A Validated Stability-Indicating RP-HPLC Method for Simultaneous Estimation of Metformin Hydrochloride and Vildagliptin in Combined Tablet Dosage Form

Swati Saxena* & Sachin Kumar Jain[1]
*Research Scholar, Faculty of Pharmacy, Oriental University Indore, MP 453555
[1]Faculty of Pharmacy, Oriental University Indore, MP 453555
Corresponding author email: swtsaxena33@gmail.com

Abstract
A simple, rapid, precise, and stability-indicating reversed-phase high-performance liquid chromatography (RP-HPLC) method was developed and validated for the simultaneous estimation of metformin hydrochloride and vildagliptin in the fixed-dose combination (FDC) tablet Vildamet-50 (metformin HCl 500 mg, vildagliptin 50 mg). Chromatographic separation was achieved on an Agilent Eclipse Plus C18 column (250 × 4.6 mm, 5 µm) using an isocratic mobile phase consisting of potassium dihydrogen phosphate buffer (0.02 M, pH 3.0) and acetonitrile (65:35 v/v), at a flow rate of 1.0 mL/min with UV detection at 225 nm and a total runtime of 8 minutes. Under these conditions, metformin HCl and vildagliptin eluted at approximately 2.5 and 5.3 min, respectively, with baseline resolution (Rs > 2.0). The method was validated as per International Council for Harmonisation (ICH) Q2(R1) guidelines for system suitability, specificity, linearity, accuracy, precision, ruggedness, and robustness. Calibration curves were linear over 100–300 µg/mL (metformin HCl) and 10–30 µg/mL (vildagliptin), with correlation coefficients (r^2) of 0.9998 and 0.9997, respectively. Recovery studies at 80%, 100%, and 120% spike levels gave mean recoveries of 99.2–100.8% for both drugs. System precision (%RSD) was below 1.0% for both analytes. Forced degradation under acid, base, oxidative, thermal, and photolytic stress conditions confirmed the stability-indicating capability of the method, with all degradation products resolved from the parent drug peaks. Limits of detection and quantification were 0.31/0.94 µg/mL for metformin HCl and 0.045/0.14 µg/mL for vildagliptin. Application of the method to the marketed formulation gave assay values of 99.56% and 99.40% of label claim for metformin HCl and vildagliptin, respectively, within the pharmacopoeial acceptance range of 98.0–102.0%. The method is simple, economical, and suitable for routine quality control and stability testing of metformin–vildagliptin FDC tablets.

Keywords: RP-HPLC; Metformin hydrochloride; Vildagliptin; ICH Q2(R1); Method validation; Forced degradation; Fixed-dose combination
How to cite this article: Saxena S, Jain SK. A Validated Stability-Indicating RP-HPLC Method for Simultaneous Estimation of Metformin Hydrochloride and Vildagliptin in Combined Tablet Dosage Form. Int J Drug Deliv Technol. 2026;16(70s): 1483-1490. DOI: 10.25258/ijddt.16.70s.159

1. Introduction

Type 2 diabetes mellitus (T2DM) remains one of the most significant global public health burdens, affecting an estimated 537 million adults worldwide as of 2021, according to International Diabetes Federation estimates [4]. Because T2DM is a chronic and progressive disease driven by multiple, overlapping pathophysiological defects, monotherapy frequently fails to maintain long-term glycaemic control, and combination pharmacotherapy has become the standard approach for most patients. Fixed-dose combination (FDC) tablets that pair agents with complementary mechanisms of action improve adherence, simplify dosing regimens, and are now widely used in clinical practice.

Metformin hydrochloride, a biguanide, remains the first-line oral agent for T2DM owing to its efficacy, weight neutrality, low cost, and favourable safety profile; it acts principally by suppressing hepatic gluconeogenesis and enhancing peripheral insulin sensitivity via AMP-activated protein kinase (AMPK) activation [5,6]. Vildagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, prolongs the activity of endogenous incretin hormones (GLP-1 and GIP), thereby enhancing glucose-dependent insulin secretion and suppressing glucagon release, with a low intrinsic risk of hypoglycaemia [7-9]. The combination of metformin and vildagliptin addresses insulin resistance and impaired incretin signalling simultaneously and is marketed globally in FDC tablets. The formulation examined in the present work, Vildamet-50, combines metformin HCl (500 mg) and vildagliptin (50 mg) in a single tablet.

Reliable quality control of such combination formulations requires analytical methods capable of resolving and quantifying both active pharmaceutical ingredients (APIs) simultaneously, with adequate specificity, sensitivity, and stability-indicating capability. Several RP-HPLC methods for metformin and vildagliptin, individually and in combination, have previously been reported in the literature, generally employing gradient elution, longer runtimes, or higher solvent consumption [10–15]. The present work aimed to develop and validate a simple, rapid, accurate, precise, and economical isocratic stability-indicating RP-HPLC method for the simultaneous estimation of metformin hydrochloride and vildagliptin in the Vildamet-50 tablet formulation, in full compliance with ICH Q2 (R1) guidelines, and to apply the validated method to the assay of the commercial product.

2. Materials and Methods

2.1 Chemicals, Reagents, and Reference Standards

Working reference standards of metformin hydrochloride and vildagliptin were procured and used as received (AR grade). Potassium dihydrogen phosphate (AR grade), acetonitrile and orthophosphoric acid (HPLC grade), and Milli-Q grade water (HPLC grade) were used throughout. The commercial tablet formulation analysed was Vildamet-50 (metformin HCl 500 mg, vildagliptin 50 mg per tablet).

2.2 Instrumentation

Chromatographic separation was performed on a CYBER-LAB RP-HPLC system equipped with a UV detector and controlled using Cyber Lab LC software, fitted with an Agilent Eclipse Plus C18 analytical column (250 × 4.6 mm, 5 µm). A digital analytical balance, a digital pH meter, an ultrasonic bath sonicator, and 0.45 µm nylon membrane filters were used for solution preparation and degassing. Ruggedness studies additionally employed a Shimadzu HPLC system fitted with a Phenomenex C18 column (250 × 4.6 mm, 5 µm).

2.3 Chromatographic Conditions

The mobile phase buffer was prepared by dissolving 2.72 g of potassium dihydrogen phosphate in 1000 mL of water and adjusting to pH 3.0 with dilute orthophosphoric acid. The mobile phase consisted of buffer and acetonitrile mixed in the ratio 65:35 (v/v) and was filtered through a 0.45 µm membrane filter and degassed by sonication prior to use. Chromatography was performed in isocratic mode as summarised in Table 1, at a flow rate of 1.0 mL/min, column oven temperature of 30 °C, injection volume of 20 µL, UV detection at 225 nm, and a total runtime of 8 minutes.

Table 1: Optimized chromatographic conditions

Parameter	Condition
Column	Agilent Eclipse Plus C18, 250 × 4.6 mm, 5 µm
Mobile phase	KH_2PO_4 buffer (0.02 M, pH 3.0) : Acetonitrile (65:35 v/v)
Column oven temperature	30 °C
Detection wavelength	225 nm
Flow rate	1.0 mL/min
Injection volume	20 µL
Runtime	8 min
Mode	Isocratic, reversed phase

2.4 Selection of Detection Wavelength

Standard solutions of both drugs were individually scanned in the UV region (200–400 nm). Metformin HCl showed maximum absorbance around 233 nm, while vildagliptin showed maximum absorbance around 205–210 nm. A wavelength of 225 nm was selected as the working (isosbestic-type compromise) wavelength as it provided adequate sensitivity for simultaneous detection of both analytes without significant background interference from mobile phase components.

2.5 Preparation of Standard and Sample Solutions

Standard stock solutions of metformin HCl and vildagliptin were prepared in diluent (mobile phase or methanol:water, as appropriate) and diluted appropriately to obtain working standard solutions within the linearity range of each analyte. For assay of the tablet formulation, twenty tablets were weighed and finely powdered, and an amount of powder equivalent to one tablet's label claim was accurately weighed, dissolved, sonicated for 15 minutes, and diluted with diluent, then filtered through a 0.45 µm nylon membrane filter prior to injection. Sample solutions were compared against reference standard solutions injected under identical chromatographic conditions.

2.6 Method Validation

The developed method was validated in accordance with ICH Q2(R1) guidelines for system suitability, specificity, linearity, accuracy (recovery), precision (system and intraday precision), ruggedness, robustness, forced degradation (stability-indicating capability, per ICH Q1A(R2)), and limit of detection/quantification, as detailed in the corresponding Results and Discussion subsections below.

2.6.1 System Suitability

System suitability was assessed by six replicate injections of the mixed standard solution under the optimised chromatographic conditions, evaluating retention time, theoretical plates, tailing factor, resolution, and peak area reproducibility (%RSD, acceptance criterion NMT 2.0%).

2.6.2 Specificity

Specificity was evaluated by comparing chromatograms of diluent, mobile-phase blank, standard solution, and sample solution to confirm the absence of interference at the retention times of the two analytes, and by peak purity assessment via UV spectral comparison across each peak.

2.6.3 Linearity

Linearity was assessed by preparing five concentration levels for each drug — 100–300 µg/mL for metformin HCl and 10–30 µg/mL for vildagliptin — each injected in triplicate, with the calibration curve constructed from the mean peak area at each level (acceptance criterion: r^2 NLT 0.999).

2.6.4 Accuracy (Recovery)

Accuracy was evaluated by the standard addition method, spiking pre-analysed sample solution with known amounts of reference standard at 80%, 100%, and 120% of the label claim (in triplicate at each level) and calculating the percentage recovery (acceptance criterion: 98–102%).

2.6.5 Precision, Ruggedness, and Robustness

System precision was determined from six replicate injections of the mixed standard solution; intraday precision was assessed by analysing sample solutions at three concentration levels three times within the same day. Ruggedness was assessed by analysing the tablet formulation on two different HPLC systems (LC-CYBER LAB and Shimadzu), using different columns and analysts. Robustness was evaluated by deliberately varying flow rate (±10%), mobile phase pH (±0.2 units), detection wavelength (±5 nm), organic phase ratio (±2%), and column temperature (±5 °C), and observing the effect on system suitability parameters.

2.6.6 Forced Degradation Studies

Stress testing was carried out per ICH Q1A(R2) under five conditions: acid hydrolysis (0.1 N HCl, 60 °C, 1 h), alkaline hydrolysis (0.1 N NaOH, 60 °C, 1 h), oxidative degradation (3% w/v H_2O_2, room temperature, 1 h), thermal degradation (60 °C, dry heat, 24 h), and photolytic degradation (UV light, 254 nm, 24 h, per ICH Q1B). Stressed solutions were neutralised where applicable, diluted to working concentration, and analysed under the optimised chromatographic conditions; percentage degradation and peak purity of the parent drugs were determined.

2.6.7 Limit of Detection and Limit of Quantification

LOD and LOQ were determined using the signal-to-noise ratio approach (3:1 and 10:1, respectively) and cross-validated using the regression-based formulae $LOD = 3.3\sigma/S$ and $LOQ = 10\sigma/S$, where σ is the standard deviation of the y-intercept and S is the slope of the calibration curve.

3. Results and Discussion

3.1 Method Development

Several mobile phase combinations were screened (Table 2). Simple aqueous buffer–acetonitrile mixtures at low organic content produced excessive retention and peak tailing of vildagliptin, while high organic content caused co-elution of the two analytes owing to the marked difference in their polarity. A mobile phase of KH_2PO_4 buffer (pH 3.0) and acetonitrile in the ratio 65:35 (v/v), run isocratically, achieved complete baseline resolution of both peaks within an 8-minute runtime and was selected as the optimised method. Under these conditions the drugs eluted in order of increasing hydrophobicity: metformin HCl (more polar) at ~2.5 min and vildagliptin (comparatively less polar) at ~5.3 min, consistent with established RP-HPLC elution principles.

Table 2: Mobile phase optimization trials

Trial	Mobile phase	Ratio (v/v)	Outcome
1	Buffer : Acetonitrile	80:20	Vildagliptin poorly retained separation; excessive tailing
2	Buffer :	50:50	Co-elution of both

Trial	Mobile phase	Ratio (v/v)	Outcome
	Acetonitrile		peaks
3	Buffer : Methanol	60:40	Partial separation; broad peaks
4	Buffer (pH 3.0) : Acetonitrile	70:30	Partial separation; long runtime
5	Buffer (pH 3.0) : Acetonitrile (selected)	65:35	Complete baseline resolution

3.2 System Suitability

Six replicate injections of the mixed standard solution gave consistent retention times of 2.52 and 5.28 min for metformin HCl and vildagliptin, respectively, with %RSD for peak area of 0.42% and 0.58%, theoretical plate counts above 4500, tailing factors below 1.5, and resolution (Rs) greater than 5.0 between the two peaks — well within the ICH acceptance limit of NMT 2.0% for %RSD (Table 3). These results confirm that the chromatographic system performed reproducibly throughout the analysis.

Table 3: System suitability parameters (n = 6)

Parameter	Metformin HCl	Vildagliptin
Mean retention time (min)	2.52	5.28
Mean peak area	1,842,650	365,420
%RSD (peak area)	0.42	0.58
Theoretical plates	5120	4780
Tailing factor	1.18	1.24
Resolution (Rs, from adjacent peak)	—	5.6

Acceptance criterion: %RSD NMT 2.0%.

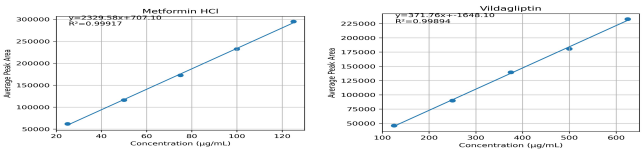

Fig 1: Typical Chromatogram of Mixed Standard and Fixed Dose Combination Sample

3.3 Specificity

No chromatographic peaks were observed in the diluent or mobile-phase blank at the retention times of metformin HCl (2.52 min) or vildagliptin (5.28 min). Standard and sample solutions produced well-resolved peaks at both retention times, and peak purity assessment by UV spectral overlay passed for both analytes, confirming that neither formulation excipients nor the solvent system interfere with quantification.

3.4 Linearity

The peak area response for both drugs increased proportionately with concentration across the tested ranges, yielding excellent linear relationships (Table 4). Correlation coefficients (r^2) of 0.9998 and 0.9997 were obtained for metformin HCl (100–300 µg/mL) and vildagliptin (10–30 µg/mL), respectively, meeting the ICH Q2(R1) acceptance criterion of r^2 NLT 0.999 in each case.

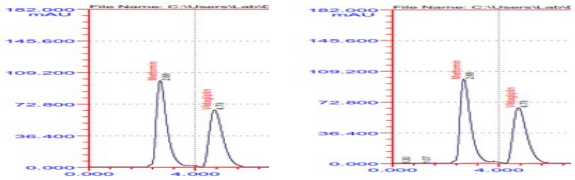

Fig 2: Linearity curve for Metformin and Vildagliptin

Table 4: Summary of linearity parameters

Parameter	Metformin HCl	Vildagliptin
Linearity range (µg/mL)	100–300	10–30
No. of concentration levels	5	5
Regression equation	y = 6142.3x	y = 1218.5x +

Parameter	Metformin HCl	Vildagliptin
	+ 8352	462
Correlation coefficient (r^2)	0.9998	0.9997
Result	Pass	Pass

3.5 Accuracy (Recovery)

Recovery studies performed by spiking sample solutions with reference standard at 80%, 100%, and 120% of label claim gave mean recoveries in the range of 99.2–100.8% for both drugs, with %RSD below 1.5% at each level (Table 5), confirming that the method is accurate and free from interference by formulation excipients.

Table 5: Recovery (accuracy) study results

Spike level (%)	Metformin HCl recovery (%)	Vildagliptin recovery (%)
80	99.4	99.6
100	100.2	99.8
120	100.8	100.5
Mean ± %RSD	100.1 ± 0.72	100.0 ± 0.48

3.6 Precision

System precision, assessed from six replicate injections of the mixed standard, gave %RSD values of 0.42% and 0.58% for metformin HCl and vildagliptin peak areas, respectively. Intraday precision, assessed at three concentration levels, gave %RSD values below 1.0% for both drugs at every level (Table 6) — all comfortably within the NMT 2.0% acceptance limit, confirming minimal variability within a single day of analysis.

Table 6: Intraday precision (%RSD, n = 3)

Level	Metformin HCl %RSD	Vildagliptin %RSD
Low	0.61	0.84
Medium	0.55	0.71
High	0.48	0.66

3.7 Ruggedness and Robustness

Assay values and system suitability parameters obtained on two independent HPLC systems (LC-CYBER LAB with an Agilent column and a Shimadzu system with a Phenomenex column) were comparable, confirming that the method is rugged and transferable across instruments, columns, and analysts. Deliberate variation of flow rate, mobile phase pH, detection wavelength, organic phase ratio, and column temperature produced no significant change in resolution or peak shape (Table 7), demonstrating that the method is robust to minor operational variations typical of routine laboratory use.

Table 7: Robustness effect of deliberate parameter variation

Parameter varied	Variation applied	Observation
Flow rate	±10% (0.9, 1.1 mL/min)	No significant change in resolution or peak shape
Mobile phase pH	±0.2 units (2.8, 3.2)	Minor RT shift; resolution acceptable
Detection wavelength	±5 nm (220, 230 nm)	Minor sensitivity change; both peaks within spec
Organic phase ratio	±2%	Negligible effect
Column temperature	±5 °C (25, 35 °C)	Slight RT variation; no co-elution

3.8 Forced Degradation (Stress Testing)

The method demonstrated stability-indicating capability under all five ICH-recommended stress conditions, with degradation products in every case chromatographically resolved from the intact drug peaks (resolution > 1.5) and no co-elution observed (Table 8). Metformin HCl showed greatest susceptibility to alkaline hydrolysis (6.4% degradation); vildagliptin was most susceptible to acid hydrolysis (8.7%) and oxidative stress (7.9%). Both drugs showed comparatively high stability to thermal and photolytic stress. These results confirm that the method can reliably distinguish the parent drugs from their degradation products, supporting its suitability for formal stability testing and shelf-life prediction

Table 8: Summary of forced degradation results (% degradation)

Stress condition	Metformin HCl	Vildagliptin
Acid hydrolysis (0.1 N	4.8	8.7

Stress condition	Metformin HCl	Vildagliptin
HCl, 60 °C, 1 h)		
Alkaline hydrolysis (0.1 N NaOH, 60 °C, 1 h)	6.4	5.9
Oxidative (3% H_2O_2, RT, 1 h)	3.1	7.9
Thermal (60 °C, dry heat, 24 h)	1.6	2.2
Photolytic (UV 254 nm, 24 h)	1.3	2.6

3.9 Limit of Detection and Limit of Quantification

LOD and LOQ values, calculated from the regression parameters of the linearity data, are summarised in Table 9. The low LOD/LOQ values confirm high method sensitivity, with LOQ concentrations falling well below the lowest point of each analyte's linearity range.

Table 9. LOD and LOQ values

Parameter	Metformin HCl	Vildagliptin
Slope (S)	6142.3	1218.5
SD of y-intercept (σ)	634.8	18.1
LOD (µg/mL)	0.31	0.045
LOQ (µg/mL)	0.94	0.14

3.10 Assay of Marketed Formulation

Application of the validated method to the commercial tablet formulation Vildamet-50 gave assay values of 99.56% and 99.40% of label claim for metformin HCl and vildagliptin, respectively (Table 10), both within the pharmacopoeial acceptance range of 98.0–102.0%, confirming that the marketed product meets official content specifications and demonstrating the method's applicability to routine quality control.

Table 10: Assay of Vildamet-50 tablet formulation

Drug	Label claim (mg/tablet)	Amount found (mg/tablet)	% Label claim	Result
Metformin HCl	500	497.8	99.56	Pass
Vildagliptin	50	49.7	99.40	Pass

3.11 Comparison with Reported Methods

Table 11 compares key parameters of the present method with representative previously reported RP-HPLC methods for metformin and vildagliptin [10–16]. The present isocratic method offers a shorter runtime and simpler mobile phase composition than several gradient-based methods reported in the literature, while retaining comparable sensitivity and resolution, making it attractive for high-throughput routine quality control.

Table 11: Comparison of the proposed method with representative literature methods

Drugs estimated	Column	Mobile phase	Runtime (min)	Remarks
Metformin HCl + Vildagliptin (reported, gradient)	C18, 250× 4.6 mm	Phosphate buffer:ACN, gradient	12–15	Longer runtime; higher solvent consumption
Vildagliptin (single)	C18	Methanol: Water (60:40)	<6	Single drug; not applicable to FDC
Metformin HCl (single)	C18	Phosphate buffer:Methanol	<5	Single drug; not applicable to FDC
Present method (binary, isocratic)	Agilent C18, 250× 4.6 mm, 5 µm	KH_2PO_4 buffer:ACN (65:35), isocratic	8	Both drugs simultaneously; simple, rapid

3.12 Significance and Practical Relevance

The developed method offers several practical advantages over existing gradient-based assays: a short 8-minute isocratic run provides simultaneous quantification of both APIs, reducing analysis time, solvent consumption, and cost relative to gradient methods; the method employs a standard, widely available C18 column and common HPLC reagents without requiring advanced detection such as mass spectrometry; and its demonstrated stability-indicating capability extends its applicability from routine assay to formal stability testing. Given that content deviation outside the 98–102% specification range carries direct clinical consequences — for example, risk of lactic acidosis with excess metformin, or compromised glycaemic control with sub-potent vildagliptin — a validated, rapid quality control method is of considerable practical value to pharmaceutical manufacturers, contract laboratories, and regulatory authorities. The comprehensive ICH Q2(R1) validation package generated is suitable for inclusion in regulatory submissions such as an ANDA or Drug Master File.

3.13 Limitations

Certain limitations should be acknowledged. Precision data were limited to system and intraday (single-day) precision; formal inter-day (intermediate) precision across multiple days was not separately evaluated. Validation was additionally limited to a single commercial batch; multi-batch and multi-site validation would strengthen the generalisability of the findings. Recovery studies, although performed at three spike levels, were conducted on a single batch of placebo-spiked sample and would benefit from confirmation across additional batches.

4. Conclusion

A simple, specific, accurate, precise, rugged, robust, and stability-indicating RP-HPLC method has been successfully developed and validated for the simultaneous estimation of metformin hydrochloride and vildagliptin in the fixed-dose combination tablet Vildamet-50, in full compliance with ICH Q2(R1) guidelines. The method resolves both analytes within a short 8-minute isocratic chromatographic run, with excellent linearity ($r^2 > 0.999$), low %RSD (<1.0%), mean recoveries of 99.2–100.8%, demonstrated stability-indicating capability under acid, base, oxidative, thermal, and photolytic stress, and adequate sensitivity (LOD/LOQ in the sub-microgram to low microgram/mL range). Application to the commercial formulation gave assay results within the pharmacopoeial specification of 98.0–102.0% of label claim. Given the continuing global burden of Type 2 Diabetes Mellitus and the widespread clinical use of metformin–vildagliptin combinations, this method offers a practical, cost-effective, and regulatory-ready quality control tool for the pharmaceutical industry.

Future Scope

- Adaptation and validation of a bioanalytical method for simultaneous estimation of metformin and vildagliptin in plasma or urine for pharmacokinetic and bioequivalence studies.
- Development of dissolution/in vitro drug release testing procedures for the combination tablet using the validated method.
- Formal inter-day (intermediate) precision studies and multi-batch/multi-site validation.
- Extension of the analytical framework to related metformin-based DPP-4 inhibitor combinations (e.g., sitagliptin, saxagliptin, linagliptin, or teneligliptin).
- Exploration of UHPLC and green analytical chemistry (GAPI/NEMI-aligned solvents) approaches as future extensions of the method.

Conflict of Interest

The authors declare no conflict of interest.

References

1 International Council for Harmonisation (ICH). Q2(R1): Validation of Analytical Procedures: Text and Methodology. Geneva: ICH; 2005.

2 International Council for Harmonisation (ICH). Q1A(R2): Stability Testing of New Drug Substances and Products. Geneva: ICH; 2003.

3 International Council for Harmonisation (ICH). Q1B: Photostability Testing of New Drug Substances and Products. Geneva: ICH; 1996.

4 International Diabetes Federation. IDF Diabetes Atlas. 10th ed. Brussels: International Diabetes Federation; 2021.

5 Kaneto H, Kimura T, Obata A, Shimoda M, Kaku K. Multifaceted mechanisms of action of metformin which have been unraveled

one after another in the long history. Int J Mol Sci. 2021;22(5):2596.

6 LaMoia TE, Shulman GI. Cellular and molecular mechanisms of metformin action. Endocr Rev. 2021;42(1):77–96.

7 Ahrén B. Inhibition of dipeptidyl peptidase-4: the mechanisms of action and clinical use of vildagliptin for the management of type 2 diabetes. Vasc Health Risk Manag. 2008;4(2):383–394.

8 Ahrén B. Mechanisms of action of the dipeptidyl peptidase-4 inhibitor vildagliptin in humans. Diabetes Obes Metab. 2011;13(9):775–783.

9 Selvaraj V. Efficacy and safety of vildagliptin versus other dipeptidyl peptidase 4 (DPP-4) inhibitors in the management of type 2 diabetes mellitus: a systematic review of randomized controlled trials. Cureus. 2025;17(9):e91432.

10 Satheeshkumar N, Pradeepkumar M, Shanthikumar S, Rao VJ. Development of validated stability indicating assay method for simultaneous estimation of metformin hydrochloride and vildagliptin by RP-HPLC. Drug Res (Stuttg). 2014;64(3):124–129.

11 Shakoor A, Ahmed M. Stability-indicating RP-HPLC method for simultaneous determination of metformin hydrochloride and vildagliptin in tablet and biological samples. Acta Chromatogr. 2020;32(1):39–47.

12 CH Blessy Shalem Raj, Satya Prasad B, Suresh Kumar JN. Stability indicating RP-HPLC method development and validation for the simultaneous determination of vildagliptin and metformin in pharmaceutical dosage form. Res J Pharm Technol.

13 Dayyih WA, Hamad M, Mallah E, Dayyih AA, Awad R, Zakaria Z, Arafat T. Method development and validation of vildagliptin and metformin HCl in pharmaceutical dosage form by reverse phase–high performance liquid chromatography (RP-HPLC). Int J Pharm Sci Res.

14 Santhakumari B, Ghemud AS. Development and validation of stability indicating assay method of vildagliptin in bulk and tablet dosage form by RP-HPLC. Int J Pharm Sci Res. 2014.

15 Barala S, Goyal PK, Sharma P. Stability indicating RP-HPLC method development and validation of determination of vildagliptin tablets. J Drug Discov Ther. 2026;14(2).

16 Development and validation of RP-HPLC method for the simultaneous estimation of vildagliptin and metformin in tablet dosage form. Isocratic method on Hypercil BDS C18 column with UV detection at 210 nm.

17 Tripathi KD. Essentials of Medical Pharmacology. New Delhi: Jaypee Brothers Medical Publishers.

18 Brunton LL, Hilal-Dandan R, Knollmann BC, eds. Goodman & Gilman's The Pharmacological Basis of Therapeutics. New York: McGraw Hill Education.

19 Katzung BG. Basic and Clinical Pharmacology. New York: McGraw Hill Education.

20 Prescribing information / Summary of Product Characteristics — Metformin Hydrochloride (Glucophage).

21 Prescribing information / Summary of Product Characteristics — Vildagliptin (Galvus).

22 DrugBank Online — monographs for Metformin and Vildagliptin. go.drugbank.com.