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Comparison of Process Parameter of Lab Batches, Scale-Up Batches Exhibit Batches Commercial Batches

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ABSTRACT

The aim of the present work is to evaluate the critical process parameters and techniques and improve the quality and reduce cast and scaling up time. The pharmaceutical industry R & D refers to the process of successful progress from drug discovery to product development. The need to the target market are identified alternative product concept are generated and evaluate and single concept of selected for future development. The concept is a description of the from function and features a product and a usefully. The Scale up is the process as define to increasing the batch size or increasing different physical parameter the output of volume. The old process scale up techniques doesn't involve studying the critical process parameters (Raw Process). The scale up batches industry to improve quality of the product in moving from Scale up batches/Exhibit Batches and validation batches. To improve the batches quality scale up of a process Transformation of small scale lab batches into commercial scale depended on experience and probability and involving the more technique. Due to this probability of success is less understanding of critical process parameters and process enables control of critical step process parameter during manufacturing and successful transformation from lab scale to Exhibit batches and commercial batches.

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INTRODUCTION

Historical data shows that the R&D Expenditure in pharmaceutical firms, which is between 14% and 18% of their annual sales. Is about five times more than average R&D Expenditure in others industries. The pharmaceutical industry R&D refers to the process of successful progress from drug discovery to product development. The scale up batches industry to improve quality of the product in moving from Research and Development (R&D) to production, Scale up batches/Exhibit Batches and validation batches to improve the batches quality scale up of a process can also be viewed as a procedure for applying the same process to different output volumes [1]. Transformation of these small-scale up observations into the large-scale development mostly requires entirely varied design strategies and equipment which may result in differences in quality. The process of new product development

is based on cooperation between designers, different department of the company and suppliers and clients. The process consists of four stages.

1. Stages I – Feasibility study; this stage lasts from 2 to 5 weeks.
2. Stages II – Design phase; This phase can lasts up to 6 months.
3. Stages III – Preparation of the prototype, Final costs and price estimation this stage lasts up to 5 months.
4. Stages IV – Manufacturing.

The novel stage of Scale-up is defined as the process of increasing batch size [Table 1]. Scale-up of a process viewed as a procedure for applying the same process to different output volumes. There is a subtle difference between these two definitions: batch size enlargement does not always translate into a size increase of the processing volume [2].

Concept of Product Development

The need to the target market are identified alternative product concept are generated and evaluate and single concept of selected for future development. The concept is a description of the from function and features a product and a usefully [Figure 1].

METHOD

The current procedure of process of exhibit batches depends on country to country and followed the various processes.

In United States

1. R&D Trial batches
2. Lab scale up batches
3. Process batches/Exhibit batches/Submissition batches
4. Pivotal batches/Exhibit/Submission batches
5. Process validation batches (Divided into three batches) [3].

In Japan States

1. R&D Trial batches
2. Dissolution method development
3. Lab scale up batches
4. ProcessOptimization batches/ Trial batches
5. Pivotal batches/Exhibit batches/Submission batches
6. Process validation batches (Divided into three batches first batch accidental second batches quality is regulatory quality third batches is validation) [4].

Selection and Function of Raw Materials

The raw material is basic excipients with a mycophenolate mofetil tables are prepared. It is procured form other company and depends upon the grade & quality [Tables 2 and 3].

Precaution

Mycophenolate Mofetil is used as immunosuppression agent use nose mask hand gloves and respirator during processing to avoid exposure to powder inhalation.

Mycophenolate

Mycophenolate Mofetil is the 2-morpholinoethyl ester of Mycophenolic acid (MPA), an Immunosuppressive agent inosine Monophosphate dehydrogenase (IMPDH) inhibitor [Figure 2] [Table 4] [5].

The raw material is basic excipients with a Mycophenolate Mofetil Microcrystalline

Cellulose

Microcrystalline cellulose grades used in the formulation development are (Avicel PH101) and (Avicel PH 102). These excipients are generally recommended as diluent microcrystalline cellulose grades use of the tablets diluent of concentration 20-90% using in microcrystalline cellulose grades is incompatible with strong oxidizing agents [6].

Croscarmellose Sodium

Croscarmellose sodium (Ac-Di-Sol) used in the generally recommended as disintegrant Croscarmellose sodium id disintegrant in tablets 0.5-5.05 using. Croscarmellose sodium is a stable though hygroscopic material.

Povidone

Povidone K 90 was selected in the formulation it is used in the formulation as a binder 0.5-5.0% povidone is suspending agent upto 5.05%.

Magnesium Stearate

Magnesium stearate was selected as lubricant it is used as a lubricant in tablets manufacture at concentration between 0.25-5.0% using.

Opadry Purple

It is a ready-mix grade of film coating composition supplied from colorcon. This coating material is recommended as Non- functional film coating

in the immediate release tablets dosage forms and it contains HPMC29/10 Hypromellose and hydroxypropyl cellulose as a film former, polyethylene glycol as plasticizer and titanium oxide as opacifier FD & C Blue 2 is permitted in the United States indigo carmine Aluminium 3% -5% and iron oxide red as colorants.

Manufacture Procedure

Dispensing

In this the raw material of mycophenolate mofetil & excipient is dispensed to prepare mycophenolate mofetil tablets of dispense product depend upto batch size [7, 8].

Sifting

Microcrystalline cellulose (Avicel PH 101) through mesh # 40

Croscarmellose sodium (Ac-di-Sol) through mesh # 40 [9].

Preparation of Binder Solution

Weight quality of purified water in a S.S (Plasdone K-90) slowly to the purified water of while stirring and continue the clear solution is obtained [10, 11].

Dry mixing

Transfer Mycophenolate Mofetil & sifted material of into rapid mixer granulator and mix for 10 minute with impeller at slow speed and chopper off and record the amperage reading of impeller motor [12].

Figure 1: Various stages for Mycophenolate Mofetil Tablets USP 500mg

Granulation

Add binder solution of over a period of 2 minute while mixing with impeller at slow speed and chopper off. Based on granulation consistency add additional quality of purified water over a period of 1 minute with impeller at slow speed and chopper off. Knead the wet mass over a period of 1 minute with impeller and chopper at fast speed. Discharge the wet mass at impeller slow speed through co-mill with 12.0mm screen into fluid bed dryer bowl.

Drying

Drying the wet mass of an inlet temperature of 50^0C $\pm$ 5^0C in fluid bed dryer till to get LOD in the range of 1.0 to 2.0% w/w at 80^0C by auto mode using suitable moisture analyzer.

Milling

Mill the dried granules by using suitable mill, fitted with 1.5mm screen at medium speed /knives forward direction until all the granules are passed through the screen.

Extra-Granular Material Sifting

Microcrystalline cellulose (Avicel PH 101) & Croscarmellose sodium (Ac-di-sol) together through mesh # 40Sift magnesium stearate through mesh # 60

Pre Lubrication

Microcrystalline cellulose (Avicel PH 101) & Croscarmellose sodium (Ac-di-sol) into suitable blender and blend for 10 minutes at 12 rpm.

Lubrication

Magnesium stearate Lubricated blend for 5 minutes at 12 rpm.

Compression

Tooling Details

17.80 $\times$ 8.90mm capsule shape deep bevel concave punches embossed with 'H' on lower punch and "MRV" on upper punch.

Coating (Film Coating Suspension)

Take weighed quantity of water filled in a container equipped with a propeller stirrer. Add Opadry II complete film coating system 85F200021 Purple slowly to the purified water while stirring. Increase the speed of stirrer if necessary continue stirring for 45 minutes or till a smooth homogeneous suspension is obtained. Transfer core tablets into coating pan tablets bed temperature reaches approximately 40 $\pm$ 5^oC. The weight gain of the tablets as per the standard operating procedure. Stop the coating when the average tablets gain is 2.5 $\pm$ 0.5% w/w of core tablets weight [13].

Table 1: Pharmaceutical formulation and process can be designed using the following statistical tools

Desired Product Quality		
ICH Q8 (R2) Pharmaceutical Development	ICH Q9 quality risk Management	ICH Q10 Pharmaceutical Quality systems

Table 2: Regulatory Authority

Country	Regulatory Authority	Full Name
India	CDSCO	Central drugs standard control organization
USA	USFDA	Food and drug administration
Canada	HC	Health Canada
Europe	EMEA	European medicine agency
UK	MHRA	Medicines and Healthcare products regulatory agency
Japan	PMDA	Pharmaceuticals and medical devices agency
Russia	MOH	Ministry of Health
Brazil	ANVISA	Ministry Sanitary Surveillance Agency
Indonesia	NADFC	National agency of drug and food control of republic of Indonesia
South Africa	MCC	Medicine control authority
Thailand	FDA-Thailand	Food and drug administration Thailand
China	SFDA	State food and drug administration
Singapore	HAS	Health sciences authority
Malaysia	DCA	Drug control authority
Philippines	BFDA	Bureau of food and drug administration
Srilanka	MOH	Ministry of health

Table 3: Selection of Excipients

Excipient	Category
Tablets Core	
Mycophenolate Mofetil USP	API
Microcrystalline cellulose (Avicel PH101)	Diluent
Microcrystalline cellulose (Avicel PH102)	Diluent
Croscarmellose sodium (Ac-di-sol)	Disintegrant
Povidone (Plasdone K-90)	Binder
Magnesium stearate (LIGAMED MF-2-V)	Lubricant
Coating	
Indigo carmine lacquer	Colorant
Hydroxypropyl cellulose	Film forming agent
Hydroxypropyl methyl cellulose	Film forming agent
Polyethylene glycol 400	Plasticizer
Red iron oxide	Colorant
Titanium dioxide	Opacifying agents

Table 4: Chemistry of Mycophenolate Mofetil USP

Details	Description
Description	White or almost white crystalline powder.
Structure	[Figure 3]
Chemical name	2-(Morpholin-4-yl)ethyl(4E)-6-(4-Hydroxy-6-methoxy-7-methyl-3-oxo-1,3- dihydroisobenzofuran-5-yl)-4-methylhex-4-enoate.
Molecular formula	C23 H31 NO7
Molecular weight	433.50
Solubility	Freely soluble in acetone, sparingly soluble ethanol and slightly soluble in water
Polymorphism	It does not show polymorphism
Melting point	Between 94^0C and 98^0C
ka	5.6
Therapeutic category	Immunosuppression agents
Pharmacopoeia status	Drug substance and drug product both are official in USP
BSC Classification	Class-II (Low solubility and High permeability)

Table 5: Showing variable affecting wet granulation method

Process variable	Product variable	Apparatus variable
Impeller chopper rotation speed	Amount of liquid binder	Shape & size of mixing chamber
Load of the mixer	Characteristic of liquid binder a) Surface tension b) Viscosity	Shape & size of impeller

Table 6: Different capacity Blender equipment of Tip Speed Calculation

Different Capacity	Research & Development			Production
	2 liters (Gansons)	10 liters (Gansons)	10 Liters (Sainath)	50 liters (Gansons)
Impeller Slow (RPM)	85.0	36.0	207.0	155
Impeller Fast (RPM)	170.0	72.0	415.0	310
Diameter (m)	0.56	1.32	0.355	0.43
PI	3.14	3.14	3.14.0	3.14
		Tip speed (m/s)		
Impeller Slow	2.49	2.49	3.85	3.50
Impeller Fast	4.98	4.97	7.71	7.01
		Froude Number		
Impeller Slow	0.11	0.05	0.43	0.29
Impeller Fast	0.46	0.19	1.73	1.18

Table 7: Comparison of parameters for Blending between 450 L blender and 4000 L Blender in terms of tangential velocity

S.No	Parameter	450L	4000L
1	Diameter (m)	1.603	2.670
2	Radius (m) (r)	0.802	1.335
3	Blender rpm (N)	9	= 2*π*r*N (m/min) =2*3.14*1.335 = 8.384 = 45.33/8.384 = 5.41
4	=2*3.14*1.335 = 8.384	45.33	Actual : 45.36 (considering 5.41 rpm)
	Calculation	2*3.14*0.802*9= 45.33	Actual : 2*3.14*1.335*5.41= 45.36
5	Total revolutions for lubrication	45	45
6	Total time for lubrication (min)	5 min	9 min

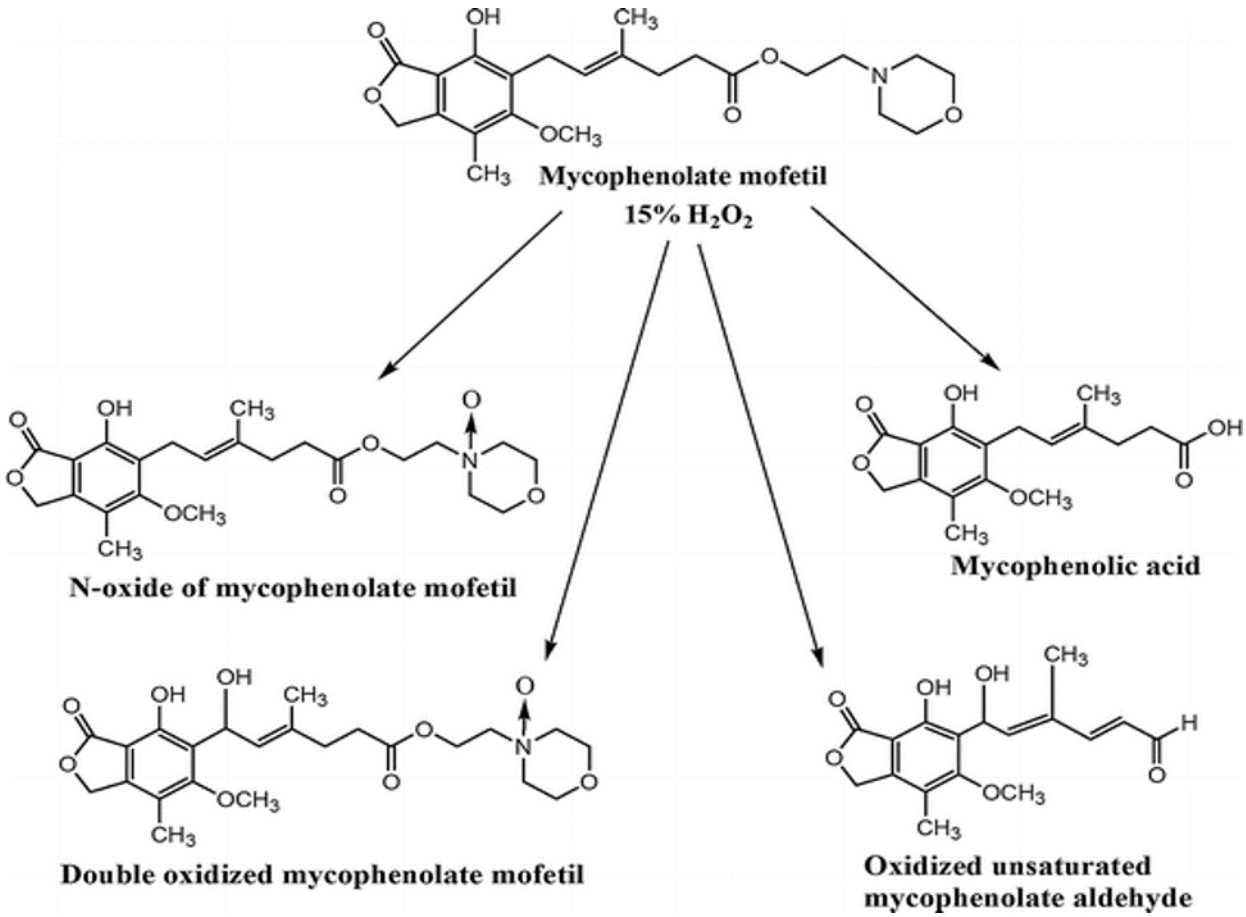

Figure 2: Mycophenolate Mofetil Synthesis

Table 8: The commercial batches is prepared successfully and sent for market Compiled Date for Technology Dozier

Parameters	R&D Trials Batches	Scale up Batches	Exhibit Batches	Commercial Batches
Batches size (Maximum)	2500 Tablets	1,50,000 Tablets	11,25,000 Tablets	50,00,000 Tablets
Dispensing weight (Maximum)	820mg	12.3kg	92.25kg	410.0mg
Sifting sieve	40mm	40mm	40mm	40mm
RMG Capacity	2 litre	200 litre	750 litre	2000 litre
Mixing time for RMG	5 minutes	6 minutes	5 minutes	8 minutes
RMG rpm	30 rpm	40 rpm	60 rpm	130 rpm
Milling hole size	8.0rpm	8.0rpm	8.0rpm	8.0rpm
Fluid bed dryer	5kg	150kg	200kg	500kg
Drying Time	45 minutes	58 minutes	62 minutes	85 minutes
Drying Temperature	50 ± 5^{0} C	50 ± 5^{0} C	50 ± 5^{0} C	50 ± 5^{0} C
Drying LOD	1.08%	1.33%	1.40%	1.58%
Dry Milling Size	1.5mm	1.5mm	1.5mm	1.5mm
Milling rpm	600rpm	500-600rpm	600-800rpm	800-1000rpm
Blender Capacity	2 litre	400 litre	800 litre	1500 litre
Blender rpm	12 rpm	12 rpm	12 rpm	12 rpm
Pre Lubrication time	10 minutes	10 minutes	10 minutes	10 minutes
Lubrication time	5 minutes	5 minutes	5 minutes	5 minutes
Tooling	D-Tooling	D-Tooling	D-Tooling	D-Tooling
Rotary	Single	Single	Double	Double
Tablets punching machine station	8 Station	27 Station	27 Station	55 Station
Compression	20 rpm	27 rpm	27 rpm	45 rpm
Shape	Capsule Shape Deep Bevel Concave	Capsule Shape Deep Bevel Concave	Capsule Shape Deep Bevel Concave	Capsule Shape Deep Bevel Concave
Individual tablets weight	820mg	822mg	821mg	825mg
Thickness	6.00mm	6.10mm	5.70mm	6.10mm
Hardness	15-17kp	15-16kp	16-17kp	18-19kp
DT	1min 5sec	1min 15sec	1min 10sec	1min 20sec
Coating machine name	Neocota	Neocota	Neocota	Neocota
Pan capacity	12 inches	36 inches	36 inches	48 inches
Pan speed	2-6rpm	2-5rpm	2-4rpm	1-3rpm
No.of spray guns	1 gun	1 gun	1 gun	1 gun
Spray rate	3-5rpm	3-5rpm	3-5rpm	3-5rpm
Inlet temperature	$50 – 60^{0}$ C	$55 – 62^{0}$ C	$52 – 58^{0}$C	$55 – 60^{0}$ C
Bed temperature	$40 – 42^{0}$ C	$35 – 40^{0}$ C	$35 – 40^{0}$ C	$36 – 41^{0}$ C
Individual tablets weight	832mg	835mg	830mg	833mg
Thickness	6.25mm	6.26mm	6.22mm	6.28mm
Hardness	22-23kp	22-23kp	22-23kp	22-23kp
DT	2 min 20 sec	2min 10sec	2min 30sec	2min 45 sec

Tip Speed Calculation

The constant Impeller Tip Speed means same shear rate in both the RMGs which [14] is an alternative to constant power in relative swept volume [Tables 5 and 6].

$$Tip\ Speed\ =\ \pi \times N \times D/t$$

where, N = RPM of the impeller; D = Diameter of the impeller, t = Kneading or Mixing time

1. Blender sweep Diameter (m) of 150L: 1.136 m
2. Blender sweep Diameter (m) of 300L: 1.449 m
3. Blender sweep Diameter (m) of 450L: 1.603 m
4. Blender sweep Diameter (m) of 1200L: 2.043 m
5. Blender sweep Diameter (m) of 4000L: 2.670m

Based on above calculation, 9 rpm in 450L blender is almost equivalent to 5 rpm in 4000L blender maintaining the Tangential velocity constant. So for 4000L blender the equivalent Lubrication time is 9minutes at 5 rpm for Mycophenolate Mofetil USP tablets 500mg. Comparison of parameters for Blending between 300L blender and 4000L Blender in terms of tangential velocity [Table 7].

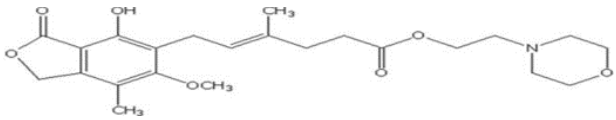

Figure 3: Structure of Mycophenolate Mofetil USP

Blender

These industrial blenders are sturdily constructed in precise dimension and offer high performance without any hassle. Keeping ourselves abreast of cutting edge technology [13]. They find application for the purpose of mixing and lubricating the granules homogeneously.

Reasons for Blend Testing

To optimize the blend time during development phase. To demonstrate lack of segregation in bins/drums during material handling to confirm that specified blend conditions produce acceptable uniformity during validation. Blend assays can be used to release finished product. The type of blending like Double cone blender, Octagonal blender, Ribbon blender, Coata blender, V-blender [13, 15].

R &D Trials Batches

The batch size of lab scale batches is 820mg or 2500 Tablets. The shape of Mycophenolate Mofetil Tablets is round and get individual average weight of tablets is 820mg of lab batches (500mg API +320mg Excipients) for the preparation of granules stated with dispensed so the 500gm raw material dispensed including excipient and sift by 40mm (#40) sieve and wet granulation method for using RMG Capacity 10 litre and mixing speed 5 minutes [16]. Wet milling 8.0mm and drying for 45 minutes at $50^oC \pm 5^oC$ in fluid bed dryer till to get LOD in the range of 1.08% w/w at 80^oC and Extra granular into two part one is pre lubrication 10 minutes and lubrication 5 minutes for 12 rpm The mixed by octagonal blenders mixer. After mixer the product and compresses the tablets by 20rpm speed at 8 stations. The compressed tablets moved for next step i.e evaluation of tablets parameters. The weight of randomly selected tablets 820.000 $\pm$ 5% (Maximum Acceptable 779.000 to 861.000) The Hardness of randomly selected tablets 17.5kp (Maximum Acceptable 10.0 to 20.0kp) measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rotate by 100rpm. The result of Friability loss than is NMT 1.0% the tablets taken form Disintegration is 45-50sec (Maximum Acceptable NMT 10min). The Thickness of tablets is 6.00 $\pm$ 0.30% (Maximum Acceptable 5.70 - 6.30mm) measured by Digital Vernier Caliper. The Film coated of tablets the about parameters of spray rate 2-4 rpm pan capacity 36 inches Inlet temperature about 50 to 60^oC bed temperature about 40 to 42^oC The weight of randomly selected tablets 832.000 $\pm$ 5%. The Hardness of randomly selected tablets 19.2kp measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rorate by 100rpm. The tablets taken form Disintegration is 2min 30sec (Maximum Acceptable NMT 10min). The Thickness of tablets is 6.26mm measured by Digital Vernier Caliper as shown in Table 8.

The R&D Trials batches is Acceptable & Successful within limit further go for scale up batches

The batch size of lab scale batches is 12.3kg or 150000 Tablets. The shape of Mycophenolate Mofetil Tablets is round and get individual average weight of tablets is 820mg of lab batches (500mg API + 320mg Excipients) for the preparation of granules stated with dispensed so the 500gm raw material dispensed including excipient and sift by 40mm (#40) sieve and wet granulation method for using RMG Capacity 100 litre and mixing speed 6 minutes. The Wet milling 8.0mm and drying for 58 minutes at $50^oC \pm 5^oC$ in fluid bed dryer till to get LOD in the range of 1.33% w/w at 80^oC and Extra granular into two part one is pre lubrication10

minutes and lubrication 5 minutes for 12 rpm The mixed by octagonal blenders mixer. After mixer the product and compresses the tablets by 36rpm speed at 27 Stations. The compressed tablets moved for next step i.e evaluation of tablets parameters. The weight of randomly selected tablets 820.000 ± 5% (Maximum Acceptable 779.000 to 861.000) The Hardness of randomly selected tablets 17.5kp (Maximum Acceptable 10.0 to 20.0kp) measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rorate by 100rpm. The result of Friability loss than is NMT 1.0% the tablets taken form Disintegration is 45-50sec (Maximum Acceptable NMT 10min). The Thickness of tablets is 6.00 ± 0.30% (Maximum Acceptable 5.70 -6.30mm) measured by Digital Vernier Caliper. The Film coated of tablets the about parameters of spray rate 2-4 rpm pan capacity 36 inches Inlet temperature about 50 to 60^{o}C bed temperature about 40 to 42^{0}C The weight of randomly selected tablets 832.000 ± 5%. The Hardness of randomly selected tablets 19.2kp measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rorate by 100rpm [17]. The tablets taken form Disintegration is 2min 30sec (Maximum Acceptable NMT 10min). The Thickness of tablets is 6.26mm measured by Digital Vernier Caliper as shown in Table 8.

The Scale up batches is Acceptable & Successful with in limit further go for Exhibit batches

The batch size of lab scale batches 82.00kg or 11,00,000 Tablets. The shape of Mycophenolate Mofetil Tablets is round and get individual average weight of tablets is 820mg of lab batches (500mg API + 320mg Excipients) for the preparation of granules stated with dispensed so the 500gm raw material dispensed including excipient and sift by 40mm (#40) sieve. And wet granulation method for using RMG Capacity 750 litre and mixing speed 5 minutes. Wet milling 8.0mm and drying for 62 minutes at 50^{o}C ± 5^{o}C in fluid bed dryer till to get LOD in the range of 1.40% w/w at 80^{0}C and Extra granular into two part one is pre lubrication 10 minutes and lubrication 5 minutes for 12 rpm The mixed by octagonal blenders mixer. After mixer the product and compresses the tablets by 20rpm speed at 8 stations. The compressed tablets moved for next step i.e evaluation of tablets parameters. The weight of randomly selected tablets 820.000 ± 5% (Maximum Acceptable 779.000 to 861.000). The Hardness of randomly selected tablets 17.5kp (Maximum Acceptable 10.0 to 20.0kp) measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rorate by 100rpm. The result of Friability loss than is NMT 1.0% the tablets taken form Disintegration is 45-50sec (Maximum Acceptable NMT 10min).The Thickness of tablets is 6.00 ± 0.30% (Maximum Acceptable 5.70 - 6.30mm) measured by Digital Vernier Caliper. The Film coated of tablets the about parameters of spray rate 2-4 rpm pan capacity 36 inches Inlet temperature about 50 to 60^{o}C bed temperature about 40 to 42^{o}C The weight of randomly selected tablets 832.000 ± 5%. The Hardness of randomly selected tablets 19.2kp measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rorate by 100rpm. The tablets taken form Disintegration is 2min 30sec (Maximum Acceptable NMT 10min) [18]. The Thickness of tablets is 6.26mm measured by Digital Vernier Caliper as shown in Table 8.

The Exhibit Commercial batches is prepared Successful and sent for regulatory authority for market approval

The batch size of lab scale batches 820.00Kg or 10,00,000 Tablets. The shape of Mycophenolate Mofetil Tablets is round and get individual average weight of tablets is 820mg of lab batches (500mg API + 320mg Excipients) for the preparation of granules stated with dispensed so the 500gm raw material dispensed including excipient and sift by 40mm (#40) sieve. And wet granulation method for using RMG Capacity 2000 litre and mixing speed 5 minutes. Wet milling 8.0mm and drying for 85 minutes at 50^{o}C ± 5^{o}C in fluid bed dryer till to get LOD in the range of 1.58% w/w at 80^{0}C and Extra granular into two part one is pre lubrication 10 minutes and lubrication 5 minutes for 12 rpm The mixed by octagonal blenders mixer. After mixer the product and compresses the tablets by 20rpm speed at 8 stations. The compressed tablets moved for next step i.e evaluation of tablets parameters. The weight of randomly selected tablets 820.000 ± 5% (Maximum Acceptable 779.000 to 861.000) The Hardness of randomly selected tablets 17.5kp (Maximum Acceptable 10.0 to 20.0 Kp) measured by using (Kraemer Hardness) tester and next Friability measured by Electrolab Type Friabilitor Measured rorate by 100rpm. The result of Friability loss than is NMT 1.0% the tablets taken form Disintegration is 45-50 Sec (Maximum Acceptable NMT 10min). The Thickness of tablets is 6.00 ± 0.30% (Maximum Acceptable 5.70 - 6.30mm) measured by Digital Vernier Caliper. The Film coated of tablets the about parameters of spray rate 2-4 rpm pan capacity 36 inches Inlet temperature about 50 to 60^{o}C bed temperature about 40 to 42^{o}C The weight of randomly selected tablets 832.000 ± 5%. The Hardness

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RESULT & DISCUSSION

Scale up batches

The batch size of lab scale batches is many required post approval changes that affected in the formulation site and manufacturing process or equipment 12.3kg or 1,50,000 Tablets small scale up batch with different capacity of equipments, tip speed calculation data and analytical report find the from the regulatory standpoint, scale up and scale-down are treated with the same degree of scrutiny The Scale-up batches is Acceptable & Successful with in limit further go for Exhibit batches.

Exhibit batches

This technique has some limitation which are these techniques useful for commercial batch maximum batch size for 1500kg batch that affected in the formulation site and manufacturing process or equipment 82.00kg or 11, 00,000 Tablets the Exhibit batches is prepared Successful and sent for regulatory authority for market approval.

Commercial batches

The Novel Validation batch is run successfully and collects all the increased amount of tablet from techniques useful for commercial batch maximum batch size for 1500kg batch that affected in the formulation site and manufacturing process or equipment 410.0kg or 50,00,000 Tablets the commercial batches is prepared Successful and sent for regulatory authority for market approval. The commercial batches is prepared successfully and sent for market.

CONCLUSION

The aim of this research work is about the various a novel observer critical parameter & techniques a scale up batches & Exhibit batches to reduce the time and with limit. Transformation of these Small-Scale observation of different in quality (Tip speed calculation RMG Occupancy blender calculation, compression machine and Neocota machine various techniques) A comparison between fixed and variable speed operations has been made to show the performance of the proposed different machine capacity, Time the scale up batches Exhibit batches so our target is time saving and techniques problem.

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Conflict of Interest

The authors attest that they have no conflict of interest in this study.

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