^{-1}	Rabbit plasma	38

	from Phenomenex. Mobile phase containing acetonitrile and 20 mM phosphate buffer (pH 6.3) (60:40, v/v) containing 25 mM SDS (Sodium dodecyl sulfate), λ_{em} = 389 nm, λ_{ex} =250 nm.					
HPLC-UV	Column: Nucleosil C_{18} (250mm x 4.6 mm, 10µm), mobile phase: methanol: acetonitrile (85:15 v/v pH 3.0 adjusted by phosphoric acid 85 %). Flow rate was 1.0 mL min^{-1}. λ = 240 nm.	2.5-1000 µg ml^{-1}	4.0 ng mL^{-1}	12.1 ng mL^{-1}	Bulk, formulations and human serum	39
HPLC-RLS	Gemini 5µ C18 reversed phase column (250 mm × 4.6 mm; 4 µm). The mobile phase consisted of methanol (B) and ammonium acetate–formic acid buffer solution (25 mM; pH = 3.0) (D). The gradient elution performed was: 0–9 min hold at 18% B, 82% D; 9–20 min, turn from initial conditions to 30% B, 70% D. The RLS signal was monitored at $\lambda_{ex} = \lambda_{em}$ = 354 nm.	0.075–3.0 µg l^{-1}	0.065 µg l^{-1}	-	Separation of Prazosin, doxazosin and terazosin	40
HPTLC	Silica gel G 60 F254 plates (10 cm w×10 cm h) with 250 mm thickness. Mobile phase composed of acetonitrile and phosphate buffer (0.02 mole=L) adjusted to pH 3.0 (30:70, v=v). λ = 332 nm	15–75 ng/band	6.91 ng/band	13.81 ng/band	Dosage forms and in human plasma	41
HPLC-UV	Mobile phase acetonitrile: methanol: water: (10:55:35 v/v, pH 2.65±0.02), on a Nuclosil 100-10 C-18 (250×4.6mm), 10 µ column. λ = 240 nm. Flow rate 1 ml^{-1}	5–100 µg ml^{-1}	0.0328 µg ml^{-1}	0.0994 µg ml^{-1}	Bulk and dosage form	42
HPLC-F	Column: A Purospher® RP-18 (125mm × 4mm i.d., 5 µm). Mobile phase: 70.0 ml of methanol, 1.0 ml of acetic acid 99.8%, 0.02 ml of triethylamine, and 30.0 ml of distilled water, pH 3.83. λ_{ex} = 244 nm ($\lambda_{em} \geq$ 389 nm)	0.02–2.43 mg l−1	0.007 mg l^{-1}	-	dissolution studies and quality control	43
HPLC-F	μBondapak C-18 (3.9×300mm), 10 µ. Mobile phase: Water:ACN: Triethylamine (75:25:0.1). Flow rate 1.5 ml/min. λ_{ex} = 250 nm, λ_{em} = 370 nm.	0.5-50 ng/ml	0.1 ng/ml	0.5 ng/ml	Pharmacokinetics	44
HPLC-UV	Spherisorb RP-C-18 column (250mm×4.6mm id, 5 µm) using water/acetonitrile/methanol/glacial acetic acid/diethylamine (25:35:40:1:0.017). flow rate 1 ml min^{-1}. λ = 254 nm	50–500 µgml^{-1}	-	-	Stability Indicating method	45
HPLC-UV	Kromasil C18 column (250 × 4.6 mm, 5.0 µm). Mobile phase A: ACN–diethylamine (0.05 ml), B: methanol, and C: 10 mM Ammonium acetate	2–500 µg/ml	0.033 µg/ml	0.102 µg/ml	Stability Indicating method	46
HPLC-UV	Kromacil C18 column. Methanol mobile phase. Flow rate 1.1 ml/min	10-60 µg/ml	0.511 µg/ml	1.549 µg/ml	In tablets	47
HPLC-UV	Waters Spherisorb ODS2 column (250 mm× 4.6 mm i.d, 5 µm) acetonitrile:water:acetic acid:diethyl amine (65:35:1:0.2). Flow rate 1 ml min^{-1}. λ = 254 nm	-	-	-	Stress degradation studies	48
HPLC-UV	IBM Cyano, 5µ spherical particles, 4.5 mm (id) × 250 mm, 650 ml. Mobile phase: 0.05M monobasic sodiun phosphate solution and 350 ml acetonitrile pH was adjusted to 3.0 with phosphoric acid. λ = 268 m for PRZ and 254 for impurities.	50-1250 ng/ml	0.6 ng/ml	-	Stability indicating assay for each drug substance and its impurities. (Prazosin and polythiazide combination)	49
HPLC-F	Stainless-steel tube (250 × 5 mm I.D.) packed with Spherisorb S5W silica (5 µm). Mobile phase 10 mM ammonium perchlorate in methanol adjusted to pH 6.7 by the addition of 1 ml/l methanolic sodium hydroxide (0.1 M), flow-rate of 2.0 ml/min. λ_{ex} 250 nm, λ_{em} 370--700 nm.	2-300 µg/L	1 µg/L	-	Prazosin and terazosin in biological fluids	50
HPTLC	Silica gel aluminum plates 60F254 (20 × 15 cm, 200 µm thickness) mobile phase composed of methylene chloride:n-hexane:methanol (8.8:0.3:0.9, by volume). λ = 254 nm	200–2000 ng/spot	4.62 ng/spot	14.00 ng/spot	Formulations	51
HPLC-UV	Cyano column (150 x 4.6 mm), mobile phase: acetonitrile: methanol: water (45:5:50% v/v) and 3 mM heptane sulphonic acid sodium. λ = 230 nm. Flow rate was 1-5 ml/min.	0.5-7 µg/ml	0.05 µg/ml	-	Formulations	52
HPTLC	60F–254 plates, [20 × 10 cm with 250 µm thickness Mobile phase: chloroform and methanol in the ratio 9.5:0.5.	0.8-1.2 mg/ml	0.017 mg/ml	0.053 mg/ml	Separation with other alpha blockers	53
HPLC-UV	Kromasil C18 column (250 × 4.6 mm, 5.0 µm), a UV detector at 230 nm and a elution was performed under a gradient mobile phase composed of (A) ACN diethylamine (0.05 mL), (B) methanol, (C) 10 mM ammonium acetate and (D) Water. Flow rate: 1 ml/min	4-16 µg/ml	0.1 µg/ml	0.33 µg/ml		

Table 3: Summary of different chromatography methods

Principle	Dosage form	Method	Limit	Ref
HPLC-UV	Prazosin tablet	Chromatography condition: Column (200×4 mm, 5µm), Zorbax Sil, Mobile phase: (0.01% diethylamine in glacial acetic acid, water and methanol in 2:2:96 ratio. Dilutions prepared in glacial acetic acid, water and methanol in 2:2:96 ratio. Flow rate 1 ml/min, λ = 254 nm.	90-110 % of stated amount	54
HPLC-UV	Prazosin tablet	Chromatography condition: Column (200×4 mm, 5µm), Mobile phase: (0.01% diethylamine in glacial acetic acid, water and methanol in 2:2:96 ratio. Dilutions prepared in glacial acetic acid, water and methanol in 2:2:96 ratio. Flow rate 1 ml/min, λ = 254 nm.	Not less than 98.5% and not more than 101.0 %	55
Potentiometry	Prazosin HCl	0.35 gm in 20 ml formic acid and 30 ml acetic anhydride. Titrate with 0.1 M perchloric acid.	Not less than 90.0% and not more than 110.0%	
HPLC-UV	Prazosin HCl	Chromatography condition: Column (250×4.6 mm, 5µm), Mobile phase: methanol, water, acetic acid and diethylamine (3500: 1500: 50:1). Flow rate is adjusted to RT 8 min, λ = 254 nm.	Not less than 97.0% and not more than 103.0%	56
HPLC-UV	Prazosin HCl	Chromatography condition: 4.6-mm × 25-cm column contains packing L3. Mobile phase: mixture of 700 ml of methanol, 300 ml of water, 10 ml of glacial acetic acid and diethylamine 0.2 ml. Dilutions prepared in methanol water mixture in ratio (7:3). Flow rate adjusted to RT between 6 and 10 minutes, λ = 254 nm.	Not less than 97.0 % and not more than 103.0 %	57
HPLC-UV	Prazosin HCl capsules	Mobile phase, Chromatographic system, and Procedure are sme as Prazosin HCl. Dilutions are prepared in Acid–methanol solution (300 ml water+0.85 ml HCl and diluted to 1000 ml with methanol).	Not less than 90.0 % and not more than 110.0 % of the labeled amount	

2.3 Other methods

Modern electrochemical methods are now sensitive, selective, rapid and easy techniques applicable to analysis in the pharmaceu-tical fields, and indeed in most areas of analytical chemistry. They are probably the most versatile of all trace pharmaceutically active compound analysis [58,59]. Some methods based on electroanalytical techniques are also available including potentiometry, amperometry, voltametry, capillary electrophoresis and electrochemical sensors. All of these reported methods are described in Table 4.

Table 4: Summary of some electroanalytical methods reported in literature

Principle	Method	Linear range	LOD	LOQ	Application	Ref
Potentiometric	Plastic membrane electrode based on incorporation of an ion pair complex of phosphotungstate (PT) anion with prazosinium cation in a poly (vinylchloride) (PVC) matrix plasticized with dioctylphthalate (DOP)	2.7×10^{-6} to10^{-2} M	2×10^{-6} to 1×10^{-5} mol dm^{-3}.	-	Solution and tablets	60
Potentiometric PVC-membrane sensor	Electrode made up of liquid plasticized PVC and was based on a water-insoluble Prazosin–tetraphenyl borate ion-pair complex as an ion-exchanger.	1×10^{-5} and 1×10^{-2} mol L^{-1}	6.3×10^{-6} mol L^{-1}	-	Tablets	61
Flow injection analy sis with multiple-pulse amperometric (FIA-MPA) detection	Boron-doped diamond film electrode.	2 to 200 µmol L^{-1}	0.5 µmol L^{-1}	-	Tablets	62
Capillary electrophoresis	Capillaries (50 and 75 µm I.D., 200 pm O.D., 64 cm long with 48 cm effective length) UV absorbance detector set at 220 nm.	0.5-30 µg/ml	-	-	human urine	63
Capillary electrophoresis	50 cm×75 µm i.d. capillary using a buffer containing 20% acetonitrile, 60 mM ammonium acetate, and 1.0% glacial acetic in methanol medium, with applied voltage and capillary temperature of 23 kV and 25 °C, respectively. λ = 220 nm.	5.0–250 µg mL^{-1}	0.5 µg mL^{-1}	-	Tablets	64
Differential pulse voltammetry (DPV)	Three-electrode system was used: a platinum counter, an Ag:AgCl reference and a nafion modified carbon paste electrode (NMCPE) as working electrode.	4.0×10^{-11} to 4.0×10^{-8} M	3.1×10^{-11} M	-	Urine and tablets	15
Electrochemical sensor based on in situ modification of graphite electrode via graphene nanosheets (GNs)	Adsorptive stripping differential pulse voltammetry (Ads-DPV)	0.09–100 mM	0.02 mM	-	In urine samples and tablets	65

3. Conclusion

Hypertension is one of the most serious diseases of the XXI century concerning about 20 to 30% of the world population of adults [66]. Prazosin is largely free of toxic or major symptomatic side effects, with the exception of postural hypotension and syncope after first doses or large dose increments [67]. This review highlights the various analytical methods for the determination of prazosin in different matrices. The spectrophotometry, chromatography, pharmacopoeial and electroanalytical methods were presented in a systematic way in Table 1, 2, 3 and 4 respectively. This review is helpful for the scientists engaged in the study of Prazosin.

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