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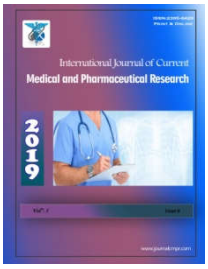

Research Article

DEVELOPMENT AND VALIDATION OF U.V SPECTROSCOPIC METHOD FOR ESTIMATION OF CANAGLIFLOZIN IN BULK AND THE PHARMACEUTICAL DOSAGE FORM

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ABSTRACT

A simple, sensitive and precise U.V spectroscopic method have been developed and validated for determination of Canagliflozin in bulk and pharmaceutical formulations as per ICH guidelines. Canagliflozin showed absorption maxima at 291nm and was linear for a range of 2-10µg/ml with correlation coefficient 0.9999with having line equation y=0.1933X+0.893. The validation of above proposed method was done by carrying out precision and accuracy studies. The analytical method showed good precision with relative standard deviation 0.022% which is less than 2. The percentage recovery at three different levels i.e. 80, 100%, 120% was found to be 98.75%, 99.89%, 100.18%respectively.Percentage assay of Canagliflozin tablets (SULISENT®) was found to be100.03%.The results of analysis were validated statistically and by recovery study. The proposed method can be applied for the routine analysis of Canagliflozin from tablet formulation.

INTRODUCTION

Canagliflozin is a novel, potent, and highly selective sodium glucose co-transporter (SGLT) 2 inhibitor. It has been proved that Canagliflozin can increase urine glucose excretion by reducing the renal glucose threshold and by decreasing the filtered glucose re-absorption. Canagliflozin was approved by FDA in March 2013. The chemical name (IUPAC) of Canagliflozin is (2S, 3R, 4R, 5S, 6R)-2-{3-[5-(4-flurophenyl)-thiophen-2-ylmethyl]-phenyl} 6 hydroxy methyl tetra hydro-pyran-3, 4, 5-triol. The structure was shown in figure 1. It is white to off white solid with melting point of 95-105°C.canagliflozin is soluble in phosphate Buffer, methanol, dimethylsulfoxide, acetonitrile. But insoluble in aqueous media.it is a product of a division of Johnson and Johnson and marketed with the brand names of INVOKANA®,SULISENT® in strengths 100 and 300mg respectively.(1)

Figure 1 Canagliflozin

MATERIALS AND METHODS

Instrumentation

A double beam UV-spectrophotometer(ELICO SL-210) consisting of two matched quartz cells with 1cm, spectra treats software used for recording and measuring spectra and absorbance, Electronic analytical weighing balance and a sonicator.

Chemicals and Reagents

Analytically pure sample of Canagliflozin, marketed tablet formulation (SULISENT®) was procured from local market with label claim 100mg.

Selection of Analytical Wavelength

Canagliflozin is soluble in organic solvents like methanol, Acetonitrile,phosphate buffer.so acetonitrile was selected throughout the study. Canagliflozin 10µg/ml of standard solution was scanned in between 200nm to 400nm and showed maximum absorption at 291nm by U.V spectrophotometer figure 2.

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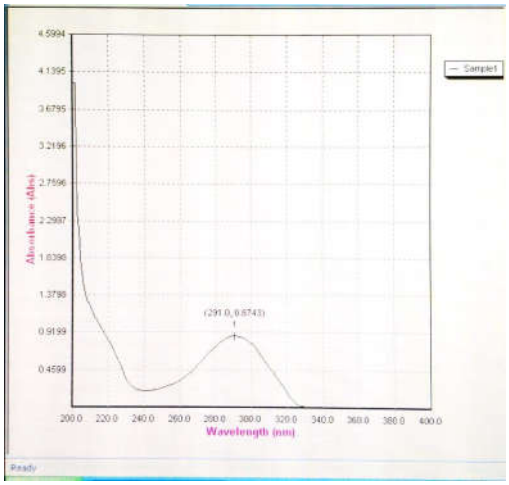

Figure 2 u.v spectrum of the standard Canagliflozin
Preparation of standard stock solution

Canagliflozin standard stock solution (1000µg/ml): A 10mg of standard Canagliflozin was weighed and dissolved in acetonitrile and made up to mark to 10ml volumetric flask.
Canagliflozin working solution (100µg/ml): from stock solution, further 1ml was transferred in10ml volumetric flask and made up to mark with acetonitrile.

Preparation of Sample Solution: 5 tablets of were weighed and calculate the average weight of each tablet then the weight equivalent to 5 tablets was transferred into a 10ml volumetric flask, 5ml of Diluent added and Sonicated for 30min,further the volume made up with Diluent and filtered. From the filtered solution 0.1ml was pipette out into a 10ml volumetric flask and made up to mark with Diluent.

Preparation of Calibration curve

From working solution, appropriate dilutions were made to get the final concentration of 2, 4,6,8,10µg/ml and absorbance was taken at λmax 291nm.averages of such 5 sets of values were taken for standard calibration curve, and the calibration curve was plotted.

Method Validation: parameters such as linearity, accuracy, precision, robustness, ruggedness, LOQ, LOD were performed according to the ICH guidelines Q2 (R1).

Linearity and Range: Linearity of developed UV spectroscopy was studied by obtaining calibration curve of Canagliflozin at five different concentrations levels ranging from 2-10µg/ml. Table 1 shows the linearity data of Canagliflozin. The linearity of Canagliflozin is shown in figure 3. The equation of regression line was **y=0.1955X-0.1215.** The correlation coefficient value was found to be **0.996**.

Table 1 Linearity data

Concentration	Absorbance
2ppm	0.1032
4ppm	0.2987
6ppm	0.4877
8ppm	0.6898
10ppm	0.8743

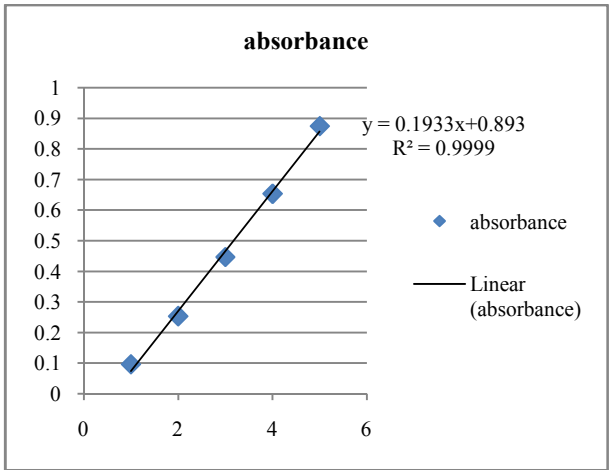

Figure 3 linearity curve of Canagliflozin

Precision

System Precision: six replicate recording of absorbance at 291nm of 10µg/ml concentration standard solution showed %RSD less than 2,which indicates acceptable reproducibility and thereby the precision of the system. System precision results are tabulated in table 2.

Method Precision: method precision was determined by performing assay of sample under the tests of 6 replicates recording of absorbance at 291nm of 10µg/ml concentration sample solution showed %RSD less than 2. Method precision results are tabulated in table 3.

Table 2 results of system precision

Concentration	system precision (Absorbance-standard)
10ppm	0.8874
10ppm	0.8820
10ppm	0.8830
10ppm	0.8858
10ppm	0.8838
10ppm	0.8849
% R.S.D	0.02218%

Table 3 results of method precision

Concentration	Method precision(absorbance-sample)
10ppm	0.5839
10ppm	0.5838
10ppm	0.5852
10ppm	0.5836
10ppm	0.5850
10ppm	0.5859
% R.S.D	**0.1456%**

Accuracy

To study the reliability, suitability and accuracy of the method, recovery studies were carried out.to the formulation equivalent to 10mg of Canagliflozin at levels of 80%,100% and 120% were added. The concentration of drugs present in resulting solution was determined using assay method; percentage recovery and percentage RSD were calculated. The results for the recovery study are given in Table 4.

Table 4 Results of accuracy

Level	Amount added	Absorbance	%recovery	%mean recovery	%r.s.d
80	4+2	0.6589	98.75%		
80	4+2	0.6588	98.71%	**98.75**%	0.07%
80	4+2	0.6590	98.79%		
100	4+4	0.7962	99.9%		
100	4+4	0.7959	99.86%	**99.89**%	0.10%
100	4+4	0.7901	99.92%		
120	4+6	1.0862	100.19%		
120	4+6	1.0859	100.14%	**100.18**%	1.10%
120	4+6	1.0865	100.23%		

Ruggedness

Ruggedness is reproducibility under normal but variable conditions. It is done by 2 methods.in one method, three working standard dilutions of 10µg/ml by 2 different analysts were prepared and tested their absorbance at fixed wavelength in same equipment and in another method, three working standard dilutions of 10µg/ml were prepared by the same analyst and the measurement of absorbance was done at 2 different systems. The results for the ruggedness are given in table5.

Table 5 Results of ruggedness

Concentration	Analyst-1 (Absorbance)	Analyst-2 (Absorbance)
10ppm	0.8898	0.8874
10ppm	0.8904	0.8892
10ppm	0.8891	0.8882
10ppm	0.8911	0.8865
10ppm	0.8884	0.8765
10ppm	0.8913	0.8902
%R.S.D	0.1277%	0.6032%

Robustness: Robustnesswas determined by performing the same concentration (10µg/ml) of solution at different wavelengths 290nm and 291nm. The analysis showed %RSD less than 2 and indicates that the method developed is robust Table 6

Table 6 Results of robustness

Concentration	290nm	292nm
10ppm	0.8879	0.8845
10ppm	0.8878	0.8833
10ppm	0.8873	0.8864
10ppm	0.8889	0.8840
10ppm	0.8891	0.8842
10ppm	0.8889	0.8825
%R.S.D	0.0837%	0.1488%

Analysis of Marketed Formulation

The validated method was applied to the determination of Canagliflozin in tablets.5tablets were assayed and the results are shown in (table 6) indicating that the amount of drug in tablet samples was in good agreement with the label claim of the formulation as indicated by %recovery(**99.70%).**

RESULTS AND DISCUSSION

Analytical method development was done based on the detection of wavelength. Selection of solvent was done based on solubility of Canagliflozin. The calibration curve was plotted using absorbance and concentration of standard solutions. The results revealed that linear regression equation for Canagliflozin was **y=0.*1933X+0.893***with correlation coefficient value **0.9999**respectively. The precision studies were carried out and the mean,standard deviation and percentage %RSD were calculated and found to be within the limit that is less than 2%. Accuracy is reported as % nominal of the analyzed concentration. The result indicates that the recovery of Canagliflozin was consistent at all levels and the percentage nominal of Canagliflozin was in between 80% to 120% respectively. The method found to be rugged and robust since there was no change in the results.

Parameters	Result
Detection wavelength(nm)	291
Beer's law limits(µg/ml)	2-10
Regression equation (y=mx+c)	1.933X+0.893
Correlation coefficient	0.9999
Slope(m)	1.933
Intercept(c)	0.893
Precision	
System precision	0.22%
Method precision	0.14%
Accuracy (%mean recovery)	
80%	98.75%
100%	99.89%
120%	100.18%
Ruggedness (2 analysts)-%RSD	≤ 2
Robustness (wavelength ±1nm) %RSD	≤2

CONCLUSION

It could be concluded that the developed method for estimation of Canagliflozin in pharmaceutical dosage form and in bulk is simple sensitive, accurate, precise, reproducible and economical. The proposed method can be used for routine quality control analysis of Canagliflozin in bulk and pharmaceutical formulation.

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Abbrevations Used

UV-ultra-violet, LOD- limit of detection, LOQ- limit of quantification, SGLT2-sodium glucose co-transporter2,µg-microgram, ICH-international conference on harmonization, RSD-relative standard deviation.

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