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Method Validation of Oral Non-Steroidal Anti-Inflammatory Drug: Aspirin

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ABSTRACT

The objective of the present study was to develop Method Validation of Oral Non-Steroidal Anti-Inflammatory Drug: Aspirin and the release of the drug from the Oral Non-Steroidal Anti-Inflammatory. The main purpose behind process validation is to provide documented evidence that the manufacturing process of Aspirin 400 mg coated tablet meets the predefined control parameters. This involves in-process monitoring of critical processing steps and end product testing of current production can document evidence to show that the manufacturing process is in a state of control.

KEYWORDS: Anti-Inflammatory Drug, Validation, Quality Assurance, validation, process.

INTRODUCTION:

QUALITY ASSURANCE

Is a wide ranging concept covering all matters that individually or collectively influence quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of quality required for their intended use. Quality assurance therefore incorporates GMP and other factors, such as product design and development. Significance and applications of QA in Pharmaceutical Industry: The system of quality assurance appropriates the manufacture of pharmaceutical products & should ensure that; Medicinal products are designed and developed in a way that takes account of the requirements of Good Manufacturing Practice (GMP), Good Laboratory Practice (GLP) and Good Clinical Practice (GCP).

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VALIDATION

"VALIDATION is defined as a documented procedure for obtaining, recording and interpreting data required to show that a process will consistently comply with predetermined standards." Validation is a scientific study of process:

- To improve that the process is consistently doing what it is supposed to do (i.e.that the process is under control)
- To demonstrate the process variables, acceptable limits for these variables and to set up appropriate in-process controls.

Materials and Methods:

The project entitled "Process validation of oral non-steroidal anti-inflammatory drug: Aspirin 400 mg tablet" was carried out at **Wockhardt Pharmaceutical Ltd.**, Aurangabad, Maharashtra. The study involves validating the process variables of this product to show that the process was under control. The study was conducted on a batch size of 3.12 Lac, which includes the validation of critical steps of manufacturing such as dry mixing, blending, compression, coating and blister packing.

2.1 METHODS: Procedure

2.7.1 DISPENSING: Environmental conditions were monitored during dispensing stage. Temperature: Not more that 27 ^{o}C, Relative Humidity: Not more than 50 %, Differential Pressure: NLT 0.4 MMWC. Ensure that weighing balance is cleaned, calibrated and adjusted to zero. Brought materials in original packs for dispensing and verify that all the materials bear QC approved label.

Transferred of each weighed material in to separate polythene bag and store in tightly closed container in quarantine area.

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2.7.2 SIFTING: Weighed all material separately by using calibrated weighing balance. All materials sifted or sieved by using sieve of 20#, for uniform distribution of particle size.

Table 14: Sampling and testing plan for sifting

S.No.	Stage	Sampling location	Sample Quantity
1	Sifting	After completion of sifting pooled sample from container	100 gm

Table 15: Physical parameters & acceptance criteria during sifting.

S.No	Stage	Sample Quantity	Test	Specification
1	Sifting	100 gm.	Appearance	White colored free flowing powder
			Sieve 20#	Should comply.
			Integrity before and after use.	Should be OK
			% powder retained	NMT 1 %

$$\text{Powder retained \%} = \frac{\text{Powder Retained}}{\text{Powder Taken}} \times 100$$

Table 16: Sampling and testing plan for prelubrication

S.No.	Stage	Sampling location	Sample Quantity
1	Blend (Prelubricated)	From container 3 point pooled sampling	100gm

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Testing parameters & acceptance criteria after Blending pre lubrication:

Table 17: Physical parameters & Acceptance criteria after pre lubrication.

S.No.	Stage	Test	Specification
1	Blending (Pre- lubrication)	Appearance	White colored free flowing powder
		Bulk density	0.5–1.0 g/ml
		Tapped Density	0.5–1.0 g/ml.

Sampling location: Top: 1, Middle: 1, Bottom: 1, by using sampling rod.

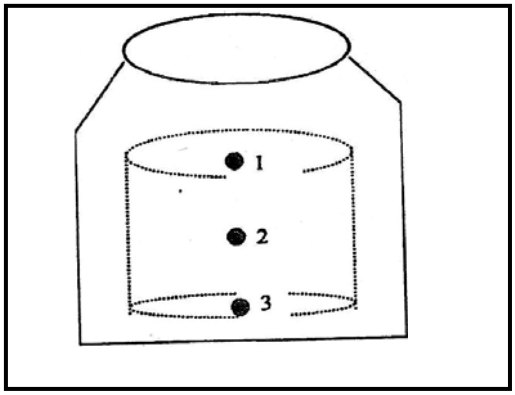

Fig.3: Container

Formula: For Bulk Density and Tapped Density

$$\text{Bulk Density} = \frac{\text{Weight of sample}}{\text{Apperent volume of sample}}$$

$$\text{Tapped density} = \frac{\text{Weight of sample}}{\text{Final tapped volume}}$$

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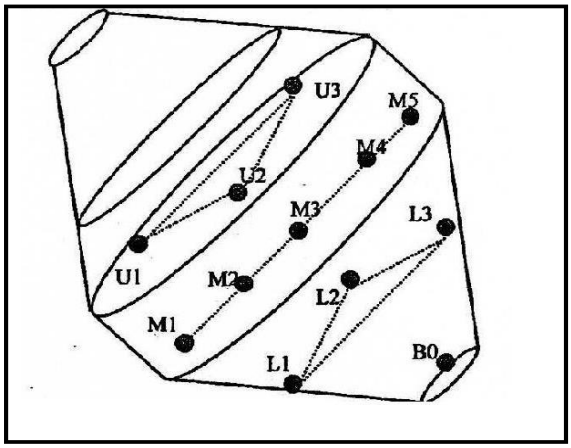
Sampling Location: Double Cone Blender: 12 - Point sampling.



Sampling Location: Double Cone Blender

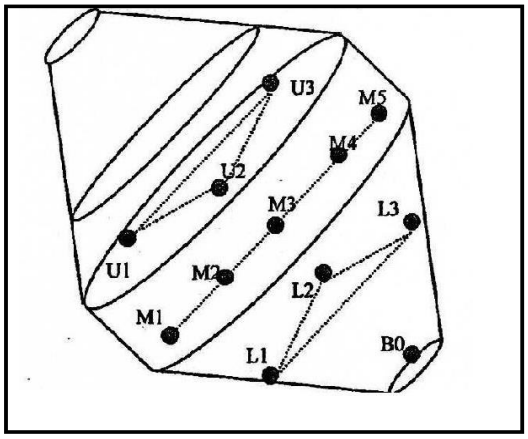


Fig.4: Double Cone Blender

Top samples : 3 (U_1, U_2, U_3)
Middle samples : 5 (M_1, M_2, M_3, M_4, M_5) Lower samples : 3 (L_1, L_2, L_3)
Bottom sample : 1 (B_0)

Blend uniformity by using HPLC:

Procedure:

Preparation of mobile phase: Mixed 1000 ml of methanol to 400 ml of distilled water and added 40 ml of Acetic acid.

Preparation of extracting solution: Mixed 1000 ml of methanol to 1000 ml of distilled water.

Standard preparation of Aspirin: Weighed 200 mg of Aspirin and dissolved in 30 ml of extracting solution, sonicated until dissolve and made up volume to 200 ml with extracting solution.

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Sample preparation: Weighed about 320 mg ± 2.5 % fine powder of blend equivalent to 200 mg of Aspirin added 30 ml of extracting solution, sonicated until dissolve and made up volume to 200 ml with extracting solution. Filter the solution through 0.45 µ filter. Again dilute to 10 to 25 ml of extract

Chromatographic condition:

Table 20: Chromatographic condition

Column	Silica – Octracarber equivalent
Wavelength	254 nm
Flow rate	1.0 ml/min
Oven temp.	30 °C
Run time	10 min.
Injection volume	20 µl

Formula:

$$\text{Blend uniformity} = \frac{AT}{AS} \times \frac{MS}{100} \times \frac{P}{MT} \times M$$

AS – Average % area of standard

(100 %) AT – % Area of Aspirin

in sample

MT – Mass of powder taken sample equivalent to 200 mg of

Aspirin. MS – Mass of standard powder taken 200 mg.

M – Average mass X (640 mg)

P – Purity of standard Aspirin (99.5 %).

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% Blend uniformity

If 400 mg = 100%
x mg = ?

X = Value from Blend Uniformity.

Table 24: Testing of physical parameters for core tablet

S.No.	Parameter	Standards	No. of tablets to be taken for testing
1	Description	White circular, biconvex tablet, plane on both sides.	As per AQL.
2	Weight of 20 tablets	12.8 gm ± 5% (12.16 gm – 13.44 gm)	20 tablets
3	Average weight	640 mg ± 2.5%	20 tablets
4	Weight variation	640 mg ± 5%	20 tablets
5	Hardness	NLT 20 N (2.05 Kg/cm^2)	10 tablets
6	Thickness	6.70 – 7.10 mm	10 tablets
7	Disintegration time	NMT 15 min.	6 tablets
8	Friability	NMT 1 % w/w	20 tablets
9	Assay	380 – 420 mg; 100 ± 5 %	10 tablets

Assay of core tablet by using HPLC: Procedure:

Preparation of mobile phase: Mixed 1000 ml of methanol to 400 ml of distilled water and added 40 ml of Acetic acid.

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Preparation of extracting solution: Mixed 1000 ml of methanol to 1000 ml of distilled water.

Standard preparation of Aspirin: Weighed 200 mg of Aspirin and dissolved in 30 ml of extracting solution, sonicated until dissolve and made up volume to 200 ml with extracting solution.

Sample preparation: Weighed 320 mg ± 2.5 % fine powder of 20 tablets equivalent to 200 mg of Aspirin added 30 ml of extracting solution, sonicated until dissolve and made up volume to 200 ml with extracting solution. Filter the solution through 0.45 µ filter.

Same procedure followed for individual core tablet.

Procedure: Injected 20 µl of blank, standard solution 1 five times, sample solution 2 times, record the chromatogram and measure the peak area of standard and sample solution.

Chromatographic condition:

Table 25: Chromatographic condition for core tablet

Column	Silica – Octracarber equivalent
Wavelength	254 nm
Flow rate	1.0 ml/min
Run time	10 min
Oven temp.	30 °C
Injection volume	20 µl

Formula:

$$\text{Assay} = \frac{AT}{AS} \times \frac{MS}{100} \times \frac{P}{MT} \times M$$

AS – Average % area of standard (100%).

AT – % Area of Aspirin in sample.

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MT – Mass of individual tablet powder equivalent to 200 mg of Aspirin.

MS – Mass of standard powder taken (200 mg)

M – Average mass of tablet 640 mg.

P – Purity of standard Aspirin (99.5 %).

% Assay

If 400 mg – 100%
x mg = ?

X = Value from assay

Sampling and testing plan for coating:

Table 27: Sampling and testing plan after coating

S.No.	Stage	Sampling location	Sample Quantity
1	During coating	From Coating Pan After completion of coating, draw 5-point samples for each lot.	100 tablets
2	Finished product (after coating)	Pooled sample after completion of coating from all containers.	100 tablets (pooled sample)

Finished product analysis and acceptance criteria for coated Tablet: Table 28: Finished product analysis for coated tablet

S.No.	Parameter	Standards	No. of tablets to be taken for testing
1	Description	White, round, biconvex, Sugar Coated Tablet.	As per AQL.
2	Weight of 20 tablets	16.40 gm ± 5% (15.58 gm – 17.22 gm)	20 tablets

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3	Average weight	820 mg± 5% (779 to 861 mg)	20 tablets
4	Thickness	7.20 – 8.0 mm	10 tablets
5	Disintegration time	NMT 30 min	6 tablets
6	Weight Builds Up	160 – 190 mg	20 tablets
7	Assay	380-420 mg 100 ± 5 %	10 tablets

3.1 RESULTS:

3.2 Three batches each of 3.12 lac were taken for the Process validation of Aspirin tablets. For each of three batches the critical steps were identified and variables studied.

3.2.1 SIFTING: By using 20# sieves.

% sample retained for Batch A, B, C:

Table 32: Sifting % sample retained result of three batches

S.No.	Batch no.	Sample taken (gm)	Sample retained (gm)	Result (%)
1	A	10.05	0.025	0.24
2	B	10.06	0.028	0.27
3	C	10.05	0.026	0.25

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Sieve integrity for Batch A, B, C:

Table 33: Sieve integrity for three batches after sifting

Batch no.	Sieve used as per BMR	Sieve Integrity	
		Before Use	After Use
A	20#	OK	OK
B	20#	OK	OK
C	20#	OK	OK

Appearance of powder: White free flowing powder

Table 34: Appearance of powder after sifting

S.No.	Batch no.	Appearance
1	A	Complies
2	B	Complies
3	C	Complies

3.2.2 BLENDING (prelubrication):

Bulk Density for Batch A, B, C:

Table 35: Results of Bulk Density for three batches after pre lubrication

S.No.	Batch No.	Weight of sample (A) gm	Apparent volume (B) ml	Bulk density (g/ml)
1	A	10.02	15.0	0.668
2	B	10.08	15.2	0.663
3	C	10.04	15.1	0.664

Tapped Density for Batch A, B, C

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Table 36: Results of Tapped Density for three batches after pre lubrication

S.No.	Batch No.	Weight of sample (A) gm.	Tapped vol. 10 tap.(ml)	Tapped vol. 500 tap.(ml)	Tapped vol. 1250 tap.(ml)	Final Tapped vol. (ml) (G)	Tapped density (g/ml).
1	A	10.02	13.0	11.5	11.3	11.3	0.886
2	B	10.08	13.4	11.8	11.5	11.5	0.876
3	C	10.04	13.2	11.6	11.4	11.4	0.880

Appearance: White free flowing powder

Table 37: Appearance of three batches after pre lubrication

S.No.	Batch no.	Appearance
1	A	Complies
2	B	Complies
3	C	Complies

3.2.3 BLENDING (Lubrication):

Appearance for Batch A, B, C: White free flowing powder

Table 38: Appearance of three batches of lubricated blend

S.No.	Batch no.	Appearance
1	A	Complies
2	B	Complies
3	C	Complies

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Blend uniformity after lubrication for Batch A,

B, C: Table 39: Details of three batches for blend

uniformity

S.No.	Location	Batch A	Batch B	Batch C
1	U1	98.35	98.45	100.20
2	U2	100.21	97.26	95.24
3	U3	97.65	98.02	99.46
4	M1	98.08	97.30	99.55
5	M2	95.13	96.56	97.23
6	M3	96.02	97.04	97.45
7	M4	100.54	96.42	100.01
8	M5	98.00	97.03	98.55
9	L1	97.08	100.14	96.53
10	L2	98.80	97.25	99.23
11	L3	100.45	98.43	97.53
12	B0	99.23	98.46	100.05
13	**Minimum**	95.13	96.42	95.24
14	**Maximum**	100.54	100.14	100.20
15	**Mean**	98.29	97.69	98.41
16	**% RSD (NMT 5%)**	1.69	1.04	1.60
Acceptance Criteria: Between 90 to 110 % of Aspirin				

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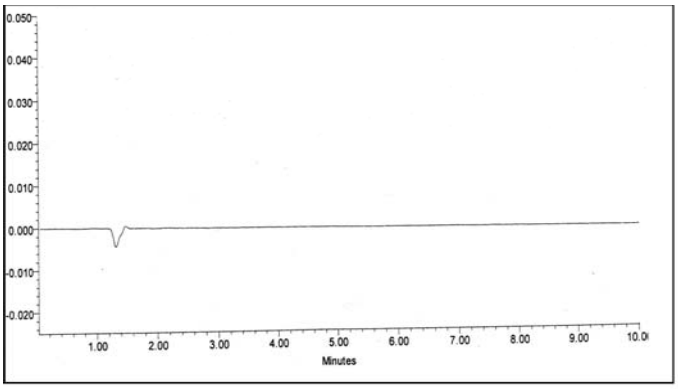
BLANK GRAPH BY USING HPLC: Using solvent without active drug.

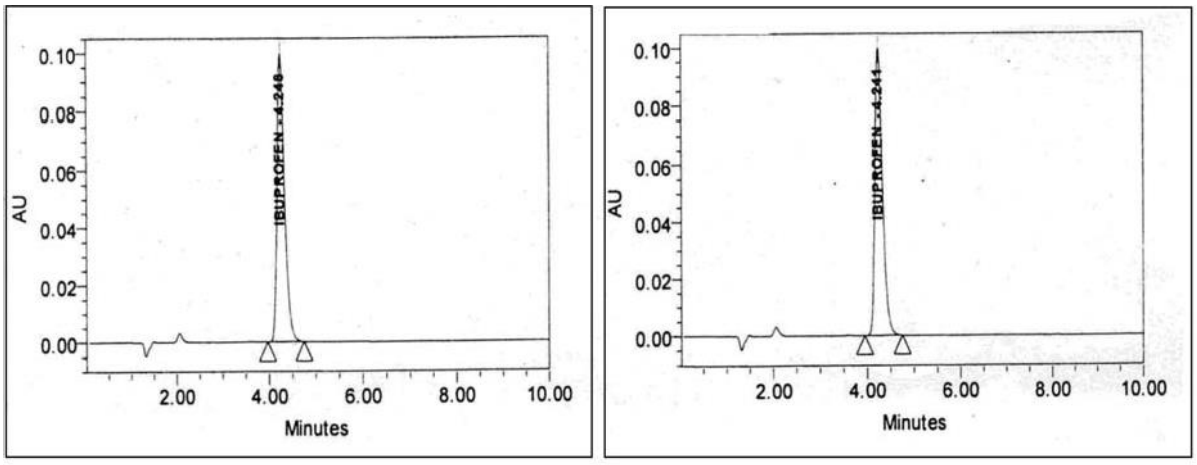
Fig.7: Blank graph by using HPLC



Sample Information	
Sample name	Blank
Acquired method	Aspirin
Flow rate	1.0 ml/min
Run time	10.0 min
Vial	1
Injection	1

STANDARD GRAPH OF ASPIRIN BY USING HPLC

Fig.8: Standard HPLC graph of Aspirin 1, 2, 3, 4, 5.



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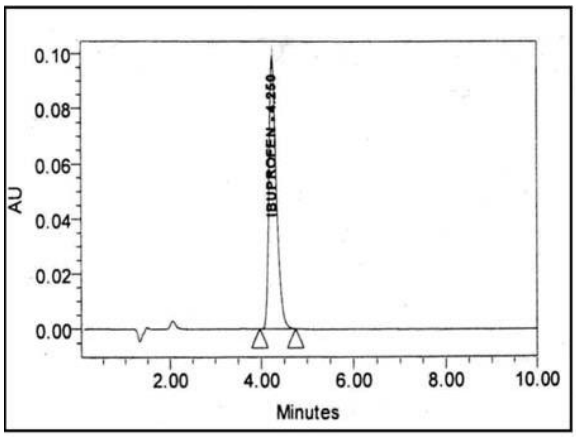

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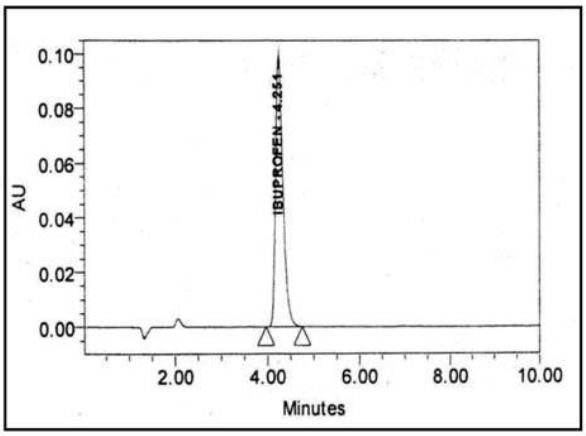

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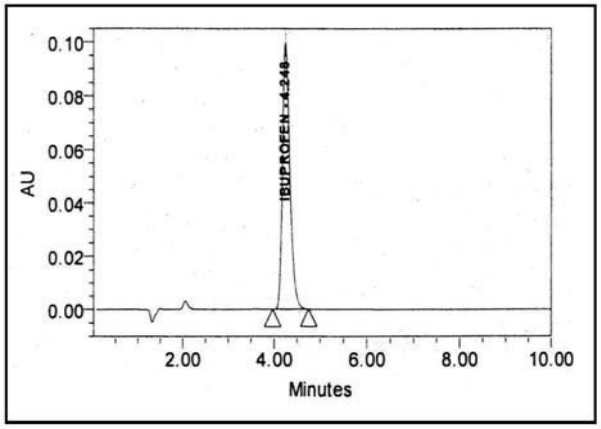

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Table 40: RT & area of Aspirin standard

Sample Information	
Sample name	Standard
Acquired method	Aspirin
Flow rate	1.0 ml/min
Run time	10.0 min
Vial	2

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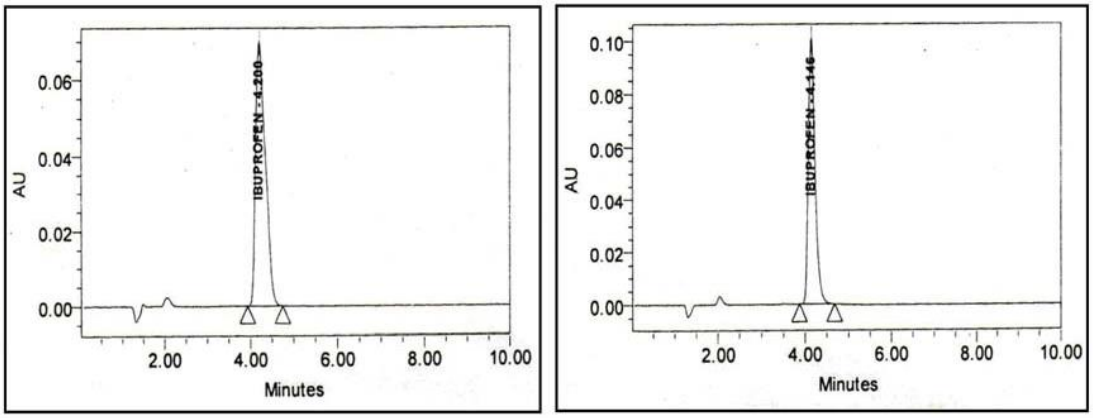
Sr.no.	Name	Sample name	Vial	Injection	RT	Area	% Area
1	Aspirin	Standard# 2	2	1	4.248	1111889	
2	Aspirin	Standard# 2	2	2	4.241	1100869	
3	Aspirin	Standard# 2	2	3	4.250	1113880	100 %
4	Aspirin	Standard# 2	2	4	4.251	1114560	
5	Aspirin	Standard# 2	2	5	4.248	1111946	
Mean					4.2476	1110629	

DETERMINATION OF BLEND UNIFORMITY OF BLEND BY USING

HPLC: Blend Uniformity for Batch A, B, C.

Fig.9: Blend uniformity by HPLC for Batch A, B, C



Batch A: Upper 1 **Batch B: Middle 1**

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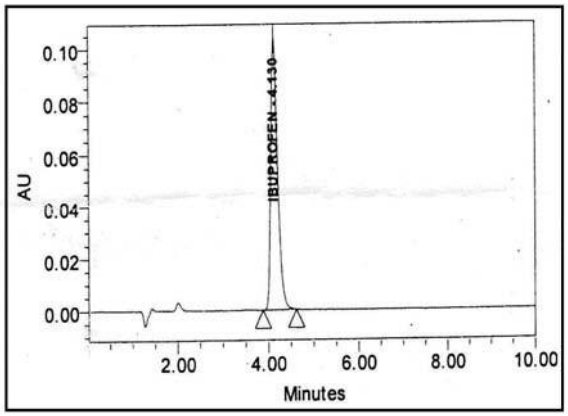

Sample Information	
Sample name	BU
Acquired method	Aspirin
Flow rate	1.0 ml/min
Run time	10.0 min

Batch C: Lower 1

Table 41: RT & area of Aspirin Blend

Sr.no.	Sample Name	Vial	Injection	RT	Area	% Area
1	BU Batch A U1	3	1	4.200	1102356	99.25
2	BU Batch B M1	6	1	4.146	1101849	99.20
3	BU Batch C L1	11	1	4.130	1094568	98.55
Mean				4.158	1099591	99.00

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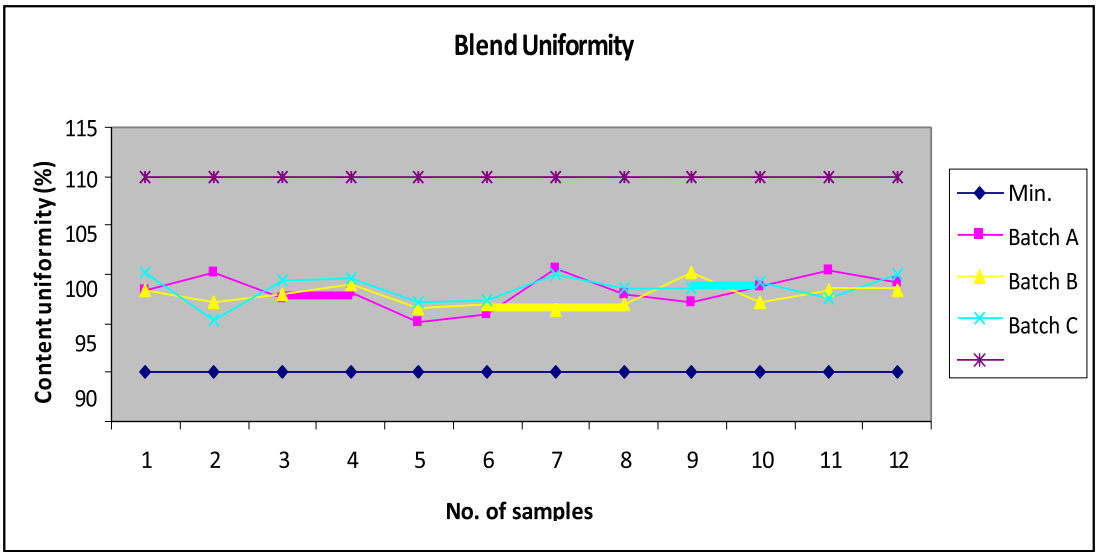
BLEND UNIFORMITY (LUBRICATION)

Fig.10: Comparative Blend uniformity for Batch A, B, C.



3.2.4 SLUGGING AND MILLING: Sample taken after sifting

% sample retained test: Batch A.

Table 42: % sample retained test after sifting for Batch A.

S.No.	Sieve no.	Sample taken (gm)	Sample retained (gm)	Result %
1	20#	10.0058	0.0486	00.49 %
2	40#	10.0151	0.4010	04.00 %
3	60#	10.0186	1.0117	10.10 %
4	80#	10.0064	1.4887	14.88 %
5	100#	10.0360	1.8058	17.99 %

% sample retained test: Batch B.

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Table 43: % sample retained test after sifting for Batch B

S.No.	Sieve no.	Sample taken (gm)	Sample retained (gm)	Result %
1	20#	10.0060	0.0485	00.48 %
2	40#	10.0150	0.402	04.01 %
3	60#	10.0186	1.020	10.18 %
4	80#	10.0060	1.480	14.79 %
5	100#	10.0350	1.790	17.83 %

% sample retained test: Batch C.

Table 44: % sample retained test after sifting for Batch C

S.No.	Sieve no.	Sample taken (gm)	Sample retained (gm)	Result %
1	20#	10.0050	0.0470	00.46 %
2	40#	10.0000	0.3800	03.80 %
3	60#	10.0180	1.0120	10.10 %
4	80#	10.0045	1.4750	14.74 %
5	100#	10.0300	1.8500	18.44 %

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Sieve Integrity for Batch A, B, C:

Table 45: Sieve Integrity after sifting

Batch no.	Sieve used as per BMR	Sieve Integrity	
		Before Use	After Use
A	20#, 40#, 60#, 80#, 100#.	OK	OK
B	20#, 40#, 60#, 80#, 100#.	OK	OK
C	20#, 40#, 60#, 80#, 100#.	OK	OK

Bulk Density for three batches:

Table 46: Results of Bulk Density for three batches of lubricated blend

S.No.	Batch No.	Weight of sample(A) gm	Apparent volume(B) ml	Bulk density (g/ml)
1	A	10.045	13.0	0.772
2	B	10.066	13.5	0.745
3	C	10.055	13.2	0.761

Tapped Density three batches:

Table 47: Results of Tapped Density for three batches of lubricated blend

S.No	Batch No.	Weight of sample (A) (gm)	Tapped vol. 10 tap.(ml)	Tapped vol. 500 tap.(ml)	Tapped vol. 1250 tap. (ml)	Final Tapped vol. (ml) (G)	Tapped density A g/ml.
1	A	10.045	12.0	11.2	11.0	11.0	0.913
2	B	10.066	12.5	11.5	11.2	11.2	0.898
3	C	10.055	12.4	11.3	11.1	11.1	0.905

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3.2.5 COMPRESSION:

Physical parameters of compressed tablets at different speeds: Weight variation: Batch A

Table 48: Weight variation: Batch A

S.No.	Parameter	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Weight Variation 640 mg ± 5%	638.20	649.47	628.24
2		642.55	644.65	632.25
3		632.00	642.30	628.23
4		640.24	644.64	634.11
5		630.12	648.29	638.36
6		646.22	644.10	635.42
7		635.55	646.50	635.42
8		636.24	646.80	631.24
9		642.02	650.67	638.41
10		628.08	646.39	632.18
11		628.56	646.48	627.01
12		640.35	636.42	634.56
13		638.65	648.25	630.12
14		632.13	650.29	641.01
15		630.47	644.41	625.56
16		635.21	639.30	630.23
17		628.32	647.58	628.32
18		640.56	649.32	629.50
19		635.14	645.40	636.42
20		636.86	649.24	635.02
21	**Min.**	**628.08**	**636.42**	**625.56**
22	**Max.**	**646.22**	**650.49**	**641.01**
23	**Wt. of 20 Tab.**	**12.71**	**12.92**	**12.65**
24	**Average**	**635.87**	**646.02**	**632.58**

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Hardness and thickness: Batch A

Table 49: Hardness and thickness for Batch A

S.No.	Parameter	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Hardness NLT 20 N (2.05 Kg/cm^2)	25.12	24.21	28.02
2		29.13	25.03	26.16
3		26.02	28.32	25.31
4		26.13	28.65	26.14
5		27.00	24.13	24.13
6		24.24	30.11	28.54
7		25.31	23.31	25.78
8		30.12	25.12	24.46
9		26.10	26.10	26.63
10		27.06	29.50	32.85
11	**Min.**	**24.24**	**23.31**	**24.13**
12	**Max.**	**30.12**	**30.11**	**32.85**
13	**Average**	**26.62**	**26.44**	**26.80**
1	Thickness 6.70 – 7.10 mm	6.84	6.82	6.85
2		6.84	6.84	6.87
3		6.85	6.88	6.86
4		6.84	6.82	6.84
5		6.86	6.88	6.82
6		6.85	6.84	6.85
7		6.83	6.85	6.84
8		6.85	6.87	6.83
9		6.84	6.85	6.81
10		6.80	6.89	6.87

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11	**Min.**	**6.80**	**6.82**	**6.81**
12	**Max.**	**6.86**	**6.89**	**6.87**
13	**Average**	**6.84**	**6.85**	**6.84**

Physical parameter at different speed Batch A:

Table 50: Physical parameters at different speeds compressed tablet: Batch A

S.No.	Parameter	Specification	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Appearance	White, biconvex tablet. Plain on both the sides.	Complies	Complies	Complies
2	Weight of 20 tablets	12.8 gm ± 5% (12.16 gm – 13.44 gm)	12.71	12.92	12.65
3	Average weight (mg)	640 mg ± 2.5% (624 to 656 mg)	635.87	646.02	632.58
4	Thickness(mm) (Avg.)	6.70 – 7.10 mm	6.84	6.85	6.84
5	Hardness (kg/cm^2) (Avg.)	NLT 20 N (2.05 Kg/cm^2)	26.62	26.44	26.80
6	Friability (% w/w)	NMT 1 % w/w	0.23	0.15	0.16
7	Disintegration time	NMT 15.0 min	1.52	2.20	2.05

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Physical parameter at different speed for
Batch B: Weight variation: Batch B
Table 51: Weight variation: Batch B

S.No.	Parameter	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Weight Variation 640 mg ± 5%	650.12	639.45	638.23
2		644.55	641.38	639.88
3		647.56	639.56	646.41
4		640.24	640.25	639.23
5		649.65	640.39	637.46
6		648.21	638.56	640.42
7		646.47	635.12	639.27
8		648.23	639.38	636.24
9		646.88	640.36	643.22
10		637.45	637.54	640.18
11		649.12	644.00	639.21
12		645.45	638.04	634.01
13		648.42	644.45	638.56
14		639.24	646.56	641.46
15		646.01	647.25	646.40
16		648.45	645.45	640.02
17		638.56	640.46	644.62
18		640.56	645.43	648.45
19		649.42	644.00	639.42
20		646.42	643.75	642.23
21	**Min.**	**637.45**	**635.12**	**634.01**
22	**Max.**	**650.12**	**647.25**	**648.45**
23	**Wt. of 20 Tab.**	**12.91**	**12.83**	**12.81**
24	**Average**	**645.55**	**641.56**	**640.74**

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Hardness and thickness: Batch B:

Table 52: Hardness and thickness for Batch B

S.No.	Parameter	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Hardness NLT 20 N (2.05 Kg/cm^2)	24.22	25.26	24.23
2		24.33	24.23	26.84
3		25.02	28.00	24.66
4		27.12	25.21	29.14
5		27.06	29.15	23.13
6		24.21	30.10	25.54
7		26.31	25.59	25.13
8		24.12	24.12	24.66
9		32.10	29.20	28.23
10		26.06	29.45	25.65
11	**Min.**	**24.12**	**24.12**	**23.13**
12	**Max.**	**32.10**	**30.10**	**29.14**
13	**Average**	**26.05**	**27.03**	**25.72**
1	Thickness 6.70–7.10 mm	6.79	6.85	6.80
2		6.87	6.83	6.86
3		6.84	6.87	6.87
4		6.82	6.85	6.83
5		6.80	6.82	6.84
6		6.83	6.86	6.84
7		6.85	6.84	6.86
8		6.82	6.86	6.85
9		6.84	6.87	6.86
10		6.88	6.83	6.84

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11	**Min.**	**6.79**	**6.82**	**6.80**
12	**Max.**	**6.88**	**6.87**	**6.87**
13	**Average**	**6.83**	**6.84**	**6.84**

Physical parameters at different speeds compressed tablet Batch B:

Table 53: Physical parameters at different speeds compressed tablet: Batch B

S.No.	Parameter	Specification	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Appearance	White, biconvex tablet. Plain on both the sides.	Complies	Complies	Complies
2	Weight of 20 tablets	12.8 gm ± 5% (12.16 gm – 13.44 gm)	12.91	12.83	12.81
3	Average weight	640 mg ± 2.5% (624 to 656 mg)	645.55	641.56	640.74
4	Thickness (mm) (Avg.)	6.70 – 7.10 mm	6.83	6.84	6.84
5	Hardness (kg/cm^2) (Avg.)	NLT 20 N (2.05 Kg/cm^2)	26.05	27.03	25.72
6	Friability (% w/w)	NMT 1 % w/w	0.31	0.23	0.38
7	Disintegration time	NMT 15 min	1.59	2.10	2.16

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Physical parameter at different speed for
Batch C: Weight variation: Batch C
Table 54: Weight variation: Batch C

S.No.	Parameter	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Weight Variation 640 mg ± 5%	635.56	649.65	650.45
2		640.55	638.48	644.08
3		631.32	642.60	636.12
4		640.24	642.65	640.05
5		630.65	638.13	638.45
6		640.10	644.21	641.20
7		631.47	649.22	647.21
8		630.21	646.64	646.48
9		642.88	642.45	644.11
10		637.45	648.73	640.70
11		641.42	648.56	646.55
12		635.40	646.85	640.65
13		636.25	648.63	647.44
14		632.28	644.89	648.70
15		641.23	649.10	643.47
16		636.36	639.22	646.20
17		632.56	648.02	647.62
18		634.24	644.25	648.46
19		636.42	646.35	649.56
20		632.23	644.23	644.20
21	**Min.**	**630.21**	**638.13**	**636.12**
22	**Max.**	**642.88**	**649.65**	**650.45**
23	**Wt. of 20 Tab.**	**12.71**	**12.90**	**12.89**
24	**Average**	**635.94**	**645.14**	**644.58**

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Hardness and thickness for Batch C:

Table 55: Hardness and thickness for Batch C

S.No.	Parameter	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Hardness NLT 20 N (2.05 Kg/cm^2)	28.26	24.45	27.10
2		25.13	28.03	26.11
3		27.32	24.21	25.25
4		26.65	26.26	24.24
5		27.13	26.32	26.33
6		25.64	25.01	24.54
7		27.31	26.25	25.38
8		25.12	25.13	24.26
9		23.80	29.35	23.73
10		32.56	28.26	28.35
11	**Min.**	**23.80**	**24.21**	**23.73**
12	**Max.**	**32.56**	**29.35**	**28.35**
13	**Average**	**26.89**	**26.32**	**25.52**
1	Thickness 6.70 – 7.10 mm	6.86	6.87	6.85
2		6.88	6.85	6.82
3		6.85	6.88	6.88
4		6.86	6.84	6.87
5		6.81	6.85	6.86
6		6.85	6.85	6.89
7		6.89	6.82	6.84
8		6.84	6.82	6.80
9		6.86	6.88	6.86
10		6.78	6.84	6.80

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11	**Min.**	**6.78**	**6.82**	**6.80**
12	**Max.**	**6.89**	**6.88**	**6.89**
13	**Average**	**6.84**	**6.85**	**6.84**

Physical parameter at different speed for Batch C:

Table 56: Physical parameters at different speeds compressed tablet: Batch C

S.No.	Parameter	Specification	1600 Tab/min	2000 Tab/min	2400 Tab/min
1	Appearance	White, biconvex tablet. Plain on both the sides.	Complies	Complies	Complies
2	Weight of 20 tablets	12.8 gm ± 5% (12.16 gm – 13.44 gm)	12.71	12.90	12.89
3	Average weight	640 mg ± 2.5% (624 to 656 mg)	635.94	645.14	644.58
4	Thickness (mm) (Avg.)	6.70 – 7.10 mm	6.84	6.85	6.84
5	Hardness (kg/cm^2) (Avg.)	NLT 20 N (2.05 Kg/cm^2)	26.89	26.32	25.52
6	Friability (% w/w)	NMT 1 % w/w	0.32	0.11	0.24
7	Disintegration time	NMT 15.0 min	1.46	1.58	2.15

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Physical parameters of tablets at Optimum Speed of 2000 tab/min.:
Batch A Weight variation: Batch A
Table 57: Weight variation at Optimum Speed: Batch A

S.No.	Parameter	Initial	Middle	End
1	Weight Variation 640 mg ± 5%	649.47	641.15	645.60
2		644.65	641.32	646.40
3		642.30	632.30	643.23
4		644.64	641.03	646.30
5		648.29	641.75	635.56
6		644.10	640.36	638.80
7		646.50	640.26	642.32
8		646.80	642.20	639.42
9		650.67	639.52	642.24
10		646.39	636.30	647.25
11		646.48	640.16	639.60
12		636.42	638.05	641.26
13		648.25	633.23	644.42
14		650.29	640.28	638.36
15		644.41	636.13	636.89
16		639.30	633.32	646.42
17		647.58	635.05	645.36
18		649.32	638.23	643.44
19		645.40	640.35	641.43
20		649.24	640.18	642.43
21	**Min.**	**636.42**	**632.30**	**635.56**
22	**Max.**	**650.49**	**642.20**	**647.25**
23	**Wt. of 20 Tab.**	**12.92**	**12.77**	**12.84**
24	**Average**	**646.02**	**638.56**	**642.33**

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Hardness and thickness: Batch A

Table 58: Hardness and thickness at Optimum Speed: Batch A

S.No.	Parameter	Initial	Middle	End
1	Hardness NLT 20 N (2.05 Kg/cm^2)	24.21	26.55	27.10
2		25.03	26.46	25.13
3		28.32	26.01	28.75
4		28.65	33.16	24.46
5		24.13	28.36	26.36
6		30.11	23.81	26.40
7		23.31	28.23	26.12
8		25.12	24.56	30.47
9		26.10	24.58	26.48
10		29.50	28.42	29.56
11	**Min.**	**23.31**	**23.81**	**24.46**
12	**Max.**	**30.11**	**33.16**	**30.47**
13	**Average**	**26.44**	**27.01**	**27.08**
1	Thickness 6.70 – 7.10 mm	6.82	6.78	6.80
2		6.84	6.87	6.84
3		6.88	6.84	6.86
4		6.82	6.79	6.85
5		6.88	6.83	6.84
6		6.84	6.79	6.82
7		6.85	6.75	6.79
8		6.87	6.80	6.83
9		6.85	6.83	6.82
10		6.89	6.81	6.81
11	**Min.**	**6.82**	**6.75**	**6.79**
12	**Max.**	**6.89**	**6.87**	**6.86**
13	**Average**	**6.85**	**6.80**	**6.82**

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Physical parameters of tablets at Optimum Speed: Batch A

Table 59: Physical parameters of tablets at Optimum Speed: Batch A

S.No.	Parameter	Specification	Initial	Middle	End
1	Appearance	White, biconvex tablet. Plain on both the sides.	Complies	Complies	Complies
2	Weight of 20 tablets	12.8 gm ± 5% (12.16 gm – 13.44 gm)	12.92	12.77	12.84
3	Average weight	640 mg ± 2.5% (624 to 656 mg)	646.02	638.56	642.33
4	Thickness (mm) (Avg.)	6.70 – 7.10 mm	6.85	6.80	6.82
5	Hardness (kg/cm^2) (Avg.)	NLT 20 N (2.05 Kg/cm^2)	26.44	27.01	27.08
6	Friability (% w/w)	NMT 1 % w/w	0.38	0.15	0.21
7	Disintegration time	NMT 15.0 min	1.52	2.20	1.45

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Table 62: Physical parameters of tablets at Optimum Speed: Batch B

S.No.	Parameter	Specification	Initial	Middle	End
1	Appearance	White, biconvex tablet. Plain on both the sides.	Complies	Complies	Complies
2	Weight of 20 tablets	12.8 gm ± 5% (12.16 gm – 13.44 gm)	12.83	12.82	12.76
3	Average weight	640 mg ± 2.5% (624 to 656 mg)	641.56	641.17	638.86
4	Thickness (mm) (Avg.)	6.70 – 7.10 mm	6.84	6.85	6.82
5	Hardness (kg/cm^2) (Avg.)	NLT 20 N (2.05 Kg/cm^2)	27.03	26.93	26.11
6	Friability (% w/w)	NMT 1 % w/w	0.39	0.23	0.47
7	Disintegration time	NMT 15.0 min	1.45	2.19	1.58

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Hardness and thickness: Batch C

Table 64: Hardness and thickness at Optimum Speed: Batch C

S.No.	Parameter	Initial	Middle	End
1	Hardness NLT 20 N (2.05 Kg/cm^2)	24.45	28.25	27.12
2		28.03	27.54	27.16
3		24.21	28.40	25.43
4		26.26	29.54	24.03
5		26.32	28.47	26.30
6		25.01	26.57	26.45
7		26.25	30.71	27.38
8		25.13	28.32	28.26
9		29.35	24.21	31.34
10		28.26	28.13	28.32
11	**Min.**	**24.21**	**24.21**	**24.03**
12	**Max.**	**29.35**	**30.71**	**31.34**
13	**Average**	**26.32**	**28.01**	**27.17**
1	Thickness 6.70 – 7.10 mm	6.87	6.84	6.82
2		6.85	6.83	6.86
3		6.88	6.84	6.88
4		6.84	6.89	6.87
5		6.85	6.86	6.86
6		6.85	6.86	6.80
7		6.82	6.86	6.84
8		6.82	6.87	6.85
9		6.88	6.86	6.86
10		6.84	6.89	6.83
11	**Min.**	**6.82**	**6.83**	**6.80**
12	**Max.**	**6.88**	**6.89**	**6.88**
13	**Average**	**6.85**	**6.86**	**6.84**

Physical parameters of table

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