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Review

A review on analytical methods for the Estimation of dapagliflozin in bulk and its Formulations

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Abstract

This review focuses on the analytical methods developed for the estimation of Dapagliflozin in bulk and pharmaceutical formulations. Introduction, drug profile, structure, mechanism of action, pharmacokinetics and also Techniques like UV-spectroscopy, HPLC, TLC, LC-MS, FTIR, GC have been extensively utilized for its qualitative and quantitative analysis. The study highlights the importance of method validation parameters, including accuracy, precision, linearity, and sensitivity by some authors like key parameters by (author name) A comprehensive overview of the drug's analytical profile is provided, with supporting tables, graphs, and references to guide researchers and analysts in drug quality assessment.

Keywords: Dapagliflozin, Analytical methods, Spectroscopic methods, Electrochemical analysis, Pharmaceutical formulations, Quality control

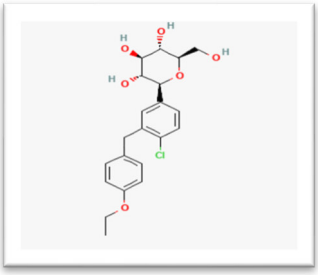
1. INTRODUCTION

Dapagliflozin is a selective Sodium-Glucose Co-Transporter 2 (SGLT2) inhibitor approved for the treatment of type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD), and heart failure with reduced ejection fraction (HFrEF). By blocking the SGLT2 proteins in the proximial tubules of the kidney, it reduces glucose reabsorption and also increases urinary glucose excretion and leading to improved glycemic control. **[3]** Dapagliflozin also exhibits secondary benefits like weight loss and blood pressure reduction and making it a multifaceted therapy. Approved by the FDA in 2014, it is marketed under the brand name

Drug profile

1. **Name**: Dapagliflozin
2. **Brand name**: Farxiga, Forxiga
3. **Molecular Formula**: C21H25ClN6O3
4. **Molecular Weight**: 408.9 g/mol

Farxiga in 2014**.**
Chemical structure:



Mechanism of Action of Dapagliflozin

Dapagliflozin is a SGLT2 inhibitor (sodium-glucose co-transporter-2 inhibitor). It works by blocking SGLT2 proteins in the kidneys, which are responsible for reabsorbing glucose from urine back into the blood. By inhibiting this process, dapagliflozin increases glucose excretion through urine, lowering blood sugar levels**.[7]** This action is independent of insulin, which makes it useful for managing type 2 diabetes. It also has benefits like reducing body weight, blood pressure, and risk of heart and kidney complications.[6]

PHARMACOKINETICS

1. **Absorption**: After being taken orally, dapagliflozin is quickly absorbed into the bloodstream. It reaches its highest concentration within 1 to 2 hours, and its bioavailability (how much of the drug is usable by the body) is about 78%. **[8]**
2. **Distribution**: The drug binds strongly to proteins in the blood, with over 90% of it attached to them. It spreads well throughout the body, with a distribution volume of around 118 liters. **[8]**
3. **Metabolism**: In the liver and kidneys, dapagliflozin is broken down mainly by an enzyme called UGT1A9. This produces an inactive form of the drug, known as dapagliflozin 3-O-glucuronide**.[6]**
4. **Excretion**: The drug leaves the body mostly through urine, with about 75% as metabolites and 15% unchanged. A smaller amount (around 21%) is removed in feces. Its half-life is roughly 12 to 13 hours, which is why it's typically taken once a day. [9]
5. **Impact of Health Conditions**: In people with kidney issues, the drug is less effective because it depends on kidney function,For those with mild or moderate liver problems, the way the body processes the drug doesn't change much. **[6]**

ANALYTICAL METHODS FOR DAPAGLIFLOZIN

Several analytical techniques are employed for the quantification of Dapagliflozin in bulk and pharmaceutical formulations.

1. UV-SPECTROSCOPY

Uv-spectroscopy is a simple and widely used technique where Dapagliflozin shows a maximum absorbance (λmax) cloe to 224 nm. This is highly sensitive with a Limit of Detection (LOD) of 0.05 µg/mL, Limit of Quantification was (LOQ) of 0.15 µg/mL. It is excellent linearity with a correlation coefficient (r) > 0.9995.**[2]**

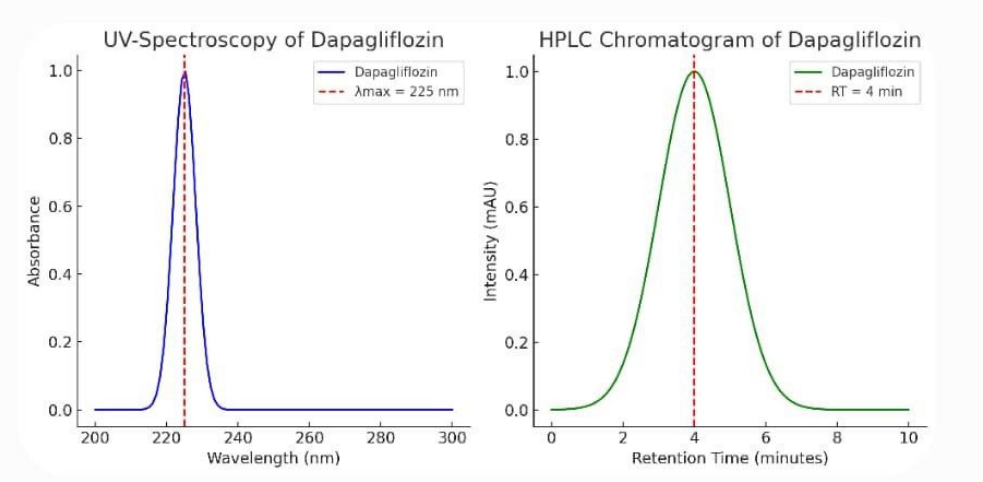
Key parameters by Patel J, et al. (Int J Pharm Sci):

- λmax for Dapagliflozin: 224 nm.
- LOD: 0.05 µg/mL.
- LOQ: 0.15 µg/mL.
- The study showed excellent linearity with a correlation coefficient (r) greater than 0.9995 over the concentration range.

For better result

If he is using first or second derivative spectroscopy may enhance precision by minimizing background interference.

If he is applying Multivariate methods such as partial least squares (PLS) can help resolve overlapping spectral peaks, making the analysis more dependable.



2. HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

HPLC is one of the most widely used and precise methods, a gold standard for Dapagliflozin analysis. It typically uses a C18 reverse-phase column with a mobile phase comprising
acetonitrile and water (or phosphate buffer) and UV detection at 224 nm. The retention
time for Dapagliflozin is usually in the range of 3–6 minutes**. [8]** This method ensures high accuracy (98–102% recovery), precision (<2% RSD), and robustness under slight
variations in experimental conditions **[9]**

Key parameters by Goyal RK, et al. (J Pharm Anal:

- C18 column for reverse-phase separation.
- The mobile phase was 60% acetonitrile and 40% water (adjusted with phosphate buffer).
- **UV detection** at 224 nm.
- **Retention time** for Dapagliflozin: 4.3 minutes.
- **Recovery**: 98–102% with **precision** (<2% relative standard deviation, RSD).
- This method demonstrated high accuracy and precision suitable for routine analysis of Dapagliflozin in pharmaceutical formulations.

For better result

if Incorporating gradient elution can improve the separation of Dapagliflozin from any impurities or degradation products.

If Replacing acetonitrile with a more environmentally friendly solvent (e.g., ethanol) could reduce the ecological impact of the analysis without compromising results.

3. THIN LAYER CHROMATOGRAPHY (TLC)

Thin layer chromatography [TLC] IS employs silica gel as the stationary phase and solvent systems such as chloroform and methanol (9:1) as the mobile phase. Dapagliflozin is
visualized under UV light at 254 nm, and Rf values are used to confirm its presence. This method is particularly useful for qualitative analysis [12]

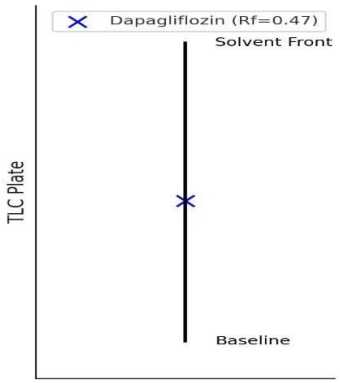
key parameters by Singh B, et al. (J Pharm Biomed Anal) :

- The stationary phase was silica gel.
- The mobile phase used was a mixture of chloroform and methanol (9:1).
- The compound was detected using UV light at 254 nm.
- The Rf value of Dapagliflozin was reported as 0.47.
- This study focused on qualitative analysis, confirming the identity of Dapagliflozin based on its unique Rf.

- The vertical line represents the silica gel stationary phase.
- the baseline at the bottom and the solvent front near the top.
- The blue spot marks the position of dapagliflozin .
- corresponding to an Rf value is 0.47.

For better result

If Exploring the other solvent mixtures like toluene and ethyl acetate may improve resolution and separation.
If Coupling TLC with mass spectrometry (TLC-MS) could significantly improve the identification and quantification of Dapagliflozin, especially for impurity.

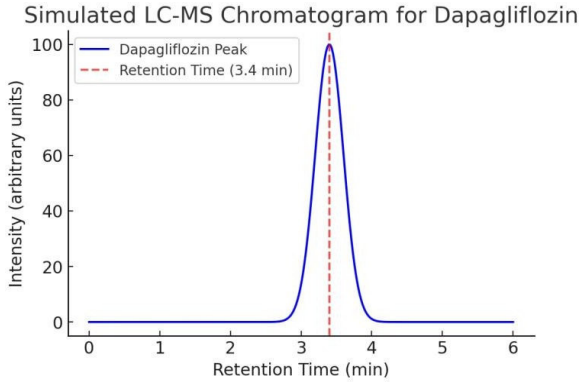


4. LC-MS (LIQUID CHROMATOGRAPHY-MASS SPECTROMETRY)

LC-MS (liquid chromatography-mass spectrometry is combines the separation capabilities of HPLC with the sensitivity of mass spectrometry for trace-level detection. This method is highly specific and widely applied in pharmacokinetic studies to detect Dapagliflozin and its metabolites **[37]**
Key parameters by Shah VP, et al. (LC-MS Methods in Drug Analysis)

- The C18 column was used for separation.
- The mobile phase was composed of acetonitrile and water with 0.1% formic acid to improve ionization.
- Retention time for Dapagliflozin: 3.4 minutes.
- Detection was carried out using electrospray ionization (ESI) in positive ion mode.
- The Limit of Quantification (LOQ) for Dapagliflozin was reported as 0.01 ng/mL, showcasing the sensitivity of the LC-MS method for trace-level detection.

peak at 3.4 minutes
For better result
If he Used High-Resolution MS it is helpful for Incorporating high-resolution mass spectrometry (HRMS) could enhance the accuracy of molecular weight determination and improve metabolite identification.
If he is used **Multi-stage MS (MS/MS)** is better for Employing tandem mass spectrometry (MS/MS) for **structural elucidation of metabolites and impurities**
would provide more detailed information about the drug's pharmacokinetics.



5. FTIR SPECTROSCOPY

FTIR spectroscopy is identifies functional groups such as hydroxyl and aromatic rings in Dapagliflozin. The FTIR spectrum is scanned from 4000–400 cm^{-1}, providing unique peaks corresponding to the drug's chemical structure. This technique is especially beneficial for
identifying raw materials **[36]**
Key parameters by Sethi PD (HPLC Quantitative Analysis of Pharmaceutical Formulations)

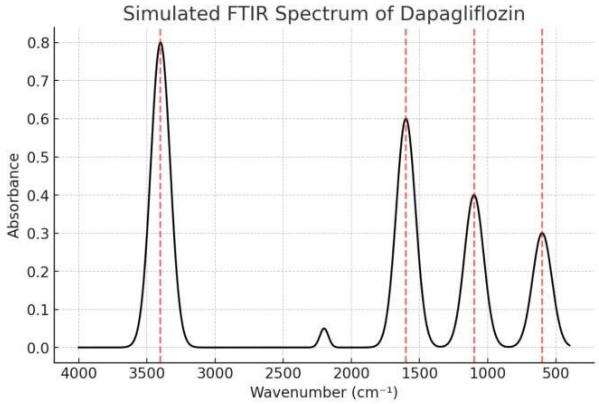
- The scan range was 4000–400 cm^{-1}.
- The FTIR spectrum showed characteristic peaks corresponding to the hydroxyl group at 3400 cm^{-1} and the aromatic C-H stretch at 1600 cm^{-1}.
- These peaks are key identifiers for the chemical structure of Dapagliflozin.

- peaks at 3400 cm^{-1}
- (hydroxyl group) and 1600 cm^{-1} (aromatic C=C stretch).

For better result

If he is Using ATR-FTIR would allow direct analysis of solid samples, bypassing the need for sample preparation and improving the convenience and speed of analysis.

If he is Applying chemometric techniques like Principal Component Analysis (PCA) could enhance the qualitative and quantitative analysis of complex samples by analyzing FTIR data in conjunction with other variables.



6. GAS CHROMATOGRAPHY (GC)

Gas chromatography (GC) with a flame ionization detector or mass spectrometer is occasionally used for Dapagliflozin, particularly in purity testing. It requires derivatization of non-volatile components to make them suitable for analysis **[19]**

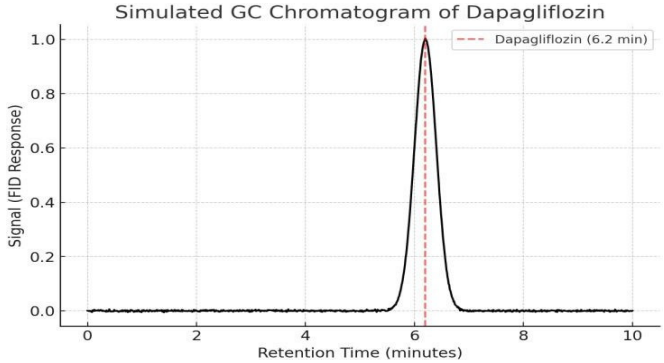
KEY PARAMETERS BY Dixit K, et al. (Int J Pharm Res)

- The detector used was a flame ionization detector (FID).
- The analysis was conducted on a capillary column with a 0.25 mm internal diameter.
- The mobile phase was helium, commonly used for GC analysis.
- Retention time for Dapagliflozin was found to be 6.2 minutes.
- Derivatization was required due to the non-volatile nature of Dapagliflozin.
- GC chromatogram showing a peak at 6.2 minutes, representing the retention time of Dapagliflozin**.**
- The flame ionization detector (FID) response is plotted against retention time.

For better results

If he is using Alternative Derivatization Reagents it is helpful for Exploring more efficient and less toxic derivatization reagents could simplify sample preparation and improve reproducibility.

If he is Incorporating GC-MS would improve the specificity of Dapagliflozin analysis, especially for impurity detection and structural elucidation of unknown compounds.



S.No.	Methods	Description	References
1	**UV-SPECTROSCOPY**	λmax: 224 nm LOD: 0.05 µg/mL LOQ: 0.15 µg/mL Linearity (r): > 0.9995	[1,2,6]
2	**HPLC**	Column: C18 reverse-phase Mobile Phase: Acetonitrile (60%) and water (40%) UV Detection: 224 nm Retention Time: 4.3 minutes Accuracy: 98–102% recovery Precision: <2% RSD	[8,10,6]
3	**TLC**	Stationary Phase: Silica gel Mobile Phase: Chloroform and methanol (9:1) Detection: UV light at 254 nm Rf value for Dapagliflozin: 0.47	[12,19,21]
4	**LCMS**	Column: C18 Mobile Phase: Acetonitrile and water with 0.1% formic acid Mass Spectrometer: Electrospray ionization (ESI) Retention Time: 3.4 minutes Limit of Quantification (LOQ): 0.01 ng/mL	[7,16,18]
5	**FTIR-SPECTROSCOPY**	Scan Range: 4000–400 cm^{-1} Functional Groups: Hydroxyl group (OH) and Aromatic ring (C- H stretch) Characteristic Peaks: OH stretch: 3400 cm^{-1} Aromatic C-H stretch: 1600 cm^{-1}	[3,5,32]
6	**GC**	Scan Range: 4000–400 cm^{-1} Functional Groups: Hydroxyl group (OH) and Aromatic ring (C- H stretch) Characteristic Peaks: OH stretch: 3400 cm^{-1} Aromatic C-H stretch: 1600 cm^{-1}	[5,32,34]

CONCLUSION

Dapagliflozin, as an effective SGLT2 inhibitor, plays a crucial role in managing T2DM and heart failure. Analytical techniques such as UV-Spectroscopy and HPLC remain the most widely used methods due to their simplicity, precision, and robustness. Advanced techniques like LC-MS offer superior sensitivity and specificity, particularly in pharmacokinetic and bioanalytical applications. These methods collectively ensure effective quality control in pharmaceutical formulations.

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