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Research Article

Process Validation of Oral Solid Dosage Form-Tablet containing Anti Tubercular Agent

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ABSTRACT

The purpose of study is to validate process of Rifampin 150mg and Isoniazid 75mg tablet and to create a robust formulation. The critical process parameter was identified with the help of optimization batches of process capability and evaluated by challenging specification. Three process validation batches of same size, manufacturing process, equipment & validation criteria was taken. The critical parameter involved in sifting, dry mixing, preparation of granulating agent, wet mixing, wet milling, drying, sizing, lubrication and compression stages were identified and evaluated. The outcome indicated that this process validation data provides high degree of assurance that manufacturing process produces product meeting its predetermined specifications and quality attributes.

Key words - Rifampin, Isoniazid, Process validation, Uniformity of mixing.

INTRODUCTION: [3, 4, 5]

The FDA in its new guidelines had made some changes in the aspects of process validation and defined it as "The collection and evaluation of data, from the design stage throughout production, which establishes scientific evidence that a process is capable of consistently delivering quality products."Process validation is nothing but giving an assurance to the quality of product in a document form, which establishes the flexibility and constraints in the manufacturing process controls in the attainment of desirable attributes in the drug product and which preventing undesirable properties. It gives scientific evidence with a systemic approach for identifying, measuring, evaluating, documenting and re-evaluating series critical steps in the manufacturing process and requires control to ensure a reproducible final product. Validation[3] is considered to be integral part of GMP essentially worldwide, compliances with validation requirements is necessary for obtaining approval to manufacture and to introduce new products. The FDA cGMP refer to the concepts of the validation in both sections 21 CFR 210 and 211. 21 CFR 211.100 states. GMP [4, 7] requires written procedures and process controls be established to assure that the drug products have the identity, strength, quality and purity they purport or are represented to possess. Quality its self cannot be inspected or tested into the finished product. Each step of the manufacturing process must be controlled to maximize the probability that the finished product meet all quality and design specification.

Type of validation [4, 6]

Prospective validation (pre marketing validation): Prospective validation is nothing but need of qualification for completion of experimental trails before the process is put into commercial use.

Retrospective validation: The retrospective validation is an establishment processes that are stable and in routine use have not under gone a formally documented validation process. In this retrospective validation the manufacturing method has to remain in unchanged for period of time.

Concurrent validation: This validation involves in process monitoring of critical processing steps and product testing, this helps to generate the document evidence to show that the production process is in a state control. Normally three batches are recorded fully on a part of initial concurrent validation program

Revalidation [7, 8, 11]: Revalidation may be divided into two broad categories:

- Revalidation after any changes.
- Periodic revalidation carried out at scheduled intervals.

Revalidation may be required in following cases: Change in formulation, procedure or quality of pharmaceuticals ingredients. Change in equipment, addition of new equipment and major breakdown (Maintenance, which affect the performance of the equipment).Major change of process parameters, change in site, batch size change, on appearance of negative quality trends. Periodic revalidation is well known that process changes may occur gradually even if experienced operators work correctly according to established methods. Similarly, equipment wear may also cause gradual changes.

MATERIALS AND METHODS

Material: Isoniazid (Amsal Chem Pvt Ltd), Rifampin (Lupin Ltd Tarapur), Microcrystalline cellulose USP/NF (RANQ Pvt Ltd), Pregletinized Starch BP/EP (Roquette Signet), Crospovidone USP/ NF (ISP Technologies), Magnesium stearate (Healthcare Ltd.), Ascorbic acid colloidal silicon and Purified Water was used for this Formulation. All material used of USP/NF/BP grade and

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Table 1 Dry mixing

Sample taken	Sample no	Blend uniformity of Rifampin and Isoniazid					
		Batch.1		Batch.2		Batch.3	
		RIFA	INH	RIFA	INH	RIFA	INH
After 6 mints	Location 1	99.2	99.3	99.6	99.3	98.5	99.5
	Location 2	102.7	99.9	101.0	99.9	97.2	100.2
	Location 3	100.7	105.4	96.5	105.4	98.2	98.2
	Location 4	101.4	101.o	101.1	101.7	99.5	99.5
	Location 5	100.2	100.8	100.4	98.6	101.2	100.8
	Location 6	103.5	102.8	10.8	97.8	99.6	101.2
	Average	101.3	101.5	99.9	101.43	99.03	99.9
	% of RSD	1.56	2.48	1.7	2.72	1.39	1.07
After 8 mints	Location 1	102.7	99	101.0	98.9	102.5	102.5
	Location 2	102.7	100.5	101.0	101.3	102.0	99.9
	Location 3	100.8	100.4	100.9	100.8	102.1	99.7
	Location 4	102.1	101.4	100.8	100.3	98.8	101.8
	Location 5	102.4	99.9	100.7	99.4	101.7	99.3
	Location 6	102.2	100.0	100.6	100.3	102.3	99.9
	Average	102.2	100.4	101.8	100.2	101.6	100.5
	% of RSD	0.7	0.6	0.2	0.9	1.4	1.3
After 10 mints	Location 1	97.3	99.3	99.3	98.3	99.8	99.2
	Location 2	99.6	99.9	99.9	99.9	99.6	102.7
	Location 3	99.8	105.4	105	105.4	99.1	100.7
	Location 4	100.5	103.7	101.6	101.0	97.5	101.3
	Location 5	100.2	101.0	101.5	100.8	96.5	100.2
	Location 6	100.8	100.8	100.2	102	100.2	101.4
	Average	99.7	101.68	101.25	101.5	98.78	103.30
	% of RSD	1.25	2.32	2.01	2.35	1.47	1.14

Table 2 Wet mixing

Process validation batch no.		Chopper (speed & Time in minute)		Impeller (speed & Time in minute)		Ampere Reading	Dough Mass Consistency
Speed		Slow	Fast	Slow	Fast		
Batch.1	RIFA	2	1	2	1	24.1	Excellent
	INH	2	4	2	4	21.0	Excellent
Batch.2	RIFA	2	1	2	1	24.2	Excellent
	INH	2	4	2	4	21.2	Excellent
Batch.3	RIFA	2	1	2	1	24.0	Excellent
	INH	2	4	2	4	21.4	Excellent

chemicals used in the analysis in the study were of analytical grade.

Equipments : Weighing Balance (JAY pan), Rapid Mixer Granulator with turbo sifter (700 L) (Saral Mumbai,) Fluid Bed Drier 200 L (Alliance Mumbai)Turbo sifter cum mill Vibratory Sifter(RP Products Mumbai),Pillar Blender (RP Products Mumbai),Double Rotary Compression Machine (Sejong), Coating machine (Gansons Mumbai) UV visible spectrophotometer (Jasco), HPLC (Agilent 1100), Dissolution apparatus 8000 (Labindia), Portable digital hardness tester (Vinsyst technologies), Disintegration and friability test apparatus(Electo lab).

Method of manufacturing process:

1. Dispensing: Dispensed the raw materials as per the standard operating procedure.

2. Sifting: Separately sifted the materials Isoniazid, Microcrystalline Cellulose and Rifampin, Microcrystalline, Cellulose Crospovidone, Pregelatinized Starch (Starch 1500) through 8 mesh S.S. sieve fitted to turbo-sifter and collected it in Rapid mixer granulator.

3. Dry mixing: Dry Mixing of sifted intragranular materials Isoniazid and Rifampin was carried separately in Rapid mixer granulator (700 L) for 8 minutes while keeping impeller at "slow" speed and chopper "off "condition. In this processes challenges were taken at different times points 6, 8, 10 mints sample were collected and it determines the uniformity of mixing of ingredient.

4. Granulation: Pregelatinized starch dispersion was used as a binder for Isoniazid and Pregelatinized Starch (Starch 1500) and Ascorbic Acid dispersion was used as a binder for Rifampin. Added the binder within 1 to 3 minutes into contents of Rapid mixer granulator and kneading was carried by keeping impeller and chopper at "slow" speed. Then scrapping was carried out and again kneading was carried by keeping impeller and chopper at "Fast" speed to

Table 3 Loss on drying

Process validation batch no.		Loss on drying (%W/W)								
Outlet	RIFA	46^0C^0			48^0C			50^0C		
Temperature	INH	40^0C			42^0C			44^0C		
Layer		T	M	B	T	M	B	T	M	B
Batch.1	RIFA	1.67	1.71	1.83	1.77	1.57	1.56	1.93	1.71	1.89
	INH	1.40	1.32	1.34	1.25	1.35	1.31	1.32	1.40	1.36
Batch.2	RIFA	1.60	1.61	1.93	1.59	1.68	1.66	1.73	1.70	1.73
	INH	1.19	1.22	1.15	1.27	1.23	1.18	1.38	1.42	1.36
Batch.3	RIFA	1.66	1.89	1.66	1.67	1.68	1.66	1.73	1.73	1.72
	INH	1.36	1.28	1.22	1.34	1.34	1.35	1.28	1.29	1.27

T =Top, M=Middle, B= Bottom

Table 4 Lubrication

Sample taken	Sample no	Blend uniformity of Rifampin and Isoniazid					
		Batch.1		Batch.2		Batch.3	
		RIFA	INH	RIFA	INH	RIFA	INH
After 3 mints	Location 1	100.4	100.4	99.1	99.1	100.6	102.1
	Location 2	100.2	104.6	98.9	98.9	100.2	99.9
	Location 3	99.7	100.2	95	95	98.1	97
	Location 4	98.4	102.1	101.0	101.6	101.	104.5
	Average	100.9	101.5	98.24	100.4	100.3	99.8
	% of RSD	1.49	1.89	2.66	2.88	1.37	3.16
After 5 mints	Location 1	100.9	99.7	101.0	96.8	99.7	102.0
	Location 2	100.0	98.7	102.5	99.9	99.6	102.2
	Location 3	103.9	103.8	102.4	98.9	101.5	98.6
	Location 4	102.2	102.3	101.7	99.4	98.9	101.4
	Average	101.3	99.0	101.9	99.1	99.4	100.6
	% of RSD	1.8	2.7	0.7	2.5	1.5	2.9
After 7 mints	Location 1	99.4	100.3	101.2	100.3	100.2	100.3
	Location 2	99.6	100.9	102.8	100.9	99.8	96
	Location 3	99.8	103.5	97	103.0	101.8	103.0
	Location 4	98.5	102.8	99.5	98.5	99.5	107
	Average	100.2	102.52	100.29	101.18	101.47	101.66
	% of RSD	1.09	1.85	2.00	2.23	1.57	3.09
			90				

get required consistency mass recorded the ammeter reading of impeller and chopper at granulation end.

5. Drying: The wet granules of Isoniazid and Rifampin were dried separately using FBD. Initially air-drying was carried out for 10 minutes. The inlet temperature of the FBD was controlled 60 - 65°C for Isoniazid and 65 - 70°C for Rifampin and outlet temperature monitored, both of which were later correlated with the corresponding LOD of the granules.

6. Sizing: Milling of dried granules was carried by using turbo sifter cum miller with 1.5 mm sifter & 1.5 mm miller S. S. Screen for Isoniazid and 1.0 mm sifter & 1.0 mm miller S. S. Screen for Rifampin.

7. Blending and Lubrication Blending: The milled granules of Rifampin part and Isoniazid part were loaded in 1350 L pillar blender bin and mixed for 15 minutes at 12 RPM. Then added in pillar blender bin 40 mesh sifted extra granular materials i.e. Microcrystalline Cellulose (PH101), Colloidal Silicon Dioxide (Aerosil 200) and Crospovidone (Polyplasdone) and mixed for 10 minutes at 12 RPM.

Lubrication: 40 mesh Sifted Magnesium Stearate added to the contents of Pillar blender Bin and lubricated for 05 minutes at12 rpm challenges were taken at different set point 3, 5, 7 minutes.

8. Compression: The Lubricated blend was compressed using 47 station 'B' tooling double rotary compression machine using capsule shape biconvex punches with break line on upper punches & lower punches are plain. The compressed tablets passed through metal detector to removed tablets with any metallic impurities.

9. Coating: The coating was performed on Ganscoater. Inspected the Coated tablets through tablet Inspection machine for removing defected tablets.

ANALYSIS

Formulation sample subjected to HPLC by keeping flow rate 1.5ml/min wave length 238 nm, injection volume20 µl, column 250x4.6 mm and 5micron hypersil BDS with column temperature 30°c. Weighed quantity equivalent to 80mg of Rifampin and Isoniazid 40mg into individual 500 ml volumetric flask, dissolve 100ml methanol sonicated to dissolve and diluted to volume up to mark.

Dissolution: Six tablets were placed in each of 6 dissolution flasks containing 900 ml of 0.1 N HCl,

Table 5 Assay of lubricated blend of composite sample

Description	Limit	Batch no		
		Batch 1	Batch 2	Batch 3
Assay of composite Blend	Rifampin USP 142.5 to 165.0 mg	100.4	99.8	98.0
	Isoniazid USP 71.5 to 78.75mg (95.0 to 105.0%)	97.6	97.9	99.1

Table 6 Compression result at different speed

Stage	Test	Batch-1	Batch-2	Batch-3
Low speed	Uniformity of weight (mg)	complies	complies	complies
	average Weight of tablets(g)	0.3525	0.3675	0.3540
	Friability (%)	0.44	0.65	0.53
	Disintegration	2:5	2:48	2:08
	Thickness(mm)	4.27	4.34	4.31
Target speed	Uniformity of weight (mg)	complies	complies	complies
	average Weight of tablets(g)	0.3600	0.3650	0.3599
	Friability (%)	0.24	0.81	0.68
	Disintegration	2:30	2:48	2:08
	Thickness(mm)	4.27	4.34	4.31
Higher speed	Uniformity of weight (mg)	complies	complies	complies
	average Weight of tablets(g)	0.3650	0.3660	0.3644
	Friability (%)	0.65	0.78	0.67
	Disintegration	2:18	2:03	2:10
	Thickness(mm)	4.28	4.35	4.31

previously maintained at 37±0.5°C and the basket was set at 100 rpm the apparatus was run for 45 minutes. A suitable volume of sample was withdrawn at regular intervals of time and filtered through 0.45 µm membrane filter. Amount of Rifampin dissolved determined by UV spectrophotometer at 475 nm and Isoniazid determined by the HPLC at 254 nm.

RESULTS AND DISCUSSION

Dry mixing: In this processes challenges were taken at different times points 6, 8, 10 mints. Uniformity dry mixing was obtained by assay of 6 locations per batch and individual sample 90 to 110% of mean value and % RSD NMT 5%, for effective mixing was calculated by mean assay of all location shown in table-1.

In dry mixing process the results of three batches at different time intervals show that the % RSD within the limit that NMT 5%.So, that the proper mixing was done. Comparing to the other time interval dry mixing at 8 mints is optimum.

Wet Mixing: Dough mass consistency of granulating agent was found excellent with respect to speed of impeller and chopper results shown in table-2. Dough mass formed satisfactory within the 6 minutes for Isoniazid ampere reading 21-21.4 Ampere and 3 minutes for Rifampin ampere reading 24-24.2 Ampere.

Loss on drying: In this stage challenges were taken at different outlet temperature loss on drying is obtained from 3 different location of FBD. LOD should between 1.0 % to 2.0 % w/w at 105°C by moisture analyzer for Isoniazid LOD between 1.0 % to 2.0 % w/w at 80°C by moisture analyzer of Rifampin for effective drying shown in table-3.

In process loss on drying the results of three batches at

Table 7 Compression result at different hardness level

Stage	Test	Batch 1		Batch 2		Batch 3	
		RIFA	INH	RIFA	INH	RIFA	INH
90N-100N	Dissolution	93	94	93	91	94	91
		99	100	94	95	97	96
		97	93	94	97	95	95
		98	98	90	93	99	94
		98	96	98	94	90	98
		94	95	91	95	91	97
100N-110N		93	91	94	89	93	88
		91	97	100	96	97	94
		99	98	98	97	95	90
		95	97	97	92	90	92
		98	96	96	93	98	91
		92	95	95	94	92	92
110N-120N		90	91	95	90	93	89
		96	98	90	90	90	92
		93	90	96	92	95	90
		89	94	88	94	90	87
		93	94	92	90	92	94
		90	95	98	91	96	93

Table 8 Compression at different hopper level

Stage	Sample no	Hopper level (Content uniformity)					
		Batch.1		Batch.2		Batch.3	
		RIFA	INH	RIFA	INH	RIFA	INH
Initial of hopper	Tablet 1	103.2	100.6	101.4	100.3	98.6	98.8
	Tablet 2	103.2	101.5	101.0	100.2	99.3	101.5
	Tablet 3	102.6	101.4	101.1	98.5	99.9	99.8
	Tablet 4	102.4	100.9	100.7	99.8	99.3	99.2
	Tablet 5	104.9	101.3	100.7	97.7	99.4	99.6
	Tablet 6	102.9	100.1	100.9	99.7	97.8	100.8
	Tablet 7	104.8	101.1	99.9	98.0	98.2	101.3
	Tablet 8	103.0	103.0	99.8	99.6	97.9	101.0
	Tablet 9	103.0	100.8	99.7	97.9	99.7	101.1
	Tablet 10	102.3	101.3	101.0	97.1	97.4	100.3
	Average	103.2	101.2	100.6	98.9	102.4	100.3
	% of RSD	0.9	0.8	0.6	1.2	0.9	0.9
Middle of hopper	Tablet 1	100.5	99.4	100.3	100.3	103.1	103.3
	Tablet 2	101.8	101.6	100.2	100.2	101.3	99.5
	Tablet 3	101.0	100.0	98.5	98.5	103.3	103.3
	Tablet 4	100.9	99.5	99.8	99.8	102.8	102.6
	Tablet 5	100.9	99.6	97.7	97.7	102.0	99.0
	Tablet 6	101.5	100.8	99.7	99.7	102.4	98.6
	Tablet 7	101.5	100.2	98.0	98.0	102.2	99.5
	Tablet 8	100.9	100.8	99.6	99.6	102.0	99.5
	Tablet 9	103.9	101.3	97.9	97.9	98.6	98.4
	Tablet 10	101.1	99.9	97.1	97.1	103.6	100.5
	Average	101.4	100.3	99.4	98.1	102.1	100.4
	% of RSD	0.9	1.8	0.9	0.8	1.4	1.9
End of Hopper	Tablet 1	102.2	99.1	99.9	98.6	103.7	100.9
	Tablet 2	102.1	100.2	99.1	99.3	101.8	99.2
	Tablet 3	102.0	100.4	99.6	99.9	101.2	99.9
	Tablet 4	101.6	99.7	99.4	99.3	100.0	99.5
	Tablet 5	104.1	100.2	101.6	99.4	100.1	97.4
	Tablet 6	101.9	98.6	99.6	97.8	102.6	100.3
	Tablet 7	104.2	100.2	97.8	98.2	100.4	99.5
	Tablet 8	101.9	101.6	98.7	97.9	102.7	99.5
	Tablet 9	101.2	99.1	99.1	99.7	101.1	97.9
	Tablet 10	101.6	100.4	97.5	97.4	101.2	97.9
	Average	102.3	100	99.2	98.7	101.5	99.2
	% of RSD	1.0	0.9	1.1	0.9	1.2	1.1

Table 9 End process checking

Sr. No.	parameter	Specification	Batch numbers		
			I	II	III
1	Description	Pink oblong tablet	Complies	Complies	Complies
2	Identification	The retention time of major peak in the chromatogram of the assay preparation corresponds to that in the chromatogram of the standard preparation as obtained in the assay	Complies	Complies	Complies
3	Dissolution	Not less than 80.0% (Q) of the stated amount of Rifampin and Isoniazid at 30 mints	RIFA 94	97	99
			INH 100	97	96
4	Uniformity of dosage Units(assay)	NLT-85%-NMT-115%	RIFA 99.7	97.8	97.6
			INH 98.9	102.2	99.2
5	Disintegration	Not more than 15 minutes	2min48sec	3min	2min59sec
6	Individual know impurities				
	IMP A	NMT-2%	0.39%	0.38%	0.37%
	IMP B	NMT0-2%	0.10%	0.11%	0.05%
	IMP C	NMT-1%	0.24%	0.24%	0.24%
	Total impurities	NMT-4%	0.73%	0.73%	0.66%

Table 10 Dissolution of Rifampin and Isoniazid Tablet

Sr. No.	Time (mints)	Cumulative % drug release	
		Rifampin	Isoniazid
1	5	90	91
2	10	97	96
3	15	101	104
4	30	105	105
5	45	110	109

different outlet temperatures show that the LOD was within the limit that 1.0 % to 2.0 % w/w So that the proper drying was achieved between 40˚C – 44°C Outlet temperature for Isoniazid and 46˚C – 50°C between for Rifampin.

Lubrication: In this processes challenges were taken at different times points 3, 5, 7mints uniformity blending was obtained by assay of 10 locations per batch and individual sample 90 to 110% of mean value and % RSD NMT 5%, for effective mixing was calculated by mean assay of all location shown in table-4.

In process lubrication the results of three batch's at different time intervals show that the % RSD was with the limit that NMT 5%.So, that the proper mixing was done. Comparing to the other time interval Lubrication at 5 mints is optimum.

Lubricated Blend composite sample: Results are shown in table-5.

Assay of Rifampin and Isoniazid for all three validation batches was found within Specification. Rifampin USP (142.5 to 165.0 mg) 95 to 100% Isoniazid USP (71.5 to 78.75) 95.0 to 105.0%

Table 11 Weight Variation

Sr. No.	Weight variation (mg)		
	Batch I	Batch II	Batch III
1	362	375	365
2	365	370	367
3	375	372	370
4	369	374	373
5	377	365	370
6	370	359	370
7	378	365	375
8	375	375	380
9	359	380	355
10	355	379	369
11	385	378	370
12	380	376	359
13	370	380	358
14	372	359	378
15	375	358	370
16	369	360	360
17	369	365	365
18	367	361	370
19	374	378	375
20	375	375	375
Min	355	358	355
Max	385	380	380
Ave	371.05	370.2	368.7

Table 12 Thickness and Hardness

Sr. No.	Thickness(4.2-4.7mm)			Hardness(NLT 50 Newton)		
	Batch no.			Batch no.		
	I	II	III	I	II	III
1	4.29	4.34	4.34	114	102	105
2	4.30	4.28	4.35	110	108	111
3	4.34	4.31	4.37	108	115	97
4	4.29	4.34	4.29	102	111	120
5	4.37	4.38	4.34	105	114	109
6	4.38	4.31	4.39	108	112	109
Ave	4.32	4.32	4.34	107	115	100
Min	4.29	4.28	4.29	102	108	107
Max	4.38	4.38	4.39	114	106	105

Table 13 Friability

Sr. No.	Batch no.	Result
1	Batch I	0.15
2	Batch II	0.11
3	Batch III	0.18

Compression: Stage challenges were done by speed challenge at minimum and maximum speed, hardness challenge at minimum and maximum hardness. Flow of granule at different hopper levels, result are shown in table-6, 7, and 8.

Acceptance criteria: content uniformity NLT-85%-NMT-115%and RSD NMT-5.0%, dissolution NLT 80% at Q point-30, disintegration within 15mins,friability NMT 1%, weight variation in between 345mg-375mg. In the compression process at the different granule at hopper levels the dissolution of each tablet at Q point 30 shows NLT 80% and the target hardness (100N-110N) results were optimum**.** At the different speed levels the tablets were under go different test and results of the test were within the limit and at target speed results were optimum. Among the different levels of the hopper the middle of hopper have content uniformity drug was present compare to initial and end of the hopper.

Coating: The coating of all three batches has been validated for Pan Load, Pan RPM, Inlet & outlet

Table 14 *Invitro* dissolution of three batches

Sr. No.	product		Rifampin (NLT 80% in 30 min)				
			5	10	15	30	45
1	Batch 1	Tablet 1	94	100	104	107	112
		Tablet 2	91	99	104	106	112
		Tablet 3	91	99	103	106	111
		Tablet 4	94	100	102	106	100
		Tablet 5	93	100	103	105	114
		Tablet 6	92	98	102	104	113
2	Batch 2	Tablet 1	90	98	102	107	115
		Tablet 2	90	98	102	108	110
		Tablet 3	91	97	102	105	112
		Tablet 4	91	98	101	106	114
		Tablet 5	91	99	101	107	113
		Tablet 6	91	99	103	106	111
3	Batch 3	Tablet 1	90	100	101	105	114
		Tablet 2	94	99	104	107	115
		Tablet 3	92	101	102	105	110
		Tablet 4	93	97	103	108	109
		Tablet 5	92	102	102	104	111
		Tablet 6	90	101	101	107	111

Table 15 *Invitro* dissolution of three batches

Sr. No.	product		Isoniazid (NLT 80% in 30 min)				
			5	10	15	30	45
1	Batch 1	Tablet 1	91	94	97	99	99
		Tablet 2	93	96	97	98	98
		Tablet 3	92	95	100	96	98
		Tablet 4	94	98	105	100	100
		Tablet 5	95	97	101	105	104
		Tablet 6	89	96	96	102	101
2	Batch 2	Tablet 1	94	97	104	96	97
		Tablet 2	91	96	105	94	97
		Tablet 3	94	97	98	98	98
		Tablet 4	95	97	102	101	97
		Tablet 5	88	104	99	109	100
		Tablet 6	89	98	97	94	99
3	Batch 3	Tablet 1	91	96	94	103	97
		Tablet 2	86	98	105	99	104
		Tablet 3	98	99	98	97	99
		Tablet 4	88	97	97	101	105
		Tablet 5	90	96	106	109	106
		Tablet 6	92	102	106	105	104

temperature, gun distance, atomization and spray rate and the results are comparable among all the three batches. The tablets were collected and checked for purity, Dissolution, uniformity of dosage related impurities assay results are shown in table-9, 10 and figure-1.

Dissolution of Rifampin in coated tablet was found in the range of 90-110 % in 5 min, 10 min, 15 min., 20 min., 30 min, and 45 min and dissolution of Isoniazid in coated tablet was found in the range of 91-109% in 5 min., 10 min, 15 min, 20 min, 30 min, and 45 min.

Evaluation of tablets –Tablets were evaluated by applicable parameters as study of weight variation results are shown in table-11 and figure-2, hardness and thickness results are shown in table -12 and figure-3, 4. Friability results are shown in table -13 and dissolution study results are shown in table -14, 15.The values were found within the limit [9, 10] the weight variation was found between the range of 355-385mg. Thickness of tablet was found within the 4.2-4.8, hardness was found NLT 50 Newton. Friability was found NMT 1% and dissolution release profile of all the three batches were not less than 80% at Q 30 minute.

CONCLUSION

Process validation is a key element in assuring that these principles and goals are met. In this study concurrent process validation was carried out for one product. In tablet dosage form, critical parameters were taken up for

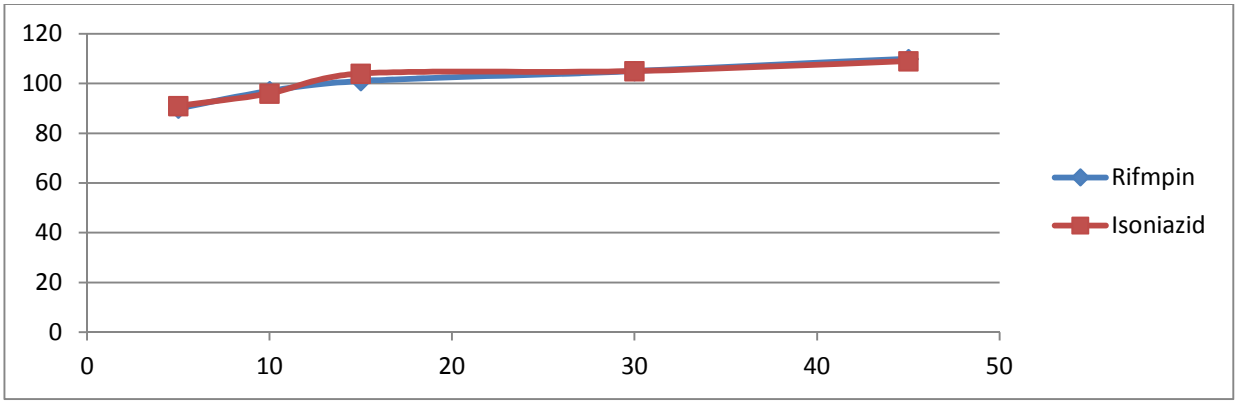

Figure 1 Dissolution profile of Rifampin and Isoniazid tablet

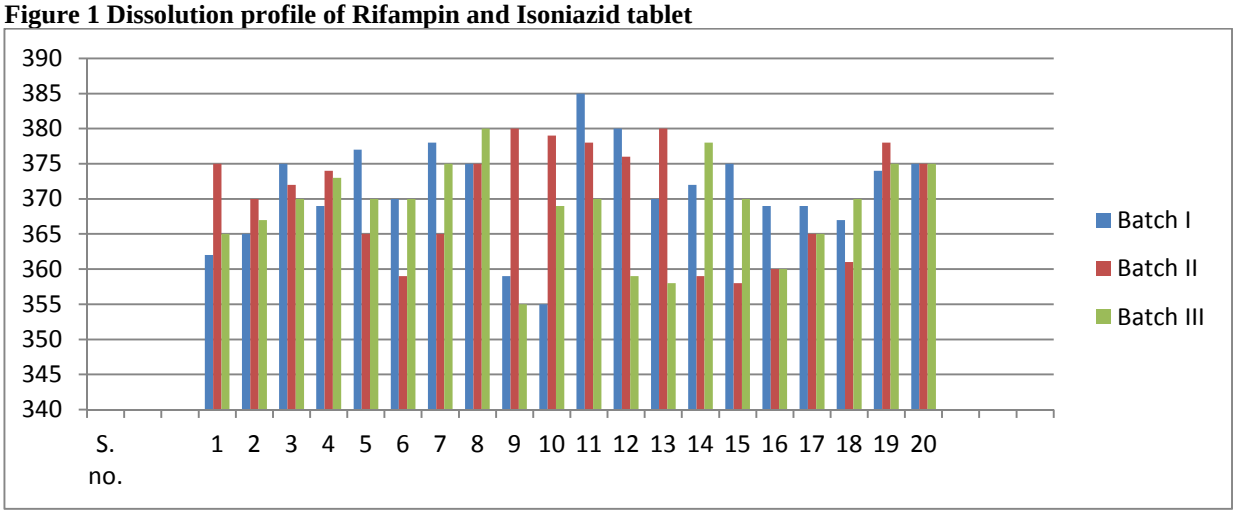

Figure 2 weight variation

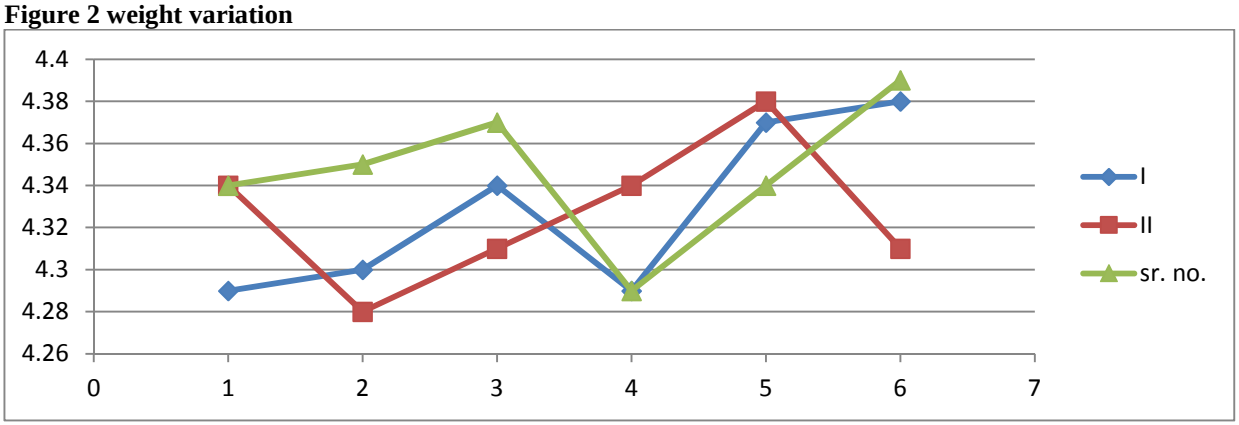

Figure 3 Thickness

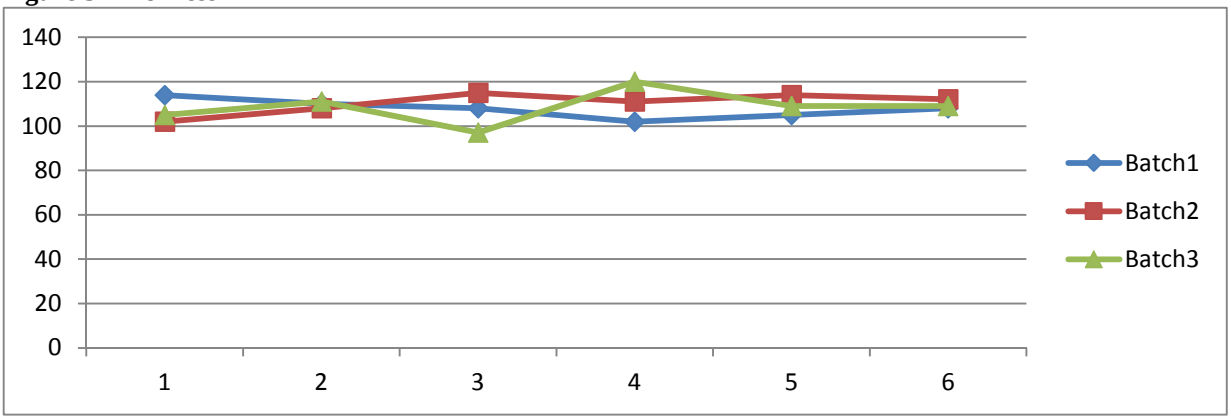

Figure 4 Hardness

validation studies and the results shown that the process was validated.

ACKWOLEDGEMENT

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