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SIMPLE COST EFFECTIVE METHOD DEVELOPMENT FOR THE ESTIMATION OF DAPAGLIFLOZIN IN MARKETED FORMULATION

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ABSTRACT

In the present study, an attempt was made to develop a simple, precise and accurate method for the estimation of Dapagliflozin in pharmaceutical dosage form and validate as per International Conference on Harmonization (ICH) guidelines. This Method involves solving of simultaneous equations based on measurement of absorbance at two wavelengths 242 nm λ_{max} of Dapagliflozin in water. Both the drugs obey the Beer's law in the concentration ranges 2-10µg/ml. % Recovery for both the drugs were in the range of near to 100 indicating excellent accuracy. The methods were precise, with a relative standard deviation of less than 2% for both drugs. The developed methods were validated according to ICH guidelines and values of accuracy, precision and other statistical analysis were found to be in good accordance with the prescribed values.

Key words: Dapagliflozin, Method development, Validation, ICH guidelines.

INTRODUCTION:

Analytical chemistry, which is both a theoretical and a practical science, is practiced in a large number of laboratories in many diverse ways. Methods of analysis are routinely developed, improved, validated, collaboratively studied, and applied (Albert, 1984). Dapagliflozin is chemically called as (1S)-1, 5-anhydro-1-C-[4- chloro-3-[(4-ethoxyphenyl) methyl] phenyl]-D-glucitol. It is a highly selective, sodium-Glucose Co-Transporter 2 (SGLT2). Dapagliflozin blocking the activity of the sodium-glucose transport proteins, which is regulates for at least 90% of the glucose reabsorption in the kidney and obstructs the transporter mechanism causes blood glucose to be removed through the urine. Dapagliflozin is

improved the glyceamic control in patients with type 2 Diabetes Mellitus (Vithoba et al., 2017). A survey of literature revealed the availability of number of analytical methods (Santos-Montes et al., 1994; Santos-Montes et al., 1993; Santos-Montes; 1999) for the quantitative determination of Dapagliflozin alone or combination with other drugs. The reported methods were mainly based on liquid chromatographic estimation using UV-VIS, fluorescence, electrochemical or mass spectrometry detectors. However, no UV-Spectrophotometric method is available for determination of the Dapagliflozin in combined pharmaceutical dosage form. In the present study, an attempt was made to develop a simple, precise and accurate method for the estimation of Dapagliflozin in pharmaceutical dosage form and validate as per International Conference on Harmonization (ICH) guidelines.

MATERIALS AND METHODS

Determination of λ_{max} of Dapagliflozin

The λ_{max} of Dapagliflozin was determined by running the spectrum of drug solution in double beam ultraviolet spectrophotometer. Accurately weighed 10 mg of drug was dissolved in 10 ml of water solution in 10 ml of volumetric flask. The resulted solution 1000µg/ml and from this solution 1 ml pipette out and transfer into 10 ml volumetric flask and volume make up with water prepare suitable dilution to make it to a concentration range of 2-10 µg/ml. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+). The spectrum peak point graph of absorbance of Dapagliflozin versus wave length was shown in figure 1.

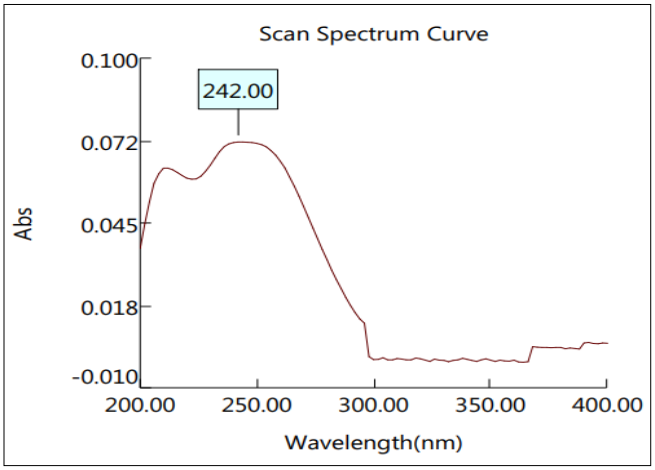

Figure 1: Wavelength maxima of Dapagliflozin in water

Validation

Linearity

Linearity of analytical procedure is its ability (within a given range) to obtain test, which are directly proportional to absorbance of analyte in the sample. The calibration plot was constructed after analysis of five different (from 2 to 10µg/ ml) concentrations and absorbances for each concentration were recorded three times, and mean absorbance was calculated.

Table 1: Calibration curve of Dapagliflozin

Conc. µg/mL	2	4	6	8	10
1	0.295	0.562	0.786	0.988	1.196
2	0.296	0.562	0.785	0.988	1.196
3	0.295	0.561	0.784	0.989	1.197
Mean	0.295	0.562	0.785	0.988	1.196

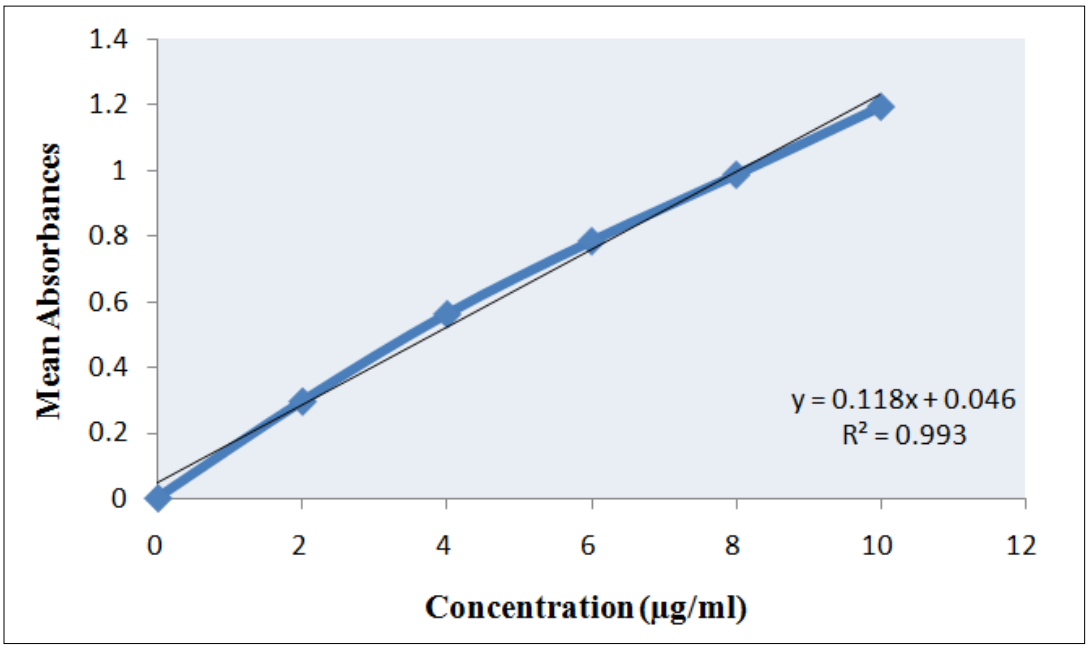

Figure 6.3 Calibration curve of Dapagliflozin water at 242nm

The linear regression analysis was done on Absorbance data points. The results are as follow for standard curve

Slope = 0.118

The intercept = 0.046

The correlation coefficient (r^2) = 0.993

Result of Analysis of Tablet formulation

Twenty tablets were accurately weighed and their mean weight was determined. The tablets were grinded to fine powder, an accurately weighed quantity of powder equivalent to 10 mg of Dapagliflozin was transferred to 10 ml volumetric flask containing distilled water. The solution was sonicated for 25 min and the

final volume was made with mobile phase. The mixture was then filtered through a 0.45 µm filter. The stock solution was further diluted sufficiently with water to get sample solution of drug concentration of 10µg/mL. The amounts of Dapagliflozin in tablets formulation were calculated by extrapolating the value of absorbance from the calibration curve. Analysis procedure was repeated six times with formulation. Results of tablet analysis are reported in table 2.

Accuracy

Recovery studies were performed to validate the accuracy of developed method. To preanalysed sample solution, a definite concentration of standard drug (80%, 100%, and 120%) was added and then its recovery was analyzed.

Table 2: Assay of Tablet Formulation

Dapagliflozin		
Label Claim	**Amount Found**	**% Purity**
Dapagliflozin	11.95	99.58

Table 3: Recovery Studies for Accuracy of Tablet formulation

Level of Recovery (%)	**80**	**100**	**120**
Amount Present	10	10	10
	10	10	10
	10	10	10
Amount of Std. Added	8	10	12
	8	10	12
	8	10	12
Amount Recovered	7.90	9.98	11.78
	7.80	9.96	11.65
	8.01	9.95	11.74
% Recovery	98.75	99.80	98.17
	97.50	99.60	97.08
	100.13	99.50	97.83

Precision

Repeatability

Standard dilutions were prepared and three replicates of each dilution were analyzed in same day for repeatability and results were subjected to statistical analysis. Standard dilutions were prepared and three replicates of each dilution were analyzed in different days and by different analysts. Statistical analysis was carried out.

Table 4: Results of analysis Data of synthetic mixture

Drug	Label claim	Amount found*	Label claim (%)	S.D.	% RSD
Dapagliflozin	12	11.92	99.33	0.215	0.285

LOD (Limit of Detection)

The Limit of Detection (LOD) is the smallest concentration of the analyte that gives the measurable response. LOD was calculated using the following formula and shown in 6.11.

$$\mathbf{LOD = 3.3\ (\sigma / S)}$$

Where, S = slope of calibration curve**,** σ = standard deviation of the response.

LOQ (Limit of Quantification):-

The Limit of Quantification (LOQ) is the smallest concentration of the analyte, which gives a response that can be accurately quantified. LOQ was calculated using the following formula and shown in Table 6.11.

$$\mathbf{LOQ = 10\ (\sigma / S)}$$

Where, S = slope of calibration curve**,** σ = standard deviation of the response.

Table 5: Results of LOD and LOQ of Dapagliflozin

S. No.	Parameter	Results
1.	LOD	0.45
2.	LOQ	1.50

Conclusion

Analytical method is an important quality control tool for estimation of percentage of drug in formulation. Dapagliflozin play an important role in the maintenance of human health. This is where analytical method plays important role to estimation the content of drug in marketed formulations. In present work the analytical method was developed for estimation of Dapagliflozin in Tablet formulations by UV spectrophotometric method. Statistical analysis proves that the methods are reproducible and selective for the estimation of Dapagliflozin in Tablet formulation. The method described for the determination Dapagliflozin in tablet formulation can successfully employed for the determination of Dapagliflozin in Tablet formulations for routine analysis in quality control laboratories.

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