IJPSR (2021), Volume 12, Issue 10 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 23 October 2020; received in revised form, 11 February 2021; accepted, 23 June 2021; published 01 October 2021

CONCURRENT PROCESS VALIDATION OF GLIBENCLAMIDE 2.5 MG TABLET

Prashant B. Patil [1], Vilas L. Badgujar [2], Rajendra D. Wagh [2] and Kundan H. Deore [*3]

H. R. Patel Institute of Pharmaceutical Education & Research [1], Shirpur - 425405, Maharashtra, India.
DCS's A.R.A. College of Pharmacy [2], Nagaon, Dhule - 424005, Maharashtra, India.
NES's Gangamai College of Pharmacy [3], Nagaon, Dhule - 424005, Maharashtra, India.

Keywords:

Glibenclamide, Assay, Concurrent, Tablets

Correspondence to Author:
Mr. Kundan Hemant Deore

Assistant Professor,
NES's Gangamai College of Pharmacy, Nagaon, Dhule - 424005, Maharashtra, India.

E-mail: kundan2321994@gmail.com

ABSTRACT: The present study of concurrent process validation delivers an extraordinary degree of quality assurance that a specific process for manufacturing of Glibenclamide Tablets will consistently manufacture a product that meets its predetermined quality attributes and specifications. Glibenclamide is generally suggested for the treatment of type II diabetes mellitus and it is mainly a sulfonylurea derivative. It mainly comprises the stages to be followed to evaluate and qualify the acceptability of the manufacturing process of Glibenclamide 2.5 mg tablets. The process is limited to the three batches H, I, and J manufactured of specific batch size with the help of specified equipment's and different quality control parameters for tablets. It involves all parameters related to each step were evaluated by the respective standard test involved in the manufacturing. All analytical results of each stage were found to be within the acceptable limit and criteria. Other tests related to compression such as hardness, thickness, disintegration and dissolution for all three batches were also found within the acceptable limit.

INTRODUCTION: Validation is defined as the process of founding through a documented database program, which provides a high degree of assurance that a specific process will constantly produce a product meeting its pre-determined specifications and critical quality attributes. The word validation simply means 'assessment of validity' or 'action of proving effectiveness' a validated manufacturing process is one, which has been proved to do what it purports to or is represented to do.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(10).5407-13

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(10).5407-13

Validation essentially contains process qualification (the qualification of materials, equipment, system, buildings and personnel, *i.e.*, Design Qualification, Installation Qualification, Operation Qualification, Performance Qualification).

Process Validation is defined as the collection and evolution of data from the process design stage throughout production, which establishes scientific evidence that a process can consistently deliver quality products. It assures Quality, Safety and efficacy. The process validation is the analysis of data collected throughout the design and manufacturing of a product to endorse that the process gives consistent production of products with a given standard. The main aim of process validation of Glibenclamide is to ensure various inputs lead to consistent and great quality productions and its continuing process that must be

regularly improved as manufacturing feedback is gathered. Glibenclamide, also known as glyburide, is an anti-diabetic drug in the class of medications known as sulfonylurea and thoroughly related to sulfonamide antibiotics. Glibenclamide, it's a second-generation sulfonylurea commonly used to treat type II diabetes mellitus. Glibenclamide was firstly granted FDA approval on May 01, 1984 and formulation with metformin was granted FDA approval on July 31, 2000. Glibenclamide is a sulfonylurea derivative and is recommended for the treatment of type II diabetes mellitus. Glibenclamide goes through the hepatic first-pass effect in its oral administration, such that only 45% of the drug is absorbed and considering its short half-life, the persistent has to take the drug in several divided doses to maintain the desired therapeutic effect. Gastrointestinal adverse effects of Glibenclamide have been reported for the drug, which decreases the patients' compliance.

Process Validation Should Proceed in the following Condition

- Processes remained finished products tests are poor
- When implementing new processes for manufacturing of the product
- When new equipment's are installed or used in the manufacturing process
- Process and equipment which are having altered suit changing the priority

MATERIALS AND METHODS: Concurrent process validation was performed on the three batches of Glibenclamide 2.5 mg Tablets. The three consecutive batches were labeled as (Batch E, Batch F and Batch G) [3-9]. List of Equipment and Stages indicate a list of equipment used in the manufacturing process of Glibenclamide 2.5 mg tablets and listed the involved equipment in which manufacturing stage details are mentioned in **Table 1**.

Details of input material indicate material or ingredients used in manufacturing Glibenclamide 2.5 mg tablets with their category, which is shown in **Table 2**. Sampling and Testing Plan indicates the planning for sampling and testing with their manufacturing stage, procedure, quantity to be sampled, and acceptance criteria for sampling to manufacture Glibenclamide 2.5 mg tablets described in **Table 3**. The manufacturing process flow chart indicates the manufacturing stages of the manufacturing process of Glibenclamide 2.5 mg tablets depicted in **Fig. 1**.

TABLE 1: LIST OF EQUIPMENT'S

Equipment	Stages Involved In
Weighing balance	All stages
Vibratory sifter (30inch)	Sifting of raw materials
Rapid Mixer Granulator	Dry mixing and granulation
Fluid bed drier (250 kg)	Drying
Multi-mill(50 T0 250 Kg/Hrs)	Sizing
Octagonal Blender (1200 Lit)	Blending
Compression machine.	Compression
Friability test apparatus	To check friability
Hardness tester	To check hardness
Dissolution Apparatus	Dissolution Testing
Disintegration apparatus	To check disintegration time
Blister Packing Machine	For Packing of Tablets
UV Spectrophotometer	For Analysis
HPLC	For Analysis

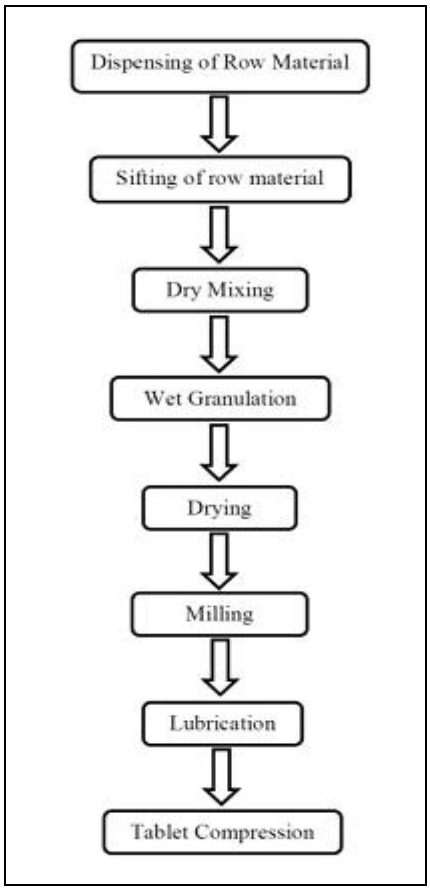

FIG. 1: MANUFACTURING PROCESS FLOW CHART OF GLIBENCLAMIDE 2.5 mg TABLET

TABLE 2: LIST OF INGREDIENTS

Ingredients	Used purpose
Glibenclamide	Active Ingredient
Lactose Monohydrate	Diluents
Maize Starch	Binder
Povidone K30	Diluents
Magnesium Stearate	Lubricant
Purified Water	Solvent

RESULTS AND DISCUSSION: These results and discussion are limited to evaluating three consecutive batches of Glibenclamide 2.5 mg tablets for concurrent process validation. Three manufacturing batches are validated in concurrent process validation; the batches are labeled as Batch E, Batch F, Batch G at blend stage, compression stage and packing stage.

TABLE 3: SAMPLING AND TESTING PLAN

Stage	Sample Location	Test
Dry mixing	After completion of drying, draw a composite sample from 11 different location of RMG after 5 min, 10 min and min of mixing of API and excipients	Blend uniformity
Drying	Samples of dried granules shall be withdrawn from the five different sampling points	Loss on Drying
Lubrication Stage	Unit dose samples shall be withdrawn from the eleven different locations of the octagonal blender	Blend uniformity
Lubricated Blend	Approximately 300 g of the lubricated bulk blend to be sampled for a characteristic physical evaluation.	Physical characteristics Description Bulk density Tapped density Angle of repose Particle size analysis Assay Sieve analysis.
Compression Stage Minimum speed Optimum speed Maximum speed	During compression, samples to be collected & mixed from both sides of the press(RHS and LHS) at the initial, middle and at the end of the compression operation	Description Average weight Uniformity of Weigh Friability Hardness Thickness Dissolution Content uniformity
Finished Product	After the final compression of tablets before packing, this analysis is carried.	Assay Dissolution Content Uniformity

Product Details-Product Name: Glibenclamide Tablets 2.5 mg.

Dry Mixing: Dry mixing was carried out in Rapid Mixer Granulator for 10 minutes, and samples were collected from eleven different six locations for Blend Uniformity. The blend uniformity test was performed and the acceptance criteria for it is individual values should be between 90.0% to 110.0% of the labeled amount of Glibenclamide with RSD not more than 5%; the results are described in **Table 4**. The RSD of Glibenclamide Tablets for all three validation batches were within found within the specification. Based on % RSD data of Glibenclamide Tablets for three validation batches, it was evident that the dry mixing throughout the sampling locations and all their results are found within acceptable limit.

TABLE 4: DRY MIXING STAGE BLEND UNIFORMITY RESULTS

S. no.	Location	Acceptance Criteria	Batch E	Batch F	Batch G
1	T1	Individual values should be between 90.0 % to 110.0 % of labeled amount of Glibenclamide with RSD NMT 5%.	101.7	101.7	101.7
2	T2		101.3	101.3	101.3
3	T3		101.0	101.0	101.0
4	B1		100.6	100.6	100.6
5	B2		101.1	101.1	101.1
6	B3		101.3	101.3	101.3

	Minimum	100.6	100.6	100.6
	Maximum	101.7	101.7	101.7
	Mean	101.6	101.6	100.6
	% RSD	0.3	0.3	0.3

T: Top, B: Bottom

Drying Analysis: The drying analysis carried for the % LOD of dried granules of Glibenclamide analysis with the help of or air oven. The samples were collected from the fluidized bed dryer bowl from the top, middle and bottom side and their results are shown in **Table 5**. % loss of drying of dried granules of Glibenclamide was within the range 7.32 to 7.81 w/w at 120 °C for 20 min respectively for all three validation batches, which were within the acceptable limit.

TABLE 5: RESULTS OF DRYING HOMOGENEITY ANALYSIS

S. no.	Limit 7.3 to 8.0 w/w at 120 °C for 20 min	Batch E	Batch F	Batch G
1	Top	7.32	7.31	7.34
2	Middle	7.81	7.87	7.82
3	Bottom	7.88	7.83	7.90

Analytical Data for Lubricated Blend: Blending was carried out in the Octagonal Blender for 13 minutes, and samples were collected from 12 different locations (12-points) for test Blend Uniformity such as upper site, middle site, lower side, and bottom. The results are as follows in **Table 6**. % RSD of Glibenclamide for all three validation batches were within the range 1.08 to 1.16, which were found within the acceptance criteria. % RSD of Glibenclamide for all three validation batches. It was evident that no segregation occurs in the blender and mixing is homogeneous throughout the sampling locations and their points are depicted in **Fig. 2**.

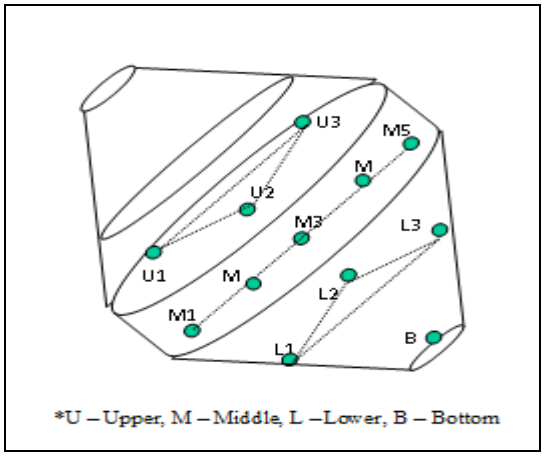

FIG. 2: SAMPLING LOCATION IN DOUBLE CONE BLENDER

TABLE 6: RESULT OF BLEND UNIFORMITY OF LUBRICATED BLEND

S. no.	Location	Acceptance Criteria	Batch E	Batch F	Batch G
1	U1	Individual values should be between 90.0 % and	97.0	96.9	96.8
2	U2	110.0 % of labeled amount of Glibenclamide with	98.9	99.0	98.8
3	U3	RSD not more than 5.0 %	98.3	98.4	98.6
4	M1		100.2	100.4	100.3
5	M2		98.4	98.3	98.5
6	M3		98.4	98.6	98.4
7	L1		98.7	98.6	98.5
8	L2		100.5	100.7	100.6
9	L3		100.1	100	100.2
10	BO		99.1	99.3	99.4
		Minimum	97.0	96.9	96.8
		Maximum	100.5	100.7	100.6
		Mean	97.0	96.9	99.01
		% RSD	0.79	0.88	1.05

Analysis of Lubricated Blend: Lubricated blend analysis is done by different parameters like blend, assay, loss on drying, bulk density, tapped density, and sieve test parameters; their results are described in **Table 7**. Description, Assay, loss on drying, bulked density, tapped density sieve test of the lubricated blend of Glibenclamide for three validation batches were within the acceptable specification and criteria.

TABLE 7: RESULTS OF ASSAY OF LUBRICATED BLEND

Test	Acceptance Criteria		Observation		
			Batch E	Batch F	Batch G
Description	White granules free from extraneous matter (blend)		Complies	Complies	Complies
Assay	2.375 mg to 2.625 mg of Glibenclamide per average weight of Blend NMT 95.0% and NMT 105.0% of label claim of Glibenclamide		97.4	98.0	98.3
Loss on Drying	For information only		8.67	8.80	8.35
Bulk Density	For information only		0.6948 mg/ml	0.7132 mg/ml	0.6890 mg/ml
Tapped Density	For information only		0.83 g/ml	0.88 g/ml	0.91 g/ml
		Sieve no.			
		20 #	93.3%	94.5%	93.6%
Sieve Test	For information only	40 #	70.0%	69.0%	69.4%
		60 #	60.3%	60.0%	61.3 %
		80 #	57.1%	57.4%	56.9%
		100 #	47.0%	47.4%	46.5%

Physical Characteristics of Lubricated Blend: Physical characteristics of the lubricated blend were done by a description of the lubricated blend, bulk density, tapped density, loss on drying, angle of repose, and particle size distribution parameters, and their results are shown in **Table 8**. The physical parameter of a lubricated blend, such as description, bulk density, tapped density, loss on drying, and particle size distribution for three validation batches was satisfactory and found consistent within the acceptable limit. No significant observation related to the flow of the blend was observed throughout the compression activity.

TABLE 8: PHYSICAL CHARACTERISTIC OF LUBRICATED BLEND

S. no.	Parameter	Batch E	Batch F	Batch G
1	Description	White Colored Powder blend	White Colored Powder blend	White Colored Powder blend
2	Bulk density gm/ml	0.67	0.64	0.67
3	Tapped density gm/ml (500taps)	0.70	0.70	0.71
4	Loss On Drying	2.0%	1.53%	1.57%
5	Angle of Repose	24.11	23.40	24.11
6	Particle Size Distribution	Cumulative Retention (%)	Cumulative Retention (%)	Cumulative Retention (%)
	Above 20#	1.74 %	98.5 %	98.5 %
	Above 60#	24.61 %	49.6 %	75.6 %
	Above 80#	40.63 %	28.4 %	59.6 %
	Above 100#	45.58 %	24.3 %	54.8 %

Compression Stage Physical Parameters: During compression, samples from the compression machine at minimum speed and maximum speed were collected from three consecutive batches for performing physical parameters. The physical parameters checks as description, average weight, uniformity of weights, thickness, hardness, friability, disintegration, assay, dissolution test performed. The results are as follows in **Table 9**. The physical parameter of Glibenclamide tablet at Minimum Speed (2200 Tabs/min) and Maximum Speed (2750 Tabs/ Min) of compression for three validation batches X, Y, Z were found in the range within the acceptance criteria and specification.

TABLE 9: COMPRESSION STAGE PHYSICAL PARAMETERS BACH X, BATCH Y, AND BATCH Z

Test	Acceptance Criteria	Minimum Speed (2200 Tabs/min)		Maximum Speed (2750 Tabs/ Min)	
		LHS	RHS	LHS	RHS
		Batch E			
Description	White circular tablets debossed with GL/2.5 on one side	Complies	Complies	Complies	Complies
Average Weight	80.0 mg ± 5 % (76.0 to 84.0 mg)	83.9 mg	82.5 mg	81.1 mg	80.9 mg
Uniformity Weight	NMT 2 tablets deviate by more than ± 10 % from the average	-2.05 to +1.57%	-1.60 to +2.09%	-2.37 to +2.62%	-3.37 to +5.35%

	weight and none deviate by ±20 % from the average weight				
Hardness	19.6 N to 49.0 N	Min – 33 Max - 45	Min – 32 Max - 36	Min – 30 Max – 36	Min – 29 Max – 33
Thickness	2.50 to 3.00 mm	Min – 2.82 Max – 2.88	Min – 2.76 Max – 2.82	Min – 2.76 Max – 2.82	Min – 2.75 Max – 2.84
Friability	Not more than 1 % w/w	0.27 %	0.23 %	0.25 %	0.23 %
Disintegration	Not more than 8 minutes	01 min 49 sec	01 min 7 sec	01 min 17 sec	01 min 37 sec
			Batch F		
Description	White circular tablets debossed with GL/2.5 on one side	Complies	Complies	Complies	Complies
Average Weight	80.0 mg ± 5 % (75.0 to 85.0 mg)	81.8 mg	82.5 mg	80.8 mg	83.2 mg
Uniformity Weight	NMT 2 tablets deviate by more than ± 10 % from the average weight and none deviate by ±20 % from the average weight	-2.02 to +1.50%	-1.53 to +2.07%	-2.26 to +2.57%	-3.31 to +5.34%
Hardness	19.6 N to 49.0 N	Min – 31 Max - 40	Min – 29 Max - 34	Min – 30 Max – 37	Min – 25 Max – 29
Thickness	2.50 to 3.00 mm	Min – 2.57 Max – 2.88	Min – 2.66 Max – 2.80	Min – 2.78 Max – 3.00	Min – 2.71 Max – 2.85
Friability	Not more than 1 % w/w	0.35 %	0.33 %	0.32 %	0.30 %
Disintegration	Not more than 8 minutes	01 min 45 sec	01 min 29 sec	01 min 25 sec	01 min 30 sec
			Batch G		
Description	White circular tablets debossed with GL/2.5 on one side	Complies	Complies	Complies	Complies
Average Weight	80.0 mg ± 5 % (75.0 to 85.0 mg)	83.5 mg	81.7 mg	81.7 mg	82.7 mg
Uniformity Weight	NMT 2 tablets deviate by more than ± 10 % from the average weight and none deviate by ±20 % from the average weight	-2.14 to +1.56%	-1.52 to +2.10%	-2.28 to +2.63%	-3.37 to +5.37%
Hardness	19.6 N to 49.0 N	Min – 39 Max - 25	Min – 35 Max - 43	Min – 33 Max – 40	Min – 33 Max – 37
Thickness	2.50 to 3.00 mm	Min – 2.58 Max – 2.80	Min – 2.74 Max – 2.87	Min – 2.70 Max – 2.90	Min – 2.75 Max – 2.90
Friability	Not more than 1 % w/w	0.35 %	0.29 %	0.31 %	0.27 %
Disintegration	Not more than 8 minutes	01 min 30 sec	01 min 26 sec	01 min 17 sec	01 min 23 sec

Compression Stage Analytical Results: Compression stage analysis in their content uniformity, assay by HPLC and dissolution were checked at minimum speed and maximum speed as same as to physical parameters and results described in **Table 10**. % dissolution of Glibenclamide at Optimum speed of compression for three validation batches E, F & G were found in the range within the acceptance criteria.

TABLE 10: COMPRESSION STAGE ANALYTICAL RESULTS

Test	Acceptance Criteria		Batch E		Batch F		Batch G	
			Min Speed	Max Speed	Min Speed	Max Speed	Min Speed	Max Speed
Uniformity of dosage (by content uniformity)	Less than or equal to 15.0		4.8	4.4	4.5	5.3	4.9	5.1
Assay (By HPLC)	95.0 % to 105.0 % of label amount of glibenclamide		97.8%	96.2%	97.2%	99.0%	97.4%	98.8%
Dissolution Profile in %	Limit between 45 % to 70 % after 30 min	Min	56	58	57	59	58	59
		Max	60	62	61	63	59	61
		Avg.	58	60	59	61	59	60

Analysis of Compressed Tablet: The analysis of compressed tables is done by assay, content uniformity and dissolution rate of Glibenclamide compressed tablets results are shown in **Table 11**. Assay, content uniformity, and dissolution rate of Glibenclamide at initial, middle, end and composite stage of compression at optimum were found within the acceptable limit of Glibenclamide 2.38 to 2.63 mg/tablets.

TABLE 11: RESULTS OF ANALYSIS OF COMPRESSED TABLET

Parameter	Acceptance limit	Observation		
		Batch E	**Batch F**	**Batch G**
Assay (HPLC)	Glibenclamide 2.36 to 2.65 mg/tablets	2.46 mg/tablets	2.48 mg/tablets	2.49 mg/tablets
Content Uniformity	Less than or equal to 15.0	4.8	4.7	4.9
Dissolution	45 to 70 % after 30 min	Min – 57 %	Min – 58 %	Min – 57 %
		Max- 61 %	Max- 62 %	Max- 61 %
		Avg – 59 %	Avg – 60 %	Avg – 59 %

*Min: Minimum, Max: Maximum, Avg: Average

CONCLUSION: The concurrent process validation of Glibenclamide 2.5 mg tablet has been performed for three batches X, Y, and Z. All the parameters and results were found within the acceptance limit at all stages, such as dry mixing, wet granulation, drying, milling, lubrication and compression. Based on the results of the validation data for three batches X, Y and Z, it was concluded that the manufacturing process used for the formulation of Glibenclamide 2.5 mg tablet will consistently produce the stable product meeting its predetermined specifications and quality attributes. Hence, it can be concluded that the method employed in the manufacture of the given Glibenclamide 2.5 mg tablet is considered to be validated and can be routinely followed.

ACKNOWLEDGEMENT: The authors are thankful to Wockhardt Ltd., Aurangabad.

CONFLICTS OF INTEREST: The authors declare that there is no conflict of interest regarding the publication of this paper.

REFERENCES:

1. Prashant BP, Rupesh K and Zamir GK: Process Validation of Bethanechol Chloride Tablet 25 mg. International Journal of Pharmaceutical, Chemical & Biological Sciences 2016; 6(2): 167-81.
2. Agalloco J: Validation: an unconventional review and reinvention. PDA Journal of Pharmaceutical Science and Technology 1995; 49(4): 175-9.
3. Global Harmonization Task Force (GHTF), Quality Management System, Process Validation Guidance, Study Group – 3, January 2004: 6-7.
4. Patil PB, Nandwalkar RK and Khan ZG: Prospective Process Validation Study of Nifedipine Extended Release Tablets. Inventi Rapid: Pharm Analysis & Quality Assurance 2016; 3: 1-7.
5. Kour G: Process Validation of Metered Dose Inhaler, Inter. Jour of Res Pharm 2012; 3(3): 55-59.
6. Patil PB, Nandre AN, Bari SB and Khan ZG: Concurrent process validation study of cilnidipine and chlorthalidone tablets. Inventi Rapid: Pharm Analysis & Quality Assurance 2016; 4: 1-7.
7. Vinod J: Process Validation of Atrovastatine Tablet 1 mg. Indo American Jour of Pharma Res 2013; 3(12): 1438-50.
8. Guidance for Industry Process Validation: General Principles and Practices (PDF). Food and Drug Administration. Retrieved 16 December 2014.

How to cite this article:
Patil PB, Badgujar VL, Wagh RD and Deore KH: Concurrent process validation of glibenclamide 2.5 mg tablet. Int J Pharm Sci & Res 2021; 12(10): 5407-13. doi: 10.13040/IJPSR.0975-8232.12(10).5407-13.