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Captopril and Hydrochlorothiazide: Insights on Pharmacology and Analytical Chemistry Profile

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ABSTRACT

Many categories of drugs are used today for hypertension such as captopril which belongs to ACE inhibitors family and hydrochlorothiazide which consider a diuretic drug.In this literature review, we will focus on their pharmacological effect as well as most of the recent reported analytical methods that have been established for their determination in their pure form, combination form with other medications, combined form with its metabolites, and in biological materials.

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Introduction

One of the most common diseases in the world is Hypertension, which is usually defined as persistent blood pressure (BP) of 140/90 mm Hg in the medical office, and it is one of the leading causes of premature morbidity and mortality in the United States [1,2]. Hypertension has no recognized cause and raises the risk of brain, cardiac, and renal problems. In developed countries, the chance of getting hypertensive (blood pressure >140/90 mm Hg) during one's lifespan is greater than 90%. Other cardiovascular risk factors such as age, obesity, insulin resistance, diabetes, and hyperlipidaemia frequently coexist with essential hypertension [3]. Many categories of drugs are being used to control hypertension as a diuretic, calcium channel blocker (CCB), angiotensin-converting enzyme (ACE) inhibitor, beta-blocker, and angiotensin receptor blocker (ARB). Moreover, even though diuretics were first used to treat hypertension nearly five decades ago, they are still an important therapy option today. Despite the fact that their popularity as preferred antihypertensive medications have waned, diuretics are still routinely used to treat hypertension, either alone or in combination with other types of drugs [4]. Thiazide diuretics as hydrochlorothiazide are the most commonly prescribed diuretics for hypertension, but other classes of diuretics may be useful in alternative circumstances. Although diuretics are no longer considered the preferred agent for the treatment of hypertension in adults and children, they remain acceptable first-line options [5]. In addition, ACE inhibitors, like Captopril, a drug that has been widely used to treat hypertension and congestive heart failure in individuals, which inhibit ACE activity and thereby reduce the synthesis of angiotensin II, are also used. Furthermore, ACE inhibitors limit the breakdown of bradykinin, enhancing its vasodilatory and other effects [6,7].

Pharmacology

Captopril (CAP) (figure 1), is an (ACE) inhibitor, and it has been shown in animal and human trials to reduce left ventricular remodeling (structural enlargement and alterations) following myocardial infarction, which can lead to left ventricular dysfunction and an increased risk of death. In several animal studies, ventricular remodeling(structural changes such as infarct expansion and thinning caused by stretching of the infarct zone and rearrangement of myocytes) was reduced after myocardial infarction, and survival in the rat model of myocardial infarction was significantly improved.

These findings have now been verified in human trials and are thought to be the result of CAP's balanced reduction in preload and afterload, other processes such as a reduction in coronary blood flow, increase prostaglandin synthesis, limit catecholamine release, and potentiation of bradykinin action [6, 8, 9]. CAP lowers plasma angiotensin II and raises angiotensin I concentrations, and this leads to increasedplasma renin activity or renin concentration, and decreased aldosterone concentration or urinary aldosterone excretion, respectively [10]. CAP has an oral bioavailability of around 60% in healthy fasting volunteers, and co-administration of food or antacids lowers CAP bioavailability by 25 to 50%. The peak plasma CAP concentration at 1 hour after delivery [6].

Hydrochlorothiazide (HCT) (figure 1)is an anti-hypertensive diuretic drug, it does its action via the prevention of sodium reabsorption as it blocks the membrane [11, 12]. Stimulation of the renin-angiotensin-aldosterone (RAAS) and sympathetic nerve systems are results of the decrease in cardiac output caused by thiazide-associated volume depletion, leading to progressive salt and NCCT (the electroneutral sodium-chloride cotransporter) which is founded on the distal convoluted tubule's apical water retention. The compensatory salt and water reabsorption brings

the ECF volume to baseline after 4–6 weeks. Surprisingly, thiazide's antihypertensive impact persists despite normalization of ECF volume due to a decrease in peripheral vascular resistance [13, 14]. The factors involved for vasodilation and long-term blood pressure reduction are unclear, but they appear to involve both a direct and indirect action on the vascular endothelium and/or muscular [15]. It has a lower duration of action and is less potent than ACE inhibitors [16, 17]. Moreover, hydrochlorothiazide Increases hydrogen and potassium ion secretion and calcium reabsorption as it increases the expression of a sodium-calcium exchange channel [18]. Thiazide diuretics can be given once daily or every other day in some cases. The initial dose of hydrochlorothiazide can range from 6.25 to 12.5 mg per day, with some people later requiring doses of up to 25 to 50 mg per day. Thiazides lose efficacy when excessive salt is consumed, in patients with renal failure, and in patients using nonsteroidal anti-inflammatory medications [19].

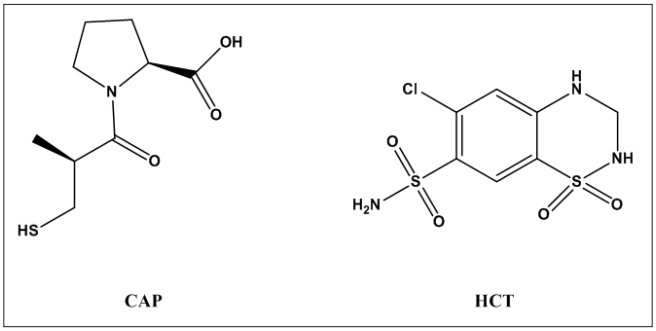

Figure 1: Chemical structures of captopril (CAP) and hydrochlorothiazide (HCT)

We have reported before review articles for many analytical techniques that have been used for the determination of important drugs in different forms [20-49]. As such, to continue our strategy of reviewing the analytical methods, in this review article, CAP and HCTwhich are usually prescribed as a combined dosage form have been studied in respect of pharmacology, mode of action and most reported analytical methods that have been developed for determination of both drugs in different matrices.

Analytical Methods

1. Capillary electrophoresis methods:

Drugs	Matrix	Capillary	Buffer (base electrolyte)	Detector	Linearity range	LOD	Ref
CAP, HCT and their impurities	Tablets	Fused-silica capillary (50 µm inner diameter, 375 µm outer diameter, total length 33.0 cm)	100 mM borate buffer pH 8.55, 64 mM sodium cholate, 6.1 %v/v n-butanol, 12 mM γ-cyclodextrin; voltage, 27 kV; temperature, 21°C	UV at 220 nm	CAP (2.40-4.80 mg/mL) HCT (1.20-2.40 mg/mL)	-----	[50]
CAP & HCT	Human serum albumin	Uncoated fused silica capillary (35 cm × 50 m ID with 26.5 cm effective length)	67 mM phosphate buffer, pH 7.4, I = 0.17, 37 ◦C	UV at 210 nm	CAP (5-100 µg/mL)	-----	[51]
CAP	Human urine and pharmaceutical preparations	Fused-silica capillaries with a total length of 57 cm, a detection length of 50 cm, and an id of 75 mm were employed.	20 mM phosphate buffer adjusted to pH 12.0	LIFD at 488 nm	3.5–6000 ng/mL	0.5 ng/mL	[52]
CAP	Tablets	Fused uncoated silica capillary of 67.5cm total and 57.5 cm effective length and of small (50 µm) internal diameter (ID) and an outer diameter (o.d.) of 360 µm .	20 mM phosphate buffer adjusted to pH 7.0	UV at 214 nm	5-70 µg/mL	1.5 µg/mL	[53]
CAP and its degradation products	Tablets	Fused-silica capillary 60 cm in total length (52.5 cm to the detector) and 75 mm internal diameter (ID).	0.025 mM cetyltrimethylammonium bromide (CTAB) added to a sodium phosphate buffer (pH 5.5; 100 mM)	UV at 214 nm	10–80 mg/mL (purity control) & 80–400 mg/mL (quantitative determination)	0.15%	[54]
CAP and Indapamide	Tablets and Human Plasma	50.2 cm long × 50 µm ID fused-silica capillary	100 mM borate at pH 9.0	UV at 220 nm	1–100 mg/L	0.075 mg/L	[55]
CAP, lisinopril, perindoprilat, quinaprilat and benazeprilat	-----	Uncoated fused-silica capillaries of 31.2 cm (21 cm from the injection side to the detector)375 mm ID	150 mM HEPES (2-[4-(2-hydroxyethyl)-1-piperazine] ethane sulfonic acid) adjusted with 1 M NaOH to pH 8.0 at 37◦C	UV at 230 nm	-----	-----	[56]

HCT and Telmisartan	Pharmaceutical preparations	Uncoated fused-silica capillary of 38 cm length (30 cm effective length) x 50 µm ID	25 mM phosphate buffer at pH 2.50 (CZE method)	UV at 230 nm	0.010-0.500 mg/mL	0.008 mg/mL	[57]
HCT and Telmisartan	Pharmaceutical preparations	Uncoated fused-silica capillary of 38 cm length (30 cm effective length) x 50 µm ID	50 mM borate buffer at pH 9.50 containing 25 mM sodium dodecyl sulfate as surfactant (MEKC method)	UV at 230 nm	0.010-0.500 mg/m L	0.062 mg/mL	[57]
HCT and Carvedilol	Tablets	Fused silica capillary (55 cm×75 µm id)	Phosphate buffer (12.5 mM, pH 7.4)–methanol (95+5, v/v)	UV at 226 nm	0.2–150 µg/mL	0.07 µg/mL	[58]
HCT and Metoprolol	Tablets	50.2-cm long × 50 µmIDfused-silica capillary	50 mmol/L phosphate at pH 9.5	UV at 214 nm	2.5–250 µg/mL	0 0.01 µg/mL	[59]
HCT, chlorothiazide, salamide, and Zofenopril	Tablets	Uncoated fused-silica capillary (50 µm ID × 48.5 cm and 40 cm effective length)	Sodium borate (pH 9.15; 10 mM)	UV at 225.0 nm	10.0–100.0 µg/mL	2.78 µg/mL	[60]
HCT, Valsartan and Amlodipine besylate	Tablets	Fused-silica capillary of 57.0-cm-long (50.0-cm effective length) and 75.6m ID	40 mM phosphate buffer at pH 7.5	UV at 230 nm	2-20 µg/mL	0.65 µg/mL	[61]
HCT, Benazepril and Amlodipine besylate	Tablets	Fused silica capillary (78.5 cm total length, 70 cm effective length, and 75 µm ID)	40 mM phosphate buffer at pH 7.5	UV at 225 nm	10–80 µg/mL	1.224 µg/mL	[62]
HCT, enalapril, lisinopril, quinapril, fosinopril, ramipril, and cilazapril	Tablets	Fused-silica capillary 52 cm total length (44.5 cm to the detector) with an internal diameter of 75 mm.	Sodium phosphate buffer (pH 7.25; 100 mM).	UV at 214 nm	0.016–0.200 mg/ml (Enalapril maleate & HCT)	-----	[63]
					0.020–0.400 mg/ml (Lisinopril dihydrate & HCT) (Quinapril. HCl & HCT) (Ramipril & HCT) (Cilazapril & HCT)		[63]
					0.010–0.200 mg/ml (Fosinopril sodium &HCT)		
HCT, candesartan, eprosartan mesylate, irbesartan, losartan potassium, telmisartan, and valsartan.	Tablets	Fused-silica capillary was used, 85 cm in total length (33 cm to the detector), and 50 mm internal diameter (ID)	60 mM sodium phosphate buffer pH 2.5 (CZE method)	UV at 214 nm	0.04-0.20 mg/ml (Irbesartan & HCT)	-----	[64]
					0.03-0.15 mg/ml (Losartan potassium & HCT)		
HCT, candesartan, eprosartan mesylate, irbesartan, losartan potassium, telmisartan, and valsartan.	Tablets	Fused-silica capillary was used, 85 cm in total length (33 cm to the detector), and 50 mm internal diameter (ID)	55 mM sodium phosphate buffer pH 6.5 containing 15 mM SDS (MEKC method)	UV at 214 nm	0.02-0.10 mg/ml (Losartan potassium & HCT)	-----	[64]
					0.05-0.25 mg/ml (Valsartan & HCT)		
losartan with chlorthalidone or HCT	Capsules	Fused-silica capillaries coated with polyacrylate 48.5 cm (40 cm effective length) ´ 75 µm ID ´ 375 µm O.D.	50 mmol/L^{-1} of sodium carbonate buffer at pH 10.3	UV at 226 nm	-----	0.07980 mg	[65]

2. Chromatographic methods

2.1. HPLC methods

Drug	Matrix	Column	Mobile phase	Detector	Linearity range	LOD	Ref.
CAP and cimetidine	Tablet	Purospher star C_{18} (5µm, 25 × 0.46 cm)	Methanol: water (60:40 v/v)	UV at 225 nm	9.3 - 150 µg/mL	1.75 ng/mL	[66]
CAP	Human plasma	C18 column (5 µm, 150 mm × 4.6 mm)	Methanol (75%, v/v) and phosphate buffer (25%, pH = 8, 0.01 M	UV at 290 nm	3–2000 ng/mL	0.9 ng/mL	[67]
CAP & HCT	Human urine	Zorbax C_8 column	0.05M sodium acetate, acetonitrile, methanol (14:17:4; pH 6.5)	UV at 254 nm	CAP (8 - 160ng) HCT (6 -140 ng)	3 and 2 ng for both	[68]
CAP	Pharmaceutical dosage forms	Luna C_{18} column at 50 °C	Phosphoric acid 15 mm and acetonitrile	UV at 210 nm.	5.05-50.5 µg/mL	1,130 µg/mL	[69]
CAP	Tablets	Zorbax SB-C_8 Solvent Saver Plus (3 × 100 mm, 3.5 µm)	Phosphoric acid (c = 15 mmol) in water-acetonitrile (w = 60–40 %),	UV at 260 nm	12–100 µg/mL	0.1 µg/mL	[70]
CAP & HCT	Tablets	Beckman Ultrasphere ODS (4.6 mm x 15 cm, 5µm)	Methanol/water (45:55 v/v). The pH 3.8 with 85% orthophosphoric acid	UV at 210 nm	CAP (0.02–0.2 mg/mL) HCT (0.01–0.1 mg/mL)	CAP (5 µg/mL) HCT (2 µg/mL)	[71]
HCT	Human plasma	Shim-pack® cyanopropyl column (250 × 4.6 mm, 5 µm)	10 mm ammonium acetate solution (pH 6.0)–methanol (65:35, v/v)	UV at 270 nm	0.31–3.12 (µg/mL)	0.043 (µg/mL)	[72]
Amlodipine Besylate; Valsartan; HCT	Tablet	Phenomenex Kinetex (150 × 4.6 mm)	Acetonetrile-phosphate buffer (0.05 M) with pH 2.8 ± 0.2 (40/60, v/v)	UV at 227 nm.	1-12 µg/mL	0.39 µg/mL	[73]
CAP	Plasma sample	Hypersil BDS C_8 (250 X 4.6 mm)	Phosphate buffer: acetonitrile (75:25 v/v) pH adjusted at 2.8 with o-phosphoric acid	UV at 205 nm	50-2.000 ng/mL.	1.65 ng/mL	[74]
Enalapril maleate and HCT	Tablet	Li Chrosorb RP-18 (250 x 4.6 mm, 10 µm)	0.02 M phosphate buffer (pH 3.0)-acetonitrile (50: 50 v/v).	UV at 225 and 233 nm	0.5-30 ng/mL	50 ng/mL	[75]
CAP	Bulk material, pharmaceutical formulation and serum.	Purospher Start C_{18} (250cm x 4.6mm, 5µm) and Hypersil ODS C_{18} (150× 4.6mm, 5 µm)	Methanol-water 50:50(v/v) pH 3.0 adjusted by phosphoric acid	UV at 215, 220, 225 nm.	1.25-50 µg/mL	2.0 ng/mL	[76]
CAP	Plasma	µbondapak NH_2 column (300×3.9 mm)	Isocratic consisting of *n*-hexane–2-propanol–methanol–acetic acid (68:15:15:2).	UV at 246 nm	12.5–500 ng/ml.	3.03 ng/ml.	[77]
CAP and Statins	Pharmaceutical preparations and human serum	Purospher Star C_{18} (5mm, 250 x 4.6 mm)	Acetonitrile:water (60:40 v/v) adjusting pH to 2.9.	UV at 230 nm	2.5-100 µg/mL	2.3 ng/mL .	[78]
Carvedilol and HCT	Tablet	Zorbax SB-C_8 column (4.6 × 250 mm, 5 µm)	0.025 M phosphoric acid and acetonitrile	UV at 271 nm	5-200 µg/mL	0.30 µg/mL	[79]
Amlodipine Besylate, Valsartan, and HCT	Tablet	Phenomenex Luna C_{18} column - RP 150 mm × 4.6 mm, 5-µm)	Acetonitrile :methanol:50 mm phosphate buffer adjusted to pH 3 with orthophosphoric acid	UV at 239 nm	1–10 µg/mL	0.1636 µg/mL	[80]
CAP & HCT	Human plasma	DIAMONSIL C_{18} column (150 mm × 4 mm, 5 µm)	Acetonitrile–trifluoroacetic acid–water gradient elution	UV at 263nm	CAP (20–4000 ng/mL) HCT (10–1200 ng/mL)	CAP (7 ng/mL) HCT (3.3 ng/mL)	[81]
CAP	Human plasma	Spherisorb C_{18} column (250 x 4 .6mm)	Water:acetonitrile: acetic acid mixture (44:55:0.2, v/v/v)	UV at 258 nm	5–500 ng/mL	2 ng/mL	[82]

HCT	Pharmaceutical Formulations and Biological Fluid	ODS Hypersil C_{18} (250 mm×4.6 mm, 5 µm)	Acetonitrile (10.6%), methanol (16.2%),	UV at 210 nm	1.25–12.75 µg/mL	1.09 µg/mL	[83]
HCT, amlodipine, and losartan	Tablet	phenomenex luna 5µ CN 100R, 250 × 4.60 mm, 5 micron	Acetonitrile, water and 0.4% of potassium dihydrogen phosphate buffer pH 2.7 adjusted with orthophosphoric acid (45:35:20).	UV at 230 nm	12.5–62.5 µg/mL	0.03 µg/mL	[84]
Zofenopril and HCT	Tablets	Agilent LiChrospher C_{18} column (250 × 4.0 mm, 5 µm)	Water–TFA (99.9:0.1 v/v) and (B) acetonitrile–TFA (99.1:0.1 v/v)	UV at 224 nm	1.0–20 µg/mL	0.019 µg/mL	[85]
CAP	Rabbit plasma	ODSI C_{18} (250 mm × 4.6 mm, 5 µm)	Water: acetonitrile (60:40 v/v), pH adjusted to 2.5 by using 85% orthophosphoric acid	UV at 203 nm	3.125–100 µg/mL	3.10 ng/mL	[86]
CAP	Human plasma	Acquity UPLC BEH shield RP (1.7µm, 2.1 x 150 mm))	Methanol: water containing 0.1% Formic acid (10: 90 v/v for 1 min then 95: 5 v/v till the end of the run)	MS	10–2000 ng/mL	3.03 ng/mL	[87]
Bisoprolol and HCT	Human plasma	Purosphere® STAR C_8 (125 mm × 4 mm, 5 µm)	Ammonium acetate solution (1 mM) with formic acid (0.2%): methanol and acetonitrile (65:17.5:17.5, v/v/v (%))	MS-MS/ESI.	1.00–80.00 ng/mL	1.00 ng/mL	[88]
CAP	Tablets	Phenomenex® Luna 5 µm (C18) column	Phosphate buffer (adjusted to pH 3.0): acetonitrile in a ratio of 70:30 (v/v)	ESA Coulometric detector at 300	2–70 µg/mL	0.6 µg/mL	[89]
CAP	Blood samples	a Genesis C_8 column, (150 mm x 4.6 mm)	Acetonitrile (70%), water (30%) and trifluoroacetic acid (0.1%),	MS-MS /EIS	2 - 4000 ng/mL	0.6 ng/mL	[90]
CAP	Dried blood spot samples	Zorbax Eclipse Plus C_8 column (150 mm x 3.0 mm, 3.5 µm)	Acetonitrile containing 0.1% v/v formic acid (eluent A), water containing 0.1% v/v formic acid (eluent B) and isopropanol (eluent C). This was delivered at 0.5 ml/min with gradient elution.	HRMS	10-400 ng/ml	-----	[91]
Irbesartan and HCT	Human plasma	Acquity U-HPLC BEH C_{18} column	A gradient mpbile phase with solvent A (0.1% formic acid in water) and solvent B (acetonitrile)	MS-MS/ESI	0.5–300 ng/mL	0.15 ng/mL	[92]
HCT	Human plasma	Onix C_{18} Monolitic column (Phe- nomenex, (50 x 4,6 mm)	Acetonitrile and water (80:20, v/v), add 5% Isopropyl alcohol	MS-MS/ESI.	5–400 ng/mL	1.15 ng/mL	[93]
Triamterene and HCT	Human plasma	Zorbax Eclipse Plus RRHD C_{18} column (2.1 mm × 50 mm, 1.7 µm)	0.1% formic acid:methanol:acetonitrile 5:4:1 and 0.1% formic acid in water at a flow rate of 0.4 ml/min.	MS	2.5–400 ng/mL	0.75 ng/mL	[94]

2.2. HPTLC methods

Drugs	Matrix	Stationary phase	Mobile phase	Detector	Linearity range	LOD	Ref.
CAP	Tablets	Silica gel, chromatographic plates 60 F254 "Merck", and "Sorbfil"	Cloroform R-propanol R (9:1)	UV at 254 nm	-----	0,4 µg	[95]
CAP	Tablets	Precoated silica gel 60 F	Methanol: ethyl acetate: glacial acetic acid (5: 5: 0.5, v/v/v)	UV at 241 nm	6–30 µg/band	0.022 µg	[96]
lisinopril and HCT	Pharmaceutical tablets.	Merck HPTLC aluminum plates of silica gel 60 F254,	Chloroform–ethylacetate–acetic acid (10:3:2, v/v/v)	UV absorption and first derivative spectra of the mixture. 210 and 275 nm	-----	-----	[97]
Valsartan and HCT	Tablet Dosage Form	Precoated silica gel 60 F(254)	Chloroform: methanol: toluene: glacial acetic acid (6:2:1:0.1, v/v/v/v)	UV at 260 nm	100 - 600 ng/ spot	30 and 100 ng/ spot	[98]

3. Spectroscopic methods

3.1. Spectrophotometric methods

Drugs	Matrix	Method-reagent	λ_{max} (nm)	Linearity range	LOD	Ref.
Enalapril, HCT and walsartan	Complex pharmaceutical preparations	Derivative spectrophotometry	-----	0.96-26.00 µg/mL	0.31 µg/mL)	[99]
Triamterene and HCT	Tablets	Zero-crossing technique	255.7 and 283.2	1.25- 6.25 µg/mL	0.25 µg/mL	[100]
Metoprolol and HCT	Pharmaceutical preparations	Zero-crossing	282	12.5 - 37.5 µg/mL	1.5 µg/mL	[101]
HCT, Atenolol and Losartan potassium	Tablet	Simultaneous equation method First order derivative method	272.5, 224 and 250 280.5, 233 and 244	1-60 µg/mL 0.5-30 µg/mL	-----	[102]
Carvedilol and HCT	Combined dosage form	Dual wavelength analysis	266 and 289.4	-----	-----	[103]
Olmesartan medoxamil, amlodipine besylate and HCT	Tablets	Ratio subtraction method	315	2-40 µg/mL	0.819 µg/mL	[104]
Olmesartan medoxomil and HCT	Tablet	Absorption ratio spectrophotometric method	272.8	10-30 µg/mL	0.44 µg/mL	[105]
HCT, indapamide and xipamide	Pharmaceutical tablets	Ternary complex formation with eosin and lead (II) in the presence of methylcellulose as surfactant	543	8-40 µg/mL	-----	[106]
HCT and Olmesartan Medoxomil	Combined dosage form	UV spectrophotometric method	271.5 and 257	5-25 µg/mL	-----	[107]
HCT and amiloride hydrochloride	Pharmaceutical dosage forms	Isoabsorptive point	274.7	10-80 µg/mL	0.39 µg/mL	[108]
HCT and telmisartan	Tablet dosage form.	Simultaneous equation method	258 and 299	2-20 µg/mL	0.079 µg/mL	[109]

3.2. Spectrofluorimetric methods:

Drugs	Matrix	Fluorogenic reagent (method)	λex (nm)	λem (nm)	Linearity range	LOD	Ref.
CAP	Tablets	Cerium (IV) in the presence of sulphuric acid	256	354	0.1–1.3 µg/mL	0.016 µg/mL	[110]
HCT and timolol	Tablets	--------	270	375	4-12 µg/mL	0.0104 mg/L	[111]
HCT and TELM	Tablets	1 M sodium hydroxide	230	365	50–400 ng/mL	------	[112]
HCT	Tablets	Carbon dot via inner filter effect (IFE) and resonance Rayleigh scattering (RRS)	310	434	0.17-2.50 µg/mL	0.11 µg/mL	[113]
HCT	Tablets	Acetonitrile at ph 6.2 and Tb3+ ion doped in sol–gel matrix	370	545	5.0×10^{-10} - 5.0×10^{-6} mol/L	2.2×10^{-11} mol/L	[114]

4. Electrochemical methods:

Drug	Matrix	Electrode	Linearity range	LOD	Ref.
CAP & HCT	Tablet and Urine	Graphene/ferrocene composite carbon paste (GR/Fc/CP)	CPT (1.0–430 µM) HCT (0.5–390 µM)	------	[115]
CAP	Tablet	Platinum electrode in a 0.1 M HNO_3 solution at 1.2 V versus a saturated silver-silver chloride	1.2×10^{-6} - 3.2×10^{-4} M	9.2×10^{-7} M	[116]
CAP & HCT	Tablet and Urine	Carbon ionic liquid modified with copper hydroxide nanoparticles	CPT (0.7–70 µM) HCT (3–600 µM)	12 nM 60 nM	[117]
CAP	Urine	Zinc oxide nanoparticles and a new ferrocene-derivative modified carbon paste	0.09–450.0 µmol/L	0.05 µmol/L	[118]
CAP	Urine	Ferrocene-dicarboxylic acid modified carbon paste	3.0×10^{-7} - 1.4×10^{-4} M	9.1×10^{-8} M	[119]
CAP	Urine	Catechol-derivative-multiwall carbon nanotubes paste	6.4×10^{-8} - 3.2×10^{-48} mol/L	3.4×10^{-8} mol/L	[120]
CAP, acetaminophen, tyrosine and HCT	Tablet and Urine	Nio/cnts and (2-(3, 4-dihydroxyphenethyl) isoindoline-1, 3-dione) (DPID).	CAP (0.07–200.0 µM) HCT (10.0–600.0 µM)	9.0 nM 5.0 µM	[121]
HCT	Tablet and Urine	Glassy carbon	24–320 ng/mL	5.0 ng/mL	[122]
CAP	Serum and pharmaceutical formulations	A three-electrode system containing the static mercury drop electrode (SMDE), Pt auxiliary electrode and Ag/agcl reference electrode was used throughout	0.5–50.0 µg/mL	6.28×10^{-3} µg/mL	[123]
CAP	Urine	Amalgam film (Hg(Ag)FE)	0.05–1 µM	1.9 nM	[124]
CAP	Injection	Boron-doped diamond thin film electrode	50 µM - 3 mM	25 µM	[125]
HCT	Urine	Electrochemically pretreated pencil graphite electrode (EPPGE) using cyclic voltammetry (CV), differential pulse voltammetry (DPV) and square wave voltammetry (SWV)	DPV (4 µM - 140 µM) SWV (1 µM - 20 µM)	3.25 µM/L 0.421 µM/L	[126]
CAP	Urine	Manganese supported on an organo-modified sio2/Al2O3	3.0×10^{-7} - 300×10^{-4} mol/dm3	9.0×10^{-8} mol/dm^3	[127]
	Tablet and Urine	Two dimensional single-crystal hexagonal gold nanosheets (schgnss) were prepared by microwave heating of a solution of haucl4 in an ionic liquid	2-400 nM and 4.0-50 µM	0.3 nM	[128]
HCT	Urine	Nickel hydroxide	1.39×10^{-5} - 1.67×10^{-4} mol/L	7.92×10^{-6} mol/L	[129]

CAP	Urine	Nio nanoparticle modified (9, 10-dihydro-9, 10-ethanoanthracene-11, 12-dicarboximido)-4-ethylbenzene-1, 2-diol carbon paste electrode	0.035 - 550 µmol/L	0.007 µmol/L	[130]
Methyldopa and HCT	Tablet, Urine and Pill	A molybdenum (VI) complex-ionic liquid–zno NP modified carbon paste electrode (MCILZNMCPE)	0.05 - 300.0 µM	-------	[131]
CAP	Tablet and Urine	Multiwall Carbon Nanotubes Paste Electrode in the Presence of Isoproterenol as a Mediator	0.3 - 90 µmol/L	0.1 µmol/L	[132]
CAP		Glassy carbon in the presence of 4, 4'-biphenol	25–300 µM	3.34 µM	[133]
CAP, acetaminophen, tryptophan, folic acid, and L-cysteine	Urine and Plasma	A novel carbon paste electrode (CPE) modified with 2,2′-[1,7–hepta nediylbis(nitrilomethylidene)]-bis(4-hydroxyphenol) (DHB) and carbon nanotubes (cnts)	7.0–100.0 and 100.0–2,500.0 µM	2.43 µM	[134]
HCT	Tablets	A Trypan Blue modified combined pencil graphite electrode system (tyb-GGG)	DPV (0.5–7 µM) SWV (0.1–5 µM)	0.1327 µM 0.0320 µM	[135]
metoprolol and HCT	Urine	Cathodically pretreated boron-doped diamond (BDD)	0.51–18.7 µmol/L	0.376 µmol/L	[136]

Conclusion

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

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