



**International Journal of Biology, Pharmacy
and Allied Sciences (IJBPAS)**

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

**AN UPDATED REVIEW ON ANALYTICAL METHODS FOR ESTIMATION
OF TENELIGLIPTIN AND DAPAGLIFLOZIN**

PATEL H, CHAKRABORTHY GS* AND PATEL P

Department of Quality Assurance, Parul Institute of Pharmacy & Research, Parul University,
Limda, Vadodara, Gujarat, India

*Corresponding Author: Dr. . G.S. Chakraborty: E Mail: g.chakraborty19159@paruluniversity.ac.in

Received 15th Feb. 2023; Revised 27th April 2023; Accepted 19th July 2023; Available online 1st March 2024

<https://doi.org/10.31032/IJBPAS/2024/13.3.7880>

ABSTRACT

Today diabetes become a global concern and recent report reveal that 422 million people suffer form the diabetes. 90 – 95 % case are type 2 diabetes. An update on spectrophotometric and chromatographic techniques for determining teneligliptin and dapagliflozin is the major goal of this review. The concentrations of Teneligliptin and Dapagliflozin are measured using UV, HPLC, HPTLC, UPLC, and LC/MS methods. Extensive studies describing various analytical methods have been conducted on dapagliflozin and teneligliptin. Spectrophotometric (UV) methods for Teneligliptin and Dapagliflozin alone and in combination with other drugs include parameters like a solvent, λ_{max} , Range, Regression Coefficient etc. chromatographic methods (HPLC, HPTLC, and UPLC) for Teneligliptin and Dapagliflozin alone and combination with other drug include parameter like stationary phase, mobile phase, flow rate, λ_{max} , Range, Regression Coefficient, retention time and Rf value etc. Additionally, this review gives comprehensive details on the circumstances for the separation of Teneligliptin and Dapagliflozin both alone and in combination with other medications, as well as the existence of its degradation products.

Keywords: Teneligliptin, Dapagliflozin, HPLC, HPTLC, LC-MS, UPLC, UV

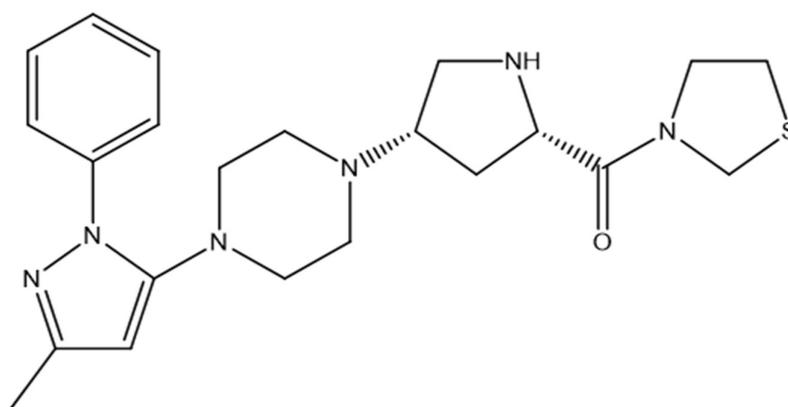
INTRODUCTION:

Teneligliptin is chemically [(2S,4S)-4- [4-(5-methyl-2-phenylpyrazol 3-yl) piperazin-1-yl] pyrrolidin-2-yl]- (1,3-thiazolidin-3-yl)

methanone, has a molecular mass of 426.6 g/mol and the chemical formula C₂₂H₃₀N₆O₅. It was removed through

excretion from the kidney and metabolism involving specific enzymes, which had a half-life of 24.2 hours in human plasma. It is a fine, white powder that dissolves freely in water, sparingly in methanol, only little in ethanol, and not at all in acetonitrile. Dipeptidyl peptidase-4 inhibitors, often known as "Gliptins," include the medication

teneligliptin, which is used to treat Type-2 mellitus diabetes. Teneligliptin inhibits the action of DPP-4 enzymes and slows down the rapid degradation of incretins. It also increases insulin synthesis by the pancreas and decreases glucagon levels which are counter-hormone of insulin, thereby further decreasing blood sugar levels.



teneligliptin

Dapagliflozin (DAPA) is a drug of gliflozin class. Chemically it is (2S, 3R, 4R, 5S, 6R)-2- (4-chloro-3- (4-methoxybenzyl) phenyl)-6- (hydroxymethyl)tetrahydro-2H-pyran-3, 4,5-triol with molecular formula of $C_{21}H_{25}ClO_6$ and 408.875g/ mol as its molecular weight. It is a white, crystalline substance that is soluble in DMSO, dimethylformamide, and ethanol, among other organic solvents. It melts at 55 and 60 °C. Dapagliflozin has antihyperglycemic effect as a selective sodium-glucose co-transporter subtype 2 (SGLT2) inhibitor. Compared to SGLT1, the co-transporter of

glucose in the gut, dapagliflozin specifically and strongly inhibits SGLT2, boosting glucose excretion through the urine and lowering blood sugar levels. Its mode of action is unrelated to insulin sensitivity and pancreatic cell activity, by inhibiting SGLT2, Dapagliflozin blocks reabsorption of filtered glucose in the kidney, increasing urinary glucose excretion and reducing blood glucose levels. Its mechanism of action is independent of pancreatic β cell function and modulation of insulin sensitivity [1].

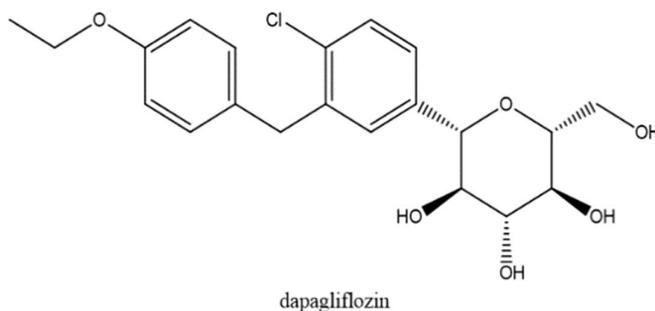


Table 1: Reported Method for Estimation of Teneiglipptin

Sr. No.	Drugs	Method	Method Description	Ref. No.
1.	Teneiglipptin and Remogliflozin	UV	Method: First-Order Derivative Method λ_{max} : ROSU: 243 nm TENE: 296 nm Range: 5-15 $\mu\text{g/ml}$	[2]
2.	Vildagliptin and Remogliflozin /Teneiglipptin and Remogliflozin	RP-HPLC	Column: Zorabx C18 Mobile Phase: Acetonitrile: Phosphate Buffer (58:42 v/v) Flow Rate:1.2 ml/min λ_{max} : 210 nm Retention Time: VLG: 1.26 min TNG: 1.65 min RGE: 2.48 min Range: VLG: 5-100 $\mu\text{g/ml}$ RGE: 5-100 $\mu\text{g/ml}$ TNG: 2-60 $\mu\text{g/ml}$	[3]
3.	Remogliflozin Etabonate and Teneiglipptin	RP- HPLC	Detector: UV Column: Cosmosil C18 column (250-4.6 mm) Mobile phase: Acetonitrile: water (80:20 v/v) Flow rate: 1ml/min λ_{max} : 245 nm Range: REMO:10-80 $\mu\text{g/ml}$ TENE: 1-8 $\mu\text{g/ml}$	[4]
4.	Teneiglipptin Hemihydrate Hydrobromide and Rosuvastatin Calcium	Stability indicating HPTLC	Stationary Phase: silica gel 60 F ₂₅₄ plates Mobile Phase: Ethyl acetate: Toluene: Acetonitrile: Formic Acid (6:3.5:0.5:0.2 v/v/v/v) Range: 50-500 ng/spot	[5]
5.	Teneiglipptin	GC-MS	Columns: (HP-5, DB-1, and SPB-624) HP-5: (30 m length \times 0.32 mm \times 1 μm film thickness) DB-1: (30 mm \times 0.32 mm \times 1 μm) Flow rate: 1.0-1.5 ml/min Range: 0.38-56 $\mu\text{g/ml}$	[6]
6.	Dapagliflozin and Teneiglipptin Hydrobromide Hydrate	UV	Model: Double beam UV/Visible spectrophotometer1700 Shimadzu Method: 1. simultaneous Equation: λ_{max} : DAPA: 223 nm TEN: 243 nm 2.Q-absorbance ratio λ_{max} : DAPA and TEN: 230 nm 3.First Derivative:	[7]

			DAPA: 251 nm Ten: 243 nm Range: TEN and DAPA: 5-75 µg/ml	
7.	Teneligliptin Hydrobromide and Metformin Hydrochloride	HPTLC	Stationary phase: silica gel G60 F254 aluminium sheets Mobile Phase: Methanol: Ammonium sulphate: Triethylamine (9: 2.7: 0.5 v/v/v) λ_{max} : 237 nm Range: TH: 4-28 ng/band MH: 100-700 ng/band	[8]
8.	Rosuvastatin and Teneligliptin Hydrobromide Hydrate	HPTLC	Stationary phase: Silica gel 60F 254 plates Mobile phase: Ethyl acetate: Toluene: Acetonitrile: Formic Acid (6:3.5:0.5:0.2 v/v/v/v) Rf values: ROS: 0.37 ± 0.01 TEN: 0.76 ± 0.01 Range: 50-500 ng/spot	[9]
9.	Rosuvastatin Calcium and Teneligliptin Hydrobromide Hydrate	UV	Model: UV-1800 Shimadzu Method: First-order Derivative: λ_{max} : TEN:230.03 ROSU:222.66 Range: 1-42 µg/ml	[10]
10.	Teneligliptin	UV	Model: I700AD Shimadzu λ_{max} : 246 nm Range: 5-10 µg/ml	[11]
11.	Teneligliptin and its impurity in Tablet	RP-HPLC	Column: C18 (250 mm x 4.6 mm, 5µm) Mobile Phase: Potassium dihydrogen phosphate: Acetonitrile (80:20 v/v) Flow Rate: 1 ml/min λ_{max} : 242 nm Range: TEN: 500-3000 µg/ml	
11.	Teneligliptin and its impurity in Tablet	RP-HPLC	Column: C18 (250 mm x 4.6 mm, 5µm) Mobile Phase: Potassium dihydrogen phosphate: Acetonitrile (80:20 v/v) Flow Rate: 1 ml/min λ_{max} : 242 nm Range: TEN: 500-3000 µg/ml Impurity B and Impurity G: 5-30 µg/ml	[12]
12.	Teneligliptin	RP-HPLC	Detector: UV Column: Zorbax C18column (100 mm × 4.6 mm, 5µm) Mobile phase: Acetonitrile: phosphate: buffer (55:45 v/v) Flow Rate: 1.2 ml/min λ_{max} : 210 nm Range: 10-100 mcg/ml	[13]
13.	Teneligliptin and Metformin HCl	RP-HPLC	Column: thermo, C18, (250 mm x 4.6 mm, 5 µm) Mobile Phase: KH ₂ PO ₄ : Methanol (60:40 v/v) Flow Rate: 1.0 ml/min λ_{max} : 280 nm Retention Time: TNG: 4.421 min MET: 3.421 min Range: TNG: 50 µg/ml -150 µg/ml MET Hcl: 50 µg/ml -150 µg/ml	[14]

14.	Teneligliptin	RP-HPLC	Column: Kromasil C18 analytical column (150 mm x 4.6 mm, 5.0 μ m) Mobile Phase: A: Acetonitrile: Water: Trifluoroacetic acid B: Acetonitrile: Trifluoroacetic acid Flow Rate: 1.0 ml/min λ_{\max} : 245 nm Retention Time: 11.2 min Range: 50-150 μ g/ml	[15]
15.	Teneligliptin	UV	Model: Shimadzu UV 1700 AD Solvent: Methanol λ_{\max} : 246 nm Range: 10-50 μ g/ml	[16]
16.	Teneligliptin and Metformin	UV	Model: UV-1800 double beam spectrophotometer (shimadzu) Method: Simultaneous equation method: Solvent: Methanol λ_{\max} : 237 nm Range: 5-25 μ g/ml	[17]
17.	Teneligliptin and Metformin	UV	Model: UV-1800 double beam Solvent Methanol Method: Simultaneous equation method: Solvent: Methanol λ_{\max} : TEN: 219.60 nm MET: 223.33 nm Range: TEN: 100 μ g/ml MET: 30 μ g/ml	[18]
18.	Teneligliptin	RP-UFLC	Column: Phenomenex Kinetex C18 (250 mm x 4.6 mm, 5 μ) Mobile Phase: Methanol: ACN (60:40 v/v) Range: 10-50 μ g/ml	[19]
19.	Teneligliptin and Teneligliptin Sulfoxide	LC-MS/MS	Range: TEN: 5-1000 ng/ml TEN SUL: 2.5-500 ng/ml Retention Time: TEN:1.83 min TEN SUL:1.53 min	[20]
20.	Teneligliptin Hydrobromide and Metformin Hydrochloride	UV	Method: 1. Simultaneous equation method λ_{\max} : TEN: 230 nm MET: 245nm 2.Absorbance ratio method λ_{\max} :TEN: 230 nm MET: 240nm Range: TEN: 2-12 μ g/ml MET: 5-55 μ g/ml	[21]
21.	Gemigliptin and Teneligliptin	UPLC	Column: C-18 (100 mm x 2.1 mm, 2.7 μ m) Retention Time: GEM: 6.56 min TEN: 4.12 min Range: GEM: 509.8-1529.4 ng/ml TEN: 510.6-1531.7 ng/ ml	[22]
22.	Teneligliptin	RP-HPLC	Column: Cosmosil C18(250 mm x 4.6 mm, 5 μ) Detector: UV-3000-M Mobile Phase: Phosphate buffer pH:3 (70:30 v/v) Flow Rate: 0.8 ml/min λ_{\max} : 246 nm Range:10-50 μ g/ml	[23]

23.	Teneligliptin	UV	<p>Model: UV-2450, Shimadzu, Japan Mobile Phase: Methanol: water (50:50 v/v) λ_{\max}: 245 nm Range: 10-35 $\mu\text{g/ml}$</p>	[24]
24.	Teneligliptin and Metformin	Stability indicating RP-HPLC	<p>Column: Kromasil C18 (250 mm x 4.6 mm, 5 μm) Mobile Phase: Buffer: Acetonitrile: Methanol (65:25:10 v/v/v) Diluent: Acetonitrile: water (50:50 v/v) Flow Rate: 1.0 ml/min λ_{\max}: 254 nm Retention Time: TNG: 2.842 min MET: 2.017 min Range: TNG: 5-30 $\mu\text{g/ml}$ MET: 125-750 $\mu\text{g/ml}$</p>	[25]
25.	Teneligliptin Hydrobromide Hydrate and Metformin Hydrochloride	UV	<p>Solvent: MET HCl: Methanol, Water TENE: water λ_{\max}: TEN: 233 nm MET HCl: 249.20 nm Range: 6-16$\mu\text{g/ml}$</p>	[26]
26.	Teneligliptin Hydrobromide Hydrate and Glimepiride	RP-HPLC HPTLC	<p>RP-HPLC: Mobile Phase: Acetonitrile: phosphate buffer (65:35 v/v) Flow rate: 1ml/min λ_{\max}: 246 nm Retention Time: Teneligliptin hydrobromide hydrate: 5.8 min Glimepiride: 9.41 min Range: Teneligliptin hydrobromide hydrate: 5-25 ng/ml Glimepiride: 0.25-1.25 ng/ml HPTLC: Stationary Phase: Merck TLC aluminium sheets of silica gel60F Mobile Phase: Toluene, Methanol, Triethylamine (1: 3: 1 v/v/v) λ_{\max}: 246 nm Rf value: Glimepiride: 0.48 Teneligliptin hydrobromide hydrate: 0.60 Range: Glimepiride: 2000-20000 ng/spot Teneligliptin hydrobromide hydrate: 100-1000 ng/spot</p>	[27]
27.	Teneligliptin Hydrobromide	Stability indicating RP-HPLC	<p>Column: Kromasil C8 Mobile Phase: Phosphate buffer (pH-5): Acetonitrile (70: 30 v/v) Flow Rate: 1.0ml/min λ_{\max}: 246 nm Range: 10-60 $\mu\text{g/ml}$</p>	[28]
28.	Teneligliptin	RP-HPLC UV	<p>HPLC System: Shimadzu HPLC series 1100 Column: Shodex C18-4E (250 mm x 4.6 mm, 5 μm) Mobile Phase: Methanol: Phosphate buffer (pH 7.2) (70:30 v/v) Flow Rate: 1 ml/min λ_{\max}: 245.6 nm Range: 10-60 $\mu\text{g/ml}$</p>	[29]

Table 2: Reported Method for Estimation of Dapagliflozin

Sr. No.	Title	Method	Method Description	Ref. No.
1.	Dapagliflozin	Stability indicating RP-HPLC	Stationary Phase: ZORBAX C ₁₈ column (250 x 4.6 mm, 5 µm) Mobile Phase: Phosphate Buffer: Acetonitrile: Methanol (55:40:05, %v/v/v) Flow Rate: 1.0 ml/min λ _{max} : 225 nm Retention Time: 2.12 min Range: 10-120 µg/ml	[30]
2.	Dapagliflozin Propanediol Monohydrate and Metformin Hydrochloride	Stability indicating HPTLC	Stationary Phase: Pre-coated silica gel 60F ₂₅₄ Mobile Phase: Methanol: Ethyl Acetate: Ammonium Acetate (6:4:0.1, v/v) λ _{max} : 220 nm Retention Factor: DAPA: 0.79 MET: 0.31 Range: DAPA: 20-100 ng/spot MET: 500-2500 ng/spot	[31]
3.	Dapagliflozin and Saxagliptin	Stability indicating RP-HPLC	Stationary Phase: BDS C ₁₈ column (150 x 4.6 mm, 5 µm) Mobile Phase: Ammonium Acetate Buffer: Acetonitrile (40:60, %v/v) Detector: DAD Flow Rate: 1.0 ml/min λ _{max} : 220nm Retention Time DAPA: 2.207 min SAXA: 2.889 min Range: DAPA: 0-15 µg/ml SAXA: 0-8 µg/ml	[32]
4.	Dapagliflozin and Saxagliptin	HPLC	Stationary Phase: SPOLAR C ₁₈ column (250 x 4.6 mm, 5 µm) Mobile Phase: Acetonitrile: Phosphate Buffer, pH 5.8 (26:74, %v/v) Detector: UV Detector Flow Rate: 0.96 ml/min λ _{max} : 236 nm Retention Time DAPA: 3.5 min SAXA: 5 min Range: DAPA: 0.2-300 µg/ml SAXA: 0.1-150 µg/ml	[33]
5.	Dapagliflozin and Metformin Hydrochloride in pharmaceutical dosage form	Stability indicating HPLC	Stationary Phase: THERMO fisher ODS C ₁₈ column Mobile Phase: Water: Acetonitrile (65:35, %v/v) Detector: UV-Visible Detector Flow Rate: 1.0 ml/min λ _{max} : 240 nm Retention Time: DAPA: 5.41 min MET: 2.13 min Range: DAPA: 1-6 µg/ml MET: 100-600 µg/ml	[34]
6.	Dapagliflozin in pharmaceutical dosage formulations	RP-HPLC	Stationary Phase: C ₁₈ column (250 x 4.6mm, 5µm) Mobile Phase: Acetonitrile: Water (40:60, %v/v) Detector: UV-Visible Detector Flow Rate: 1.0 ml/min λ _{max} : 277 nm. Retention Time: 7.029 min Range: 1-16 µg/ml	[35]
7.	Dapagliflozin Forced	RP-HPLC	Stationary Phase: C ₁₈ column (250 x 4.6mm, 5µm) Mobile Phase: Acetonitrile: Water (50:50, %v/v)	[36]

	degradation		<p>Detector: UV-Visible Detector Flow Rate: 0.5 ml/ min λ_{max}: 235 nm Retention Time: 4.11 min Range: 10-1200 ng/ml</p>	
8.	Dapagliflozin and Saxagliptin in fixed-dose combination	UV	<p>UV- Spectrophotometer: Lab India model-3000+ series λ_{max}: DAPA: 276 nm SAXA: 222 nm Solvent: Phosphate Buffer pH 6.8 Range: DAPA: 5-25 $\mu\text{g/ml}$ SAXA: 5-25 $\mu\text{g/ml}$</p>	[37]
9.	Dapagliflozin and Saxagliptin	HPTLC	<p>Stationary Phase: Silica gel 60 F₂₅₄ Aluminium plates Mobile Phase: Hexane: Methanol: Ethyl Acetate (4:2:4, v/v/v) λ_{max}: DAPA: 225 nm SAXA: 210 nm Retention Factor: DAPA: 0.6 SAXA: 0.18 Range: 50-550 ng/spot</p>	[38]
10.	Dapagliflozin, Saxagliptin, Metformin	HPLC	<p>Stationary Phase: Agilent C₁₈ column (4.6 x 250 mm) Mobile Phase: Acetonitrile: Acidified aqueous phase Detector: DAD Flow Rate: 0.8 ml/min λ_{max}: 230 nm Retention Time: DAPA: 7.17 min SAXA: 3.78 min MET: 2.83 min Range: DAPA: 20-160 $\mu\text{g/ml}$ SAXA: 80-300 $\mu\text{g/ml}$ MET: 10-120 $\mu\text{g/ml}$</p>	[39]
11.	Dapagliflozin, Saxagliptin, Metformin	HPTLC	<p>Stationary Phase: Merck HPTLC silica gel plates Mobile Phase: Chloroform: Methanol: Water: Acetic Acid (7.4:2.6:0.5:0.01, v/v) λ_{max}: 224 nm Retention Factor: DAPA: 0.66 SAXA: 0.50 MET: 0.14 Range: DAPA:250-3000 ng/spot SAXA:700-7500 ng/spot MET:150-1750 ng/spot</p>	[40]
12.	Dapagliflozin and Metformin Hydrochloride	UV	<p>UV- Spectrophotometer: ELICO Double beam SL 210 UV-Visible spectrometer Method: Q absorption ratio method λ_{max}: DAPA: 232 nm MET: 222 nm Solvent: Water Range: DAPA: 2-32 $\mu\text{g/ml}$ MET: 1-20 $\mu\text{g/ml}$</p>	[41]
13.	Metformin, Dapagliflozin and Saxagliptin	Stability indicating RP-UPLC	<p>Stationary Phase: BEH C₁₈ column (50 x 2.1 mm, 1.7 μm) Mobile Phase: Water: Methanol (70:30 %v/v) Flow Rate: 0.3 ml/min λ_{max}: 222 nm Retention Time: MET: 1.06 min DAPA: 1.50 min</p>	[42]

			<p>SAXA: 2.17 min Range: MET: 250-1500 µg/ml DAPA: 2.5-15 µg/ml SAXA: 1.25-37.5 µg/ml</p>	
14.	Dapagliflozin in bulk drug and marketed tablet formulation	Stability indicating HPTLC	<p>Stationary Phase: Merck HPTLC plates precoated with silica gel 60 F₂₅₄ Mobile Phase: Methanol: Toluene: Ammonium Acetate (6.9:3:0.1, v/v/v) λ_{max}: 250 nm Range: 100-1000 ng/band Retention Factor: 0.29 ± 0.05</p>	[43]
15.	Dapagliflozin in bulk and tablet dosage form	HPTLC	<p>Stationary Phase: Merck TLC plates Silica gel 60F₂₅₄ (10 x10 cm) Mobile Phase: Chloroform: Methanol (9:1, v/v) λ_{max}: 223 nm Range: 400-1200 ng/band Retention Factor: 0.21 ± 0.004</p>	[44]
16.	Dapagliflozin and Metformin Hydrochloride	RP-HPLC	<p>Stationary Phase: Cosmosil C₁₈ column (250mm × 4.6mm, 5µm) Mobile Phase: Methanol: Potassium dihydrogen phosphate buffer with pH 3.0 (80:20, %v/v) Detector: UV Detector Flow Rate: 1.0 ml/min λ_{max}: 228nm Retention Time: DAPA: 5.2 min MET: 3.6 min Range: DAPA: 1-5 µg/ml MET: 100-500 µg/ml</p>	[45]
17.	Metformin and Dapagliflozin	LC-MS/MS	<p>Stationary Phase: Reversed-phase ACE 5CN (150 × 4.6 mm, 5 µm) column Mobile Phase: Acetonitrile-15 mM Ammonium Acetate, pH 4.5 (70:30% v/v) Range: DAPA:0.10-200 ng/ml MET:1.00-2000 ng/ml</p>	[46]
18.	Dapagliflozin and Saxagliptin	UV	<p>UV- Spectrophotometer: UV-spectrophotometric method λ_{max}: DAPA: 276 nm SAXA: 222 nm Solvent: Phosphate buffer pH 6.8 Range: DAPA: 5-25 µg/ml SAXA: 5-25 µg/ml</p>	[47]
19.	Saxagliptin and Dapagliflozin	RP-HPLC	<p>Stationary Phase: Discovery C₁₈ column (250 x 4.6 mm, 5 µm) Mobile Phase: Acetonitrile: Ortho phosphoric acid (0.1%) (50:50, %v/v) Flow Rate: 0.98 ml/min λ_{max}: 210 nm Retention Time: DAPA: 3.49 min SAXA: 2.81 min Range: DAPA: 25-150 µg/ml SAXA: 12.5-75 µg/ml</p>	[48]
20.	Saxagliptin and Dapagliflozin	HPLC	<p>Stationary Phase: Eclipse XDB C₁₈ (150 x 4.6 mm, 5 µm) Mobile Phase: 0.1% ortho phosphoric acid: acetonitrile (50:50, %v/v) Detector: UV Flow Rate: 1.0 ml/min λ_{max}: 254 nm Retention Time DAPA: 5.17 min</p>	[49]

			SAXA: 2.74 min Range: DAPA: 0.05-2 µg/ml SAXA: 0.01-0.5 µg/ml	
21.	Empagliflozin, Dapagliflozin, Canagliflozin	HPLC	Stationary Phase: Agilent Zorbax RX-C ₈ column (150 mm x 4.6 mm, 5 µm) Mobile Phase: Acetonitrile: Aqueous 0.1% trifluoroacetic acid (40:60, %v/v) Detector: DAD Flow Rate: 1.0 ml/minutes λ _{max} : 210 nm Retention Time EMPA: 2.047 min DAPA: 2.819 min CANA: 4.889 min Range: EMPA: 2-2500 ng/ml DAPA: 3.5-2500 ng/ml CANA: 1.1-2500 ng/ml	[50]
22.	Metformin, Gliclazide, Pioglitazone, Dapagliflozin, Empagliflozin, Saxagliptin, Teneligliptin and Linagliptin	HPLC	Stationary Phase: Waters Reliant™ HPLC Columns (250 mm x 4.6 mm, 5 µm) Mobile Phase: Acetonitrile: Water (6:4, %v/v) Detector: DAD Flow Rate: 1.0 ml/min λ _{max} : 230 nm Retention Time: MET: 1.31 min SAXA: 6.44 min LINA: 4.96 min TENELI: 1.96 min EMPA: 3.42 min PIO: 2.71 min DAPA: 8.41 min GLI: 7.49 min Range MET: 10-70 µg/ml GLI, PIO, SAXA, TENE: 50-350 µg/ml LINA: 10-70 µg/ml EMPA: 30-210 µg/ml DAPA: 30-210 µg/ml	[51]
23.	Dapagliflozin and major degradation product and Metformin.	UHPLC	Stationary Phase: C ₁₈ column (100 x 2.1 mm, 2.2 µm) Mobile Phase: Potassium dihydrogen Phosphate Buffer pH (3.5): Acetonitrile (50:50, %v/v) Detector: UV Flow Rate: 0.4 ml/min λ _{max} : 225 nm Retention Time DAPA: 1.5 min MET: 0.9 min Range: DAPA: 1-50 µg/ml MET: 0.5-100 µg/ml	[52]
24.	Dapagliflozin in its tablet dosage form	Stability indicating HPLC	Stationary Phase: Zorbax Eclips XDB C ₁₈ (150 x 4.6 mm, 5 µm) Mobile Phase: Buffer: Acetonitrile: Methanol (60:37:03, %v/v/v) Flow Rate: 1.0 ml/min λ _{max} : 220 nm Retention Time: 1.63 min Range: 12-36 µg/ml	[53]
25.	Dapagliflozin	RP-HPLC	Stationary Phase: Princeton C ₁₈ column Mobile Phase: Acetonitrile: Triethylamine (50:50, % v/v) Flow Rate: 1.0 ml/min λ _{max} : 224 nm Retention Time: 5.16 min Range: 10-70 µl/ml	[54]

CONCLUSION:

The presented review depicts the information about the various methods available in the literature for the determination of Teneligliptin and Dapagliflozin including that the different analytical methods are reported for estimation Teneligliptin and Dapagliflozin individual and other combination like UV Spectroscopy, HPTLC, HPLC, UPLC, LC-MS etc. Hence all methods found to be simple, accurate, economic, precise and reproducible in nature. This review will help in future to develop the analytical methods for this new combination and also gives the knowledge about its characteristics of both drugs. This review provided a summary of the most recent, cutting-edge analytical techniques for determining Teneligliptin and Dapagliflozin, which will be useful for future studies on this combination. Knowing the important solvents and their available set of instruments in the analytical laboratory would also be helpful after reading the review.

REFERENCES:

- [1] Tripathi KD. Essentials of medical pharmacology. JP Medical Ltd; 2013 Sep 30.
- [2] Drashti A. Mandale, Chairesh Shah and Rakesh Jatt. Simultaneous Estimation of Rosuvastatin and Teneligliptin in Synthetic Mixture by UV Spectrometer. World Journal

of Pharmacy and Pharmaceutical Sciences, 2022, 11(7), 84-93.

- [3] Attimarad, M., Venugopala, K. N., Nair, A. B., Sreeharsha, N., & Deb, P. K. Experimental design approach for quantitative expressions of simultaneous quantification of two binary formulations containing remogliflozin and gliptins by RP-HPLC. Separations, 2022, 9(2), 21-23.
- [4] Vashi Dhara and Gamit Dharmistha. Development and validation of RP-HPLC method for simultaneous estimation of Remogliflozin Etabonate and Teneligliptin in pharmaceutical dosage form. World Journal of Pharmacy and Pharmaceutical Sciences, 2022,11(8), 04-16.
- [5] Saiyed Javedmiya Mukhtiyarmiya and Dr. Sibaji Sarkar. Stability indicating Analytical Method Development and Validation for Simultaneous Estimation of Teneligliptin Hemihydrate Hydrobromide and Rosuvastatin Calcium in Synthetic Mixture. World Journal of Pharmacy and Pharmaceutical Sciences, 2022,11(1), 16-52.
- [6] M. Manivannan, P. Parthiban and P. Ilayaraja. Analytical Method Development and Validation of

- Genotoxic Impurity p-Anisaldehyde in Teneiglipitin using GC-MS. *Rasayan Journal of Chemistry*, 2022, 15(3), 55-60.
- [7] Patel A, Jadeja P, Mashru R. Analytical Method Development and Validation For Simultaneous Estimation of Dapagliflozin and Teneiglipitin Hydrobromide Hydrate From Synthetic Mixture By Three Different UV Spectrophotometric Methods. *World Journal of Pharmaceutical Research*, 2022, 11(7), 70-83.
- [8] Patel M, Patel D, Shah U, Kachhiya H. Simultaneous quantification of teneiglipitin hydrobromide and metformin hydrochloride: an improved HPTLC method with implementation of Plackett-Burman design. *Journal of Chemical Metrology*, 2021, 15(1), 75-85.
- [9] Saiyed Javedmiya Mukhtiyarmiya and Dr. Sibaji Sarkar. Stability indicating analytical method development and validation for simultaneous estimation of teneiglipitin hemihydrate hydrobromide and rosuvastatin calcium in synthetic mixture. *world journal of pharmacy and pharmaceutical sciences*, 2021, 11(1), 16-52.
- [10] Vyas A, Godhaniya J, Patel A, Patel A, Patel N, Shah S, Sheth D. Development and Validation of UV-Spectroscopic First Order Derivative Method for Simultaneous Estimation of Rosuvastatin Calcium and Teneiglipitin Hydrobromide Hydrate in Synthetic Mixture. *Chemical Methodologies*, 2021, 5(4), 17-23.
- [11] Maruthi R, Chandan RS, Barath M, Datta GN, D'silva M, Kumari KM, Ahmad F, Geetha R. Analytical method development and validation of teneiglipitin by UV spectroscopy. *Research Journal of Pharmacy and Technology*, 2021, 14(1), 75-80.
- [12] Bhoomi Dineshkumar Patel, Nidhi J. Dharsandiya, Ankit Chaudhary. Development and Validation of RP-HPLC Method for Estimation of Teneiglipitin and its Impurity in Tablet: *International Journal of Pharmaceutical Sciences Review and Research*, 2021, 69(2), 127-133.
- [13] Gunnam, S., Choppari, T., Lakshmi, N. C., Cherla, P. M., & Siddiqui, S. I. Development and Validation of Teneiglipitin Stereoisomers by HPLC Using Cellulose Based Immobilized

- Polysaccharide Chiral Stationary Phase. *Current Pharmaceutical Analysis*, 2021,17(10), 1317-1322.
- [14] Shirisha. K, Amina begum. K, Sravya. K, Swarna. K, Neelima. K, S. Srinivasa Rao. Analytical Method Development and Validation of Teneligliptin and Metformin HCl by Using RP-HPLC Method: *Journal of Global Trends in Pharmaceutical Sciences*, 2020,11(3), 8051-56.
- [15] Biswas, B., Kumar, M., Sharma, J. B., Saini, V., & Bhatt, S. Method Development and Validation for Estimation of Teneligliptin in Tablet Dosage Form by RP-HPLC. *Research Journal of Pharmacy and Technology*,2020, 13(4), 1774-1778.
- [16] Maruthi, R., Chandan, R. S., Barath, M., Datta, G. N., D'silva, M., Kumari, M. K., ... & Geetha, R. Analytical method development and validation of teneligliptin by RP-UFLC. *Research Journal of Pharmacy and Technology*,2020, 13(9), 4035-4040.
- [17] Naik, R. R., & Pratyusha, S. M. Simultaneous spectrophotometric determination of compounds: Application to an anti-diabetic formulation of Teneligliptin and Metformin. *Research Journal of Pharmacy and Technology*,2020, 13(4), 1938-1942.
- [18] Annapurna, M. M., Pratyusha, S. M., & Naik, R. R. New validated spectrophotometric methods for the combined dosage form of Teneligliptin and Metformin. *Research Journal of Pharmacy and Technology*, 2020,13(1), 270-274.
- [19] Annapurna, M. M., Naik, R. R., & Pratyusha, S. M. Simultaneous spectrophotometric determination of compounds: Application to an anti-diabetic formulation of Teneligliptin and Metformin. *Research Journal of Pharmacy and Technology*, 2020, 13(4), 1938-1942.
- [20] Prafulla M Patil, Savita J Sonawane and Sanjay J Surana. UV-AUC Spectrophotometric Method for Quantitative Estimation of Teneligliptin. *Current Pharmaceutical Analysis*, 2019, 3(6), 332-339.
- [21] Maruthi R, Chandan RS, Barath M, Datta GN, D'silva M, Kumari MK, Ahmad F, Geetha R. Analytical method development and validation of teneligliptin by RP-

- UFLC. Research Journal of Pharmacy and Technology, 2020, 13(9), 35-40.
- [22] Park, J. W., Kim, K. A., & Park, J. Y. Development of a liquid chromatography/tandem-mass spectrometry assay for the simultaneous determination of teneligliptin and its active metabolite teneligliptin sulfoxide in human plasma. Biomedical Chromatography, 2020, 34(2), 21-29.
- [23] Chandra, A., Rathod, R., Ali, F., Prakash, A., Kumar, R., & Singh, G. N. Development and Validation of a Rapid and Sensitive Method for the Simultaneous Estimation of Gemigliptin and Teneligliptin in Bulk and Dosage Forms by Using Liquid Chromatography-tandem Mass Spectrometry. Current Pharmaceutical Analysis, 2020, 16(8), 1104-1111.
- [24] Lokhande, D. P. Analytical method development and validation of teneligliptin by using RP-HPLC with ICH guidelines. Int. J. Trend. Sci. Res. Dev., 2019, 3(1), 259-263.
- [25] Pritam S Jain, Prafulla M Patil, Savita J Sonawane and Sanjay J Surana. UV-AUC Spectrophotometric Method for Quantitative Estimation of Teneligliptin. Current Pharmaceutical Analysis, 2019, 3(6), 332-339.
- [26] Vetapalem, R., Yejella, R. P., & Atmakuri, L. R. Development and validation of a stability indicating RP-HPLC method for simultaneous estimation of teneligliptin and metformin. Turkish Journal of Pharmaceutical Sciences, 2020, 17(2), 141.
- [27] Annapurna, M. M., Pratyusha, S. M., & Naik, R. R. New validated spectrophotometric methods for the combined dosage form of Teneligliptin and Metformin. Research Journal of Pharmacy and Technology, 2020, 13(1), 270-274.
- [28] Jadhav, S. B., Kupkar, S. K., Dharam, D. L., Jangam, A. M., & Chaudhari, P. D. Development and validation of RP-HPLC and HPTLC methods for simultaneous estimation of sitagliptin phosphate and metformin hydrochloride in bulk and dosage form. Ind J Pharm Edu Res, 2019, 47(1), 13-16.
- [29] Lata P. Kothapalli, Rachana S. Bhimanwar, Ankita P. Malani, Asha B. Thomas. Validated Stability Indicating High

- Performance Liquid Chromatography (HPLC) Method for Determination of Teneligliptin Hydrobromide in Presence of its Degradation Products: Application to its Kinetic Degradation Study. *Pharmaceutical Resonance*, 2019, 1(2), 39-43.
- [30] Lokhande DP. Analytical method development and validation of teneligliptin by using RP-HPLC with ICH guidelines. *Int. J. Trend. Sci. Res. Dev.*, 2019, 3(1), 259-63.
- [31] Murugesan, A. R. U. L. S. E. L. V. A. N., & Annapurna, M. Simple Quantified and Validated Stability Indicating Stress Degradation Studies of Oral Anti-Diabetic Agent Dapagliflozin by RP-HPLC Method. *Int J App Pharm*, 2022, 14(1), 231-7.
- [32] Surati, J. S., & Patel, V. B. Study of the degradation behavior of dapagliflozin propanediol monohydrate and metformin hydrochloride by a stability-indicating high-performance thin-layer chromatographic method. *JPC-Journal of Planar Chromatography-Modern TLC*, 2020, 34(3), 243-252
- [33] Manasa, M., & Aanandhi, V. M. Stability indicating simultaneous method development and validation of dapagliflozin and saxagliptin by RP-HPLC. *Research Journal of Pharmacy and Technology*, 2021, 14(2), 1045-1049.
- [34] Gurralla, S., Raj, S., Subrahmanyam, C. V. S., & Anumolu, P. D. Multivariate optimization of liquid chromatographic conditions for determination of dapagliflozin and saxagliptin, application to an in vitro dissolution and stability studies. *Future Journal of Pharmaceutical Sciences*, 2021, 7(1), 1-11.
- [35] Dhale C R, Rao J R. Stability indicating HPLC Method Development and Validation for the Simultaneous Estimation of Metformin Hydrochloride and Dapagliflozin in api and Pharmaceutical Dosage Form. *Int. Res. J. Pharm.*, 2021, 12 (8), 1-10.
- [36] Krishnaveni Nagappan et al. A Quantitative, Sensitive and Rapid Validated Analytical RP-HPLC Method for the Estimation of Dapagliflozin in Bulk and Pharmaceutical Dosage Formulations. *Int. J. Res. Pharm. Sci.*, 2020, 11(2), 2543-2548.
- [37] Ameeruzzafar, El-Bagory, I., Alruwaili, N. K., Imam, S. S.,

- Alomar, F. A., Elkomy, M. H., ... & Elmowafy, M. Quality by design (QbD) based development and validation of bioanalytical RP-HPLC method for dapagliflozin: forced degradation and preclinical pharmacokinetic study. *Journal of Liquid Chromatography & Related Technologies*, 2020, 43(1-2), 53-65.
- [38] Patel, A., Omray, D. L., & Soni, P. Method development for simultaneous estimation of Dapagliflozin and saxagliptin in fixed-dose combination and validation on UV spectroscopy. *J Pharm*, 2020, 9(3), 2536-43.
- [39] Ahmed, H. M., Omar, M. A., Batakoushy, H. A., & Hamid, M. A. A. HPTLC-densitometric analysis of selected antidiabetic drugs in presence of their degradation products. *Microchemical Journal*, 2020, 154, 104560.
- [40] El-Shoubashy, O. H. E., Beltagy, Y. A. E. M., Issa, A. E., & El-Kafrawy, D. S. Comparative study of HPLC-DAD and HPTLC for the simultaneous determination of a new multitarget antidiabetic ternary mixture in combined tablets. *JPC–Journal of Planar Chromatography–Modern TLC*, 2020, 33, 59-70.
- [41] El-Shoubashy, O. H. E., Beltagy, Y. A. E. M., Issa, A. E., & El-Kafrawy, D. S. Comparative study of HPLC-DAD and HPTLC for the simultaneous determination of a new multitarget antidiabetic ternary mixture in combined tablets. *JPC–Journal of Planar Chromatography–Modern TLC*, 2020, 33, 59-70.
- [42] Bhavyasri, K., Surekha, T., & Sumakanth, M. A Novel Method Development and Validation of Dapagliflozin and Metormin Hydrochloride using Simultaneous Equation Method by UV–Visible Spectroscopy in Bulk and Combined Pharmaceutical Formulation including Forced Degradation Studies. *Journal of Pharmaceutical Sciences and Research*, 2020, 12(8), 1100-1105.
- [43] Karthikeyan, V. A Stability Indicating RP-UPLC Method for the Simultaneous Estimation of Metformin, Dapagliflozin and Saxagliptin in Bulk and Tablet Dosage Form (Doctoral dissertation, JKK Nattraja College of Pharmacy, Kumarapalayam) 2020.

- [44] Snehal R. Karmankar, Madhukar R. Tajne. A Validated Stability indicating High Performance Thin Layered Chromatographic Method for the Analysis of Dapagliflozin in Bulk Drug and Marketed Tablet Formulation. *Asian Journal of Chemistry*, 2019, 31(7), 1457-1460.
- [45] Nachiket S. Dighe, Priyanka R. Varade, Ganesh S. Shinde, Priya S. Rao. Quantitative Estimation and Validation of Dapagliflozin and Metformin Hydrochloride in Pharmaceutical Dosage form by RP-HPLC. *Asian J. Research Chem*, 2019, 12(3), 136-142.
- [46] Shah, P. A., Shrivastav, P. S., Shah, J. V., & George, A. Simultaneous quantitation of metformin and dapagliflozin in human plasma by LC-MS/MS: Application to a pharmacokinetic study. *Biomedical Chromatography*, 2019, 33(4), 44-53.
- [47] Bhadauria, R. S., & Agarwal, V. Development and Validation of UV Spectroscopic Method for Simultaneous Estimation of Dapagliflozin and Saxagliptin in marketed formulation. *Journal of Drug Delivery and Therapeutics*, 2019, 9(4), 1160-1164.
- [48] Gundala, A., Prasad, K. V. S. R. G., & Koganti, B. Application of quality by design approach in RP-HPLC method development for simultaneous estimation of saxagliptin and dapagliflozin in tablet dosage form. *Brazilian Journal of Pharmaceutical Sciences*, 2019, 55.
- [49] Donepudi, S., & Achanta, S. Simultaneous estimation of saxagliptin and dapagliflozin in human plasma by validated high performance liquid chromatography-ultraviolet method. *Turkish Journal of Pharmaceutical Sciences*, 2019, 16(2), 227.
- [50] Mabrouk, M. M., Soliman, S. M., El-Agizy, H. M., & Mansour, F. R. Ultrasound-assisted dispersive liquid-liquid microextraction for determination of three gliflozins in human plasma by HPLC/DAD. *Journal of Chromatography B*, 2020, 1136, 121932.
- [51] Kant, R., Bodla, R. B., Kapoor, G., & Bhutani, R. Optimization of a single HPLC-PDA method for quantifying metformin, gliclazide, pioglitazone, dapagliflozin,

empagliflozin, saxagliptin, linagliptin and teneligliptin using central composite design. *Bioorganic Chemistry*, 2019, 9(1), 103-111.

- [52] Zaghary, W. A., Mowaka, S., & Hendy, M. S. Kinetic degradation study of dapagliflozin coupled with UHPLC separation in the presence of major degradation product and metformin. *Chromatographia*, 2019, 82, 777-789.
- [53] Vaghela, Y. V., Patani, P., & Patel, D. Development and Validation of Stability Indicating Estimation Method of Dapagliflozin in Its Tablet Dosage Form. *Int. J. Res. Anal. Rev*, 2019, 6, 206-213.
- [54] Mante, G. V., Hemke, A. T., & Umekar, M. J. RP-HPLC Method for Estimation of Dapagliflozin from its Tablet. *International Journal of Chem. Tech Research*, 2018, 11(01), 242-248.