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Development and Validation of UV Spectrophotometric Method for Simultaneous Estimation of Vildagliptin and Dapaglipflozin in Tablet Dosage Form

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Abstract: *A UV spectrophotometric approach for quantifying Vildagliptin and Dapagliflozin in fixed-dose Combinations that is simple, fast, sensitive, accurate, and exact. The absorbance of Vildagliptinand Dapagliflozin was measured at two different wavelengths 260 nm and 227 nm, respectively. The Isosbestic point was discovered to be 250 nm in diameter. Vildagliptin (r2=0.9994) and Dapagliflozin(r2=0.9991) both showed linearity in the 64µg/ml to 96µg/ml and 50µg/ml to 75µg/ml range Respectively. A recovery study was carried out to confirm the methods' accuracy. In the recovery Study, the % RSD was less than 2. The methods were validated in accordance with ICH guidelines.*

Keywords: Vildagliptin, Dapagliflozin, Simultaneous Estimation, UV.

I. INTRODUCTION

INTRODUCTION TO ANALYTICAL CHEMISTRY:

Ultraviolet-visible (UV-Vis) spectroscopy is a widely used technique in many areas of science Ranging from bacterial culturing, drug identification and nucleic acid purity checks and Quantitation, to quality control in the beverage industry and chemical research. This article will Describe how UV-Vis spectroscopy works, how to analyze the output data, the technique's Strengths and limitations and some of its applications. Analytical studies use spectrophotometric techniques including derivative and ratio spectra Spectrophotometry, which are related to quality control and routine analysis of commercial Items in research or industry laboratories. Compared to hyphenated analytical instruments or Techniques like LC-MS, GC-MS, LC-NMR, etc., which always involve prior steps like Extraction and other time-consuming analytical processes during analysis, these Spectrophotometric procedures are found to be preferred. However, the associated methods With intricate parts are expensive and time-consuming.

Qualitative analysis: Finding non-numerical information about a chemical species, a Reaction, etc. is known as qualitative analysis. A couple of examples would be Witnessing a reaction cause a change in hue or witnessing gas popping up out of Solution. Although qualitative analysis is frequently much simpler, quicker, and less Expensive to conduct than quantitative research, it is not as reliable. The method of Conducting a systematic analysis to determine the composition of inorganic material is Covered.

Quantitative analysis: The determination of the absolute or relative abundance (typically stated as a concentration) of one, many, or all specific substance(s) present In a sample is known as quantitative analysis in analytical chemistry. UV Spectroscopy uses ultraviolet light to determine the absorbency of a substance. In simple Terms, the technique maps the interaction between light and matter and measures. As matter Absorbs light it undergoes either excitation or de-excitation, which generates what is known as A spectrum. Ultraviolet-visible (UV-Vis) spectroscopy is a widely used technique in many areas Of science ranging from bacterial culturing, drug identification and nucleic acid purity checks And quantitation, to quality control in the beverage industry and chemical research.

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Analytical Method of Development:

Analytical method development is a process whose main purpose is to prove if any analytical Method in the pharmaceutical industry is suitable for use in the measurement of drug substances Or drug products. It plays a vital role in the development and manufacture of pharmaceuticals Drug substances or drug products

• Aim of an Analytical Method Development:

Analytical method development is the creation of a set of experimental conditions to perform Analytical procedures in chemical samples. Developed analytical methods can be used to Identify, separate, quantify, and learn more about the chemical components in drug products Intended for commercial manufacturing.

• Need for Method Development:

Method development and validation are essential components of drug development and Chemistry manufacturing and controls (CMC). The goal of method development and validation Isto ensure that the methods used to measure the identity, purity, potency, and stability of drugs Are accurate, precise, and reliable.

▪ Analytical Method:

Analytical method development is the creation of a set of experimental conditions to perform Analytical procedures in chemical samples. Developed analytical methods can be used to Identify, separate, quantify, and learn more about the chemical components in drug products

Intended for commercial manufacturing.

SPECTROPHOTOMETRY:

▪ INTRODUCTION:

A method in which the absorption or transmission properties of a material is quantitatively
Measured as a function of wavelength. The basic principle behind this method is that: Each
Compound absorbs or transmits light over a certain range of wavelength.

▪ UV Visible Spectroscopy:

UV-Vis spectroscopy is an analytical technique that measures the amount of discrete

AIM AND SCOPE

AIM:

Development and Validation of UV Spectrophotometric Method for Simultaneous Estimation Of Vildagliptin and Dapagliflozin in Tablet Dosage Form .

SCOPE:

An analytical method development is simple, precise, accurate method for investigation of drug And it helps in the Discovery, Development, and Manufacture of pharmaceuticals. Stability Indicating method is a validated analytical procedure that accurately measure active ingredient Free from process impurities, excipients and degradation products and it monitors the results During stability studies in order to guarantee safety, efficacy and quality

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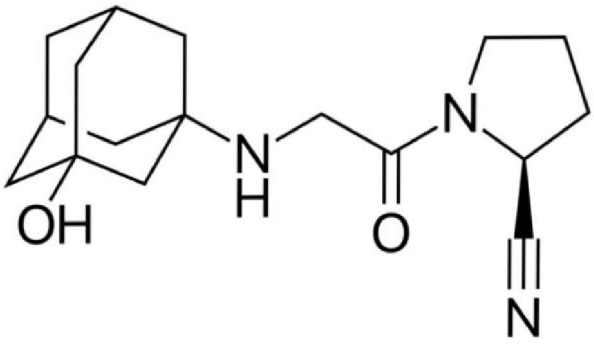
DRUG PROFILE

DRUG PROFILE OF VILDAGLIPTIN

	Drug Profile Drug Profile Of Vildagliptin
Chemical structure	
Chemical IUPAC Name	(S)-1-[N-(3-Hydroxy-1-adamantyl)glycyl]pyrrolidine-2-carbonitrile
Chemical Formula	C17H25N3O2
Molecular Weight	303.399g/mol
BCS Class	The absorption of Vildagliptin is completely controlled by its permeability as it belongs to Class I BCS drugs
Melting point	149-155°C
pKa value	14.71
Lambda max	202.5nm
Solubility	Soluble in Ethanol ,methanol

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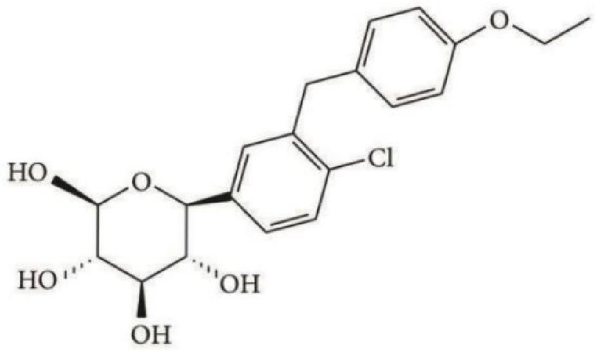
	Drug Profile Drug Profile Of Dapagliflozin
Chemical structure	
Chemical IUPAC Name	(1S)-1,5-anhydro-1-C-{4-chloro-3-[(4-ethoxyphenyl)methyl]phenyl}-D-glucitol
Chemical Formula	C21H25ClO6
Molecular Weight	408.873
BCS Class	Dapagliflozin is non-ionisable; thus, its aqueous solubility and partition coefficient are not affected by changes in pH. Dapagliflozin is a Biopharmaceutical Classification System (BCS) Class III drug.
Melting point	65-70°C
pKa value	12.6
Lambda max	233.66nm
Solubility	Soluble in methanol
State	Solid

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State	Solid
Plasma protein binding	9.3%
Administration	When used in dual combination with a sulphonylurea, the recommended dose of vildagliptin is 50 mg once daily administered in the morning
Volume of distribution	Vildagliptin is minimally bound to plasma proteins (9.3%) and, on the basis of a volume of distribution of 71 L, it is considered to distribute extensively into extravascular spaces.
Route of elimination	The principal pathways of Vildagliptin elimination are biliary and renal.
Plasma half life	The mean elimination half-life of fexofenadine was 14.4 hours following administration of 60 mg, twice daily, in normal volunteers.
Mechanism of action	Vildagliptin is minimally bound to plasma proteins (9.3%) and, on the basis of a volume of distribution of 71 L, it is considered to distribute extensively into extravascular spaces.
Toxicity	patients experienced muscle pain, mild and transient paresthesia, fever, edema, and a transient increase in lipase levels at a dose of 400 mg.

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Plasma protein binding	Approximately 95%
Administration	Dapagliflozin any time of day, just try to take it at the same time every day. Swallow the tablets whole with a drink of water. Do not chew them. You can take them with or without food..
Volume of distribution	The steady-state volume of distribution of Dapagliflozin averages 118 litres.
Metabolism	Liver & Kidney
Route of elimination	Dapagliflozin and its metabolites are excreted via the renal pathway.
Plasma half life	The mean plasma terminal half-life (t1/2) for dapagliflozin is approximately 12.9 hours following a single oral dose of 10 mg..
Mechanism of action	By inhibiting SGLT2, dapagliflozin blocks reabsorption of filtered glucose in the kidney, increasing urinary glucose excretion and reducing blood glucose levels. Its mechanism of action is independent of pancreatic β cell function and modulation of insulin sensitivity.
Toxicity	Its adverse effects include orthostatic hypotension, dehydration and urinary tract and genital infections caused by glycosuria.

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UV spectra Vildagliptin and Dapagliflozin at 208nm and 225 nm respectively. Mobile phase is Used for this good peaks, good absorbance and better sensitivity. Both drugs absorbed at same
Point shown in Figure no.

SIMULTANEOUS ESTIMATION OF VILDAGLIPTIN AND DAPAGLIFLOZIN:
In the Simultaneous Method, we used absorbance at two selected wavelengths. To determine The λmax of both the drugs we scan in the range of 200- 400 nm. Standard solutions of different Concentrations of both drugs were prepared in the mobile phase. The absorbance of Vildagliptin (5000 µg/ml) and Dapagliflozin (500 µg/ml) were recorded at two wavelengths 231 nm and 285 nm by using the simultaneous equation method.[16]
Cx = A2ay1- A1ay2/ ax2ay1- ax1ay2 and
CY = A1ax2- A2ax1/ ax2ay1- ax1ay2
Where,
Cx= concentration of Vildagliptin
Cy= concentration of Dapagliflozin
Ax1and ax2= absorptivity value of Vildagliptin at 231 nm and 285 nm
Ay1and ay2= absorptivity value of Dapagliflozin at 231 nm and 285 nm
A1=absorbance of the standard mixture at 231 nm
A2=absorbance of the standard mixture at 285 nm

Analysis of Combination Formulation:
A fixed dose combination was prepared for assay were used to stimulate the conditions of actual Product. The 60mg of Vildagliptin and 4 mg Dapagliflozin and was weighed and mixed with Diluent and sonicate for 5 minutes. (Stock conc of Vildagliptin= 5000 µg/ml and Dapagliflozin= 500 µg/ml). 1 ml of above solution was further diluted to 10 ml (Conc of & Vildagliptin = 500 µg/ml and Dapagliflozin = 50 µg/ml). Individual samples of and Vildagliptin and Dapagliflozin were prepared of 500 µg/ml and 50µg/ml, respectively.

METHOD VALIDATION:
Validation of an analytical method is the process to establish that the performance characteristics Of the developed method meet the requirements of the intended analytical application. The UV Linearity was studied by plotting a graph of absorbance directly proportional to the concentration. A series of standard solutions of Vildagliptin concentration range is 30 µg/ml to 70 µg/ml and Dapagliflozin was prepared in the concentration range of about 3 µg/ml to 7 µg/ml is shown in Below Tables 2 & 3. The absorbance values for Vildagliptin and Dapagliflozin were measured at Respective wavelength for each drug separately.

PRECISIO
Six separate solutions comprising concentrations of 40,50,6 µg/ml of Vildagliptin and 4,5,6 µg/ml Of Dapagliflozin were analyzed for repeatability. The absorbance was measured three times each Day to determine intra-day and inter-day variation. The %RSD was determined to be less than 2,

ACCURACY
This parameter is used to calculate how closely the test results match the true value, which is Represented as a percentage of recovery. The same amount of concentration listed above in the Table for both Vildagliptin and Dapagliflozin was spiked at three different levels (80%, 100%, and 120%). To calculate the percentage RSD, samples were analyzed three times. The recoveryPercentage was also computed beneath Table 8 and 9.

LOD/ LOQ:
The limit of Quantitation is 3 times more than the limit of detection respectively. The LOD value Of Vildagliptin and Dapagliflozin was found to be 2.89 µg/ml and 0.78 µg/ml respectively and The LOQ value of Vildagliptin and Dapagliflozin were found to be 10.49 µg/ml and 2.14 µg/ml

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Respectively. It was calculated for both drugs by using the ANOVA techniq

II. RESULT AND DISCUSSION

METHOD 2: UV SPECTROPHOTOMETRIC METHOD

Development and Validation of an Analytical Method for Simultaneous Estimation of Vildagliptin and Dapagliflozin by UV in Fixed -Dose Combination From the individual spectra Of Vildagliptin and Dapagliflozin in Methanol at concentration of 60ug/ml of Vildagliptin and 4 Mg/ml of Dapagliflozin, two wavelengths 208nm and 225nm were selected for simultaneous Estimation of drugs respectively. The relation between concentration and absorbance for Individual drug was studied. Vildagliptin and Dapagliflozin individually follow the BeerLamberts law over concentration range 64µg/ml to 96µg/ml and 50µg/ml to 75µg/m respectively.

Selection of UV Spectra:

Overlay spectrum of Vildagliptin and Dapagliflozin maximum absorbance at 208nm and 225 nm. Graph of spectra was studied by plotting a graph of absorbance v/s wavelength. The spectra of Both drugs are shown in the following figures

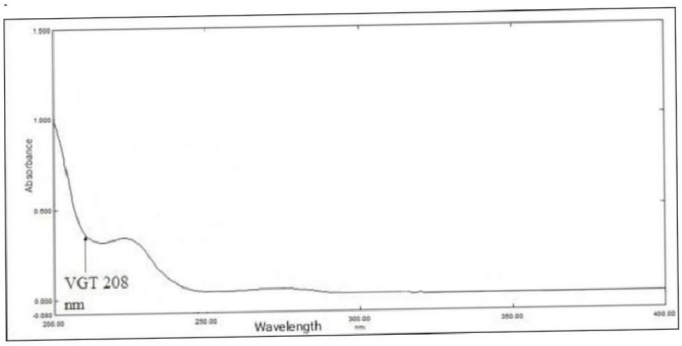


Fig. 1: Wavelength of Vildagliptin at 208nm

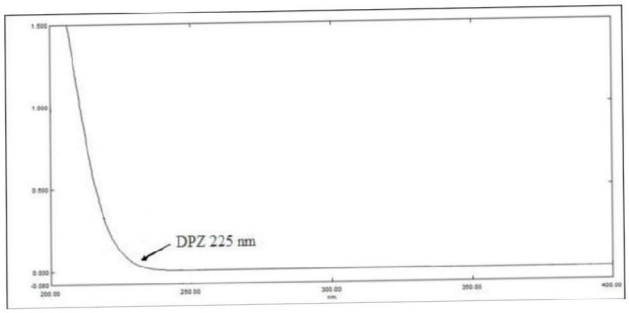
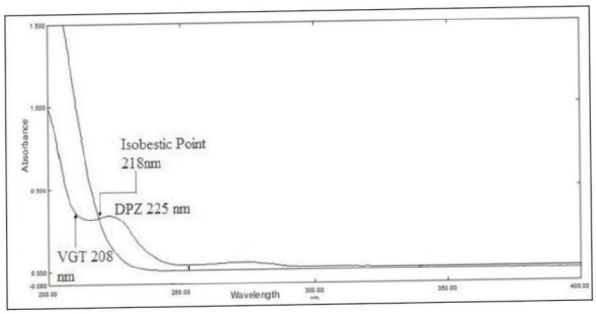


Fig. 2: Wavelength of Dapagliflozin at 225nm



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RECISION:
Six separate solutions comprising concentrations of 72, 80, and 88 µg/ml of Vildagliptin and 56.25,62.5, and 68.75 µg/ml of Dapagliflozin were analysed for repeatability. The absorbance was measured three times each day to determine intra-day and inter-day variation. The %RSD was determined to be less than 2

Accuracy:
This parameter is performed to determine the closeness of the test results with that of The true value which is expressed as % recovery. Recovery studies were carried out at Three different levels (80%,100%, and120%) by spiking the same amount of Concentration given above in the table for both Vildagliptin and Dapagliflozin. Samples Were analysed in Triplicate to calculate % RSD. The % recovery was also calculated

III. CONCLUSION

A simple, precise, accurate, & economical UV spectrophotometric method was developed for VILDA & DAPA in Fixed combined dosage forms for simultaneous estimation. The outcomes Discussed in the UV Spectrophotometric method tables were promising & this method can be Used for the routine determination of VILDA & DAPA in Combined dosage forms.The ICH guidelines are followed throughout the study for method validation and thus proposed Method has wide industrial application

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