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A Review on Analytical Methods for Estimation of Dapagliflozin and Vilagliptin in Tablet Dosage Form

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ABSTRACT

Dapagliflozin and Vildagliptin are comes under new class of sodium-Glucose Co-transporter 2 (SGLT-2) and dipeptidyl peptidase-4 (DPP-4) inhibitor respectively. The discovery, development and production of pharmaceuticals depend heavily on the development and validation of analytical methods. As more pharmaceuticals enter the market each year, it is imperative to create a new testing approach for these drugs. It is now important to validate the new analytical technique after development. The process of method development demonstrates that an analytical method is appropriate for application. Information on numerous phases and parameters, such as accuracy, precision, linearity, limit of detection, limit of quantification, specificity, range and robustness is provided through the validation of analytical methods. Validation should be carried out in accordance with regulatory standards, like the ICH standards. The development and validation of analytical methods are reviewed in this article. Dapagliflozin and Vildagliptin are alone estimated by RP-HPLC, UV, RP-UPLC method.

INTRODUCTION

Dapagliflozin is chemically known as (2S, 3R, 4R, 5S, 6R)-2-[4-Chloro-3-(4-ethoxybenzyl) phenyl]-6-(hydroxymethyl)tetrahydro-2H-pyran-3,4,5-triol, CAS no. 461432-26-8, molecular formula $C_{21}H_{25}ClO_6$ with molecular weight of 408.9 g/mol.[1]

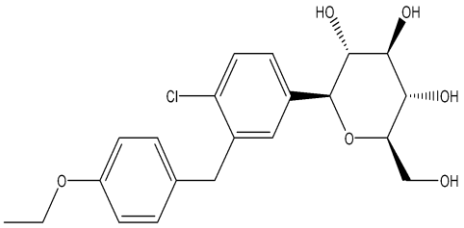

Figure No. 1: Chemical structure of Dapagliflozin

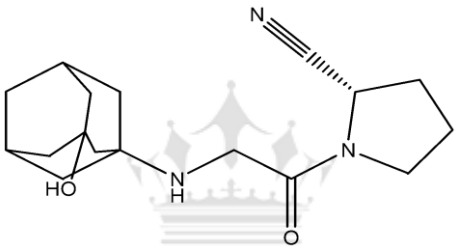

Figure No. 2: Chemical structure of Vildagliptin

Vildagliptin is chemically known as (2S)-1-[2-[(3-hydroxy-1-adamantyl)amino]acetyl]pyrrolidine-2-carbonitrile, CAS no. 274901-16-5, molecular formula $C_{17}H_{25}N_3O_2$ with molecular weight of 303.4 g/mol.[2]

MECHANISM OF ACTION

1. Dapagliflozin: Dapaglifozin is a recently developed medicine used to treat early and late type 2 diabetes. Dapaglifozin is a selective sodium glucose cotransporter or sodium-glucose linked transporter (SGLT) agent. It increases urine glucose excretion and inhibits glucose reabsorption in the kidney. All glycemic indicators develop as a result of glucose excretion and falling plasma levels. This method of action, which is unrelated to the effects of insulin, depends on blood glucose levels as well as other thiazolidinedione actions (mediated by

GLUTs). As a result, there is little chance of hypoglycemia and little danger of beta cells becoming over stimulated or worn out. Because its mechanism of action is dependent on normal renal glomerular-tubular function, the effectiveness of SGLT-2 is reduced in those with renal impairment.[3]

2. Vildagliptin: With a minimal risk of hypoglycemia, gliptin inhibits dipeptidyl peptidase-4 (DPP-4) to prevent the breakdown of glucagon-like peptide-1 (GLP-1) and lowers blood sugar levels in people with type 2 diabetes mellitus. Gliptin causes persistent enzyme inhibition by covalently attaching to the catalytic site of DPP-4. This increases intact GLP-1 levels both after meals and throughout a fast. Gliptin has been demonstrated to increase insulin secretion and decrease glucagon secretion in a manner that is glucose-dependent. Additionally, gliptin increases insulin sensitivity while inhibiting the generation of hepatic glucose, mostly through modifications in islet hormone secretion.[4]

MARKETED FORMULATION

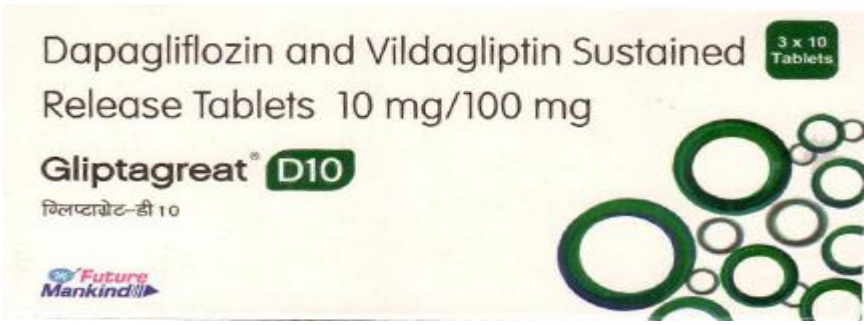

Figure No. 3: Marketed formulation

LITRATURE REVIEW

DAPAGLIFLOZIN

Table No. 1: Reported methods for Dapagliflozin in single dosage form

Sr. No	Drug	Method	Description	Detection Mode	Ref No
01	Dapagliflozin	Simple UV Spectrophotometric method	Mobile Phase: Distilled water Linearity: 5-40 µg/mL r^2 : 0.985	224 nm	5
02	Dapagliflozin	RP-HPLC	Mobile phase: Phosphate buffer : Acetonitrile (60:40 v/v) Linearity: 10-60 µg/ml r^2 : 0.9957 LOD: 0.02µg/ml LOQ: 0.06µg/ml	237 nm	6
03	Dapagliflozin	Stability indicating HPLC	Mobile phase: Buffer (dipotassium hydrogen phosphate) : Acetonitrile (60:40 v/v) Linearity: 50-150 µg/ml r^2 : 0.997 LOD: 5.14 µg/ml LOQ: 15.6 µg/ml	222 nm	7
04	Dapagliflozin	Stability indicating RP-HPLC	Mobile phase: Acetonitrile: ortho phosphoric acid Linearity: 25-150 µg/ml r^2 : 0.999LOD: 0.6 µg/ml LOQ: 1.8 µg/ml	245 nm	8

Table No. 2: Reported methods for Dapagliflozin in combined dosage form

Sr. No.	Drug	Method	Description	Detection Mode	Ref No
01	Dapagliflozin and Metformin	First derivative UV spectro-photometric method	Mobile phase: Methanol Linearity: Dapa: 0.5-2.5 µg/ml Met: 25-125 µg/ml r^2: Dapa: 0.984 Met: 0.982 LOD: Dapa:0.009 µg/ml Met: 0.013µg/ml LOQ: Dapa:0.039 µg/ml Met: 0.041 µg/ml	Dapa: 235 nm Met: 272 nm	9
02	Dapagliflozin and Metformin	RP-HPLC method	Column: Phenomenex Luna C18 (4.6mm I.D. × 250mm, 5µm) column Mobile phase: Acetonitrile: water (75:25 v/v) Linearity: Dapa: 10-50 µg/ml Met: 20-100 µg/ml r^2: Dapa: 0.999 Met: 0.9991 LOD: Dapa: 3.7 µg/ml Met: 5 µg/ml LOQ: Dapa: 11.4 µg/ml Met: 15.2 µg/ml	285 nm	10
03	Dapagliflozin and Saxagliptin	Stability indicating HPLC method	Column: Xterra RP18 (4.6×150 mm,5 µm size) column Mobile phase: Acetonitrile: water (60:40) Linearity: Dapa: 100-500 µg/ml Saxa: 50-250 µg/ml r^2: Dapa: 0.9998	248 nm	11

			Saxa: 0.9998 LOD: Dapa: 3.00 µg/ml Saxa: 3.02 µg/ml LOQ: Dapa: 9.98 µg/ml Saxa: 10.01 µg/ml		
04	Dapagliflozin and Saxagliptin	RP-UPLC method	Column: reverse phase C18 column (2.1 × 100 mm) Mobile phase : 0.1% ortho phosphoric acid and acetonitrile (40:60) Linearity: 25-150% r^2: Dapa: 0.9997 Saxa: 0.999 LOD: Dapa: 0.53 µg/ml Saxa: 0.13 µg/ml LOQ: Dapa: 1.59 µg/ml Saxa: 0.38 µg/ml	254 nm	12

VILDAGLIPTIN

Table No. 3: Reported methods for Vildagliptin in single dosage form

Sr. No.	Drug	Method	Description	Detection Mode	Ref No
01	Vildagliptin	Simple UV spectrophotometric method	Mobile phase: 0.5M HCl Linearity: 10-40 µg/ml r^2: 0.999 LOD: 0.055 µg/ml LOQ: 1.666 µg/ml	202.5 nm	13
02	Vildagliptin	RP-HPLC method	Column: Xterra® Waters C18 column (150mm×4.6mm, 5µm) Mobile phase: Phosphoric acid (pH 9.5) : Methanol	210 nm	14

			(60:40 v/v) Linearity: 5-200 µg/ml r^2: 0.9997 LOD: 1.47 µg/ml LOQ: 4.90 µg/ml		
03	Vildagliptin	Stability indicating RP-HPLC assay method	Column: C18 column (250 X4.6 mm i.d.,5 µm) Mobile phase: Buffer: Acetonitrile (50:50 v/v) Linearity: 10-60 µg/ml r^2: 0.996 LOD: 0.025 µg/ml LOQ: 0.054 µg/ml	220 nm	15
04	Vildagliptin	UPLC method	Column: chiralcel OD-RH column Mobile phase: 20 mM borax buffer (pH 9.0 ±0.05), ACN, and 0.1% Triethylamine (50:50:0.1, v/v/v) Linearity: 1-12 µg/ml r^2: 0.999 LOD: 0.024 µg/ml LOQ: 0.075 µg/ml	210 nm	16

Table No. 4: Reported methods for Vildagliptin in combined dosage form

Sr. No.	Drug	Method	Description	Detection Mode	Ref No
01	Vildagliptin and Nateglinide	UV+HPLC	Mobile phase: Acetonitrile: phosphate buffer (70:30% v/v) Linearity: Vilda: 5-25 µg/mlµg/ml Nate: 9-45 µg/ml	Vilda: 270 nm Nate: 253 nm	17

			r^2: Vilda: 0.997 Nate: 0.995 LOD: Vilda: 0.602 µg/mlNate: 0.638 µg/ml LOQ: Vilda: 1.986 µg/ml Nate: 2.105 µg/ml		
02	Vildagliptin and Metformin HCl	RP-HPLC	Column: Xterra C18 column (250 mmL×4.6 mm I.D × 5µ) Mobile phase: Acetonitrile: Phosphate buffer: water (65: 20:15v/v/v) Linearity: Vilda: 5-25 µg/ml Met: 10-50 µg/ml r^2: Vilda: 0.9999 Met: 0.9998 LOD: VLD: 0.0040 µg/ml MET: 0.025 µg/ml	239 nm	18
03	Vildagliptin and Remogliflozin Etabonate	Stability indicating UPLC method	Column: Acquity UPLC BEH C18 (2.1 × 50 mm, 1.7 µm) Mobile phase: 0.1 M acetate buffer : methanol 25:75 (v/v) Linearity: Remo: 5-30 µg/ml Vilda: 2.5-15 µg/ml r^2: Remo: 0.9995 µg/ml Vilda: 0.9995 µg/ml LOD: Remo: 0.015 µg/ml Vilda: 0.03 µg/ml LOQ: Remo: 0.05 µg/ml Vilda: 0.01 µg/ml	215 nm	19

CONCLUSION

There have been several reported techniques for determining dapagliflozin and vildagliptin. According to the article, RP-HPLC assay techniques were used to assess the amounts of dapagliflozin and vildagliptin. In several publications, the pharmacological dosage forms of

dapagliflozin, vildagliptin, metformin, saxagliptin, and remogliflozin are determined. Also reported are UV techniques. Additionally reported are studies on UPLC.

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