Quantification Of Novel Dpp4 Inhibitor - Vildagliptin By Spectrophotometric And Chromatographic Techniques: Brief Review

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ABSTRACT:
A review is presented on different analytical techniques used for quantitative analysis of novel Dipeptidyl peptidase-4 inhibitor (DPP-4) - Vildagliptin. Endeavours have been made to examine all the pertinent references to the degree conceivable. The review discusses the pros and cons of the cited analytical techniques, which will aid to give understand into the methods used for determination of Vildagliptin, from clinical isolates and from its pharmaceutical dosage forms. The major focus of this review is the basic as well as advanced analytical techniques established for determination of Vildagliptin. The procedures outlined here have been exhibited to be helpful for assessment of Vildagliptin and may discover application in dissecting other related properties.

KEYWORDS: Vildagliptin, DPP-4, HPLC, UV, Diabetes.

INTRODUCTION:

Vildagliptin, sold under the trade mark of Galvus, is a novel oral hypoglycemic (anti-diabetic drug) of the dipeptidyl peptidase-4 (DPP-4) inhibitor class. It also available in combination – Galvus Met consists of Vildagliptin with Metformin are the active constituents. Vildagliptin (Galvus) was first synthesized in May 1998 and was named after Edwin B. Villhauer. It was discovered when researchers at Novartis examined adamantyl derivatives that had proven to be very potent. The 'vil' in vildagliptin was in recognition of Ed Villhauer's contribution. (https://en.wikipedia.org/wiki/Vildagliptin). Vildagliptin is chemically (2R)-1-[2-[(3-Hydroxy-1-adamantyl) amino] acetyl] pyrrolidine-2-carbonitrile (Fig.1) and CAS Number is 274901-16-5. Vildagliptin is used as monotherapy or in combo with other drugs for the treatment of type 2 diabetes[1,2]. When used alone or added to other OADs, it effectively improves glycemic control, preserves both the α- and β-cell function, and reduces lipotoxicity and insulin resistance.

This drug is well tolerated and is weight-neutral. Dipeptidyl-peptidase IV (DPP-4) inhibitors prevent the degradation of the incretins, glucagon- like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP). This article gives a highlight on the activity of DPP-4 inhibitors in the human body and targets on their development and their significant physiological actions with related to the treatment of type 2 diabetes[3,4].

Figure 1. Structure of Vildagliptin

The importance of method development:

The chief reason for scientific techniques is to get information with respect to productivity (which could be directly connected with the necessity of a identified dose), impurity (related to safety of the medication), bioavailability (uniformity of drug and release of drug), stability (shows the degradation product), and effect of producing parameters to verify that the assembly of drug product is steady[5,6]. Many anti-diabetic drugs and their combination drugs are determined by UV, RP-HPLC, HPTLC, LC and GC[(7-12)].

Quantification of Vildagliptin by Spectrophotometric methods:

Spectrophotometric method utilized for the quantitative analysis of Vildagliptin was cited by Ramzia I.El-Bagary et al (2011)[13] published basic and accurate spectrophotometric techniques for the estimation of Sitagliptin and Vildagliptin in active pharmaceutical ingredient form and its formulated dosage forms. In this method were

supported on the charge transfer complexes of sitagliptin phosphate and vildagliptin with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), 7,7,8,8-tetra cyano quino dimethane (TC NQ) and tetrachloro-1,4-benzoquinone (p-chloranil). In this study, all the parameters were studied and as well as optimized the reaction conditions. Beer's law was obeyed to sitagliptin with the concentration limits of 50-300 µg/ml, 20-120 µg/ml and 100-900 µg/ml with DDQ, TCNQ and p-chloranil, respectively. Beer's law was obeyed to Vildagliptin with the concentration limits of 50-300 µg/ml, 10-85 µg/ml and 50-350 µg/ml with DDQ, TCNQ and p-chloranil, respectively. Samer Housheh et al (2019)[14] created spectrophotometer method to determine the Vildagliptin in bulk. In this method absorbance of Vildaglptin was found at λmax 202.5 in 0.5 M HCl. This proposed method was precise because RSD less than 2%. Linearity test was affirmed inside scope of 10-40 µg/ml for with correlation coefficient (R2) of 0.999. LOQ and LOD were 0.166µg/ml and 0.055µg/ml, respectively with Accuracy of 100.17%. Marwa S. Moneeb et al (2013)[15] was developed a basic and accurate spectrophotometric method to estimation of saxagliptin and vildagliptin in API and its formulated preparations. In this method were depend on derivatization of the investigated drugs with two reagents such as 1, 2 – naphthoquinone – 4 - sulfonic acid sodium salt (NQS) and 4-chloro-7-nitrobenzofurazan (NBD-Cl). To increase the sensitivity, the D1 spectra of the reaction products were also recorded. For NQS reaction, Beer's law was obeyed over the limits of 5–30 and 7–45 µg mL1 for the absorbance readings; and 3–32 and 5–50 µg mL1 for the derivative readings of Saxagliptin and Vildagliptin, respectively.

Sujan Banik et al (2015)[16] created UV spectrophotometric technique for the quantitative analysis of vildagliptin and linagliptin in API and its formulated dosage forms. Calibration curves limit of 8-32 µg/ml and 5-25 µg/ml respectively. P. V. Prasad et al (2017)[17] studied Vildagliptin in manufactured tablet formulation. In 0.1% NaOH exhibited absorption maxima at 216.00 nm. The Vildagliptin obeyed Beers-Lamberts Law in the concentration limit of 10-100 µg/mL along with Correlation Coefficient (R_2) was 0.997. Baokar Shrikrishna et al (2013)[18] established spectrophotometric method for quantitative analysis of Vildagliptin and Metformin in combined pharmaceutical dosage form. The combined drugs obeyed Beers-Lamberts law in concentration limit of 30-70 µg/ml for vildagliptin with Correlation Coefficient (R_2) was 0.999 and 5-25 µg/ml for metformin Correlation Coefficient (R_2) was 0.999.

Omar Abdel-Aziz et al (2014)[19] developed spectrofluorimetric technique for the quantitative analysis of vildagliptin and saxagliptin in API and their tablet forms at 455nm after excitation at 345 nm. Beer's law in a concentration limit of 100-600 µgml^{-1}. The 2nd suggested spectrophotometric technique is related to the charge transfer complex of saxagliptin with tetrachloro-1, 4-benzoquinone (p-chloranil). The created charge transfer complex was determined spectrophotometrically at 530 nm. Beer's law of 100-850 µgml^{-1}. The 3rd proposed spectrophotometric method was related to the condensation reaction of the primary amino group of saxagliptin with formaldehyde and acetyl acetone to create a yellow coloured product known as hantzsch reaction, measured at 342.5 nm with Beer's law limit of 50-300 µgml^{-1}. B. Amani et al (2017)[20] developed Pregabalin and Vildagliptin in pharmaceutical preparation. In this method, the stock solution and subsequent dilution of Pregabalin and Vildagliptin were done in 0.2M Hcl. Solution of Pregabalin in 0.2M Hcl showed λmax at 217.00 nm and solution of Vildagliptin in 0.2M Hcl showed λmax at 204.00nm. These two drugs obeyed beer's law with the concentration limits of 60-100 µg/ml and 1-10 µg/ml for Pregabalin and Vildagliptin, respectively. The RSD of both intra-day and inter-day precision were found as below 2%. The LOD and LOQ were found to be 1.2 µg/ml and 3.69 µg/ml for Pregabalin and 1.06 µg/ml and 3.19 µg/ml for Vildagliptin, respectively. Karajgi Santosh Raveendra et al (2016)[21] developed an easy and precise analytical technique for the quantitative analysis of Vildagliptin and Metformin in combined pharmaceutical dosage forms. In this proposed method utilizes measurement of λmax of Vildagliptin and Metformin using water as a solvent. Absorbance maxima were found as 218.25 nm for Vildagliptin and 225.5 nm for Metformin, respectively. Hydrochloride has absorbance maxima at 225.5 nm in water. Both Vildagliptin and Metformin obeyed Beer's law in concentration limit of 60-100 µg/ml for Vildagliptin and 10-50 µg/ml for Metformin Hydrochloride, respectively. Both these drugs mean recovery were found as 100% for Vildagliptin and Metformin hydrochloride, respectively.

Dr. Safila Naveed et al (2014)[22] established a validated method for vildagliptin using UV spectrophotometer. The proposed method utilizes measurement of λmax of vildagliptin using water as a solvent. Linear calibration curve limits of 12.5-200 µg/ml for vildagliptin with the correlation coefficient of 0.985. Usharani Gundala et al (2013)[23] developed for the quantitative analysis of Vildagliptin and Metformin in combined pharmaceutical formulations. Before this study, there are no reported UV methods for the quantitative analysis of Vildagliptin and Metformin in their pharmaceutical combined formulation. Thus, a requirement was felt to create new methods to analyse the drugs simultaneously. The estimation was achieved by multi-wavelength method, such as 217 nm and 234 nm over the concentration limits of 0.7µg/ml and 7 µg/ml for both drugs Vildagliptin and Metformin respectively.

Amanda T. Barden et al (2018)[24] studied two analytical methods, by second-order derivative UV spectrophotometric by HPLC, for estimation of vildagliptin. This newly created methods were validated as per ICH and USP. UV derivative technique were done at 220 nm, which was the zero-crossing point of excipient solutions. Optimized HPLC technique was achieved utilizing a Zorbax Eclipse Plus RP-C8 column (150 mm × 4.6 mm, 5 µm), detected at 207 nm, and potassium phosphate buffer solution pH 7.0: acetonitrile (85:15, v/v) as mobile phase. In dissolution test, the conditions utilised were 0.01 mol L^{-1} HCl acid in 900 mL of dissolution medium, USP apparatus 2 (paddle) with 50 rpm stirring speed. Both these created methods were successfully performed for analysis of dissolution samples from vildagliptin pharmaceutical dosage form.

Quantification of Vildagliptin by Chromatographic methods:

K. Hanumantha Rao et al (2014)[25] developed RP-HPLC technique for the qualitative analysis of Vildagliptin in pharmaceutical formulation with Altima C18 column and mobile phase containing dilute orthophosphoric acid solution pH 2.6±0.5 as buffer and acetonitrile (72:28 v/v) was used. 1.0 ml/min flow rate and effluents were monitored at 266 nm. The Vildagliptin retention time were found as 3.25 min. LOD and LOQ were found 0.06 µg/ml and 0.21 µg/ml respectively and recovery of Vildagliptin from tablet formulation was found 99.73%. Aparajita Malakar et al (2012)[26] created technique for the qualitative analysis of Vildagliptin in pharmaceutical formulation. The separation was performed on a Xterra® Waters C18 column using mobile phase containing a mixture of aqueous phase (1 ml of 25% ammonium hydroxide was dissolved in 1000 ml of water for chromatography, pH of the solution was adjusted to the value of 9.5 using a 50% solution of phosphoric acid) and organic phase (methanol) with the proportion of 60 : 40 v/v and 1.0 ml/min of flow rate at 210nm. The retention time was found to be 6.3 min with linear between 5- 200µg/ml (r2 = 0.9997). LOD and LOQ were 1.47 and 4.90 µg/mL, respectively. K. Manohar et al (2014)[27] established a RP-HPLC technique for the qualitative analysis of Metformin and Vildagliptin in pure and tablet dosage form with Phenomex column, phosphate buffer and acetonitrile in the ratio of 75:25 v/v as mobile phase. 1.0 ml/min flow rate and UV detection at 260 nm were fixed. The retention time were found to be 2.4 min, 3.4 min for Metformin and Vildagliptin respectively. The linear detector response was found between 25-250 µg/ml, 2.5-25 µg/ml for MET, VIL respectively.

B. Santhosha et al (2012)[28] developed a RP-HPLC technique for the quantitative analysis of Metformin and Vildagliptin in pure and pharmaceutical formulation with Dionex C18 column and mobile phase contains dipotassium hydrogen phosphate (0.01M) buffer and water in the proportion of 90:10 v/v. 1.5ml/min flow rate with UV detection at 215nm. The retention time for Metformin was 2.390 min and for Vildagliptin was 4.601 min. The linear detector response was found between 500-1500µg/ml for Metformin and 50-150µg/ml for Vildagliptin respectively. In the linearity study, the regression equation and correlation coefficient were found to be (y = 124986x, r2 = 1) for Metformin Hydrochloride, (y = 21377x, r2 = 0.9999) for Vildagliptin, respectively. Satheesh kumar N et al[29] established stability-indicating HPLC technique for the quantitative analysis of metformin and vildagliptin in pharmaceutical formulations. The separation was done on Grace Cyano column with isocratic flow. 1.0 mL/min flow rate with mobile phase of 25 mM ammonium bicarbonate buffer and acetonitrile (65:35, v/v) detected at 207 nm. The linear detector response was found between 25-125 µg/mL for Metformin and 50-250 µg/mL for Vildagliptin respectively. LOD and LOQ for Metformin were 0.36 µg/mL and 1.22 µg/mL, and for Vildagliptin were 0.75 µg/mL and 2.51 µg/mL respectively.

Ramesh Jayaprakash et al (2017)[30] developed stability-indicating RP-HPLC technique for quantitative analysis of vildagliptin and metformin in pharmaceutical formulation with Kromasil-C18 column and mobile phase of 0.05 mmol potassium dihydrogen phosphate buffer: acetonitrile [80:20 v/v] with flow rate of 0.9 ml/min at 263 nm. This chromatographic method, the peak retention times were found to be 2.215 min and 2.600 min for metformin and vildagliptin, respectively. A linear detection achieved in the concentration limit of 5-17.5 µg/ml and 50-175 µg/ml for vildagliptin and metformin, respectively. The LOD and LOQ for Vildagliptin were 0.0182µg/mL and 0.0553µg/mL and for metformin were 0.4451µg/mL and 1.3490µg/mL respectively. Khushabu R. Patil et al[31] established reverse phase liquid chromatographic technique for the quantitative analysis of vildagliptin and metformin in mixed dosage form. This chromatographic separation was performed using a mobile phase of 2mM potassium phosphate buffer and Acetonitrile with pH 2.5 adjusted with ortho phosphoric acid with the proportion of 70: 30%v/v. Cosmosil C18 column was used with 1 ml / min flow rate. The PDA detection was achieved at 227 nm. A linear detection response was achieved with the concentration limit of 1-5 µg/mL for Vildagliptin and 10-50 µg/mL for Metformin respectively. The retention times were found to be 2.08 for Vildagliptin and 6.50 min for

Metformin respectively. The Vildagliptin's LOD and LOQ was 0.0604, 0.1831 respectively. Metformin's LOD and LOQ was 0.6802, 2.6821 respectively.

Subhakar Nandipati et al (2012)[32] developed a RP-HPLC technique for the quantitative analysis of Vildagliptin and Metformin in pharmaceutical formulation. The estimation was achieved by the using of 2 phases. Thermo hypersil ODS C18 column utilized as a stationary phase and mobile phase contains 0.1M Potassium hydro phosphate and Acetonitrile at the proportion (60:40%v/v) Adjust the pH:7.0 by using Ortho phosphoric acid. 1ml/min flow rate and detection done at 263nm. 2.1min and 3.5min retention times for Metformin and Vildagliptin respectively. Lakshmana Rao et al (2013)[33] established an easy, precise and rapid HPLC technique for the quantitative analysis of Metformin and Vildagliptin in pharmaceutical formulation. Sunfire BDS C8 column was utilized and the mobile phase comprised of disodium hydrogen phosphate pH 7.0±0.05 as buffer and acetonitrile in the ratio of 60:40 v/v and ultrasonication was done for degassing. 1.0ml/min flow rate was adjusted and the effluent was detected at 263 nm. The retention times were found to be 2.07 min for Metformin and 3.52min for Vildagliptin, respectively. The linear calibration curve was found in the concentration limit of 1000.60 – 300.80 µg/ml and 100.20 – 300.60 µg/ml for Metformin and Vildagliptin, respectively. The percentage recoveries of Metformin and Vildagliptin were found to be 98.8 to 101.9 and 98.5 to 102.1 respectively.

Wael Abu Dayyih et al (2018)[34] established a RP-HPLC separation method was applied using an Xterra C18 column with acetonitrile: phosphate buffer (pH 6.0): water (65: 20:15v/v/v) as a mobile phase and flow rate was 1.0 ml/min. The UV detection was done at 239 nm. In this RP-HPLC method, the LOD was found to be 0.0040 µg/ml and 0.025 µg/ml for vildagliptin, metformin respectively. Linear response was found between 4-34 µg/mL for Vildagliptin and 8-54 µg/ml for Metformin respectively. Meetali M. Chaphekar et al (2016)[35] developed QbD approached RP-HPLC method using Design of Experiments and subsequent validation for analysis of Vildagliptin in raw bulk drug and its pharmaceutical formulation. This competent experimental design has all 3 key components of the RP-HPLC technique such as Buffer pH, Organic Phase - % acetonitrile, Organic Modifier - Methanol. The proposed technique was validated and Forced degradation studies were also carried out in order to determine the stability-indicating nature of the method. In this RP-HPLC method, Jasco CrestPack RP C18 (250 × 4.6 mm, 5µ) column used for separation and Buffer (pH 6): Acetonitrile: Methanol (70:10:20 v/v) employed as mobile phase and detection was achieved using Photo-Diode Array (PDA) detector at 210 nm. Linear response was found between 5-15 µg/mL for Vildagliptin. In this proposed method, the percentage Relative Standard Deviation of both precision and accuracy were found to be less than 2%. Forced Degradation studies revealed that the method was found to be stability-indicating.

Pragati Ranjan Satpathy et al (2014)[36] developed a new RP-HPLC technique with ambiguous UV detection for the quantitative analysis of Vildagliptin in pharmaceutical formulation. Within 4 min separation were achieved with Reverse phase and linearity was found between 50–90 µg/mL ($r2 = 0.999$). C18 column used for the separation and a mixture of pH 8.2 buffer, acetonitrile and methanol employed as the mobile phase. Ambiguous UV detection was achieved at 254 nm. 3.9 ± 0.1 min retention time was found for Vildagliptin. The LOD and LOQ was found to be 2.98 g/m and 9.94 g/mL for Vildagliptin respectively. Mohammed M. Amin et al (2017)[37] established a new isocratic HPLC method for determination of Vildagliptin, Pioglitazone Hydrochloride and Glimepiride in pure and tablet dosage forms with Hypersilgold® C18 column, acetonitrile and 0.05M potassium dihydrogen phosphate buffer, adjusted by orthophosphoric acid to a pH of 3.5 with a proportion of (45:55 v/v) as employed as mobile phase with Isocratic elution system were used. 1.5 ml/min flow rate and the effluent were monitored at 200 nm. A calibration curves was found as linear at a concentration limit of 5–75, 3–45 and 1–8 µg/ml for Vildagliptin, Pioglitazone and Glimepiride respectively with correlation coefficients not less than 0.9996. Sai Lohit et al (2014)[38] developed an easy, precise, specific, RP-HPLC method to determine simultaneously the quantity of Metformin and Vildagliptin at single wavelength at210 nm. Quantification of these drugs by this method was achieved using a Hypercil BDS detector at 210 nm. The linearity was found to be the concentrations between 12.5µg/ml–75µg/ml for Metformin and 1.25µg/ml – 7.5µg/ml for Vildagliptin, respectively. The LOD and LOQ for metformin and vildagliptin were found to be 1.75 and 5.29 µg/ml and 0.46 and 1.39 µg/ml, respectively.

Thangabalan Boovizhikannan et al (2013)[39] studied RP-HPLC technique for the quantitative analysis of vildagliptin in API form and in pharmaceutical dosage form with Agilent XDB C18 column. The mobile phase of 0.1M Phosphate buffer and acetonitrile in the proportion of 85:15% v/v with flow rate 1.0 mL/min and the detection were done at 210 nm. The linear response was between concentration limit of 10 - 150 mg/mL and retention time was 3.04 min. The proposed technique was performed at 50, 100 and 150% of test concentration (50 mg/mL) levels. The

LOD was 0.0329 mg/mL and LOQ was 0.0998 mg/mL for vildagliptin, respectively. Hitesh P. Inamdar et al (2013)[40] developed an easy, accurate and stability-indicating HPLC technique for the quantitative analysis of anti-diabetic drugs. The gradient elution method was done on ACE 3 150mm*4.6mm, 3.5µm column with buffered mobile phase consist of 10mM sodium hexane sulphonate monohydrate and 10mM Potassium dihydrogen phosphate buffer with acetonitrile and methanol in gradient proportion at a flow rate of 1.5 mL min^{-1}**.** The UV detection was achieved at 210 nm. The retention time for vildagliptin was found as 1.5minutes. B. Mohammed Ishaq et al (2012)[41] developed a basic, easy and precise reversed phase-HPLC method to determine simultaneously the quantity of Metformin and Vildagliptin at single wavelength (258 nm) in order to assess estimation in its pharmaceutical dosage form and carried out its stability studies. Water's C18 column used as a stationary phase with an isocratic elution system were performed. The mobile phase comprises of 0.1 M Dipotassium Phosphate buffer (pH 7) and acetonitrile in the ratio of 70:30 v/v. The PDA detection was achieved at 258 nm. The linear calibration curve was found in the concentration limit of 1000 - 3000 µg/ml for metformin and 100 - 300 µg/ml for vildagliptin were studied. Intra and inter-day precision were below 2%. The LOD and LOQ of metformin were found as 1.1 and 3.6 ng/ml. The LOD and LOQ of vildagliptin were found as 0.3 and 0.8 ng/ml.

Shrikrishna B. Baokar et al (2013)[42] studied and evaluated for the simultaneous estimation of Vidagliptin and Metformin hydrochloride in API and pharmaceutical dosage form. In this proposed method carried on Warers HPLC and Lichrocart C18 column was employed. Mobile phase was 0.05 M KH_2PO_4: Acetonitrile (70:30 v/v pH 3.5 with Ortho Phosphoric Acid) with the flow rate 1.0 ml/min and detected at 215 nm. The VIDA and MET retention times were found to be 6.64 and 5.18 minutes respectively.

Atul R. Bendale et al (2018)[43] established stability indicating HPTLC technique of vildagliptin and metformin in pharmaceutical formulations. In this study, system suitability test, stress study, alkali hydrolysis, acid hydrolysis, neutral hydrolysis, oxidative stress degradation, dry heat degradation, wet heat degradation, photodegradation study has been used. In this proposed method, optimization done by altering different parameters, such as organic solvent, the combination of the mobile phase, acid or base changer used in the mobile phase (by varying one parameter and keeping all other conditions constant).in this proposed method, Metformin (500 ng/band) 10 µl stock solution and Vildagliptin (100 ng/band) 2 µl stock solution were applied to TLC plates. The end solutions were applied on the HPTLC plates and these were created as per the optimized densitometry conditions. From the spectra, it was noticed that metformin and vildagliptin showed good absorbance at about 217 nm. Both metformin and vildagliptin were exhibited degradation with extra peaks at R_f values of 0.16 and 0.81, respectively. This proposed process was validated in terms of various parameters as per ICH guidelines. Mixture of Hexane: Methanol: Acetonitrile: Glacial Acetic Acid (2:3.5:2.5:0.2 v/v/v/v) was used as a mobile phase and retardation factor (Rf) values were found as 0.22±0.01 for MET and 0.73±0.02 for VIL. Eman I. El-Kimary et al (2016)[44] developed a single, easy, specific and validated HPTLC technique for the quantitative analysis of linagliptin (LGP), saxagliptin (SGP), vildagliptin (VGP) in their binary mixtures with metformin (MET) in pharmaceutical preparations using environmentally preferable green mobile phase system. In this proposed method, Merck HPTLC aluminum sheets of silica gel 60 F254 used as a stationary phase and mobile phase was mixture of methanol–0.5% w/v aqueous ammonium sulphate (8 : 2, v/v). Densitometric measurement of the spots was achieved at 225 nm for LGP/MET mixture and at 208 nm for both SGP/MET and VGP/MET mixtures. The linear regression analysis data were used for the regression line in the limit of 0.05–0.5 µg/band for LGP and SGP and 0.2–2 and 5–40 µg/band for VGP and MET, respectively.

Amanda Thomas Barden et al (2012)[45] developed RP-HPLC technique was created and evaluated for the estimation of vildagliptin in pharmaceutical formulation, the separation was achieved within 6 min. The linear calibration curve was found in the concentration limit of 20–80 mg/mL (r2 5 0.9999). The LOD and LOQ were found as 0.63 and 2.82 mg/mL, respectively. 6,345 of theoretical plates and 0.99 of peak asymmetry. The R_f value was 3.60. This proposed method reports show that linearity, system suitability for the intended analysis.

Manal Mohamed Fouad et al (2015)[46] established UPLC for determination of two binary mixtures; vildagliptin with metformin and ciprofloxacin with dexamethasone. Phenomenex C18 column was used as a stationary phase and mixture of potassium di-hydrogen phosphate (pH 4): acetonitrile in the proportion of 70:30 (v/v) was used as mobile phase for vildagliptin/metformin mixture or 80:20 (v/v) for ciprofloxacin/dexamethasone mixture. In this proposed method, ambient temperature maintained with flow rate 1 mL/min. The UV detection was achieved at 220 or 254 nm for the two mixtures, respectively. A good linearity was achieved in the concentration limit of 0.5-5 µg/mL for vildagliptin, 5-50 µg/mL for metformin and 2-20 µg/mL for both ciprofloxacin and dexamethasone. Sharifa Sultana

et al (2017)[47] developed a QbD-based rapid, simple, precise and robust RP-UHPLC method for the regular analysis of vildagliptin in raw drug and in pharmaceutical dosage formulations with X-bridge C18 column and phosphate buffer (pH 6.8) and acetonitrile in the proportion of 67:33(v/v) used as mobile phase with the rate of flow was 1.0 ml/min. Photo-diode array plus detection was reached at 239 nm. In this proposed method, method optimization done by QbD approach using Design of Experiments. The chromatographic process design was made with two factors utilized. They are (i) independent variables which comprising percentages of acetonitrile in mobile phase and rate of flow and (ii) co-variates which include the retention time, tailing factor and theoretical plates. This proposed technique was evaluated in terms of ANOVA, normal plot of residual, box-cox plot for power transform, perturbation, counter plot and 3D response surfaces plots.

A. B. Pharne et al (2012)[48] developed an easy and cost-effective Reverse-Phase HPLC method for determination of vildagliptin in plasma. In the management of type 2 diabetes mellitus, Vildagliptin is used as a potent DPP-IV inhibitor. In this proposed method, Tolbutamide is used as an internal standard. In this proposed method, a Perkin Elmer Series 200 HPLC system equipped with XBridge Shield C18 column. The flow rate of mobile phase was 1.0mL/min composed of 50mM ammonium bicarbonate (pH 7.8) (solvent A) and acetonitrile (solvent B) at 210 nm. The retention times were 11.2 min for of vildagliptin and 13.4 min for tolbutamide, respectively. A good linearity was achieved in the concentration limit of 10μg/ml to 120μg/ml. Mahesh Attimarad et al (2014)[49] established HPLC technique for the quantitative analysis of metformin and vildagliptin in drug formulation and human plasma. Fast monolithic column used as a stationary phase and a combination of sodium dihydrogen phosphate and sodium dodecyl sulfate and acetonitrile at pH 4.5 utilized as the mobile phase. The proposed technique exhibited good correlation coefficients ($r \geq 0.997$) in the limit of 0.05-20 μg/mL and 0.1-40 μg/mL for metformin and vildagliptin, respectively. The accuracy and intra-interday precision values were between the allowable limit for both the analytes. The mean extraction recoveries of metformin and vildagliptin from human plasma were 97.51% and 97.18%, respectively.

CONCLUSION:

Most of the techniques like Spectrophotometric and chromatography such as- HPLC, HPTLC, Liquid chromatography, UPLC methods and quality by design (QbD), which was application to pharmacokinetic, dynamic, bioavailability, drug metabolism-disposition and bioequivalence studies were reported. The above cited methods for the estimation of Vildagliptin in pure API, its marketed formulations like alone or combinations and also in biological matrices followed by various tissue extractions, the drug Vildagliptin was quantified. As far as we know there is not a single research paper which refers to the quantification of Vildagliptin for the applicability of chemometric assisted method as well as very few available related with UPLC method and quality by design (QbD). Hence there is still scope for the development of new selective and specific analytical techniques for quantification of Vildagliptin.

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