Development and Validation of Analytical Method for the Estimation of Drugs Dapagliflozin and Vildagliptin Phosphate by FTIR

[1]Utkarsha R. Yadav, [2]Krishna S. Pathade

[1]M Pharmacy, [2]M Pharmacy

[1]Department of Pharmaceutical Chemistry,

[1]Appasaheb Birnale College of Pharmacy, Sangli, Maharashtra, India 416416

ABSTRACT: The Fourier Transform Infrared (FTIR) Spectroscopy technique has been used to establish a novel analytical approach for the quantification of dapagliflozin and vildagliptin in their pure and pharmaceutical dose forms. In transmittance mode, the spectra were obtained between 4000 cm-1 and 400 cm-1. Vildagliptin and dapagliflozin's FTIR spectra were used to pinpoint certain functional groups. The O-H stretching at 3369.3 cm-1 and 3295.0 cm-1, the C-H stretching at 2880.2 cm-1 and 2847.7 cm-1, and the C-O stretching at 1271.0 cm-1 for dapagliflozin were all visible in the spectra of the two drugs. Vildagliptin's spectrum showed similar amounts of stretching. During the procedure, pure drug samples and pharmacological formulations were scanned in the 4000-400 cm-1 range. Using OPUS, the device's software, the spectra were analysed. A robustness, linearity, accuracy, and precision assessment were conducted on the developed technique. The goal of this investigation is to promote a fundamental, precise, reliable, and workable logical approach for evaluating antiemetic medications in accordance with ICH guidelines. to provide a time-efficient, reliable approach for quickly estimating large numbers of samples.

Key words: Dapagliflozin, Vildagliptin, FT-IR, Analytical Method Development, Validation

INTRODUCTION:

Dapagliflozins Chemical name: (2S, 3R, 5S, 6R)-2-[4-chloro-3-[(4-ethoxyphenyl) methyl] phenyl]-6- (hydroxymethyl) oxane-3,4,5-triol.
Drug class: Sodium-glucose co-transporter 2 (SGLT-2) inhibitors.
By lowering the renal glucose threshold and decreasing filtered glucose reabsorption, the SGLT2 inhibitor Dapa enhances the excretion of glucose in the urine. The enzyme SGLT2, which is expressed in the proximal renal tubules, is primarily in charge of filtered glucose reabsorption via the tubular lumen.

Vildagliptins Chemical name: (2S)-1-[2-[3-hydroxy-1-adamantyl) amino] acetyl] pyrrolidine-s2- carbonitrile.
Drug class: Dipeptidly peptidase-4 (DPP-4) inhibitor.

Blood glucose levels are regulated and glucose homeostasis is maintained by the incretin hormones glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide-1 (GLP-1). It is estimated that GLP-1 and GIP activity accounts for around 70% of the insulin response to an oral glucose challenge.
They stimulate the secretion of insulin in a glucose-dependent manner through GLP-1 receptor signalling and G-protein-coupled GIP.

MATERIALS AND METHODS:

Reagents and chemicals:

The standard Dapagliflozin were procured from Lupin, Pune. Vildagliptin from CTX Life Sciences, Surat.

The solvents used Methanol, Ethanol and Water of HPLC grade were bought from Research lab fine industries.

Equipment's used: Analytical balance: Shimadzu AUX-220, Japan.

pH meter: Eeuiptronics.

FT-IR: Jasco V-750, Japan.

MATERIALS AND METHODS

DAPAGLIFLOZIN

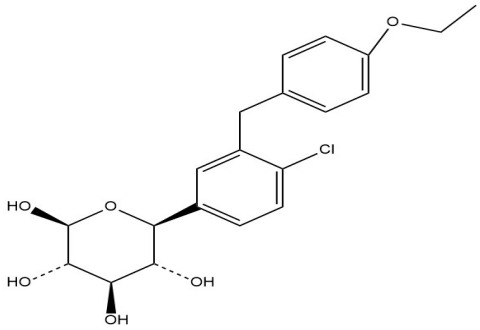

Figure 1 structure of Dapagliflozin

IR spectroscopic analysis of DAPAGLIFLOZIN, a standard medication:

Dapagliflozin's infrared spectroscopy was conducted using a Bruker FT-IR Spectrophotometer with a wing ALPHA. We checked the anvil, ATR crystal, and sample surface for cleanliness; this was an easy and uncomplicated procedure. The sampling area's center is where the sample is placed. The sample is applied sparingly enough to thoroughly envelop the ATR crystal. The anvil is pressed onto the sample, taking care to apply the optimum contact pressure to press it on the ATR crystal. After the spectrum has been acquired, the pressure application device is raised once more, and the sample is taken.

VILDAGLIPTIN

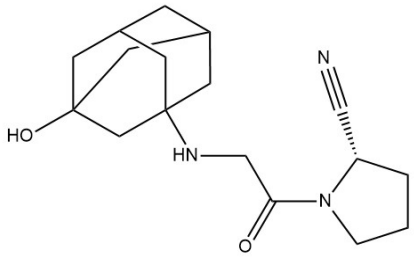

Figure 2 Structure of Vildagliptin

IR spectroscopic analysis of VILDAGLIPTIN, a standard medication:

Using an ALPHA Bruker FT-IR Spectrophotometer, Vildagliptin's infrared spectroscopy was carried out. An uncomplicated and basic technique was used to assess the cleanliness of the

anvil, ATR crystal, and sample surface. Samples are placed in the centre of the sampling zone. The appropriate amount of sample is used to thoroughly cover the ATR crystal. The sample is pushed against the ATR crystal using the anvil, with caution used to apply the proper contact forces. The sample is taken and the pressure application device is raised once more once the spectrum has been acquired.

EXPERIMENTAL WORK FOR FT-IR METHOD

METHOD DEVELOPMENT: FTIR Spectroscopic method was developed by using a liquid sampling technique.

Selection of Measurement Mode: DAPA and VILDA's IR spectra were analyzed quantitatively using transmittance mode. Transmittance of functional peaks were determined at different wavenumbers(cm-1).

Selection of detector: The Mercury cadmium telluride detector was selected.

Solvent Selection: Selected according to solubility profile.

Dapagliflozin- Water.

Vildagliptin- Ethanol.

Sample Preparation: Weighed the drug sample (as per concentration to me made) transfer to volumetric flask and add the solvent up to the mark.

METHOD VALIDATION: The developed method was validated according to the ICH guidelines Q2(R1).

Linearity: The working standard solutions of 2,4,6,8,10 mg/ml were prepared. Transmittance of the solution were recorded. Standard calibration curve were plotted.

LOD and LOQ: The LOD and LOQ were calculated by the equation method

$LOD = 3.3\times \sigma/S$

$LOQ = 10 \times \sigma/S$

Where, σ = the substandard deviation of the response

S = slope of the calibration curve

Precision: The precision of the instrument was checked by repeated scanning and measuring the transmittance of solution of dapagliflozin and vildagliptin.

Accuracy: Accuracy of the method was expressed in terms of % recovery.

RESULTS AND DISCUSSIONS:

Spectrophotometric methods for the simultaneous determination of DAPA and VILDA were developed and validated according to ICH Q2B guidelines which are used for validation of

analytical procedures in order to determine the linearity, LOD, LOQ, precision and accuracy for the analytes and data complying with the standards were obtained. The results of validation parameters for the developed methods are reported.

Validation parameters:

Table No.1 Validation Parameters

	Dapagliflozin	Vildagliptin
Linearity range (mg/spot)	1-5mg	1-5mg
Regression equation (Y=mX+C)	Y= 0.0001x-0.0263	Y= 0.0234x-0.0288
Correlation Coefficient r^2	0.9128	0.8767
Slope (S)	0.019	0.023
Intercept	0.022	0.028
Mean standard deviation of responses (σ)	0.152752	0.152757
LOD	0.087 mg/ml	0.093mg/ml
LOQ	0.42 mg/ml	0.57 mg/ml

FTIR spectra and λ_{max} by UV of DAPA:

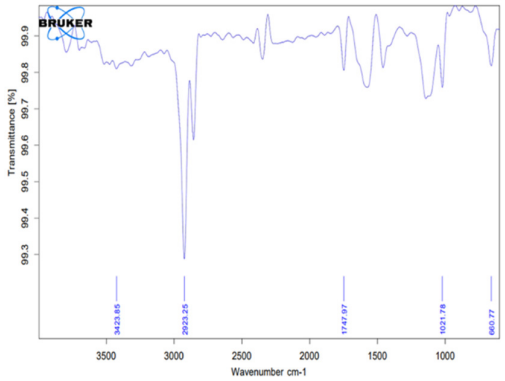

Figure 3 FTIR spectra of Dapagliflozin

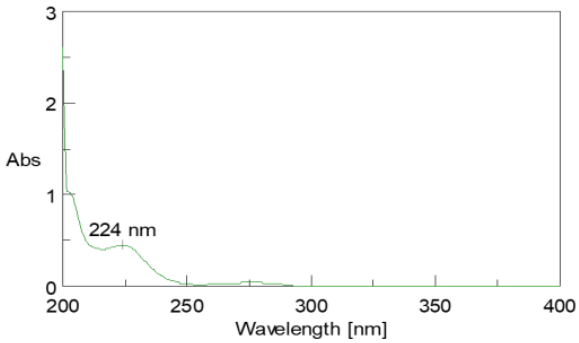

Figure 4 λmax for DAPA

FTIR spectra of DAPA in water by liquid sampling technique:

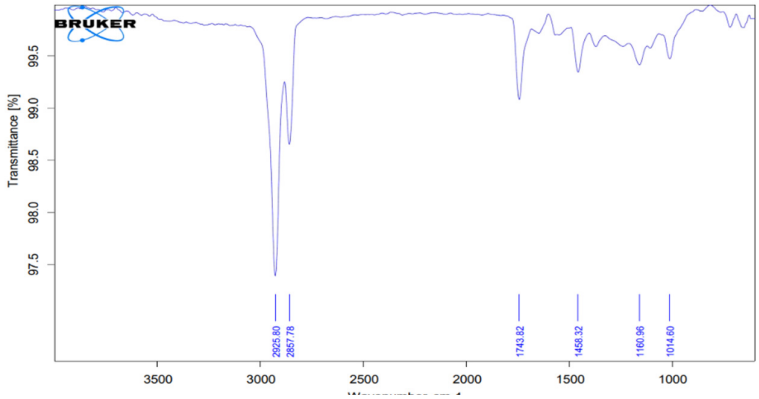

Figure 5 FTIR spectra of DAPA in water by liquid sampling technique

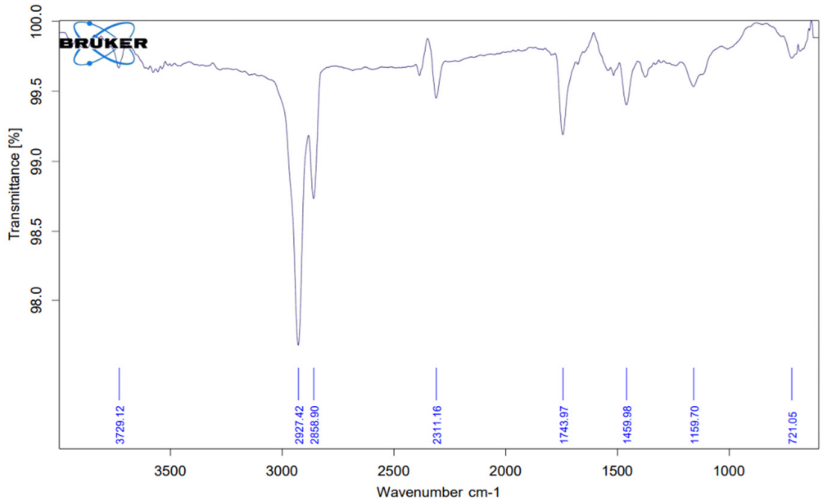

Figure 6 FTIR spectra of DAPA in water by liquid sampling technique

Standard Calibration Curve data for Dapagliflozin:

Track	Sample volume in mg	Amount fraction in mg	Absorbance	±SD	Correlation coefficient (r^2)
1	2	1	0.00516	0.485946	0.9128
2	4	2	0.01207	1.507878	
3	6	3	0.02709	0.853939	
4	8	4	0.04511	1.671779	
5	10	5	0.08422	1.752025	

Standard Calibration Curve for Dapagliflozin:

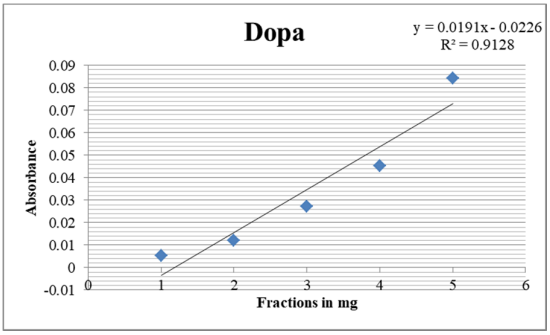

Figure 7 Standard Calibration Curve for Dapagliflozin

FTIR spectra and λ_{max} by UV of VILDA:

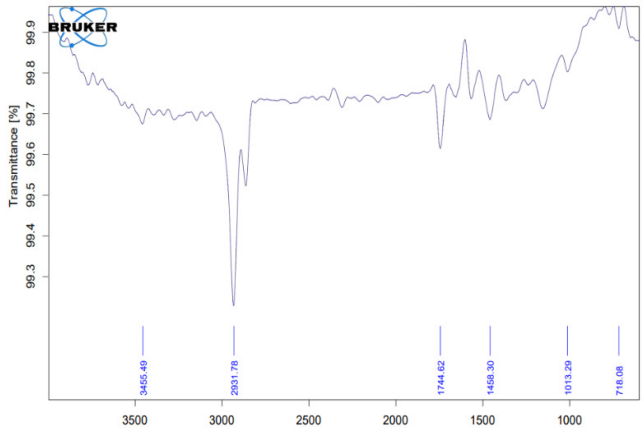

Figure 8 FTIR spectra of Vildagliptin

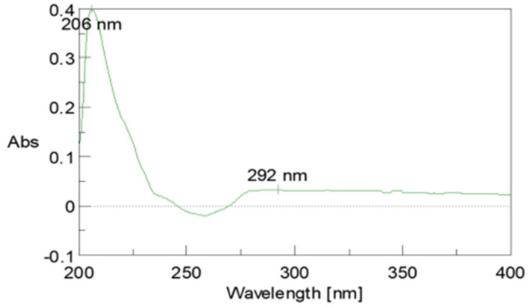

Figure 9 λmax for VILDA

FTIR spectra of VILDA in water by liquid sampling technique:

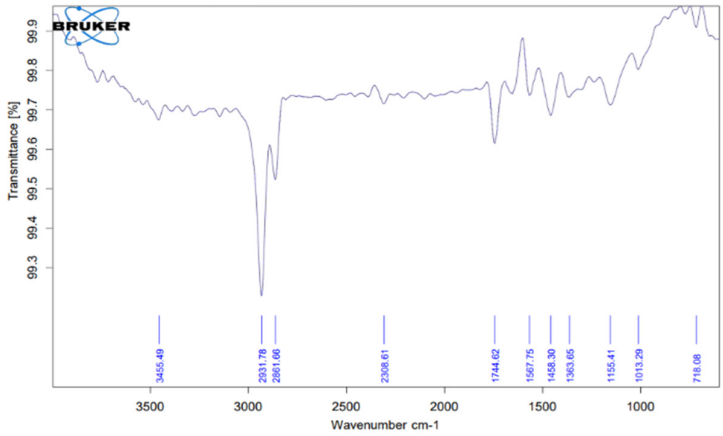

Figure 10 FTIR spectra of VILDA in ethanol by liquid sampling technique

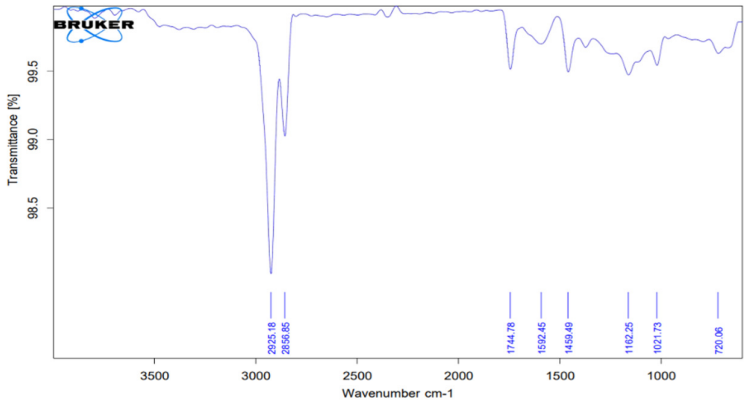

Figure 11 FTIR spectra of VILDA in ethanol by liquid sampling technique

Standard Calibration Curve data for Vildagliptin:

Track	Sample volume inmg	Amount fraction inmg	Absorbance	Correlation coefficient (r^2)
1	2	1	0.00710	0.9128
2	4	2	0.01408	
3	6	3	0.02907	
4	8	4	0.05218	
5	10	5	0.10521	

Standard Calibration Curve for Vildagliptin:

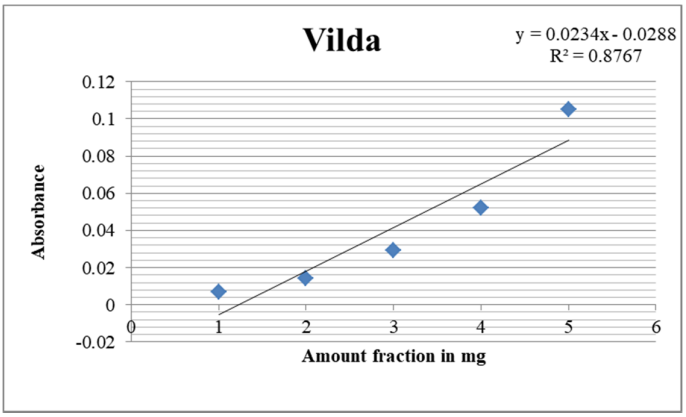

Figure 12 Standard Calibration Curve for Vildagliptin

Conclusion: The principal application of FTIR in the transmission mode, as described in all compendium pharmacopeia's, is to identify functional groups in raw materials and final products. The FTIR method is rarely employed for quantitative analysis. In this work, a novel FTIR approach was developed to detect dapagliflozin and vildagliptin. The approach met the majority of validation criteria for a concentration range appropriate for medication quality control in both pure and solid dose forms. Furthermore, the FTIR approach consumes less solvent and requires no reagents. Hence, the devised approach was shown to be appropriate for the detection of dapagliflozin and vildagliptin in medications. The approach was accurate, precise, linear, and resilient, making it appropriate for quality control and regulatory applications.

REFERENCES:

1. Desai S, Maradia RB, Suhagia BN. A Comprehensive and Critical Review on Analytical and Bioanalytical methods for Metformin Hydrochloride, Dapagliflozin, and Saxagliptin. Current Pharmaceutical Analysis. 2023 Jan 1;19(1):20-50.
2. Savale SK. Development and validation of RP-HPLC for Estimation of Vildagliptin. Asian Journal of Biomaterial Research. 2017;3(5):6-11.
3. Patel A, Jadeja P, Mashru R. Analytical method development and validation for simultaneous estimation of dapagliflozin and teneligliptin hydrobromide hydrate from synthetic mixture by three different UV spectrophotometric methods.2022;11(7).
4. Attimarad M, Venugopala KN, Al-Dhubiab BE, Elgorashe RE, Shafi S. Development of ecofriendly derivative spectrophotometric methods for the simultaneous quantitative analysis of remogliflozin and vildaglitin from formulation. 2021 Oct 12;26(20);6160.
5. Elhassan MM, Mahmoud AM, Hegazy MA, Mowaka S. Univariate and Multivariate Determination of Dapagliflozin and Saxagliptin in Bulk and Dosage Form. Journal of AOAC International. 2023 May 1;106(3):794-803.
6. Deepam T, MV Basaveswara Rao, MD Dhanaraju. Development of validated stability indicating assay method for simultaneous estimation of metformin and dapagliflozin by RP-HPLC. European Journal of Applied Sciences.9(4):189-199,2017.
7. Attimarad M, Islam MM, Shafi S, David M, Rahman A, Molina EI. Smart eco-friendly mathematically manipulated UV spectroscopic methods to resolve severely overlapped spectra of a binary mixture of dapagliflozin with sitagliptin and vildagliptin. Microchemical Journal. 2023 Jul 1; 190:108700.
8. Oh DW, Chon J, Kang JH, Han CS, Shin DH, Kim JY, Rhee YS, Chun MH, Kim DW, Park CW. Physicochemical characterization of dapagliflozin and its solid-state behavior in stress stability test. Drug development and industrial pharmacy. 2021 May 4;47(5):685-93.
9. Patel BH, Teraiya NH. (2024) Simultaneous Estimation and Stability Indicating Method of Vildagliptin and Dapagliflozin by Rp-hplc in Pharmaceutical Dosage Form.
10. Sen AK, Khatariya SB, Sen DB, Maheshwari RA, Zanwar AS, Velmurugan R. Various innovative UV spectroscopic methodologies for concurrent estimation of dapagliflozin and vildagliptin in combined tablet. Journal of Applied Pharmaceutical Science. 2023 Sep 4;13(9):213-23.
11. Prajapati P, Rana B, Pulusu VS, Shah S. Simultaneous Chromatographic Estimation of Vildagliptin and Dapagliflozin Using Hybrid Principles of White Analytical Chemistry and Analytical Quality by Design. Journal of AOAC International. 2024 Jan 1;107(1):212-22.
12. Jayaprakash R, Natesan SK, Lalitha K. Stability indicating RP-HPLC method development and validation for the simultaneous determination of vildagliptin and metformin in pharmaceutical dosage form. International Journal of Pharmacy and Pharmaceutical Sciences. 2017;9(3):150-7.
13. Joshi A, Birla A, Prasad A, Warrier S. Bioequivalence study of a fixed-dose combination of Dapagliflozin/Vildagliptin Sustained Release tablets in healthy adult

male subjects: A Randomized, Open-Label, Crossover Study. Journal of Drug Delivery and Therapeutics. 2022 Nov 15;12(6):105-9.

14. Tanajak P, Sa-Nguanmoo P, Sivasinprasasn S, Thummasorn S, Siri-Angkul N, Chattipakorn SC, Chattipakorn N. Cardioprotection of dapagliflozin and vildagliptin in rats with cardiac ischemia-reperfusion injury. Journal of Endocrinology. 2018 Feb 1;236(2):69-84.
15. Abdelrahman AE, Maher HM, Alzoman NZ. HPTLC method for the determination of metformin hydrochloride, saxagliptin hydrochloride, and dapagliflozin in pharmaceuticals. Current Analytical Chemistry. 2020 Aug 1;16(5):609-19.
16. Surendran S, Paul D, Pokharkar S, Deshpande A, Giri S, Satheeshkumar N. A LC-MS/MS method for simultaneous estimation of a novel anti-diabetic combination of saxagliptin and dapagliflozin using a polarity switch approach: application to in vivo rat pharmacokinetic study. Analytical methods. 2019;11(2):219-26.
17. Dalal D, Kant R, Badhwar R. A Review on Analytical Method of Dapagliflozin and Empagliflozin by QBD Approach. Mathews Journal of Pharmaceutical Science. 2023 Mar 20;7(1):1-6.
18. Akash MS, Rehman K, Akash MS, Rehman K. Introduction to spectrophotometric techniques. Essentials of pharmaceutical analysis. 2020:19-27.
19. Kartikey A, Gupta A, Gupta V. FORMULATION AND EVALUATION OF BILAYER TABLET OF DAPAGLIFLOZIN AND VILDAGLIPTIN. Journal of Population Therapeutics and Clinical Pharmacology. 2023 Jan 14;30(1):714-23.
20. Sen AK, Khatariya SB, Sen DB, Maheshwari RA, Akabari AH, Velmurugan R. Development and validation of high-performance thin layer chromatographic method for concurrent estimation of dapagliflozin and vildagliptin in combined tablet. Separation Science Plus. 2024 Jan;7(1):2300132.