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Research Article

METHOD DEVELOPMENT AND VALIDATION FOR THE ESTIMATION OF DAPAGLIFLOZIN IN BULK AND TABLET DOSAGE FORMBY UV VISIBLE SPECTROSCOPY

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ABSTRACT

Simple, precise and accurate UV-Spectrophotometric methods for estimation of dapagliflozin were developed and validated as per ICH guidelines. The lambda max of dapagliflozin was found to be 225nm. All the developed methods obeyed beer's Lambert's law. The results of the developed methods linearity correlation coeffient was found to be 0.996, precision, robustness and ruggedness were found to be within the limits.

INTRODUCTION

Dapagliflozin is a sodium glucose co-transporter 2 inhibitor, which prevents glucose reabsorption in the kidney using Dapagliflozin leads to heavy glycosuria (glucose excretion in the urine), which can lead to weight loss and tiredness. It is chemically known as (2S,3R,4R,5S,6R)-2-(4-chloro-3-(4-ethoxybenzyl)phenyl-6-(hydroxymethyl)tetrahydro-2HPyran-3,4,5-triolIt has molecular formula $C_{21}H_{25}ClO_6$ with molecular weight 408.98

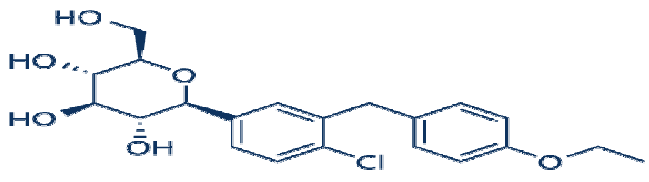

Figure 1 Chemical Structure of Dapagliflozin

The main objective of proposed work is to develop a new rapid, simple, precise, accurate and economical analytical method for the estimation of dapagliflozin in bulk and tablet dosage form. To validate and developed method in accordance with the ICH guidelines.

MATERIALS AND METHODS

Chemicals: Dapagliflozin standard is obtained from Larus Labs, dapagliflozin tablets label claim 10mg manufactured by Forxiga, were purchased from local market, chemical usedmethanol obtained from Rankem.

Instruments: ELICO SL 210 double beam UV-Vis spectrophotometer, cuvetts quartz, software spectra treats.

Preparation of stock solution

10mg of dapagliflozin was weighed and taken in to 10ml volumetric flask and then dissolved with methanol and made up to the mark (1000ppm)

Preparation of working standard solution

From the stock solution take 1ml of the solution and was transferred into another volumetric flask and made up to the mark with methanol (100ppm)

Take 1ml of the solution from the stock solution into another volumetric flask and made up to the mark with same diluent methanol (10ppm)

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Selection of wavelength

10ppm of dapagliflozin was scanned under UV-Spectrophotometer within the range 200-400nm.
The drug lambda was found to be 225nm.

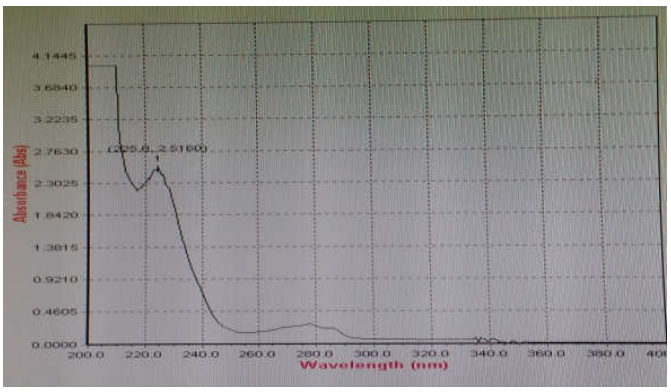

Figure 2 lambda max of dapagliflozin

Assay

To determine the content of dapagliflozin from marketed tablets, 10 tablets were weighed, powdered and average weight was calculated and amount of tablet powder equivalent to 10mg of dapagliflozin was weighed accurately transferred to a 10ml volumetric flask. Sufficient amount of methanol was added and sonicated for 10 minutes and the solution was diluted up to the mark with the same solvent and filtered through what mann filter paper. From the filterate, measured volume was taken and diluted with methanol to get the final concentration. The absorbances were measured at selected wave length.

Weight of 10 tablets = 2559mg

Average weight of 10 tablets =2559/10= 255.9

$$\text{Weight to be taken} = \frac{\text{Weight to be taken X equivalent weight}}{\text{Label claim}}$$

$$= 255.9 \quad \frac{255.9 \text{ X } 10}{10}$$

$$\text{Assay} = \text{X} \frac{\text{Absorbance}_{\text{sample}}}{\text{Absorbance}_{\text{standard}}} \frac{\text{Concentration}_{\text{standard}}}{\text{Concentration}_{\text{sample}}}$$

$$= \text{X} \quad \text{X} \quad 100 = 99.08\% \qquad \frac{0.9037\ 10}{0.912010}$$

Method Validation

Calibration curve and linearity

A calibration graph was constructed with dapagliflozin concentration on X- axis and absorbance on Y-axis. A linear relationship was found in the concentration range 2-10µg/ml (r^2-0.999)

From 100ppm solution, appropriate dilutions were made to get series of concentration i.e., 2ppm, 4ppm, 6ppm, 8ppm, 10ppm and their absorbance were observed at the selected wavelength 225nm. Results were shown below in table 1

Acceptance criteria: correlation coefficient (r^2)- 0.999

Table 1 linearity

Concentration	Absorbance
2ppm	0.3808
4ppm	0.5199
6ppm	0.6582
8ppm	0.7901
10ppm	0.9165

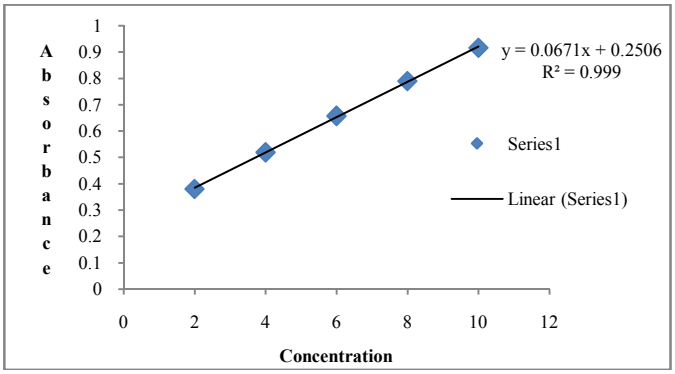

Figure 3 Linearity graph

Precision

The precision of the analytical method expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. Results were shown below table 2
Acceptance Criteria: less than 2

$$\text{Standard deviation } (\sigma) = \frac{\sqrt{\Sigma(x-\bar{x})^2}}{n} \qquad (1)$$

$$\%\ \text{RSD} \quad \frac{\sigma}{\bar{x}} \quad \text{X } 100 \qquad (2)$$

Table 2 Precision

Concentration	Absorbance
10	0.9141
10	0.9113
10	0.9142
10	0.9124
10	0.9145
10	0.9160
%RSD	0.18

Accuracy

The accuracy of the proposed method was determined through a recovery study. The known amount of pure drug dapagliflozin was spiked to pre-analyzed tablet formulation. Analysis of dapagliflozin was carried out at concentrations 50%, 100%, 150%. The percentage recovery of the proposed method was calculated. Results were shown below in table 3

Table 3 Accuracy

Level	Standard + sample	Absorbance	Recovery	Mean	%RSD
50%	4+1	0.5962	99.8	0.03	0.03%
	4+1	0.5963	99.8		
	4+1	0.5966	99.9		
100%	4+2	0.6778	100	0.03	0.04%
	4+2	0.6774	99.9		
	4+2	0.6779	100		
150%	4+3	0.7990	99.8	0.02	0.06%
	4+3	0.7994	99.8		
	4+3	0.7993	99.8		

Robustness

The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage.

This procedure was carried out by changing the lambda max and checks the absorbance of the prepared drug concentration. Standard deviation and percentage RSD were calculated by using equation 1 and 2. Results were shown below in table 4

Table 4 Robustness

Concentration	Wavelength 224nm Absorbance	Wavelength 226nm Absorbance
10ppm	0.9168	0.9106
10ppm	0.9123	0.9095
10ppm	0.9171	0.9085
10ppm	0.9180	0.9079
10ppm	0.9160	0.9099
10ppm	0.9187	0.9099
%RSD	0.24	0.10

Ruggedness

The inter day precision and intraday precision of method was determined. A repeatability study (intraday) was performed by analyzing the dapagliflozin solution (10µg/ml) repeatedly within a day. An inter day precision was performed by analyzing the dapagliflozin solution (10µg/ml) repeatedly on different days. Standard deviation percentage and RSD was calculated by using equation 1 and 2. Results were shown below in table 5

Table-5:Ruggedness

Instrument name: ELICO SL210			Instrument name: Systronics	
	Day-1		Day-2	
Concentration	Analyst -1 Absorbance	Analyst-2 Absorbance	Analyst -1 absorbance	Analyst -2 Absorbance
10ppm	0.9100	0.9105	0.878	0.876
10ppm	0.9193	0.9115	0.877	0.876
10ppm	0.9102	0.9100	0.875	0.877
10ppm	0.9109	0.9120	0.878	0.878
10ppm	0.9124	0.9102	0.877	0.877
10ppm	0.9114	0.9102	0.876	0.878
%RSD	0.38	0.08	0.13	0.10

Limit of detection and limit of quantification

The limit of detection and limit of quantification were calculated by using the formula

$$LOD = (3.3 \times \sigma) / S \quad (3)$$

$$LOQ = (10 \times \sigma) / S \quad (4)$$

σ = standard deviation, S = slope of calibration curve.

Table 6 LOD and LOQ

Parameters	Results
Measured wavelength	225nm
Linearity range	2-10µg/ml
Slope	0.0671
Intercept	0.2506
Correlation coefficient (r^2)	0.999
LOD	10.4µg/ml
LOQ	31.6µg/ml

CONCLUSION

The UV-Spectroscopic methods were developed for the determination of Dapagliflozin. The methods were validated and fund to be simple, sensitive, accurate, and precise. Hence it is used for the routine analysis.

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