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ORIGINAL ARTICLE



Review on Analytical Method for Quantitative Estimation of Dapagliflozin Propanediol Monohydrate, Sitagliptin Phosphate Monohydrate and Metformin Hydrochloride

¹Aditi Patel, *Pinkal Patel²

Parul Institute of Pharmacy and Research, Parul University, Vadodara, Gujarat-391760, India Corresponding Author: Pinkal Patel *Email id: pinpharmacy@gmail.com

ABSTRACT

This review focuses on the analytical techniques used to determine the quantitative amounts of Dapagliflozin Propanol Monohydrate, Sitagliptin Phosphate Monohydrate, and Metformin Hydrochloride in various pharmaceutical dosage forms. The three active pharmaceutical ingredients (APIs) mentioned above are frequently used to treat type 2 diabetes mellitus. The final pharmaceutical formulations' quality, efficacy, and safety depend on the precise measurement of these ingredients. This review covers a broad spectrum of analytical methods, including as spectroscopic, chromatographic, and hybrid techniques. Along with its validation parameters and regulatory issues, each method's benefits, drawbacks, and scope are reviewed. This review intends to help researchers, analysts, and regulatory agencies choose suitable approaches for the quantitative analysis by giving a thorough overview of different analytical methodologies.

Keywords: Dapagliflozin Propanediol Monohydrate, Sitagliptin Phosphate Monohydrate, Metformin Hydrochloride, Analytical methods

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INTRODUCTION

Over the course of human history, there have been advancements in our understanding and classification of diabetes mellitus. A notable development was the separation of Type 1 and Type 2 diabetes in 1936, which was followed by the identification of Type 2 diabetes as a crucial element of the metabolic syndrome in 1988. The latter discovery clarified the intricate interplay between genetics, environment, and behaviour influencing its development [1] [2].

It is a sodium-glucose co-transporter 2 inhibitor that stops the kidneys from reabsorbing glucose. A first-generation, selective SGLT inhibitor called dapagliflozin prevents the transport of glucose while being around 100 times more selective for SGLT2 than SGLT1 [3].

Sitagliptin functions by preventing the breakdown of incretin hormones like GLP-1 (glucagon-like peptide-1) by the enzyme DPP-4. Sitagliptin raises levels of GLP-1 and GIP (glucose-dependent insulinotropic polypeptide) via inhibiting DPP-4. By enhancing insulin release and reducing the synthesis of glucose in the liver, these incretin hormones aid in blood sugar regulation [4].

Although the precise mechanism of action of Metformin is not entirely understood, it is known that it largely reduces glucose synthesis in the liver, lowers intestinal glucose absorption, and raises insulin sensitivity in peripheral organs like muscle cells [5].

Official Methods for Dapagliflozin Propanediol Monohydrate:

There is no official method for Dapagliflozin Propanediol Monohydrate in any pharmacopoeia.

DRUG PROFILE:

Table: 1 Drug Profile					
Drug	Dapagliflozin Propanediol	Sitagliptin Phosphate	Metformin Hydrochloride [8]		
Name	Monohydrate [6]	Monohydrate [7]			
Mol.	$C_{21}H_{25}ClO_6 \cdot C_3H_8O_2 \cdot H_2O$	$C_{16}H_{15}F_6N_5O\cdot H_3PO_4\cdot H_2O$	C ₄ H ₁₁ N ₅ · HCl		
Formula					
Chemical		F			
Structure	QH	F + H ₂ PO ₄ • H ₂ O			
	HO OH H ₃ C				
	•H ₂ O	N N			
	HO	ŕ ví			
		CFa			
IUDAC	(29) propage 1.2 dial	(2D) 2 amino 1 [2	2 (diaminamathylidana) 11		
IUPAL	(25)-propane-1,2-dioi (25 3R 4R 55 6R)-2- $(4-ch)$ oro-	(5K)-5-dillillo-1-[5- (trifluoromethyl)-6.8-dihydro-	dimethylguanidine:hydrochlorid		
Name	3-[(4-	5H-[1,2,4]triazolo[4,3-	e		
	ethoxyphenyl)methyl]phenyl}	a]pyrazin-7-yl]-4-(2,4,5-	c		
	-6-(hydroxymethyl)oxane-	trifluorophenyl)butan-1-			
	3,4,5-triol hydrate	one;phosphoric acid; hydrate			
Mol	502 99 g/mol	165.63 g/mol	523 32 g/mol		
Weight	302.99 g/ mor	105.05 g/ 1101	323.32 g/ mor		
weight					
State	Solid	Solid	Solid		
Appearanc	White to light yellow	white to off-powder,	White,		
e		crystalline powder	crystalline powder		
Solubility	Dimethyl Sulphoxide ethanol,	ethanol, acetone and	Water, acetonitrile, and		
	and dimethyl formamide	acetonotrile	methanol		
brand	Forxiga Edistride	Ianuvia	Gluconhage Gluconhage XB		
name	i or Aigu, Duistriue	Junavia	Fort met. Glumetza		
CAS	960404-48-2	654671-77-9	657-24-9		
Number	500101102	0310/17/7	037 21 7		
Melting	74-78° C	216-219° C	221-228° C		
point					
рКа	12.57	8.78	12.4		
Log P	2.11	1.26	2.64		
<u></u>	2000	2002	2500		
Storage	-20°C	-20°C	-25°C		
Category	Sodium - glucose Cotransport-	Dipentidyl Pentidase-4(DPP-	Biguanide (AMPk Activator)		
Gutegory	2 (SGLT- 2) Inhibitors	4) Inhibitors	Eigunnae (min Kneuvator)		

Official methods for Sitagliptin Phosphate Monohydrate:

Table: 2.1 Official methods fo	r Sitagliptin Phos	phate Monohydrate
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Sr.no.	Title	Method	Description	Ref. no.
1	Indian	Liquid	Stationary Phase: A stainless steel	[9]
	Pharmacopoeia	Chromatography	column (15 cm × 4.6 mm, 5 μm)	
	2022		Mobile Phase: A mixture of 15	
			volumes of acetonitrile and 85 velum of	
			buffer solution prepared by diydrogen	
			phosphate in about 900ml of water,	
			adjusted to pH 2 with orthophosphoric	
			acid and diluted to 1000 ml with water.	
			Flow rate: 1 ml/min.	
			Detection Wavelength: 205 nm	
			Injection volume: 20 μl	

	Tubici II		riction min my ar ocmorriae	
1	Indian Pharmacopoeia	Liquid	Stationary Phase: A stainless steel	[10]
	2022	Chromatography	column (30 cm × 4 mm, 10μm)	
			Mobile Phase: A solution containing	
			0.087 % w/v of Sodium pentane	
			sulphonate and 0.12% w/v of sodium	
			chloride, adjusted to pH 3.5 using 1%	
			v/v solution of orthophosphoric acid.	
			Flow rate: 1 ml/min	
			Detection Wavelength: 218 nm	
			Injection volume: 20 μl	
2	British Pharmacopoeia	Liquid	Stationary Phase: Stainless steel	[11]
	2009	Chromatography	column (12.5cm × 4.5cm, 5µm)	
			Mobile Phase: A 1.7 %w/v solution	
			of ammonium dehydrogenase	
			Orthophosphate adjusted to pH 3.0	
			with orthophosphoric acid.	
			Flow rate: 1 ml/min	
			Detection wavelength: 218nm	
			Injection volume: 20 μl	

Official methods for Metformin Hydrochloride: Table: 2.2 Official methods for Metformin Hydrochloride

Reported Methods for Dapagliflozin Propanediol Monohydrate:

Table: 2.3 Reported Methods for Dapagliflozin Propanediol Monohydrate

Sr.no	Title	Method	Description	Ref.
				no.
1	Dapagliflozin	UV-	Model: Jasco V-630 and Shimadzu-1700	[12]
		visible	Solvent: Distilled water	
			Detection wavelength: 224 nm	
			Linearity range: 2– 10 µg/ml	
2	Dapagliflozin	RP-	Stationary Phase: Waters C18 column (25 cm	[13]
		HPLC	× 4.6 mm, 5 μm)	
			Mobile Phase: Acetonitrile: Phosphate Buffer	
			(40:60 %v/v)	
			Flow Rate: 1.0 ml/min	
			Detection Wavelength: 237 nm	
			Retention time: 3.461 min	
			Injection Volume: 20µl	
			Detector: PDA detector	
3	Saxagliptin + Dapagliflozin	RP-	Stationary Phase : C18 column (250 mm × 4.6	[14]
		HPLC	mm, 5 μm)	
			Mobile Phase : 0.1% Orthophosphoric acid:	
			Acetonitrile (50:50%v/v)	
			Flow Rate: 0.98 ml/min	
			Detection Wavelength: 210 nm	
			Retention time : 2.81 min and 3.49 min	
			Injection Volume : 20µl	
			Detector: PDA (Shimadzu, SPD-20A) detector	
4	Dapagliflozin	RP-	Stationary Phase: ZORBAX (C18) column (250	[15]
		HPLC	mm × 4.6 mm, 5 μm)	
			Mobile Phase: Phosphate Buffer: Acetonitrile:	
			Methanol (55:40:05 %v/v/v)	
			Flow Rate: 1 ml/min	
			Detection Wavelength: 225 nm	
			Retention time : 2.12 ± 0.5 min	
			Injection Volume : 10 μl	
			Detector: UV detector	

5	Dapagliflozin + Metformin	RP-	Stationary Phase: C18, X- bridge column,	[16]
		HPLC	Xterra. Phenomenex Luna C18 (4.6 mm × 150	
			mm, 5 μm)	
			Mobile Phase: Water : Acetonitrile	
			25:75%v/v)	
			Flow Rate: 0.5 ml/min	
			Detection Wavelength: 240 nm	
			Retention time: 3.202 and 5.463 mins	
			Injection Volume: 10µl	
			Detector: UV detection	
6	Dapagliflozin +	RP-	Stationary Phase: C18 column (Acquity UPLC	[17]
	Saxagliptin	UPLC	ethylene bridge hybrid (BEH) (2.1 mm× 100	
			mm, 1.7 μm)	
			Mobile Phase: 0.1% Ortho Phosphoric Acid:	
			Acetonitrile (40: 60%v/v)	
			Flow Rate: 0.3 ml/min	
			Detection Wavelength: 254 nm	
			Detector: PDA detection	
7	Dapagliflozin +	UV-	Model: Labindia model-3000+ series	[18]
	Saxagliptin	visible	Solvent: Phosphate Buffer (pH 6.8)	
			Detection Wavelength : Saxagliptin: 222 nm,	
			Dapagliflozin: 276 nm	
8	Dapagliflozin +	UV-	Model: UV/Visible spectrophotometer (1700)	[19]
	Teneligliptin	visible	A Shimadzu	
	Hydrobromide Hydrate		Solvent: Distilled Water	
			Detection Wavelength : Dapagliflozin: 223 nm,	
			Teneligliptin Hydrobromide Hydrate: 243 nm	
9	Dapagliflozin Propanediol	RP-	Stationary Phase: C18 column Bridge Ethylene	[20]
		UPLC	Hybride (BEH) (50 mm × 2.1 mm, 1.7μm).	
			Mobile Phase: Acetonitrile: Water (40:60	
			%v/v)	
			Flow Rate: 0.5ml/min	
			Detection Wavelength: 223 nm	
			Injection Volume : 10 µl	
			Detector: Photodiode array detector	50.15
10	Dapagliflozin	HPLC	Stationary Phase: agilent C18 (4.6mm ×	[21]
			150mm , 5μm)	
			Mobile Phase: Acetonitrile : Di-Potassium	
			Hydrogen Phosphate (pH-6.5) (40: 60% v/v)	
			Flow Rate: 1ml/min	
			Detection Wavelength: 223 nm.	
			Injection Volume : 10 µl	
			Detector : Photodiode array detector	

Reported Methods for Sitagliptin Phosphate Monohydrate:

Table: 2.4 Reported Methods for Sitagliptin Phosphate Monohydrate

ſ	11	Sitagliptin + Metformin	UV-	Model: Shimadzu 1800	[22]
		Hydrochloride	Vis	Solvent: Distilled Water	
				Detection Wavelength: 231nm MTF, 267nm SPM	
				Linearity range: MTF: 2-10 µg/ml, SPM: 20-60 µg/ml	
I	12	Sitagliptin Phosphate	RP-	Stationary Phase: Shimadzou® C18 column (250 mm × 4.6	[23]
			HPLC	mm, 5μm)	
				Mobile Phase: Methanol :Water (40:60 % v/v)	
				Flow Rate: 1 ml/min	
				Detection Wavelength: 260 nm	
				Retention time: 1.96 and 3.70 min	
				Injection Volume : 20 μl	
				Detector: PDA detector	

13	Sitagiiptin Phosphate Monohydrate + Metformin Hydrochloride	UPLC	Stationary Phase : BEH C8 (100 mm × 2.1 mm, 1.7μm) Mobile Phase : Buffer 10 mm Potassium Diydrogen Phosphate And 2 mm Hexane-1-Sulfonic Acid Sodium salt (pH adjusted to 5.50 with diluted Phosphoric Acid) and Acetonitrile Flow Rate : 0.2 ml/min Detection Wavelength : 210 nm Retention time : 1.96 and 3.70 min Injection Volume : 0.5 ul	[24]
14	Metformin Hydrochloride + Sitagliptin Phosphate	RP- HPLC	Stationary Phase: C18 (100mm × 4.6 mm, 5 μm) Mobile Phase: Acetonitrile: Methanol: Phosphate buffer (35:20:45 % v/v/v) Flow Rate: 1 ml/min Detection Wavelength: 254 nm	[25]
15	sitagliptin phosphate	UV- Vis	Model: Labindia UV/VIS double beam spectrophotometer Solvent: Distilled Water Detection Wavelength: 267 nm	[26]
16	Sitagliptin Phosphate	RP- HPLC	Stationary Phase: Phenomenex RP C18 (250mm × 4.6mm, 5 μm) Mobile Phase: Water : Acetonitrile (40:60 % v/v) Flow Rate: 1 ml/min Detection Wavelength: 272 nm Injection Volume : 20 μl Detector: PDA detector	[27]
17	Sitagliptin + Simvastatin	RP- HPLC	Stationary Phase: Prontosil,ODS,C18 (250 × 4.6mm, 5 μm)Mobile Phase: Water : Methanol : Acetonitile (30:50:20%v/v/v)Flow Rate: 0.80 ml/minDetection Wavelength: 261 nmInjection Volume: 10 μlDetector: UV detector	[28]

Reported Methods for Metformin Hydrochloride:

Table: 2.5 Reported Methods for Metformin Hydrochloride

18	Metformin	UV-Vis	Model: Shimadzu UV-1800 240V	[29]
			Solvent: Distilled Water	
			Detection Wavelength: 234 nm	
			Linearity: 10 - 50 μg/ml	
19	Metformin Hydrochloride	UV-Vis	Model: Shimadzu UV mini1700	[30]
			Solvent: 0.01N NaOH	
			Detection Wavelength: 233 nm	
			Linearity: 01-25 μg/ml	
20	Metformin Hydrochloride	UV-Vis	Model: Shimadzu UV1700	[31]
			Solvent: Methanol	
			Detection Wavelength : 233 nm	
			Linearity: 08-13 μg/m	
21	Metformin Hydrochloride	RP-	Stationary Phase: Cosmosil C18 (250 mm × 4.6	[32]
		HPLC	mm, 5μm)	
			Mobile Phase: Phosphate buffer (pH-3):	
			Methanol : (30:70 %v/v)	
			Flow Rate: 1 ml/min	
			Detection Wavelength: 238 nm	
			Retention time: 4.2 min	
			Injection Volume : 10 μl	
			Detector: UV detector	
			Linearity: 10-50 μg/ml	
22	Metformin Hydrochloride	RP-	Stationary Phase: Hypersil ODS C18, (250mm ×	[33]
		HPLC	4.6mm, 5μm)	
			Mobile Phase: Phosphate buffer (pH- 5.75) :	
			Acetonitrile (35:65 %v/v)	
			Flow Rate: 1 ml/min	
			Detection Wavelength: 233 nm	

			Retention time: 7.168 min	
			Linearity:50-150 µg/ml	
23	Metformin Hydrochloride	RP-	Stationary Phase: Zorbax - SCX C18, (250 mm ×	[34]
		HPLC	4.6 mm, 5 μm)	
			Mobile Phase: Acetonitrile: Ammonium-	
			Dihydrogen Phosphate buffer (pH-3) (50:50	
			(0, 0, 0)	
			Detection Wavelength: 218 pm	
			Retention time: 11 12 min	
			Linearity: 20-60 µg/ml	
24	Metformin Hydrochloride	RP-	Stationary Phase: Inertsil - Extend C18, (250 mm	[35]
	5	HPLC	× 4.6 mm, 5 μm)	
			Mobile Phase: Acetonitrile: 1-Octane sulfonic	
			acid (20:80 %v/v)	
			Flow Rate: 1 ml/min	
			Detection Wavelength: 232 nm	
			Retention time: 10.78 min	
			Linearity: 01-250 µg/ml	
25	Metformin Hydrochloride +	HPTLC	Stationary Phase: Silica gel 60 F254	[36]
	Pioglitazone + Glibenclamide		Mobile Phase: Glacial acetic acid: 1,4-dioxane :	
			Butanol (2:3:5 $\%$ V/V/V)	
			Detection wavelengtn : 226 nm	
			Linearity: Mettormin hydrochloride: 2000- 18000 ug/ml Diaglitazona: 60.540 ug/ml	
			Cliberclamide: $10-100 \text{ µg/ml}$	
			Rf value : Metformin hydrochloride: 0.15	
			Pioglitazone: 0.72. Glibenclamide: 0.85	
26	Metformin Hydrochloride +	HPTLC	Stationary Phase: Silica Gel 60 F254	[37]
	Glibenclamide		Mobile Phase: Water : Methanol : 0.4 % Sodium	
			Sulphate in Water (5:7:11 %v/v/v)	
			Detection Wavelength: Glibenclamide: 238 nm,	
			Metformin Hydrochloride: 232 nm	
			Linearity: Glibenclamide: 250-1750 µg/ml,	
			Metformin Hydrochloride: 250-1750 µg/ml	
			Rf value : Glibenclamide: 0.80, Metformin	
27			Hydrochloride: 0.27	[20]
27	Sitagliptin + Metformin	HPILC	Stationary Phase: Precoated silica gel 60 F254	[38]
	Hydrochloride		Mobile Phase: Glacial Aceuc Acid: Ammonia : Methanol (0.2:0.4:0.4.0($x/x/x$)	
			$\mathbf{Detection Wavelength} \cdot 214 \text{ nm}$	
			Detection wavelength. 214 mm	
			Linearity: Metformin Hydrochloride: 1000-	
			Linearity : Metformin Hydrochloride: 1000- 11000 ug/ml. Sitagliptin: 100-1100 ug/ml	
			Linearity : Metformin Hydrochloride: 1000- 11000 μg/ml, Sitagliptin: 100-1100 μg/ml Rf value : Metformin Hydrochloride: 0.28.	
			Linearity : Metformin Hydrochloride: 1000- 11000 μg/ml, Sitagliptin: 100-1100 μg/ml Rf value : Metformin Hydrochloride: 0.28, Sitagliptin: 0.61	
28	Gliclazide + Metformin	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) :	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity:MetforminHydrochloride:1000-11000 μg/ml, Sitagliptin:100-1100 μg/mlRfvalue:MetforminHydrochloride:0.28,Sitagliptin:0.61Stationary Phase:Silica gel 60 F254Silica gel 60 F254Silica gel 60 F254Silica gel 60 F254Mobile Phase:AmmoniumSulphate(0.25%):Acetonitrile:Ethanol:Toluene(3:4:4:4)	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v)	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm Linearity: Gliclazide: 200-1000µg/ml, Metformin	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm Linearity: Gliclazide: 200-1000µg/ml, Metformin Hydrochloride: 200-1000µg/ml	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm Linearity: Gliclazide: 200-1000µg/ml, Metformin Hydrochloride: 200-1000 µg/ml Rfvalue: Gliclazide: 0.69, Metformin Hydrochloride: 0.27	[39]
28	Gliclazide + Metformin Hydrochloride	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm Linearity: Gliclazide: 200-1000µg/ml, Metformin Hydrochloride: 200-1000 µg/ml Rfvalue: Gliclazide: 0.69, Metformin Hydrochloride: 0.37	[39]
28	Gliclazide + Metformin Hydrochloride Metformin Hydrochloride +	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm Linearity: Gliclazide: 200-1000µg/ml, Metformin Hydrochloride: 200-1000 µg/ml Rfvalue: Gliclazide: 0.69, Metformin Hydrochloride: 0.37 Stationary Phase: Silica gel 60 F254 Mobile Phase: Watar : Classial Acatia Acid	[39]
28	Gliclazide + Metformin Hydrochloride Metformin Hydrochloride + Sitagliptin Phosphate	HPTLC	Linearity: Metformin Hydrochloride: 1000- 11000 µg/ml, Sitagliptin: 100-1100 µg/ml Rf value: Metformin Hydrochloride: 0.28, Sitagliptin: 0.61 Stationary Phase: Silica gel 60 F254 Mobile Phase: Ammonium Sulphate (0.25%) : Acetonitrile: Ethanol: Toluene (3:4:4:4 %v/v/v/v) Detection Wavelength: 228 nm Linearity: Gliclazide: 200-1000µg/ml, Metformin Hydrochloride: 200-1000 µg/ml Rfvalue: Gliclazide: 0.69, Metformin Hydrochloride: 0.37 Stationary Phase: Silica gel 60 F254 Mobile Phase: Water : Glacial Acetic Acid : Butanol (2:2:6 %v/v/v)	[39]

			Detection Wavelength: 227 nm	
			Linearity: Metformin Hydrochloride: 500-10000	
			ug/ml. Sitagliptin Phosphate: 50-1000 ug/ml	
			Rf value: Metformin Hydrochloride: 0.35.	
			Sitagliptin phosphate: 0.75	
30	Empagliflozin+ Linagliptin +	UPLC	Stationary Phase: RSLC 120 C18 Column (100	[41]
	Metformin		mm × 2.1mm, 2.2μm)	
			Mobile Phase: Methanol : Potassium dihydrogen	
			phosphate buffer (pH-4) (50:50%v/v)	
			Flow Rate: 0.4 ml/min	
			Detection Wavelength: 225nm	
31	Metformin + Empagliflozin	RP-	Stationary Phase: C18 BEH (Ethylene Bridged	[42]
		UPLC	Hybrid) UPLC (100 mm × 2.1mm, 1.7μm)	
			Mobile Phase: Methanol : -0.1%OPA buffer	
			(PH3.4) with 0.1 N NAOH solution (60:40%v/v)	
			Flow Rate: 0.25 ml/min	
			Detection Wavelength: 254 nm	
			Retention Time: Empagliflozin: 3.471min,	
			Metformin: 0.882min	
			Detector: PDA	
32	Metformin HCl +	UPLC	Stationary Phase : BEH C18 Column (2.5 mm × 50	[43]
	Empagliflozin		mm, 3μm)	
			Mobile Phase: Phosphate buffer (pH-3) :	
			Acetonitrile (30:70% v/v)	
			Flow Rate: 0.3ml/min	
			Detection Wavelength: 220 nm	
			Retention time: Empagliflozin: 1.294 min,	
			Metformin HCl: 0.879 min	

CONCLUSION

In conclusion, this study has offered a thorough examination of various analytical techniques for the quantitative assessment of Dapagliflozin Propanediol Monohydrate, Sitagliptin Phosphate Monohydrate, and Metformin Hydrochloride in pharmaceutical dosage forms. We have assessed the appropriateness, accuracy, and precision of existing techniques, including UV-Vis spectroscopy HPLC, RP-HPLC, HPTLC, UPLC, Stability-indicating RP-HPLC Method, and others, for pharmaceutical quality control.

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