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Analytical Method Development and Validation of Antidiabatic drugs Dapagliflozin Propanediol Monohydrate and Gliclazide

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ABSTRACT:

This study reports the Method Development and Validation for Anti Diabetic Drugs By RP-HPLC. The drug analysis is playing a vital position within the improvement of medicine, their manufacture and therapeutic use for the simultaneous estimation of medicine present in dosage forms, lot, of suitable techniques are adopted like uv – spectrophotometer HPLC. The chromatographic separation was achieved on a C18 column using a mobile phase composed of acetonitrile and an aqueous buffer containing 0.1% formic acid, delivered at a controlled flow rate. The detection wavelength was set to optimize the response of all three analytes. Forced degradation studies under acidic, basic, oxidative, thermal, and photolytic conditions demonstrated the method's capability to effectively resolve the drugs from their degradation products, confirming its stability-indicating nature. Validation according to ICH guidelines revealed excellent linearity, precision, accuracy, and robustness over the specified concentration ranges, with recovery rates between 97% and 102%. This method offers a rapid, sensitive, and reproducible analytical procedure suitable for routine quality control of tablet formulations containing these active pharmaceutical ingredients.

Keywords: Method development, Validation, RP-HPLC method, Gliclazide, Dapagliflozin Propanediol Monohydrate, Anti Diabetic Drugs

1. INTRODUCTION[1]

Diabetes Mellitus

Derived from the Greek "diabetes" meaning "to pass through" and the Latin "mellitus" meaning "sweet," diabetes mellitus has a historical origin. The term "diabetes" was initially introduced by Apollonius of Memphis between 250 and 300 BC. Multiple ancient cultures, including the Greeks, Indians, and Egyptians, noticed the sweet quality of urine in people with diabetes, giving rise to the name "Diabetes Mellitus."

The literature review disclosed that a Dapagliflozin is SGLT2 inhibitors (Sodium-Glucose Co-Transporter 2 inhibitors) and works by blocking the reabsorption of glucose by the kidneys, promoting the excretion of excess glucose through urine. Gliclazide is sulfonylurea class of insulin secretagogues and it helps to control diabetes by increases the amount of insulin your pancreas makes. Insulin reduces blood sugar by helping the cells use/store glucose. The combination of dapagliflozin and gliclazide is more effective than many other marketed drugs because it provides strong glycemic control, low risk of hypoglycemia, weight benefits, and cardiovascular and renal protection, all in a cost-effective.

Diabetes is a metabolic condition, characterized by higher than-normal blood glucose levels. It includes different subtypes or categories, such as:

1.Type 1 diabetes mellitus (T1DM): Typically presents in children or adolescents and results from defective insulin secretion.

2.Type 2 diabetes mellitus (T2DM): Commonly affects middle-aged and older adults and is associated with prolonged hyperglycemia due to lifestyle and dietary factors.

3.Maturity-onset diabetes of the young (MODY): A rare form of diabetes with a genetic basis.

4.Gestational diabetes: Occurs during pregnancy and can affect both the mother and the baby.

5.Neonatal diabetes: A rare condition that develops in the first six months of life.

6.Secondary diabetes: Results from underlying medical conditions or medication use, such as steroids.

Adapting to healthy lifestyle and monitoring of blood glucose levels allow individuals to be free from long term complications of diabetes such as diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, increased risk of heart attack/stroke, etc.

Antidiabetic medications are designed to regulate blood sugar levels by enhancing insulin release or addressing insulin resistance, helping to maintain blood sugar within healthy ranges

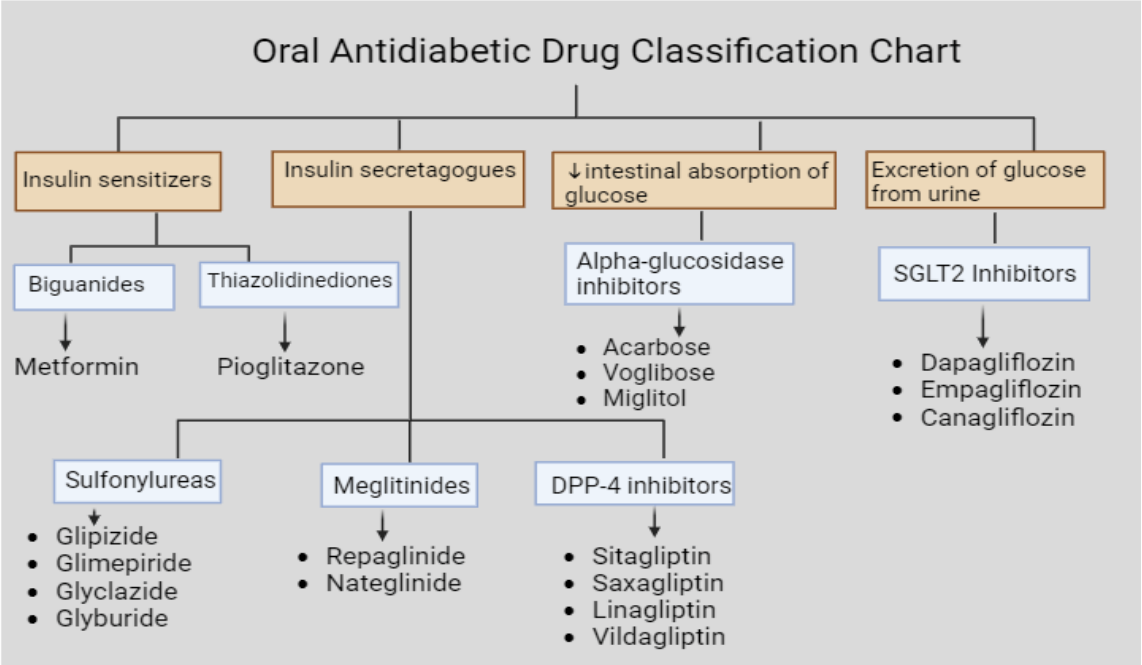
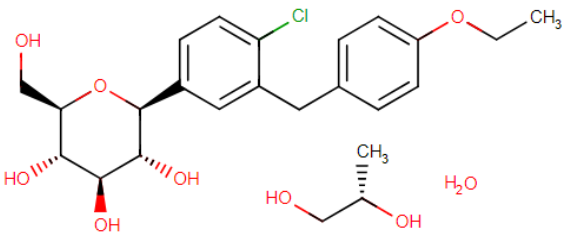


Figure 1: Classification of Anti-diabetic drug

2. DRUG INTRODUCTION

2.1 Dapagliflozin Propanediol Monohydrate

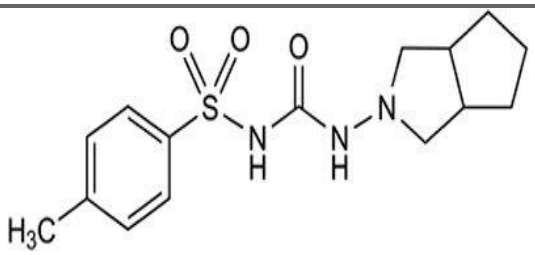
Table 1: Drug profile of Dapagliflozin propanediol monohydrate

Name	**Dapagliflozin propanediol monohydrate**[2,3]
Chemical Structure	
Molecular Formula	$C_{24}H_{35}C_lO_9$
Molecular Weight	503.0 g/mol
IUPAC Name	(2S)-propane-1,2-diol (2S,3R,4R,5S,6R)-2-{4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl}-6-(hydroxymethyl)oxane-3,4,5-triol hydrate
Solubility	solubility of water is approximately 0.39 mg/mL and soluble in methanol.
pKa (Strongest Basic)	9.86
pKa (Strongest Basic)	-3
Log P	2.5
Melting Point	74° - 78°C
Pharmacological Class	Gliclazide belongs to drug class sulfonylurea and is used for the treatment of non-insulin- dependent diabetes mellitus (NIDDM). Dapagliflozin is a sodium-glucose cotransporter 2 (SGLT2) inhibitor, and it was the first SLGT2 inhibitor to be approved, is also indicated for managing NIDDM. SGLT2 inhibitors in dual combination with sulfonylurea is recommended by the American Diabetes Association and European Association for the Study of Diabetes to treat patients with NIDDM.
Dosage Form:	Dapagliflozin is marketed under the trade names of Forxiga® in the EU91 and in the US as Farxiga®. 18

	It is available in 5 mg or 10 mg strengths. It is also available in combination with metformin, under the trade name of Xigduo®, in 5 mg/850 mg or 10 mg/850 mg (dapagliflozin/metformin) strengths.
Pharmacodynamics	
Mechanism of Action	Dapagliflozin inhibits SGLT2, lowering blood glucose. When combined with sulfonylurea, it reduces HbA1c in type 2 diabetes patients. It also alleviates heart failure by reducing intravascular volume, relieving cardiac workload and improving left ventricular function.
Therapeutic indication	Non-Insulin-Dependent Diabetes Mellitus. Additionally, dapagliflozin has been found to have benefits in reducing the risk of heart failure in certain patients with type 2 diabetes
Route of Administration	Oral
Adverse effects	Feeling or being sick Stomach pain Feeling thirsty Mild skin rash
Pharmacokinetics	
Bioavailability	High oral bioavailability (approximately 78%).
Distribution	It primarily targets the kidneys, where it inhibits SGLT2.
Metabolism	Dapagliflozin undergoes minimal hepatic metabolism
Excretion	It is primarily eliminated unchanged through the urine

2.2 Gliclazide

Table 2: Drug profile of Gliclazide

Name	**Gliclazide** [4,5]
Chemical Structure	
Molecular Formula	$C_{15}H_{21}N_3O_3S$
Molecular Weight	323.41 g/mol
IUPAC Name	1-(3,3a,4,5,6,6a-hexahydro-1H-cyclopenta[c]pyrrol-2-yl)-3-(4-methylphenyl) sulfonylurea
Solubility	Soluble in methanol.
pKa (Strongest Basic)	5.8
Log P	1.52
Melting Point	160-166°C
Pharmacological Class	sulfonylurea class of insulin secretagogues
Dosage Form	Dosage should be initiated at 40mg (1/2 tablet) daily and may be increased, if necessary, up to 320 mg daily (4 tablets). Doses up to 160mg daily may be taken in a single dose, preferably at the same time each morning. Doses in excess of 160mg should be taken in divided doses in the morning and the evening. The severity of glycaemia will determine the dosage, requiring adjustment to obtain the optimal response at the lowest dosage. Use of gliclazide does not obviate the necessity of regulating diet.
Pharmacodynamics	
Mechanism of Action	Gliclazide is a sulfonylurea medication used to treat type 2 diabetes. Its mode of action involves stimulating insulin secretion from pancreatic beta cells, increasing cellular uptake of glucose, and reducing blood sugar levels. This helps control diabetes by enhancing the body's response to insulin and promoting better glucose utilization.

Route of Administration	Oral
Therapeutic indication	Non-Insulin-Dependent Diabetes Mellitus
Adverse effects	Hypoglycaemia, Headache
Pharmacokinetics	
Absorption	Gliclazide is absorbed in the gastrointestinal tract and can be affected by food.
Distribution	It targets pancreatic beta cells and binds to plasma proteins in the bloodstream.
Metabolism	Gliclazide is metabolized in the liver, mainly by the CYP2C9 enzyme.
Excretion	The drug is primarily eliminated via the kidneys,

3. LITERATURE REVIEW

Official Methods

Table 3: Official method for Gliclazide

Sr. No.	Title	Chromatographic Parameters	References
1.	Indian pharmacopoeia 2022	Mobile Phase: Triethylamine: trifluoroacetic Acid: acetonitrile: Water: 45:55%v/v. Column: Stainless steel C18 Flow Rate: 0.9 ml/min. Wavelength: 235nm.	6
2.	European pharmacopoeia	Mobile Phase: Triethylamine: Trifluoroacetic acid: acetonitrile: Water (0.1:0.1:45:55 v/v/v/v). Column: C18 Flow Rate: o.9ml/min. Wavelength: 235nm.	7
3.	British pharmacopoeia 2023	Mobile Phase: Triethylamine: Trifluoroacetic acid: acetonitrile: Water (0.1:0.1:45:55). %v/v. Column: C8 Flow Rate: 0.9 ml/min. Wavelength: 235 nm.	8
4.	Japanese pharmacopoeia 2016	Mobile Phase: Water: Acetonitrile: Triethylamine: Trifluoroacetic acid (550:450:1: 1). %v/v. Column: C18 25 Flow Rate: Adjust so that Rt will be 14 minutes Wavelength: 235nm	9

- Dapagliflozin monograph is not given in IP, USP, BP, JP or EP.

Table 4: Published method for Dapagliflozin

Sr. No.	Title	Chromatographic Parameters	References
1.	Development and validation of dapagliflozin by RP-HPLC method and its degradation studies	Mobile phase: Buffer: acetonitrile (60:40) %v/v. Column: Hypersil BDS Flow rate: 1 mL/min. Wavelength:245nm.	10
2.	RP-HPLC Method for Estimation of Dapagliflozin from its Tablet	Mobile phase: Acetonitrile: 0.1% Triethylamine (pH-5.0) in the ratio of 50:50 %v/v Column: Princeton C18 column Flow rate: 1 mL/min Wavelength: 224 nm	11
3.	A New RP-HPLC Method Development and Validation of	Mobile phase: Phosphate buffer: acetonitrile: 60:40 %v/v. Column: Waters C18	12

	Dapagliflozin in Bulk and Tablet Dosage Form	Flow rate: 1.0 mL/min. Wavelength: 237 nm.	
4.	Analytical Method Development, Validation, and Forced Degradation Study of Dapagliflozin by RP-HPLC	Mobile phase: acetonitrile: water (52:48) %v/v. Column: Kromasil 100-5-C8 Flow rate: 1.0 mL/min Wavelength:224nm	13
5.	Development and Validation of stability-Indicating RP-HPLC method for determination of Dapagliflozin	Mobile Phase: Mixture of acetonitrile and ortho phosphoric acid (55:45) %v/v. Column: BDS column Flow Rate: 1 ml/min Wavelength: 245 nm	14

Table 5:Published methods for Dapagliflozin in combination with other drug

Sr. No.	Title	Chromatographic Parameters	References
1.	Development and validation of QBD assisted RP-HPLC method for dapagliflozin and metformin HCL in bulk and its combined dosage for	Mobile phase: ACN (Acetonitrile): KH2PO4 pH 4.5 (65:35% v/v) Column: Intersil ODS column Flow rate: 1 mL/min Wavelength: 222 nm and 232 nm for Dapagliflozin and Metformin HCl respectively.	15
2.	Simultaneous Estimation of Saxagliptin and Dapagliflozin in Human Plasma by Validated High Performance Liquid Chromatography - Ultraviolet Method	Mobile Phase : 0.1% ortho phosphoric acid :acetonitrile : 50:50%v/v. Column: Eclipse XDB C18 Flow Rate: 1 mL/min. Wavelength:260nm	16
3.	Application of quality by design approach in RP-HPLC method development for simultaneous estimation of saxagliptin and dapagliflozin in tablet dosage form	Mobile Phase: Acetonitrile: Water (60:40) %v/v. Column: Xterra RP18 Flow Rate: 1 mL/min Wavelength: 248 nm	17
4.	RP-HPLC Method for Dapagliflozin and Metformin HCL in Bulk and Combined Formulation	Mobil Phase: water : methanol:50:50%v/v. Column: Phenomenex C18 Flow Rate: 1.0 mL/min. Wavelength: 230 nm.	18
5.	Stability Indicating RP-HPLC Method for Determination of Saxagliptin and Dapagliflozin in Bulk and Tablet Dosage Forms	Mobile Phase: Methanol and 0.1% o-phosphoric acid (60:40). %v/v. Column: RP C18 (Thermo) Flow Rate: 1 ml/min. Wavelength: 220 nm.	19
6.	Stability-indicating HPLC method development and validation for simultaneous estimation of metformin, dapagliflozin, and saxagliptin in bulk drug and pharmaceutical dosage form	Mobile phase: A mixture of 60% phosphate buffer (pH = 3) and 40% acetonitrile. % v/v. Column: Kromasil C18 Flow rate: 1.0 mL/min Wavelength:230nm	20
7.	Development and Validation of a New HPLC Method for the Simultaneous Estimation of Saxagliptine and Dapagliflozin and Its Application in Pharmacokinetic Studies	Mobile Phase: Phosphate buffer (pH 4) : Acetonitrile (50:50 v/v). %v/v. Column: XTerra C18 Flow Rate: 1ml/min Wavelength:225nm	21

Table 6: Published methods for Gliclazide

Sr. No.	Title	Chromatographic Parameters	References
1.	Analytical method validation of gliclazide related substance by HPLC method	Mobile Phase: acetonitrile: water:450ml:550ml%v/v. Column: LiChroCART Supersher RP-8 Flow Rate: 1.2ml/min Wavelength :235 nm	22
2.	Development and Evaluation of Robust RP-HPLC Method for Gliclazide Estimation Integrating Box Behnken Design	Mobile Phase: Methanol: 0.02 M potassium dihydrogen orthophosphate (70:30 %v/v) Column: Phenomenex C18 column Flow Rate: 1.2 ml/min Wavelength: Detection at 210 nm	23
3.	HPLC Method for Determination of Gliclazide in Human Serum	Mobile Phase: Acetonitrile: methanol: water (50:30:20,% v/v), pH 3 Column: C18 column Flow rate: 1.2ml/min Wavelength: 230nm	24
4.	HPLC Estimation of Gliclazide in Formulations and In Pharmacokinetic Studies	Mobile Phase: Water 0.1% w/v: sodium phosphate monobasic (pH adjusted to 2.1 using phosphoric acid): acetonitrile (34:66) %v/v. Column: RP C-18 column Flow rate: 1.2ml/min Wavelength: 230 nm	25

Table 7: Published methods for Gliclazide in combination with other drugs

Sr. No.	Title	Chromatographic Parameters	References
1.	HPLC method for simultaneous determination of metformin and gliclazide	Mobile Phase: 20 mM ammonium phosphate buffer (pH 3.5): acetonitrile:45:55 (%v/v). Column: Alltima CN column using isocratic mode. Flow rate:1mL/min Wavelength:227nm	26
2.	RP-HPLC Method for the Simultaneous Estimation of Rosiglitazone and Gliclazide in Tablets	Mobile Phase: ammonium phosphate buffer: acetonitrile: methanol : 50:35:15 %v/v. Column: Phenomenex Gemini C18 Flow Rate: 1 mL/min Wavelength:254nm.	27
3.	Simultaneous HPLC Assay of Gliclazide and Ciprofloxacin in Plasma and its Implementation for Pharmacokinetic Study in Rats	Mobile Phase: acetonitrile: KH_2PO_4 (0.01 M, 0.1%v/ v: triethylamine, pH 2.7) %v/v. Column: C18 column Flow Rate: 1 mL/min Wavelength: 229 nm gliclazide:277 nm ciprofloxacin	28
4.	HPLC Method Development, Validation and Application to Determining In-Vitro Effect of Levofloxacin on the Availability of Gliclazide	Mobile Phase: Methanol: phosphate buffer (pH 3.0) %v/v. Column: Stainless steel analytical column C18 Flow Rate: 0.8 mL/min Wavelength: 228 nm	29
5.	Rapid RP-HPLC Method for Simultaneous Estimation of Some Antidiabetics; Metformin, Gliclazide and Glimepiride in Tablets	Mobile Phase: MeOH:0.025M KH_2PO_4 (pH 3.20) with ortho-phosphoric acid:70:30 (%v/v). Column: BDS Hypersil C8 Flow Rate: 1 mL/min. Wavelength: 235 nm.	30
6.	Development and validation of a	Mobile phase: Methanol: water (65:35 %v/v, pH adjusted to 3.0	31

	reversed-phase HPLC method for the determination of lisinopril and gliclazide in pharmaceuticals	triethylamine-orthophosphoric acid buffer). Column: Zorbax C8 analytical column Flow rate: 1.0 mL/min Wavelength: 237nm	

5. CONCLUSION

The oral anti-diabetic drug .it is approved by Approval by CDSCO: 29 NOV 2023. The above study gives the analytical methods for analysis of oral anti-diabetic drug in bulk and tablet dosage form. Literature survey reveals that various methods are reported for the development and validation of various drugs. at present review illustrates various analytical approaches exercised for the evaluation of oral anti-diabetic drug numerous investigations had perform including HPLC in bulk, and pharmaceutical dosage form. These methods are reported for the development and validation of various drugs. Analysis of drug plays a significant role during formulation to identify the drug and its metabolites.

6. RESULT

Firstly, Identification of procured API, Dapagliflozin and Gliclazide was done to confirm its identity of both drugs.
A novel RP-HPLC method was used to estimate dapagliflozin and gliclazide. The separation was achieved at 1.0 ml/minute using a stationary phase of Inertsil ODS 3V C18 (150 mm x 4.6 mm x 5µ) and a mobile phase of Buffer: Methanol (30:70) %v/v. Colum temperature was preset at 25°C, and UV wavelength kept constant at 220 nm. Retention time for DAPA and GLICLA were 3.7 min and 6.13 min, respectively.
Method was validated using ICH Q2 (R1) recommendations and yielded linear results for dapagliflozin, and gliclazide in the ranges of 25 - 75 µg/ml, and 75 – 225 µg/ml, respectively. The method demonstrated great selectivity and specificity; there was no interference identified in the blanks at the retention durations of, dapagliflozin, and gliclazide, and there was a good connection between the peak area and drug concentration under ideal circumstances.
The percentage recoveries for dapagliflozin and gliclazide ranged from 100.5% - 100.7%and 99.6% - 100.8%.The suggested approach is precise and robust, as demonstrated by the low level of %RSD during repeatability, intraday and interday accuracy, and robustness testing. %RSD remained below 2, when small deliberate changes were made in method, hence developed method is robust.
The proposed technique is new, simple, precise, linear, sensitive, robust, and accurate for simultaneous estimation of DAPA and GLICLA in tablet formulation, according to the results of the experiment. For routine analysis, this approach was more stable and cost-effective.

7. REFERENCES

1. Sapra, A., & Bhandari,P. “Diabetes.”National library of medicine, 2023.
2. Dapagliflozin/Drug bank. https://search.app/uQFrVePbxX21WeoS6 29th September 2024.
3. Dapagliflozin/Pubchem. https://search.app/BuRk8cz3svTiWY3F6 29th September 2024.
4. Gliclazide/Drug bank. https://search.app/8YUUwU17DTH7XzHM9 2nd October 2024.
5. Gliclazide/Pubchem. https://search.app/ACQC8RzVriNX7MsZ8 2nd October 2024.
6. Gliclazide/Indian pharmacopoeia, 2022, vol 2, pp 2176.
7. Gliclazide/European pharmacopoeia, 10.0, pp 2748.
8. Gliclazide/British pharmacopoeia, 2023, vol-3, pp 733.
9. Gliclazide/Japanese pharmacopoeia, 2016, pp 1068
10. Basha, S. S., & Sravanthi, P. “Development and validation of dapagliflozin by reversed-phase high-performance liquid chromatography method and its forced degradation studies.” Asian journal of pharmaceutical and clinical research, 2017, 10(11), 2455-3891.
11. Mante, G. V., Hemke, A. T., & Umekar, M. J. “RP-HPLC Method for Estimation of Dapagliflozin from its Tablet.” International Journal of ChemTech Research, 2018, 11(01), 242-248.
12. Debata, J., Kumar, S., Jha, S. K., & Khan, A. "A new RP-HPLC method development and validation of Dapagliflozin in bulk and tablet dosage form." International Journal of Drug Development & Research, 2017, 9(2), 48-51.
13. Chaudhari, U., Sahu, J. K., & Dande, P. R. “Analytical Method Development, Validation, and Forced Degradation Study of Dapagliflozin by RP-HPLC.” Drug Metabolism and Bioanalysis Letters,2023, 16
14. Sanagapati, M., Dhanalakshmi, K., Reddy, G. N., & Sreenivasa, S. “Development and Validation of Stability-Indicating RP-HPLC Method for Determination of Dapagliflozin.” Journal of Advanced Pharmacy Education & Research, 2014, 4(3), 350-353.
15. Dave, V., & Patel, P. U. “Development and Validation of QbD-Assisted RP-HPLC Method for Dapagliflozin and Metformin HCL in Bulk and Its Combined Dosage Form.” International Journal of Pharmaceutical Sciences and Research, 2023, 14(2), 788-794.
16. Donepudi, S., & Achanta, S. “Simultaneous Estimation of Saxagliptin and Dapagliflozin in Human Plasma by Validated High-Performance Liquid Chromatography-Ultraviolet Method.” Turk J pharm sci., 2019, 16(2), 227–233.

17. Braz. J. Pharm. Sci. "Application of quality by design approach in RP-HPLC method development for simultaneous estimation of saxagliptin and dapagliflozin in tablet dosage form" Braz. J. Pharm. Sci., 2019, 55.
18. Bhavyasri K, Surekha T, Begum S, Sumakanth M. "RP-HPLC Method for Dapagliflozin and Metformin HCL in Bulk and Combined Formulation." Arch Pharm Pract, 2021, 12(4):106-10.
19. Md. Rageeb Md. Usman, Sufiyan Ahmad, Chandrakant Deore, Tanvir Shaikh, Bharat Jain, Md. Imran. "Stability Indicating RP-HPLC Method for Determination of Saxagliptin and Dapagliflozin in Bulk and Tablet Dosage Forms. J. Pharm. Sci. & Res., 2020, 12(4), 499-506.
20. Vankalapati, K. R., Alegete, P., & Boodida, S. "Stability-Indicating HPLC Method Development and Validation for Simultaneous Estimation of Metformin, Dapagliflozin, and Saxagliptin in Bulk Drug and Pharmaceutical Dosage Form." Wiley Analytical Science, 2022, 36(7).
21. Kommineni, V., Chowdary, K. P. R., & Prasad, S. V. U. M. "Development and Validation of a New HPLC Method for the Simultaneous Estimation of Saxagliptine and Dapagliflozin and Its Application in Pharmacokinetic Studies." International Research Journal of Pharmacy and Medical Sciences (IRJPMS), 2018, 1(6), 16-24.
22. SABHYATHA T. S., & NARAYANA BABU. "Analytical method validation of Gliclazide related substances by high-performance liquid chromatography method." International Journal of Current Pharmaceutical Research, 2022
23. Mansi S. Dholakia, Hardik B. Rana, Saloni Desai, Mukesh C. Gohel, Kalpana G. Patel, Vaishali T. Thakkar, Tejal R. Gandhi. "Development and Evaluation of Robust RP-HPLC Method for Gliclazide Estimation Integrating Box Behnken Design." Research J. Pharm. and Tech, 2019, 12(1),135-141.
24. Ghai, D., & Lakshmi Ganesh, G. "HPLC Method for Determination of Gliclazide in Human Serum." Asian Journal of Chemistry, 2009, 21(6), 4258-4264.
25. Chowdary, K.P.R., & Tripura Sundari, P. "HPLC Estimation of Gliclazide in Formulations and In Pharmacokinetic Studies." Asian Journal of Chemistry, 2009, 21(7), 5221-5227.
26. Gedawy, A., Al-Salami, H., & Dass, C. R. "Development and validation of a new analytical HPLC method for simultaneous determination of the antidiabetic drugs, metformin and gliclazide. "Journal of Food and Drug Analysis, 2019, 27(1), 315-322.
27. Rathinavel, G., Uma Nath, U., Valarmathy, J., Samueljoshua, L., Selvin Thanuja, C., Ganesh, M., Sivakumar, T., & Priyadarsini, R. "RP-HPLC Method for the Simultaneous Estimation of Rosiglitazone and Gliclazide in Tablets." Journal of chemistry, 2009, 6 (4), 1188-1192.
28. Sasongko, L., Pratiwi, G. K., Leo, M., & Adiwidjaja, J. "Simultaneous HPLC Assay of Gliclazide and Ciprofloxacin in Plasma and its Implementation for Pharmacokinetic Study in Rats." Journal of Chromatographic Science, 2021, 59(4), 338–346.
29. Chhitajed, S. S., Sonawnae, S. S., More, P. K., Chaudhari, H., & Kshirsagar, S. J. "HPLC Method Development, Validation and Application to Determining In-Vitro Effect of Levofloxacin on the Availability of Gliclazide." Pharmaceutical Chemistry Journal, 2023, 57(5), 445–450.
30. Sebaiy, M. M., El-Adl, S. M., Baraka, M. M., & Hassan, A. A. "Rapid RP-HPLC Method for Simultaneous Estimation of Some Antidiabetics; Metformin, Gliclazide and Glimepiride in Tablets." Egyptian Journal of Chemistry,2019, 62(3), 429-440.
31. Şenkardeş, S., Özaydın, T., Uğurlu, T., & Küçükgüzel, Ş. G. "Development and validation of a reversed-phase HPLC method for the determination of lisinopril and gliclazide in pharmaceuticals." Marmara Pharmaceutical Journal, 2017, 21(2), 338-344.