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PROCESS VALIDATION OF PANTOPRAZOLE GASTRO-RESISTANT AND DOMPERIDONE PROLONGED-RELEASE CAPSULES IP

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ABSTRACT

Validating a process is gathering and analyzing data from a method's ability to consistently produce a high-quality medicinal component from the process design stage to production in order to create scientific evidence. The purpose of the validation is to ensure that quality is integrated throughout the system rather than just assessed for at the conclusion. It comprises the collection and evaluation of data, beginning with the process design stage and continuing through production, that establishes scientific confirmation that a method is capable of reliably producing a high-quality pharmacological ingredient. A study demonstrates the efficacy of the pantoprazole gastro-resistant and the delayed release capsule for domperidone. Sifting, dry mixing, granulation, extrusion of wet mass, semi-drying, size reduction/milling, drying, final sifting, reprocessing, capsule filling, inspection, and packing were among the process variables that were observed for the process validation batch at the granulation stage. In accordance with the protocol for approved process validation, the sample was removed at various points. All of the analytical findings were deemed to be satisfactory and to be well within the specification parameters.

KEYWORDS: cGMPValidation of the process, capsule filling, and packing.

1. INTRODUCTION

In the middle of the 1970s, workers, first proposed the concept of validation to improve the standard of pharmaceuticals. Process validation is an essential part of quality assurance, according to cGMP. Validation and quality assurance will work together to ensure the products' high level of quality. A few factors that contribute to product quality assurance are the choice of high-quality parts and materials, proper product and process design, process

control, and in-process and end-product testing.[1,2,3] Only a few tests on finished products are highly sensitive. Final product testing doesn't always take into account all potential product changes, which could have an impact on safety.[4,5] According to the FDA's 1987 Guideline, process validation is "establishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes." Process validation was defined as "The collection and evaluation of data, from the design stage through production, which establishes scientific evidence that a process is capable of consistently delivering quality products" in the FDA's new guidelines. The handling of powder is extensive during the manufacturing of solid dosage forms. To ensure uniformity, the powder must be blended and either compressed or encapsulated into the dosage form.[6,7,8] The active ingredients and excipients in tablets are normally in the form of powder that has been compressed or pressed into a solid. disintegrates to facilitate the tablet's digestion; flavors or sweeteners to enhance flavors; In order to regulate the pace at which the active ingredient is released from the tablet, increase environmental resistance (and hence shelf life), make the tablet smoother and easier to swallow, and enhance tablet aesthetics, a polymer is often coated on it. Depending on the output volume, different manufacturing and accompanying facilities will have different sizes. Regardless of whether the facility produces thousands or millions of tablets or capsules daily, the essential validation principles will always apply.[9,10,11] It is required to show that the facility where the dosage form is made complies with the numerous technical and legal standards of cGMP in order to manufacture high-quality medications anywhere. The validation effort should be supported by the quality system's (infrastructure) quality system through document control, calibration preventive maintenance, and other techniques. These are important elements that affect how well process validation works. The process's crucial points should be determined in full and run using the system's extremes at those points (worst case scenario). The region should correspond to the requirements of validation before approval.[12,13,14] To demonstrate product consistency statistically, adequate run (data) are needed. The validation document's requirements should be followed when executing the protocol, and any variations from those criteria should be adequately documented.[15,16]

MATERIAL AND METHODS

Batch Manufacturing of Validation Batch details

Table 1: Product Details.

1	Generic name	Pantoprazole gastro resistant and Domperidone prolonged release capsules IP
2	Label Claim	Each film coated tablet contains:Pantoprazole and domperidone
3	Batch Size	Open batch size
4	Storage Condition	(77 °F) at 25 °C for storage Excursion allowed between 59 and 86 °F (15 to 30 °C)
5	Shelf Life	24 Months

Protocol for concurrent process Validation of the pantoprazole Gastric-Release and Domperidone prolonged release capsule

Table no -2.

S. No.	Section Title
1.	Objective
2.	Scope
3.	Responsibility
4.	Process Validation Team Members
5.	Number of batches subjected for validation
6.	Equipment Detail
7.	Raw Material & Packing Material
8.	Process Flow Chart
9	Manufacturing process risk assessment of process validation batches
10	Process parameter
11	Analytical Results
12	Finished Product Analytical Results

Pre-process validation requirements

Pre-requisites for process validation

- Batches must be manufactured in compliance with a valid batch manufacturing record (BMR) and specification.
- Space and equipment need to be suitable.
- Before being used, the packaging materials and raw materials for manufacture must be purchased from authorised vendors and pass a quality inspection.

METHODOLOGY

Validation of the manufacturing process is required for batches with open batch sizes. Phase III will see the product's production.

- In order to assess the product's important process parameters for quality features.

- Process control must be assessed in relation to the authorised specification.
- The final drug product must be analysed in accordance with test protocols and meet the established specification.
- Charges for stability are required for both rapid and long-term completion.

Granulation Raw Materials Details

Table 3: Raw material requisition.

Ingredient	SAP item code	Spec	AR. No/batch no			QTY reqd/lac	Qty Dispensed		
			E20937	E20950	E21054		E20937	E20950	E21054
Granules of sodium bicarbonate (SF005632)									
Dry mixing									
Sodium bicarbonate	1001559	IP	10000342768	10000342768	10000342768	16.170kg	88.550	80.850	80.850
Lactose	1000255	IP	10000354889	10000354889	10000354889	3.570kg	18.488	17.850	17.850
crospovidone	1000101	USNF	10000356181	10000356181	10000356181	0.630kg	3.450	3.150	3.150
HPMC (E3)	10001551	IP	10000342790	160374	160374	0.630kg	3.4	3.4	3.4
Binder preparation									
Purified water	NA	IP	1706	2206	0807	2.200kg	11	12	12
DOMPAM DSR CAPSULES (SF079031)									
Pantoprazole enteric coated pellets 22.5% w/w (yellow)	1001760	IH	10000356764	10000356764	10000356764	17.800Kg	89	89	89
Domperidone sustained release pellets 30%w/w (orange)	1001771	IH	10000356765	10000356765	10000356765	10.00Kg	50	50	50
Dummy granules (sodium bicarbonate)	SF005632	IH	E20937	E20937	E20937	20.000kg	100	95.310	93.310
Hard gelatin caps size ‘0’(transparent red cap/transparent clear body)	1001761	IH	10000340816	10000340816	10000340816	100000nos	5,00,000	5,00,000	5,00,000

Table 4: Packing material requisition.

Ingredients	SAP item code	A.r no/Batch no			QTY.Reqd/Lac	QTY. Dispensed / Batch no		
		E20941	E20970	E21055		E20941	E20970	E21055
DOMPAN DSR CAP: 142X0.025MM PTD BL FL FRNT-SL	2008404	10000343278	10000343278	10000343278	9.600kg	56.950	37.400	52.450
DOMPAN DSR CAP: 146X0.13MM PTD COLDBL FLM-SL	2008405	10000343468	10000343468	10000343468	34.100kg	184.020	115.7	191.1
DOMPAN DSR CAP: CARTON (10X10) SALE	2008406	10000342928	10000342928	10000342928	1000nos	5000	2900	5000
CORRU BOXES 5 PLY J-56	2008420	10000343310	10000343310	10000343310	17nos	85	50	85
GENERAL PACKING SLIPS (S)	2000132	10000354858	10000354858	10000354858	17nos	85	50	85

2.5 Packing style

Table 5: Packing style.

S.no	Stage	Pack style
1	Blister	10 capsules
2	Carton	10 X 10 capsules
3	Corrugated box	60X10X10 capsules

RESULT AND DISCUSSION

Dummy granules of sodium bicarbonate

Sifting: The sifting process in the pharmaceutical industry involves the separation of particles of different sizes. It is essential to the pharmaceutical industry's drug manufacturing process.

Table 6: Sifting.

S.no	Ingredient	Sieve size	Observed in batch nos		
			E20937	E20950	E21054
1	Sodium bicarbonate	#40	#40	#40	#40
2	Lactose	#40	#40	#40	#40
3	Crospovidone	#40	#40	#40	#40
4	HPMC (E3)	#40	#40	#40	#40

The Table 5 describes the values after executing the shifting process using different ingredients such as sodium bicarbonate, Lactose, Crospovidone and HPMC (E3) with specified sieve size #40 against the unique batch numbers such as E20937, E20950 and E21054. The outcomes revealed that the observed values fall under the specified safety range in order to manufacture the appropriate drug in the pharma industry.

Dry mixing: The blending process greatly impacts a drug's stability, visual appeal and ability to deliver an accurate dosage. Because dry blending is normally the first step in tablet production, a high-quality pharmaceutical mixing process is essential to ensure a uniform and effective finished dosage form.

Table 7: Dry mixing.

S.no	RMG parameter	Specification	Observed in batch nos		
			E20937	E20950	E21054
1	Impeller	On	On	On	On
2	Chopper	Off	Off	Off	Off
3	Speed	Slow	Slow	Slow	Slow
4	Mixing time	10min	10min	10min	10min

In Table 6, The observation values have been discussed using the different RMG parameters

such as Impeller, Chopper, Speed and Mixing time under the different setting to evaluate the results by implementing the dry mixing process to authenticate the drug stability. The batch numbers like E20937, E20950 and E21054 shows the desired results using RMG parameters as discussed in order to ensure the uniformity and effectiveness of the finished dosage form.

Granulation: It is the important step in making dosage forms for drugs by expanding the particles by an agglomeration procedure.

Table 8: Granulation.

Step	**RMG parameter**	**Specification**	**Speed**	**Observed in batch nos**		
				E20937	**E20950**	**E21054**
Binder addition	Impeller	On	Slow	6min	6min	5min
	Chopper	Off	NA			
Wet mixing	Impeller	On	Slow	2min	2min	2min
	Chopper	Off	NA			
Discharge of wet mass	Impeller	On	Slow	2min	2min	2min
	Chopper	Off	NA			
Extrusion of wet mass						
parameters	**Specification**	**Observed in batch**				
		E20937		**E20950**		**E21054**
Extrude wet mass through extruder	1.0mm die	1.0mm die		1.0mm die		1.0mm die
Semi-drying						
Parameters	**Limit**	**Observed in batch**				
		E20937		**E20950**		**E21054**
Semi dry the extrudes in FBD	Inlet below 50^0C	48^0C		49^0C		48^0C
	Outlet	33^0C		32^0C		33^0C
Size reduction						
Sieve		**Observed in batch**				
		E20937		**E20950**		**E21054**
#30		#30		#30		#30
Drying						
Parameters	**Limit**	**Observed in batch**				
		E20937		**E20950**		**E21054**
Drying time	---	40min		50min		40min
Inlet temperature	Below 50^0C	49^0C		49^0C		49^0C
Exhaust temperature	---	36^0C		37^0C		37^0C
Loss on drying						
Parameters	**Limit**	**Observed in batch**				
		E20937		**E20950**		**E21054**
LOD (5gm	NMT 1.5% w/w	1.04%		1.08%		0.82%

sample qty)	at 70^0C for 10minutes			
Reprocessing of 30# pass(under size extrudes)				
Details	**Weight**	**Observed in batch**		
		E20937	**E20950**	**E21054**
Quantity of (B) &(D) [under size granules)	…….kg	44.900kg	47.900kg	41.250kg

The Table 7 represents the result values after performing the granulation. The result values have been obtained under different conditions such as wet mass, Semi-wet mass, drying, loss of drying and reprocessing using different RMG parameters against the unique batch number such as E20950, E20950 and E21054. For example, the values obtained in case of drying in which set temperature condition is below 50^0C for inlet temperature and the obtained values falls under the desired limit i.e., 49^0C. against the different batch numbers of the drugs which helps to initiate the crucial particle expanding procedure by an agglomeration process.

Quality control analytical parameters: (dummy granules):- Different parameter (water content, bulk density, tapped density, sieve analysis) are use for the quality control analysis.

Table 9: Quality control analytical.

Parameters		**Specification**	**Observed in batch**		
			E20937	**E20950**	**E21054**
Water content by K.F		For information	17.13%	15.897%	11.06%
Bulk density			0.817g/ml	0.884 g/ml	0.590 g/ml
Tapped density			0.906 g/ml	0.914 g/ml	0.738 g/ml
Sieve analysis	20#		9.55%	10.24%	26.76%
	40#		2.75%	2.97%	7.00%
	60#		2.74%	2.86%	6.50%

In Table 8, The test result values of quality control using different variables such as water content, sieve analysis, bulk and tapped density has been mentioned. The quality control analysis has been performed against the unique batch number of the drugs in order to find the optimal value under the permissible limits. Based on the standard set protocols the parameter values comes under the desired quality range which shows the superiority of the drug. For example, Bulk density has been computed against the E20950, E20950 and E21054 batch number and the obtained values are 0.817g/ml, 0.884 g/ml, and 0.590 g/ml respectively which shows the high end quality of the used drug.

CAPSULE FILLING: Powder is transferred from a container into the capsule's interior

using filling bands.

Parameters	Limit	Observed in batch		
		E20941	E20970	E21055
Target speed	90SPM	90SPM	90SPM	90SPM
Description	Size ‘0’ capsule with transparent red cap/transparent clear body containing light yellow to yellow, light orange to orange pellets and white to off-white granule	Complies	Complies	Complies
Separate weight of pellets in size ‘0’ capsule	Domperidone SR pellets(orange colour) 100mg±5% (95mg-105mg)	96mg	104mg	102mg
	Pantoprazole EC pellets 22.5%(yellow colour) 178±5% (169.10mg-186mg)	178mg	172mg	177mg
	Dummy granules (white colour) 200mg ± 5% (190mg-210mg)	201mg	195mg	203mg
Weight of 20 filled capsules	11.48gm ±3.0% (11.136gm-11.824gm)	11.287gm	11.463gm	11.503gm

Parameters	Limit	Observed in batch																	
		E20941						E20970						E21055					
		Filled capsules		Empty capsule		Net content		Filled capsules		Empty capsule		Net content		Filled capsules		Empty capsule		Net content	
Individual weight of 20 capsules	Weight of filled capsule: 574.00mg ±7.5% (530.95-617.05mg) Net content weight 478.00mg ±5% (454.10-501.90mg) Empty capsule weight 96.00mg ±10% (86.40-105.6mg)	572	572	95	99	477	473	577	574	99	98	478	476	573	579	99	98	474	481
		559	555	97	91	462	464	571	578	95	104	476	471	578	586	100	99	478	487
		579	565	101	93	478	472	575	571	98	96	471	475	578	586	96	97	477	473
		561	566	96	94	465	472	570	569	99	95	473	474	573	587	98	93	475	461
		572	564	102	98	470	466	571	572	98	99	475	473	573	570	101	98	480	482
		55	579	99	99	456	480	577	577	102	101	476	476	581	554	98	99	493	480
		568	566	100	99	468	467	571	570	95	97	477	473	591	580	100	101	470	479
		554	556	97	98	457	458	577	571	100	95	472	476	570	579	95	98	476	464
		551	558	96	92	455	466	576	571	104	93	475	478	571	580	98	99	475	466
		562	573	98	97	464	476	572	573	97	95	476	478	573	562	99	98	478	465
Average weight of filled capsule	574.00mg ±5%	567.90mg						573.15mg						575.15mg					
Uniformity weight of filled capsule	Not more than 2 of the individual weights deviate from the average weight of filled capsule by more than ±7.5% & none deviate by more than ±15%	+2.60% -2.37%						+0.85% -0.72%						+2.76% -3.68%					

Table 10: Setting parameters (physical parameters).

Parameters	Limit	Observed in batch					
		E20941		E20970		E21055	
Locking length of filled capsule	21.30mm ± 3.0 % (20.66mm-21.94mm)	21.32mm	21.28mm	21.40mm	21.29mm	21.36mm	21.33mm
		21.38mm	21.39mm	21.59mm	21.49mm	21.42mm	21.52mm
		21.30mm	21.66mm	21.46mm	21.45mm	21.25mm	21.24mm
		21.60mm	21.55mm	21.42mm	21.51mm	21.44mm	21.18mm
		21.72mm	21.36mm	21.56mm	21.53mm	21.39mm	21.47mm

In Table 9, the result values have been obtained using the capsule filling process by setting the standard limit for quality assurance to meet the acceptance criteria. The different parameters haven been examined such as target speed, weight of the filled and unfilled capsule, individual weight, average weight, uniformity weight of the capsule and locking length of the capsule against the E20941, E20970, and E21055 batch number of the drugs. For example, average weight of the capsule falls under the accepted criteria i.e., 567.90mg and 573.15mg which is within the limits.

Speed & compressed air challenge test (min & max speed)

Table 11: Minimum and maximum speed.

Min& Max. Speed	Parameters	Limit	Observed in batch no		
			E20941	E20970	E21055
Max speed (98 SPM)	Average wt. of filled capsule	574.00mg± 5% (545.30mg-602.70%)	565.23mg	577.11 mg	562.68 mg
	Average wt. of net content	478.00mg± 5% (454.10mg- 501.90mg)	469mg	477.13 mg	466.45 mg
	Locking length	21.30mm±3% (20.66mm-21.94mm)	21.15 mm	21.15 mm	21.15 mm
Min speed 80SPM	Average wt. of filled capsule	574.00mg± 5% (545.30mg-602.70%)	573.56mg	575.12 mg	572.35 mg
	Average wt. of net content	478.00mg± 5% (454.10mg- 501.90mg)	475.22 mg	479.55 mg	478.81 mg
	Locking length	21.30mm±3% (20.66mm-21.94mm)	21.28mm	21.39mm	21.46mm

In Table 10, the values obtained from speed challenge test using different physical parameters has been mentioned. The physical parameters are average wt. of the filed capsule, net content, locking length against the minimum and maximum speed such as 80SPM and 98SPM respectively. In case of average wt of net content for max. speed are 469.08mg, 477.13mg and 466.45 mg against E20941, E20970, and E21055 respectively. Similarly, average wt of net content for min. speed are 475.22mg, 479.55mg and 478.81mg against E20941, E20970, and E21055 respectively.

Table 12: Minimum and maximum compressed air.

Min& Max. comp. air	Parameters	Limit	Observed in batch no		
			E20941	E20970	E21055
7Kg/cm^2	Average wt. of filled capsule	574.00mg± 5% (545.30mg-602.70%)	578.49mg	573.98mg	575.68 mg
	Average wt. of net content	478.00mg± 5% (454.10mg-501.90mg)	485.51mg	479.14mg	479.6 mg
	Locking length	21.30mm±3% (20.66mm-21.94mm)	21.44mm	21.29 mm	21.39mm
5Kg/cm^2	Average wt. of filled capsule	574.00mg± 5% (545.30mg-602.70%)	570.56mg	572.12 mg	571.35 mg
	Average wt. of net content	478.00mg± 5% (454.10mg-501.90mg)	474.22 mg	476.55 mg	475.81 mg
	Locking length	21.30mm±3% (20.66mm-21.94mm)	21.36mm	21.55mm	21.32mm

In Table 11, the values obtained from compressed air challenge test using different physical parameters has been mentioned. The physical parameters are average wt. of the filed capsule, net content, locking length against the max. and min. speed such as 7Kg/cm^2 and 5Kg/cm^2 respectively. In case of average wt of net content for max. compressed air are 485.26mg, 479.28mg and 479.32 mg against E20941, E20970, and E21055 respectively. Similarly, average wt of net content for min. compressed air are 474.83mg, 476.33mg and 475.85mg against E20941, E20970, and E21055 respectively.

Assay results at capsule filling stage

Table 13: Capsule filling assay.

Assay	Specification	Observed in batch no		
		E20941	E20970	E21055
Pantoprazole sodium eq. to pantoprazole	90.0%-110% of labelled amount	100.7%	102.7%	102.6%
Domperidone	90.0%-110% of labelled amount	100.9%	104.6%	104.4%

In table 12, assay results at capsule filling stage have been analyzed and obtained values have been mentioned for pantoprazole and Domperidone with specified limit. The obtained values through the test for different batch number in case of pantoprazole are 100.7%, 102.7% and 102.6% against E20941, E20970, and E21055 respectively. Similarly, for Domperidone the obtained values through the test for different batch number in case of pantoprazole are 100.9%, 104.6% and 104.4% against E20941, E20970, and E21055 respectively.

Content uniformity:-The pharmaceutical industry uses a criterion called "Uniformity of Content" for controlling the quality of capsules. Several capsules are chosen at random, and their contents are then analyzed using the most appropriate technique.

Table 14: Uniformity.

API	Specification	Observed in batch no		
		E20941	**E20970**	**E21055**
Pantoprazole	For 10 dosage units 85% to 115% of average content. For 30 dosage units- 85% to 115% of average content and none unit should be outside- 75% to 125% of average content.	Min. 95.6%	Min 98.9%	Min 98.7%
Domperidone		Max. 104.1%	Max. 101.5%	Max.102.1%
		Avg. 100.0%	Avg.100%	Avg. 100.0%
		Min 98.2%	Min. 97.1%	Min 97.9%
		Max. 105.5%	Max. 102.1%	Max. 103%
		Avg. 100%	Avg.100.0%	Avg.100%

In table 13, content uniformity has been analyzed and obtained values have been mentioned for pantoprazole and Domperidone. For pantoprazole, the obtained average values are 100% for each batch number. Similarly, For Domperidone. The obtained average values are 100% for every batch number drug. It outcomes ensure the content uniformity in the drug which presents the quality of the formulated drug.

DISSOLUTION

To make a solution, a solute must first dissolve in a solvent, which may be either a gas, liquid, or solid.

Table 15: Dissolution.

Parameter	Limit	Observed in batch no		
		E20941	**E20970**	**E21055**
Pantoprazole (by HPLC)				
In acid medium	NMT 10% of the labelled amount is dissolved in 120minutes	Min. 2.0%	Min. 1.0%	Min. 4.0%
		Max.5.0%	Max. 9.0%	Max. 8.0%
		Avg. 3.5%	Avg. 6.0%	Avg. 5.5%
In buffer medium	NLT 70% (D) of the labelled amount is dissolved in 45min	Min. 93%	Min. 95%	Min. 93%
		Max.103%	Max.99%	Max.102%
		Avg. 97%	Avg. 97%	Avg. 98%
Domperidone (by HPLC)				
1 hour	20-50%	Min. 36%	Min. 33%	Min. 27%
		Max.43%	Max. 38%	Max. 41%
		Avg. 38%	Avg. 36%	Avg. 34%
4 hour	45-75%	Min. 61%	Min. 61%	Min. 52%
		Max.71%	Max. 67%	Max. 64%

		Avg. 67%	Avg. 64%	Avg. 61%
12 hour	NLT 75%	Min. 90%	Min. 85%	Min. 80%
		Max.93%	Max. 90%	Max. 91%
		Avg. 92%	Avg. 88%	Avg. 85%

In table 14, the outcomes after the dissolution test obtained have been mentioned, the test is performed for Pantoprazole (HPLC) and Domperidone(by HPLC) using different conditions under different mediums and time limits. In case of Pantoprazole (HPLC), under acidic medium average values are 3.5%,6% and5.5% against different batch number drug i.e., E20941, E20970 and E21055 respectively. Similarly, in case of Domperidone(by HPLC), consider the 4th hour for average value calculation, the obtained average values are 67%, 64% and 61% against different batch number drug i.e., E20941, E20970 and E21055 respectively.

RELATED SUBSTANCE

Table 16: Related substance.

Parameter	**Limit**	**Observed in batch no**		
		E20941	**E20970**	**E21055**
Pantoprazole (by HPLC)				
Related compound A	NMT 0.5%	Not detected	Not detected	Not detected
Related compound B	NMT 0.3%	0.02%	0.01%	0.01%
Related compound D &F	NMT 0.75%	0.03%	0.11%	0.14%
Any other secondary impurity	NMT 0.5%	0.49%	0.10%	0.11%
Total impurities	NMT 1.5%	0.69%	0.20%	0.24%
Domperidone (by HPLC)				
Any other secondary impurity	NMT 0.5%	0.07%	Not detected	0.09%
Total impurities	NMT 2%	0.07%	Not detected	0.09%

In Table 15, related substance values have been computed for Pantoprazole (HPLC) and Domperidone(byHPLC) using different conditions under different impurity conditions such as compound A, B, D &F, Any other impurity and Total impurity. In case of Pantoprazole (HPLC), the total impurity, the values are 0.66%, 0.20% and 0.24% against different batch number drug i.e., E20941, E20970 and E21055 respectively. Similarly, in case of Domperidone(byHPLC), consider the total impurity, the obtained values are 0.07%, not detected and 0.09% against different batch number drug i.e., E20941, E20970 and E21055 respectively.

Water content by K.F:- Itis a method of determining the water content of solid, liquid and gaseous samples.

Table 17: Water content.

Test	Limit	Observed in batch no		
		E20941	E20970	E21055
Water content	For information	8.0081%	10.84%	7.7601%

The Table 16 represents the test values obtained from the water content test using K.F. The moisture level in the drug has been examined and the values obtained for different batch number drugs such E20941, E20970 and E2155 comes under the permissible range which ensure the drug quality. The water content obtained for E20941, E20970 and E2155 are 8.0081%, 10.84%, and 7.7601% respectively.

PACKING

Table 18: Physical parameter.

Test	Limit	Observed in batch no		
		E20941	E20970	E21055
Sealing temperature	---	157.4^{0}C	152.8^{0}C	159.5^{0}C
Speed	---	30cycles/min	33 cycles/min	33 cycles/min
Horizontal cutting	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Vertical cutting	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Pocket filling	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Sealing & knurling	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Leak test	Should pass	Pass	Pass	Pass
Appearance	Satisfactory	Satisfactory	Satisfactory	Satisfactory

It is noticed that the Table 17 shows the acceptance criteria of physical parameters involved in the evaluation of the drug quality control. Before the final pacing of the drug capsule a certain set of tests such as Sealing, temperature, Speed Horizontal, cutting, Vertical cutting, Pocket filling, Sealing & knurling, Leak test and appearance have been conducted to ensure the quality of the drug capsule. The shows that used drug obtained satisfactory and pass remarks after the undergoes in the examination against the unique batch numbers such as E20941, E20970 and E2155. In case of Appearance the drug show satisfactory result, hence the packing of the drug can be done.

Finished samples

Table 19: Analytical parameter.

Test	Limit	Observed in batch no		
		E20941	E20970	E21055
Pantoprazole sodium eq. to pantoprazole	90%-110% of labelled amount	101.9%	103.7%	104.9%
Domperidone	90%-110% of labelled amount	103.6%	107.8%	109.2%

In Table 18, the finished samples have been analyzed against the Pantoprazole and Domperidone for different batch numbers such as E20941, E20970 and E2155. It is observed that the obtained values come under the permissible limit for different batch numbers in case of pantoprazole i.e., 101.9%, 103.7% and 04.9% against E20941, E20970 and E2155 respectively. In a similar manner, finished samples values have been observed for the Domperidone are 103.6%, 107.8% and 109.2% respectively. The obtained values shows that the results falls under the acceptance criteria.

MICROBIAL TEST: The pharmaceutical, beauty products, and food and drink sectors all utilize microbiological testing to ensure their goods are safe for human consumption. Testing for bioburden, mycoplasma, pathogens, spoilage, pyrogens, sterility, air quality, and surface cleanliness are only some of the methods frequently used to guarantee public health and legal conformity.

Table 20: Microbial limit test.

Parameter	**Observed in batch no**			
		E20941	**E20970**	**E2155**
Total aerobic microbial count- NMT 1000cfu/gm		35cfu/g	35cfu/g	25cfu/g
Combined yeast and mould count-NMT 100cfu/gm		Nil	Nil	Nil
Pathogens	E.coli should be absent/g	Absent	Absent	Absent
	Pseudomonas aeruginosa should be absent/g	Absent	Absent	Absent
	Staphylococcus aureus should be absent/g	Absent	Absent	Absent
	Salmonella species should be absent/g	Absent	Absent	Absent

The table 19shows the microbial limit test for the different batch numbers such as E20941, E20970 and E2155 against different parameters such as Total aerobic microbial count, Combined yeast and mould count, and Pathogens. The presence of the pathogens hand yeast and microbial count has been analyzed in order to ensure the health safety of the consumer. In the obtained observation, it is noticed that harmful pathogens were absent and microbial count falls under the safety limit such as 35cfu/g, 35cfu/g, and 25cfu/g against the E20941, E20970 and E2155 batch number respectively.

YIELD STATUS

Table 21: Yield status.

Stage	**Observed in batch no**		
	E20941	**E20970**	**E2155**
Lubrication	95.68%	96.41%	96.50%
Capsule filling	98.90%	97.41%	98.03%
Inspection	NA	NA	NA
Packing	97.50%	97.49%	98.10%

The Table 20 depicts the Yield status of the observed batch numbers such as E20941, E20970 and E2155 at different stages such as Lubrication, Capsule filling, Inspection and packing. The different stages involved the unique proportion based of the set protocols. The Distinct values in terms of percentage has been observed against the different batch number, for example, Lubrication stage consist of 95.68%, 96.41% and 96.50% for E20941, E20970 and E2155 batch number respectively. Similarly, the proportion has been computed for other stages based on the standard protocols.

SUMMARY AND CONCLUSION

According to the sampling plan of the approved Process validation Protocol, all process variables were observed throughout various stages of the production of the products pantoprazole and domperidone capsule. The production procedure was carried out in accordance with the batch manufacturing and packing record that was approved.

For the process validation batch, B. Nos. E20941, E20970, and E21055, the following process variables were monitored: sifting, dry mixing, granulation, extrusion of wet mass, semi-drying, size reduction/milling, drying, final sifting, reprocessing, capsule filling, inspection, and packing. In accordance with the protocol for approved process validation, the sample was removed at various points. All of the analytical findings were deemed to be satisfactory and to be well within the specified bounds. For succeeding batches of process validation, the protocol was applicable. The intermediate process validation report, however, is created following batch completion. After the batch is finished, a final process validation report must be created in accordance with the addendum protocol.

Samples were collected in accordance with protocol, and the findings of the packing machine assessment for sealing temperature and packing machine speed were found to be satisfactory and within specification limits.

CONCLUSION

Pantoprazole and domperidone capsule validation batches were created in accordance with batch production records that were approved. The results of all necessary validation tasks were finished, and they are compiled in this report. Critical process parameters were observed during the validation research as specified in the protocol. The results of the in-process tests revealed that every parameter was well within the allowed range. All of these validation batches were manufactured using the same manufacturing process. When all of these batches

were tested in accordance with the authorised specification, there were no anomalies found in the testing parameters.

This validation report demonstrates that the production of pantoprazole and domperidone capsules is reliable, consistent, and upholds the necessary standards of quality. Based on the interim assessment, this batch may be made available for sale and distribution.

Conflict of interest

None.

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