*https://doi.org/10.48047/AFJBS.6.14.2024.7221-7236*

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

# A Process Validation Study of Empagliflozin Tablet 25mg

**NEETOO SINGH*, RITA SAINI AND SHIVANAND PATIL**

DEPARTMENT OF PHARMACY, SHREE DEV BHOOMI INSTITUTE OF EDUCATION SCIENCE AND TECHNOLOGY, UTTARAKHAND TECHNICAL UNIVERSITY, DEHRADUN, UTTARAKHAND-248011

Volume 6, Issue 14, Aug 2024

Received: 15 June 2024

Accepted: 25 July 2024

Published: 15 Aug 2024

*doi: 10.48047/AFJBS.6.14.2024.7221-7236*

**ABSTRACT:**

Empagliflozin Tablet is an oral anti-diabetic drug used to treat type 2 diabetes mellitus. The objective of this research study is to execute/manufacture the process validation batches at the manufacturing site as per data generated from lab scale batches at R&D. Process validation batches are executed to demonstrate the process performance for reproducibility and consistency within its range of operation as per process design.

This data was generated for regulatory filling, process evaluation, and optimization of the scale-up batch of Empagliflozin Tablets 25mg.

As a part of submission batches execution at the manufacturing site, complete requisite and qualified equipment status mapped and accordingly scale-up calculation done. Based on the scale-up calculation further master documents have been prepared to execute validation batches. The process mapping at the qualified equipment train can produce the drug product, which gives the defined quality attribute during, the intermediate and finished product stages.

After the execution of validation batches, the outcome indicated that the process design for manufacturing the Empagliflozin Tablet 25mg is robust enough to manufacture a quality drug product. The validated products give the specified quality attribute results and meet its predetermined specification criteria.

**Keywords:** Empagliflozin Tablets, Process Validation, Food and Drug Administration, Quality Attribute of Drug Product, Scaleup batch.

## INTRODUCTION:

As per USFDA guidance (2008) “Proces validation is establishing documented evidence which provides a high degree of assurance that a specific process (such as the manufacturing of pharmaceutical dosage forms) will consistently produce a product meeting its predetermined specifications and quality characteristics.” As per USFDA guidance (2011) “Process validation is carried in three phases of study, Phase 1 is called as, “Product Design”, which covers all activities resting to product research and development, formulation pilot batch studies. [1][2]

Phase 2 is called, "**Process Qualification",** which covers scaleup batch execution with assurance of ***Process Validation/ Process Performance Qualification*** with three consecutive batches (or batches based on risk assessment) at the manufacturing site, intended to define the commercial batch manufacturing process.

Phase 3 is called, "**Continuous Process Verification**", it provides the manufacturer with assurance that a process remains validated during the routine manufacturing phase of the product lifecycle.

The principal elements of validation include documented evidence, a high degree of assurance, specific processes, consistency, and predetermined specifications.[3] [4] There are different types of validations, including Prospective validation: which establishes documented evidence prior to process implementation that a system does what it proposed to do based on pre-planned protocols Concurrent validation: establishes documented evidence that a process does what it purports to do, based on information generated during actual implementation of the process; Revalidation: repeats the original validation effort or any part of it, and includes investigative review of existing performance data. This approach is essential to maintain the validated status of the plant, equipment, manufacturing processes, and computer systems. [5]

Empagliflozin Tablets 25 mg is an oral anti-diabetic drug from the SGLT-2 class used mainly to treat type 2 diabetes mellitus and, in some countries, prediabetes. It is sold under the brand name Jardiance. Empagliflozin was approved for medical use in the United States and the European Union in 2014. It is an inhibitor of the sodium-glucose co-transporter-2 (SGLT-2) and works by increasing sugar loss in urine. [19]

A clinical trial carried out with Empagliflozin Tablet [Jardiance] showed an impressive 21% relative risk reduction for the composite primary endpoint of cardiovascular death or hospitalization for heart failure in adults with heart failure with preserved ejection fraction (HFpEF). Results from the EMPEROR-Preserved phase III trial were presented today at the European Society of Cardiology Congress 2021 and published in The New England Journal of Medicine.[27] Key secondary endpoint analyses from the trial showed that Jardiance also reduced the relative risk of first and recurrent hospitalizations for heart failure by 27% and significantly slowed kidney function decline. [8][9]

## PROCESS VALIDATION OF EMPAGLIFLOZIN TABLETS:

### a) Pre-validation Assessment and Plan of Work:

Every pharmaceutical industry has addressed the quality theme, in their equipment, product, process, personnel, and company through validation. A validation program encompasses various components within a pharmaceutical organization. It is important to grasp this concept to have a successful validation programmed validation is the only part of the overall picture towards the goal of a high quality of standard.

In consideration of providing affordable quality drug products, lab scale data was generated at R&D batches. Further scaleup at the manufacturing site was carried out to generate the process validation data as well as stability data of the product throughout the recommended shelf life. This data is required for further drug product regulatory filling. In this study, the scope of scale-up calculation and further process validation batch execution for commercial product manufacturing has been explored.

Taking into consideration of same as mentioned above, three consecutive validation batches are planned to be executed at the manufacturing site to ensure the process designed to manufacture the drug product is adequate and well-validated.

Pre-requisites before Process Validation Batches execution assessed and documents have been designed accordingly. As a part of the Prerequisites, manufacturing Equipment selection, Scaleup calculation for Raw Materials, and Process variables & control design were carried out.

### Manufacturing Equipment Selection:

The list of equipment used in the manufacturing of products has been selected based on manufacturing process design, scaleup calculation, and facility/utility assessment criteria. The equipment train has been decided as per the manufacturing process of the product Empagliflozin Tablets 25mg.

***Table 1: Equipment Details Used in Manufacturing of Batches***

| Sr. No. | Equipment Name | Size/Capacity |
|---|---|---|
| 1 | Sifter | 20 Inches |
| 2 | Rapid mixer granulator | 25 lts. |
| 3 | Multi mill | --- |
| 4 | Tray Drier | --- |
| 5 | Double Cone Blender | 25 L |
| 6 | Tablet Compression Machine | 35 Stations |
| 7 | Conventional coating pan | 20 Kg |
| 8 | Colloid mill | --- |
| 7 | Strip Packing Machine | 40 - 60 cuts/min |
| 8 | Weighing Balance | 220 g |
| 9 | Weighing Balance | 60 Kg |

**List of Raw Materials:**

Materials used in the manufacturing of the batch have been taken from approved documents and formula designed from R&D and further scaleup calculations were carried out at the manufacturing site for the proposed batch size of 0.03M Tablets. The details of the ingredients are mentioned below in the table:

***Table 2: Details of Raw Material Used for Manufacturing of Tablets***

| Sr. No. | Name of Raw Materials | Qty./Tablets (mg) | Qty./Batch (Kg) |
|---|---|---|---|
| 1. | Empagliflozin | 25 | 0.75 |
| 2. | Microcrystalline cellulose | 102.2 | 3.066 |
| 3. | Hydroxypropyl cellulose | 13 | 0.39 |
| 4. | Croscarmellose Sodium (Ac-di-sol) | 8.3 | 0.249 |
| 5. | Ferric oxide Yellow | 0.5 | 0.015 |
| 6. | Purified water | q.s. | q.s. |
| 7. | Croscarmellose Sodium (Ac-di-sol) | 9.6 | 0.288 |
| 8. | Aerosil 200 | 1.6 | 0.048 |
| 9. | Magnesium Stearate | 1.6 | 0.048 |
| 10. | Sodium Stearyl Fumarate | 3.2 | 0.096 |
| **Coating Material** | | | |
| 11. | Hydroxy propyl methyl cellulose E 15 | 0.083 | 0.0249 |
| 12. | Talc | 0.017 | 0.0051 |
| 13. | Titanium dioxide | 0.017 | 0.0051 |
| 14. | Propylene glycol | 0.025 | 0.0075 |
| 15. | Polyethylene glycol 6000 | 0.025 | 0.0075 |

**Process Steps, Process Variables, and Measuring Controls Design:**

Process steps, process variables, and measuring controls for **Empagliflozin 25mg Tablets** are designed, and accordingly, process mapping is carried out throughout the validation batch execution. This will give accurate data for process robustness evaluation and assessment; it also gives information about the process being stable and gives the quality drug product throughout the execution i.e. intermediate and finished product stages.

***Table 3: Details of Process Variables and Control Measures***

| **PROCESS** | **VARIABLES** | **MEASURING CONTROLS** |
|---|---|---|
| SIFTING | ➢ Visual Inspection | ➢ Sieve Integrity |
| DRY MIXING & GRANULATION | ➢ Occupancy<br>➢ Granulator RPM<br>➢ Mixing Time | ➢ Content Uniformity |
| DRYING | ➢ Drying Temperature<br>➢ Drying Time | ➢ Drying Time<br>➢ LOD |
| BLENDING / LUBRICATION | ➢ Occupancy<br>➢ Blender RPM<br>➢ Blending Time | ➢ Bulk density<br>➢ Blend Uniformity by Assay<br>➢ Particle Size Distribution |
| COMPRESSION | ➢ Machine RPM<br>➢ Hopper Level | ➢ Description<br>➢ Uniformity of weight<br>➢ Disintegration Time<br>➢ Hardness<br>➢ Thickness<br>➢ Friability<br>➢ % Assay & CU |
| COATING | ➢ Spray rate<br>➢ Coating pan RPM<br>➢ Bed temperature | ➢ Description<br>➢ Weight gain<br>➢ Dissolution |
| STRIP PACKING | ➢ Sealing Temperature<br>➢ Machine Speed | ➢ Strip Quality<br>➢ Leak Test<br>➢ Finished Product Quality Attribute |

**b) Manufacturing of Empagliflozin Tablets 25mg Validation Batches:**

Manufacturing of validation batches (consecutive three batches) carried as per the assessed and defined process of validation protocol. As part of the first step, dispensing of raw material i.e. Active Pharmaceutical Ingredient (Empagliflozin) and excipients have been carried out as per approved batch size (according to scaleup calculation). The raw materials were dispensed as per the standard operating procedure and approved batch records. The weights and AR numbers are mentioned in the dispensing recorded to ensure the quantity of drug product dispensed as per the calculated approved batch size. The weighing balance used in dispensing was assured about calibration status and only calibrated balance was used to avoid any dispensing error in raw material quantity. After the dispensing of raw materials, the active ingredient and other excipients were sifted in the vibratory sifter with #60 & #40 sieves as per the approved batch manufacturing record.

The sifted raw materials were loaded in the rapid mixture granulator for wet granulation of drug products. As process is designed with a wet granulation process, hence after loading of Empagliflozin and other Raw materials. Dry mixing in RMG was carried out for 10 minutes and after that dry mix blend sample for assay analysis. After the dry mixing, further wet granulation was carried out with purified water addition (purified water was used as a binding solution). The chopper and impeller amperage load and time of granulation are considered process variable factors. After completion of wet granulation, granules were unloaded in bins.

Granules were loaded in a tray drier and dried till they attained the specified LOD, i.e. NMT 3.0% w/w. After achieving the desired LOD in the drying process, further dried granules were milled in multi-mill with screen size 40#. The milled granules were loaded in a double-cone- blender for blending and lubrication with specified RPM and recommended time. Sampling has been carried out for different time intervals of blending as per the approved protocol to ensure blend uniformity and drug content.

The lubricated blend after complying with the blend uniformity confidence level criteria and meeting the specification limit was processed to the next stage of manufacturing i.e. compression. Tablet compression was carried out on a compression machine with the specified punches and dies as per the approved validation protocol and Batch manufacturing record. The in-process checks of compressed tablets are also performed to ensure the physical attributes of compressed tablets are within the approved limit. It also provides confidence in

the validation process at the compression stage and provides a high degree of confidence to establish the critical process parameters, such pre -compaction force, main compaction force, speed of compression machine, punch penetration, cylindrical height & etc.

Content Uniformity is also assured by sampling tablets at different time points and analyzed to assure as per ASTM sampling criteria. Content uniformity results give the confidence level of the process about manufacturing quantity drug products throughout the validation process. After the compression of the tablets, the compressed tablets were subjected to coating. The coating of tablets was carried out in pan coater with proper optimization and validation of critical process parameters. After achieving the target weight buildup during the coating process, the coating stage was validated. Further primary packing is carried on a strip packing machine, with assurance of variable of strip packing machine speed and sealing temperature.

Finished products were analyzed as per the standard testing procedure and the results evaluation carried with the approved product specifications.

**RESULT AND DISCUSION:**

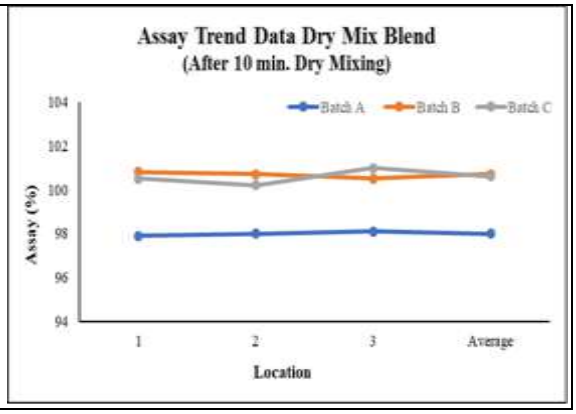
As part of process validation study, sampling of drug product carried at different stage of manufacturing. These samples were analyzed as part of in-process checks as well as subjected in Quality Control department for analysis. The sampling of drug product carried as per approved validation protocol. The analytical results of drug product give the confidence and assurance about manufacturing process is well-validated. Sampling and Analytical Results of Validation Batches discussed in below sections;

**Dry Mixing Blend Sample from RMG and Results:**

The dispensed sifted active drug and the excipients were dry mixed for 10 minutes and sampled and checked for assay value from three different locations. The observed data from three batches were compiled in the table.

***Table 4: Analytical results of dry mix blend from RMG***

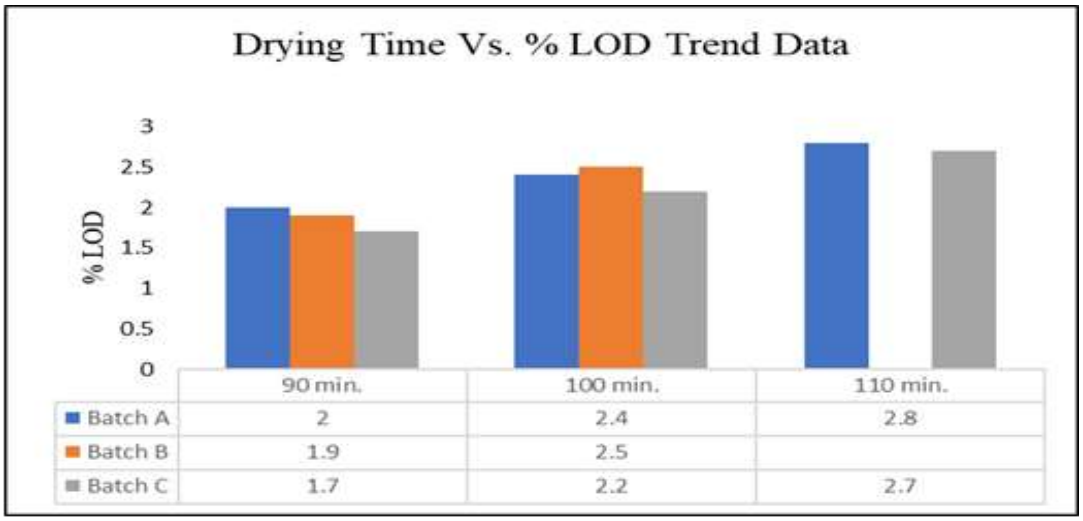
| Location | Observation on 10 minutes Assay of Empagliflozin (%) | | | Limits |
|---|---|---|---|---|
| | **Batch A** (AR: 1167599) | **Batch B** (AR: 1167600) | **Batch C** (AR: 1167601) | |
| 1 | 97.9 % | 100.8 % | 100.5 % | 95.0 % – 105.0 % |
| 2 | 98.0 % | 100.7 % | 100.2 % | |
| 3 | 98.1% | 100.5 % | 101.0 % | |
| Minimum | 97.9 % | 100.5 % | 100.2 % | - |
| Maximum | 98.1 % | 100.8 % | 101.0 % | - |
| Average | 98.0 % | 100.7 % | 100.6 % | - |
| % RSD | 0.1 % | 0.1 % | 0.3 % | NMT 5 % |




***Inference:*** *Based on the evaluation of trend data of assay results, it has been concluded that the dry mixing at 10 minutes gives adequate mixing and gives the desirable quality attribute result in the product.*

**Drying Stage Sampling and LOD Results of Granules:**

The granulated mass was dried in a tray drier and the samples were observed for loss on drying at specific time intervals. The observed data for the three batches were compiled below:



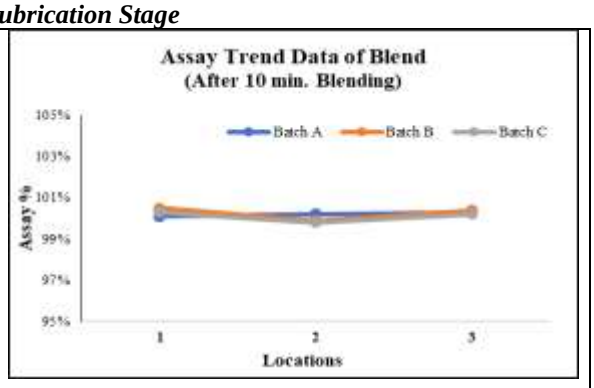
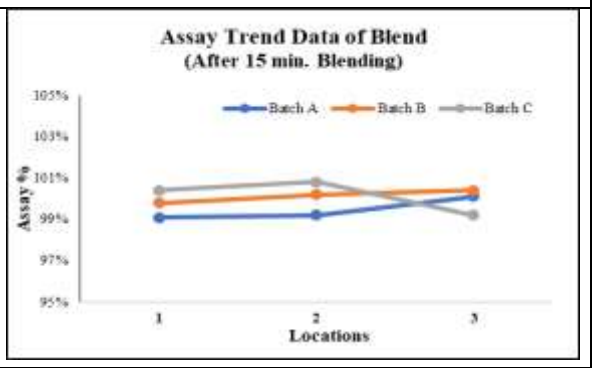
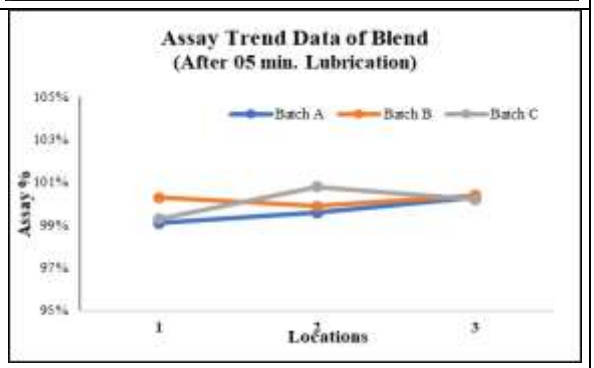

***Note:*** *In Batch B target LOD was achieved with 100 minutes of drying, hence further additional 10 minutes of drying was not performed*

***Inference:*** *The observed data from the three batches A, B, and C confirms that the drying time required to achieve the targeted LOD, i.e. within the specified limits NMT 3.0 %, is required from 100 to 110 min. drying as per process validation data.*

**Blending Stage Sampling and Lubricated Blend Results**

The blending process of dried & milled granules was carried out in a Double-cone blender. During the blending process samples were collected from two time points of the blending stage and one time point i.e. after the Lubrication stage. A total of 15 minutes of blending of milled granules and 5 minutes of lubrication has been carried out in all three validation batches.

***Table 5: Analytical results at Blending & Lubrication Stage***

| Location | Observation on 10 minutes Blending Assay of Empagliflozin (%) | | | Limits | |
|---|---|---|---|---|---|
| | **Batch A** (AR: 1167003) | **Batch B** (AR: 1167004) | **Batch C** (AR: 1167005) | | |
| 1 | 100.1 % | 100.5 % | 100.3 % | 95.0 % – 105.0 % |   |
| 2 | 100.2 % | 99.9 % | 99.8 % | | |
| 3 | 100.3 % | 100.4 % | 100.2 % | | |
| Minimum | 100.1 % | 99.9 % | 99.8 % | - | |
| Maximum | 100.3 % | 100.5 % | 100.2 % | - | |
| Average | 100.2 % | 100.3 % | 100.1 % | - | |
| % RSD | 0.1 % | 0.3 % | 0.2 % | NMT 10 | |
| **Location** | **Observation on 15 minutes Blending Assay of Empagliflozin (%)** | | | **Limits** | |
| | **Batch A** (AR: 1167006) | **Batch B** (AR: 1167007) | **Batch C** (AR: 1167008) | | |
| 1 | 99.1 % | 99.8 % | 100.4% | 95.0 % – 105.0 % |   |
| 2 | 99.2 % | 100.2 % | 100.8 % | | |
| 3 | 100.1 % | 100.4 % | 99.2 % | | |
| Minimum | 99.1 % | 99.8 % | 99.2 % | - | |
| Maximum | 100.1 % | 100.4 % | 100.8 % | - | |
| Average | 99.5 % | 100.1 % | 100.1 % | - | |
| % RSD | 0.5 % | 0.2 % | 0.7 % | NMT 10 | |
| **Location** | **Observation on 5 minutes Lubrication Assay of Empagliflozin (%)** | | | **Limits** | |
| | **Batch A** (AR: 1167009) | **Batch B** (AR: 1167010) | **Batch C** (AR: 1167011) | | |
| 1 | 99.1 % | 100.3 % | 99.3 % | 95.0 % – 105.0 % |   |
| 2 | 99.6 % | 99.9 % | 100.8 % | | |
| 3 | 100.3 % | 100.4 % | 100.2 % | | |
| Minimum | 99.1 % | 99.9 % | 99.3 % | - | |
| Maximum | 100.3 % | 100.4 % | 100.8 % | - | |
| Average | 99.7 % | 100.2 % | 100.1 % | - | |
| % RSD | 0.5 % | 0.2 % | 0.6 % | NMT 10 | |

***Inference:*** *Based on the analytical data of Blending stage samples, it has been evident that the product process is validated to give adequate quality attributes in manufactured drug products. RSD of assay results at the blending stage was found from 0.1% to 0.7%, which clearly expresses that the process of manufacturing is robust.*

## Compressed Tablets Sampling and Results:

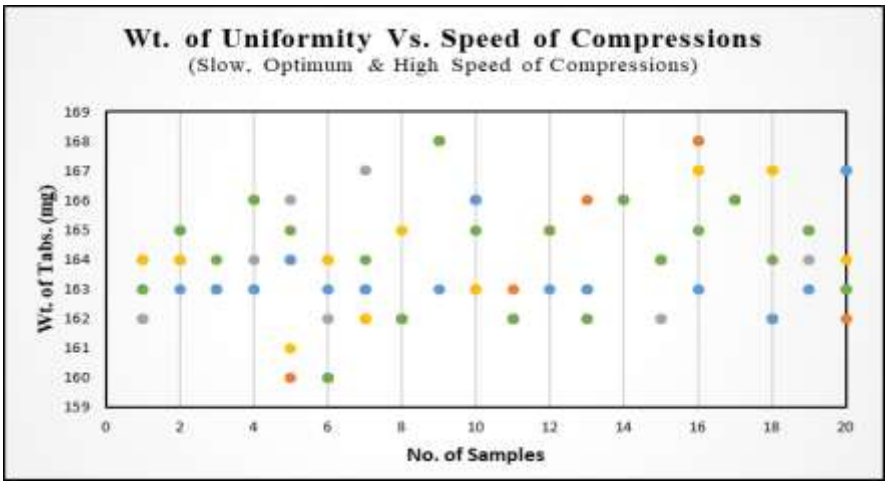
As per the designed and mapped manufacturing process, the lubricated blend of Empagliflozin product was compressed at a Double Rotary 35 station compression machine. As a part of the validation process evaluation, defined challenge tests have been carried out by sampling and in-process testing of compressed tablets at different speeds of compression machines.

***Table 6: Analytical results of compressed tablets***

| Parameter | Observation | | | |
|---|---|---|---|---|
| | **Batch A** | **Batch B** | **Batch C** | **Acceptance Criteria** |
| Uniformity of weight | 162 - 169 | 162 - 167 | 162 - 168 | 165mg ± 7.5 % (153 – 177 mg) |
| Thickness | 3.00 -3.14 | 3.07 – 3.15 | 3.08 – 3.12 | 3.10± 0.20 mm |
| Hardness | 6 | 5 | 6 | NLT 3 Kg / Cm2 |
| Friability | 0.11 % | 0.10 % | 0.12 % | NMT 1.0 % w/w |
| Disintegration Time | 4’55” | 4’55” | 4’50” | NMT 15 Minutes |
| Assay | 100.8 % | 100.9 % | 100.7 % | Assay (Limit: 95.0 – 105.0 %) |

***Table 7: Weight of uniformity of compressed tablets at different speeds of machine***

| **Uniformity of Weight Limit: 165 mg ± 7.5 % (153mg to 177 mg)** | | | | | | |
|---|---|---|---|---|---|---|
| **No. of Sample** | **Low Speed (25 RPM)** | | **Optimum Speed (30 RPM)** | | **High Speed (35 RPM)** | |
| | **LHS** | **RHS** | **LHS** | **RHS** | **LHS** | **RHS** |
| 1 | 164 | 162 | 162 | 164 | 163 | 163 |
| 2 | 165 | 164 | 164 | 164 | 163 | 165 |
| 3 | 163 | 163 | 163 | 163 | 163 | 164 |
| 4 | 166 | 166 | 164 | 163 | 163 | 166 |
| 5 | 164 | 160 | 166 | 161 | 164 | 165 |
| 6 | 160 | 164 | 162 | 164 | 163 | 160 |
| 7 | 163 | 162 | 167 | 162 | 163 | 164 |
| 8 | 162 | 162 | 162 | 165 | 162 | 162 |
| 9 | 168 | 168 | 168 | 168 | 163 | 168 |
| 10 | 166 | 163 | 166 | 163 | 166 | 165 |
| 11 | 162 | 163 | 162 | 162 | 162 | 162 |
| 12 | 165 | 165 | 165 | 165 | 163 | 165 |
| 13 | 163 | 166 | 162 | 163 | 163 | 162 |
| 14 | 166 | 166 | 166 | 166 | 166 | 166 |
| 15 | 164 | 164 | 162 | 164 | 164 | 164 |
| 16 | 168 | 168 | 167 | 167 | 163 | 165 |
| 17 | 166 | 166 | 166 | 166 | 166 | 166 |
| 18 | 162 | 167 | 162 | 167 | 162 | 164 |
| 19 | 165 | 165 | 164 | 165 | 163 | 165 |
| 20 | 167 | 162 | 163 | 164 | 167 | 163 |
| **Min.** | 160 | 160 | 162 | 161 | 162 | 160 |
| **Max.** | 168 | 168 | 168 | 168 | 167 | 168 |
| **Average** | 164.5 | 164.3 | 164.2 | 164.3 | 163.6 | 164.2 |
| **RSD** | 1.3 | 1.3 | 1.2 | 1.1 | 0.9 | 1.1 |




***Inference:*** *Based on the verification and evaluation of in-process checks and analytical data, it has been revealed that the product process at the compression stage is well-validated. The compression process was challenged at the speed range of the compression machine from 25 rpm to 35 rpm. The product compressed at a compression machine gives quality attributes as per designed specification criteria. Hence process is considered validated till the compression stage.*

**Coating stage sampling and results:**

To check the weight gain and various parameters including the appearance of the tablets during coating, samples are drawn at different intervals of coating from the coating pan. However, after 120 minutes of coting the required weight gain was achieved, hence spraying was stopped after that and the dried tablet was sampled from the coating pan and submitted to Quality Control for analytical assessment. The results are compiled in the below table:

***Table 8: In-process and Analytical results of coated tablets***

| Parameter | Observation | | | |
|---|---|---|---|---|
| | **Batch A** | **Batch B** | **Batch C** | **Acceptance Criteria** |
| **Weight gain (%)** | 3.03 % | 3.01 % | 3.02 % | 2.8% - 3.2% weight gain from average wt. of core tablets |
| **Description** | White to off white Circular shallow concave tablets with both side plain. | White to off white Circular shallow concave tablets with both side plain. | White to off white Circular shallow concave tablets with both side plain. | White to off white Circular shallow concave tablets with both side plain. |
| **Thickness** | 3.20 – 3.26 | 3.19 – 3.27 | 3.16 – 3.19 | 3.10± 0.20 mm |

| Parameter | Observation | | | |
|---|---|---|---|---|
| | **Batch A** | **Batch B** | **Batch C** | **Acceptance Criteria** |
| **Diameter** | 8.02 - 8.05 | 8.02 - 8.05 | 8.01 – 8.04 | 7.9 – 8.1 mm |
| **Assay** | 99.5 % | 100.6 % | 99.5 % | Assay (Empagliflozin should be 95.0 – 105.0 % of the label claim) |

***Inference:*** *From the observed data, it was confirmed that the weight gain and the appearance of the tablets were within the specified limit during the coating stage. The coating process was completed in 120 minutes. Analytical data confirms that the product exerts quality attributes throughout the manufactured drug product till the coating stage. Hence process was considered well-designed and product validation was successful, to give the desired quality attribute product.*

**Packing in-process checks and results of Finished product**

The finished product was packed at the strip packing. The sealing quality of strip packs has been evaluated by validating the packing process at different speeds of the machine with variable sealing temperatures of 130 to 150 degree celcius. Packing process CPPs (critical process parameters) and observation are mentioned below in the table.

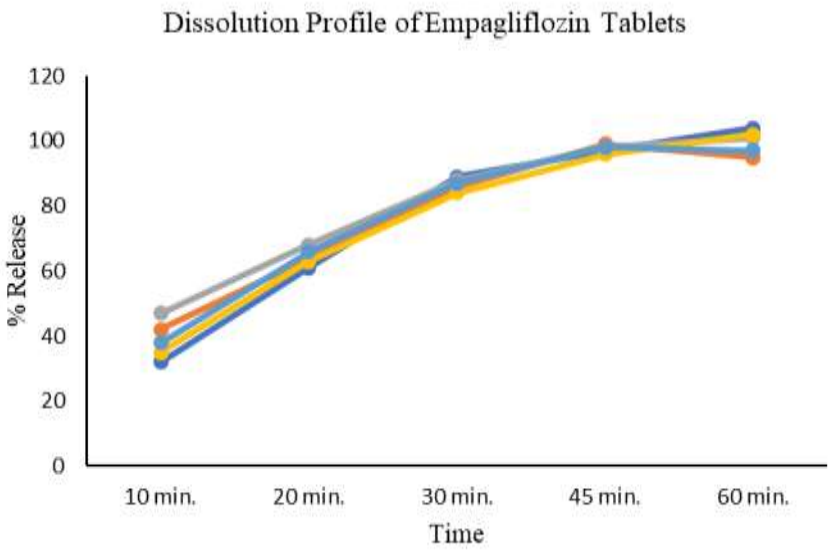
***Table 9: In-process details of the packing stage***

| Parameter | Observation | | | |
|---|---|---|---|---|
| | **Batch A** | **Batch B** | **Batch C** | **Acceptance Criteria** |
| Strips Quality | Complies | Complies | Complies | Strip packs are well sealed and the knurling of strips adequate with proper cutting |
| Machine Speed | 30 to 40 cuts/min. | 30 to 40 cuts/min. | 30 to 40 cuts/min. | 30 to 40 cuts/min. |
| Sealing Temperature | $130^0$c to $150^0$c | $130^0$c to $150^0$c | $130^0$c to $150^0$c | $130^0$c to $150^0$c |
| Leak test | Passes | Passes | Passes | The leak test complies as per approved procedure |

Finished products were sampled from the initial, middle, and end of packing stages of three validation batches and a pooled sample of each batch was sent to the quality control department to analyze the quality attribute of the manufactured drug product.

***Table 10: Finished Product Result***

| Parameter | Observation | | | |
|---|---|---|---|---|
| | **Batch A** | **Batch B** | **Batch C** | **Specification Limit** |
| **Description** | White to off white Circular shallow concave tablets with both side plain. | White to off white Circular shallow concave tablets with both side plain. | White to off white Circular shallow concave tablets with both side plain. | White to off white Circular shallow concave tablets with both side plain. |
| **Assay** | 99.8 % | 99.6 % | 100.4 % | Assay of Empagliflozin should be 95.0 – 105.0 % of the label claim. |
| **CU** | 5 | 4 | 4 | Acceptance Value (AV) NMT-15 |
| **Dissolution** | 97% | 99% | 102% | Dissolution of Empagliflozin content Not Less Than 80% in 45min. |
| **Unknown individual Impurity** | 0.03% | 0.02% | 0.02% | NMT - 0.1 % |
| **Total impurity** | 0.05% | 0.04% | 0.04% | NMT – 1.0% |




***Inference:*** *Based on the evaluated analytical data of the finished product it has been revealed that the manufactured & packed good of Empagliflozin Tablets 25mg is meeting the defined quality attribute. All test results are meeting the specification criteria. It confirms that the product manufacturing & packing process is well-validated.*

## CONCLUSION

The outcome indicated that the process validation data provides a high degree of assurance that the manufacturing process produces a product meeting its predetermined specification and quality attribute.

## DATA AVAILABILITY STATEMENT

This article contains all of the data generated or analyzed during this validation study.

## ETHICAL APPROVAL

Because in present study, animals were not used as result of this, ethical approval was not required.

## ACKNOWLEDGEMENT

The authors are grateful to Guide and Director of Shree Dev Bhoomi Institute of Education Science and Technology, who gave permission to involve in the validation batches.

## REFERENCE:

[1] FDA Guidance for industry-Process Validation: General Principles and Practices (Draft Guidance) November 2008.

[2] FDA Guidance for industry-Process Validation: General Principles and Practices January 2011.

[3] David J. Ingram., “Six Sigma and Process Validation Strategies”. Journal of Validation Technology, Volume 6, May 2000, P – 657 – 662.

[4] David W. Vincent, "Cleaning Validation for the Biotechnology and Biological Industries – part II", Journal of Validation Technology, Volume August 2000. P – 710 to 712.

[5] Donald M. Rosendale, “Validation of Pharmaceutical process Equipment”.

[6] Frederick J. Carleton and James P. Agalloco, Validation Pharmaceutic process (Sterile products), 2nd edition, revised and Expanded Marcel Dekker Inc., P – 131 to 150.

[7] Global Harmonization Task Force study Group #3 draft Process Validation Guidance – June 1, 1998.

[8] Guidelines on General Principles of Process Validation, FDA, May '87.

[9] Guide to Good Manufacturing Practice for Medical products, version pH 1/97 (rev.3) dated 15 January 2002. Published by Pharmaceutical Inspection Corporation scheme

(PIC / S.) Australian Code of Good Manufacturing Practice of Medicinal Products, 16 August 2002.

[10] Guide to inspections of Oral Solid Dosage Forms per / post approval for development and Validation, January 1994.

[11] Kenneth G. Chapmann, "Proposed Validation Standard VS – I, Non–aseptic Pharmaceutical process". Journal of Validation Technology, Volume 6, P – 502 to 518.

[12] Lachman Libermann and Kang., 3rd Edition, Theory and practice of Industrial Pharmacy.

[13] Leonard A. Grunbaum, " Do It Right The First Time", Journal Validation Technology, Volume 6, February 200, P – 535.

[14] S.Sree Rama Murthy and K. Saravana Kumar, "Validation". The Eastern Pharmacist, Volume XI, No.476, July 2001, P – 451 to 457.

[15] Nash R.A.Berry, I.R. Pharmaceutical Process Validation 2nd edition, Marcel Dekker Inc., P – 351 to 368.

[16] S.I. Haider, Validation Standard Operating Procedure a step-by-step guide for achieving compliance in the Pharmaceutical Medical Device and Biotech industry.

[17] S.K. Sharma, "Validation of Pharmaceutical Products & Process", the Eastern Pharmacist, volume XI, IV, No.523., July 2001, P – 21 to 23.

[18] Validation guidelines for pharmaceutical process, Health products and Food Branch Inspection Guidance document (Date Issued 2000 – 05 – 01)

[19] "Empagliflozin (Jardiance) Use During Pregnancy". Drugs.com. 30 August 2018. Archived from the original on 5 August 2019. Retrieved 10 February 2020.

[20] ^ Jump up to:a b c d e f g h "Empagliflozin Monograph for Professionals". Drugs.com. AHFS. Archived from the original on 6 April 2019. Retrieved 21 December 2018.

[21] ^ "AusPAR: Empagliflozin". Therapeutic Goods Administration (TGA). 8 November 2017. Retrieved 24 March 2022.

[22] "Empagliflozin (Jardiance) Use During Pregnancy". Drugs.com. 30 August 2018. Archived from the original on 5 August 2019. Retrieved 10 February 2020.

[23] Empagliflozin Monograph for Professionals". Drugs.com. AHFS. Archived from the original on 6 April 2019. Retrieved 21 December 2018.

[24] Davies MJ, D'Alessio DA, Fradkin J, Kernan WN, Mathieu C, Mingrone G, et al. (December 2018). "Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)". Diabetologia.

[25] FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes". U.S. Food and Drug Administration (FDA). 9 February 2019. Archived from the original on 13 December 2019. Retrieved 18 March 2019.

[26] British National Formulary: BNF 76 (76 ed.). Pharmaceutical Press. 2018. p. 691. ISBN 9780857113382.

[27] Empagliflozin - Drug Usage Statistics". ClinCalc. Retrieved 14 January 2024.

[28] Kovacs CS, Seshiah V, Swallow R, Jones R, Rattunde H, Woerle HJ, et al. (February 2014). "Empagliflozin improves glycaemic and weight control as add-on therapy to pioglitazone or pioglitazone plus metformin in patients with type 2 diabetes: a 24-week, randomized, placebo-controlled trial". Diabetes, Obesity & Metabolism.