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Open Access **Research Article**

Process Validation of Solid Antioxidant Skin Supplement Tablets

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Abstract

Antioxidants, protects the skin from cell damage and harmful rays. So, there is a need to kill the skin problems. The Aim of this present work is to study about oral antioxidants and its benefits for our skin and body hence this formulation can be used as health supplements. The purpose of this work is to prepare and perform process validation of antioxidant tablet formulation. The study consists of manufacturing of the three batches of 1 lakh tablets each of solid Antioxidant tablets. Each batch of Antioxidant tablets consists of Reduced L-Glutathione, Pycnogenol, Alpha Lipoic Acid, Vitamin C Coated and Grape Seed Extract as active antioxidant components. The results demonstrate that the manufacturing process was under control throughout all stage between batches. The process validation of, the all three batches were conducted, for a batch size at dry mixing, Blending, Compression, Coating and Packing stage. The three validation batches of tablets, containing all active components complies with the approved in-process and raw materials and finished product specifications defined for the formulation. Finished product reports of all the three batches shows that product meets the in-house specifications. The overall review of results shows consistency and reproducibility within and between all three batches. Hence it was concluded that the manufacturing process and the equipments adopted were strong enough and produce product meets pre-determined standards and quality attributes, therefore the process stands validated.

Keywords: Validation, Process validation, Antioxidant, Quality, Tablet, manufacturing, Solid dosage form.

INTRODUCTION:

A tablet comes under solid dosage forms. The manufacturing of solid dosage forms involves extensive powder handling.[1]Tablets are hard, compressed, biconvex solid dosage form they contain one or more medicament with excipients (Binders, Glidants, Disintegrating agents, diluents and organoleptics etc.

A series of unit operation are involved in manufacturing of tablet which include powder blending for content uniformity and converted into solid mass form either through wet granulation or direct compression. Various unit operation are used which include weighing, sieving, dry mixing/blending, wet mixing drying milling and sieving, blending, compression coating and packing.[1]

An antioxidant are compound of many different chemical forms and that inhibit the oxidation of other molecules and delays or prevent to oxidative damage.5Antioxidants are naturally occurring plant substances that protect the body from damage caused by harmful molecules called free radicals.[2] Antioxidants help prevent oxidation, which can cause damage to cells and may contribute to aging. They may improve immune function and perhaps lower the risk for infection, cardiovascular disease, and cancer. Antioxidants exist as vitamins, minerals and other compounds in foods. A diet containing plenty of fruits and vegetables, whole grains and nuts can supply all the antioxidants your body needs. Diets rich in antioxidants can be very beneficial.[3]

Validation is the process of establishing documentary evidence demonstrating that a procedure, process, or activity carried out in testing and then production maintains the desired level of compliance at all stages. The purpose of setting validation parameter is to monitor the online and offline performance of the manufacturing process and here validate it. Validation is essential part of Good manufacturing practices .it is therefore, an element of the quality assurance programmers associated with the particular product or process. Validation is concept that has involved in United stated in 1978.The concept of validation has expended through the year to embrace a wide range of activities from analytical methods used in quality control of drug substance and drug product to computerized system for clinical trials, labeling or process control.

In all stages of the product lifecycle, good project management and good archiving that capture scientific knowledge will make the process validation program more effective and efficient. The following practices should ensure uniform collection and assessment of information about the process

and enhance the accessibility of such information later in the product lifecycle.

MATERIALS AND METHODS:

Weighing of Excipients and API: For weighing and dispensing clean container is want and the area in which process is done is known as weighing room, central weigh for weighing ofExcipients Weighing balance apparatus is use.

Sifting or Milling: Sifting **mechanical shifter** is use.

Sieving: For sieving **#20** and **#40** sieve. Sieve is fitted in mechanical shifter.

Dry Mixing: The mixing and blending is occur during tablet manufacturing process and for uniform distribution of material **Rapid mixer granulator** is used. And also items are considered for mixing: Mixing or blending technique, mixing or bleeding speed, druguniformity and Excipients uniformity. The following physical properties of drug and Excipients are creating a uniform mix and blend: Bulk density, water content, Surface areaof particle, Particle shape and size.

The API Reduced L-Glutathione, Pycnogenol, Alpha Lipoic Acid , Vitamin C Coated , Grape Seed Extract and Excipients Dibasic calcium phosphate, Lactose, Sodium methyl paraben, Sodium propyl paraben, Sodium starch glycolate, Cross Carmellose sodium are loaded in RMG.

Slugging: The Excipients powder put in Slugging machine and powder are formed in ribbon.

Sifting: Mechanical sifter equipped with milled granules in #20sieves. **Multi mill** equipped and milling is used to break up the lumps and enhance the drying of granulation. Such factors are consider in milling: Mill type, screen size, mill speed, feed rate.

Pre-lubrication & Lubrication: For **lubrication bender** is use. The percentage of mixing of lubricating agent in a control manner because it also have critical and create defects in tablet like when the ratio of lubricating agent is low it cause such type of problems: Picking, Sticking, Capping, Binding in the die cavity and the ratio is high it cause hardness of tablet is decrease, compression of tablets is not proper, disintegration times of tablet is increase (DTs), dissolution is also decrease and it also affect other property of tablet. PVP K-30, Starch, Aerosil, Talcum powder, Magnesium stearate, Sodium lauryl sulphate are placed in blender.

Compression: Compression to be carried not as per batch manufacturing record using

8.0 mm normal concave plain lower and upper punches and 8.0 mm dies. Set the machineat three different speeds of 15, 25 & 35 RPM. Set the compression machine at desired parameter and collect the sample for pre- compression studies. Set the compression machine at lower and higher thickness and collect samples for dissolution. Divide the total compression time into three equal cycles. Run the compression machine at three different speeds in three cycles respectively and withdraw samples for content uniformity, dissolution and impurity at each speed. And check the physical parameters at each speed.

Dissolution profile: Check the dissolution profile on 12 tablets at 15 min, 20 min, 30min, 45 min, and 60 min from the pooled sample after the completion of film coating.

SAMPLING LOCATION IN COATING PAN:

Coating was carried as per BMR. Before starting coating, average weight of core tablets was recorded. After coating process the appearance and weight gain during coating was tested. After completion of coating check for Description, Weight variation of 20 tablets, LOD and Weight buildup.

1. After loading the pan with tablets, it is rotated for 1 minute for de-dusting and pre heatingof tablets.
2. Inlet air temperature: 50 - 60ºc
3. Outlet air temperature: 45 - 50ºC
4. Atomization air pressure: 3.0 - 5.0 kg/cm2
5. Pan RPM: 3-5
6. Spray gun distance: 20 - 26 cm
7. Spray rate: 40 - 60 ml/gun/min

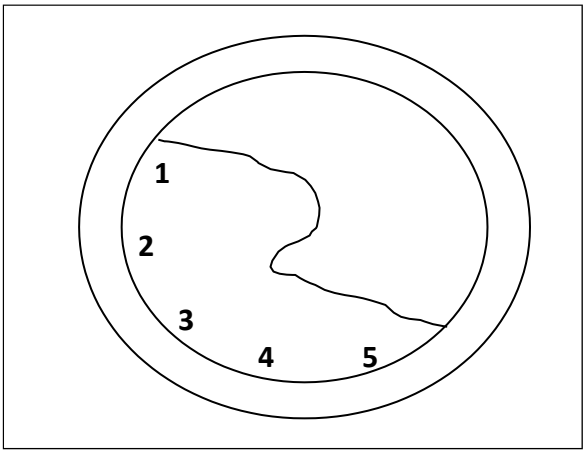

Fig. No. 1 Sampling location in Coating Pan

Table No. 1: In-Process Specification (Dry mixing):

S. No.	Test	Specification
1.	Description	Light brown to brown granular powder.
2.	Bulk density	0.30 to 0.40 g/cc.
3.	Tapped density	0.25 to 0.35 g/cc.
4.	Particle size distribution(By sieve analysis)	# 20 sieve (% retain)
		# 40 sieve (cumulative % retain)
		# 60 sieve (cumulative % retain)

Table No. 2: In-Process Specification (Core Tablets):

S. No.	Test	Specification
1.	Appearance	Light Brown color uncoated tablets.
2.	Targeted weight	1.50 gm
3.	Average weight of 20 tablets	30.0 gm ± 5%
4.	Thickness	6.00 mm ± 0.1 mm
5.	Width	8.50 ± 0.1 mm
6.	Length	21.10 ± 0.1 mm

Table No. 3: In-Process Specification (Coated Tablets):

S. No.	Test	Specification
1.	Description	Brown color, elongated shape biconvex scored film coated tablet.
2.	Average weight	1.600 gm ± 5 %

Table No. 4: Sampling and IPQC plan:

Processing time	No. of sample	Quantity of sample	Test to be performed
Mixing (blending) stage:			
After completion of mixing	10 sample	15.0 gm to 25.00 gm	Loss on drying, Uniformity of blend.
Slugging stage			
After completion of slugging	5 sample	Approx. 10 g	Content Uniformity, Moisture content
Lubrication stage			
After completion oflubrication process	Take a composite sample from 5different locations.	150 mg to 350 mg	Uniformity of blend Description, Bulk density, tapped density,Particle size.
After Unloading	In SS bin	180 mg to 410 mg	
Compression stage			
Different speed at OptimalHardness (sample from RHS andLHS)	Slow speed = 1 sample Optimal speed =1 sample High Speed =1 sample	20 tablet 10 tablets Take tablets eq. to 1.6 gm	Appearance, Average weight, uniformity ofweight Thickness, Hardness Friability test.
Different Hardnessat optimal speed (samp le from RHS and LHS)	Low hardness =1 sampleOptimum hardness =1 sample High hardness =1 sample	20 tablet 10 tablets Take tablets eq. to 1.6 gm	Appearance, Averageweight, uniformity of weight Thickness, Hardness Friability test.

RESULT AND DISCUSSION:

Table No. 5: Observation of Dry Mixing process

Batch No.	Observation in %								
	Batch 1			Batch 2			Batch 3		
Mixing time	10 min	15 min.	20 min	10 min.	15 min	20min	10 min.	15 min	20 min
Top	95.3	94.4	94.3	97.18	93.3	95.36	95.21	92.36	99.13
Middle Left	99.2	98.3	91.4	94.36	94.32	97.89	99.95	99.10	95.26
Middle	95.3	93.9	92.3	97.25	99.33	92.63	99.32	97.23	97.10
Middle Right	98.8	94.6	98.2	95.81	96.23	98.23	98.25	99.63	95.36
Bottom	96.7	95.1	98.6	94.38	97.06	96.96	98.63	97.23	95.26
Min.	95.3	93.9	91.4	94.36	93.3	92.63	95.21	92.36	95.26
Max.	99.2	98.3	98.6	97.25	99.33	98.23	99.95	97.23	95.36

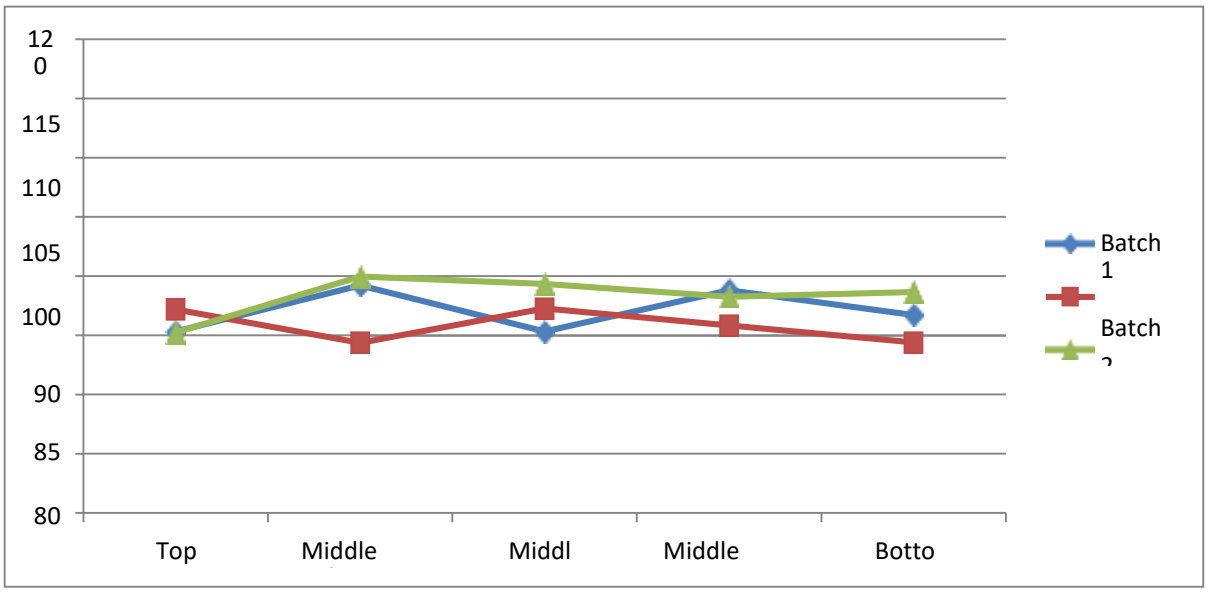

Fig No. 2: Graph of batch no. 1. content of dry mixing (10 minutes)

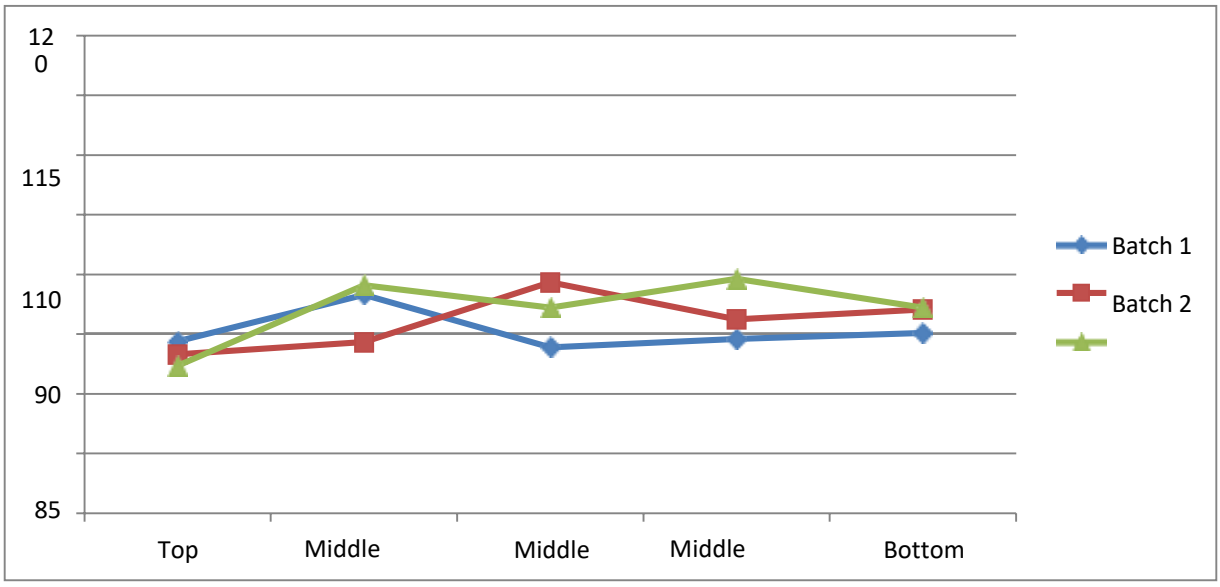

Fig No. 3: Graph of batch no. 2. content of dry mixing (15 minutes)

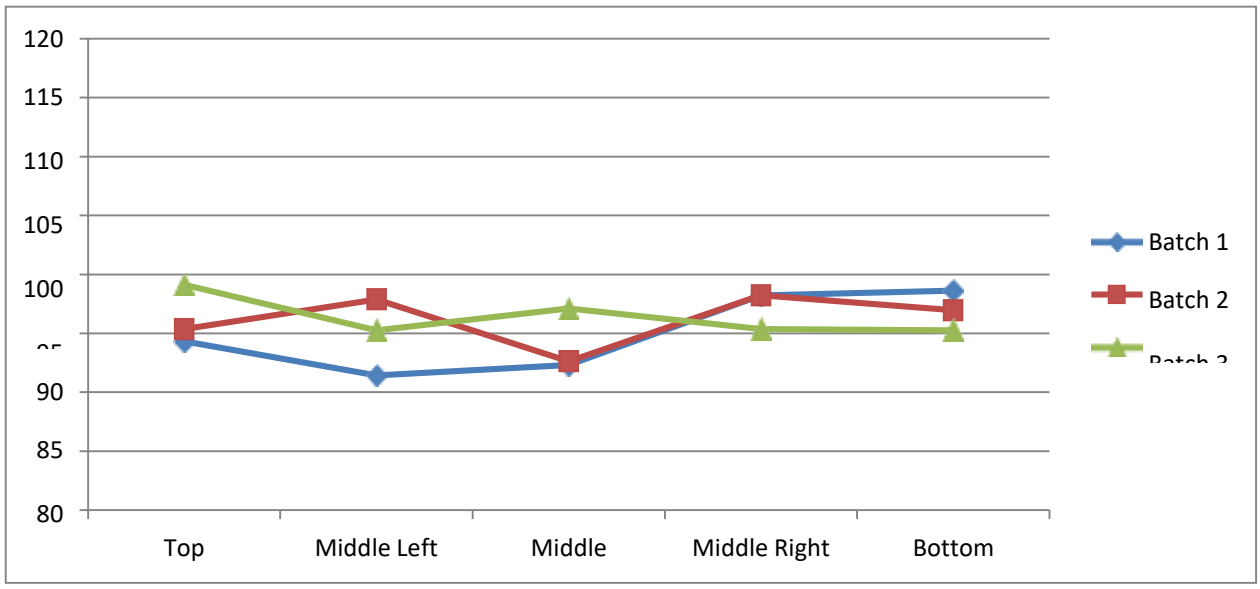

Fig No. 4: Graph of batch no. 3. content of dry mixing (20 minutes)

Observations: It is observed from the compiled analytical data of the content uniformity and it'safter 5 minutes dry mix the values of the three batches are well within the acceptance criteria as per specifications. The distribution of API is well acceptable at 5 minutes of dry mixing as shown by the samples analyzed data. The results show closer homogeneity of drugdistribution in the dry mix stage.

SLUGGING:

1. Temperature and relative humidity of room were 27 ºC and 54 % respectively.
2. Binder solution preparation sufficient quantity of water was added and mixed slowly.And powder was formed in ribbon.

Table No. 6: Observation of Loss on drying at slugging process

Batch No.	Observation		
	Batch No. 1	Batch No. 2	Batch No. 3
Top	0.33%	0.36%	0.33%
Middle Left	0.31%	0.39%	0.26%
Middle	0.32%	0.23%	0.30%
Middle Right	0.21%	0.23%	0.32%
Bottom	0.23%	0.20%	0.36%

GRANULE SIFTING:

20# sieve was used. No damage of sieve was observed.

Integrity of the sieve before and after was found intact.

LUBRICATION:

Temperature and relative humidity were 27 ºC and 54 % respectively.

Direction of knives was clockwise at 10 rpm speed. Lubrication Time was 30 min.

Table No. 7: Observation of Lubrication process

Test	Acceptance Criteria	Observation		
		Batch 1	Batch 2	Batch 3
Description	Brown or light brown powder	Complies	Complies	Complies
Bulk density(gm/cc)	--	0.37	0.35	0.38
Tapped density (gm/cc)	--	0.28	0.25	0.30

Blend Uniformity and Blending time:

All the results of composite sample for physical parameters were found within the acceptance criteria.

Table No. 8: Observation of Blend Uniformity:

Batch No.	% of Blend Uniformity								
	Batch No.1			Batch No.2			Batch No.3		
Blending time	10 min.	20 min.	30 min	10 min.	20 min.	30 min	10 min.	20 min.	30 min
Top	115.3	124.4	117.3	117.18	112.30	115.36	125.21	120.36	119.13
Middle Left	110.2	126.3	111.4	124.36	114.32	117.89	119.95	119.10	115.26
Middle	112.3	103.9	119.3	117.25	119.33	115.63	109.32	107.23	117.10
Middle Right	115.8	112.6	118.2	115.81	115.23	111.23	108.25	119.63	115.36
Bottom	116.7	125.1	119.6	132.36	121.06	115.96	108.63	117.23	117.36
Min.	110.2	103.9	111.4	115.81	121.06	111.23	108.25	107.23	115.26
Max.	116.7	126.3	109.6	132.36	112.30	117.89	125.21	120.36	117.36

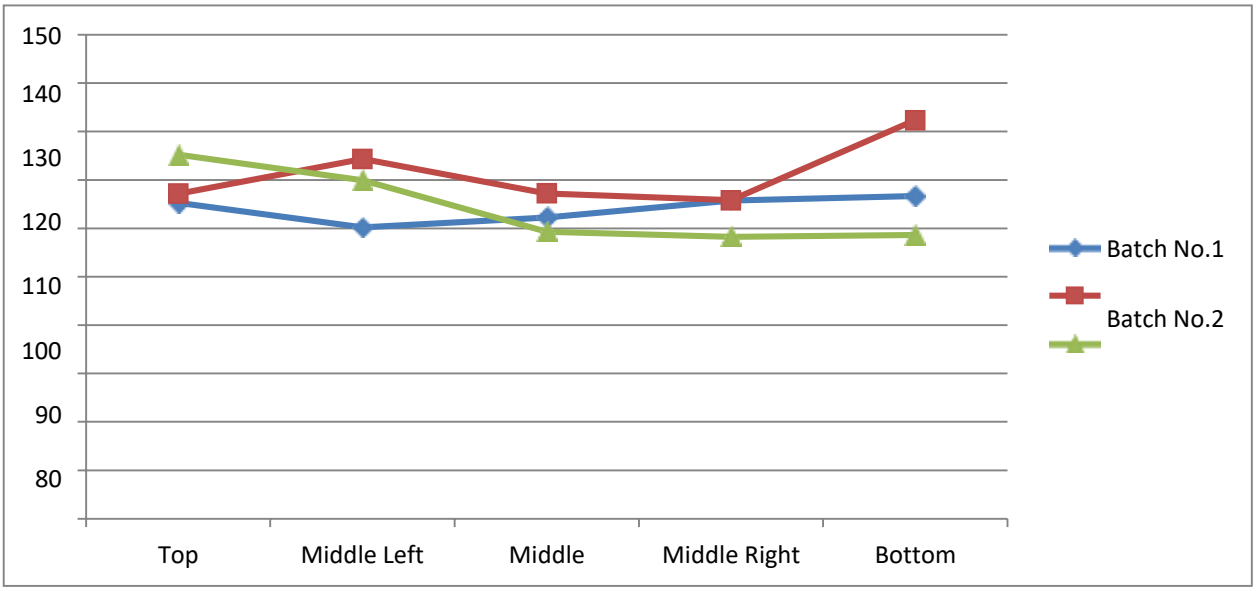

Fig No.5: Graph of blend uniformity at 10 minutes

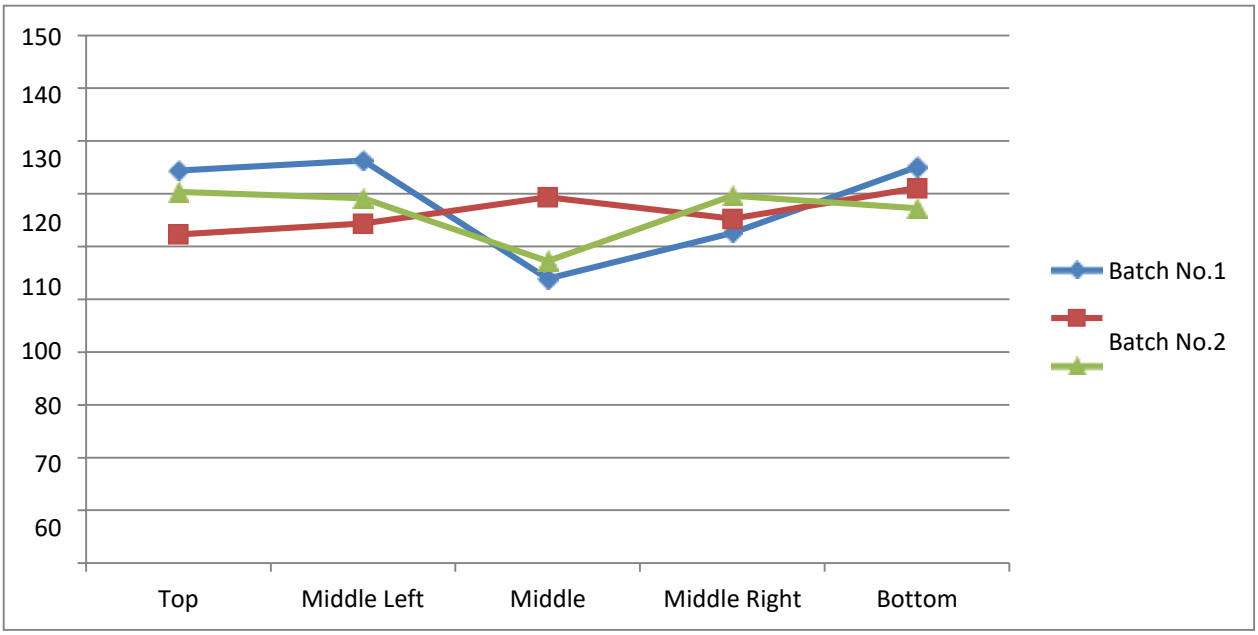

Fig No.6: Graph of blend uniformity at 20 minutes

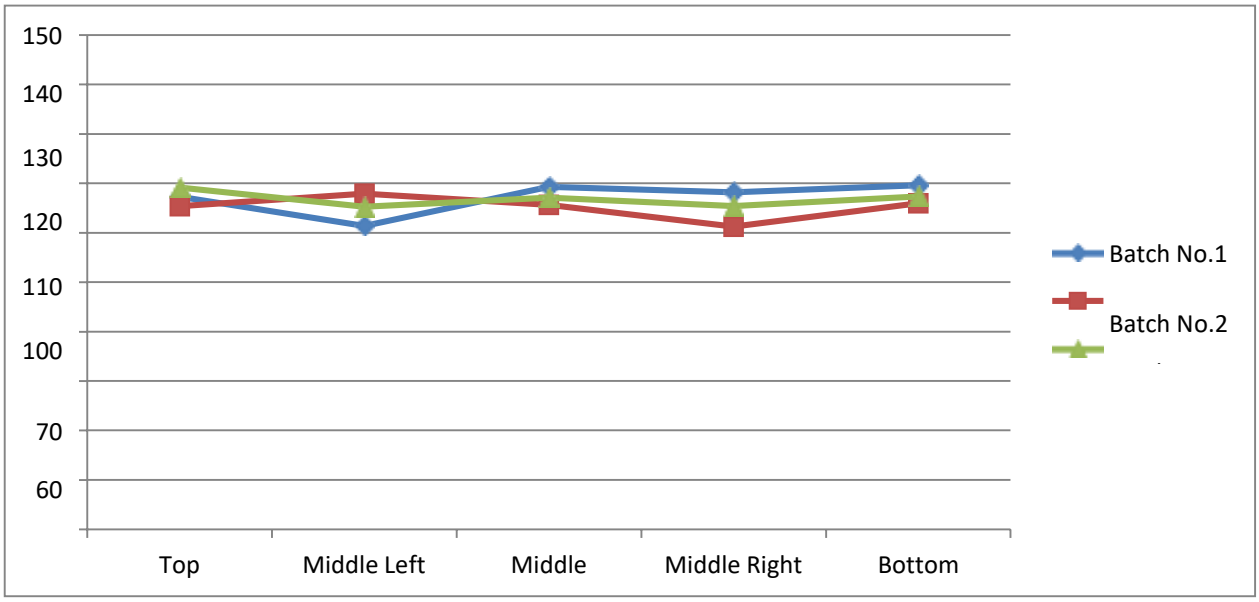

Fig No. 7: Graph of blend uniformity at 30 minutes

Table No. 9: Observation of Compression process

S. No.	Test	Specification	Batch No.1	Batch No.2	Batch No.3
1.	**Appearance**	Light Brown color elongated shape biconvex tablet.	Light Brown color elongatedshape biconvex tablet.	Light Brown color elongatedshape biconvex tablet.	Light Brown color elongatedshape biconvex tablet.
2.	**Weight of 20 tablet**	30.00 gm ± 5 %	30.1398 gm	30.1380gm	30.1395gm
3.	**Average weight of tablet**	1.500 gm ± 5 %	1.5300 gm	1.5339 gm	1.5350 gm
4.	**Disintegration time**	Not more than 15 minutes.	2 min. 45 sec.	2 min. 01 sec.	2 min. 11 sec.
5.	**Thickness of tablet**	6.00 mm ± 0.1 mm	6.01 mm	6.01 mm	5.59 mm
6.	**Width**	8.50 mm ± 0.1 mm	8.51 mm	8.52 mm	8.50 mm
7.	**Length**	21.10 ± 0.1 mm	21.15 mm	21.17 mm	21.17 mm

CONCLUSION:

The pharmaceutical process validation and process controls are important steps in manufacturing of solid dosage form with consistent to meet the regulatory required standard such as identity, strength, quality, purity and stability in the final solid dosage form tablet. The process validation of Antioxidant tablets for the three batches was conducted for a batch size of 1 lakh tablets at dry mixing, Blending, Compression, Coating and Packing stage. Finished product reports of all the three batches of 01, 02 & 03 shows that final product meets the finished product in-house specifications.

The results demonstrate that the manufacturing process was under control throughout all stage within and between batches. The three validation batches of tablet containing Reduced L- Glutathione, Pycnogenol, Alpha Lipoic Acid, Vitamin C Coated, Grape Seed Extract comply with the approved in-process and finished specifications defined for the product. The overall review of result shows consistency and reproducibility within and between batches.

Hence, it is concluded that the manufacturing process and the equipments adopted were strong enough and produce product meeting pre-determined standards and quality attributes, therefore the process stands validated.

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