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Process Validation of Sitagliptin Film Coated Tablets 100 mg

Pratibha Thapliyal[*1], Neha Sodiyal[2], Shivanand Patil[3]

[1]MPHARM (Quality Assurance) student, Department of Pharmacy, Shree Dev Bhoomi Institute of Science & Technology, Dehradun, Uttarakhand.

[2]Associate Professor (Guide), Department of Pharmacy, Shree Dev Bhoomi Institute of Science & Technology, Dehradun, Uttarakhand.

[3]Professor (Director), Department of Pharmacy, Shree Dev Bhoomi Institute of Science & Technology, Dehradun, Uttarakhand

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KEYWORDS

Introduction, Sitagliptin, Process validation, Critical process parameters (CPPs), critical quality attributes (CQAs), and Regulatory guidelines of Process Validation.

ABSTRACT:

Introduction: Sitagliptin is an antidiabetic medication used to treat type-2 Diabetes Mellitus. As a member of the dipeptidyl peptidase-4 (DPP-4) inhibitor class, Sitagliptin works by inhibiting the enzyme DPP-4, thereby increasing the levels of incretin hormones, which help regulate blood sugar levels. Process validation refers to the documented evidence that ensures the consistency and reliability of a manufacturing process that produces a product meeting predetermined specifications and quality attributes.

Objectives: This project is about the process validation of Sitagliptin film-coated tablets 100 mg, ensuring that the manufacturing process consistently produces a product of the highest quality, in compliance with regulatory requirements, and in line with industry standards.

Methods: The methodology outlines the steps for conducting the process validation study, from the formulation and manufacturing process to the analytical testing of the Sitagliptin Film-Coated Tablets 100 mg.

Results: Sampling of products performed at different stages of manufacturing, i.e., granulation, compression, coating & finished stage as per the validation protocol. The analytical test results assure that the manufacturing processes are well-validated.

Conclusions: The process validation of Sitagliptin Film-Coated Tablet 100 mg, which had not been previously performed, was initiated through a novel approach. Process validation of the product Sitagliptin Film-Coated Tablet 100 mg to be carried out with three consecutive batches. During the process validation, critical process parameters and critical quality attributes were checked at the granulation, compression stage, and coating stage.

1. Introduction

Sitagliptin, an oral dipeptidyl peptidase-4 (DPP-4) inhibitor, improves glycemic control by inhibiting DPP-4 inactivation of the incretin hormones glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide. This increases active incretin, and insulin levels and decreases glucagon levels and post-glucose-load glucose excursion. Validation is the documented act proving that any procedure, process, equipment, material, activity, or system leads to the expected result..

Process validation is the documented proof that ensures the consistency and reliability of the manufacturing process that produces a product of the highest quality, in compliance with regulatory requirements, and in line with industry standards. It guarantees uniformness of the dosage form across batches, meeting critical quality attributes like dissolution, hardness. Overall, process

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validation plays an important role in the maintenance of product consistency, quality, and compliance in tablet manufacturing..

DRUG PROFILE

Sitagliptin is an oral medication used in the treatment of type 2 diabetes mellitus (T2DM). It is a member of the DPP-4 inhibitors class, which works by increasing the levels of incretin hormones in the body, such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP). These hormones help regulate blood sugar levels by stimulating insulin release from the pancreas in response to meals and inhibiting glucagon release, which reduces liver glucose production. Sitagliptin is marketed under the brand name Januvia, but it is also available in generic forms. The drug is often prescribed alone or in combination with other antidiabetic agents such as metformin, sulfonylureas, or thiazolidinediones, depending on the patient's clinical condition and response to treatment.

Brand name: Januvia

Drug class: Dipeptidyl Peptidase-4 (DPP-4) Inhibitors

Chemical name: 7-[(3R)-3-amino-1-oxo-4-(2,4,5-trifluorophenyl)butyl]-5,6,7,8-tetrahydro-3-(trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine phosphate monohydrate.

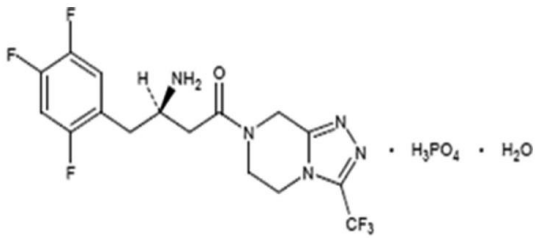
Molecular formula:

Sitagliptin- $C_{16}H_{15}F_6N_5O$

Sitagliptin phosphate monohydrate

$C_{16}H_{15}F_6N_5O•H_3O_4P•H_2O$

Structure



Molecular weight

Sitagliptin-407.314 g/mol

Sitagliptin phosphate monohydrate- 523.329 g/mol

Description- White to off-white, crystalline, non-hygroscopic powder.

VALIDATION

Validation is the documented act of proving that any procedure, process, equipment, material, activity, or system leads to the expected result.

Importance of Validation

1. Process parameters and controls are determined during the validation of any process or system.

2. It helps to determine the worst case and risks that may rise during the manufacturing of the products.

3. It helps to investigate deviation caused during the process.

4. The risk of regulatory non- compliance is minimized after validation.

5. A validated process required less process control and the finished product testing.

6. Batch to batch variation is minimized due to the validation of processes, system and equipment.

7. Reduces production cost of the product.

8. Increases the production of manufacturing facility due to the minimized rework and rejection.

PROCESS VALIDATION

In pharmaceutical manufacturing, process validation refers to the documented evidence ensuring that the manufacturing process consistently produces a product that meets predetermined specifications and quality attributes. This process plays a critical role in meeting regulatory requirements set by agencies such as the FDA, EMA, and ICH (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use).

Process validation is a step-by-step procedure to ensure that a manufacturing process can consistently produce quality products. Generally, process validation is carried out before releasing a new product, or when applying any change to an existing product, and periodically verifying the process.

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History of Process Validation

This concept was first introduced in the mid 1970's for improving the quality of pharmaceuticals by two Food and drug administration (FDA) officers, Ted Byers and Bud Loftus. [1]

In 1987, the FDA released the first process validation guidance. [4]

The fundamental approach was testing the process to ensure it worked, along with periodic retesting of the manufacturing process to assure it was continuing to work.

In the mid-2000s, regulatory agencies developed ICH Q8 – Pharmaceutical Development to provide foundational concepts required for companies to develop high-quality manufacturing processes. The final 2009 guidance provided several definitions intended to provide the basis for very important concepts for building processes. [5]

The most important PV concepts begin with the following terms defined in ICH Q8 (R2):

- Critical Process Parameter (CPP)
- Critical Quality Attribute (CQA)
- Design Space (DS)
- Control Strategy (CS)
- Quality by Design (QbD)
- Real-Time Release Testing (RTRT)

In addition, acknowledging that developing and manufacturing pharmaceuticals was primarily a risk management and control exercise, regulatory agencies in 2006 developed and issued ICH Q9 – Quality Risk Management. [6]

Types of Process Validation

1. Prospective process validation- also known as pre-market validation. Prospective process validation is executed after the completion of the R & D SITA to produce the product for commercial purposes. This type of validation is generally connected with the introduction of new drug products into the market and involves studies of all their manufacturing processes.

2. Retrospective process validation- The Retrospective process validation establishes documented evidence that a system does what it is supposed to do based on a review and analysis of historic information. It is normally conducted on a product already being commercially distributed and is based on accumulated production, testing and control data.

3. Concurrent process validation- Concurrent validation is a type of validation that occurs during the routine production of the product. It involves collecting and analyzing data from each batch or lot to verify that the process or system operates within the specified limits and produces consistent results. Concurrent validation can also be used as an alternative to prospective validation in some cases, such as when there is a lack of historical data, when the product has a short shelf life, or when the product is urgently needed.

4. Revalidation process validation- Revalidation means repeating the original validation. Revalidation is performed if there is any sort of change in the batch size, formulation or when the consecutive batches of the manufacturing unit doesn't meet specification as stated in its product, when changes are made in the site location, equipment size and capacity or new advance equipment are introduced for further processing or when new manufacturing methods and control are to be followed or changes are made in them.

Approaches in Process Validation

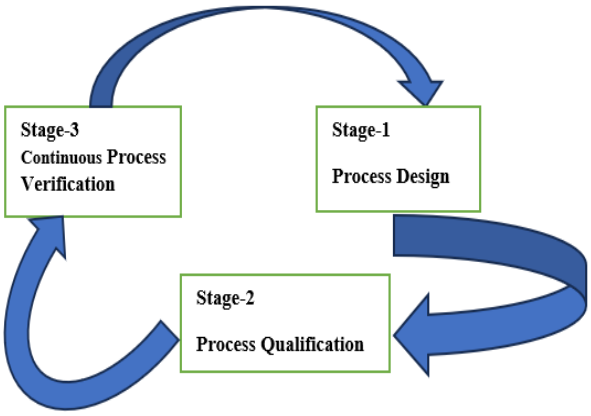

Figure-1 Approaches of Process Validation

Stage-1 Process Design:

The commercial manufacturing process is defined during this stage based on knowledge gained through development and scale-up activities. [7] This stage also

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involves process control, planning strategies to reduce input variation and/or adjust for it during manufacturing. Following sources and methods to capture process information:

- Product development activities
- Functionality and limitations of production equipment.
- Predicted contributions to variability
- Design of experiment (DOE) studies
- Risk analysis tools
- Experiments or demonstrations at laboratory or pilot scale
- Computer-based or virtual simulations.

Stage-2 Process Performance:

During this stage, the process design is evaluated to determine if the process is capable of reproducible commercial manufacturing.[7] This stage has two elements:

a) Design of the facility and qualification of the equipment and utilities

b) Process Performance Qualification (PPQ)

a) **Design of the facility and qualification of the equipment and utilities**

Proper design of a manufacturing facility is required under part 211, subpart C, of the CGMP regulations on Buildings and Facilities. It is essential that activities performed to assure proper facility design and commissioning precede PPQ.

Process Performance Qualification (PPQ) combines the actual facility, utilities, equipment (each now qualified), and the trained personnel with the commercial manufacturing process, control procedures, and components to produce commercial batches. A successful PPQ will confirm the process design and demonstrate that the commercial manufacturing process performs as expected. Process performance qualifications should be executed through a protocol and documented in a report:

- The manufacturing conditions include operating parameters, processing limits, and component (raw material) inputs.
- The data to be collected and when and how it will be evaluated.
- Tests to be performed (in-process, release, characterization) and acceptance criteria for each significant processing step.
- The sampling plan, including sampling points, number of samples, and the frequency of sampling for each unit operation and attribute.
- Criteria and process performance indicators that allow for a science- and risk-based decision about the ability of the process to consistently produce quality products.

Stage-3 Continuous Process Verification:

Ongoing assurance is gained during routine production that the process remains in a state of control. The goal of the third validation stage is continually assurance that the process remains in a state of control (the validated state) during commercial manufacture. Good process design and development should anticipate significant sources of variability and establish appropriate detection, control, and/or mitigation strategies, as well as appropriate alert and action limits. The equipment and facility qualification data should be assessed periodically to determine whether re-qualification should be performed and the extent of that re-qualification. Maintenance and calibration frequency should be adjusted based on feedback from these activities.

2. Objectives

The primary aim of this research work is to evaluate and document the verification, assurance of Sitagliptin tablets, confirming about the manufacturing process which is continuously yields highest quality material, in accordance with the agency guidelines, in line with industry standards. By assessing key process parameters, critical quality attributes, and validation stages, the thesis aims to contribute to the optimization and standardization of the production process for Sitagliptin tablets.

3. Methods

The Materials and Methodology section provides a detailed outline of the resources, experimental design, and procedures that will be used in the process validation of Sitagliptin Film-Coated Tablet 100 mg. This section is crucial for ensuring that the validation process is carried out systematically and in compliance with regulatory requirements.

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Table 1: Materials used in the formulation

S.No.	Ingredients	Purpose
1.	Sitagliptin phosphate monohydrate	Active Pharmaceutical Ingredients
2.	Lactose Monohydrate	Used as a filler and binder.
3.	Microcrystalline Cellulose (MCC)	Binder and diluent.
4.	Povidone	Binder
5.	Magnesium stearate	Lubricant
6.	Croscarmellose sodium	Disintegrants
7.	Colloidan Silicon dioxide	Glidant

Table 2: Equipment & Apparatus

S.No.	Equipment	Purpose
1.	High-Performance Liquid Chromatography (HPLC)	Content uniformity testing and Quantification of Sitagliptin.
2.	Dissolution Testing Apparatus (USP Type II)	Evaluating the dissolution rate of the Sitagliptin tablets.
3.	Hardness Tester	Assessment of Mechanical strength.
4.	Friability Test Apparatus	Determination of breakability.
5.	Blender (e.g., V-blender or Paddle Mixer)	Determination of uniform blending of the tablet formulation components.
6.	Granulator	For Wet granulation.
7.	Tablet Compression Machine	For compressing the tablets into granules.
8.	pH Meter	Determination of pH.

Table 3: Reagents and Chemicals

S.No.	Reagent/Chemical	Purpose
1.	Phosphate Buffer (pH 6.8)	For dissolution testing
2.	Methanol	For HPLC analysis
3.	Acetonitrile	For HPLC analysis
4.	Water (HPLC-grade)	For preparing buffers and solvents

METHODOLOGY

The methodology outlines the steps for conducting the process validation study, from the formulation and manufacturing process to the analytical testing of the Sitagliptin Film-Coated Tablets.

Process Validation Protocol of Sitagliptin Film-Coated Tablet 100mg

- **Step 1:** Manufactured three consecutive validation batches under conditions determined during process optimization.
- **Step 2:** For each batch, monitor and document Critical Process parameters such as:

Table 4: Critical Process Parameters to be monitored

S.No.	Process	Parameter
1.	Sifting	Sieve Size
2.	Mixing	
3.	Dry Mixing	Mixing Time
	Wet Mixing	Mixing Time Granulation Time
4.	Drying	i.Inlet temperature i.Drying time

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S.No.	Process	Parameter
		i.Loss on Drying
5.	Sizing	Size of granules
6.	Blending	i.Blending time i.RPM of blender
7.	Compression	i.Description i.Average weight i.Uniformity of weight v.Hardness v.Friability i.Thickness i.Disintegration time i.Dissolution test x.Assay
8.	Coating	i.Description i.Average weight i.Uniformity of weight v.Disintegration time v.Dissolution test i.Assay

- **Step 3:** After production, sample the tablets for analytical testing and evaluate them for:

➢ **Content Uniformity:** Test at least 10 tablets from each batch using HPLC.
➢ **Dissolution Rate:** Test the dissolution of tablets at 30 minutes using the USP Type II apparatus.
➢ **Tablet Hardness:** Test at least 6 tablets from each batch using a hardness tester.
➢ **Disintegration Time:** Test 6 tablets from each batch to determine how quickly they disintegrate in simulated gastric fluid.
➢ **Friability:** Test 10 tablets for friability using a friability tester.

Flow Chart of Manufacturing Process

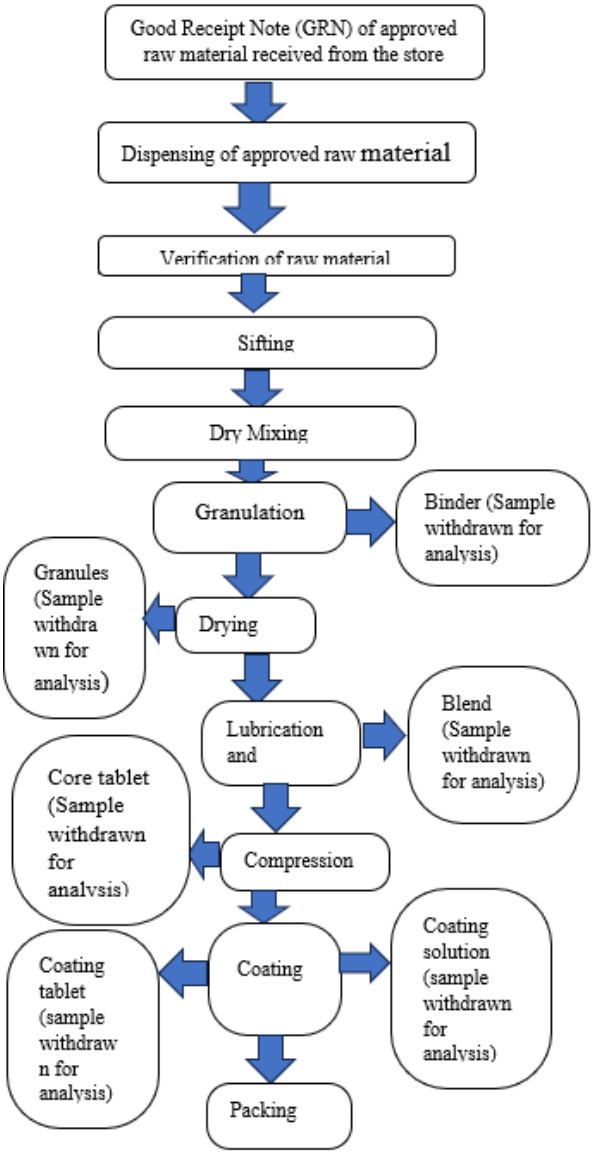

Figure 2: Flow Chart of Manufacturing Process

3. Result And Discussion

Sampling of products performed at different stages of manufacturing, i.e., granulation, compression, coating & finished stage as per the validation protocol. The analytical test results assure that the manufacturing processes are well-validated. Product sampling and analytical results of the validation batches are discussed below:

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Table 5: Critical Process Parameters (CPPs) Analytical Results

Parameters	Acceptance Criteria	Batch No.: SITA-1	Batch No.: SITA-2	Batch No.: SITA-3
SIFTING:				
Sieve Size	30#	30#	30#	30#
Sieve Integrity Before Use	Should be intact	Intact	Intact	Intact
Sieve integrity after use	Should be intact	Intact	Intact	Intact
DRY MIX				
Mixing time	10 min.	10 min.	10 min.	10 min.
Mixing Speed	For informa	40 RPM	40 RPM	40 RPM
ACTIVE SOLUTION/BINDER PREPARATION				
Mixing Time	To be recorde	10 min.	10 min.	10 min.
WET GRANULATION				
Mixing time (binder solution addition)	01-02 min.	02 min.	02 min.	02 min.
Slow Impeller Speed	For Inform ation	40 RPM	40 RPM	40 RPM
Mixing time (After adding purified water)	01-02 min.	02 min.	02 min.	02 min.
Slow Impeller Speed	For Inform ation	40 RPM	40 RPM	40 RPM
(Slow Chopper)				
Mixing Time (After Raking)	01-02 min.	01 min.	02 min.	01 min.
Fast impeller speed (Fast chopper speed)	For Inform ation	103 RPM	103 RPM	103 RPM
SEMI DRYING				
Air drying Time	10 - 20 min.	20 min.	20 min.	20 min.
Sieve size	12#	12#	12#	12#
Dutch mesh Integrity before use	Should be intact	Intact	Intact	Intact
Dutch mesh Integrity after use	Should be intact	Intact	Intact	Intact
FINAL DRYING				
Drying time	To be recorde d	30 min.	30 min.	30 min.
Inlet Temp.	60 ± 5 °C	62 °C	62 °C	62 °C
Outlet Temp.	30 - 35 °C	32 °C	32 °C	32 °C
LOD at Drying Stage	1.0 to 2.0 %	1.28 %	1.47%	1.30%

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Parameters	Acceptance Criteria	Batch No.: SITA-1	Batch No.: SITA-2	Batch No.: SITA-3
SIFTING & MILLING				
Sieve Size	24#	24#	24#	24#
Sieve integrity before	Should be intact	Intact	Intact	Intact
Sieve integrity after	Should be Intact	Intact	Intact	Intact
Screen Size	1.0 mm	1.0 mm	1.0 mm	1.0 mm
Screen Integrity before	Should be intact	Intact	Intact	Intact
Screen integrity after	Should be intact	Intact	Intact	Intact
Knives direction	Forward	Forward	Forward	Forward
SIFTING OF LUBRICATION MATERIAL				
Sieve Size	40#, 60#	40#, 60#	40#, 60#	40#, 60#
Sieve integrity before	Should be intact	Intact	Intact	Intact
Sieve integrity after	Should be Intact	Intact	Intact	Intact
MIXING				
Mixing Time	10 min.	10 min.	10 min.	10 min.
Mixing Speed	For Information	12 RPM	12 RPM	12 RPM
LUBRICATION				
Mixing Time	05 min.	05 min.	05 min.	05 min.
Mixing Speed	For Information	12RPM	12 RPM	12 RPM

Table 6: Analytical Results of Lubricated Granules:

Sampling Point	Parameters	Acceptance Criteria	Observed Results		
			Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
Composite	Description	White to off white coloured granular powder.	Complies	Complies	Complies
	Identification	The retention time of the major peak in the chromatogram of the test solution should correspond to the peak in the chromatogram obtained with reference solution (a) as directed in the assay.	Complies	Complies	Complies
	LOD	1.0 to 2.0 %	1.62 %	1.65 %	1.68 %

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Sampling Point	Parameters		Acceptance Criteria	Observed Results		
				Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
	Bulk Density		To be Recorded	0.60 g/ml	0.68 g/ml	0.77 g/ml
	Tapped Density		To be Recorded	0.70 g/ml	0.80 g/ml	0.81 g/ml
Composite	Compressibility Index		To be Recorded	0.14	0.15	0.05
	Angle of repose		To be Recorded	28.37°	32.82°	29.68°
	Hausner Ratio		To be Recorded	1.17	1.18	1.05
Sieve analysis		20#	To be Recorded	100% Passed	100 % Passed	100 % Passed
		40#		96.8 % Passed	69.5 % Passed	82.3 % Passed
		60#		96.6 % Passed	69.5 % Passed	51.8 % Passed
		80#		83.2 % Passed	52.2 % Passed	36.6 % Passed
		100#		80.5 % Passed	51.4 % Passed	33.0 % Passed
Assay						
Sitagliptin Phosphate			95.0 % to 105.0 %	100.5 %	99.8 %	103.4 %

Table 7: Blend Uniformity Results

Blend Uniformity:					
Sampling Point	**Parameters**	**Acceptance Criteria**	**Observed Results**		
			Batch No.: SITA-1	**Batch No.: SITA-2**	**Batch No.: SITA-3**
Top Left (S1)	Blend Uniformity	±10% of absolute mean	99.48 %	99.33 %	101.36 %
Tope Right (S2)			97.78 %	98.47 %	100.42 %
Top Centre (S3)			96.15 %	100.08 %	103.59 %
Middle Left (S4)			100.56 %	100.39 %	102.34 %
Middle Right (S5)			98.00 %	98.91 %	103.28 %

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Blend Uniformity:					
Middle Rear (S6)			99.87 %	97.76 %	100.58 %
Middle Front (S7)			100.01 %	100.18 %	101.86 %
Bottom Left (S8)			98.18 %	101.42 %	102.18 %
Bottom Right (S9)			96.55 %	99.83 %	101.12 %
Bottom Centre (S10)			98.12 %	97.39 %	101.77 %
Mean			98.47 %	99.38 %	101.85 %
Relative standard deviation (RSD)		NMT 5 %	1.502 %	1.262 %	1.028%

Table 7: Critical Process Parameters (Compression Stage)

Process	**Critical Process Parameter (CPP)**	**Critical Quality Parameter (CQP)**
Compression Process	Compression RPM	Description, Average weight, Uniformity of weight, Thickness, Hardness, Length, Width, Friability, Assay, Dissolution

Table 8: Observed Results (Critical Process Parameters – Compression Stage)

S.NO.	**Test Parameter**	**Acceptance Criteria**	**Batch no. SITA-1**	**Batch no. SITA-2**	**Batch no. SITA- 3**
1.	Tablet compression Machine speed (RPM)	12-25	18	18	18

Table 9: Analytical Results of Compressed Tablet (CQPs)

S.NO.	**Test Parameter**	**Acceptance Criteria**	**Batch no. SITA-1**	**Batch no. SITA-2**	**Batch no. SITA- 3**
1.	Description	Light Brown coloured, round, biconvex, film-coated tablets, plain on both sides.	Complies	Complies	Complies
2.	Group weight of 20 tablets	8.00 g ± 3%	8.02 g	8.04 g	8.05 g
3.	Average weight	400 mg ± 3%	403.30 mg	402.87 mg	407.02 mg
4.	Diameter	10.0 mm ± 0.20 mm Min.	10.08 mm	10.08 mm	10.08 mm

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S.NO.	Test Parameter	Acceptance Criteria		Batch no. SITA-1	Batch no. SITA-2	Batch no. SITA- 3
			Max.	10.12 mm	10.25 mm	10.13 mm
5.	Thickness	4.30 mm to 0.20 mm	Min.	4.25 mm	4.12 mm	4.25 mm
			Max.	4.32 mm	4.20 mm	4.34 mm
6.	Hardness	NLT 10.0 kgf	Min.	5.12kgf	5.17 kgf	4.75 kgf
			Max.	5.45 kgf	5.45 kgf	5.17 kgf
7.	Disintegration Time	NMT 8.0 minutes		02 min. 18 sec.	02 min. 07 sec.	02 min. 07 sec.
8.	Friability (≥ 6.5 g/100	NMT 1.0 %w/w		0.29% w/w	0.37% w/w	0.27 % w/w
9.	Uniformity of weight	400 mg ± 7.5 %	Min.	398.9mg	397.60 mg	398.0 mg
			Max.	404.4mg	403.9 mg	404.2 mg
10.	Dissolution	Not less than 75.0% of labeled amount	Min.	99.4 %	101.7 %	82.3 %
			Max.	102.9 %	107.0 %	92.0 %
			Avg.	101.2 %	103.6 %	97.3 %
11.	Assay: Each film-coated tablet contains:					
	Sitagliptin Phosphate Monohydrate IP eq. to Sitagliptin.. . 100mg	95.0 to 105.0% of the labeled amount		99.2 %	98.2%	100.3 %

Table 10: Critical Process Parameters (Coating Stage)

Process	CPP	CQA
Coating Process	Pan RPM, Peristaltic pump RPM, Bed to gun distance, Inlet air temperature, bed temp., outlet temp., atomization air gauge, fan air, gauge. Number of guns, spray rate, spray gun aperture, weight gain	Description, Average weight, Uniformity of weight, Thickness, Diameter, Assay, Dissolution, Residual Solvent.

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Table 11- Observed Results (Critical Process Parameters – Coated stage)

Processing Stage	CPP	Acceptance Criteria	Observed Results		
			SITA- 1	SITA 2	SITA 3
Preparation of film dispersion	Stirring Time	45 min	45 min	45 min	45 min
	Description	Homogeneous dispersion	Homogeneous dispersion	Homogeneous dispersion	Homogeneous dispersion
Coating Process	Pan RPM	1 -5 RPM	1-3.5 RPM	1-4 RPM	1-2 RPM
	Peristaltic pump RPM	30-45 RPM	30 RPM	35 RPM	35 RPM
	Inlet air temperature	45°C° to 55°C	50-54 °C	50-54 °C	52-54 °C
	Bed temperature	32°C to 42°C	38-41°C	38-40°C	39-40°C
	Outlet temperature	30°°C to 40°C	35-39 °C	36-38°C	34-35°C
	Spray Gun Aperture	1.5 mm	1.5 mm	1.5 mm	1.5 mm
	Spray Rate	120 to 220gm/min	130.59 g/min.	155.86 g/min.	136.68 g/min.
Drying of Film Coated Tablet	Bed Temperature	40 °C to 45 °C	42.6 °C	42.2 °C	42.4 °C
	Drying time	10 – 15 min	12	12	12
In-Process Check for Film Coated Tablet	Description	Light Brown coloured, round, biconvex, film-coated tablets, plain on both sides.	Complies	Complies	Complies
	Average weight	400 mg ± 3%	403.30 mg	402.87 mg	407.02 mg
	% of weight gain	4.00 ± 0.50 % m/m	4.07 % m/m	4.19 % m/m	4.06 % m/m

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Table 12- Analytical results of coated tablets:

S.NO.	Test Parameter	Acceptance Criteria		Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
1.	Description	Light Brown coloured, round, biconvex, film coated tablets, plain on both sides.		Complies	Complies	Complies
2.	Identification	The retention time of the major peak in the chromatogram of test solution should correspond to the peak in the chromatogram obtained with reference solution (a) as directed in the assay.		Complies	Complies	Complies
3.	Diameter	9.90 mm to 10.30 mm	Min.	10.13 mm	10.14 mm	10.10 mm
			Max.	10.16 mm	10.17 mm	10.15 mm
4.	Thickness	4.10 mm to 4.50 mm	Min.	4.34 mm	4.14 mm	4.20 mm
			Max.	4.38 mm	4.35 mm	4.27 mm
5.	Disintegration Time	Not more than 15 minutes		02 min. 18 sec.	02 min. 07 sec.	02 min. 07 sec.
6.	Average weight	397.70 to 422.30 mg		411.29 mg	412.22 mg	412.98 mg
7.	Uniformity of weight	Not more than 2 tablets in 20 deviates from the average weight by more than 5%. No tablet deviates from the average weight by more than 10%.		-1.44 to + 0.90 %	-3.16 to + 1.78 %	-1.96 to + 3.29 %
8.	Dissolution (D) 70%	Not less	Min.	83.7%	77.6 %	77.2 %

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S.NO.	Test Parameter	Acceptance Criteria		Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
		than 75.0 % of labeled amount	Max.	96.1%	86.6 %	92.0 %
			Avg.	90.3%	83.3 %	84.5 %
9.	Related Substance					
	Single Maximum Unknown Impurity	Not more than 0.2%		Below Disregard Limit	Below Disregard Limit	Below Disregard Limit
	Total Impurities	Not more than 0.5%		Below Disregard Limit	Below Disregard Limit	Below Disregard Limit
10.	Residual Solvent					
	Isopropyl Alcohol	Not more than 5000 ppm		105 ppm	392 ppm	81 ppm
	Dichloromethane	Not more than 600 ppm		Not Detected	Not Detected	Not Detected
	Assay: Each film coated tablet contains:					
11.	Sitagliptin Phosphate Monohydrate IP eq. to Sitagliptin...100mg	95.0 to 105.0% of labeled amount		98.2%	98.2 %	98.2 %

Table 13- Finished Product Results:

S.NO.	Test Parameter	Acceptance Criteria	Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
1.	Description	Light Brown coloured, round, biconvex, film coated tablets, plain on both sides.	Complies	Complies	Complies

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S.NO.	Test Parameter	Acceptance Criteria		Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
2.	Identification	The retention time of the major peak in the chromatogram of test solution should correspond to the peak in the chromatogram obtained with reference solution (a) as directed in the assay.		Complies	Complies	Complies
3.	Diameter	9.90 mm to 10.30 mm	Min	10.13 mm	10.14 mm	10.10 mm
			Max	10.16 mm	10.17 mm	10.15 mm
4.	Thickness	4.10 mm to 4.50 mm	Min	4.34 mm	4.14 mm	4.20 mm
			Max	4.38 mm	4.35 mm	4.27 mm
5.	Disintegration Time	Not more than 15 minutes		02 min. 18 sec.	02 min. 07 sec.	02 min. 07 sec.
6.	Average weight	397.70 to 422.30 mg		411.29 mg	412.22 mg	412.98 mg
7.	Uniformity of weight	Not more than 2 tablets in 20 deviates from the average weight by more than 5%. No tablet deviates from the average weight by more than 10%.		-1.44 to + 0.90 %	-3.16 to + 1.78%	-1.96 to + 3.29 %
8.	Dissolution 70% (D)	Not less than 75.0% of labeled amount	Min.	83.7 %	77.6%	77.2 %
			Max.	96.1 %	86.6%	92.0 %
			Avg.	90.3 %	83.3%	84.5 %
9.	Related Substance					

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S.NO.	Test Parameter	Acceptance Criteria	Batch No. SITA-1	Batch No. SITA-2	Batch No. SITA-3
	Single Maximum Unknown Impurity	Not more than 0.2%	Below Disregard Limit	Below Disregard Limit	Below Disregard Limit
	Total Impurities	Not more than 0.5%	Below Disregard Limit	Below Disregard Limit	Below Disregard Limit
10.	Residual Solvent				
	Isopropyl Alcohol	Not more than 5000 ppm	105 ppm	392 ppm	81 ppm
	Dichloromethane	Not more than 600 ppm	Not Detected	Not Detected	Not Detected
11.	Assay: Each film coated tablet contains:				
	Sitagliptin Phosphate Monohydrate IP eq. to Sitagliptin...100 mg	95.0 to 105.0% of labeled amount	98.2 %	98.2%	98.2 %

5. Conclusion

The process validation of Sitagliptin Film-Coated Tablet 100 mg, which had not been previously performed, was initiated through a novel approach. Process validation of the product Sitagliptin Film-Coated Tablet 100 mg to be carried out with three consecutive batches. During the process validation, critical process parameters and critical quality attributes were checked at the granulation, compression stage, and coating stage. Three initial validation batches were executed using identical methods, equipment, and validation criteria. Critical parameters across various stages, including sifting, mixing, granulation, drying, sizing, compression, and coating, were identified and assessed according to the validation master plan. During the evaluation of critical quality attributes, samples were collected at different locations of the coating pan, and a composite sample was made from different locations of the pan. The composite sample was analyzed by Quality Control (QC) as per the finished product specification, and all analytical results were found within the specified limit.

Based on the observed results at different stages, it is concluded that process validation of Sitagliptin Film-Coated Tablet 100 mg was carried out as per the respective protocol, and the observed results of critical process parameters and critical quality attributes were found within the specified limit. The finished product results of the batch were **found within the specified limit recommendation.**

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