WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 13, 1365-1373. Research Article ISSN 2277–7105

A NOVEL UV SPECTROPHOTOMETRIC METHOD DEVELOPMENT AND VALIDATION OF DAPAGLIFLOZIN IN BULK AND PHARMACEUTICAL DOSAGE FORM

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Article Received on
16 May 2025,

Revised on 05 June 2025,
Accepted on 25 June 2025

DOI: 10.20959/wjpr202513-37423

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ABSTRACT

The quantification of Dapagliflozin in pharmaceutical dosage forms and bulk drug has been accomplished through the development and validation of a new, precise, and effective zero-order derivative UV spectroscopic method. In acetonitrile and ethanol (70:30), Dapagliflozin shows its maximum absorbance at 224 nm, and its concentration ranges between 3 and 18 µg/mL according to Beer's Law. A correlation coefficient (R2) of 0.998 demonstrated the method's strong linearity, indicating high consistency and reliability throughout the range under study. The recovery rates ranged from 99.51% to 101.35%, while the limits of detection (LOD) and quantification (LOQ) were found to be 0.0985 µg/mL and 0.298 µg/mL, respectively. Relative standard deviation (%RSD) values were less than 2%, indicating that the method was also very precise. The ICH guidelines were followed in evaluating the following validation parameters: linearity, accuracy, precision, robustness, ruggedness, LOD, and LOQ. This verified spectroscopic method is a reliable and repeatable way to routinely analyse Dapagliflozin in different pharmaceutical preparations.

KEYWORDS: Dapagliflozin, Zero order derivative spectroscopy, Validation, Pharmaceutical formulation.

INTRODUCTION

Dapagliflozin is a highly selective sodium-glucose cotransporter-2 inhibitor (SGLT2) used for the treatment of type 2 DM. Dapagliflozin is a new class of anti-diabetic agents that effectively reduce blood glucose levels, body weight, and systolic blood pressure. In addition to that, they have newly shown cardiovascular safety. The glucose-reducing effect of dapagliflozin has been approved in many randomized controlled clinical trials that showed notable reducing effects of Dapagliflozin in fasting blood glucose, glycosylated hemoglobin (HbA1c), and postprandial blood glucose levels. Furthermore, Dapagliflozin appeared to have a cardioprotective effect, by reducing blood pressure, lowering body weight, uric acid, and triglyceride, and enhance insulin resistance .Dapagliflozin is an oral, selective SGLT2 inhibitor that has displayed a significant improvement in glycemic control. Across universal clinical development programs including analysis of Phase IIB/III trial, treating with Dapagliflozin alone as monotherapy or in conjunction with pre-existing OADs was linked with a significant lowering in glycosylated hemoglobin (HbA1c), fasting blood glucose and also help in lower or stabilize the body weight and systolic blood pressure (SBP) in patients with T2 diabetes mellitus.[1] Dapagliflozin inhibits subtype 2 of the sodium-glucose transport proteins (SGLT2), which is responsible for at least 90% of the glucose reabsorption in the kidney. Blocking this transporter causes blood glucose to be eliminated through the urine. It also reduce the body weight, and systolic blood pressure. In addition to that, they have newly shown cardiovascular safety.[2]

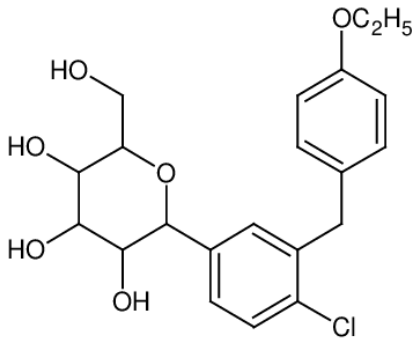

Fig. 1: Chemical Structure of Dapagliflozin.

Dapagliflozin is selected in order to assess the potency in pure and tablet dosage form. A thorough review of the literature reveals that only few spectrophotometric techniques,[3-10] RP-HPLC,[11-21] HPTLC.[22] and UPLC[23] are effective for determining the presence of Dapagliflozin alone or in combination in a variety of pharmaceutical formulations and biological fluids, including stability studies. This information provides details about the

analyte's synthesis, physical and chemical properties, solubility, and pertinent analytical techniques. For the regular determination of dapagliflozin in pure and tablet form, newer, easier, more sensitive, quick, accurate, and reproducible spectrophotometric and chromatographical approaches are therefore required.

MATERIALS AND METHODS

Instrument: UV-Visible double beam spectrophotometer, SHIMADZU (model UV-1800) with UV probe software.All weights were taken in analytical balance.

Chemicals: Dapagliflozin pure drug was obtained as a gift sample from Althera Laboratories, Bengaluru and its pharmaceutical dosage Dapagliflozin 20 tablets (DAPANORM) labelled claim 10mg from alkem laboratories ltd.

Solvent: Acetonitril and Ethanol (70:30) is used as a solvent.

Selection of analytical wavelength: Appropriate dilutions of Dapagliflozin were prepared from standard stock solution and using spectrophotometer solution was scanned in the wavelength range 200-400 nm. The absorption spectra obtained and show maximum absorbance at 224 nm, as the wavelength for detection.

Preparation of standard stock solution: 100mg of Dapagliflozin was weighed accurately transferred into 100 ml of volumetric flask and diluted in acetonitrile and ethanol (70:30) upto the mark. From this, the solution was further diluted into 100µg/ml and pipetted out 0.3, 0.6, 0.9, 1.2, 1.5 and 1.8 ml into 10 ml individual volumetric flask and diluted in acetonitrile and ethanol (70:30) upto the mark, this gives 3, 6, 9, 12, 15 and 18 µg/ml concentration.

Preparation of sample solution: 20 tablets of Dapagliflozin marketed formulations was weighed and powdered. A quantity of tablet powder equivalent to 10mg of Dapagliflozin was transferred into 100ml volumetric flask then it was diluted with acetonitrile and ethanol (70:30) makes upto the mark.

METHOD AND VALIDATION

The method was validated according to the ICH guidelines.[24-26]

RESULT AND DISCUSSION

METHOD: ZERO ORDER DERIVATIVE SPECTROSCOPY

Linearity: The linearity of an analytical method is its capacity to show the test results that are directly proportional to the concentration to the analyte in the sample within the range. The linearity was established in the range of 3-18µg/ml was measured at 224 nm and absorbance values are shown in table 1. The calibration curve was prepared by plotting graph against the concentration and absorbance and therefore the graph shown in Fig-3 statistical variables like slope, intercept, regression equation, correlation coefficient and Sandell's sensitivity were determined and shown in table-2.

Precision: The precision of an analytical method express the closeness of series of individual analytical measurement obtained from the multiple sampling of equivalent sample. Precision was established by intra-day and inter-day was determined by analysing the same concentration for six times in a same day. Inter-day precision was analysing the same concentration daily for six days shown in table-3.

Accuracy: The accuracy of an analytical method says that closeness of test results obtained by that method of the true value .To assess the accuracy of the developed method, recovery studies were carried out at three different levels at 50%, 100% and 150%. In which the formulation concentration kept constant and varied pure drug concentration. Shown in table-4.

Ruggedness: The ruggedness is defined as the reliability of results when the method is performed under the variation in condition. This includes distinct analyst, laboratories, instruments, temperature etc. Ruggedness was determined between different analyst, the value of %RSD was found to be less than 2.(Table-5)

LOD and LOQ: The limit of detection is an individual analytical method is the smallest amount of analyte in the sample which can be reliably detected by the analytical method. The limit of quantification is an individual analytical procedure is the smallest amount of analyte in the sample which can be quantitatively determined. LOD and LOQ were calculated by using following formula.

$$LOD = 3.3(SD)/S \text{ and } LOQ = 3(LOD)$$

LOD and LOQ value of Dapagliflozin found be 0.098 µg/mL and 0.298µg/ml.

Table 1: Results of calibration curve at 224nm by zero order derivative spectroscopy.

Sl No.	Concentration in µg/ml	Absorbance ±Standard deviation
1	0	0
2	3	0.150±0.0010
3	6	0.285±0.0011
4	9	0.435±0.0012
5	12	0.543±0.0012
6	15	0.705±0.0014
7	18	0.833±0.0013

*Average of six determinations

Table 2: Regression parameters of Dapagliflozin by Zero order spectroscopy.

Regression Parameter	Results
Range	3-18 µg/ml
λ_{max}	224nm
Regression equation	Y=0.0272x-0.0099
Slope(b)	0.045
Intercept (a)	0.0131
Correlation coefficient (r^2)	0.998
Sandell's sensitivity	0.020
Limit of detection (µg/ml)	0.098
Limit of quantification (µg/ml)	0.298

Y=bx+a**

Table 3: Determination of Precision results for Dapagliflozin at 224 nm by Zero order spectroscopy.

Concentration (µg|ml)	Intra-day Absorbance ±Standard deviation*	%RSD**	Inter-day Absorbance ±Standard deviation*	%RSD**
3	0.150±0.0010	0.666	0.158±0.0010	0.632
6	0.285±0.0011	0.385	0.267±0.0011	0.411
9	0.435±0.0012	0.275	0.427±0.0011	0.257
12	0.543±0.0012	0.220	0.562±0.0017	0.302
15	0.705±0.0014	0.198	0.713±0.0012	0.168
18	0.833±0.0013	0.156	0.862±0.0013	0.150

*Average of six determinations, ** Percentage relative standard deviation.

Table 4: Determination of accuracy results for Dapagliflozin at 224nm by Zero order spectroscopy.

Spiked evels	Amount of sample (µg|ml)	Amount of standard (µg|ml)	Amount recovered	%Recovery± Standard deviation*	%RSD**
50	9	4.5	13.65	101.35%±0.377	0.37
100	9	9	17.91	99.51%±0.234	0.23
150	9	13.5	22.71	100.96%±0.176	0.17

*Average of six determinations, ** Percentage relative standard deviation.

Table 5: Determination of ruggedness results of Dapagliflozin at 224nm by Zero order spectroscopy.

Analysts	Analyst 1	Analyst 2
Mean absorbance	0.427	0.427
± Standard deviation*	0.0011	0.0016
%RSD**	0.257	0.374

*Average of six determinations, ** Percentage relative standard deviation.

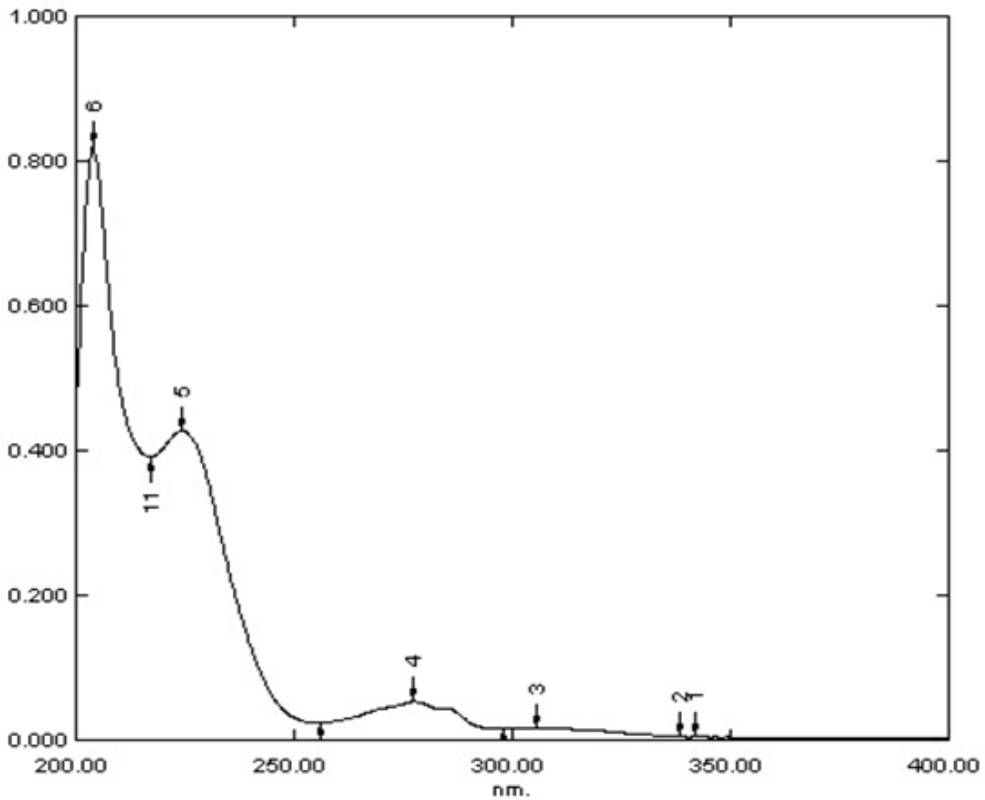

Fig. 2: Zero order spectrum of Dapagliflozin at 224nm.

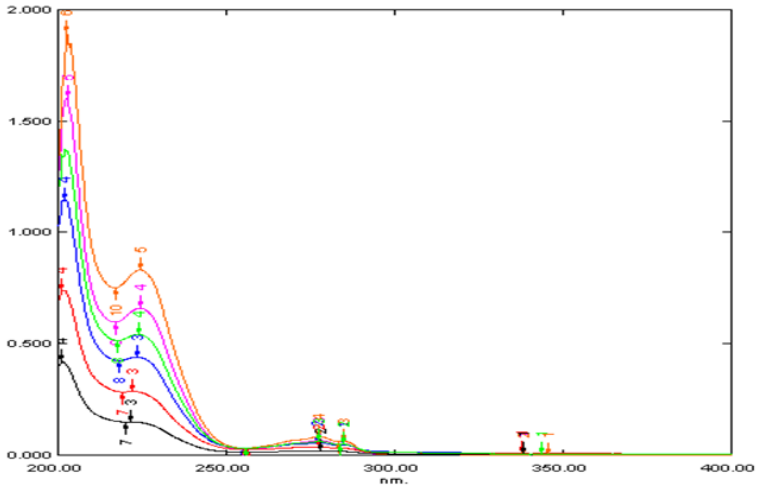

Fig. 3: Zero order overlain spectra of Dapagliflozin showing absorbance at 224nm.

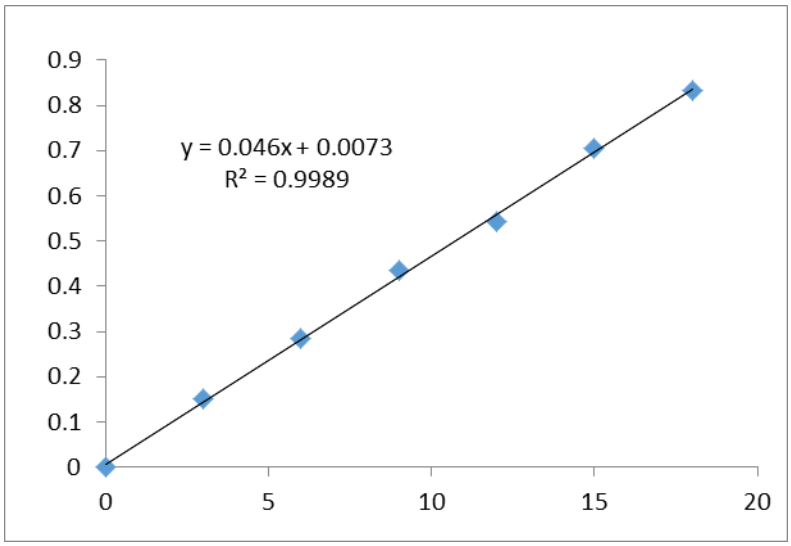

Fig. 4: Calibration curve of Dapagliflozin by Zero order derivative spectroscopy.

CONCLUSION

The analytical method developed for Dapagliflozin was validated as per ICH guidelines demonstrating simplicity, specificity, accuracy, economy, and sensitivity. This method is suitable for regular analysis of Dapagliflozin in both bulk form and pharmaceutical preparations.

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