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A Review on Estimation of Metformin Hydrochloride and Vildagliptin in Pharmacutical Dosage Form

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ABSTRACT

The aim of this review to focus on comprehensive update of different analytical methods for determination of oral anti-diabetic drugs like Metformin hydrochloride and Vildagliptin for the treatment of type 2 diabetes mellitus (T2DM), such as biguanides and sodium /glucose co –transportaer 2 inhibitors in their bulk materials and in pharmaceutical dosage forms. This review provides detailed information of development and validation for Metformin hydrochloride and Vildagliptinin bulk and in pharmaceutical preparations either alone or in combination with other hypoglycemic agent.

KEYWORDS: *Metformin HCL, Vildagliptin, Analytical methods, Antidiabetic*

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INTRODUCTION

Diabetes mellitus is a combination of heterogeneous disorders commonly presenting with episodes of hyperglycaemia and glucose in tolerance, as a results of lack of insulin, defective insulin action, or both. Such complications arise due to derangements in the regulatory systems for storage and mobilization of metabolic fuels, including the catabolism and anabolism of carbohydrates, lipids and proteins emanating from defective insulin secretion, insulin action, or both.

Classification of diabetes mellitus is based on its a etiology and clinical presentation. As such, there are four types or classes of diabetes mellitus viz; type 1 diabetes, type 2 diabetes, gestational diabetes,

Classification of diabetes mellitus is based on its aetiology and clinical presentation. As such, there are four type or classes of diabetes mellitus viz; type 1 diabetes, type 2 diabetes, gestational diabetes, and other specific type. The incidence of type 1 diabetes is increasing in both rich and poor countries. Furthermore, a shift towards type 1 diabetes occurring in children at earlier ages is imminent.85 to 95% of all diabetes in high-income countries are of type 2 accounting for an even higher dominance in developing countries.

It is intimately associated with improper utilization of insulin by target cell and tissues. It is currently a common and serious health concern globally. According to WHO, this problem has been aggravated by rapid cultural and social dynamics, ageing populations, increasing urbanization, dietary changes, reduced physical activity and other unhealthy lifestyle and behavioural patterns[(1)]

Metformin (Met)is a biguanide class drug which is orally administered for the management of type 2 diabetes. In patients with type 2 diabetes, MTF improves glucose tolerance, as well as lowers the postprandial and basal plasma glucose. MTF are prescribed for patients that are obese or over weight with normal kidney faction. It improver insulin

sensitivity by decreasing glucose intestinal absorption and hepatic production, and it is the most important therapy which is used in combination with other orally administered hypoglycaemic [2]

Vildagliptin (VLD) is used for the treatment of type 2 diabetes. VLG,(S)-1-[N-(3-hydroxy-1-admantyl1)glycl] pyrrolidine-2-carbonotrile, as a potent and selective DPP-IV inhibitor that improves glycaemic control in patient with type 2 diabetes mellitus by increasing α-and β-cell responsiveness to glucose [3]

Diabetes mellitus (DM) is a chronic condition characterized by high level of blood glucose due to a defect in insulin production or activity.

This disease has been a struggle for many generations. The prevalence of diabetes is expeditiously escalating, accordingly, the awareness of its treatment has of a tremendous interest among recent population.

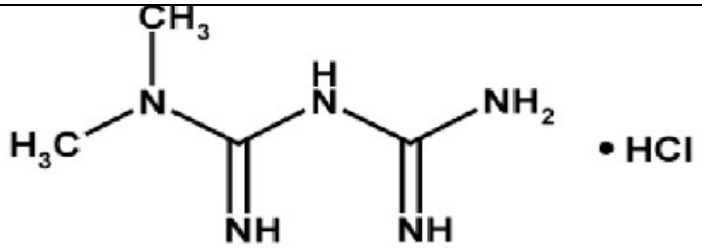
Type1 (Insulin dependent Diabetes Mellitus – (IDDM), occur mostly in juvenile and when secretion of insulin is diminished .Management of type 1 DM is achieved through intake of exogenous insulin.

Type2 (Non –insulindependent Diabetes Mellitus – NIDDM) is more common in order adults however its incidence among teenagers have boosted in the current year mainly due to unhealthy lifestyle.

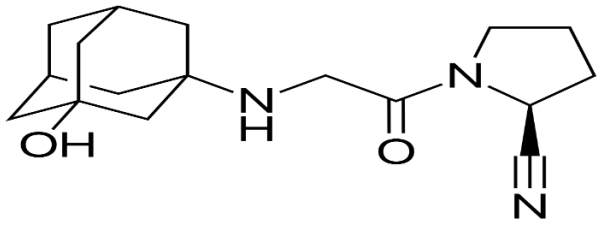
Oral anti-diabetic drug are initiated in case of type 2 DM that had inadequate response toward lifestyle change including calorie restriction and increase in physical activity [4]

Drug profile:

METFORMIN HYDROCHLORIDE:

Structure	
Chemical name	N-N –Dimethylimidodicarbomidicdiamide
Molecular formula	C4H11N5
Molecular weight	165.62g/mole.
Appearance	white to off-white crystalline compound
Category	Metformin hcl : hypoglycemic Vildagliptin : anti hypoglycemic
Melting point	221℃
Solubility	Freely soluble in water and is practically insoluble in acetone, ether and chloroform

VELDAGLIPTIN:

Structure	
Chemical name	(S)-1-[N-(3-Hydroxy-1-adamantyl)glycyl] pyrrolidine-2-carbonitril
Molecular formula	C17H25N3O2
Molecular weight	303.399g/mol
Appearance	white to slightly yellowish or slightly greyish crystalline powder
Category	Anti-diabetic
Melting point	150℃
Solubility	Freely soluble in water mg/mL

Mechanism of Action:

Metformin:

The molecular mechanism of metformin is not completely understoodActivation of AMPKwas required for metformin's inhibitory effect on liver glucose production. AMPK is an enzyme that plays an important role in insulin signalling, whole-body energy balance, and the metabolism of glucose and fats.

The molecular mechanism of metformin is not completely understood of AMPK was required for metformin's inhibitory effect on liver glucose production. AMPK is an enzyme that plays an important role in insulin signalling, whole-body energy balance, and the metabolism of glucose and fats. AMPK activation was required for an increase in the expression of small heterodimer partner, which in turn inhibited the expression of the hepatic gluconeogenic genes phospgoenolpyruvate carboxykinase and glucose 6-phosphatase. Metformin is frequently used in research along with AICA rib nucleotide as an AMPK agonist. The mechanism by which biguanidesincrease the activity of AMPK remains uncertain; however, metformin increases the concentration of cytosolic adenosine monophosphate (AMP) as opposed to a change in the total AMP or total AMP/adenosine triphosphate increased cellular. AMP has been proposed to explain the inhibition of a glucagon-induced increase in cAMP and activation of PKA. Metformin and other biguanides may antagonize the action of glucagon, thus reducing fasting glucose levels. Metformin also induces a profound shift in the faecal microbial community profile in diabetic mice and this may contribute to mode of action possibly through an effect on glucagon-like peptide-1 secretion.

Vildagliptin:

During a meal, the incretins glucagon-like peptide 1 (GLP-1) and glucose-dependent gastro intestinal polypeptide (GIP) are released by the small intestine in to the blood stream. These hormones regulate insulin secretion in a glucose-dependent manner.(GLP-1 has many role in the human body. It stimulates insulin biosynthesis, inhibits glucagon secretions, slows gastric emptying, reduces appetite and stimulates regeneration of islet β-cells.)

GLP-1 and GIP have extremely short plasma half-lives due to very rapid inactivation, catalysed by the enzymes DPP-4 .Inhibition of DPP-4 slows their inactivation. There by potentiating their action, leading to lower plasma glucose levels, it's utility in the treatment of type 2 diabetes.

TABLE 1: HPLC METHODS

S. No.	Drugs	Method	Chromatographic Conditions	Author
1	MTF and VLD	RP-HPLC	Stationary phase: Thermo Hypersil ODS C18 column (5µm,4.6 mm×250mm) Mobile phase: methanol, acetonitrile, and phosphate buffer (5:30:46,v/v,pH3.5) Wavelength: 212nm Flow rate: 0.8mL/min Temp:35℃	Abdul shakoor[2]
2	MTF and VLD	RP-HPLC	Stationary phase: Grace Cyano column (250nm×4.6mm) Mobile phase: ammonium bicarbonate buffer and acetonitrile(65:35v/v) Wavelength :207nm Flow rate: 1.0 mL/min Temp: 35℃	N. Satheeshkumar[3]
3	EMP and LIN	RP-HPLC	Stationary phase: Column :ODS 250×4.6 mm,5µ Mobile phase :Buffer: acetonitrile (70:30) Wavelength :285nm Flow rate: 1ml/min Temp:30℃	V.Sruthi[5]
4	SITA and SIMV	RP-HPLC	Stationary phase: RP-C18 Column (250mm × 4.6 mm; 5µm) Mobile phase : phosphate buffer: acetonitrile and Methanol in the range of (45:35:20v/v/v) Wavelength:255nm Flow rate: 1ml/min	P. Ravisankar[6]

5	MET and LIN	RP-HPLC	Stationary phase: Hypersil BDS C18 column Mobile phase: KH2PO4 and acetonitrile (40:60) wavelength: 245nm Flow rate: 1.0ml/min	S. Shirisha[7]
6	EMP-LIN	RP-HPLC	Stationary phase: C18(250×4.6×5) column Mobile phase:buffer: acetronitrile(68;32) Wavelength:249nm Flow rate 1ml/min	SharmilaDonepudi[8]
7	MET and EMP	New stability indicating RP_HPLC	Stationary phase; BDS (250 mm 4.6mm, 5m) Mobile phase :Orthophosphoric acid buffer:acetonitrile in the ration (50:50) Wavelength:250mm Flow rate:1ml/min Temperature:30℃	Geethasusmita[9]
8	EMP and LIN	RP-HPLC	Stationary phase: Octadecylsilyl C18 Column (5µm, 4.6mm* 250mm) Mobile Phase: Phosphate buffer and Methanol wavelength: 229 nm Flow rate: 0.8 ml/min Temperature: Ambient	Nilesh K. Bornare[10]
9	MET and SET	RP-HPLC	Stationary phase: C18 column (Phenomenex, 250 ×4.6 mm, 5 µm) Mobile phase: 0.02M Potassium dihydrogen phosphate 9KH2 PO4) and acetonitrile in the ration of 55:45 (v/v) Wavelength:252nm Flow rate:1 ml/min Temperature: Ambien	GovindasamyJeyabalan [11]
10	MET and LIN	RP-HPLC	Stationary phase:C18 column (150×4.6mm) Mobile phase: Phosphate buffer: Methanol: Acetonitrile (65:10:25) Flow rate:1ml/min	Mrs sheenaMoncy[12]
11	EMP	RP-HPLC	Stationary phase: Hypersil BDS 150mm×4.6mm Mobile phase: 0.1%OPA: Acetonitrile in the ration of (70:30 V/V) Wavelength:233nm Flow rate 1ml/min	Shyamala[13]
12	MTF and VLD	Stability indicating RP-HPLC	Stationary phase: kromasil C18 column (4.5×250mm:5µm) Mobile phase: Potassium dihydrogen phosphate buffer:acetonitrole980:20v/v) Wavelength: 263nm. Flow rate: 0.9 ml/min Temperature: Ambient	Ramesh Jayaprakash[14]
13	LIN	RP-HPLC	Stationary phase: C18 column (150×4.6mm,5µm particle size) Mobile phase: phosphate buffer and acetonitrile (70:30v/v) Wavelength: 253nm Flow rate: 1ml/min	Joy Chandra Rajbangshi[15]

14	REPA and SITA	Stability indicating RP_HPLC and UV	Stationary phase: C18 (250×4.6mm,5µm) Column Mobile phase: Acetonitrile: Phosphate buffer (65:35,v/v) Wavelength: 228nm Flow rate;1ml/min	Nusrat K. shaikh[16]
15	MET and BENT	Stability indicating RPTLC method	Stationary phase: C18 column Mobile phase: Benzene: Methanol:triethylamine (8.5:1:0.5,v/v/v) Wavelength:249nm Flow rate:1 ml/min Temprature:110℃	Ram Suresh Sakhare[17]
16	MET	RP-HPLC	Stationary phase :Hypersil ODS C18,25cm×4.6mm×5µm Column Mobile phase: acetonitrile: phosphate buffer Wavelength:233nm Flow rate 1.0ml/min	Pavan Kumar Chadalawada[18]
17	VLD	RP-HPLC	Stationary phase: VP-ODS,150×4.6mm Mobile phase:phosphate buffer (pH4.6) and acetonitrile at the ration (80:20v/v) Wavelenght:210nm Flow rate: 0.7ml/min Temperature at 25℃	RahimaKhatun[19]

CONCLUSION

The above study presents analytical method for analysis of Metformin hydrochloride and Vildagliptin in pharmaceutical dosage forms by RP-HPLC and UV Spectrophotometry. Literature survey suggested that various RP-HPLC, HPLC, UPLC, LC/MS/MS UV methods were developed and reported. The published methods were validated for various parameters as per ICH guidelines.

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