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ANALYTICAL METHODS FOR ESTIMATION OF CANAGLIFLOZIN IN PHARMACEUTICAL DOSAGE FORM - A REVIEW

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ABSTRACT

Canagliflozin is an orally well-administered drug. It is under the type of sodium-glucose co-transporter- 2 (SGLT-2) inhibitor used in the treatment of type-II diabetes patient. By inhibiting the transporter protein SGLT-2 in the kidneys, canagliflozin reduces renal glucose reabsorption, thereby increasing urinary glucose excretion and reducing blood glucose levels. Canagliflozin is estimated by RP-HPLC, RP-LC, UV-Spectrophotometer, UPLC, HPTLC, LC-MS, FT-IR methods, spectoflurimetry. There are plenty of articles which have already been published describing analytical method and method validation for the same. In present to review account, the disclosed analytical methods are outlined for the establishment of canagliflozin in its Pharmaceutical preparations and biological matrices. Most frequently used techniques such as spectrometric and liquid chromatography method for canagliflozin alone and in combination include parameters like λ max, solvent, matrix etc. and HPLC method for canagliflozin alone and in combination including parameters like matrix, stationary phase, mobile phase, composition, detection, wavelength etc. HPTLC methods including parameters like stationary phase, mobile phase combination, RF etc. This review also provides detailed information on separation condition for canagliflozin alone, in the presence combination with other drugs and in presence of its degradation products.

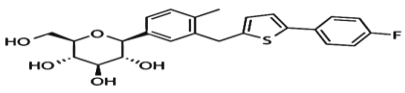
Keywords: Canagliflozin, Analytical methods and Validation Technique, HPLC, RP-LC, HPTLC, LC-MS, UPLC, UV-Spectroscopy, Fourier-transform Infra-red spectroscopy, Spectroflurimetry, Review article.

INTRODUCTION

DRUG PROFILE

Canagliflozin [C24H25FO5S] is a white to off white solid with melting range of 95-105°C is chemically named as (2S,3R,4R,5S,6R)-2-{3-[5-[4-Fluoro-phenyl)-thiophen-2-ylmethyl]-4-methyl-phenyl}-6-hydroxymethyl-tetrahydro-pyran-3,4,5-triol. It is soluble in many organic solvents (methanol, dimethyl sulfoxide) but insoluble in aqueous media. Canagliflozin is an oral anti-diabetic agent which belongs to a newly developed class. It is an inhibitory action on sodium-glucose co-transporter-2 (SGLT-2).

Structure of CANAGLIFOZIN



Mechanism of Action

The sodium-glucose co-transporter-2 (SGLT-2), is found in the proximal tubules of the kidney, and reabsorption filtered glucose from the renal tubular lumen. Canagliflozin Inhibits the SGLT-2 co-transporter. This inhibition leads to lower reabsorption of filtered glucose into the body and decreases the renal threshold for glucose [RTG], leading to increased glucose, excreted in the urine.

ANALYTICAL DETERMINATION:

1. **High Performance Liquid Chromatography (HPLC):**

HPLC is the advanced analytical technique in the pharmaceutical analysis, which is predominantly used in pharmaceutical industries [7-8] for the large variety of samples. It is the method of choice for determining the purity of new drug candidates, monitoring changes or scale-ups of synthetic procedures, evaluating new formulations, and scrutinizing quality control of final drug products.

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S. NO	STATIONARY PHASE	MOBILE PHASE	FLOW RATE AND METHOD OF DETECTION	RESULTS	REFERENCE
1.	C18 column F 250 mm length × 4.6 mm diameter × 5µm particle size	Acetonitrile : 1-octane sulphonic acid in ratio of 70:30 v/v	1.0ml/min UV at 245nm	r : 0.9997 LOD : 0.0170 µg/ml LOQ : 0.1705 µg/ml	Sreenivasulu.S *et al*.[10]
2.	C18 column (250 mm × 4.6 mm × 5 mm particle size)	Phosphate buffer : Acetonitrile (60:40 v/v)	PDA Detector 290 nm	Rt : metformin:5.4 min Canagliflozin: 7.6 min r : 0.999	Darshan Patel *et al*.[11]
3.	Non polar inertial ODS – 3(250 mm × 4.6 mm, 5 µ)	Ammonium acetate : Buffer (pH – 4.5) Acetonitrile in the ratio of 30:70 % v/v	1 mL/min UV at 252 nm	Rt : 4.5 mins Run time : 7 min LOD : 0.01 ppm LOQ : 0.04 ppm	Darshan Bhatt *et al*.[12]
4.	INERTSIL Column C18 (150 × 4.6) 5 µm	water :Acetonitrile (70:30)v/v	1 mL/min UV at 264	r : 0.999 LOD : 0.003 µg/ml LOQ : 0.011 µg/ml	Swapnasingh *et al*.[13]
5.	Cosmosil C18 (250 mm × 4.6 ID particle size : 5 micron)	Water: Methanol 50:50 at pH-3	1 ml/min UV at 254 nm Run time : 8 min	Canagliflozin:- LOD : 0.57 µg/ml LOQ : 1.70 µg/ml Metformin : - LOD : 0.16 µg/ml LOQ : 0.49 µg/ml	SunandaLekurwala *et al*.[14]
6.	K romasil C18 250 × 4.6 mm , 5µm, 120 A°	Acetonitrile : 0.1% solution of Phosphoric Acid (50 : 50)	1.5 ml/ min UV at 290 nm	LOD : 0.22 ppm LOQ : 0.70 ppm	Mohammad Tarikul Islam Boussunia *et al*.[15]
7.	K romasil C18 column [250 × 4.6 mm ; 5 mm particle size]	Mixture of 0.001 M Ammonium acetate pH adjusted to 3.5 with Ortho Phosphoric Acid Acetonitrile (65:35, v/v)	PDA Detector	Metformin LOD : 0.27µg/ml LOQ : 0.83 µg/ml Canagliflozin LOD : 0.01 µg/ml LOQ : 0.04 µg/ml	Uttampanigraphy *et al*.[16]
8.	Stainless steel column RP Amide 150 mm × 4.6 mm; 2.7 µm	Ammonium acetate buffer : Acetonitrile	0.7 ml/min Injection volume : 10 µL UV Detector : 290 nm	LOD : 0.005 LOQ : 0.015	GoutamSen et.al.[17]
9.	ODS 250mm × 4.6 mm ; 5µ particle size	Isocratic mobile phase Acetonitrile and Methanol	Rt: For Metformin- 2.7832 min Canagliflozin- 3.781 PDA Detector : 212 nm	LOD : 0.034 LOQ : 0.102	NareddyPreethi Reddy *et al*.[18]
10.	C18 250 mm × 4.6 mm; 5µ particle size	Acetonitrile and Orthophosphoric acid	1 ml/ min PDA Detector at 290 nm	Injection volume: 20 LOD : 0.41 ml LOQ : 1.24 µg/ ml	Ishpreetkaur *et al*.[19]
11.	C18 100mm × 4.6 mm	Ammonium	1-10 mg/ml	LOD : 0.0026 ng/ml	AsmitaV.Gaik

	× 3.5 µm	formate in water : Methanol (25:75 v/v)	UV at 290 nm	LOQ : 0.008 ng/ml	wad, Preetikhulbe *et al.*[20]
12.	INERTSIL ODS – 3 (250 × 4.6 mm, 5 µ)	0.02% Formic acid and Acetonitrile (40:60) 0.02% Formic acid and Acetonitrile (40:60)	1.2 ml/min UV at 230 nm	Run time : 4.4 min Injection volume:10-50 g/ml LOD : 0.00736µg/ml LOQ : 0.00414µg/	Dr.Vijaya Lakshmi Marella *et al.* [21]
13	C18 250 mm ×4.6 mm, 5 µm particle size	Acetonitrile 0.1% and Sodium acetate buffer pH 4.6, ratio of 20:80 in Isocratic mode	1 ml/min UV at 291 nm	Injection volume :2-14 µg/ml	GudipallyMounika *et al.* [22]
14.	K romasil C18 column [250 mm× 4.6 mm ×5 µm particle size]	0.1% OPA (pH : 2.8) and Acetonitrile (45:55 v/v)	1 ml/min UV Detector at 254nm	Metformin LOD : 0.17 ug/ml LOQ : 2.20 ug/ml Canagliflozin LOD : 0.01 ug/ml LOQ : 0.50 ug/ml	K.P.R Chowdhury *et al.* [23]

*LOD – Limit of Detection, LOQ – Limit of Quantitation.

2. LC-MS method for Canagliflozin

S.NO	STATIONARY PHASE	MOBILE PHASE	FLOW RATE AND METHOD OF DETECTION	RESULTS	REFERENCE
1.	C18 Analytical column (50mmx4.6mm)	0.1% Formic acid and Acetonitrile (60:40 v/v)	Run time : 5 minutes	LLOQ : Metformin : 47.24 ng/ml Canagliflozin : 11.31 ng/ml	Ola Zakaria *et al.* [24]
2.	INERTSIL ODS 5 µm C18 50 × 4.60 mm	30:70 v/v of 0.01 M Ammonium acetate and Methanol as an Isocratic mobile phase	0.8 ml/min	LOD : 1.38 LOQ : 4.17	DharsanBhatt *et al.* [25]
3.	Hypersil BDS, C18 column (100×4.6mm; 5µm)	Isocratic mobile phase 5mm Ammonium acetate with 0.1% Formic acid and Methanol (15:85 v/v)	1.0 ml/min Injection volume : 15 µL Linearity : Canagliflozin : 10.00-6028.00 Metformin : 10.00 – 3027.00	LOQ : Canagliflozin : 10.27 ng/mL Metformin : 10.03 ng/mL	Lakshmana Rao Atmakuri *et al.* [26]
4.	COS-MICSIL 100 C18 [250×4.6 mm] 5µm column	Acetonitrile: water (70:30 v/v) Detection : 282 nm PH : 3.0±0.05	1 ml/min Run time : 6 minutes Injection volume : 20L UV Detection:282nm	LOD : 0.28 g/ml LOQ : 0.78 g/ml	Dr.SatheeshaBabu B.K *et al.* [27]

*LOD – Limit of Detection, LOQ – Limit of Quantitation, LLOQ – Lower Limit of Quantitation.

3. RP-LC METHOD FOR CANAGLIFLOZIN

S.NO	STATIONARY PHASE	MOBILE PHASE	FLOW RATE AND METHOD OF DETECTION	RESULTS	REFERENCE
1.	phenomenixgemini-NX C18 column [250×4.6mm, 5 m particle size]	Acetonitrile:1-octane sulphonic acid Detection : 245 nm Ratio : 70:30 v/v	1 ml/min Concentration range : 10-100 g/ml Run time : 10 minutes UV Detection:245nm	LOD : 0.0170 g/m LOQ: 0.1705 g/ml	M.Rameswara Rao *et al.* [28]

*LOD – Limit of Detection, LOQ – Limit of Quantitation

4. UPLC METHOD FOR CANAGLIFLOZIN

S. NO	SAMPLE	DESCRIPTION	DETECTION	REFERENCE
1.	Oral Solid dosage form	Column: BEH C18 Column 50x2.1mm,1.7 µm column Mobile phase: Methanol : Acetonitrile Flow rate – 0.3ml/min LLOQ-0.100ng/ml	PDA DETECTOR	VijayakumarRekulapally *et al.* [29]

*PDA – Photodiode-Array Detection, LLOQ – Lower Limit of Quantitation.

5. HPTLC METHOD FOR CANAGLIFLOZIN

S. NO	DERIVATIZATION AGENT	STATINORY PHASE MOBILE PHASE DETECTION METHOD	Retention factor (R_f) LOD	REFERENCE
1.	CAMAG TLC IV scanner	Precoated Silica gel 60 F254 HPTLC aluminium plates (20x10 cm,0.2mm thick) Mobile phase: Toluene: Ethyl acetate :Methanol (2:2:1) Saturation time: 30min.	LOD : 0.39 LOQ : 1.19	Ishpreet Kaur *et al.* [30]

*LOD – Limit of Detection, LOQ – Limit of Quantitation.

6. UV SPECTROSCOPY METHOD FOR CANAGLIFLOZIN

S.NO	SOLVENT	FLOW RATE AND METHOD OF DETECTION	RESULT	REFEERENCE
1.	Methanol: Distilled water(1:1)	UV at 224 nm Linearity:10.66µg	LOD:0.33µg/ml. LOQ:1.00µg/ml	K.Saravanakumari *et al.* [31]
2.	Methanol	UV Visible Spectrophotometer.	For metformin LOD:0.49µg/ml LOQ1.49µg/ml For canagliflozin LOD:0.43µg/ml LOQ:1.31µg/ml	D.Sharmila *et al.* [32]
3.	Methanol and Water	UV at 290 nm	L0D:0.084 mcg/ml LOQ:0.255 mcg/ml	Ishpreet Kaur *et al.* [33]
4.	Methanol and Water(40:60)	UV at 319 nm	For canagliflozin LOD:0.3325µg/ml LOQ:1.0076µg/ml For metformin LOD:0.10431µg/ml LOQ:0.3161µg/ml	B.A.Patel *et al.* [34]

*LOD – Limit of Detection, LOQ – Limit of Quantitation.

7. FT-IR METHOD FOR CANAGLIFLOZIN

S.NO	PARAMETER	RESULTS	REFERENCE
1.	Group: O-H Wavelength(cm^{-1}) : 3000-3500 Beer's law range (µg/mg) : 3-11	Correlation coefficient, r^2:0.999 LOD:0.159677µg LOQ:0.483871µg	Nareshbabuchilamakuru *et al*.[35]

*LOD – Limit of Detection, LOQ – Limit of Quantitation.

8. SPECTROFLURIMETRIC METHOD FOR CANAGLIFLOZIN

S. NO	SOLVENT	DETECTION	RESULTS	REFERENCE
1	Methanol	UV Detection Excitation -λ max 293 nm Emission – λ max 349 nm	R^2-0.9994 LOD – 13.58ng/mL LOQ – 41.15ng/mL	Tailor Pratik *et al*. [36]

*LOD – Limit of Detection, LOQ – Limit of Quantitation.

DISCUSSION AND REPORT:

In this above review article, we had investigated the analytical development methods of canagliflozin in different pharmaceutical dosage form. Canagliflozin is the drug used for the treatment of type II diabetes patients and is available in limited Pharmaceutical dosage form (i.e. tablet).

As stated in different article, we came to a conclusion that the chromatographic technique RP-HPLC along with the UV – Visible spectroscopy has produced efficient results in the analytical development method of canagliflozin in different pharmaceutical dosage forms. So, RP-HPLC is the most preferable method.

CONCLUSION

In this review article, we discussed about the analytical development methods for estimation of canagliflozin in pharmaceutical dosage form. The proposed technique accomplished for canagliflozin are RP-HPLC, RP-LC, HPTLC, LC-MS, UPLC, UV- SPECTROSCOPY, FT-IR, Spectrofluorimetry. This above data are helpful for further research studies in analysis of canagliflozin.

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