Abstract

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Equipment and process involved during validation: e equipments and process involved during validation was given in table 3.

Dry mixing/ Blending:

1. Samples were drawn from di erent positions of double cone blender as shown in gure 2.
2. Each sample was collected in butter paper at di erent intervals from top, middle and bottom.
3. Sample size should be 1 to 3 times of the unit weight.
4. e samples were collected and subjected to analysis for assay, bulk density, tapped density, angle of repose, etc.
5. Acceptance criteria were uniform distribution of drug and other contents.

Lubrication/ Blending:

1. Lubricant (magnesium stearate) was added to initial powder blend, till the free owing powder was produced.
2. Samples were collected from di erent positions of blender as shown in gure 2.
3. Each sample was collected in butter paper at di erent interval of time.
4. e samples were subjected for further tests i.e. tapped and bulk density, angle of repose, assay.
5. Acceptance criterion was free owing powder blend.

Compression:

1. e tablets were compressed by varying compression speed and force.
2. Following tests were performed and the process variables were optimized.
3. e three optimized batches of tablets were produced and samples were collected at start, middle and bottom of each batch.

Compressed taste parameters were shown in table 4.

Coating:

1. Tablets were rst coated by varying di erent process variables of coating and samples were collected and subjected to analysis.
2. e three optimized batches of coating were produced.
3. Tablets were collected at end of coating process and checked for surface defect, friability, disintegration, dissolution and assay.

Critical steps validation:

Dry mixing: e xed parameters of dry mixing process during critical step validation were given below,

Batch size	-	250.00 gm
Batches taken for study	-	A, B, C
Variable considered for study	-	Mixing time
Acceptance criteria	-	Mixing end point by assay, bulk density, tapped density

Lubrication: e xed parameters of lubrication process during critical step validation were given below,

Batch size	-	250.00 gm
Batches taken for study	-	A, B, C
Variable considered for study	-	Blending time
Measure response	-	Assay, Tapped density, Bulk density, Angle of repose.
Acceptance criteria	-	Free owing powder blend with no lumps.

Compression: e xed parameters of compression process during critical step validation were given below,

Type of machine	-	16 station single rotary compression machine
Variables considered for study	-	Compression force and Machine speed.

Compression force and machine speed study: e objective was to study e ect of compression force and machine speed on tablet

Tablet coating

Film coating: e lm coating was done with hydroxypropylmethylcellulose and ethyl cellulose using solvent Isopropyl alcohol and dichloromethane [10]. e formulation of coating solution was given in table 5.

Coating parameters study: Di erent coating parameters were analyzed to get good coated tablets. e xed parameters of coating process during critical step validation were given below [11],

Batch size	-	50 tablets
Pan size	-	8"
Ba es	-	3
Spray nozzle	-	1 mm
Spray gun	-	1
Atomization pressure	-	1.2 kg/cm^2
Spraying	-	Continuous
Tablet bed temperature	-	33°C ± 2°C
Pre-warming	-	10 to 15 mins at slow rpm
Post drying	-	10 to 15 mins at slow rpm
Sampling	-	At end of coating
Measure response	-	Tablet physical parameters, disintegration time, dissolution and assay.

e various variable of coating parameter study for three batches given in table 6.

Normal lm coating Operation: e xed parameters of normal lm coating process during critical step validation were given below (10),

Batch size	-	50 tablets
Batches taken for study	-	A, B, C.

Other parameters were same as that applied to coating parameters study in batch II.

Determination of hygroscopicity of lm coated Ranitidine hydrochloride tablets by weight gain method

e lm coated Ranitidine hydrochloride tablet was placed in beaker and subjected to accelerated conditions of temperature and humidity (40 qC ± 1qC and 75%RH ± 3%) in humidity chamber in presence and absence of light. Increase in weight was recorded a er every 10 days for 3 months [11].

Stability study

e stability study of lm coated tablets was carried at accelerated condition of 40 qC ± 2qC temperatures and 75% ± 5% relative humidity

Determination of hygroscopicity of Ranitidine hydrochloride by weight gain method

Results of hygroscopicity of Ranitidine hydrochloride were illustrated in table 12 and gure 8.

Critical steps validation

Dry mixing: For all the batches, the speed of Double cone blender was kept at 25 rpm and samples were drawn at time interval of 5, 10, 15 and 20 minutes till the uniform distribution of all content was achieved. Samples were drawn from position as shown in gure 1.

e samples collected a er 15 min. showed uniform distribution of drug which was con rmed by assay of drug in accordance with very low standard deviation in all three batches and samples collected a er 20 min. showed almost same standard deviation as that of 15 min (Tables 13-15). So, it was observed that uniform blend was formed at mixing time of 15 minutes with blender speed of 25 rpm in all three batches; hence mixing process concluded as validated (Tables 13-15). Physical parameters like bulk density, tapped density and angle of repose was done. Observations are noted in table 16.

Lubrication: e lubrication 79 BDC /MCID24(7). 0-57(validated6rie7 i.4

low standard deviation in all three batches and samples collected a er 15 min, showed almost same standard deviation as that of 10 minutes (Table 17). So, it was observed that uniform lubricated blend was formed at lubrication time of 10 min with blender speed of 25 rpm in all three batches; hence lubrication process concluded as validated (Table 17). Physical parameters like bulk density, tapped density and angle of repose was done. Observations are noted in table 18.

Compression: Observations of e ect of compression force and machine speed on tablet are shown in table 19.

Normal production: Observation of compressed tablets evaluation of normal production batch A, B and batch C are shown in tables 20-22 respectively. Sixteen station single rotary compression machine with compression force of 4 tones and machine speed of 30 rpm produced tablets with required speci cation; hence compression process was concluded as validated.

Tablet coating

Film coating: Formulation of coating solution given in table 23. From above coated batches the batch II showed good tablets with no surface defects and evaluation of batches I, II, III is shown in tables 24 and 25 respectively.

Normal lm coating Operation: e coating of core tablets was done by applying process parameters considered for batch II. e tablets in pan were pre-heated with hot air and spray gun was started, when tablet bed temperature reaches to 33°C ± 2°C. Coated tablets were evaluated for physical parameters, disintegration time, dissolution time and assay. Observations are shown in table 26. e tablets produced in all three batches meet required speci cations; hence tablet coating process was concluded as validated.

Determination of hygroscopicity of lm coated Ranitidine hydrochloride tablets by weight gain method

e result of Determination of hygroscopicity of lm coated Ranitidine hydrochloride tablets by weight gain method study was shown in table 27 and gure 9.

Stability study

e stability study of lm coated tablets was carried at accelerated

S No	Physical Parameter	Limit	Batch A		
			Initial	Middle	End
1	Appearance	Plane tablet with no surface defects	Complies	Complies	Complies
2	Weight of 20 tablets	NLT 10.564 g and NMT 11.676 g	10.792	10.697	10.817
3	Average weight	NLT 0.528 g and NMT 0.584 g	0.54	0.535	0.541
4	Thickness	2.90 mm to 4.10mm	3.99	3.79	3.87
5	Diameter	11.90 mm to 12.10 mm	11.97	12.08	11.99
6	Hardness	8 to 12 kg/cm^2	8.74	8.91	9.1
7	Friability	NMT 1.0%	0.13	0.11	0.09
8	Disintegration Time	NMT 60 mins	9 min 12 Sec	9 min 45 Sec	10 min 45 Sec
9	Assay	NLT 90% and NMT 110%	97.99	98.41	98.07
10	Dissolution Test	NLT 80%	91.62	90.99	91.09

Table 20: Compressed tablets evaluation of normal production batch A.8

S No	Ingredient	Quantity
1	Hydroxypropylmethylcellulose	1.2 kg
2	Ethyl cellulose (7cps)	0.3 kg
3	PEG 6000 (Starch 1500)	0.04 kg
4	Propylene glycol	0.02 kg
5	Sodium lauryl sulphate	0.01 kg
6	Titanium dioxide	0.25 kg
7	Color	0.20 kg
8	Isopropyl alcohol	18 lit.
9	Methylene chloride	30 lit.

Table 23: Preparation of film coating solution.

S No	Variable	Batch		
		I	II	III
1	Pan speed (rpm)	30	25	20
2	Air temperature	50 qC	45 qC	35 qC
3	Spray rate	2.8 ml/min	2.4 ml/min	2.1 ml/min
4	Spray pattern	Narrow	Normal	Broad
5	Nozzle to bed distance (cm)	6.5	6	5.5
6	6			

parameters were analyzed to establish limits to these attributes which will lead to uniformity in dosage form.

From the study it can be concluded that the critical process parameters considered for study were relevant indicators of a controlled process. List of processes and testing criteria ensured that by scientific means, the product can be manufactured in a manner to ensure uniformity within a lot, consistency between lots within defined limits. The critical process parameters were analyzed to establish limits to these attributes which leaded to uniformity in dosage form. So these numerical ranges can be used for routine production of Ranitidine hydrochloride tablets to get constantly a good product with all required characteristics and uniformity in final dosage form from batches to batches. The process validation done in this study also helps in creating necessary documentation to support a stepwise evaluation of a pharmaceutical process.

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