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FORMULATION AND PROCESS VALIDATION OF ATORVASTATIN FILM COATED TABLET

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ABSTRACT

Atorvastatin is a selective competitive inhibitor of HMG CoA reductase. It reduces total cholesterol, low density lipoprotein (LDL). HMG CoA reductase catalyzes the HMG CoA to mevolanate, which is the limiting step in cholesterol biosynthesis. It also reduces the VLDL cholesterol and triglyceride. The present research work focused on formulation and concurrent process validation for Atorvastatin 20 mg tablets. The tablets were manufactured by wet granulation method. Since the dose is 20 mg, uniform distribution of the drug in the tablet is critical which can influence the content uniformity, assay and dissolution of the tablets. Validation is best viewed as an impartment and integral part of cGMP. Validation is therefore one element of quality assurance programs associated with a particular process. Quality cannot be assured only by doing finished product testing and in-process monitoring but it should be built into the manufacturing process. So building of quality require a special attention to a few factors like selection of material, process design, control variables, in process control and finished product testing. In this study three initial batch of Atorvastatin tablet with same size, method, equipment & validation criteria were taken. Various critical parameters during dry mixing, wet granulation, drying, lubrication, compression and coating stages were identified and evaluated as per validation protocol. The outcomes of the entire process indicate that process validation data provides a high degree of assurance that the manufacturing process will produce a product meeting its predetermined specification and quality attributes. It is concluded that the wet granulation method can ensure uniform distribution of Atorvastatin and the tablets can be effectively manufactured with the desired specifications & reproducible quality standards.

Keywords: Atorvastatin, Concurrent process, Wet granulation method, Critical parameters

INTRODUCTION

Atorvastatin (AVT), as a synthetic lipid-lowering agent, is an inhibitor of 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase which catalyzes the conversion of HMG-Co A to mevalonate, an early rate limiting step in cholesterol biosynthesis. Atorvastatin is currently used as calcium salt for the treatment of hypercholesterolemia [1].

Atorvastatin calcium ([*R*-(*R**,*R**)]-2-(4-fluorophenyl)-β,γ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino)carbonyl]-1Hpyrrol- 1-heptanoic acid, hemi-calcium salt). Is a white to off-white crystalline powder that is insoluble in aqueous solution of pH 4 and below; it is very slightly soluble in water and slightly soluble at pH 7.4 phosphate buffers and acetonitrile, slightly soluble in ethanol and freely soluble in methanol. The intestinal permeability of atorvastatin is high at the physiologically

intestinal pH (6-6.5). However, it is reported that the absolute bioavailability of atorvastatin is 12% after a 40 mg oral dose [2]. The basic principle of quality assurance is that a drug should be produced that is fit for its intended use [3]. In order to meet this principle, a good understanding of the processes and their performance is important. Quality cannot be adequately assured by in-process and finished product inspection and testing, but it should be built into the manufacturing processes. These processes should be controlled in order that the finished product meets all quality specifications. One of the major problems that affect product quality is the non-uniform distribution of drug in the dosage form. Non-uniform distribution of drug can affect critical parameters like assay, content uniformity and dissolution. The purpose of the present study is to ensure uniform distribution of the drug in the dosage form, which is manufactured by wet granulation method by concurrent process validation approach. The validation study was performed on three batches. Process validation is establishing documented evidence which provides high degree of assurance that a specific process consistently produced a product meeting its predetermined specifications and quality characteristics [4]. Process validation is intended to establish that the proposed manufacturing process is a suitable one and yields consistently a product of the desired quality. i.e. that the process is suitable and under control [5]. The main advantages to be obtained from process validation are

- ✓ Expanded real time monitoring and adjustment of process.
- ✓ Enhanced ability to statistically evaluate process performance and product variables.
- ✓ Increased confidence about process reproducibility and product quality.
- ✓ Improved ability to set target parameters and control limits for routine production.
- ✓ Enhanced reporting capability [6].

Types of Process validation

- Prospective validation
- Concurrent Validation
- Retrospective validation
- Process re-validation [7].

Prospective validation is done prior to manufacture of commercial batches. Using this well-defined process, a series of batches (generally considered acceptable that three consecutive batches/runs within the finally agreed parameters) should be produced which would give desired quality product and constitute a proper process validation.

Concurrent validation is a practical approach under certain circumstances which includes (a) When a previously validated process transferred to a third party contract manufacturer or to another manufacturing site, (b) Where the product is a different strength of a previously validated product (c) When the number of lots evaluated under the Retrospective Validation were not sufficient to obtain a high degree of assurance demonstrating that the process is fully under control, (d) When the number of batches produced are limited (e.g. orphan drugs). **Retrospective validation** is applicable to processes that are stable and in routine use which have not undergone a formally documented validation process. Documentary evidence for the validity of the processes can be provided by utilizing the historical data. Retrospective validation is only acceptable approach for well-established detailed processes that include operational limits for each critical step of the process and will be inappropriate where there is a change in operating procedures, product formulation, equipment and facility. Data from a minimum of ten consecutive batches produced will acceptable for retrospective validation.

Process re-validation provides the assurance that changes in a process and /or the process environment that are introduced do not adversely affect process characteristics and product quality. Some planned or unplanned changes that may require re-validation under following situations (a) Changes in raw materials (b) Changes in the source of active raw material manufacturer, (c) Changes in packaging material (d) Changes in process (e) Changes in the equipment (f) Changes in the plant/facility, (g) Variations revealed by trend analysis.

Materials and Methods

Atorvastatin calcium was obtained from Vitalife Laboratories Gurgaon, Haryana. HPMC, crospovidone, microcrystalline cellulose, magnesium carbonate, lactose and starch was purchased from Merck Chemicals, Germany. Other reagents and solvents used were of analytical grade.

Experiment/ Methodology

Table 1: Product profile of Atorvastatin tablets

Product Name	Atorvastatin tablets 20 mg
Dosage form	Tablet
Label claim	Each film coated tablet contains Atorvastatin calcium equivalent to AVT 20 mg
Batch size	110000 Tablets
Shelf life	36 months

The manufacturing formula for batch size of 110000 tablets is given below:

Table 2: Master formula of Atorvastatin tablet

Sr. No	Components	Specification	Weight/Tablet in mg
Dry Mixing			
1	Light magnesium carbonate	IP	145.68
2	Lactose	IP	73.54
3	Starch	IP	34.14
Binding			
4	Starch	IP	12.0
5	Polysorbate 80(tween 80)	IP	4.36
6	Purified water	HIS	Q.S
Lubrication			
7	Atorvastatin calcium	HIS	21.6
8	Anhydrous Lactose	BP	20.28
9	Colloidal silicon dioxide	IP	8.0
10	Crospovidone	BP	8.0
11	Microcrystalline cellulose	IP	13.4
12	Magnesium stearate	IP	5.0
	Total(uncoated tablet)		346.0
	Film Coating		
13	Hydroxy propyl methyl cellulose E-15	IP	4.36
14	Isopropyl alcohol#	HIS	Q.S
15	Dichloromethane#	BP + HIS	Q.S
16	Polyethylene glycol 6000	IP	0.44
17	Purified talc	IP	0.9
18	Titanium dioxide	IP	0.9
19	Diethyl phthalate	BP	0.44
20	Colour-Ponceau 4R lake	HIS	0.2
21	Isopropyl alcohol		Q.S
22	Weight build up		7.24
	Total(coated Tablet)		353.24

Manufacturing process

Granulation

A. Raw material shifting

Light magnesium carbonate (16.02kg), starch for dry mix (3.76), lactose monohydrate 8.09 kg, starch for paste (1320g) are transferred from the raw material day store to granulation area. The light magnesium carbonate, starch for dry mix & lactose is Sifted through 40 # .sift starch (for paste) through 60 #.The sifted materials are collected into cleaned container lined with double polythene bag.

B. Binder solution preparation

The weighed, 1320 gm of maize starch was taken into stainless steel tank and purified water was added into tank to make slurry. To obtain lump free paste, required quantity of boiled purified water was added to above mixture. After that, Polysorbate 80 (480g) was added under continuous stirring. The paste was cooled at 40 to 50° C.

C. Dry mixing, granulation

Light magnesium carbonate, starch, lactose monohydrate are loaded in to the rapid mixer granulator. Dry mixed material is agitated for 7 min at slow speed. Binder solution was added after dry mixing at slow agitator to obtain granules.

D. Drying, Sifting and Milling

After successful granulation, it was loaded into the FBD and inlet temperature was maintained 60°C to 70°C for 20 min. The obtained semisolid granules were passed through # 20 fitted on vibrosifter. Retained granules were passed through the sieve 1.5 mm perforator on multi mill at medium speed knife forward direction. Again dried the semidried granules till the desired LOD in between 2.5 to 3.0 % w/w is achieved.

E. Blending / Lubrication

Atorvastatin calcium (2.38kg) and anhydrous lactose (2.23kg) was transfer through sieve 40# and was considered as blend A. Colloidal silicon dioxide (880g) and crospovidone (880g) was transfer through sieve 40# and was considered as blend B. Microcrystalline cellulose and blend A was transfer through sieve 40#, was consider as blend C. Prepared blend B and blend C is sifted through sieve 40# and it was considered as blend D. Magnesium stearate (550) was sifted through 60#. Blend A and blend B was transfer into octagonal blender and mixed for 5 min at slow speed. Sifted and milled granules obtain from step (D) loaded in to blender and mix for 20 min at slow speed. At the last, magnesium stearate was added in to the blender mix for 3 min.

The lubricated granules were unloaded and store in stainless steel container 2.

Compression

After release from QC department, lubricated granules were taken for the compression. For the compression of Atorvastatin 20 mg tablet, following specification was used as per master manufacturing formula.

Compression machine -29 stations, Upper punch Size-10.0 mm, Shape-round standard concave punches embossing break line, Lower punch size -10.0 mm Shape - round standard concave punches , Die size-10.0mm, RPM 15±5rpm,Pressure- 5-6 Tone.

Coating process

Load the compressed tablet into the Ganscoater. Temperature was set for hot air inlet temperature 40-50^{0}C. Maintain exhaust temperature at 35-40^{0}C. Tablet was warm at hot air temperature till the bed temperature is attained 35-40^{0}C by inching. Coating solution is loaded of first lot in the solution vessel and stirring the coating solution during the processing. Spraying was started after achieving the bed temperature and all parameters maintained during coating. Pan RPM has been maintained 1-3 and compressed air pressure was 5-6 kg. The coated tablets were unloaded after drying.

Evaluation of tablet

The critical parameters considered during the process validation of Atorvastatin film coated tablet are Dry mixing, Wet granulation, Drying, Lubrication, Compression, Coating, Packaging, Weight variation, Hardness test, Dissolution test, Assay study.

Dry mixing

This step involves mixing of Atorvastatin Calcium with other excipients. Mixing speed and time are critical variables in this process. Since speed of the RMG is constant, proper mixing time shall be determined. Mixing is a critical step as less mixing time will result in non-uniform distribution of drug whereas more mixing time will result in de-mixing, leading to non-uniform distribution of drug and increase in disintegration time [8]. Proper mixing shall be established by checking content uniformity of drug at all the time intervals mentioned in protocol.

Wet granulation

Binding solution was added to mixed material in RMG and mixes it with slow speed until quality wet granules mass is obtained.

Drying

Water in granules or blend is important factor. If moisture is more in granules it will lead to poor flow and poor hardness. If moisture is less it will lead to capping, high friability and chipping. Drying of granules in Fluidized bed dryer (FED) controls the water. Inlet temperature of FED is most critical variable for the drying. LOD or water is checked periodically to establish the same. Drying was carried as per the batch

manufacturing record at an inlet temperature of 65-75°C till the LOD comes to not more than (NMT) 2.5 - 3.0 % w/w. Samples were withdrawn from seven places of the FED bowl after drying as per protocol and check LOD using moisture balance.

Milling and size distribution

This step involves size reduction of granules after drying. Milling was carried out in multimill at the speed of 1450 RPM. After effective size reduction, granules were subjected for sieve analysis. For sieve analysis, granules were transferred to vibro-sifter. The vibro-sifter was made up of different sives, arranged according to its aperture size in ascending order, such as 20, 40,60, 80, and 100 #

Blending

Blending involves mixing of granules with other extragranular ingredients [9]. The purpose is to get a uniform distribution of Atorvastatin Calcium with other ingredients. Blending speed and time are critical variables in this process. Since speed of the blender is constant, proper blending time shall be determined. Blending is critical as less blending will result in non-uniform distribution of drug whereas more blending will result in de-mixing, leading to non-uniform distribution of drug and increase in disintegration time. Proper blending shall be established by checking content uniformity of drug at all the time intervals mentioned in protocol. Proper blending time has been be established by checking of drug content at regular time intervals (20 + 3 min) before lubrication and after lubrication.

Lubrication

This step involves mixing of blended granules with lubricant to achieve good flow and antiadherent properties to aid satisfactory compression parameters [10]. Lubrication time and speed are critical variables in this process. Since speed of the blender is constant, proper lubrication time shall be determined. Proper lubrication shall be established by checking content uniformity of drug and physical parameters of lubricated granules.

Compression

This step involves conversion of lubricated granules into tablets as per specifications. Speed of machine and hopper levels are the major variables. So, following parameters are to be checked to establish the above-mentioned variables at regular intervals:

- Weight variation (group and individual)
- Hardness
- Thickness
- Friability
- Disintegration time
- Assay

Method of analysis

The method of analysis of samples taken at various process steps is given below:

Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if none of the individual tablet weight deviates from the average weight by more than the 7.5 % of the average weight.

Hardness

The crushing strength in Kg/cm2 of tablets was determined for 10 tablets of each batch by using Ketan hardness tester. The average hardness and standard deviation was determined.

Friability

Ten tablets were weighed and placed in the Roche friabilator and apparatus was rotated at 25 rpm for 4 minutes. After revolutions the tablets were deducted and weighed the percentage friability was measured using the formula:

$$\% F = \{1-(Wt/W)\} \times 100$$

Where % F = friability in percentage W = Initial weight of tablets Wt = weight of tablets after revolution

Thickness and diameter

The thickness and diameter of all the tablets were measured by digital vernier callipers and expressed in mm.

Disintegration

The test was carried out in disintegration test apparatus. The baskets were filled up to 75% of its capacity and temperature was checked by sensor. The temperature was set with 37 ± 2 °C. Six tablets were placed into different disintegration mesh tube and apparatus was stared. The time was noted until complete disintegration of the tablets.

***In vitro* dissolution study**

The in vitro release of Atorvastatin calcium tablets were studied for dissolution in phosphate buffer pH 6.8, an amount of 900 ml of respective dissolution fluids were used at 37°C with stirred speed of 75 rpm. 5 ml of the sample of dissolution medium was withdrawn and filter through whatman GSC filter and taken into vials. The volume withdrawn after 30 min and volume was replaced with same quantity of fresh dissolution medium. The sample was analyzed for drug release by HPLC analysis. After HPLC analysis, following calculation was used to determine drug release from tablet.

Sample area/Std area x44mg (WS)/100 x 5/100 x 900/20 x 0.9654 x potency of WS (99.99%)

Chromatographic system:

Detector: PDA detector 240 nm

Column: C18 Inertsil ODS column (250 mm x 4.6 mm,5 µm)

Column temperature: 35°C

Flow rate: 2.0 mL/min

Injection volume: 20 µL

Mobile phase system: Accurately measured quantity (1000 ml) of ammonium acetate buffer pH 4.0, 925 ml of acetonitrile and 25 ml of tetrahydrofurone, mixed together to prepare mobile phase.

Assay [11]

To carry out assay procedure, 20 tablets were crushed to get fine powder. From the powder, 80 mg equivalent to Atorvastatin calcium transfer to 500 ml of volumetric flask contained 100 ml of methanol and dispersion was sonicated. The volume was make up to 500 ml with methanol. From this resulting solution, aliquot of 5 ml was withdrawn and diluted with 10 ml of diluent solution. After HPLC analysis, following calculation was used to determine drug content from tablet.

Sample area/Std area x44mg (WS)/100 x 5/100 x 900/20 x 0.9654 x potency of WS (99.99%)

Coating

The coating process is performed in perforated auto coater. The film coating is performed at a predetermine lot size and the predetermined coating parameter. All in process were checked at regular intervals to ensure the coated tablets meet the finished product specification.

- Spray rate
- Distance b/w spray gun to tablet bed
- Inlet/outlet temperature
- Bed temperature
- Atomization pressure
- RPM of coating pan
- RPM of the peristaltic pump
- Tablet thickness
- Weight of 20 tablets
- Weight gain
- Dissolution of coated tablet

RESULTS AND DISCUSSION

In the present study, total 3 batches of Atorvastatin tablets were manufactured and subjected for process validation. The validation was done at the various stages of manufacturing of tablets such as drying, milling, blending, compression and coating. Since the amount of the drug in the tablet is around 5%, the critical process steps that can affect the distribution of drug in the tablet were evaluated. Non uniform drug distribution can affect the weight, dissolution and assay. The results are presented below.

DRYING

The drying process was performed in the FED. After the drying process, samples were collected possible poor area of drying to check the uniformity of drying. After collection of samples, it was analyzed for its moisture content on the moisture balance. The results of collected samples of all three batches were found within the acceptable limits as shown in the table 3. After the positive result of drying uniformity, the all batches were taken for further process.

Tablet 3: LOD after drying

Sample	Weight	Batch No. A		Batch No. B		Batch No. C	
		Weight taken (g)	LOD % w/w	Weight taken (g)	LOD %w/w	Weight taken (g)	LOD % w/w
Tl	2 - 5 g	2.228	2.79	2.130	2.86	2.130	2.63
T2	2 - 5 g	2.622	2.55	2.206	2.83	2.193	2.64
Ml	2 - 5 g	2.111	2.69	2.261	2.56	2.198	2.79
M2	2 - 5 g	2.469	2.70	2.152	2.73	2.104	2.82
M3	2 - 5 g	2.262	2.73	2.158	2.81	2.156	2.83
Bl	2 - 5 g	2.128	2.70	2.265	2.85	2.077	2.89
B2	2 - 5 g	2.425	275	2.179	2.93	2.254	2.93.

Milling and particle size distribution

The milling process was carried out for size reduction of prepared granules. Milling process was done successfully and granules were further subjected for size distribution by sieve analysis. The ratio of coarse granules and fine powder was found satisfactory Table 4.

Table 4: Result of sieve analysis (milled granules)

Sieve size	Weight required (composite)	Particle size distribution		
		% w/w Retention		
		Batch A	Batch B	Batch C
20#t	50 gm	8.60	1.20	3.96
40#t		29.32	19.08	39.87
60#t		17.71	43.28	16.87
80#t		22.29	22.84	19.43
100#t		3.95	0.44	3.27
		% W/W Passed Through		
100#		17.53	0.56	16.36

Tapped density, untapped density and LOD was checked and obtained result mentioned in table 5.

Table 5 Result bulk density & LOD of Milled granules

Batch no.	Tapped bulk density	Untapped bulk density	LOD at 105°C
A	**0.79 g/ml**	**0.56 g/ml**	**2,92%**
B	**0.75 g/ml**	**0.60 g/ml**	**2.85%**
C	**0.71 g/ml**	**0.56 g/ml**	**2.82%**

Blending

To check the uniform distribution of drug with granules, samples were collected from 10 different locations, at 20 minute before the lubrication and 3 minute after the lubrication. All the collected samples were subjected for content uniformity and RSD is summarized in the table 6. The tests were carried out for all three batches. After the lubrication, the granules were subjected for LOD, bulk density and particle size analysis. Result revealed that blend uniformity, LOD, bulk density and particle size analysis was found to be within the acceptable limits table 7 & 8.

Table 6 Blend uniformity of lubricated and pre-lubricated granules for batch A/B/C

Batch No.	Sample Points	% Content of Atorvastatin calcium (mg/tab.)	
		Blending Time	
		20 Min (Pre lubrication)	3 Min (Lubrication)
A	Top 1	99.0	99.6
	Top 2	102.4	100.8
	Top 3	102.2	101.2
	Top 4	98.4	100.2
	Middle 1	101.0	102.3
	Middle 2	99.5	100.6
	Middle 3	102.0	100.4
	Bottom 1	99.9	100.2
	Bottom 2	101.8	100.6
	Bottom 3	98.5	99.5
	Average	100.5	100.5
	Min	98.4	99.5
	Max	102.4	102.3
	RSD	1.56	0.80
B	Average	100.3	100.9
	Min	98.0	98.4
	Max	102.9	103
	RSD	1.35	1.34
C	Average	99.5	99.7
	Min	97.5	97.5
	Max	102.1	102.5
	RSD	1.6	1.44

Table 7 Result of bulk density-untapped/tapped and LOD (lubricated granules)

Batch No	Weight required	Tapped Bulk Density	Untapped Bulk Density	LOD at 105°C
A	50 gm	0.77 g/ml	0.63 g/ml	2.82 %
B	50 gm	0.54 g/ml	0.49 g/ml	2.87 %
C	50 gm	0.59 g/ml	0.56 g/ml	2.77 %

Table 8 Result of sieve analysis (Lubricated granules)

Sieve size	Weight required (composite)	Particle size distribution % w/w Retention		
		Batch A	Batch B	Batch C
20#t	50 gm	8.60	1.28	3.97
40#t		27.56	25.51	32.06
60#t		17.88	20.50	16.45
80#t		22.55	20.70	18.32
100#t		3.63	8.58	7.31
		% W/W Passed Through		
100#		18.57	21.33	20.95

COMPRESSION

After the successful granulation process, granules were taken for the compression. During the compression, process validation was done for all three batches (A, B, C) by challenging the parameters like maximum hardness, minimum hardness, initial stage optimum speed, middle stage optimum speed and end stage optimum speed. On the base of these parameters, various in-process tests were carried out such as description, average weight, diameter, friability, hardness, disintegration, thickness, uniformity of weight and assay. Tablets were subjected to dissolution only for the maximum and minimum compression hardness. From the result of all batches, it was observed that compression force only affected the friability & disintegration time. As the compression hardness increased, friability was decreased whereas disintegration time was increased, this might be due to more compact tablets. All the test results were complied with specifications table 9.

Tablet 9 Results of compression process

Parameter	Observation			Specification
	A	B	C	
Description	Complies	Complies	Complies	White to off white, circular, biconvex uncoated tablet having break line on one side and plane on other side
Average Weight	347.73	346.23	346.15	346.00 ± 2.5% (337.45 to 354.56)
Friability	0.17%	0.19%	0.16%	NMT 1 %
Diameter	10.05	10.02	10.00	10.00 ±0.20 (9.80-10.20)
Thickness	4. 19	4. 19	4. 18	4.20 ± 0.20 (4.00 -4.40)
Hardness	4.82	4.95	4.97	4.0 to 7.0
Dissolution %	104.3	102.7	104.6	NMT 75
Disintegration T	01 min 54 sec	01 min 55 sec	01 min 57 sec	NMT15
Assay	101.8	102.9	101.2	95.0 to 105.0

Coating process variables

At the stage of coating different parameter taken under the validation such as inlet temperature, outlet temperature, bed temperature, weight gain, uniformity of weight, % drug contain, thickness, spray rate and dissolution all the mention parameter has been checked for three batches (A,B,C) found well within the specification limit table 10 & 11.

Table 10 Result of temperature variable of coating pan during coating process, Uniformity of weight

Sr.no	Batch no	Inlet temperature	Outlet temperature	Bed temperature	Pan RPM
1	Batch A	35°C-40°C	45°C-50°C	39°C-41°C	1.2
2	Batch B	35°C-40°C	44° C - 50° C	40°C-41°C	1.3
3	Batch C	35°C-40°C	45°C-49°C	38°C-40°C	1.2

Table 11 Result of Wt. Variation, Thickness, DT, %Content uniformity of Coated Tablets

Batch no.	Wt. Variation	Thickness (mm)	D.T.	%Content uniformity
A	357	4.15	3 Min 10 Sec	98.92
B	352	4.15	2 Min 22 Sec	98.73
C	355	4.18	2 Min 42 Sec	100.58

Spray rate for all three batches has been measured and found 52 gm/min, 58gm/min, 56 gm/min respectively for batch A,B,C.

Table 12 **Dissolution profile of finished product (% drug released)**

Sample No.	Result A	Result B	Result C
1	95.53	93.90	93.25
2	96.20	95.34	95.27
3	96.50	95.98	94.32
4	95.75	95.98	95.29
5	95.43	92.33	93.25
6	95.61	95.63	95.30
Average	**95.84**	**94.86**	**94.45**

Conclusion

The concurrent process validation of Atorvastatin film coated tablet has been performed for three batches (batch A, batch B, batch C) and all the parameters and results were found within the acceptance limit. Based on the results of the validation data for three batches, it was concluded that the manufacturing process used for formulation of Atorvastatin film coated 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 product is considered to be validated and can be routinely followed.

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