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A REVIEW: ANALYTICAL DEVELOPMENT AND VALIDATION OF VILDAGLIPTIN IN BULK AND PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

Vildagliptin is approved in 2007 by USFDA. Vildagliptin s- l-[n-(3-hydroxy-1-adamantyl) glycyl] pyrrolidine-2- carbonitrile is oral anti-diabetic drug of the new potent dipeptidyl peptidase-4 inhibitor category of antidiabetic medicine. The present work category theeasy, accurate, precise analytical HPLC method. This paper could be a review analyticalHPLC techniques that are the widely-used in determination common provision issues. In these review involve information about HPLC method development like mobile phase, mobile phase ratio, column, retention time, flow rate and wavelength of UV detector, run time and Validation parameter is Linearity, percentage recovery, limit of detection and limit of quantification. Pharmaceutical analysis plays an important role in quality assurance as internal control of pure and pharmaceutical dosage form. Analytical method development has become the important activity of study.

Keywords: Vildagliptin, Drug profile, Pharmacology, Pharmacokinetic, Analytical HPLC Method

INTRODUCTION

Vildagliptin is an oral anti-diabetic drug(antihyperglycemic agent) potent dipeptidyl peptidase IV(DPP-IV) for the treatment of diabetes2. Vildagliptin IUPAC name is 2S- (3- Hydroxyadamantan- l-ylamino) acetyl pyrrolidine- 2-carbonitrile. DPP-IV inhibitors represent (vildagliptin) a brand new class of oral anti -hyperglycemic

agents to shown reduce hyperglycemia in type-2 diabetes mellitus. DPP-IV inhibitor improves fasting state and postprandially glycaemic control without hypoglycemia or weight gain. Vildagliptin inhibits dipeptidyl peptidase -IV in turn inactivation ofGLP-I and GIP by DPP-IV, allowing GLP- I and GIP which are incretin hormone that promote the secretion of insulin in the beta cells an inhibit glucagon release by the alpha cells of the islets of Langerhans in the pancreas. Literature survey disclosed that few analytical methods used for estimation of Vildagliptin and stability indicating assay method and simultaneous estimation drug with Vildagliptin from its pharmaceutical dosage form. The aim of review is get more information about method of development and validation vildagliptin bulk and pharmaceutical dosage form [1-10]. The review methodology is easy, accurate and precise method development of Vildagliptin and pharmaceutical dosage form.

Drug Profile

Drug	Vildagliptin
IUPAC Name	2S-(3- Hydroxyadamantan- l-ylamino) acetyl pyrrolidine- 2-carbonitrile
Molecular Formula	$C_{17}H_{25}N_3O_2$
Molecular Mass	303.3993g/mole
Melting Point	153-155^{0}C
Physical State	Solid
Solubility	Soluble in Methanol and water (20^{0}C)
pKa	9.03 and 14.71 Basic and strong acid
Half Life	90Min
Use	Reduce hyperglycemia in type 2 diabetes mellitus

Pharmacology

Vildagliptin may be a potent and selective, reversible, competitive DPP-IV inhibitor an accelerator and binding macromolecule tissues like the kidneys and liver, lymphocytes, and epithelial tissue cells .Vildagliptin binds covalently to DPP-IV, eliciting prolonged enzyme inhibition. DPP-IV is concerned in the inactivation of the neuropeptides and cytokines, chemokines and epithelial duct hormones. Vildagliptin inhibits dipeptidyl peptidase -4 in turn inactivation of GLP-1 and GIP by DPP-IV, allowing GLP- I and GIP which are incretin hormone that promote the secretion of insulin in the beta cells and inhibit glucagon release by the alpha cells that lowering of glucose.DPP-IV role in blood glucose regulation is thought to be through degradation of GIP and GLP-I.

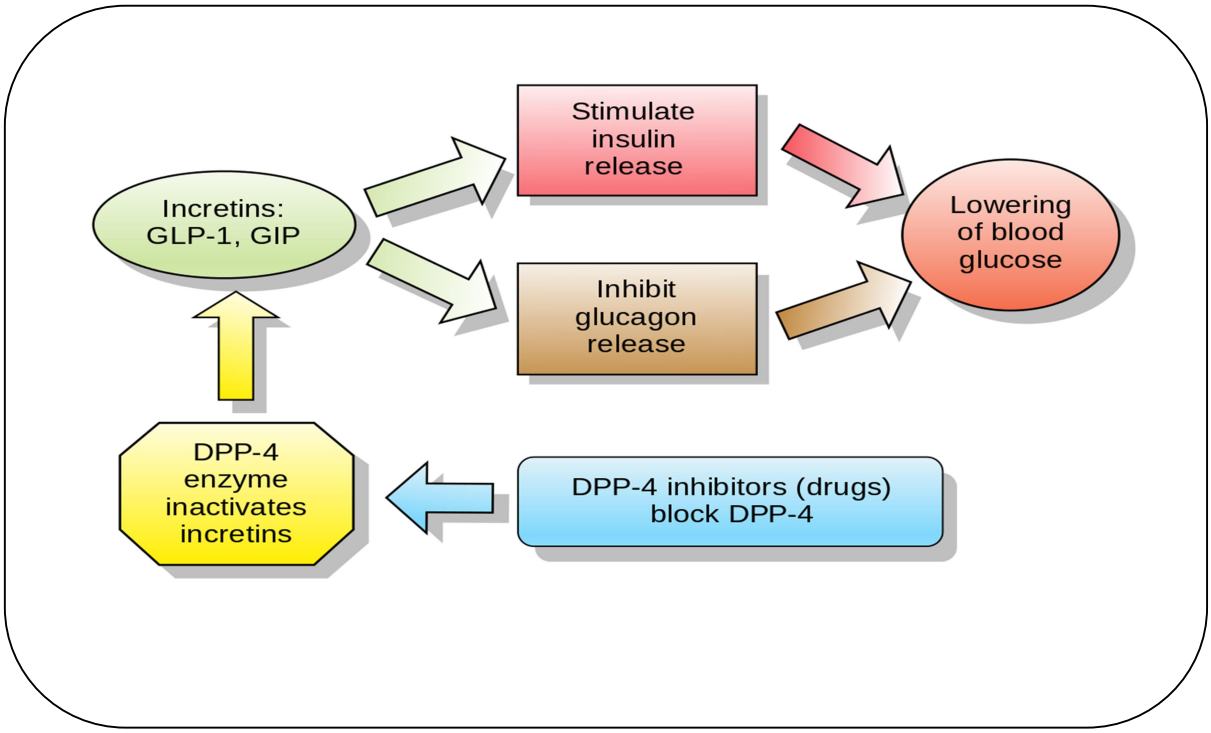

Figure 1: Mechanism of DDP-IV Inhibitor

Pharmacokinetic

Vildagliptin has been report healthy volunteers and study in patients with type 2 diabetes mellitus. Vildagliptin rapidly absorbed following oral administration. Plasma concentration of vildagliptin increase in an around dose-proportional manner. Plasma protein binding of vildagliptin is 9.3% .Peak plasma vildagliptin concentration observed at 1 to 2.Vildagliptin shown oral bioavailability of 85% in healthy volunteers and pharmacokinetics of vildagliptin was not affected by meal. Absolute bioavailability greater than 90% and the average clearance rate from plasma of 1.5 L/hr. /kg. Vildagliptin is hydrolysis to inactive metabolite CYP450 not significantly involved. Vildagliptin excreted by kidney.

Analytical HPLC method development for vildagliptin

High-performance liquid chromatography could be a specific type of chromatography employed in organic chemistry and analysis to separate, identify, and quantify the active compounds. High Performance Liquid Chromatography is the type of column chromatography and, is mostly commonly used technique in pharmaceutical industry. The principle is the sample injected at the top of column of a porous material

(stationary phase) flow along with mobile phase (liquid) and is pumped and pressurize through the chromatographic column. The separation of sample is based on the differences between in the rates of migration through the column arising from different partition of the solution between the stationary phase and mobile phase and flow rate of mobile phase. High Performance Liquid Chromatography is much versatile than gas chromatography since it is not limited to unpredictable and thermally stable samples, and the choice of stationary phaseand mobile phase is wider.

High performance liquid chromatography is an important analytical tool in assess of drug product. This article reviews the use of HPLC for chromatographic analysis of antidiabetic drugs dipeptidyl peptidase IV.

Method Validation:

Analytical methods should be validated as per International Conference on Harmonization (ICH) guidelines. Methodvalidation has ICH guideline's defines eight steps for validation:

1. Accuracy:
2. Precision
3. Specificity
4. Linearity
5. Range
6. Detection limit
7. Quantitation limit
8. Robustness
9. Ruggedness
10. Sensitivity
11. Repeatability
12. Reproducibility

Sr. No.	Author	Mobile phase	Flow Rate	Retention Time	Detection	column	Linearity
1	Sultana etal. (2013)	Acetonitrile: Buffer 50:50v/v	1.0 ml/min	5.017min	220nm	ZOBRAX Rapid Resolution HT column	10-60ug/ml
2	Rao etal. (2014)	Dilute Orthophosphoric acid (PH 2.6 as buffer):acetonitrile(72: 28v/v)	1.0 ml/min	3.258min	266nm	Altima C18 column	25-150ug/ml
3	Manohar *et al.*(2014)	0.1MPhosphate Buffer (6.8): Acetonitrile75:25	1.0 ml/min	3.9 min	260nm	PhenomexKro mosil column	2.5-25ug/ml
4	Khatun *et al.* (2013)	0.02M phosphate Buffer: Acetonitrile(PH4.6) 80:20v/v	0.7 ml/min	3.6min	210nm	Shimpack VP-ODS Shimadzu column	20-70ug/ml
5	Satpathy *et al.*(2014)	Acetonitrile: Phosphate Buffer(8.2): methanol	0.5 ml/min	3.9min	254nm	Symmetry C18 column	50-90ug/ml
6	Savale *et al.*	Di potassium	0.5	5-5.5min	263nm	Qualisil	10-60ug/ml

	(2017)	**Hydrogen(adjPH7 OPA)phosphate: Acetonitrile70:30**	**ml/min**			**BDSC18 column**	
7	**Santhosha *et al.* (2012)**	**Di Potassium (0.01M)hydrogen phosphate Buffer: water 90:10v/v**	**1.5 ml/min**	**4.601min**	**215nm**	**Dionex C18 column**	**50-150ug/ml**
8	**Imran *et al.* (2017)**	**Potassium Phosphate Buffer(3.2):Acetonitril e 60:40v/v**	**0.7 ml/min**	**-**	**225nm**	**Shimadzu Primesil C18 column**	**10-50ug/ml**
9	**Malakar *et al* (2012)**	**Ammonium hydroxide(adjust PH9.5, 50% (phosphoric acid):Methanol 60:40v/v**	**1.0 ml/min**	**6.3min**	**210nm**	**Xterra^{R} waters column**	**2-200ug/ml**
10	**Barden *et al.*(2012)**	**Acetonitrile:triethylam ine(0.3%adjustPH7.0 phosphoric acid) in ratio 15:85v/v**	**1.0 ml/min**	**3.60min**	**207nm**	**XBridge analytical,C8 column**	**20-80ug/ml**
Sr.N o	**Author**	**Mobile phase**	**Flow Rate**	**Retention Time**	**Detection**	**Column**	**Linearity**
11	**Raju *et al.*(2019)**	**01M Di Potassium Hydrogen phosphate: methanol 60:40v/v**	**0.5 ml/min**	**5.32min**	**258nm**	**Chromosil C18 column**	**20-160ug/ml**
12	**Nagalaksh mi et al.(2021)**	**Acetonitrile: methanol :water 15:60:25v/v**	**1.0 ml/min**	**2.8min**	**278nm**	**Hypersil ODS C18 column**	**1-5ug/ml**
13	**Meetali *et al.*(2016)**	**buffer(PH6):acetonitril e: Methanol 70:10:20 v/v**	**1.0 ml/min**	**7.21min**	**210nm**	**Jasco crest pack Rp column**	**5-15ug/ml**
14	**Shakoor *et al.*(2020)**	**Phosphate Buffer (6):Acetonitrile: methanol 65:30:5**	**0.8 ml/min**	**5.41min**	**212nm**	**Thermo Hypersil ODS C18 column**	**1-4ug/ml**
15	**Shaikh *et al.*(2020)**	**phosphate Buffer: Acetonitrile(3.2) 30:70v/v**	**1.0 ml/min**	**6min**	**222nm**	**A Kromstar^{R} column**	**5-25ug/ml**
16	**Reddy *et al.*(2021)**	**Acetonitrile: methanol75:25v/v**	**1.0 ml/min**	**2.545min**	**225nm**	**Kromasil C18column**	**24.9-5003.8 ug/ml**
17	**Amin *et al.*(2017)**	**Acetonitrile: potassium Dihydrogen phosphate buffer(adjust PH 3.5 OPA) 45:55v/v**	**1.5 ml/min**	**1.27min**	**200nm**	**Hypersil Gold C18 column**	**5-75ug/ml**
18	**Attimarad etal. (2014)**	**Acetonitrile: SodiumDihydrogen phosphate(10nM)SDS(10nM)(with PH4.5)30:70v/v**	**2.5 ml/min**	**2.167min**	**208nm**	**Fast monolithic C18 column**	**0.1-40ug/ml**
19	**Dhale *et al.*(2019)**	**Acetonitrile :Water(ph adjust7 triethalyamine)**	**1.0 ml/min**	**5.3min**	**220nm**	**Hypersil Gold C18 column**	**2-20ug/ml**
20	**Balamurug an *et al.* (2009)**	**Acetonitrile: potassium Dihydrogen phosphate(4.6)**	**0.4 ml/min**	**5.62min**	**220nm**	**OnyxC18 monolithic column**	**2-10ug/ml**
21	**Pharne *et al.*(2014)**	**Acetonitrile: Ammonium bicarbonate(7.8)**	**1.0 ml/min**	**11.2min**	**210nm**	**Shield C18 column**	**10-120ug/ml**
Sr. No.	**Author**	**Mobile Phase**	**Flow Rate**	**Retention Time**	**Detection**	**Column**	**Linearity**

22	**Gattu *et al*.(2014)**	**Phosphate buffer :methanol**	**1.0 ml/min**	**4.243min**	**200nm**	**Zodiac C18 column**	**7.5-17.5 ug/ml**
23	**Barden *et al*.(2018)**	**Acetonitrile: potassium phosphate buffer 85:15v/v(7)**	**1.0 ml/min**	**-**	**207nm**	**Zorbax Eclipse Plus Rp C18 column**	**10-90ug/ml**
24	**Thangabalan *et al*.(2013)**	**Acetonitrile: phosphate buffer15:85v/v**	**1.0 ml/min**	**3.04min**	**210nm**	**Agilent Eclipse XDB C18 Column**	**10-150ug/ml**
25	**Ramesh *et al*. (2017)**	**Potassium Di Hydrogen phosphate buffer: Acetonitrile 80:20v/v**	**ml/min**	**2.6min**	**263nm**	**Kromasil C18 column**	**50-175ug/ml**
26	**Abu *et al*.(2018)**	**Acetonitrile : phosphate Buffer:water65:20:15v/v(6)**	**1.0 ml/min**	**2.28min**	**239nm**	**XterraC18 column**	**5-25ug/ml**
27	**Basha *et al*.(2017)**	**Di Potassium hydrogen phosphate: Methanol (9.2)**	**0.5 ml/min**	**5.32min**	**258nm**	**Chromosil ODS C18 column**	**-**
28	**Drashti *et al*.(2021)**	**Acetate Buffer(5.6): Methanol30:70v/v**	**1.0 ml/min**	**6.334min**	**210nm**	**Xterra WaterC18 column**	**10-200ug/ml**
29	**Shirode *et al*. (2014)**	**Phosphate buffer(PH6 using KOH):Methanol: Acetonitrile 50:30:20 v/v**	**0.8 ml/min**	**4.8min**	**220nm**	**HiQsil, BDS Hypersil C18 column**	**10-60ug/ml**
30	**Ishaq *et al*.(2012)**	**Di potassium phosphate buffer(7):acetonitrile 70:30 v/v**	**1.0 ml/min**	**5.3min**	**258nm**	**Water's C18 column**	**100-300 ug/ml**

CONCLUSION:

Vildagliptin is anti-diabetic medicine used in diabetic mellitus. The above study gives the analytical high performance liquid chromatography methods for study and analysis of vildagliptin in pure form and pharmaceutical dosageform. Literature survey reveals that many methods are reported for the method development and validation parameter of various drugs. A present review illustrates various analytical approaches for the evaluation of vildagliptin had performed including HPLC in pure form, and pharmaceutical dosage form. These methods are reported for the method development and validation parameter of vildagliptin drugs. Analysis of drug plays a important role after formulation to identify the drug and its metabolites.

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