Review Article

Review Article on Various Analytical Techniques for the Estimation of Vildagliptin

Kommineni Lahari*1 Varikallu Sravani2, Vulleru Bala Murali 2, Manchi Madhavai Latha2, Khadgam Pooja2, Puttagunta Srinivasa Babu3
1Assistant Professor, Vignan Pharmacy College, Vadlamudi, Affiliated to JNTUK, AP, India.
2 Student at Vignan Pharmacy College, Vadlamudi, Affiliated to JNTUK, AP, India.
3 Professor and Principal, Vignan pharmacy college, Vadlamudi, Affiliated to JNTUK, AP, India.
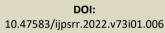***Corresponding author's E-mail:** lahari2623@gmail.com

ABSTRACT

Pharmaceutical analysis plays a very prominent role in quality assurance as well as quality control of bulk drugs and pharmaceutical formulations. The use of analytical sciences in the discovery, development and manufacture of pharmaceuticals is wide ranging. From the analysis of minute amounts of complex biological materials to the quality control of the final dosage forms, the use of analytical technology covers an immense range of techniques and disciplines. In the current scenario, approximately 463 million adults (20-79 years) were living with diabetes; by 2045 this will rise to 700 million1. New drug molecules are being developed and the analysis is also gaining equal importance. The present article focuses on the different analytical methods for the quantitative estimation of Vildagliptin, an anti-hyperglycaemic agent. A huge survey was conducted for determination of Vildagliptin from the research articles published in various pharmaceutical and analytical chemistry Journals. The present studies revealed that HPLC technique along with the spectroscopic have been most widely explored for the analysis. The investigatory review may provide the comprehensive details of various analytical techniques and their experimental condition to the researchers who are working in the area of analytical research of Vildagliptin.

Keywords: Pharmaceutical analysis, Vildagliptin, High-performance liquid chromatography, UV spectrophotometry, Gas Chromatography- Mass spectroscopy.

INTRODUCTION

The complexity and globalization of the pharmaceutical supply chain necessitate that standards are built into development and manufacturing processes – from raw materials through finished products. Standards are essential for ensuring the identity, purity, potency and performance of drugs across the product lifecycle. In a 2018 survey, 90% of industry professionals with expertise formulating and testing drugs, indicated that standards accelerated drug development, especially in the case of generics, saving about 19% in total product development time2. Medicinal products (gene therapy, personalized medicine, and other emerging therapeutic modalities) grow increasingly complex. Quality attributes of these products are also more complex, difficult to define and measure, making standards even more critical for ensuring quality. For standards to remain relevant, they must evolve in response to advances in the industry. Existing standards need to be updated, and new, fit-for-purpose standards created to ensure they include the most useful, appropriate, and feasible approaches to measuring relevant parameters.

These days, the proportion of people with type II diabetes is increasing in most countries and it is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. As such, there is a growing need for anti-hyperglycemic agents, along with their quality attributes. Vildagliptin is one such drug which is an orally active, potent & selective dipeptidyl peptidase-4 (DPP-4) inhibitor that improves glycemic control in patients with type-II diabetes primarily by enhancing pancreatic (α & β) islet function. Vildagliptin has been shown both to improve insulin secretion & to suppress the inappropriate glucagon secretion. Elevated level of GLP-1 & GIP consequently results in improved glycemic control.

Oral vildagliptin was approved by the European medicines agency in 2008 for the treatment of type-II diabetes mellitus in adults as monotherapy or in combination with metformin, a sulfonylurea, or a thiazolidinedione in patients with inadequate glycemic control following monotherapy. It is marketed as Galvus. Vildagliptin is also available as Eucreas, fixed dose formulation with metformin for adults in who do not adequately glycemic control from monotherapy. Vildagliptin is currently under investigation in the US.

Methods

Vildagliptin is estimated by so many methods like High performance liquid chromatography (HPLC), (RP-HPLC)

Reverse- phase high performance liquid chromatography, gas chromatography, Mass spectroscopy (GC-MS), UV spectrophotometric method.

A) Chromatographic methods:

In RP-HPLC &HPLC different mobile phase and stationary phase are used that also change in UV absorption or λ_{max}.

Based on the solvents and columns used there is a change in every chromatographic conditions. The chromatographic conditions and the results obtained were listed in the Table 1.

Table 1: Details of various chromatographic methods for the estimation of Vildagliptin

Technique	Chromatographic condition	Results obtained	Reference
RP-HPLC	S-phase : Xterra® waters C_{18} column (150mm *4.6m) M-phase : mixture of aqueous phase (1ml of 25%NH_4OH by using 9.5 50% solution of phosphoric acid) and organic phase (methanol) in the ratio 60:40 v/v Flow rate: 1.0ml/min Retention time: 6.3min	Absorption at 210nm, LOD was found to be 1.47µg/ml LOQ was found to be 4.90µg/ml linearity range was 5-200µg/ml	3
RP-HPLC	s-phase : Lichrocart C_{18} column (250*4.60*5) m-phase : 0.05M KH_2PO_4 : Acetonitrile (70:30v/v pH 3.5 with orthophosphoric acid) flow rate :1.0ml/min retention time : 6.64min	Absorption at 215nm linearity range was found to be 5-25µg/ml	4
RP-HPLC	S-phase : Xterra C_{18} column (250mm*4.6mm I.D-5µ) M-phase : acetonit;rile : phosphate buffer (pH6.0) :water (65:20:15v/v/v) Flow rate : 1.0ml/min	λ_{max}at 239nm LOD was found to be -0.0040µg/ml	5
RP-HPLC	Column phenomenex C_{18} column (250mm*4.6mm I.D-5µ) used as S-phase M-phase include methanol : water (60:40v/v) pH adjusted to 4.5 with orthophosphoric acid Flow rate- 0.8ml/min	UV detection at 207nm	6
RP-HPLC	S-phase : Thermo Hypersil ODS C_{18} column 5µ, 4.6mm*250mm) M-phase : methanol : acetonitrile: phosphate buffer (5:30:65) v/v/v pH- 3.5 Retention time : 5.41min Flow rate : 0.8ml/min	λ_{max}at 212nm linearity range was found to be 1-14µg/ml	7
RP-HPLC	S-phase : Jasco Crestpack RP-C_{18} (250*4.6mm I.D-5µ) M-phase : Buffer (pH-6):acetonitrile: methanol (70:10:20v/v/v)	UV detection at 210nm Linearity range was found to be 5-15µg/ml	8
RP-HPLC	S-phase : HiQsil C_{18} (4.6mm*250mm) analytical column M-phase : include phosphate buffer (Ph adjusted to 6 using 3M KOH): methanol: acetonitrile (50:30:20v/v/v) Flow rate : 0.8ml/min	LOD & LOQ -1.70µg/ml &5.15µg/ml	9
RP-HPLC	S-phase : Dionex C_{18}(250mm*4.6mm – I.D-5µ) M-phase : K_2HPO_4 (0.01M) buffer and water (90:10v/v) Flow rate : 1.5ml/min Retention time : 4.601min	UV detection – 215mm Linearity range was 50-150µg/ml	10
RP-HPLC	S-phase : Kromosil-C_{18} column was used M-phase: 0.05 mmol KH_2PO_4 Buffer: acetonitrile: (80:20:v/v) (pH adjusted to 3.5 using orthophosporic acid) Flow rate: 0.9ml/min	Absorbance at 263nm Linearity range was 5-17.5µg/ml Tailing factor -1.26	11

	Runtime: 6 min Column temp: 30^{0}C Injection volume -10µl Retention time – 2.600min	LOD & LOQ was 0.0182 & 0.0553µg/ml	
RP-HPLC	Altima C$_{18}$ column (150mm*4.6mm) is used as S-phase M-phase include dilute phosphoric acid Ph 2.6±0.5 as buffer and acetonitrile (40:60v/v) Flow rate was 0.5ml/min Runtime- 6.0min, retention time-305min Theoretical plates-5892	λ$_{max}$ at 210nm linearity range was 5-30µg/ml LOD &LOQ was found to be 1.36 & 4.12µg/ml Tailing factor-1.42	12
RP-HPLC	Column is chromosil C$_{18}$ column (250mm*4.6mm,5µ) M-phase include K$_2$HPO$_4$: methanol (60:40v/v) pH -9.2 Retention time- 5.32min	λ$_{max}$ at 258nm	13
RP-HPLC	Monolithic column is used as S-phase M-phase: acetonitrile – NaH$_2$PO$_4$ (10mM): sodium dodecyl sulphate (10mM) (30:70v/v) with pH 4.5±0.2 Flow rate: 2.5ml/min	λ$_{max}$ at 208nm	14
RP-HPLC	S-phase : column (C$_{18}$, 5µ, 4.6*250mm) Hypersil M-phase : Acetonitrile : methanol : water (15:60:25v/v) Flow rate : 1.0ml/min	λ$_{max}$ at 278nm linearity range was 1-5µg/ml LOD & LOQ – 0.154 &0.468µg/ml	15
HPLC	Altima C$_{18}$ column having 150mm*4.6mm internal diameter 5µm is used as S-phase M-phase: contains dilute orthophosphoric acid solution as a buffer pH 2.6 and acetonitrile (72:28v/v) isocratic mode, flow rate-1.0ml/min Retention time – 3.25min	λ$_{max}$at 266nm LOD & LOQ was 0.06µg/ml & 0.21µg/ml	16

B) Spectrophotometric methods:

Different UV and Visible spectrophotometric methods were done for the estimation of Vildagliptin. The spectroscopic conditions and the results obtained were listed in the Table 2.

Table 2: Details of various spectrophotometric methods for the estimation of Vildagliptin

Technique	Experimental conditions	Results obtained	Reference
UV Spectrophotometric	0.1N NaOH was used as a solvent	UV detection at 233nm Linearity range was 30-70µg/ml Correlation coefficient 0.999	17
Visible Spectrophotometric	This method was based on formation of schiff's base with PDAB in acidic ethanol	It gives yellow colour UVabsorption at 446 nm LOD & LOQ was found to be 10.633 µg/ml and 32.223µg/ml	18
UV Spectrophotmetric	Water was used as a solvent	λ$_{max}$- 218.25nm linear range was 60-100µg/ml	19
UV Spectrophotometric	0.2M HCl is used as a solvent	λ$_{max}$ – 204 nm linearity range was 1-10µg/ml LOD & LOQ was 3.69µg/ml 3.19µg/ml	20
UV Spectrophotometric	0.1 N HCl was used to dissolve the sample	λ$_{max}$ at 210nm linearity range was 5-60µg/ml LOD & LOQ was found to be 0.951µg/ml & 2.513µg/ml.	21

C) Other advanced techniques: Advanced hyphenated techniques for the analysis of Vildagliptin are listed below in the table 3

Table 3: Details of various advanced techniques for the estimation of Vildagliptin

Technique	Experimental condition	Result obtained	Reference
GC-MS	Sample was derivatized with N-Methyl-N(trimethylsilyl) trifluoroacetamide (MSTFA): Ammonium iodide: β-mercapto-ethanol at 60^0 for 30 min (100:2:6 v/v/v. 5% phenyl methylpolysiloxane capillary column is used (30m*0.25mm, I.P-025μm)200^0-300^0 C temo used, at 300^0 C held for 2 min.	LOD & LOQ was found to be 1.5 ngml^{-1}& 3.5ngml^{-1}	22

CONCLUSION

The present review discussed about different analytical approach employed for the assessment of Vildagliptin. Extensive examinations have been accomplished including, HPLC, UPLC, HPTLC, UV/Vis-Spectroscopy, LC-MS, etc. for evaluation of Vildagliptinin bulk and in its combination with other drugs from pharmaceutical formulations. Liquid chromatography with UV detection has been found to be most studied for estimation in both bulk as well as pharmaceutical dosage forms, while the advanced techniques like HPTLC, UPLC were also reported. Simple UV-Spectrophometric methods were developed which may be used for routine analysis of Vildagliptin. These compiled data may be of use for research for further studies in analysis of Apremilast or other similar drugs.

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