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Research Article

DEVELOPMENT AND VALIDATION OF UV- SPECTROPHOTOMETRIC ESTIMATION OF CANAGLIFLOZIN IN ITS PHARMACEUTICAL DOSAGE FORM

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Abstract

A simple, accurate, validated and reproducible UV-Spectrophotometric method has been developed for the estimation of Canagliflozin in tablet formulation. Canagliflozin was estimated by using the mode at 290 nm in their solution in methanol. The Beer's law obeyed the concentration range of 5-25µg/ml for Canagliflozin. Mean recovery of 100.47% for Canagliflozin signifies the accuracy of the method. This method can be used for the routine UV estimation of canagliflozin in industries and other analytical laboratories.

Keywords

Canagliflozin, Validate, UV-Spectrophotometric, Estimation, Beer's law, Analytical laboratories, Industry

Introduction

Canagliflozin is an Anti-Diabetic agent. Chemically it is (2S, 3R, 4R, 5S, 6R)-2-(3-{[5-(4-fluorophenyl) thiophen-2-yl] methyl}-4-methylphenyl)-6-(hydroxymethyl) oxane-3, 4, 5-triol. Canagliflozin binds to SGLT2 more potently (250 times) than SGLT1 in vitro. The 50% inhibitory concentrations (IC50) are 2.2-4.4 nmol/L and 684-910nmol/L for SGLT2 and SGLT1 respectively. Dose dependent decreases in renal threshold for glucose and increases in administered type 2 diabetes patients. Decreases in plasma glucose in dose dependent fashion where also noted as early as the first day of administration. When given to healthy and type 2 diabetic patients before a meal, a daily intestinal glucose absorption and a reduction in postprandial glucose was observed.

Canagliflozin does not prolong the QTc interval. Extensive literature review reveals that one high performance of liquied chromatography method for determination of anti diabetic drug Canagliflozin in human plasma. Therefore, in this communication we report a UV- Spectrophotometric estimation of the Canagliflozin drug which indicating accuracy, precision and sensitivity of the method using methanol as a solvent. All the chemicals used were of

analytical grade. Spectral and absorbance measurement were made on Shimadzu Double beam UV-spectrophotometer 1800.

Material and methods

Instruments

Spectrophotometric measurements were performed on Shimadzu UV – visible double beam spectrophotometer (Model- 1800). All weighing were done on electronic analytical balance (Wensar Dab220).

Chemicals and Reagents

The drug, Canagliflozin was obtained from Manus Akttiva Pharmaceuticals; Ahmedabad and Analytical grade methanol was procured from Merck Fine chemicals (Mumbai).

Selection of a Solvent: Methanol was selected as solvent for studying spectral characteristic of drugs.

Preparation of Standard Stock Solution

Accurately weighed 10 mg of Canagliflozin standard was transferred to separate 100 ml volumetric flask and dissolved in 100 ml methanol. The flasks were shaken and volume was made up to the mark with Methanol to give solution containing 100µg/ml Canagliflozin.

Preparation of Working Standard Solution of Valsartan and Nifedipine

From above solution of Canagliflozin pipette out 0.5, 1.0, 1.5, 2.0, 2.5 ml of the stock solution were further diluted to 10 ml volumetric flasks individually with methanol to get concentrations 5, 10, 15, 20, 25µg/ml.

Selection of Analytical Wavelength

Standard 5-25 µg/ml solutions of Canagliflozin were scanned between 400-200nm. Canagliflozin show the absorption maximum at 290nm. The calibration curves were plotted and recorded in the quantitative mode of instrument. The calibration curves for Canagliflozin is shown in fig:1. The linearity of calibration curve was calculated by least square method which showed co-efficient of correlation 0.998 for Canagliflozin.

Analysis of Lab sample by UV-Spectroscopic method:

The method was validated by analyzing the physical sample prepared in the laboratory. Three standards of Canagliflozin were prepared. The lab solution was prepared by the standard method analysis of Lab sample by UV-spectroscopic method. The prepared samples was then scanned in the Multi component mode in the range of 400-200nm using 290nm as sampling wavelength. The prepared lab samples were scanned and conc. was displayed through the instrument. The statistical data of the results was calculated.

Method Validation

Method validation was performed following ICH guidelines. The proposed method has been extensively validated in terms of linearity, accuracy and precision, limit of detection and limit of quantification.

Linearity (Calibration curve)

Appropriate volume of aliquot from Canagliflozin standard stock solution was transferred to 10 ml volumetric flask. The volume was made up to the mark with methanol to give solution containing 5-25 µg/ml Canagliflozin. All spectrums of canagliflozin was recorded using absorbance at 290 nm (n=5). Calibration curve was constructed by plotting average absorbance versus concentrations for both drugs. Straight line equations were obtained from these calibration curves. The linear regression equation of Canagliflozin was $y = 0.037x - 0.004$ ($R^2 = 0.998$).

Accuracy

Accuracy was assessed by determination of the recovery of the method by addition of standard drug to the pre quantified sample preparation at three different concentration levels 80 %, 100 % and 120 %, taking in to consideration percentage purity of added drug sample. The amounts of Canagliflozin were estimated by applying obtained values to the respective regression line equations. Each concentration was analyzed 3 times and average recoveries were measured.

Precision

The precision of an analytical procedure expresses the closeness of agreement between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions. The precision of the method was verified as repeatability, intra-day, inter-day and reproducibility.

The repeatability was evaluated by assaying 6 times of sample solution of 15µg/ml Canagliflozin prepared for assay determination without changing the parameter. The intra-day and inter-day precision study of Canagliflozin was carried out by estimating different concentration of Canagliflozin (10, 15, 20 µg/ml), 3 times on same day and on 3 different day (first, second and third).

Limit of Detection (LOD) and Limit of Quantification (LOQ)

ICH guideline describes several approaches to determine the detection and quantification limits. These include visual evaluation, signal-to-noise ratio and the use of standard deviation of the response and the slope of the calibration curve. In the present study, the LOD and LOQ were based on the third approach and were calculated according to the 3.3 × (SD/Slope) and 10 × (SD/Slope) criteria, respectively; where SD is the standard deviation of y-intercept of

regression line and S is the slop of the calibration curve.

Ruggedness:

Ruggedness is the degree of reproducibility of the results obtained under a verity of conditions. These conditions included different analysts and different instruments etc. In this method different analysts was considered. The data was subjected to statistical analysis and the results are expressed in mean, standard deviation and %RSD.

Robustness:

Robustness of the method was studied by deliberate variations of the analytical parameter such as solvent composition. The data was then subjected to statistical analysis and the results are expressed in mean, standard deviation and %RSD.

Table 1: Regression analysis data and summary of validation parameters for the proposed method

Parameter	UV Spectrophotometric
	Canagliflozin
Concentration range (µg/ml)	5-25
Regression equation	y = 0.037x - 0.004
Slope	0.039
Intercept	0.005132
Correlation Coefficient (R^2)	0.998
Accuracy (% recovery, n=3)	99.66-100.95
Repeatability (%RSD, n=6)	0.3814
Intraday (%RSD, n=3)	0.2019-0.4423
Interday (%RSD, n=3)	0.3301-0.5729
LOD (µg/ml)	0.432
LOQ (µg/ml)	1.31

Table 2: Recovery data of proposed method

Drug	Level (%)	Test amount (µg/ml)	Spiked STD Amount (µg/ml) (µg/ml)	Total Amount Recovered	%Mean recovery ± RSD. (n=3)
Canagliflozin	80	10	8	17.94	99.66 ± 0.6111
	100	10	10	20.16	100.8 ± 0.4043
	120	10	12	22.21	100.95 ± 0.2449

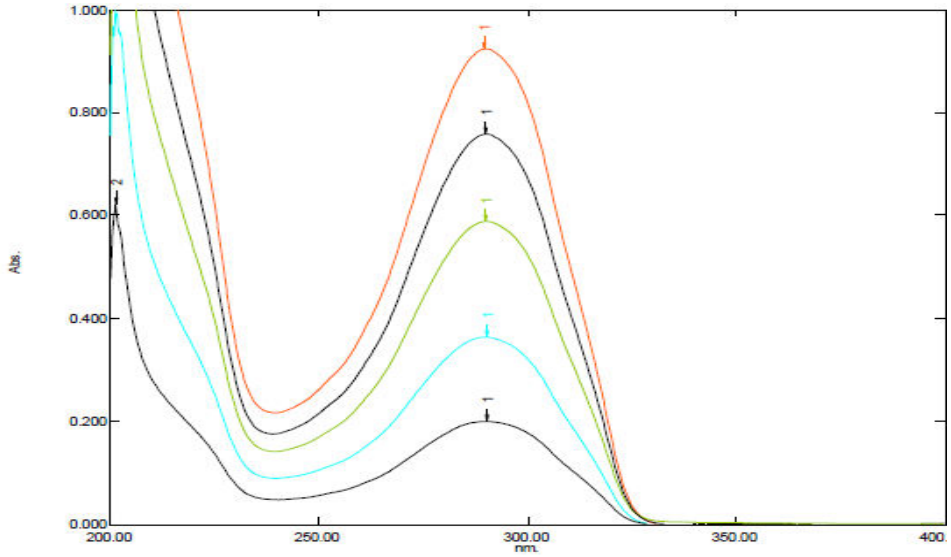

Figure 1: UV-Spectrum of Canagliflozin at 290 nm in methanol.

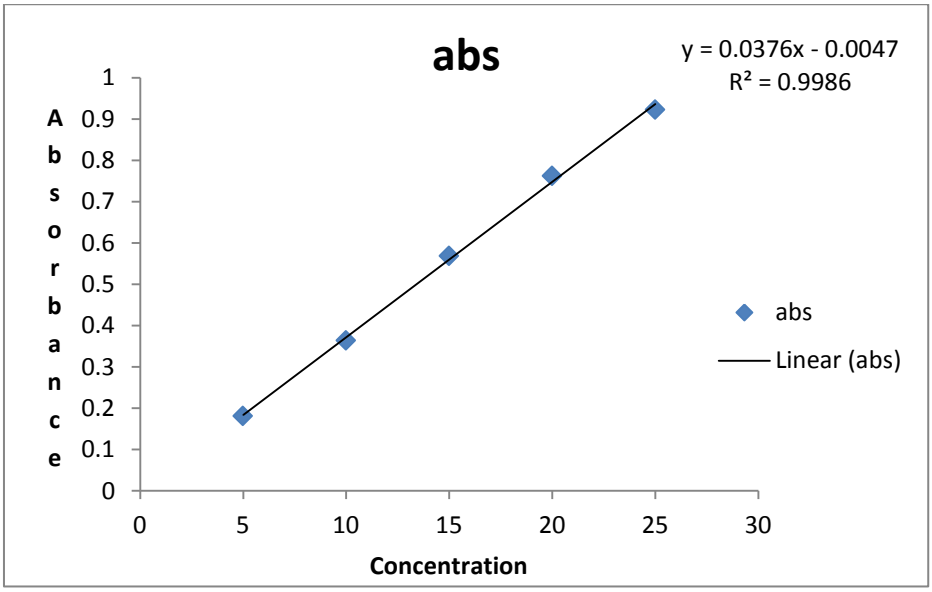

Figure 2: Calibration curve of Canagliflozin at 290 nm in Methanol.

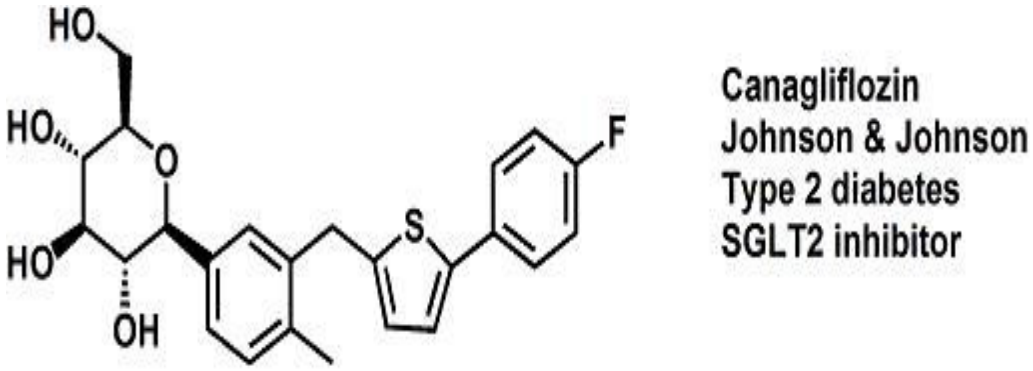

Fig-3: Structure of Canagliflozin.

Result and Discussion:

Canagliflozin obeys the Beer's limit in the range of 5-25µg/ml with the regression coefficient of 0.998. The results of recovery studies reveal that the method is accurate with the mean % recovery values between 98-102%. S.D. values

are between 0.002– 0.005 and the % R.S.D. values are between 0.2– 0.6. While performing the repeatability of the method it was found that the method is precise with the S.D. value of 0.00216 and % R.S.D. value of 0.381. The % R.S.D values of the intraday and Interday precision studies also supports this preciseness of the method.

Conclusion:

By the UV-Spectrophotometric method the API samples, as well as the marketed formulations were analyzed. The results were validated statistically and the results obtained are found well within the prescribed limits. From these results it can be concluded that, the developed UV-Spectroscopic method is simple, accurate, precise, rapid and economical. Hence, this method can be used routinely for estimation of Canagliflozin in industries and different analytical laboratories.

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