International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 3 May-June 2023, pp: 279-291 www.ijprajournal.com ISSN: 2249-7781

"Various Analytical Methods for the Determination of Dapagliflozin and Hydrochlorothiazide in Pharmaceutical Dosage Form: A Review"

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Submitted: 01-05-2023 Accepted: 08-05-2023

ABSTRACT
Current prevention strategies in patients with recurrence of kidney stones show especially in high-risk patients a diversely and in the long-term not successful outcome in a sustainable number of cases. Recent studies have revealed that Dapagliflozin has the potential to decrease risk and incidence of urolithiasis events especially in patients suffering from Diabetes. The investigators propose that Dapagliflozin has the potential to increase the metabolic situation of hyperoxaluric patients with recurrence of urolithiasis. The investigators therefore test whether Dapagliflozin can decrease the oxalate excretion compared to the current strategy with Hydrochlorothiazide. The study may open up a new way of preventing urolithiasis in patients with high-risk of recurring urolithiasis.

Keywords: Analytical method, Dapagliflozin, Hydrochlorothiazide, UV, RP-HPLC,

I. INTRODUCTION:

Kidney stone disease, is a condition in which individuals form calculi (stones) within the renal pelvis and tubular lumens. Stones form from crystals that precipitate (separate) out of the urine. Stone formation may occur when the urinary concentration of crystal-forming substances (calcium, oxalate, uric acid) is high.Approximately 80 percent of adults with nephrolithiasis have stones comprised predominately of calcium oxalate and/or calcium phosphate.The most common biochemical abnormality identified in patients with nephrolithiasis is hypercalciuria; other abnormalities may includehypercalcemia, hyperuricemia, hyperuricosuria, hyperoxaluria, hypernatriuria, and hypocitraturia. Kidney stones constitute a worldwide health care challenge with a current lifetime risk of ~18.8% in men and ~9.4% in women in Western civilisations. Recurrence rates are high, up to 40% and 75% at 5 and 10 years, respectively.Hospitalisations, surgery and lost work time associated with kidney stones cause enormous healthcare-related expenditures.

Dapagliflozin[3,4]

Dapagliflozin is sodium glucose co-transporter 2 inhibitor (SGLT2), which prevents glucose reabsorption in the kidney using Dapagliflozin leads to heavy glycosuria (glucose excretion in the urine), which can lead to weight loss and tiredness.Dapagliflozin was also shown to reduce the rate to decline in kidney function and kidney failure in adults. Dapagliflozin is an inhibitor of the sodium glucose co-transporter 2 which is found almost exclusively in the proximal tubules of nephron components in the kidneys.

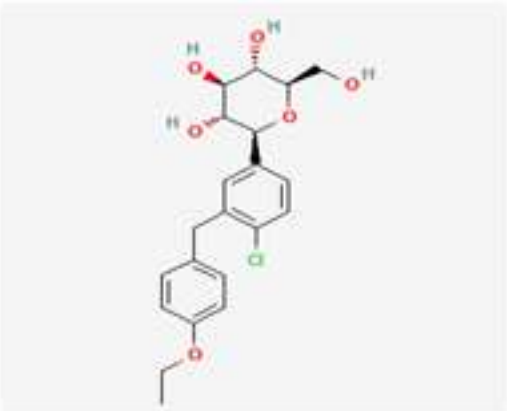

Figure No.1: Structure of Dapagliflozin [3]

Mechanism of action:[1-4]Sodium-glucose cotransporter 2, expressed in the proximal renal tubules, is responsible for the majority of the reabsorption of filtered glucose from the tubular lumen. Dapagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, Dapagliflozin reduces reabsorption of filtered glucose and thereby promotes urinary glucose excretion. Dapagliflozin

International Journal of Pharmaceutical Research and Applications
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also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. Due to their unique mode of action, SGLT2 inhibitors induce weight loss, decrease blood pressure and increase urinary volume, the latter being a very effective measure to reduce stone recurrence.

Hydrochlorothiazide[5,6]

Hydrochlorothiazide is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, there by increasing the excretion of sodium and chloride ions and consequently of water.Hydrochlorothiazide (HCT) is chemically 6-chloro-3, 4-dihydro-2h-1,2,4-bezothiadiazine-7-sulphonamide-1,1-dioxide.

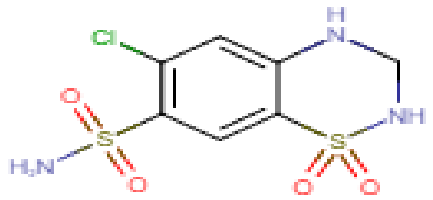

Figure No.2: Structure of Hydrochlorothiazide

Mechanism of action:[7,8] Thiazide diuretics exert their diuretic effect via blockage of the sodium-chloride (Na/Cl) channel in the proximal segment of the distal convoluted tubule (DCT). At the same time, blockage of the Na/Cl channel increases the flow of ions through the Na/Ca channel, resulting in increased calcium reabsorption into the interstitium in exchange for Na return to the DCT.By increasing calcium reabsorption from the luminal membrane into the interstitium in exchange for sodium, thiazides reduce urine calcium levels and increase blood calcium. This effect of thiazide diuretics makes thiazides useful for Urolithiasis treatment.

Table No.1: Method for determination of Dapagliflozin and Hydrochlorothiazide Single with other drugs by UV Spectroscopy, chromatography and other techniques.

Sr. No.	Method	Description	Ref No.
1.	Method development and validation for the estimation of Dapagliflozin in bulk and tablet dosage form by UV visible spectroscopy	**Solvent:** Methanol **Concentration:** 2-10 µg/ml **Wave length:** 225nm	9
2.	Estimation of Dapagliflozin from its Tablet Formulation by UV-Spectrophotometry	**Solvent**: Methanol 1000 µg/ml: Distilled water **Concentration:** 5-40 µg/mL **Wave length:** 220 nm and 224 nm	10
3.	Development and validation of UV spectrophotometric method for Estimation of Saxagliptin and Dapagliflozin in bulk and dosage form	**Solvent:** 10 ml Methanol **Concentration:** SAXA: 2-10 µg/ml, DAPA: 4-20 µg/ml **Wave length:** SAXA: 224 nm, DAPA: 274 nm	11
4.	Method Development, Validation and Stress Studies of Dapagliflozin and Metformin Hydrochloride Using Ultraviolet-Visible Spectroscopy in Bulk and Combined Pharmaceutical Formulations	**Solvent:** Water **Concentration:** DAPA: 1 – 20 µg/ml, MET: 2 – 36 µg/ml **Wave length:** DAPA: 222 nm, MET:232 nm	12
5.	Development and Validation of UV Spectroscopic Method for Simultaneous Estimation of	**Solvent:** Phosphate buffer (pH 6.8) **Concentration:** 5-25 µg/ml **Wave length:** DAPA: 222 nm SAXA:	13

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	Dapagliflozin and Saxagliptin in marketed formulation	276 nm	
6.	Development and Validation of UV Spectroscopic First Derivative Method for Simultaneous Estimation of Dapagliflozin and Metformin Hydrochloride in Synthetic Mixture	**Solvent:** Methanol **Concentration:** DAPA: 0.5-2.5 µg/ml, MET: 25-125 µg/ml **Wave length:** DAPA: 235 nm, MET: 272 nm	14
7.	Multivariate optimization of liquid chromatographic conditions for determination of Dapagliflozin and Saxagliptin, application to an in vitro dissolution and stability studies	**Stationary phase:** SPOLAR C18 (250 cm × 4.6 mm, 5 µm) **Mobile phase:** Acetonitrile: Phosphate buffer (26:74 % v/v) (pH 5.8) **Flow rate:** 0.96 ml/min **Wave length:** 236 nm	15
8.	Development and Validation of Dissolution Test Method for Dapagliflozin using RPHPLC and UV Spectrophotometer	**Stationary phase:** Princeton C18-4E (250 mm*4 mm,5 µm) **Mobile phase:** Acetonitrile: 0.1% Triethylamine (50:50 % v/v) (pH-5.0) **Flow rate:** 1 ml/min **Wave length:** 254.6 nm **UV METHOD** **Solvent:** Methanol **Concentration:** 30 µg/ml **Wave length:** 245.6 nm	16
9.	RP-HPLC Method for Estimation of Dapagliflozin from its Tablet	**Stationary phase:** PrincetonC184E (250 cm *4 mm, 5 µm) **Mobile phase:** Acetonitrile: 0.1% Triethylamine (50:50 % v/v) (pH adjusted to 5.0) **Flow rate:** 1 ml/min **Wave length:** 224 nm	17
10.	A New RP-HPLC Method Development and Validation of Dapagliflozin in Bulk and Tablet Dosage Form	**Stationary phase:** C18 (25 cm × 4.6 mm, 5 µm) **Mobile phase:** Phosphate buffer: Acetonitrile (60:40 % v/v) **Flow rate:** 1.0 ml/min **Wave length:** 237 nm	18
11.	Stability Indicating RP HPLC Method for Estimation of Dapagliflozin in Bulk and Tablet Dosage Form	**Stationary phase:** HypersilBDSC18 (250 mm * 4.6 mm, 5µm) **Mobile phase:** 0.1% Ortho phosphoric acid buffer: Acetonitrile (50:50 % v/v) **Flow rate:** 1.0 ml/ min **Wave length:** 245 nm	19
12.	Method Development and Validation of Dapagliflozin in API by RP-HPLC and UV-Spectroscopy	**Stationary phase:** BDS C8 (50 cm × 4.6 mm, 5µm) **Mobile phase:** Acetonitrile: Ortho phosphoric acid (55:45 % v/v) **Flow rate:** 1ml/min **Wave length:** 203 nm **UV METHOD** **Solvent:** Methanol: Distilled water **Concentration**: 25-150 µg/ml	20

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		Wave length: 203 nm	
13.	Development and validation of RP-HPLC method for the simultaneous Estimation of Dapagliflozin and Saxagliptin in bulk and pharmaceutical Dosage forms	**Stationary phase:** C8 (4.6 mm × 150 cm, 3.5 µm) **Mobile phase:** Buffer: Acetonitrile (70:30 % v/v) (pH 3) **Flow rate:** 1 ml/min **Wave length:** 221 nm	21
14.	RP-HPLC Method for Dapagliflozin and Metformin HCL in Bulk and Combined Formulation	**Stationary phase:** Phenomenex C18 250 cm x 4.6 mm, 5 µm) **Mobile phase:** Water: Methanol (50:50 % v/v) **Flow rate:** 5 1.0 ml/min **Wave length:** 230 nm	22
15.	A new validated RP-HPLC-photo diode array (PDA) method for the simultaneous estimation of Dapagliflozin and Saxagliptin in bulk form and pharmaceutical tablet dosage form	**Stationary phase:** Phenomenex Luna C18 (4.6 mm× 250 cm, 5µm) **Mobile phase:** Acetonitrile: Phosphate Buffer (pH 4.6) (45:55 % v/v) **Flow rate:** 1.0 ml/min **Wave length:** 245 nm	23
16.	RP- HPLC Method for Simultaneous Estimation of Dapagliflozin and Saxagliptin in Bulk Samples	**Column:** Phenomenex Luna C18 (25 cm x 4.60 mm, 5 µm) **Mobile phase:** 10 mM Phosphate buffer: Acetonitirle (40: 60 % v/v) (pH 6.8) **Flow rate:** 1.0 ml/min **Wave length:** 260 nm	24
17.	Stability indicating HPLC method for the simultaneous determination of Dapagliflozin and Saxagliptin in bulk and tablet dosage form	**Stationary phase:** Xterra RP18 (4.6 mm × 150 cm, 5 µm) **Mobile phase:** Acetonitrile: Water (60:40 % v/v) **Flow rate:** 1 ml/min **Wave length:** 248 nm	25
18.	A Highly Validated RP-HPLC Method Development for the Simultaneous Estimation of Dapagliflozin and Saxagliptin in Tablet Dosage Forms	**Stationary phase:** BDS C8 (50 cm × 4.6 mm, 5 µm) **Mobile phase:** Potassium dihydrogen phosphate: Acetonitrile (55: 45 % v/v), pH adjusted to 3.8 by dilute orthophosphoric acid. **Flow rate:** 1 ml/min **Wave length:** 210 nm	26
19.	A novel RP-HPLC method for simultaneous estimation of Dapagliflozin and Saxagliptin in bulk and pharmaceutical dosage form	**Stationary phase:** Inertsil-ODS, C18 (250 cm × 4.6 mm, 5 µm) **Mobile phase:** Methanol: Potassium dihyrogen phosphate buffer (45:55 % v/v) **Flow rate:** 1.0 ml/min **Wave length:** 210 nm	27
20.	A new high-performance thin layer chromatographic method development and validation of Dapagliflozin in bulk and tablet dosage form	**Stationary phase:** Merck precoated silica gel aluminumplate60 F_{254} (10 cm*10 cm,75-125 µm) **Mobile phase:** Chloroform: Methanol (9:1 % v/v) **R_f:** 0.21±0.004 **Wave length:** 223 nm	28
21.	TLC-Spectro densitometric method for	**Stationary phase:** Silica gel G 60 F 254	29

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	simultaneous determination of Dapagliflozin and rosuvastatin in rabbit plasma: stability indicating assay and kinetic studies	TLC (20 cm* 7 mm, 0.2 µm) **Mobile phase:** Ethyl acetate: Methanol (5: 0.1 % v/v) **R_f:** DAPA**:** 0.23, ROSV: 0.44 **Wave length:** 243 nm	
22.	Development and validation of a LC-ESI-MS/MS Based Bioanalytical Method for Dapagliflozin and Saxagliptin in Human plasma	**Stationary phase:** HypersilGoldC18 (250 cm* 4.6 nm, 5µm) **Mobile phase:** 10 mM Ammonium acetate: Methanol (20: 80 % v/v) **Flow rate:** 0.5 ml/min **Wave length:** 236 nm **Injection:** 20µl **Detector:** Triple Quadruple	30
23.	Hydrochlorothiazide (Indian Pharmacopoeia 2018) BY Thin-layer chromatography	**Stationary phase:** Coating the plate with silica gel GF254 **Mobile phase:** Ethyl acetate **Wave length:** 254 nm	31
24.	Hydrochlorothiazide Tablets (Indian Pharmacopoeia 2018) BY Thin-layer chromatography	**Stationary phase:** Coating the plate with silica gel GF254 **Mobile phase:** Ethyl acetate **Spray:** Ethanolic sulphuric acid	32
25.	Hydrochlorothiazide Tablets (British Pharmacopoeia 2022) BY Thin-layer chromatography	**Stationary phase:** Coating silica gelGF254 **Mobile phase:** Ethyl acetate **Wave length:** 254 nm	33
26.	Hydrochlorothiazide Capsules (USP 43-NF38 2020) by Liquid Chromatography	**Stationary phase:** Packing L1(4.6 mm × 25 cm, 5 µm) **Mobile phase:** Acetonitrile: Buffer (10:90 % v/v) (Adjust with 10% phosphoric acid to a pH of 3.0) **Flow rate:** 2 ml/min **Wave length:** 272 nm	34
30.	Development And Validation of UV Spectrophotometric and HPLC Method For Hydrochlorothiazide In Bulk and Tablet Dosage Form	**Solvent:** Methanol **Concentration:** 5-25 µg/ml **Wave length**: 260 nm **HPLC METHOD** **Stationary phase:** Agilent C_{18} (4.6 mm * 250 cm, 5 µm) **Mobile Phase:** Methanol: Water (30:70 % v/v) pH 7. **Flow rate:** 0.7 ml/min **Wave length:** 260 nm	35
31.	Stress Degradation Studies of Hydrochlorothiazide and Development of Validated Method by UV Spectroscopy	**Solvent:** NaOH (Sodium Hydroxide) **Concentration:** 5-30 µg/ml **Wave length:** 273 nm	36
32.	Simultaneous Determination of Hydrochlorothiazide and Losartan Potassium in Pharmaceutical Product by UV-Vis Spectrophotometric Method with Kalman Filter Algorithm	**Solvent:** NaOH (Sodium Hydroxide) **Concentration:** HCT: 12.5 µg/ml, LST: 50.0 µg/ml **Wave length:** HCT: 271 nm, LSP: 235 nm	37
33.	UV Spectroscopy Determination of Cilazapril And Hydrochlorothiazide Active Agents	**Solvent:** Methanol: 0.1 m HCl (Hydrochloric acid) **Concentration:** 100 mgL^{-1}	38

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	Used in The Treatment Of Hypertension	**Wave length:** 0.1 nm	
34.	Determination of Simultaneous Irbesartan and Hydrochlorothiazide by Ultraviolet Spectrophotometry with Dual Wavelength Method	**Solvent:** NaOH (Sodium Hydroxide) **Concentration:** IRB: 10 µg/ml, HCT: 8 µg/ml **Wave length:** IRB: 263.4 nm, 281 nm, HCT: 243.4 nm, 247.6 nm	39
35.	Simultaneous estimation of Aliskiren Hemi fumarate and Hydrochlorothiazide in combined Tablet Formulation by Simultaneous equation, Absorbance ratio and First derivative Spectroscopic Methods	**Solvent:** Methanol **Concentration:** ALI: 120 µg/ml, HCT: 10 µg/ml **Wave length:** ALI: 271 nm, 280 nm, HCT: 271nm, 280nm	40
37.	Simultaneous determination of carvedilol and hydrochlorothiazide in pharmaceutical dosage form by first order derivative UV Spectrophotometry	**Solvent:** Methanol **Concentration:** CAR 20µg/ml, HCT: 20 µg/ml **Wave length:** CAR: 301 nm HCT: 278 nm	41
38.	UV-Spectrophotometric Determination of Telmisartan and Hydrochlorothiazide in Combined Tablet Dosage Form Using Simultaneous Equation Method	**Solvent:** Methanol **Concentration:** TLM: 5-30 µg/ml, HCT: 2-12 µg/ml **Wave length:** TLM: 296.8 nm, HCT: 271.2 nm	42
39.	Validated Spectrophotometric Methods for Estimation of Telmisartan and Hydrochlorothiazide in Combined Tablet Dosage Form	**Solvent:** Methanol: Water (1:1 % v/v) **Concentration:** TEM: 4-24 µg/ml, HCT: 2-14 µg/ml **Wave length:** TEM: 273.0 nm, HCT: 295.0 nm	43
40.	Simultaneous estimation of valsartan and hydrochlorothiazide in fixed dose combination in UV Spectrophotometry	**Solvent:** NaOH (Sodium Hydroxide) **Concentration:** VAL: 2-24 µg/ml, HCT: 2-14 µg/ml **Wave length:** VAL: 249 nm- 259 nm, HCT: 261 nm- 281 nm	44
41.	Development and Validation of a UV Spectrophotometric Method for the Simultaneous Estimation of Eprosartan Mesylate and Hydrochlorothiazide in Bulk and Formulations	**Solvent:** 0.1M Sodium Hydroxide **Concentration:** EPM: 6-36 µg/ml, HCT: 1-10 µg/ml **Wave length:** EPM: 274.5 nm, HCT: 249.1 nm	45
42.	UV Spectrophotometric Determination of Hydrochlorothiazide and Olmesartan Medoxomil in Pharmaceutical Formulation	**Solvent:** Double distilled water **Concentration:** HCT: 100 µg/ml OLM: 160 µg/ml **Wave length:** HCT: 261.5 nm OLM: 257.0 nm	46
43.	Development and Validation of Novel UV Methods for Irbesartan and Hydrochlorothiazide Combination	**Solvent:** Methanol: 0.1 N HCL (Hydrochloric acid) **Concentration:** IRB: 10-50 µg/ml, HCT: 0.83-4.16 µg/ml **Wave length:** IRB: 244 nm, HCT: 275.02 nm	47
44.	Development and Validation of RP-HPLC Method for the Determination of Hydrochlorothiazide in Bulk Drug and	**Stationary phase:** InertsilcolumnODS3 (250 cm × 4.6 mm, 5 µm) **Mobile Phase:** Acetonitrile: Water (50: 50 % v/v)	48

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	Pharmaceutical Dosage Form	**Flow rate:** 1 ml/min **Wave length:** 272 nm	
45.	Development And Validation of an RP-HPLC Method For the Estimation of Hydrochlorothiazide In Tablet Dosage Forms	**Stationary phase:** KromasilC18 (150 cm x 4.6 mm, 5 µm) **Mobile Phase:** Phosphate buffer: Acetonitrile (50:50 % v/v) (pH 2.5) **Flow rate:** 0.6 ml/min **Wave length:** 254 nm	49
46.	Development and Validation of RP-HPLC Chromatographic Dissolution Method for the Simultaneous Estimation of Ramipril and Hydrochlorothiazide from Solid Dosage Formulation	**Stationary phase:** Sunniest C8 (150 cm x 4.6 mm, 5 µm) **Mobile Phase:** Buffer solution: Acetonitrile (500: 500 v/v) **Flow rate:** 1.0 ml/min **Wave length:** 210 nm	50
47.	Validation Of Stability Indicating RP-HPLC Method For the Simultaneous Estimation Of Telmisartan and Hydrochlorothiazide Content in Bulk And Pharmaceutical Dosage Form	**Stationary phase:** InertsilC8 (125 cm x 4.0 mm, 5 µm) **Mobile Phase:** A: 2g/l Ammonium dihydrogen phosphate monohydrate: Acetonitrile (85:15 % v/v) (Adjust the pH3.0±0.2 with phosphoric acid) **Flow rate:**1.2 ml/min **Wave length:** 270 nm	51
49.	Simple Analytical Method for The Simultaneous Estimation of Hydrochlorothiazide and Candesartan By RP-HPLC.	**Stationary phase:** Silanol BDS C18 (250 cm x 4.6 mm, 5 µm) **Mobile Phase:** Water: Acetonitrile (30:70 % v/v) (pH adjusted to 2.8 with ortho Phosphoric acid) **Flow rate:** 1 ml/min **Wave length:** 210 nm	52
50.	Stability Indicating RP-HPLC Method For Quantification of Impurities in Valsartan And Hydrochlorothiazide FDC Tablet Dosage Form	**Stationary phase:** L1 (250 cm × 4.6 mm, 5 µm) **Mobile Phase: A:** 0.1% Ortho phosphoric acid, **B:** 100% Acetonitrile **Flow rate:** 1.0 ml/min **Wave length:** 265 nm	53
51.	Development and Validation of RP-HPLC Method for Simultaneous Estimation of Olmesartan and Hydrochlorothiazide in Tablet Dosage Form	**Stationary phase:** C-18 (250 cm x 4.6 mm, 5 µm) **Mobile Phase:** Methanol: Acetonitrile (70:30 % v/v) (pH 2.6) **Flow rate:** 1.0 ml/min **Wave length:** 254 nm	54
52.	Analytical RP-HPLC Method Development and Validation for the Simultaneous Estimation of Ramipril and Hydrochlorothiazide in Tablet Dosage Form	**Stationary phase:** Purosphere@StarRp18 (150 cm × 4.6 mm, 5 µm) **Mobile Phase:** Acetonitrile: Sodium perchlorate buffer (3:2 % v/v) (pH 2.5) **Flow rate:** 1.0 ml/min **Wave length:** 316 nm	55
53.	Development and Validation of RP-HPLC method for simultaneous estimation of Methyldopa and Hydrochlorothiazide in	**Stationary phase:** HypersilBDSC8 (250 cm x 4.6 mm, 5µm) **Mobile Phase:** Phosphate buffer: Acetonitrile (50:50 % v/v)	56

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	Pharmaceutical Dosage Form	**Flow rate:** 1.0 ml/min **Wave length:** 287 nm	
54.	RP-HPLC Method for Simultaneous Estimation of Amlodipine Besylate and Hydrochlorothiazide in Combined Dosage Forms	**Stationary phase:** RP-C18 (250 cm, 4.6 mm, 5 µm) **Mobile Phase:** Water: Methanol (70:30 % v/v) **Flow rate:** 0.5 ml/min **Wave length:** 245 nm	57
55.	Ion pair-HPLC method for the simultaneous estimation of quinapril and hydrochlorothiazide in tablets	**Stationary phase:** RP-C18 Gemini (150 cm × 4.5 mm, 5 µm) **Mobile Phase:** 0.1% v/v Triethylamine: 1 mM of Hexane sulphonic acid: Acetonitrile (30:70 % v/v) (pH 3.5) **Flow rate:** 6 min, 1 ml/min **Wave length:** 220 nm	58
56.	A Validated RP-HPLC Method for Simultaneous Estimation of Nebivolol and Hydrochlorothiazide in Tablets	**Stationary phase:** Phenomenex Gemini C18 (25 cm × 4.6 mm, 5 µm) **Mobile Phase:** Acetonitrile: 50 mM Ammonium acetate (70:30 % v/v) (adjusted to pH 3.5 using Orthophosphoric acid) **Flow rate:** 1.0 ml/min **Wave length:** 254 nm	59
57.	RP-HPLC method for simultaneous estimation of telmisartan and hydrochlorothiazide in tablet dosage form	**Stationary phase:** ODS HypersilC18 (25 cm × 4.6 mm, µl) **Mobile Phase:** acetonitrile: 0.05 M KH2PO4 (Potassium dihydrogen phosphate) (60:40 % v/v) (pH 3.0) **Flow rate:** 1.0 ml/min **Wave length:** 271 nm	60
58.	Application Of a Validated Stability-Indicating HPTLC Method For Simultaneous Quantitative Determination of Candesartan Cilexetil And Hydrochlorothiazide In Pharmaceutical Dosage Form	**Stationary phase:** pre-coated silica gel 60 F254 aluminium plates (20.0 cm x 10.0 cm, 250 µm) **Mobile Phase:** Toluene: Chloroform: Ethanol: Glacial acetic acid (2:7:1:0.1 % v/v/v/v) **R_f:** HCT: 0.12, CDT: 0.70 **Wave length:** 270 nm	61
59.	Validated HPTLC technique for simultaneous estimation of Candesartan celexitil and Hydrochlorothiazide in pharmaceutical dosage Form	**Stationary phase:** Silica gel 60F 254 TLC pre-coated aluminium plates (10 cm × 10 cm, 0.2 µm) **Mobile Phase:** Toluene: Ethyl acetate: Formic acid (85%) (6:4:1 % v/v/v) **R_f:** CAN: 0.39±0.01, HYD: 0.73±0.01 **Wave length:** 250 nm	62
62.	A validated stability indicating HPTLC method for simultaneous estimation of irbesartan and hydrochlorothiazide	**Stationary phase:** Silica gel 60 F254 (10 cm × 10 cm, 250 µm) **Mobile Phase:** Acetonitrile: Chloroform (5:6 % v/v) **R_f:** Irbesartan:0.27±0.03, HCT: 0.45±0.03 **Wave length:** 270 nm	63

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63.	HPTLC Method for the Simultaneous Estimation of Valsartan and Hydrochlorothiazide in Tablet Dosage Form	**Stationary phase:** Precoated silica gel 60F254 aluminium sheets (10 cm × 10 cm, 0.2 µm) **Mobile Phase:** Chloroform: Methanol: Toluene: Glacial acetic acid (6:2: 1: 0.1 % v/v/v/v) **Rf:** Valsartan: 0.36±0.04, HCT: 0.63±0.03 **Wave length:** 260 nm	64
65.	Method Validation for Simultaneous Quantification of Olmesartan and Hydrochlorothiazide in Human Plasma Using LC-MS/MS And Its Application Through Bioequivalence Study In Healthy Volunteers	**Stationary phase:** UNISOL C18 (150 cm * 4.6 mm, 5 µm) **Mobile Phase:** Methanol: Buffer solution (80: 20 % v/v) (2 mM ammonium acetate pH 5.5 adjusted by acetic acid) **Flow rate:** 0.8 ml/min **Wave length:** 281 nm **Detector:** Mass spectrometer	65
66.	LC-MS/MS Method for Quantitation of Hydrochlorothiazide and Nifedipine in Human plasma	**Stationary phase: C**18 guard cartridge (4 cm* 3.0 mm, 3.0µm) **Mobile phase:** methanol: 0.1% v/v formic acid: 5 mM aqueous ammonium formate (pH 6.0) **Wave length:** HCT:296.1nm and 205.2 nm NFP: 347.2 and 347.2-315.1nm **Detector:** Electrospray Ionization	66

II. CONCLUSION

This review describes the reported Spectroscopic and Chromatographic methods developed Dapagliflozin and Hydrochlorothiazide. As per this review, it was concluded that for Dapagliflozin and Hydrochlorothiazide, different Spectroscopic and chromatographic methods are available for single-single drugs. It was observed that still, any combination method of Dapagliflozin and Hydrochlorothiazide is not available. Thus, all methods were simple, accurate, economical, precise, and reproducible. Nearly all Methods were of RP-HPLC and UV absorbance detection because these methods provided with best available reliability, repeatability, analysis time, and sensitivity.

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