International Journal of Scientific Research and Engineering Development-– Volume 7 Issue 4, July-Aug 2024
Available at www.ijsred.com

RESEARCH ARTICLE OPEN ACCESS

A Review on Analytical Methods for Vildagliptin and Metformin in Combination

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ABSTRACT
VILDAGLIPTIN : It is an antidiabetic medication belongs to dipeptidyl peptidase-4(DPP-4) enzyme inhibitor class of drug. It is used along with diet and exercise to improve blood sugar control in adults with type 2 diabetes. Vildagliptin works by increasing the release of insulin from the pancreas and decreasing the hormones that raise blood sugar levels.
METFORMIN : It is the first line drug of choice for the treatment of type 2 diabetes particularly in overweight and obese people with normal Kidney function. The review highlights the variety of analytical methods such as UV spectroscopy, high performance liquid chromatography (HPLC), GC (Gas chromatography), LCMS and High performance thin layer chromatography (HPTLC) for the estimation of Vildagliptin and Metformin in combination in pharmaceuticals.

Keywords: Vildagliptin, Metformin, UV Spectroscopy, HPLC and HPTLC.

INTRODUCTION:
Vildagliptin is an orally active antihyperglycemic agent which selectively inhibits the dipeptidyl peptidase-4(DPP-4) enzyme. Its IUPAC name is (S)-1-[N-(3-Hydroxy-1-adamantyl) glycyl] pyrrolidine-2 carbonitrile belongs to a class of drugs known as "Islet enhancers." The molecule known as N, N-(Dimethylimido1-dimethylimidocarbonimidic)diamide or Metformin (MET), is a member of the "Biguanide" class. This medication is an oral anti-hyperglycemic. Beta cells can secrete more insulin when VIDA prevents DPP4 from inactivating GLP-1[1-2] and GIP, which also prevents the pancreatic islets of Langerhans from releasing glucagon. In type 2 diabetes mellitus, VIDA has been demonstrated to lower hyperglycemia [1]

When it comes to treating type 2 diabetes, especially in individuals who are overweightor obese and have normal renal function, MET is the recommended first-line medication. It is used to treat polycystic ovarian syndrome and has been studied for additional conditions where a possible contributing factor is insulin resistance. A combination of Vildagliptin and Metformin is used to improve glycemic control whose diabetes is not controlled by them when administered alone. Numerous analytical techniques, including UV-Visible Spectroscopy, HPLC, GAS, LC-MS, and HPTLC, were discussed in this review article[2]

UV SPECTROSCOPY:

Mayur T. Narkhede et al, 2021: The simultaneous equation method was used in this paper to estimate metformin and vildagliptin in bulk drug and Formulation. The basis of this technique is the measurement of absorbance at 235 and 268 nm using Methanol as a Solvent. The observed linearity for metformin was in the range of 10–50µg/ml, while for vildagliptin was in the range of 2-32 µg/ml. The developed techniques were verified in terms of precision, accuracy (recovery), and linearity. The findings were verified in accordance with ICH criteria [3].

Baokar Shrikrishna et al, 2013: Vildagliptin (VIDA) and Metformin (MET) dosage forms in combination were estimated concurrently. The determination of absorbance using 0.1 N NaOH as a solvent at the wavelengths of maximal absorptions of VIDA and MET. The linearity was in the concentration range of 30 to 70 µg/ml for VIDA, with a correlation coefficient of 0.999, and 5 to 25 µg/ml for MET, with a correlation coefficient of 0.999, the calibration curve was linear. All of the results fell well within the acceptance requirements, demonstrating the method's great potential for simultaneous VIDA and MET measurement in a combination dosage form [4].

Usharani Gundala et al,2013: UV Visible spectrophotometry-based simultaneously estimation

of vildagliptin and metformin in pharmaceutical formulations and bulk was established using a multi-wavelength approach, the estimation was carried out at 217 and 234 nm in wavelength. Vildagliptin and metformin had concentration ranges of 0.7µg/ml and 7µg/ml, with a mean recovery of 100% for both drugs. Vildagliptin and metformin hydrochloride can be simultaneously estimated in analyses using this approach with success [5].

HPLC:

Godge R.K et al,2023: Continual testing of different HPLC method separation settings is a part of the analytical method optimization process, which also includes screening different column and eluent conditions. The detecting wavelength was 206nm with Chromasil-C_{18} column with Mobile phase Methanol:Orthophosphoric acid ratio of 80:20 V/V adjusted to pH 4 and the flow rate was 0.7 ml/min. The chromatographic conditions for metformin and vildagliptin had peak retention durations of 1.87 and 2.54 min, respectively. The technique has been verified in compliance with ICH Q2 R1 standards. It was discovered that the metformin and vildagliptin calibration curves were linear over the concentration ranges of 2–30µg/ml and 1–15µg/ml respectively. The regular dosage of metformin and vildagliptin can be administered with this technique [6].

K. Manohar et al, 2014: For the simultaneous measurement of Vildagliptin and Metformin Hydrochloride in pure and pharmaceutical dosage form, the RP- HPLC method was created using Kromosil column using Mobile phase consisting of Phosphate buffer and Acetonitrile in the ratio of 75:25 V/V with flow rate of 1ml/min with UV detection at 260 nm and validated. It was discovered that the retention durations of VIDA and MET were 3.4 and 2.4 min, respectively. The ICH-Q2B criteria were followed in determining the various analytical parameters, including accuracy, linearity, precision, robustness, limit of detection (LOD), and limit of quantification (LOQ). The RP-HPLC technique was accurate, precise, andsensitive. Consequently, it was effectively used to quantify medications in commercial dosage forms [7].

Caroline Paola Ubber et al, 2014: Vildagliptin and metformin combination in tablets can be determined simultaneously using the high-performance liquid chromatography and mass spectrometry approach. Operating at 25°C, chromatographic separations were obtained using a C8 column (150 × 4.6 mm, 5 µm particle size). Acetonitrile, water, and formic acid in the ratio of 20:80:0.1, v/v/v made up the isocratic mobile phase, which was eluted at a rate of 800 µl/min. A 20 µl injection volume was used. The calibration curves for vildagliptin and metformin, and metformin-related substances A, B, and C ranged from 5-150 ng/mL, 250-2000 ng/mL, and 2.5-25 ng/mL respectively. And all had excellent coefficients of correlation ($r > 0.99$). Based on the quantification of these chemicals in tablets, the levels of vildagliptin (95.2-101.2%) and metformin (97-104.4%) were found to be within the stated range. Using this extremely sensitive approach, no molecules related to metformin were found [8].

GAS CHROMATOGRAPHY:

Popat Mohite et al, 2024: The antidiabetic medication metformin helps to lessen the amount of glucose produced in the liver. Vildagliptin is a DPP-4 inhibitor that decreases the hormones that raise blood sugar levels and increases the pancreas' release of insulin. concurrent evaluation of Vildagliptin and Metformin in prescription dose forms and in bulk. The column measures 30 m in length, 0.25 mm in internal diameter, and 1.8 µm in film thickness with 300 °C for the injector, 250 °C for the detector, and 100 °C for the initial oven temperature. Vildagliptin had a retention period of 22.021min and metformin of 10.203 min, respectively. Linearity, detection limit (LOD), quantitation limit (LOQ), accuracy, precision, system appropriateness, and robustness of the approach were all the subjects of validation studies [9].

LC-MS:

Ramzia et al, 2011: A pair of reversed-phase liquid chromatographic (RP-LC) techniques are presented for the identification of two hypoglycemic agent binary mixtures. Vildagliptin (VDG) was measured using the first approach while 3-amino- 1-adamantanol (AAD), a synthetic intermediate and VDG impurity, was present. The second approach involved the simultaneous determination of metformin hydrochloride (MET) and pioglitazone hydrochloride (PGZ) in their binary combination. In the first mixture, isocratic elution was carried out at a flow rate of 1 ml/min using a mobile phase consisting of potassium dihydrogen phosphate buffer pH (4.6) - acetonitrile - methanol (30:50:20, V/V/V) with UV detection at 220 nm. Using potassium dihydrogen phosphate buffer pH (4.6) and acetonitrile (60:40, v/v) ata flow rate of 1 ml/min and UV detection at 210, the second approach uses isocratic elution [10].

HPTLC:

A.R Shirode et al, 2014: For the purpose of simultaneously estimating metformin hydrochloride (MET) andvildagliptin (VLD) in bulk and in their marketed combined dosage form, reversed-phase

high performance liquid chromatography (RP-HPLC) and High-performance thin layer chromatography (HPTLC) methods were developed. It was discovered that the Rfvalues for VLD and MET were, respectively, 0.55 and 0.44. It was discovered that the RP-HPLC method was linear for both MET and VLD over concentration ranges of 10–60µg/mL. The LOD and LOQ values for MET and VLD in RP-HPLC were 1.09µg/ml and 1.70µg/ml, respectively, and 3.32µg/ml and 5.15µg/ml, respectively. For MET and VLD, respectively, the HPTLC technique was found to be linear over the range of 1000-5000ng/spot and 500- 2000ng/spot [11].

CONCLUSION:

Present systematic review covers the analytical methods for the determination of Vildagliptin and Metformin in combination. UV methods were found to be most widely used for Vildagliptin and Metformin. The other analytical methods like HPLC, HPTLC, LC/MS, were also used for the determination of Vildagliptin and Metformin. The present information will be useful for the future study for researcher involved in formulation development and quality control of Vildagliptin and Metformin in combination.

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