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Review Article

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A DETAILED ANALYSIS OF THE ANALYTICAL APPROACHES FOR DAPAGLIFLOZIN AND VILDAGLIPTIN

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ABSTRACT

Dapagliflozin and vildagliptin are two broad classes of anti-diabetic glycoside pharmacological ingredients for the management of -2-disaccharides. Dapagliflozin, an SGLT-2 inhibitor, lowers blood sugar levels by increasing glucose urinary excretion while vildagliptin could be a DPP-4 inhibitor which increases insulin secretion and suppresses glucagon secretion. The accurate evaluation and quality assurance of these pharmaceuticals are vital to ensure their effectiveness and safety in pharmaceutical formulations. This encapsulates the various methods of analysis that are developed and validated for the determination of dapagliflozin and vildagliptin in bulk and in dosage form. RP-HPLC Chromatography and UV-VIS Spectroscopy have been used for this purpose. The differences between these methods have been described with respect to sensitivity, specificity, and relevance in drug testing. The reason for this review is to provide information on the analytical methods developed for dapagliflozin and vildagliptin and to help scientists and practitioners in the pharmaceutical industry choose the right methods for quality control testing.

KEYWORDS

- Dapagliflozin
- Vildagliptin
- RP-HPLC
- UV Spectrophotometry

INTRODUCTION

Medications that diagnose and treat the types of diabetes that are progressive work by lowering blood glucose levels. Except for pramlintide and the major part of GLP-1 receptor agonists such as exenatide and liraglutide, all diabetes medicines are taken by mouth and are therefore classified as oral hypoglycemic agents or oral anti-diabetic agents. The age of a person, their situation, the specific type of diabetes and other patient specifics determine which of the available types of hypoglycemic agents is appropriate to use for them.[1]

One medication for managing type 2 diabetes is dapagliflozin, known by various brand names such as Farxiga in the US and Forxiga in the EU. It is also prescribed for adults with chronic kidney disease and heart failure. Dapagliflozin works by reducing glucose reabsorption and promoting glucose excretion in the urine through the reversible inhibition of SGLT-2, a sodium-glucose transporter located in the proximal convoluted tubule of the kidney.[2][3] Vildagliptin is an oral medication used to manage high blood sugar levels in people with diabetes. It falls under the category of DPP-4 inhibitors and is sold under the brand name Galvus, among others. By inhibiting the enzyme DPP-4, vildagliptin allows the hormones GLP-1 and GIP to remain active longer, which helps stimulate insulin production from beta cells and reduces glucagon secretion from the alpha cells in the pancreatic islets of Langerhans.[4]

Diabetes is managed with a medication known as dapagliflozin combined with vildagliptin. This treatment is specifically for Type II diabetes, a chronic condition that impacts the body's ability to utilize glucose or blood sugar. The main factors contributing to Type II diabetes are insufficient insulin production and insulin resistance.[5]

DRUG PROFILE

A. DAPAGLIFLOZIN

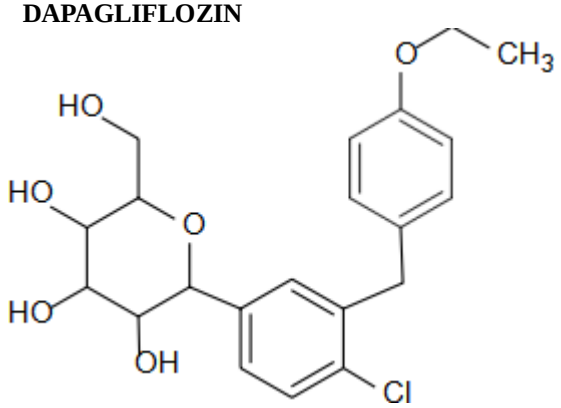

Fig.no 1: Molecular structure of Dapagliflozin.

IUPAC NAME: (2S,3R,4R,5S,6R)-2-[4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl]-6-(hydroxymethyl)oxane-3,4,5-triol
Molecular formula: $C_{21}H_{25}ClO_6$
Molar Mass: 408.9 g/mol
Melting Point: 55-58^{0}C
pKa: 12.6

Drug Category: It is sodium-glucose co-transporter 2 inhibitors for the treatment of type 2 diabetes.
Solubility: Soluble in ethanol and dimethyl formamide.

Mechanism of action: Dapagliflozin works by inhibiting subtype 2 of the sodium-glucose transport proteins (SGLT2), which play a key role in reabsorbing about 90% of glucose in the kidneys. By blocking this transporter, dapagliflozin promotes the excretion of glucose through urine. When used alongside metformin at a standard dose of 10 mg daily, it has been shown to reduce HbA1c levels by 0.54-0.84% compared to metformin alone in patients with type 2 diabetes who have not achieved adequate control and have normal kidney function. The benefits of dapagliflozin in heart failure are mainly due to its hemodynamic effects. SGLT2 inhibitors effectively decrease intravascular volume through osmotic diuresis and natriuresis, which can lead to lower preload and afterload. This reduction helps ease the workload on the heart and enhances left ventricular function.

B. VILDAGLIPTIN

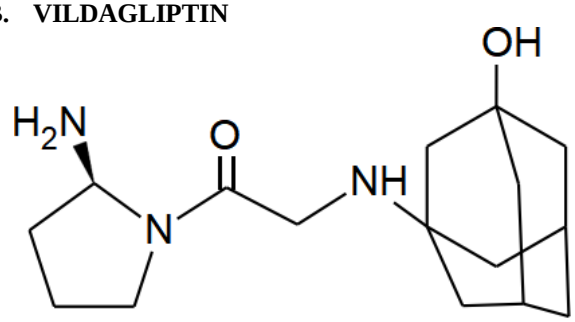

Fig.no 2: Molecular structure of Vildagliptin.

IUPAC NAME: (2*S*)-1-[2-[(3-hydroxy-1-adamantyl)amino]acetyl]pyrrolidine-2-carbonitrile

Molecular formula: $C_{17}H_{25}N_3O_2$

Molar Mass: 303.4 g/mol
Melting Point: 153-157^{0}C
pKa: 8.7
Drug Category: It is DPP-4 (Dipeptidyl Peptidase-4) inhibitors. It is used in thetreatment of type 2 diabetes to help control blood sugar levels.
Solubility: Freely soluble in water, methanol, and ethanol, but it is poorly soluble inorganic solvents such as acetone and acetonitrile.

Mechanism of action: Vildagliptin sustained release works by inhibiting DPP-4, which extends the effects of GLP-1 and GIP hormones. This process boosts insulin secretion and decreases glucagon release, resulting in better glycemic control for individuals with type 2 diabetes by lowering postprandial glucose levels while minimizing the risk of hypoglycemia.

ANALYTICAL METHODS

Various analytical methods, such as UV, HPLC, LC-MS, and HPTLC, have been developed to determine Dapagliflozin along with Vildagliptin in pharmaceutical dose and bulk forms.

Table 1: Chromatographic estimation in RP-HPLC for dapagliflozin and vildagliptin.

S.No	Author's name	Column	Mobile phase [M.P], Flow rate [F.R] & Injection Volume[I.V]	Retention time & Wavelength
1.	Kumar RR.,[2024][6]	Discovery C18 column (4.6 x 150mm, 5µm)	MP: Acetonitrile and Na2hpo4[70:30] FR: 1 ml/min IV: 10 µL	RT: VDG-2.307 minutes DGZ-2.865 minutes W: 220 nm
2.	Patel BH et al.,[2024][7]	C18 columns (250 mm x 4.6 mm, 0.5-micron particle size)	MP: Methanol: 0.01% Trifluoroacetic acid (pH-2.78) (95:05 %v/v) FR: 0.8 mL/min IV: 10 µL	RT: VDG-2.282 min DGZ- 4.070 min W: 210 nm
3.	Khagga B et	Agilent C18 column	MP:	RT: VDG-2.1

	al.,[2024][8]	(150 x 4.6 mm, 5 mm)	Orthophosphoric acid: Acetonitrile FR: 0.7 ml/min IV: 20µL	mins DGZ-3.5mins W: 224nm
4.	Boovizhikannan T et al.,[2013][9]	Agilent XDB C18, (150 × 4.6 mm, 5 µ)	MP: 0.1 M Phosphate buffer and acetonitrile (85:15% v/v) FR: 1.0 ml/min IV: 25 µL	RT: 3.04 min W: 210 nm
5.	Malakar A et al.,[2012][10]	Xterra® Waters C18 column (150mm×4.6mm, 5µm)	MP: aqueous phase (ammonium hydroxide, water, phosphoric acid all mixed) and organic phase methanol (60:40 v/v) FR: 1.0 ml/min IV: 25 µL	RT: 6.3 min W: 210nm
6.	Satpathy PR et al., [2014][11]	Symmetry C18 (4.6 x 150mm, 5mm, Make: Thermosil)	MP: buffer:Acetonitrile: methanol (450: 480:70) FR: 0.5 ml/min IV: 10µl	RT: 3.9 ± 0.1 mins W: 254nm
7.	Sultana R et al.,[2013][12]	ZORBAX Rapid Resolution HT C18 columns (150 mm x 4.6 mm)	MP: Buffer: Acetonitrile (50:50 v/v) FR: 1 mL/ min IV: 20 µL.	RT: 5.017 ±0.01 min W: 220 nm
8.	Debata J et al.,[2017][13]	Waters C18, 5 µm, 25 cm × 4.6 mm	MP: phosphate buffer: acetonitrile (60:40) FR: 1 mL/ min	RT: 3.461 minutes W: 237 nm
9.	Mante GV et al.,[2018][14]	Princeton C18column	MP: acetonitrile: 0.1% triethylamine (pH-5.0) (50:50%v/v) FR: 1 mL/ min	RT: 5.163min W: 224nm
10.	Verma MV et al.,[2017][15]	Agilent C18 column (4.6 mm150,5 µm)	MP: acetonitrile: di-potassium hydrogen phosphate (40:60%v/v) FR: 1 mL/ min	RT: 3.160 min (API) and 3.067 min (Tablet) W: 222 nm
11.	Manoharan G et al.,[2018][16]	Zorbax Eclipse Plus, Agilent Technology column (150mm x 4.6mm, 5µm)	MP: Methanol: Water (75:25 v/v) FR: 1 mL/ min IV: 20µL	RT: 3.1 min W: 230 nm

Table 2: Spectroscopic estimation of dapagliflozin and vildagliptin.

S.No	Author's name	Method	Materials & Description
1.	Mane SV et al.,[2022][17]	Shimadzu model 1800 double beam	**Wavelength:** 210 nm **Solvent:** water, 0.1 N HCl, and phosphate buffer pH 7.4 **Concentration Range:** 2-12 µg/ml **Linearity (R2):** 0.9998, 0.9994 and 0.9991
2.	Naveed S et al.,[2014][18]	UV visible 1601 Shimadzu double beam spectrophotometer	**Wavelength**: 244 nm **Solvent:** Water **Concentration Range:** 12.5-200 µg/mL **Linearity (R2):** 0.985
3.	Mante GV et al.,[2017][19]	Jasco V-630 and Shimadzu-1700 double beam	**Wavelength:** 224 nm **Solvent:** Methanol **Concentration Range:** 5-40 µg/mL **Linearity (R2):** 0.985

4.	Vadla S et al.,[2023][20]	UV-1800 SHIMADZU and UV-3200 LAB INDIA UV-Visible spectrophotometer	**Wavelength:** 220 nm **Solvent:** methanol: water (15:85) **Concentration Range:** 5–30 µg/ml **Linearity (R2):** 0.999

CONCLUSION

The examination of the expository strategies highlights how effective and uniquely tailored approaches are for measuring dapagliflozin and vildagliptin in pharmaceutical contexts. Due to its high sensitivity, specificity, and accuracy, chromatography methods like RP-HPLC are suitable for standard stability and quality control testing. Spectroscopic techniques provide reliable linearity and reproducibility, particularly UV-VIS spectroscopy, which is often a simpler and more cost-effective option. The choice of method depends on the type of analysis, regulatory compliance, or bulk drug examination. Ongoing advancements in innovative and reliable analytical methods ensure better monitoring and improved treatment outcomes for diabetes management.

ABBREVIATIONS

RP-HPLC: Reversed-phase high-performance liquid chromatography; **UV:**Ultraviolet; **HPTLC:**High-performance thin layer liquid chromatography; **LC-MS:**Liquid chromatography-mass spectrometry; **VDG:**Vildagliptin; **DGZ:**Dapagliflozin;

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