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# METHOD DEVELOPMENT AND VALIDATION OF RP-HPLC METHOD FOR DETERMINATION OF EMPAGLIFLOZIN AND LINAGLIPTIN IN BULK AND PHARMACEUTICAL FORMULATION

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**ABSTRACT**

A rapid and accurate reverse phase high performance liquid chromatography method has been developed for the validation of empagliflozin and linagliptin in pure form and in the form of tablets. Chromatography was performed on an Altima C18 column (4.6 x 150 mm, 5 µm) using water: ACN (15: 85% v / v) as the mobile phase at a flow rate of 1.0 ml / min. at 234nm. The retention time of empagliflozin and linagliptin was 2,088, 6,068 ± 0.02 min, respectively. The method produces linear responses in the concentration range of 5-25 µg / ml empagliflozin and 30-150 µg / ml linagliptin. The precision of the method for the determination of the test was lower than 2.0% RSD. The method is useful for the quality control of bulk and pharmaceutical formulations.

**KEYWORDS**

Empagliflozin, Linagliptin, RP-HPLC and Validation.

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## INTRODUCTON

The analysis can be defined as the science and art of determining the composition of materials according to the elements or compounds they contain. In fact, analytical chemistry is the science of chemical identification and the determination of the composition (atomic, molecular) of substances, materials and their chemical structure.

Quality control is a concept that aims to produce a perfect product through a series of measures designed to prevent and eliminate errors in different stages of production. The decision to release or reject a product is based on one or more types of control actions. With the growth of the pharmaceutical industry in recent years, rapid

progress has been made in the field of pharmaceutical analysis involving complex instrumentation. Providing a simple analytical procedure for complex formulation is a matter of the utmost importance. Therefore, it is necessary to develop new methods of analysis for these drugs. In summary, the reasons for developing new drug testing methods are the following:

1. The medication or combination of medications cannot be official in any pharmacopoeia.
2. An appropriate analytical procedure for the medication may not be available in the literature due to patent regulations.
3. Methods for testing a drug in combination with other medications may not be available.
4. Analytical methods to quantify the medication in body fluids may not be available.
5. Existing analytical procedures may require expensive reagents and solvents. It can also involve long extraction and separation procedures, which may not be reliable[1,2].

**DRUG PROFILE**

**Drug** : Empagliflozin
**Drug category** : Hypoglycemic Agent
**Structure** :
**Chemical name/ Nomenclature / IUPAC Name** (2S, 3R, 4R, 5S, 6R)-2-[4-chloro-3-({4-[(3S)-oxolan-3-yloxy]phenyl}methyl) phenyl]-6-(hydroxymethyl) oxane-3, 4, 5-triol.

**DRUG PROFILE**

**Drug** : Linagliptin
**Synonym** : (R)-8-(3-Aminopiperidin-1-yl)-7-but-2-ynyl-3-methyl-1-(4-methylquinazolin-2-ylmethyl)-3, 7-dihydro-purine-2, 6-dione Trajenta.
**Drug category** : Antidiabetic Agent
**Structure** :
**Chemical name/ Nomenclature / IUPAC Name** 8-[(3R)-3-aminopiperidin-1-yl]-7-(but-2-yn-1-yl)-3-methyl-1-[(4-methylquinazolin-2-yl)methyl]-2, 3, 6, 7-tetrahydro-1H-purine-2, 6-dione.

## EXPERIMENTAL WORK

**Instruments used**

**Chemicals used**

**Preparation of Standard Solution**

Accurately weigh and transfer 10 mg of Empagliflozin and 10mg of Linagliptin working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution) Further pipette 0.15ml of Empagliflozin and 0.9ml of the Linagliptin from the above stock solutions into a 10ml volumetric flask and dilute up to the mark with diluents.

**Preparation of Sample Solution**

Take average weight of Tablet and crush in a mortar by using pestle and weight 10 mg equivalent weight of Empagliflozin and Linagliptin sample into a 10mL clean dry volumetric flask and add about 7mL of Diluent and sonicate to dissolve it completely and make volume up to the mark with the same solvent.

Further pipette 0.15ml of Empagliflozin and 0.9ml of the Linagliptin from the above stock solutions into a 10ml volumetric flask and dilute up to the mark with diluents.

## PREPARATION OF DRUG SOLUTIONS FOR LINEARITY

Accurately weigh and transfer 10 mg of Empagliflozin and 10mg of Linagliptin working standard into a 10ml of clean dry volumetric flasks add about 7mL of Diluents and sonicate to dissolve it completely and make volume up to the mark with the same solvent. (Stock solution)

**Preparation of Level - I (5µg/ml of Empagliflozin and 30 µg/ml of Linagliptin)**

Pipette out 0.05ml of Empagliflozin and 0.3ml of Linagliptin stock solutions was take in a 10ml of volumetric flask dilute up to the mark with diluent.

**Preparation of Level - II (10 µg/ml of Empagliflozin and 60 µg/ml of Linagliptin)**

Pipette out 0.1ml of Empagliflozin and 0.6ml of Linagliptin stock solutions was take in a 10ml of volumetric flask dilute up to the mark with diluent.

**Preparation of Level - III (15 µg/ml of Empagliflozin and 90 µg/ml of Linagliptin)**

Pipette out 0.15ml of Empagliflozin and 0.9ml of Linagliptin stock solutions was take in a 10ml of volumetric flask dilute up to the mark with diluent.

**Preparation of Level - IV (20 µg/ml of Empagliflozin and120 µg/ml of Linagliptin)**

Pipette out 0.2ml of Empagliflozin and 1.2ml of Linagliptin stock solutions was take in a 10ml of volumetric flask dilute up to the mark with diluent.

**Preparation of Level - V (25 µg/ml of Empagliflozin and 150 µg/ml of Linagliptin)**

Pipette out 0.25ml of Empagliflozin and 1.5ml of Linagliptin stock solutions was take in a 10ml of volumetric flask dilute up to the mark with diluent.

**Procedure**

Inject each level into the chromatographic system and measure the peak area.

Plot a graph of peak area versus concentration (on X-axis concentration and on Y-axis Peak area) and calculate the correlation coefficient.

## RESULTS AND DISCUSSION

**Optimized Chromatogram (Standard)**

Mobile phase : Water: ACN (15:85% v/v)
Column : Altima C18 (4.6×150mm, 5.0 µm)
Flow rate : 1 ml/min
Wavelength : 234 nm
Column temp : 35ºC
Injection Volume : 10 µl
Run time : 14 minutes

**Observation**

From the above chromatogram it was observed that the Empagliflozin and Linagliptin peaks are well separated and they shows proper retention time, resolution, peak tail and plate count. So it's optimized trial.

**Optimized Chromatogram (Sample)**

**Acceptance criteria**

- Resolution between two drugs must be not less than 2
- Theoretical plates must be not less than 2000
- Tailing factor must be not less than 0.9 and not more than 2.
- It was found from above data that all the system suitability parameters for developed method were within the limit.

## VALIDATION

**Blank**

**System suitability**

**Acceptance criteria**

- %RSD of five different sample solutions should not more than 2
- The %RSD obtained is within the limit, hence the method is suitable.

**Acceptance criteria**

- %RSD for sample should be NMT 2
- The %RSD for the standard solution is below 1, which is within the limits hence method is precise.

## SPECIFICITY

The ICH documents define specificity as the ability to assess unequivocally the analyte in the presence of components that may be expected to be present, such as impurities, degradation products, and matrix components.

$$\%ASSAY = \frac{\text{Sample area}}{\text{Standard area}} \times \frac{\text{Weight of standard}}{\text{Dilution of standard}} \times \frac{\text{Dilution of sample}}{\text{Weight of sample}} \times \frac{\text{Purity}}{100} \times \frac{\text{Weight of tablet}}{\text{Label claim}} \times 100$$

The % purity of Empagliflozin and Linagliptin in pharmaceutical dosage form was found to be 99.6%.

## LINEARITY

**CHROMATOGRAPHIC DATA FOR LINEARITY STUDY**

**Empagliflozin**

**Linearity plot**

The plot of Concentration (x) versus the Average Peak Area (y) data of Empagliflozin is a straight line.

Y = mx + c
Slope (m) = 19725
Intercept (c) = 35332
Correlation Coefficient (r) = 0.999

**Validation Criteria**

The response linearity is verified if the Correlation Coefficient is 0.99 or greater.

**Conclusion**

Correlation Coefficient (r) is 0.99, and the intercept is 35332. These values meet the validation criteria.

**Linagliptin**

**Linearity Plot**

The plot of Concentration (x) versus the Average Peak Area (y) data of Linagliptin is a straight line.

Y = mx + c

Slope (m) = 22791

Intercept (c) = 56388

Correlation Coefficient (r) = 0.999

**Validation Criteria**

The response linearity is verified if the Correlation Coefficient is 0.99 or greater.

**Conclusion**

Correlation Coefficient (r) is 0.99, and the intercept is 56388. These values meet the validation criteria.

**Precision**

The precision of an analytical procedure expresses the closeness of agreement (degree of scatter) between a series of measurements obtained from multiple sampling of the same homogeneous sample under the prescribed conditions.

**Repeatability**

**Acceptance criteria**

- %RSD for sample should be NMT 2
- The %RSD for the standard solution is below 1, which is within the limits hence method is precise.

**Acceptance criteria**

- %RSD for sample should be NMT 2
- The %RSD for the standard solution is below 1, which is within the limits hence method is precise.

**Intermediate precision**

**Day 1**

**Acceptance criteria**

- %RSD of Six different sample solutions should not more than 2

**Acceptance criteria**

- %RSD of Six different sample solutions should not more than 2
- The %RSD obtained is within the limit, hence the method is rugged.

**Day 2**

**Acceptance criteria**

- %RSD of Six different sample solutions should not more than 2

**Acceptance criteria**

- %RSD of Six different sample solutions should not more than 2
- The %RSD obtained is within the limit, hence the method is rugged.

**Accuracy**

Accuracy at different concentrations (50%, 100%, and 150%) were prepared and the % recovery was calculated.

**Accuracy50%**

**Acceptance Criteria**

- The percentage recovery was found to be within the limit (98-102%).
  The results obtained for recovery at 50%, 100%, 150% are within the limits. Hence method is accurate.

**LIMIT OF DETECTION**

The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value.

**LOD= 3.3 × σ / s**

Where

σ = Standard deviation of the response

S = Slope of the calibration curve

**Empagliflozin response standard deviation**

**σ =** 5877.74

**S=** 19726

**Linagliptin response standard deviation**

**σ =** 17637.4

**S=** 22792

**RESULTS**

**Empagliflozin**

=3.3 × 5877.74/19726

=0.9µg/ml

**Linagliptin**

=3.3 × 17637.4/22792

=2.5µg/ml

**LIMIT OF QUANTITATION**

The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined.

**LOQ=10×σ/S**

Where

σ = Standard deviation of the response

S = Slope of the calibration curve

**RESULTS**

**Empagliflozin**

=10×5877.74/19726

= 2.9µg/ml

**Linagliptin**

=10 × 17637.4/22792

= 7.7µg/ml

**Robustness**

**Acceptance criteria**

The tailing factor should be less than 2.0 and the number of theoretical plates (N) should be more than 2000.

**Table No.1: Instruments used**

| S.No | Instruments And Glasswares | Model |
|---|---|---|
| 1 | HPLC | WATERS Alliance 2695 separation module, software: Empower 2, 996 PDA Detector. |
| 2 | pH meter | LabIndia |
| 3 | Weighing machine | Sartorius |
| 4 | Volumetric flasks | Borosil |
| 5 | Pipettes and Burettes | Borosil |
| 6 | Beakers | Borosil |
| 7 | Digital ultra sonicator | Labman |

**Table No.2: Chemicals used**

| S.No | Chemical | Brand names |
|---|---|---|
| 1 | Empagliflozin(Pure) | Sura labs |
| 2 | Linagliptin(Pure) | Sura labs |
| 3 | Water and Methanol for HPLC | LICHROSOLV (MERCK) |
| 4 | Acetonitrile for HPLC | Merck |

**Table No.3: Peak results for trail 4**

| S. No | Peak name | $R_t$ | Area | Height | USP Resolution | USP Tailing | USP plate count |
|---|---|---|---|---|---|---|---|
| 1 | Empagliflozin | 2.088 | 3425413 | 567933 | | 1.0 | 5565.5 |
| 2 | Linagliptin | 6.068 | 1629854 | 517733 | 5.6 | 1.1 | 5355.2 |

**Table No.4: Optimized Chromatogram (Sample)**

| S.No | Name | Retention time(min) | Area (µV sec) | Height (µV) | USP resolution | USP tailing | USP plate count |
|---|---|---|---|---|---|---|---|
| 1 | Empagliflozin | 2.090 | 3468547 | 567933 | | 1.0 | 5565.5 |
| 2 | Linagliptin | 6.070 | 16289441 | 517733 | 5.5 | 1.1 | 5355.2 |

**Table No.5: Results of system suitability for Empagliflozin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing |
|---|---|---|---|---|---|---|
| 1 | Empagliflozin | 2.080 | 3569412 | 567917 | 5568.0 | 1.0 |
| 2 | Empagliflozin | 2.080 | 3465125 | 517719 | 6359.2 | 1.1 |
| 3 | Empagliflozin | 2.080 | 3598154 | 567933 | 5565.5 | 1.0 |
| 4 | Empagliflozin | 2.081 | 3586491 | 517733 | 5355.2 | 1.1 |
| 5 | Empagliflozin | 2.081 | 3582694 | 567917 | 6348.0 | 1.0 |
| Mean | | | 3560375 | | | |
| Std. Dev | | | 54225.61 | | | |
| % RSD | | | 1.523031 | | | |

**Table No.6: Results of method precession for Linagliptin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing | USP Resolution |
|---|---|---|---|---|---|---|---|
| 1 | Linagliptin | 2.080 | 3582264 | 567917 | 5568.0 | 1.0 | 2.5 |
| 2 | Linagliptin | 2.080 | 3586491 | 517719 | 5359.2 | 1.1 | 2.5 |
| 3 | Linagliptin | 2.080 | 3598154 | 567933 | 5565.5 | 1.0 | 2.5 |
| 4 | Linagliptin | 2.081 | 3564125 | 517733 | 5355.2 | 1.1 | 2.5 |
| 5 | Linagliptin | 2.081 | 3569412 | 562173 | 5568.0 | 1.0 | 2.5 |
| Mean | | | 3580089 | | | | |
| Std. Dev | | | 13609.81 | | | | |
| % RSD | | | 0.380153 | | | | |

| S.No | Concentration Level (%) | Concentration µg/ml | Average Peak Area |
|---|---|---|---|
| 1 | 33.3 | 5 | 1010252 |
| 2 | 66.6 | 10 | 2049374 |
| 3 | 100 | 15 | 3072706 |
| 4 | 133.3 | 20 | 3921068 |
| 5 | 166.6 | 25 | 4952813 |

| S.No | Concentration Level (%) | Concentration µg/ml | Average Peak Area |
|---|---|---|---|
| 1 | 33 | 30 | 8040807 |
| 2 | 66 | 60 | 14318417 |
| 3 | 100 | 90 | 21087985 |
| 4 | 133 | 120 | 27913928 |
| 5 | 166 | 150 | 34584741 |

**Table No.7: Results of repeatability for Empagliflozin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing |
|---|---|---|---|---|---|---|
| 1 | Empagliflozin | 2.084 | 3569412 | 567917 | 5568.0 | 1.0 |
| 2 | Empagliflozin | 2.083 | 3465125 | 517719 | 5359.2 | 1.1 |
| 3 | Empagliflozin | 2.082 | 3598154 | 567933 | 5565.5 | 1.0 |
| 4 | Empagliflozin | 2.081 | 3586491 | 517733 | 5355.2 | 1.1 |
| 5 | Empagliflozin | 2.080 | 3582694 | 567917 | 5568.0 | 1.0 |
| Mean | | | 3560375 | | | |
| Std. Dev | | | 54225.61 | | | |
| % RSD | | | 1.523031 | | | |

**Table No.8: Results of method precision for Linagliptin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing | USP Resolution |
|---|---|---|---|---|---|---|---|
| 1 | Linagliptin | 6.056 | 1582264 | 567917 | 5568.0 | 1.0 | 5.5 |
| 2 | Linagliptin | 6.057 | 1586491 | 517719 | 5359.2 | 1.1 | 5.5 |
| 3 | Linagliptin | 6.058 | 1598154 | 567933 | 5565.5 | 1.0 | 5.5 |
| 4 | Linagliptin | 6.059 | 1564125 | 517733 | 5355.2 | 1.1 | 5.5 |
| 5 | Linagliptin | 6.060 | 1569412 | 562173 | 5568.0 | 1.0 | 5.5 |
| Mean | | | 1580089 | | | | |
| Std. Dev | | | 13609.81 | | | | |
| % RSD | | | 0.861332 | | | | |

**Table No.9: Results of Intermediate precision for Empagliflozin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing |
|---|---|---|---|---|---|---|
| 1 | Empagliflozin | 2.081 | 3481579 | 567917 | 5568.0 | 1.0 |
| 2 | Empagliflozin | 2.082 | 3458121 | 517719 | 5359.2 | 1.1 |
| 3 | Empagliflozin | 2.083 | 3426581 | 567933 | 5565.5 | 1.0 |
| 4 | Empagliflozin | 2.084 | 3465712 | 517733 | 5355.2 | 1.1 |
| 5 | Empagliflozin | 2.085 | 3451476 | 567917 | 5568.0 | 1.0 |
| 6 | Empagliflozin | 2.085 | 3452106 | 567514 | 5359.2 | 1.1 |
| Mean | | | 3455929 | | | |
| Std. Dev | | | 18188.92 | | | |
| % RSD | | | 0.5 | | | |

**Table No.10: Results of Intermediate precision for Linagliptin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing | USP Resolution |
|---|---|---|---|---|---|---|---|
| 1 | Linagliptin | 6.061 | 15481579 | 567917 | 5568.0 | 1.0 | 2.5 |
| 2 | Linagliptin | 6.062 | 15369852 | 517719 | 5359.2 | 1.1 | 2.5 |
| 3 | Linagliptin | 6.063 | 15248454 | 567933 | 5565.5 | 1.0 | 2.5 |
| 4 | Linagliptin | 6.064 | 15874692 | 517733 | 5355.2 | 1.1 | 2.5 |
| 5 | Linagliptin | 6.064 | 15236547 | 567933 | 5568.0 | 1.0 | 2.5 |
| 6 | Linagliptin | 6.064 | 15217547 | 567133 | 5359.2 | 1.1 | 2.5 |
| Mean | | | 15404779 | | | | |
| Std. Dev | | | 251289.4 | | | | |
| % RSD | | | 1.6 | | | | |

**Table No.11: Results of Intermediate precision Day 2 for Empagliflozin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing |
|---|---|---|---|---|---|---|
| 1 | Empagliflozin | 2.081 | 3481579 | 567917 | 5568.0 | 1.0 |
| 2 | Empagliflozin | 2.082 | 3458121 | 517719 | 5359.2 | 1.1 |
| 3 | Empagliflozin | 2.083 | 3426581 | 567933 | 5565.5 | 1.0 |
| 4 | Empagliflozin | 2.084 | 3465712 | 517733 | 5355.2 | 1.1 |
| 5 | Empagliflozin | 2.085 | 3451476 | 567917 | 5568.0 | 1.0 |
| 6 | Empagliflozin | 2.085 | 3452106 | 567514 | 5359.2 | 1.1 |
| Mean | | | 3455929 | | | |
| Std. Dev | | | 18188.92 | | | |
| % RSD | | | 0.5 | | | |

**Table No.12: Results of Intermediate precision for Linagliptin**

| S.No | Name | Rt | Area | Height | USP plate count | USP Tailing | USP Resolution |
|---|---|---|---|---|---|---|---|
| 1 | Linagliptin | 6.061 | 15481579 | 567917 | 5568.0 | 1.0 | 2.5 |
| 2 | Linagliptin | 6.062 | 15369852 | 517719 | 5359.2 | 1.1 | 2.5 |
| 3 | Linagliptin | 6.063 | 15248454 | 567933 | 5565.5 | 1.0 | 2.5 |
| 4 | Linagliptin | 6.064 | 15874692 | 517733 | 5355.2 | 1.1 | 2.5 |
| 5 | Linagliptin | 6.064 | 15236547 | 567933 | 5568.0 | 1.0 | 2.5 |
| 6 | Linagliptin | 6.064 | 15217547 | 567133 | 5359.2 | 1.1 | 2.5 |
| Mean | | | 15404779 | | | | |
| Std. Dev | | | 251289.4 | | | | |
| % RSD | | | 1.6 | | | | |

**The accuracy results for Empagliflozin**

| %Concentration (at specification Level) | Area | Amount Added (ppm) | Amount Found (ppm) | % Recovery | Mean Recovery |
|---|---|---|---|---|---|
| 50% | 1543793 | 7.5 | 7.51 | 101.9 | 100.9% |
| 100% | 3035883 | 15 | 15.1 | 101.4 | |
| 150% | 4451005 | 22.5 | 22.47 | 99.4 | |

**The accuracy results for Linagliptin**

| %Concentration (at specification Level) | Area | Amount Added (ppm) | Amount Found (ppm) | % Recovery | Mean Recovery |
|---|---|---|---|---|---|
| 50% | 1084420 | 45 | 45.01 | 100.2 | 99.6% |
| 100% | 2096069 | 90 | 89.9 | 99.4 | |
| 150% | 3112684 | 135 | 134.9 | 99.5 | |

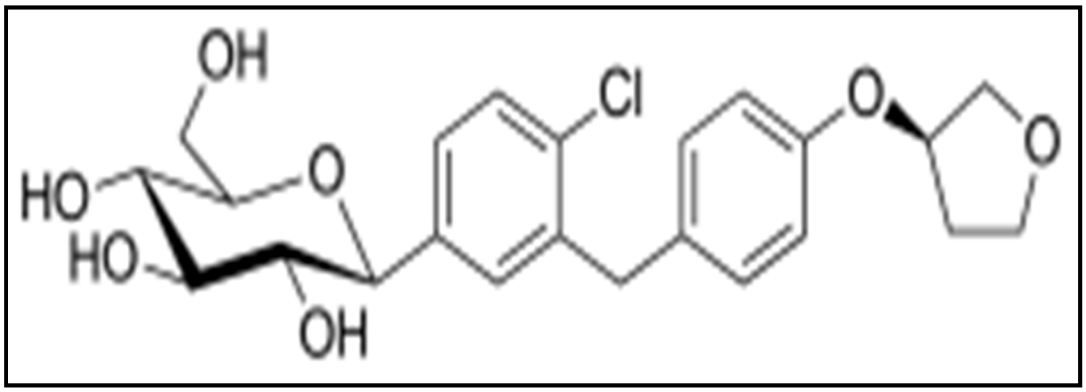
**Table No.13: Results for Robustness**

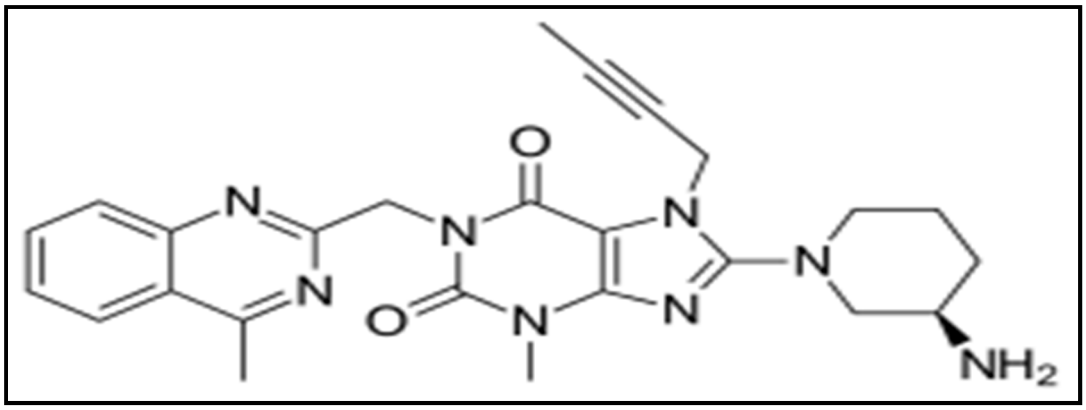
**Empagliflozin**

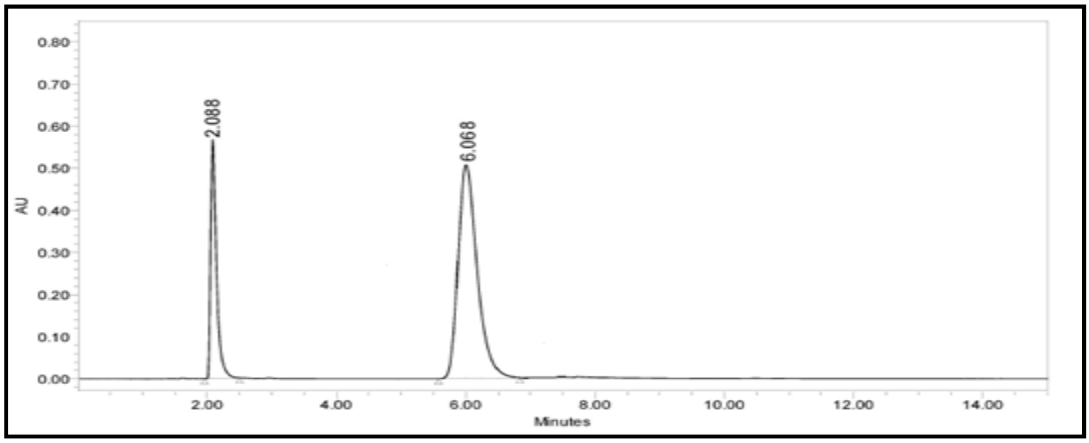
| S.No | Parameter used for sample analysis | Peak Area | Retention Time | Theoretical plates | Tailing factor |
|---|---|---|---|---|---|
| 1 | Flow rate of 1.0 mL/min | 3425413 | 2.088 | 5568.2 | 1.0 |
| 2 | Flow rate of 0.9 mL/min | 3425282 | 3.111 | 5922.2 | 1.2 |
| 3 | Flow rate of 1.1 mL/min | 3517879 | 1.880 | 5868.8 | 1.2 |
| 4 | Less aqueous phase | 3175485 | 3.101 | 5836.2 | 1.2 |
| 5 | More aqueous phase | 3365431 | 1.881 | 5282.6 | 1.1 |

**Linagliptin**

| S.No | Parameter used for sample analysis | Peak Area | Retention Time | Theoretical plates | Tailing factor |
|---|---|---|---|---|---|
| 1 | Flow rate of 1.0 mL/min | 2029854 | 6.068 | 5359.2 | 1.1 |
| 2 | Flow rate of 0.9 mL/min | 1738319 | 7.101 | 5999.1 | 1.2 |
| 3 | Flow rate of 1.1 mL/min | 1638304 | 5.007 | 5989.2 | 1.1 |
| 4 | Less aqueous phase | 1973724 | 7.108 | 5387.2 | 1.1 |
| 5 | More aqueous phase | 2102838 | 5.008 | 5938.1 | 1.1 |




**Optimized Chromatogram**

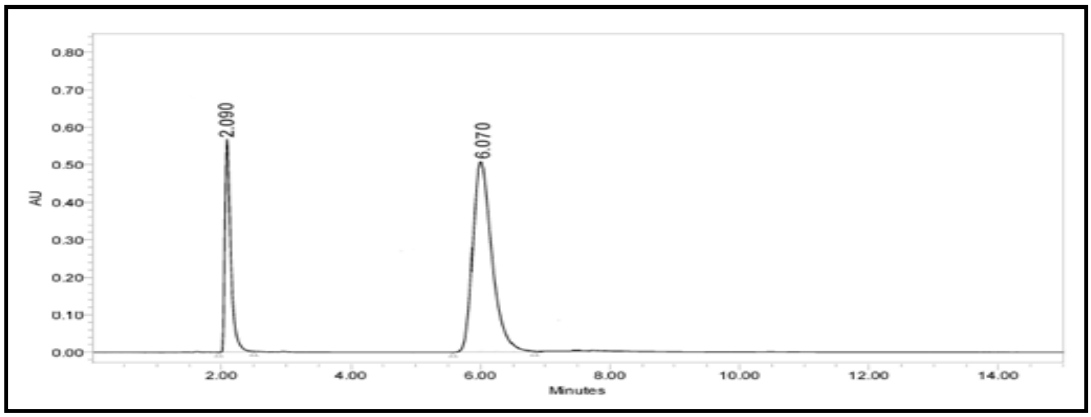



**Figure No.1: Optimized Chromatogram (Sample)**

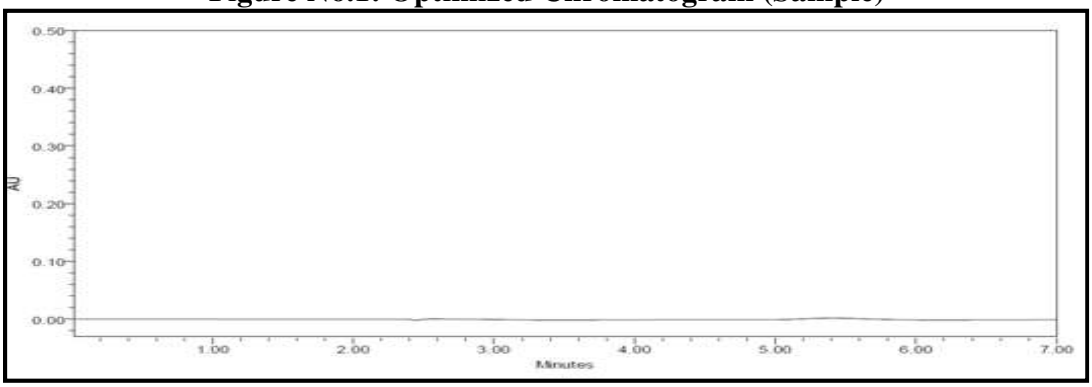



**Figure No.2: Chromatogram showing blank (mobile phase preparation)**

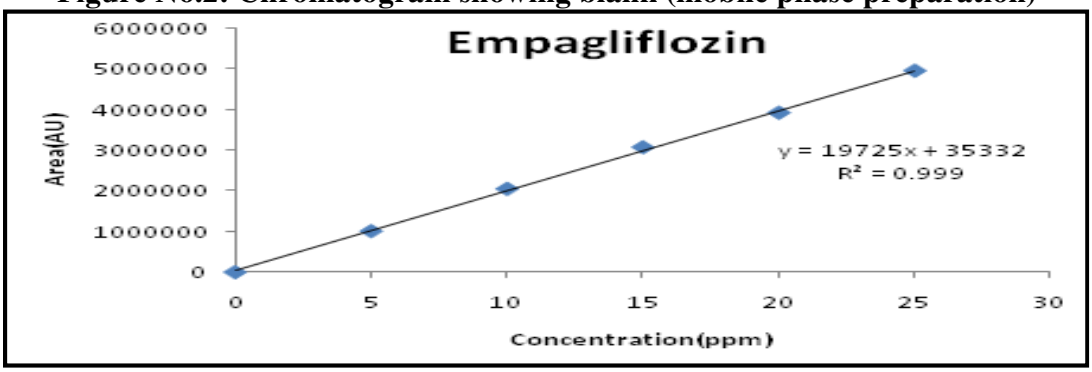



**Figure No.3: Calibration graph for Empagliflozin**

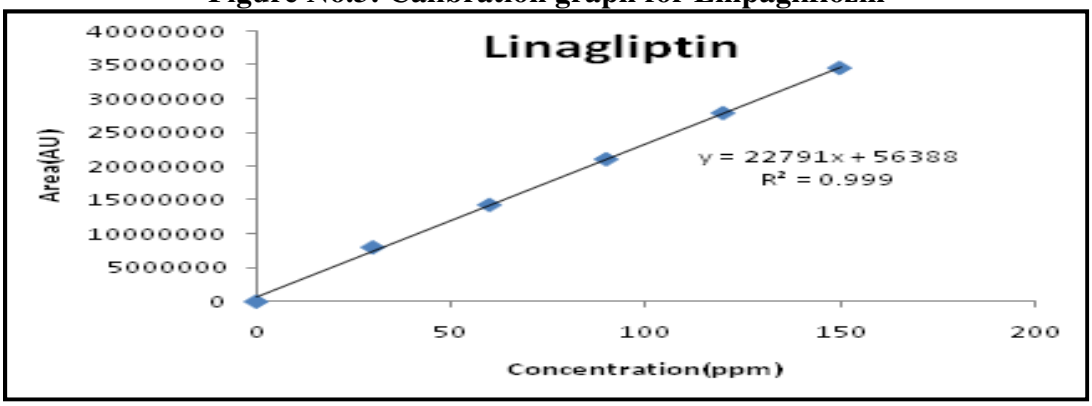



**Figure No.4: Calibration graph for Linagliptin**

## CONCLUSION

- In the present investigation, a simple, sensitive, precise and accurate RP-HPLC method was developed for the quantitative estimation of Linagliptin and Empagliflozin in bulk drug and pharmaceutical dosage forms.
- This method was simple, since diluted samples are directly used without any preliminary chemical derivatisation or purification steps.
- Linagliptin and Empagliflozin was freely soluble in ethanol, methanol and sparingly soluble in water.
- Water: ACN (15:85% v/v) was chosen as the mobile phase. The solvent system used in this method was economical.
- The %RSD values were within 2 and the method was found to be precise.
- The results expressed in Tables for RP-HPLC method was promising. The RP-HPLC method is more sensitive, accurate and precise compared to the Spectrophotometric methods.
- This method can be used for the routine determination of Linagliptin and Empagliflozin in bulk drug and in Pharmaceutical dosage forms.

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## CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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