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Original Article

Quality-By-Design Approach to Stability Indicating RP-HPLC Analytical Method Development for Estimation of Canagliflozin API and Its Validation

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ABSTRACT

Context: Stability Indicating RP-HPLC analytical method validation for estimation of Canagliflozin API have been reported, but there are not studies related to the application of Analytical Quality by Design (AQbD) concepts to the development of a comprehensive science and risk based stability indicating RP-HPLC Analytical method for the analysis of Canagliflozin Active Pharmaceutical Ingredient (API). **Aim:** Development of a comprehensive science and risk based stability indicating RP-HPLC Analytical method for the analysis of Canagliflozin Active Pharmaceutical Ingredient (API) according to Analytical Quality by Design (AQbD) concept. **Methods:** AQbD key tools - identification of ATP (Analytical Target Profile), CQA (Critical Quality Attributes) with risk assessment, Method Optimization and Development with DoE, MODR (method operable design region), Control Strategy, AQbD Method Validation, and Continuous Method Monitoring (CMM) ware studied. An efficient experimental design based on systematic scouting of all key components of the RP-HPLC Analytical method (e.g. Diluents, λ_{max}, Column and mobile phase composition) ware presented. The final method was validated according to ICH validation guideline. **Results:** The method was linear. (r2=0.999). The accuracy was 99% to 101%. The precision, ruggedness and robustness values were also within the prescribed limits (<1%). **Conclusion:** This result indicated that a consistent, reliable and cost effective method is developed for the routine analysis of Canagliflozin in quality control laboratories.

Key words: Analytical Quality by design, Analytical Target Profile, Critical Quality Attributes, Method Optimization and Method Development

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INTRODUCTION

Quality by Design (QbD)[1-2] is a concept first outlined by well-known quality expert Joseph M. Juran in various publications, most notably Juran on Quality by Design. While Quality by Design principles have been used to advance product and process quality in every industry, and particularly the automotive industry, they have most recently been adopted by the U.S. Food and Drug Administration[3-5] as a vehicle for the transformation of how drugs are discovered, developed, and commercially manufactured. Since first initiated by the U.S. Food and Drug Administration (FDA) in its "Pharmaceutical cGMPs for the twenty-first century", Quality by Design (QbD) has become an important concept for the pharmaceutical industry that is further defined in the International Conference on Harmonisation (ICH) guidance on pharmaceutical development as "a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management".

Currently QbD approach has been successfully implemented in generic formulation development. Equivalent to process QbD, the outcome of AQbD is well understood and fit for intended purpose with robustness throughout the lifecycle. AQbD life cycle has different tools such as ATP (Analytical Target Profile), CQA,[6] Risk Assessment, Method Optimization and Development with DoE, MODR (method operable design region), Control Strategy and Risk Assessment, AQbD Method Validation and Continuous Method Monitoring. Figure 1 represents the AQbD life cycle with each tool. Scientific QbD Approach for Synthesis and Analysis. ICH Q11 has explained the QbD approach for API synthetic process development but there is no specific discussion on AQbD. However, it is recommended to implement QbD approach in analytical method development termed as AQbD. Nowadays, the AQbD concept is mainly applied to the development step of the method as an alternative approach to the quality-by-testing methodology. As already widely discussed in the scientific literature[7-11] applying the Analytical quality-by-design (QbD) concept to analytical methods ensures a controlled risk-based development of a method where quality assurance will be guaranteed.

The expression of tools in QbD and AQbD is different for synthetic development and analytical development. Both QbD and AQbD tools are presented in Table 1.

Canagliflozin is (2S, 3R, 4R, 5S, 6R)-2-{3-[5-(4-fluoro-phenyl)-thiophen-2-ylmethyl]-4-methyl-phenyl}-6 hydroxymethyltetrahydro-pyran-3,4,5-triol is a white to off white powder, soluble in many organic solvents (ethanol, methanol, tetrahydrofuran, acetone) but insoluble in aqueous media. The log P of the drug substance is 3.44 at 20oC and pH=7. There is no pKa in the physiological pH range. Molecular weight of Canagliflozin is 453.53 g/mol and formula is $C_{24}H_{25}FO_5S$. For structure refer Figure 2. Canagliflozin is an orally active inhibitor of SGLT2. By inhibiting SGLT2, Canagliflozin reduces reabsorption of filtered glucose and lowers the renal threshold for glucose (RTG), and thereby increases urinary glucose excretion (UGE), lowering elevated plasma glucose concentrations by an insulin independent mechanism in patients with type 2 diabetes. Urinary

Figure 1: AQbD tools and life cycle.

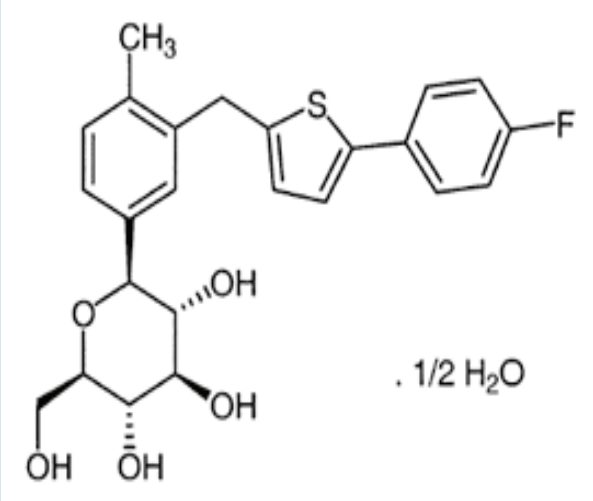

Figure 2: Structure of Canagliflozin.

Table 1: QbD tools for synthetic development and analytical development.

Steps Synthetic development (QbD)	Analytical development (AQbD)
QTPP identification	ATP (Analytical Target Profile) identification
CQA/CMA identification, Risk Assessment	CQA identification, Initial Risk Assessment
Define product design space	Method Optimization and development with DOE (Design of Experiment)
Define process design space	MODR (Method Operable Design Region)
Control Strategy with Risk Assessment	Control Strategy with Risk Assessment
Process validation	AQbD Method Validation
Continuous process monitoring	Continuous Method Monitoring

glucose excretion induced by canagliflozin leads to an osmotic diuresis, which can be associated with caloric loss and reduction in weight. The drug is commercially available in various forms of once daily oral dosage formulations including oral granules.

According to literature survey, there are some publications on RP-HPLC Analytical method development strategy but the method development approaches for RP-HPLC Analytical method specifically focused on pharmaceutical development in an AQbD environment have not been widely discussed. Therefore, there is an unmet need to develop a systematic RP-HPLC Analytical method development approach for pharmaceutical development using AQbD principles to ensure the quality of the method throughout the material lifecycle.

The primary objective of this study was to implement AQbD approach to develop and validate an RP-HPLC Analytical method for the determination of assay of Canagliflozin API to establish an in depth understanding of the method and build in the quality during the method development to ensure optimum method performance over the lifetime of the material.

The objectives of this work are as follows:

1. To develop simple, rapid and sensitive method for identification of critical attributes by AQbD approach of Canagliflozin API by RP-HPLC method.
2. To establish a validated test method as per ICH guidelines for the determination of assay of Canagliflozin API by RP-HPLC method.

MATERIALS & METHOD

Materials and reagents

Canagliflozin Active Pharmaceutical Ingredient (API) was obtained from Beijing Huikang Boyuan Chemical Tech. Co. Ltd., China. HPLC grade ethanol, Tetrahydrofuran and methanol were purchased from Merck. Phosphoric acid, GR grade was purchased from Merck. Purified water was obtained from Milli-Q water purification system (Millipore, Milford, USA).

Instrumentation

A HPLC (Perkin Elmer, Model: Lambda 25) consisting of P.E. Binary LC Pump 200B/250 (Perkin Elmer, Model: series 200), vacuum degasser, UV-VIS detector (PerkinElmer, Model: series 200), C8 and C18 reverse phase column (Kromasil, size: 250×4.60 mm, particle size 5 µm) and a sample injector system (Rheodyne) with a 200µl sample loop and Total Chrome Navigator software (version V 4.5) on computer (operated with Windows XP); Spectrophotometric determinations were carried out on 'Shimadzu' double beam UV-Visible spectrophotometer (model: UV probe) with 1 cm quartz cell.

Preparation of 1% Phosphate Buffer

10 ml of Phosphoric acid was added in 1000 ml of water respectively. Then it was sonicated.

ATP (Analytical Target Profile)

ATP identification includes the selection of method requirements such as target analytes (product and impurities), analytical technique category, and product specifications.

(a) Target Analytes Selection: The analyst for this present study is Canagliflozin API.

(b) Technique Selection: The selected technique for assay / potency determination of Canagliflozin is RP-HPLC.

(c) Method Requirements Selection: Based on RP-HPLC the requirements of this study are Diluents, Column and mobile phase composition.

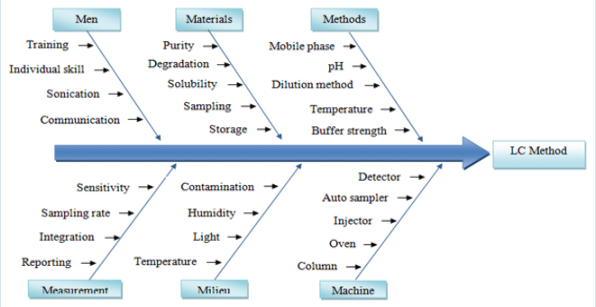

Figure 3: Fishbone for Risk identification.

CQA (Critical Quality Attributes) and Initial Risk Assessment

CQA (Critical Quality Attributes): CQA for analytical methods includes method attributes and method parameters. Each analytical technique has different CQA. In present study, RP-HPLC method's CQA are Diluents, λ_{max}, Column and mobile phase composition.

Initial Risk Assessment

Ishikawa fishbone diagram is used for risk identification and assessment. Figure 3 that show fishbone risk identification approach for this analytical test procedure.

Risk Identification:

DoE: Design of Experiments (Method Optimization and Development)

Depending on the Risk Assessment, the DoE of the present study is performed to confirm and refine the critical method variables. Here an efficient and comprehensive experimental design based on systematic scouting of all three key components of the RP-HPLC method (Diluents, λ_{max}, Column and mobile phase composition) is presented. It forms a database that will assist with method understanding, optimization and selection. In addition, it can be used to evaluate and implement change of the method, should it be needed in the future, for example should the diluent used no longer be commercially available, or not present in the lab at the time of analysis. The scouting of the parameters is shown in Table 2.

MODR (Method Operable Design Region): Method operable design region (MODR) is used for establishment of a multidimensional space based on outcomes of DoE; MODR can provide suitable method performance. Further method verification exercises can be employed to establish ATP conformance and ultimately define the MODR.

Control Strategy and Risk Assessment: Control strategy is a planned set of controls, derived from analyte nature and MODR understanding. Method control strategy does not appear dramatically different under the AQbD approach when compared to the traditional approach. However, method controls are established based on CQA, DoE, and MODR experimental data to ensure a stronger link between the method purpose and performance.

As the final method is selected against method attributes, it is highly likely that the selected method is reliable and will remain operational over the lifetime of material. Therefore, the evaluation of method robustness and ruggedness to be carried out as one of the step of method development is mainly for the method verification and finalization. A risk-based approach based on the QbD principles set out in ICH Q8 and Q9 was applied to the evaluation of method robustness and ruggedness. As per ICH Q8 guidance process robustness is defined as "Ability of a process to tolerate variability of materials and changes of the process and equipment without negative impact on quality."

Robustness

To establish the robustness of test method and to demonstrate its reliability for minor changes in method conditions.

Ruggedness

The ruggedness of analytical method is the degree of reproducibility of test results obtained by the analysis of the same samples under a variety of conditions such as different laboratories, different instruments, different lots of reagents, different assay, temperatures, different days, different analysts, etc.

As a result of robustness and ruggedness studies, the overall method understanding of method performance under various conditions can be improved and an analytical method performance control strategy along with appropriate system suitability criteria can be defined to manage risk and ensure the method delivers the desirable method attributes. If the risk is high and is hard to manage, it is an opportunity for the analyst to go back to the database described in scouting of CQA Parameters to find a more appropriate method and to go through the procedure as described to ensure method robustness and ruggedness.

AQbD Method Validation

AQbD method validation approach is the validation of analytical method over a range of different API batches. It uses both DoE and MODR knowledge for designing method validation for all kinds of API manufacturing changes without revalidation. The approach provides the required ICH validation elements as well as information on interactions, measurement uncertainty, control strategy, and continuous improvement. This approach requires fewer resources than the traditional validation approach without compromising quality.

Accuracy: Accuracy of the method was resolved by standard addition method in which standard addition of pure API at three different concentration levels of 60%, 80%, 100%, 120% and 140% was performed

Table 2: Scouting of CQA Parameters

Parameters	Description of the parameters
Diluents	Methanol, Ethanol, Dimethylsulphoxide is used to check the solubility and stability of solution. Scan the drug substance solution in the solvents in the range of 400nm-200 nm and select the desired solvent as diluent.
λ_{max}	Scan the drug substance solution in the solvents in the range of 400nm-200 nm and the maximum absorbance is fixed as λ_{max} for the drug substance.
Column	C18, C8
Mobile phase composition	Acetonitrile: Buffer Methanol: Buffer

in triplicate. Accuracy of the method is calculated in the terms of % recovery of the API.

Linearity: The linearity of an analytical method is its ability to elicit test results that are directly, or by a well-defined mathematical transformation, proportional to the concentration of analyte in sample within a given range (60%, 80%, 100%, 120% and 140% API solution.)

Precision: The standard solution was injected six times to determine the system suitability parameters. Method precision was established by determining six sample preparations under same conditions. Six replicates of sample were prepared at sample concentration by one analyst and analyzed on same day.

Limit of Detection (LOD) and Limit of Quantification (LOQ)**:** The limit of quantification (LOQ) is the lowest amount of analyte in a sample that can be determined with acceptable precision and accuracy under the stated experimental conditions, It is expressed as the concentration of analyte (e.g. parts per million) in the sample. S/N ratio not less than 10.

LOD = 3.3 σ /S, LOQ = 10 σ /S (σ = Standard deviation and S = Slop of the calibration curve)

Stability studies (Forced degradation)

Stability studies are performed according to ICH guidelines under condition of hydrolysis (acidic and alkaline), oxidation and thermal studies.

Standard Stock solution

Accurately weighed quantity of Canagliflozin (10 mg) was transferred to a 10 ml volumetric flask, dissolved and diluted up to the mark with methanol and was ultra-sonicated for 5 min (Concentration:1000 µg/ml).

Alkali induced degradation

To 1ml of stock solution of Canagliflozin 1 ml 2N sodium hydroxide was added and allowed to keep aside for 6 hur, after that 1ml of acid was added to neutralize the base to the resulting solution. Add Methanol sufficient to make up 10ml. Later, 4 ml of sample was diluted to 25 ml with methanol and analyzed.

Acid induced degradation

To 1ml of stock solution Canagliflozin, 1 ml of 2 N hydrochloric acid was added and allowed to keep aside for 6 h, then that acid was neutralized by base and diluted up to 10 ml with methanol. Then, 4 ml of sample was diluted to 25 ml with methanol and analyzed.

Hydrogen peroxide-induced degradation

To 1 ml of stock solution of Canagliflozin, 1 ml of 30 % hydrogen peroxide (H_2O_2) was added and it allowed to keep aside for 6 h. Add Methanol sufficient to make up 10 ml. Later, 4 ml of sample was diluted to 25 ml with methanol and analyzed.

Thermal degradation

A sample powder of Canagliflozin (10 mg) was exposed to a temperature of 100 °C for 48 h in hot air oven. This Canagliflozin (10 mg) was transferred to a 100 ml volumetric flask, dissolved and diluted up to the mark with methanol and was ultra-sonicated for 5 min. Later, 4 ml of sample was diluted to 25 ml with methanol and analyzed.

Continuous Method Monitoring (CMM) and Continual Improvement: Life cycle management is a control strategy used for implementation of design space in commercial stage. CMM is final step in AQbD life cycle; it is a continuous process of sharing knowledge gained during development and implementation of design space. This includes results of risk assessments, assumptions based on prior knowledge, statistical design considerations, and bridge between the design space, MODR, control strategy, CQA, and ATP. Once a method validation is completed, method can be used for routine purpose and continuous method performance can be monitored. This can be performed by using control charts or tracking system suitability data, method related investigations, and so forth. CMM allows the analyst to proactively identify and address any out-of-trend performance.

Table 3: Solubility and solution stability

Diluents	Solubility	Solution Stability (Appearance of solution)			Solvent Selection
		Day-01	Day-02	Day-03	
Methanol	Soluble	Clear	Clear	Clear	Satisfactory
Ethanol	Soluble	Clear	Clear	Clear	Satisfactory
DMSO	soluble	Clear	Clear	Clear	Satisfactory

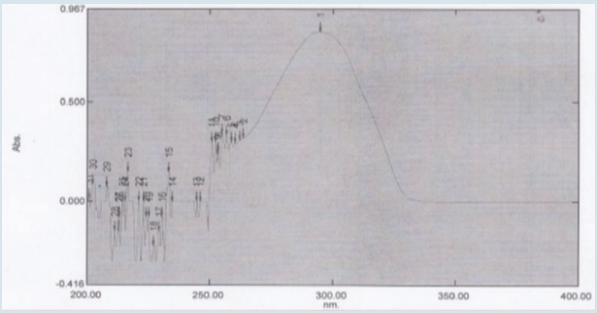

Figure 4: UV spectra of Canagliflozin (in DMSO) for detection wavelength; (λ_{max}) = 290 nm.

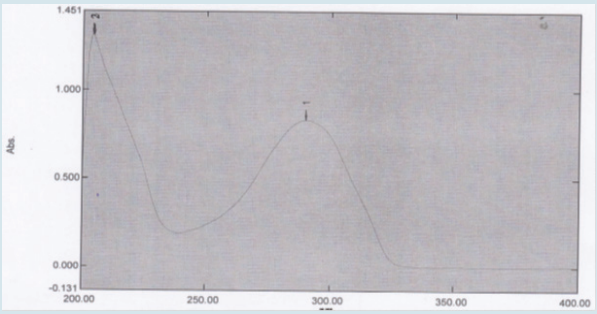

Figure 5: UV spectra of Canagliflozin(in Methanol and in ethanol) for detection wavelength; (λ_{max}) = 290 nm.

RESULTS & DISCUSSION

DoE experiment for method development

Solubility and solution stability**:** All the trials of method development on the basis of solubility and solution stability is shown in Table 3.

From the above experiment of solubility, solution stability and scanning from 200 nm to 400 nm,

λ_{max} of 290 nm was considered for experimental work. Methanol and

Table 4: Column and mobile phase composition

Trial	Trials taken		Observation	Remarks
1	Column C8	Buffer : Methanol	Peak was found to be very asymmetrical with large tailing	Not Satisfactory
2	Column C8	Buffer : Acetonitrile	Peak was found to be asymmetrical with awful shape	Not Satisfactory
3	Column C18	Buffer : Methanol	Peak was found to be asymmetrical but shape was not good	Not Satisfactory
4	Column C18	Buffer : Acetonitrile	Good asymmetrical Peak shape and tailing factor was 1.04	Satisfactory

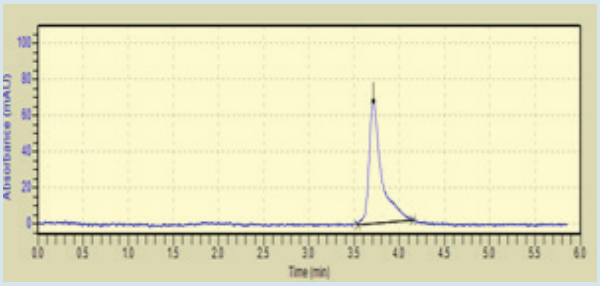

Figure 6: Chromatogram for Trial 1.

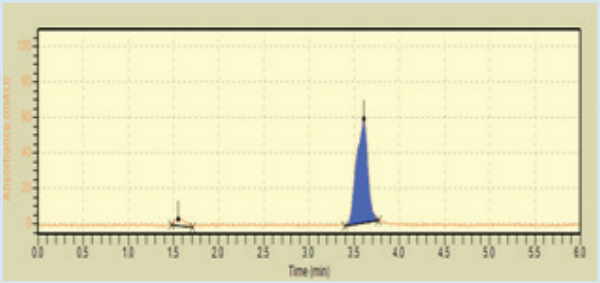

Figure 7: Chromatogram for Trial 2.

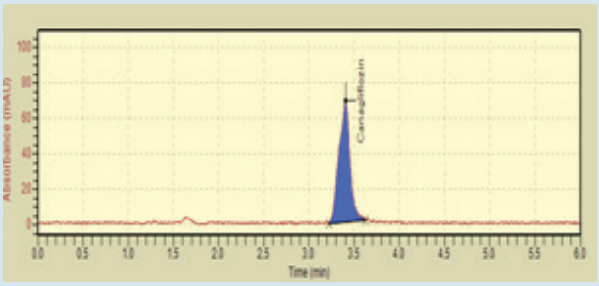

Figure 8: Chromatogram for Trial 3.

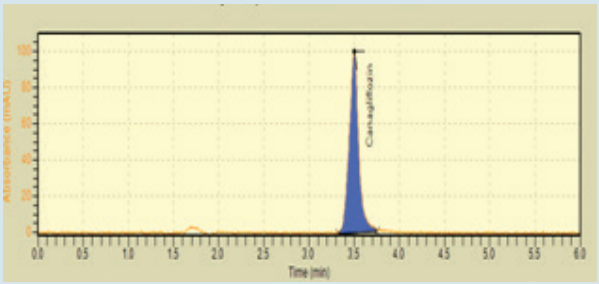

Figure 9: Chromatogram for Trial 4.

Table 5: Robustness studies of Canagliflozin

Parameter		Area (mAU)	Retention time (min)	Theoretical Plates	Tailing factor
Change in flow rate (1.5 ml/min ± 0.1 ml/min)	1.4 ml/min	590715	3.725	4857	1.006
	1.6 ml/min	591026	3.378	4122	1.058
Change in wave length (290 mn ± 1 nm)	289 nm	600081	3.442	4268	1.009
	291 nm	590956	3.506	4219	1.117

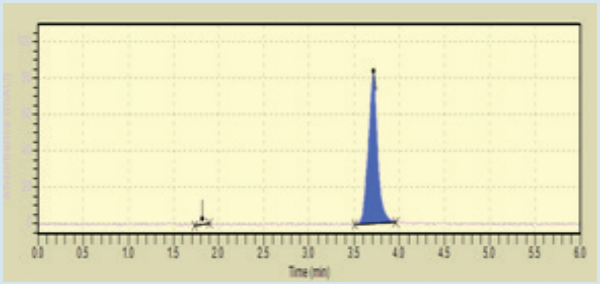

Figure 10: Chromatogram of Robustness at flow rate of 1.4 ml/min.

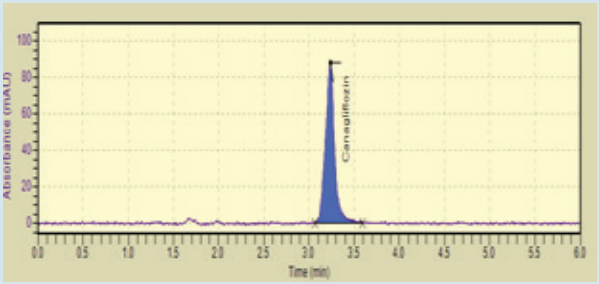

Figure11: Chromatogram of Robustness at flow rate of 1.6 ml/min.

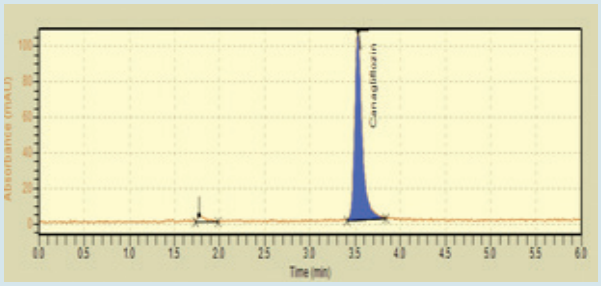

Figure 12: Chromatogram of Robustness at 289 nm.

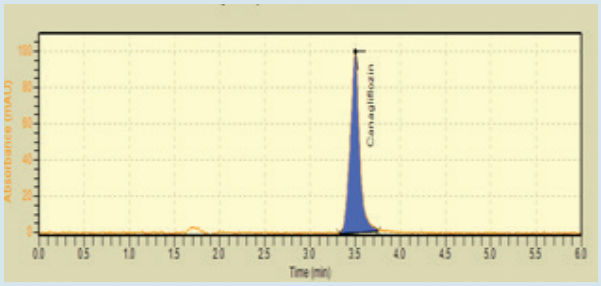

Figure 13: Chromatogram of Robustness at 291 nm.

Table 6: Ruggedness studies of Canagliflozin

Test Sample	Change in Day & Analyst	
	Day 1 & Analyst 1	Day 2 & Analyst 2
	Result 1 (%)	Result 2 (%)
1	99.38	98.65
2	99.39	98.38
3	98.88	98.38
4	98.88	98.38
5	98.38	98.39
6	99.39	98.87
SD	**0.409**	**0.436**
Mean	**99.05**	**99.01**
RSD	**0.413**	**0.440**

Table 7: Accuracy Studies of Canagliflozin

No. of sample	Sample added, mg	Sample Recovered, mg	% of Recovery	Average Recovery, %
1	8.25	8.05	99.42	
2	8.23	8.05	99.63	99.52
3	8.33	8.15	99.51	
1	10.23	10.2	99.13	
2	10.09	10.02	99.58	99.39
3	10.03	10.2	99.46	
1	12.05	12.37	99.04	
2	12.36	12.34	99.16	99.08
3	12.09	12.37	99.05	

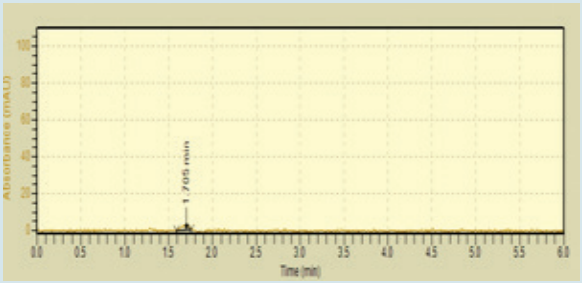

Figure 14: Chromatogram for Blank.

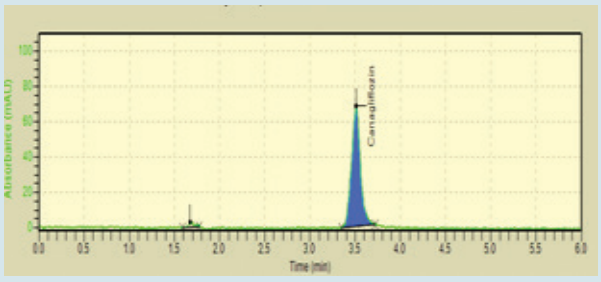

Figure 15: Accuracy Chromatogram at 80% level.

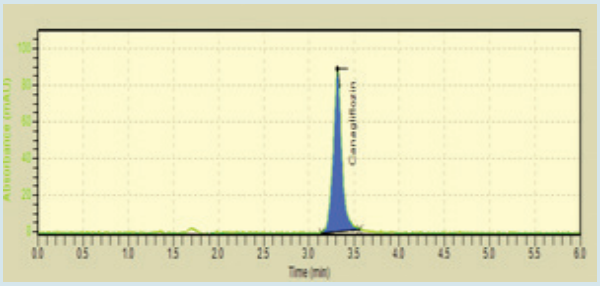

Figure 16: Accuracy Chromatogram at 100% level.

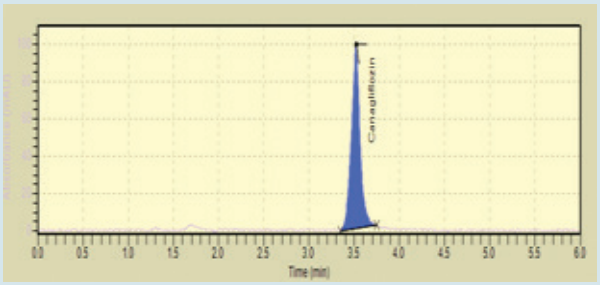

Figure 17: Accuracy Chromatogram at 120% level.

Methanol both gave a smooth curve. From the literature survey,[12] Methanol was selected as diluent.

MODR (Method Operable Design Region):

From the outcome of the above DoE, MODR is selected as follows:

The chromatographic condition is presented below:

- Chromatographic system : Perkinelmer HPLC with PDA detector
- Column : Kromasil C_{18}, 250 mm x 4.6 mm, 5µ, 120Aº
- Mobile phase : Acetonitrile : 0.1% solution of Phosphoric acid (50:50)
- Flow rate : 1.5
- Column temperature : 30°C
- Wavelength : 290 nm
- Inject volume : 20 µL

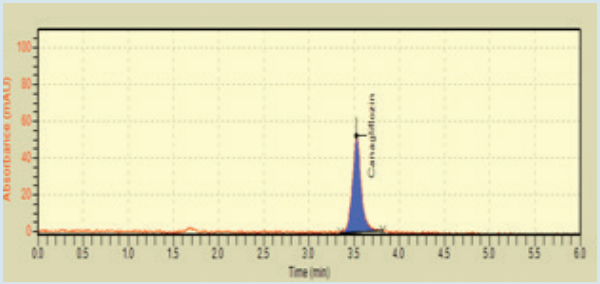

Figure 18: Linearity Chromatogram at 60%. level

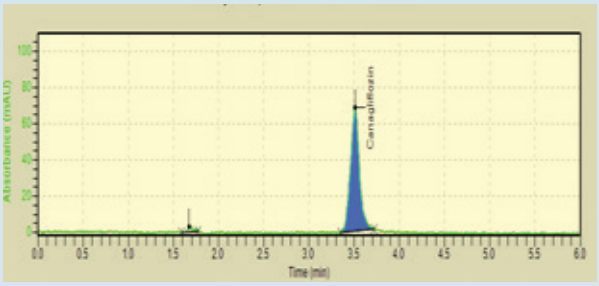

Figure 19: Linearity Chromatogram at 80%. level.

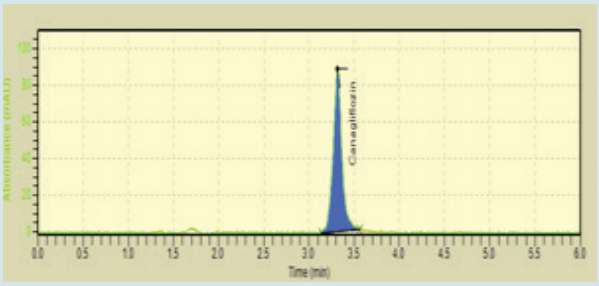

Figure 20: Linearity Chromatogram at 100% level.

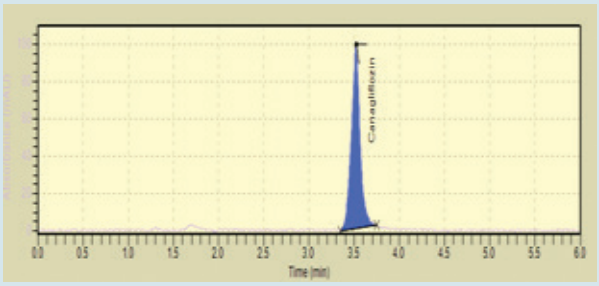

Figure 21: Linearity Chromatogram at 120% level.

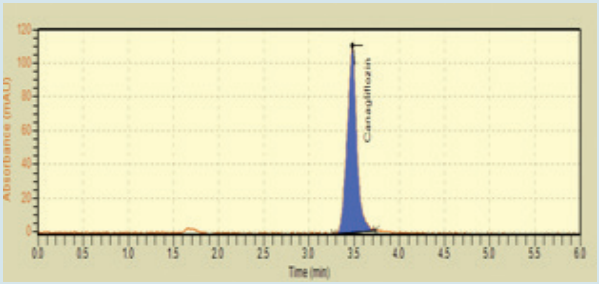

Figure 22: Linearity Chromatogram at 140% level.

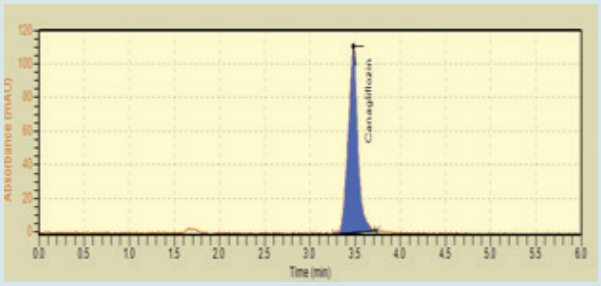

Figure 23: Calibration Curve of Canagliflozin.

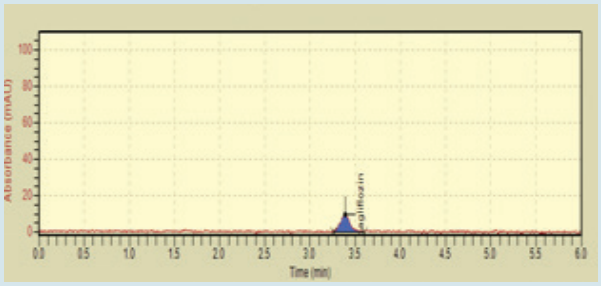

Figure 25: Chromatogram at 10% level.

Control Strategy and Risk Assessment:

Conclusion: The study proves that the method is robust under different conditions (change in flow rate and wavelength).

Conclusion: The study proves the reliability of test method for ruggedness in Spectrophotometric condition.

The study result of robustness and ruggedness ensure that the method delivers the desirable method attributes.

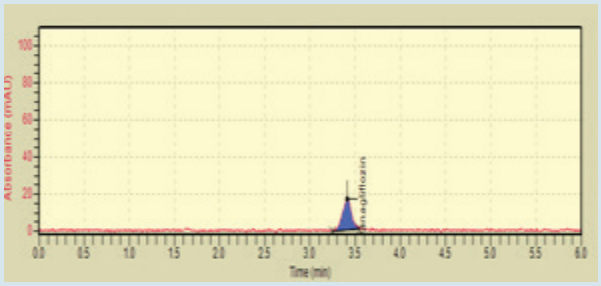

Figure 26: Chromatogram at 20% level.

AQbD Method Validation:

Conclusion:

Average recoveries at each level within 97% to 103% establish that the method is accurate.

Linearity:

The linearity results are shown in Table 8 and the graphs are shown in figure 4 (1 & 2).

Table 8: Linearity of Canagliflozin

Concentration (ppm)	Peak Area
9.6	375889
12.8	491322
16.0	607510
19.2	714936
22.4	843145

Conclusion:

From the study of concentration range (9.6 ppm to 22.4 ppm), the linear response for the analyte exist can be established.

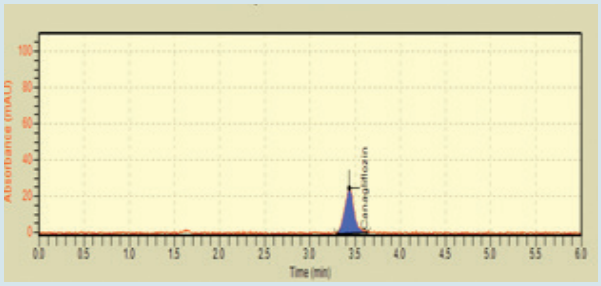

Figure 27 : Chromatogram at 30% level.

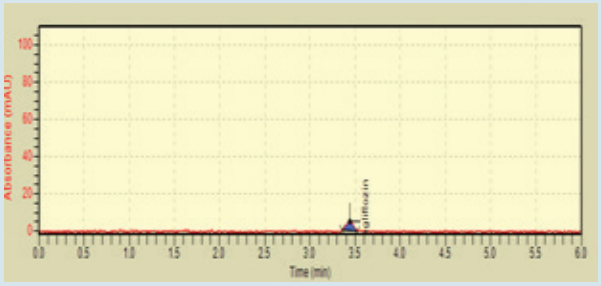

Figure 24: Chromatogram at 5% level.

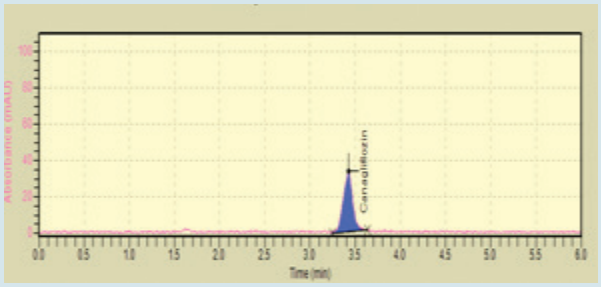

Figure 28: Chromatogram at 40% level.

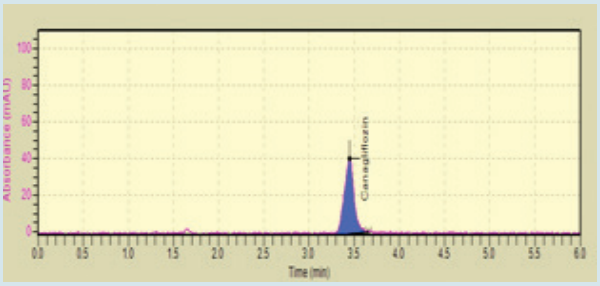

Figure 29: Chromatogram at 50% level .

Precision:

Table 9: System Suitability Parameters

Area	Retention time (min)	Area % RSD		Theoretical Plates		Tailing factor	
		Result	Acceptance limit	Result	Acceptance limit	Result	Acceptance limit
590228	3.437	1.068	< 2.0	3857	> 2000	1.016	< 2.0

Table 10: Precession studies of Canagliflozin

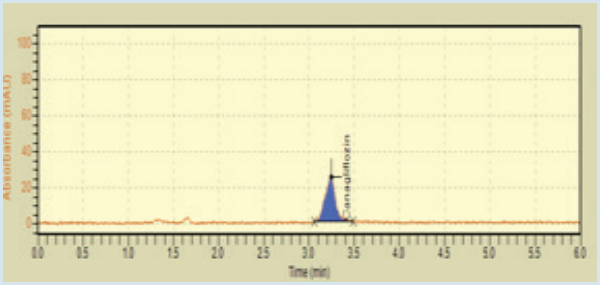

Figure 30: Chromatogram of Degradation-Acid Hydrolysis.

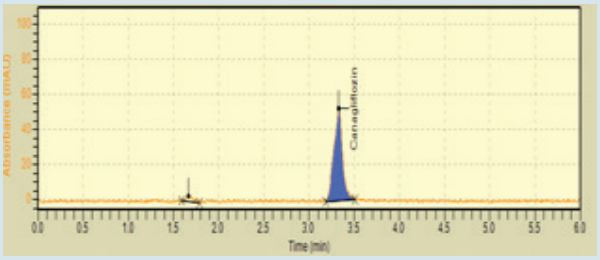

Figure 31: Chromatogram of Degradation-Alkaline Hydrolysis.

Conclusion: In forced degradation it was observed that Canagliflozin is susceptible to degradation in acid, base and oxidative stress conditions, but it is found to be stable under thermal stress conditions.

CONCLUSION

A comprehensive science and risk based stability indicating RP-HPLC Analytical method approach using QbD principles has been described. First, the method goals are clarified based on the process understanding.

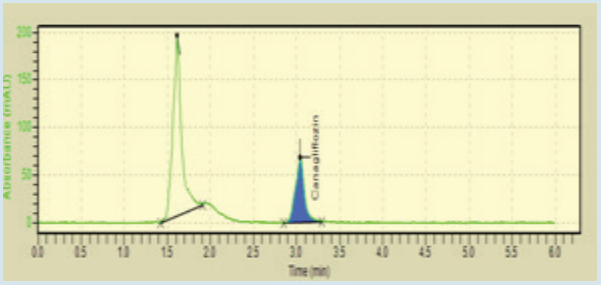

Figure 32: Chromatogram of Degradation-Oxidation.

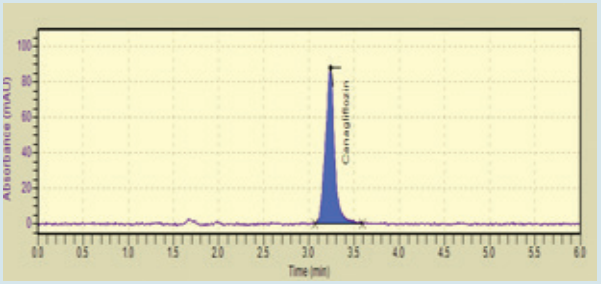

Figure 33: Chromatogram of Degradation- Thermal.

Sample	% of Canagliflozin
1	99.20
2	99.10
3	98.10
4	98.18
5	98.25
6	99.38
SD	**0.11**
Average	**99.20**
%RSD	**0.11**

Conclusion: RSD of six samples is less than 2.0% shows that the method is precise.

Limit of Detection & Limit of Quantification:

The LOD and LOQ of Canagliflozin were found 0.22 ppm and 0.70 ppm respectively.

Table 11: Stability studies of Canagliflozin (Forced degradation)

Sample	Sample used, mg	Sample recovered after degradation, mg	% of Recovery
Acid Hydrolysis	10.15	3.61	35.54
Alkaline Hydrolysis	10.11	6.97	68.90
Oxidation	10.07	7.79	77.31
Thermal	10.23	10.14	99.10

The experimental design describes the scouting of the key RP-HPLC Analytical method components including diluent, λ_{max} selection, column and composition of mobile phase. Their interrelationships are studied and the preliminary optimized conditions are obtained for each combination of diluent, λ_{max} selection, column and composition of mobile phase. Here a better understanding of the factors influencing RP-HPLC Analytical method and greater confidence in the ability of the methods to meet their intended purposes is done. Moreover, this approach provides an in-depth knowledge and enables the creation of a RP-HPLC database that can be utilized to provide alternative method conditions at a future time should changes to the method be required. Furthermore, the method development is not considered finished until a thorough risk assessment and all the necessary robustness and ruggedness studies are carried out. All the validated parameters were found within acceptance criteria. The validated method is specific, linear, precise, accurate, robust and rugged for determination. The forced degradation studies were carried out in accordance with ICH guidelines and Canagliflozin is unstable in alkaline, acidic, oxidative but stable in thermal degradations. Based on the knowledge of method obtained through the method development and the results of risk assessment along with robustness and ruggedness studies, detailed analytical method performance control strategy can be defined to manage the risk. Implementation of QbD approach resulted in more robust methods which can produce consistent, reliable, and quality data throughout the process and also save time and money. This approach has been successfully used in the laboratory to use RP-HPLC Analytical method for Canagliflozin API.

ACKNOWLEDGEMENT

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CONFLICT OF INTEREST

No conflict of interest

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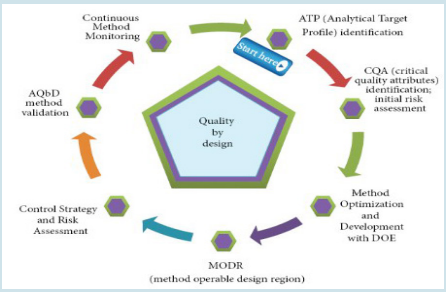
PICTORIAL ABSTRACT



SUMMARY

- The experimental design of AQbD describes the scouting of the key RPHPLC Analytical method components including diluent, λmax selection, column and composition of mobile phase.
- Their interrelationships are studied and the preliminary optimized conditions are obtained for each combination of diluent, λmax selection, column and composition of mobile phase.
- The validated method is specific, linear, precise, accurate, robust and rugged for determination.
- Implementation of QbD approach has been successfully used in the laboratory to use RP-HPLC Analytical method for Canagliflozin API.

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