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Development and Validation of UV Spectrophotometric Method for the Estimation of Canagliflozin in Bulk and Pharmaceutical Dosage Form

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ABSTRACT

To develop and validate simple, sensitive, precise, rapid and cost effective method for determination of Canagliflozin in bulk and pharmaceutical formulations as per ICH Guidelines. A simple double beam UV Spectrophotometric method has been developed and validated with different parameters such as Linearity, Precision, Repeatability, Accuracy, Robustness and Ruggedness. Canagliflozin in phosphate buffer shows maximum absorbance at 289 nm. Beer's law was obeyed in the concentration range of 1-6 mcg ml-1. A recovery of Canagliflozin in tablet formulation was observed in the range of 80-120%. Percentage assay of Canagliflozin tablets (INVOKANA®) was found to be more than 99%. The proposed method is precise, accurate and reproducible and can be used for routine analysis of Canagliflozin in bulk and pharmaceutical dosage form.

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INTRODUCTION

Canagliflozin is an anti diabetic drug used to improve glycemic control in patients with type 2 diabetes. It inhibits sodium-glucose cotransporter 2 (SGLT2) represent novel therapeutic approaches in the management they act on kidneys to decrease the renal threshold for glucose (RT_G) and increase urinary glucose excretion (UGE).[1-3] Canagliflozin is chemically (2S,3R,4R,5S,6R)-2-{3-[5-(4-fluorophenyl)-thiophen-2-ylmethyl]-4-methyl-phenyl} 6hydroxymethyltetrahydro-pyran-3,4,5-triol.[4-6] The structure of canagliflozin was shown in figure 1. It is white to off white solid with melting point of 95-105ºC. Canagliflozin is soluble in phosphate buffer, methanol, dimethyl sulfoxide. Thereby increasing urinary glucose excretion and lowering blood glucose levels. It is a product of a division of Johnson and Johnson and marketed with the brand name of INVOKANA® in strengths of 100 and 300mg respectively.[7]

Literature review revealed that they were several analytical methods like HPLC, LS-MS, HPTLC and RP-HPLC and only few UV-Spectroscopic methods were reported for the estimation of canagliflozin in bulk and pharmaceutical dosage forms. Hence the present work aimed at the development and validates a simple, precise, sensitive UV spectrophotometric method for the estimation of Canagliflozin in its bulk and pharmaceutical dosage form.[8-10]

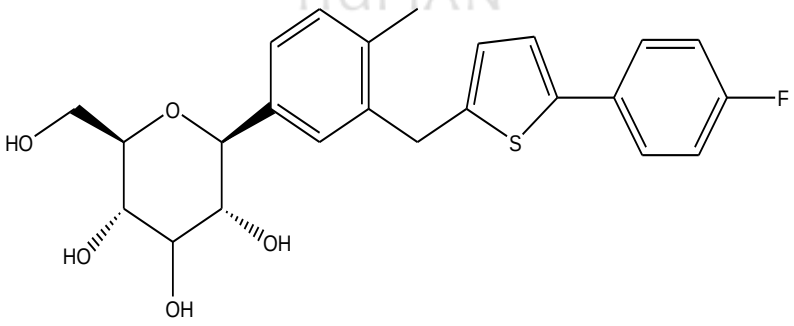

Figure 1: Canagliflozin

MATERIAL AND METHODS:

Instrumentation:

A double beam UV-visible spectrophotometer (Shimadzu 1800) consisting of two matched quartz cells with 1 cm light path and loaded with UV Solutions software (UV Probe) was used for recording and measuring of spectra and absorbance. Electronic analytical weighing balance 0.1 mg sensitivity and a sonicator (Sonica, model 1900 MH) were used in this study.

Chemicals and reagents:

Analytically pure sample of Canagliflozin was obtained from Hetero drugs, Hyderabad and marketed tablet formulation (Invokana) was procured from Johnson & Johnson, Mumbai, India with label claim 100 mg.[11-13]

Selection of analytical Wavelength:

Canagliflozin is soluble in organic solvents like phosphate buffer, Methanol and Dimethyl sulfoxide (DMSO) so Phosphate buffer was selected throughout the study. Canagliflozin 10 µg/ml of working standard solution was scanned in between 200 nm to 400 nm and showed maximum absorption at 289nm by UV spectrophotometer figure 2.

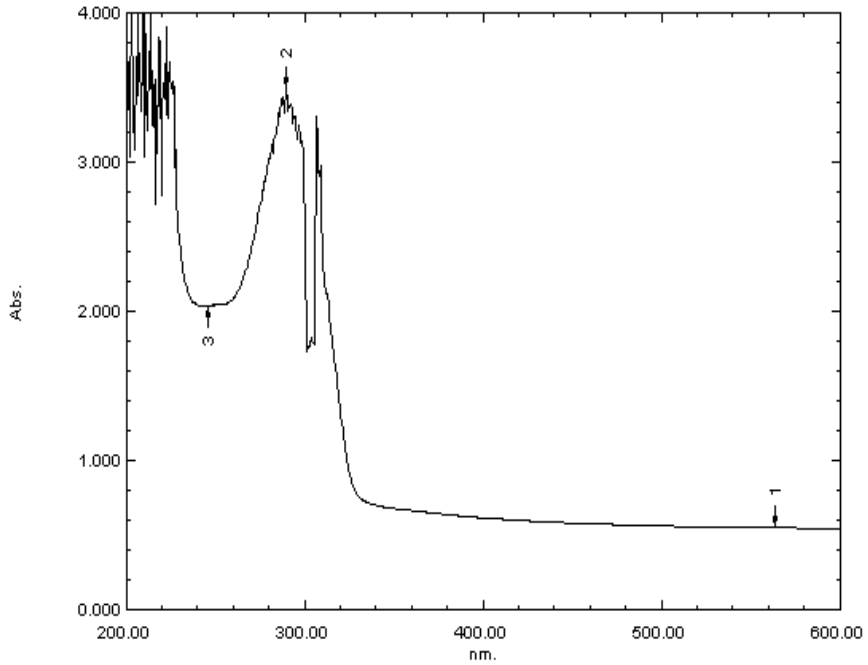

Figure 2: UV spectrum of the standard canagliflozin

Preparation of standards stock solution:

Canagliflozin standard stock solution (100µg/ml):

A 10mg of standard canagliflozin was weighed and transferred to 100ml volumetric flask and dissolved in 50ml phosphate buffer. The flask was shaken and volume was made up to the mark with phosphate buffer. From this stock solution, further 5ml was transferred in 25ml volumetric flask and diluent was added up to mark to give a solution containing 100µg/ml canagliflozin.

Preparation of calibration curve:

From this stock solution, appropriate dilutions were made to get final concentration of 1, 2,3,4,5 and 6µg/ml and absorbance was taken at λmax 289 nm. Averages of such 5 sets of values were taken for standard calibration curve, and the calibration curve was plotted.[14-17]

Method validation:

Linearity and range:

Linearity of developed UV spectrophotometer was studied by obtaining calibration curve of canagliflozin at five different concentration levels ranging from 1-6µg/ml. Table 1 show the linearity data of canagliflozin. The linearity curve of canagliflozin is shown in figure 3. The equation of regression line was y=0.047x-0.045. The correlation coefficient value was found to be 0.997.

Precision:

Precision of the method was determined by evaluating intraday and interday precision. Intra-day and Inter-day variation was analyzed by selecting three concentrations which were 1, 2 and 3µg from linearity range. Intraday analysis was carried on same day whereas Interday analysis was carried on three different days in replicates of three. The respective peak areas for different concentrations were reported in Table 2 & 3 express precision data for the method in terms of % RSD.

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 the 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.

Ruggedness:

Ruggedness is reproducibility under normal but variable laboratory conditions. It is done by 2 methods. In one method, three working standard dilutions of 1µg/ml by 2 different analysts were prepared and tested their absorbance at fixed wavelength in the same equipment and in another method, three working standard dilutions of 1µg/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 Table 5&6.[18-20]

Robustness:

Robustness was determined by performing the same concentration (1µg/ml) of solution at different wavelengths 289nm and 291. The analysis showed %RSD less than 2 and indicates that the method developed is robust Table 7.

RESULTS AND DISCUSSION:

Analytical method development was done based on the detection of wavelength. Selection of the solvent was done based on the solubility of the canagliflozin. Linearity and range of the methods were analyzed by preparing calibration curves using different concentrations range of standard canagliflozin (1 to 6µg/ml) solutions. The calibration curve was plotted using absorbance and concentration of the standard solutions. The results revealed that linear regression equation for canagliflozin was y =0.047x with correlation coefficient (R2) value 0.997 respectively. The precision studies were carried out in intraday and interday method and the mean, standard deviation (SD) 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 results indicate that the recovery of canagliflozin was consistent at all levels and the percentage nominal of the canagliflozin was in between 80% to 120%

respectively. The method was found to be rugged and robust since there was no change in the results.

Table 1: Linearity data

	Concentration (µg/ml)	Absorbance
1	0.002	
2	0.047	
3	0.098	
4	0.149	
5	0.198	
6	0.234	

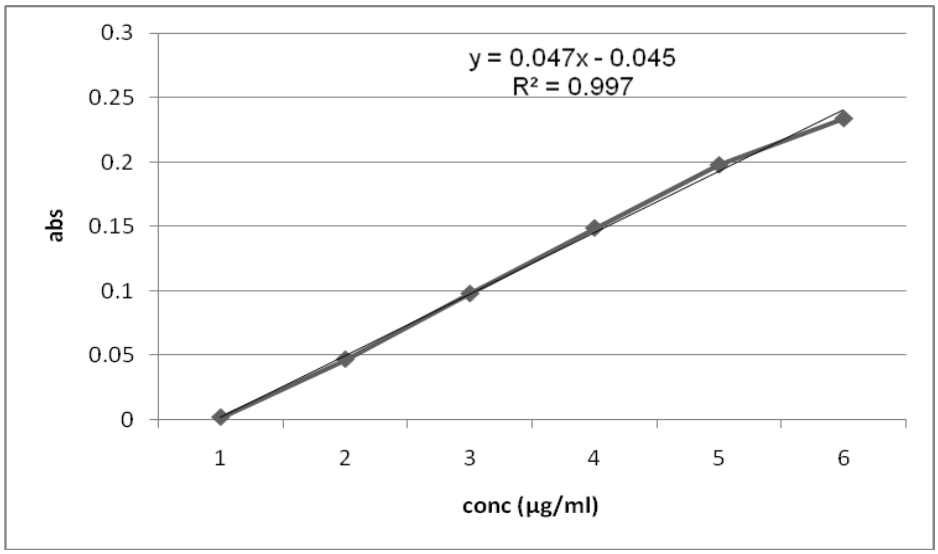

Figure: 3 Linearity curve of canagliflozin

Table 2: Results of Precision (Intraday)

Concentration (µg/ml)	Sample Absorbance	Mean Absorbance ± S.D.	%RSD
1	0.013 0.014 0.012	0.013± 0.001	7.69
2	0.047 0.044 0.042	0.044 ± 0.002	5.67
3	0.071 0.072 0.076	0.073 ± 0.003	3.62

Table 3: Results of Precision (Interday)

Concentration (µg/ml)	Sample Absorbance	Mean Absorbance ± S.D.	%RSD
	0.025		
1	0.027	0.025± 0.001	8
	0.023		
	0.057		
2	0.055	0.055 ± 0.002	2.76
	0.054		
	0.078		
3	0.080	0.079 ± 0.003	1.91
	0.081		

Table 4: Results of Accuracy

Level %	Sample Absorbance	% Recovery	Mean % Recovery	% RSD
80	0.108	98.7		
80	0.107	99.37	98.54	1.43
80	0.105	97.5		
100	0.114	99.1		
100	0.112	101.2	100.26	4.28
100	0.111	100.5		
120	0.144	101.66		
120	0.145	102.5	101.66	1.05
120	0.147	100.83		

Table 5: Results of Ruggedness (Analyst -1)

Sample Absorbance	Mean Absorbance ± S.D.	% RSD
0.194		
0.195	0.195 ± 0.002	1.06
0.198		

Table 6: Results of Ruggedness (Analyst -2)

Sample Absorbance	Mean Absorbance ± S.D.	% RSD
0.201		
0.204	0.202 ± 0.001	0.075
0.203		

Table 7: Results of Robustness

Wavelength (in nm)	Sample Absorbance	Standard Absorbance	Mean Absorbance ± S.D.	%RSD
	0.221			
289	0.219	0.198	0.221 ±0.002	1.13
	0.224			
	0.231			
291	0.229	0.201	0.229 ±0.002	1.10
	0.226			

CONCLUSION

Canagliflozin is an antidiabetic drug used to improve glycemic control in patients with type 2 diabetes. A sensitive UV spectrophotometric method was developed for the estimation of canagliflozin in bulk and pharmaceutical dosage form. Validation of the developed method was done as per the ICH guidelines Q2 (R1).

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