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PHARMACEUTICAL CONCURRENT PROCESS VALIDATION OF AMYLMETACRESOL AND 2, 4-DICHLORO BENZYL ALCOHOL LOZENGES

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ABSTRACT

Amylmetacresol is an antiseptic used to treat infections of the mouth and throat. 2,4-Dichlorobenzyl alcohol is a mild antiseptic with a broad spectrum for bacterial and virus associated with mouth and throat infections. As per ISO 17025, Validation is the documentary proof that the particular requirements for a specific intended use are fulfilled. This research aimed to study concurrent process validation for Amylmetacresol and 2,4-Dichlorobenzyl alcohol 2.5gm lozenges. The critical parameter involved in manufacturing stages were identified and evaluated as per the validation master plan. The outcome indicated that this process validation data provides a high degree of assurance that the manufacturing process produces products meeting its predetermined specifications and quality attributes.

Keywords: Amylmetacresol, 2,4-Dichlorobenzyl alcohol Process validation, Quality assurance, Lozenges

1.0. INTRODUCTION

Oral dosage forms are orally administered pharmaceutical drug products in the form in which they are marketed for use, with a specific mixture of active ingredients and inactive components, in a particular configuration, and apportioned into a particular dose [1]. Oral dosage forms can be solid, liquid, semisolid in nature e.g. tablets, capsules, sachets, powders, granules, orally dispersible films, syrups, solutions, paste, gel, creams etc. ·

Lozenges are different shaped solid preparations that contain one or more medicaments, usually in a flavored, sweetened base, that are intended to dissolve or disintegrate slowly in the mouth for localized or systemic effect [2]. They can be prepared by molding (gelatin and/or fused sucrose and sorbitol base) or by compression of

sugar-based tablets. Molded lozenges are sometimes referred to as pastilles, whereas compressed lozenges may be referred to as troches [3]. They are used for patients who cannot swallow solid oral dosage forms well as for medications designed to be released slowly to yield a constant level of drug in the oral cavity or to bathe the throat tissues in a solution of the drug [4]. Lozenges historically have been used for the relief of minor sore throat pain and irritation and have been used extensively to deliver topical anesthetics and antibacterial [5]. They are used for of drugs like analgesics, anesthetics, antimicrobials, antiseptics, antitussives, aromatics, astringents, corticosteroids, decongestants, and demulcents and other classes and combinations. They are easy to handle, the dose has been apportioned, and the excipients have a demulcent effect on throat since the ingredients are released slowly and spread uniformly over the affected mucosal membrane [6].

Amylmetacresol (AMC) is an antiseptic used to treat infections of the mouth and throat. Chemically, AMC is derivative of *m*-cresol, with a pentyl group attached to the sixth carbon atom[7]. 2,4-Dichlorobenzyl alcohol is a mild antiseptic with a broad spectrum for bacterial and virus associated with mouth and throat infections [8].

Validation is a documented practice which delivers the evidence that any of the process, procedure, material, equipment, action or system truly shows the estimated result. It acts as guidance in assisting manufacturers in in gaining knowledge of Quality management system (QMS) requirements regarding process validation [9]. In pharmaceutical industry, validation is a foremost requirement of Current Good Manufacturing Practices (cGMP) [10]. Validation is a very important a part of internal control and quality assurance. Various regulatory authorities give special emphasis on the validation of all the processes utilized in the industry [11].

“Validation is that the process by which it's established, by laboratory studies, that the performance characteristics of the strategy meet the necessities for the intended application” [12,13]. According to section 820.75 of the Quality System (QS) regulation process validation is established process by objective proof that steadily produces a result or product meeting its predetermined specifications that are fit for their intended use [14,15].

PROCESS VALIDATION

Process validation is “A documented procedure which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specification and quality attributes” [16,17]. The validated documentation obtained from the concurrent process validation can be further used in the future to perform the retrospective process validation for the reference purpose [6].The primary objective of process validation is to facilitate manufacturers in understanding the quality management system (QMS) requirements for process validation [24]. There are four subtypes of process validation, briefly discussed below:

- **Prospective validation:**Prospective process validation is executed after the completion of the R and D trial in order to produce the product for the commercial purpose. This is one of the crucial parts of the process validation as most validation efforts depends on the prospective experimentation so that data that support

the validation could be generated. This type of validation is generally connected with the introduction of new drug product into the market and involves the studies of all their manufacturing processes [19]

- **Retrospective validation:**The retrospective validation is generally performed on the established product which does not face any sort of instability and are considered stable, when the prospective validation programs cannot be justified due to the resource limitation and on the basis of economic considerations alone. Prior to commencing retrospective validation, where in the numbers of in-process or end-product test data of past manufacturing batches are exposed to the equipment, facilities, statistical analysis and sub systems involved in association with the manufacturing procedure must be practiced in conformance with CGMP necessities [20].

- **Concurrent validation:**This validation is quite similar to prospective process validation but differ in the aspect that the product will be sold by the operating firms throughout the qualification sequence among the public as its stated market value. In process supervising of critical processing phases and product testing lies under this validation which aids to produce the documented evidence showing the manufacturing procedure is proceed under a suitable state of control with quality characteristics. The validated documentation obtained from the concurrent process validation can be further used in the future to performed the retrospective process validation for the reference purpose [21].

- **Revalidation:**Revalidation basically refers to the repetition of the validation method. In any pharmaceutical plant revalidation is performed if any sort of changes is made in the batch size, formulation or when the consecutive batches of the manufacturing unit doesn't meet specification as stated in its product, when changes are made in the site location, equipment size and capacity or new advance equipment are introduced for the further processing or when new manufacturing methods and control are to be followed or changes are made in them [22].

The cGMP regulation for finished pharmaceuticals, 21CFR 210 and 211, were promulgated to enforce the requirement of the act. Although these regulations do not include a definition for process validation, the requirements is implicit in the language of 21CFR 211.100 [23], which states:

- There should be written procedure for production and process control to ensure that the drug products have the identity, strength, quality and purity that are intended to possess."
- Conducting process validation is not only a regulatory requirement, but also makes a great deal of sense from engineering as well as a business point of view. It is evident that pharmaceutical companies that are well versed in conducting process validation have a competitive advantage over those who are not. Process validation is required generally and specifically by the cGMP regulations for finished pharmaceuticals products.

The requirement of process validation is implicit in the Schedule M section 820.100, which states that "Written manufacturing specification and processing procedure shall be established, implemented, and controlled to assure that device conforms to its original design or any approved changes in that design" [24].

STAGES OF PROCESS VALIDATION ACTIVITIES [25]:

Stage 1: Process Design

This stage provides a key input to the studies that are carried without the application of good manufacturing practices, during the product development studies which ultimately helps in the various design stages such as anticipated dosage form, manufacturing route [26].

Stage 2 – Process Qualification

Process qualification is the second stage where the evaluation of process design is performed to regulate whether it is efficient of reproducible commercial production.

Stage 3 – Continued Process Verification

All the continual data assembled to sustain the quality of product are evaluated in the third stage i.e. CPV of process validation. Various data are included such as critical quality attributes, process tends and in process material attribute, critical quality attributes.

STRATEGY FOR VALIDATION OF STUDIES [27]:

The various strategies for process validation of method are:

- Preparing process flow charts and detecting the critical process variables.
- Selecting the three sequential batches, which possess same manufacturing formula and batch size.
- Process prequalification should be carried out in case of failure to encounter the prerequisite of the validation protocol on the basis of process input and output control.
- Proper documentation should be prepared for all the validation experiment and results by maintaining a validation report.
- BMR, SOPs, finished and in process product specification along with other associated documents and batch-packaging record should be maintained.
- Prepare a relevant process validation protocol of the specified product.
- In other to perform the task consistently and efficiently, SOPs should be prepared.
- Accomplishment of validation protocol effectively.
- Monitoring of all the respective process validation batches.
- Carrying out the in process testing during manufacturing of the product.

The main aim of study is to perform the pharmaceutical concurrent process validation of amylmetacresol and 2, 4-dichloro benzyl alcohol lozenges.To evaluate the key process variables and to quantify their effects on products attributes.To confirm the process conditions for each unit operation.To confirm the acceptable range or limits for process parameter.

2.0. MATERIALS AND METHODS

2.1. Materials

Amylmetacresol and 2,4-Dichlorobenzyl alcoholwas obtained as gift sample from Shreya Life science Pvt Ltd Roorkee.All other chemicals used were of reagent's grade.

2.2. Quality attributes

Table 1. Process steps and process variables:

S. No.	Process Step	Process Variables		Acceptance Criteria
1	Sugar Syrup Preparation	Syrup Preparation Temp.		85-90 ºC
		Appearance of syrup		Orange colored & transparent solution
		Brix Index of prepared syrup		75 – 80 %
2	Preparation of flavour, Medicament & Menthol Mixture	Clarity		Clear colorless & transparent liquid
		Specific gravity		0.85 – 1.10 %
3	Cooking (Cross Flow)	Syrup Flow Rate		380 – 420 Ltr/Hr.
		Cooking Temp.		140 ± 2ºC
4	Vacuum Phase	Vacuum		NLT 0.7 Bar
5	Mixing	Citric Acid Addition Rate		80 ± 2 gm/min
		Dosing rate of Flavour/ medicament		45 ±2 gm/min
6	Mass Flow Rate	Cooled Mass Flow Rate/Hour		480 Kg ± 2%
7	Transfer Belt	RPM of Motor		35 ± 2
	Batch Roller	RPM of Motor		50 ± 2
	Rope Sizer	RPM of Motor		55 ± 2
	Batch Forming Machine	RPM of Motor		66 ± 2
8	Cooling Tunnel	Temperature		23 ± 2ºC
		Relative Humidity		50 ± 5%
9	Cooling Tunnel	Conveyor Motors RPM	Upper	99 ± 2
			Middle	96 ± 2
			Lower	70 ± 2

S. No.	Process Step	Process Variables	Acceptance Criteria
10	Set Parameters of Lozenges (Lozenge)	Appearance	Circular tablets of orange Colour with menthol and orange flavor
		Average Wt.	2500 mg ± 5%
		Thickness	6.60 ± 0.2 mm
		Diameter	18.80mm

2.3. Sampling and analysis plan:

The samples were collected at various intervals at different operations as per the sampling plan tabulated below.

Table 2. Sampling and analysis plan

Stage	Test to be performed	Sampling Interval	Sample Qty.
During Batch Manufacturing	• Average weight • Content of Citric Acid • Content of Amylmetacresol • Content of 2, 4 dichlorobenzyl alcohol	➢ At an interval of 01 hours up to batch completion	40 lozenge
	• Complete analysis	➢ After completion of manufacturing	60 Lozenges
During Batch Packing	• Average weight • Content of Citric Acid • Content of Amylmetacresol • Content of 2, 4 dichlorobenzyl • alcohol	➢ High temperature & low speed ➢ Low temperature & fast speed	40 lozenge

2.4.Specification:

Table3. Specifications

S. no.	Test	Specification
1.	**Description**	Circular orange color with orange flavored tablets. Uneven coloration, presence of air bubbles in the caramel mass & insignificant unevenness of surface & edges of tablets is permissible. Emergence White coating is permissible.
2.	**Identification (BY GC)** **Amylmetacresol&2,4-dichlorobenzalalcohol**	The Retention time of two main peaks on the chromatogram of test solution must correspond to the retention time of Amylmetacresol and 2,4-dichlorobenzyl alcohol on the chromatogram of standard solution in assay procedure.
3.	**Average weight**	2500 mg, ± 5% (2375.00 mg to 2625.00 mg)
4.	**Uniformity of weight**	18 tablets out of 20 not more than ±5% of the average weight. No tablets out of 20 not more than ±10% of the average weight.
5.	**Foreign mixtures (By GC)** **2,4-dichlorobenzaldehyde**	Not be more than 2% of labeled amount of 2,4-dichlorobenzalalcohol
6.	**Citric Acid Content** **(Citric Acid anhydrous 25mg)**	(22.50 mg to 27.50 mg/tablet) (90.01 % - 110.01 % of the label claim)
7.	**Assay by GC:**	
7.a	**Amylmetacresol BP: (0.6 mg)**	0.584 mg to 0.876 mg / tablet (97.33 % - 146.00 % of the label claim)
7.b	**2, 4-Dichlorobenzyl alcohol BP : (1.2 mg)**	1.16 mg – 1.74mg / tablet (96.67 % - 145.00 % of the label claim)
8.	**Microbiological limit test:**	
8.a	**Total number of aerobic bacteria**	Not more than 1000 cfu/g
8.b	**Total number of fungi**	Not more than 100 cfu/g
8.c	**Escherichia coli**	Must be absent in 1 g

2.5.DEVIATIONS:

All protocol deviation, non-conformance and out of specification results obtained shall be investigated in accordance with corresponding SOPs and documented in the validation report.

2.6.CONCURRENT PROCESS VALIDATION OF AMYLMETACRESOL AND 2, 4-DICHLORO BENZYL ALCOHOL LOZENGES

The all three validation batches were manufactured using standard manufacturing process for amylmetacresol and 2, 4-dichloro benzyl alcohol lozenges. The samples were collected and tested as per sampling protocol. The environmental conditions were monitored during different processing step of all three validation batches and observed as

Temperature	: Not more than 25°C
Relative Humidity	: 50% ± 5%
Pressure differential	: 0.6 – 1.6 mm of water

2.6.1.Description of manufacturing process & packing process:

i) Preparation Of Sugar Syrup:

a. Take the dispensed material to the Sugar Syrup Preparation Area.

b. Take 500.0 liters of purified water in Sugar Dissolving Vessel Heated to 85°C- 90°C.

c. Then charge 1520.000 kg of Sugar (refined) under continuous stirring and heating.

d. Then start the addition of 1160.000 kg of Liquid Glucose with continuous stirring and heating. After complete addition of Liquid Glucose continue the stirring for 30 minutes at 85 – 90°C temperature.

e. Take 0.400 Kg of warm Purified Water into a suitable S.S. container; dissolve 0. 150 Kg of Sunset Yellow FCF under constant stirring until clear solution is formed.

f. Transfer the solution to the Sugar Dissolving Vessel and continue the stirring for 15 minutes.

g. Online filter the syrup through Basket Filter and transfer into holding vessel.

h. Collect the 100 ml sample from holding tank in a clean glass beaker for determination of appearance and Brix Index.

ii) Manufacturing Procedure:

- Adjust the stroke length of flavour dosing pumps and run the dosing pump.
- Start the vacuum pump on manual mode and check for sufficient vacuum NLT 0.70 bar.

- Keep the digital display of steam on a manual mode and adjust requires steam pressure to achieve temperature of cooked syrup 140±2^{0}C.
- Start the tempering belt also starts the circulation pump and circulates water below tempering belt.
- Start addition of lubricants drop wise on tempering belt from Reservoir controlling needle valve.
- Open all steam valves of steam station of sucoma and after 10 minutes, start extraction screw and mixing screw.
- Start the batch roller and switch ON heaters for batch roller, rope sizer.
- Switch ON refrigeration plant, close bypass valve and start cooling tunnel.
- Open the bottom valve of holding tank also open valve for syrup filter.
- Start the syrup transfer pump and adjust flow of syrup on manual mode and start steam valve of cooker. Set the flow rate on Control Panel P24.
- Start dosing pump and check visually for dosing. When cooked mass is coming in evaporation chamber, open the needle valve at P80 on sucoma panel and set syrupy flow on auto mode from panel. Pass cooked mass under vacuum (NLT 0.70 bar) to extraction screw and to mixing screw.
- Then take cooked mass on tempering belt, adjust the folder and kneading roller to get continuous uniform rope.
- Feed this rope from transfer belt to batch roller through distributor unit, after getting required quantity of cooked mass. Start rope sizer and batch former.
- Pass cooked mass through rope sizer into the forming machine and in the die set rope is formed to get the Tablets and set the weight by adjusting the rope sizer. Then keep sucoma controller, steam controller and vacuum controller on auto mode.

iii) Transfer Of Citric Acid, Flavour Solution And Lubricant:

a. Verify the weights of Citric acid, prepared Flavour Solution and record in the following table.

b. Transfer the Citric Acid to dosing hopper.

c. Transfer Prepared Flavour Solution in Medicament Vessel.

d. Transfer Lubricant in lubricant holding tank.

3.0. RESULTS AND DISCUSSION

3.1.Standard manufacturing process:

Table 4. Observed Critical Process Variables, Set Parameters & Rpm:

Process Steps	Process Variables		Acceptance criteria	Observations		
				Batch A	Batch B	Batch C
Sugar Syrup Preparation in sugar dissolving vessel	Temp. of purified water		85-90 ºC	87	86	86
	Stirring time after addition of sugar (refined) & liquid glucose in above heated purified water at a temp. 85-90 ºC	Clarity of solution	Clear solution	Clear solution	Clear solution	Clear solution
		Mixing time after addition into sugar syrup	15 minutes	15 minutes	15 minutes	15 minutes
	Appearance of syrup		Yellow colored & transparent solution	Yellow colored & transparent solution	Yellow colored & transparent solution	Yellow colored & transparent solution
	Brix Index of prepared syrup		75 – 80 %	78%	77.5%	77.5%
Preparation of flavour, Medicament	Clarity		Clear colorless & transparent liquid	Clear colorless & transpar	Clear colorless & transpar	Clear colorless &

& Menthol Mixture			ent liquid	ent liquid	transpare nt liquid
	Specific gravity	0.85 – 1.10 %	0.98	0.92	0.98
Cooking (Cross Flow)	Syrup Flow Rate	380 – 420 Ltr/Hr.	360 Ltr/Hr.	360 Ltr/Hr.	380 Ltr/Hr.
	Cooking Temp.	140 ± 2ºC	140ºC	140ºC	140ºC
Vacuum Phase	Vacuum	NLT 0.7 Bar	0.71	0.71	0.71
Mixing	Citric Acid Addition Rate	80 ± 2 gm/min	80 gm/min	80 gm/min	80 gm/min
	Dosing rate of Flavour/ medicament	40 ±2 gm/min	35.65 gm/min	35.46 gm/min	35.71 gm/min
Mass Flow Rate	Cooled Mass Flow Rate/Hour	480 Kg/Hr ± 2%	480 Kg/Hr	480 Kg/Hr	480 Kg/Hr
Tempering Belt	RPM of Conveyor motor (In %)	37± 2	37	37	37
Batch Roller	RPM of Motor (In %)	35 ± 2	98	98	98
Rope Sizer	RPM of Motor (In %)	50 ± 2	86	86	86
Batch Forming Machine	RPM of Motor (In %)	66 ± 2	65	65	65
Cooling Tunnel	Temperature	20 ± 2ºC	20ºC	20ºC	20ºC
	Relative Humidity	45 ± 5%	46 %	46 %	46 %
Cooling Tunnel	Conveyor Motors RPM	Upper 99 ± 2	99	99	99
		Middle 96 ± 2	96	96	96
		Lower 70 ± 2	70	70	70

Set Parameters of Lozenges (Lozenge)	Appearance	Circular tablets of orange Colour with menthol and orange flavor	Complies	Complies	Complies
	Average Wt.	2500 mg ± 5%	2501 mg	2502 mg	2503 mg
	Thickness	6.60 ± 0.2 mm	6.65 mm	6.70 mm	6.67 mm
	Diameter	18.80 ± 0.2 mm	18.84 mm	18.82 mm	18.80 mm

3.2.Results of hourly samples of batches A, B&C

Table 5: Results Of Hourly Samples Of Batches A, B & C

Batch A							
Test Performed	Acceptance Criteria	Results					
		Initial	1st Hour	2nd Hour	3rd Hour	4th Hour	5th Hour
Average Weight	2500 mg ± 5% (2375.0 mg to 2625.0 mg)	2440.14	2448.61	2455.44	2453.67	2452.41	2454.41
Citric Acid Content (25mg) By Titrimetry method	(22.50 mg to 27.50 mg/tablet) (90.00 % - 110.00 % of the label claim)	99.48	100.46	101.54	98.19	98.87	99.33

Amylmetacresol BP: (0.6 mg)	0.584 mg to 0.876 mg / tablet (97.33 % - 146.00 % of the label claim)	113.2	111.2	112.8	114.5	111.5	113.5
2, 4-Dichloro benzyl alcohol BP : (1.2 mg)	1.16 mg – 1.74mg / tablet (96.67 % - 145.00 % of the label claim)	116.3	115.3	113.5	114.0	115.1	114.7
Batch B							
Test Performed	Acceptance Criteria	Results					
		Initial	1st Hour	2nd Hour	3rd Hour	4th Hour	5th Hour
Average Weight	2500 mg ± 5% (2375.0 mg to 2625.0 mg)	2448.32	2456.44	2450.41	2452.11	2453.67	2455.89
Citric Acid Content (25mg) By Titrimetry method	(22.50 mg to 27.50 mg/tablet) (90.00 % - 110.00 % of the label claim)	100.46	103.55	106.34	100.56	102.76	104.87

Amylmetacresol BP: (0.6 mg)	0.584 mg to 0.876 mg / tablet (97.33 % - 146.00 % of the label claim)	120.2	123.72	124.78	125.76	120.89	1265.11
2, 4-Dichloro benzyl alcohol BP : (1.2 mg)	1.16 mg – 1.74mg / tablet (96.67 % - 145.00 % of the label claim)	115.3	120.89	119.78	123.76	122.90	125.44
Batch C							
Test Performed	Acceptance Criteria	Results					
		Initial	1st Hour	2nd Hour	3rd Hour	4th Hour	5th Hour
Average Weight	2500 mg ± 5% (2375.0 mg to 2625.0 mg)	2465.49	2460.65	2470.11	2464.12	2463.96	2466.34
Citric Acid Content (25mg) By Titrimetry method	(22.50 mg to 27.50 mg/tablet) (90.00 % - 110.00 % of the label claim)	99.48	98.72	96.65	96.22	95.45	94.33

Amylmetacresol BP: (0.6 mg)	0.584 mg to 0.876 mg / tablet (97.33 % - 146.00 % of the label claim)	113.2	124.78	122.09	125.34	124.87	122.77
2, 4-Dichloro benzyl alcohol BP : (1.2 mg)	1.16 mg – 1.74mg / tablet (96.67 % - 145.00 % of the label claim)	116.5	115.78	120.43	121.99	130.23	129.87

3.3. RESULTS OF COMPOSITE SAMPLE:

Table 6 :Results Of composite Samples Of Batches A, B & C

S.No.	Test	Results			
		Specification	B.no.A	B.no.B	B.no.C
1	Description	Circular orange color with orange flavored tablets. Uneven coloration, presence of air bubbles in the caramel mass & insignificant unevenness of surface & edges of tablets is permissible. Emergence White coating is permissible.	Complies	Complies	Complies

2	Identification (BY GC) Amylmetacresol &2,4-dichlorobenzalalcohol	The Retention time of two main peaks on the chromatogram of test solution must correspond to the retention time of Amylmetacresol and 2,4-dichlorobenzyl alcohol on the chromatogram of standard solution in assay procedure.			
3	Average weight	2500 mg, ± 5% (2375.00 mg to 2625.00 mg)	2452.41	2454.31	2464.61
4	Uniformity of weight	18 tablets out of 20 not more than ±5% of the average weight. No tablets out of 20 not more than ±10% of the average weight.	Complies	Complies	Complies
5	Foreign mixtures (By GC) 2,4-dichlorobenzaldehyde	Not be more than 2% of labeled amount of 2,4-dichlorobenzalalcohol	1.5	1.6	1.4
6	Citric Acid Content (Citric Acid anhydrous 25mg)	(22.50 mg to 27.50 mg/tablet) (90.01 % - 110.01 % of the label claim)	99.67	103.4	101.56
7	Assay by GC:				

7a	Amylmetacresol BP: (0.6 mg)	0.584 mg to 0.876 mg / tablet (97.33 % - 146.00 % of the label claim)	99.78	111.43	113.32
7b	2, 4-Dichlorobenzyl alcohol BP: (1.2 mg)	1.16 mg – 1.74mg / tablet (96.67 % - 145.00 % of the label claim)	113.65	112.12	116.75
8.	Microbiological limit test:				
8a.	Total number of aerobic bacteria	Not more than 1000 cfu/g	987 cfu/g	980 cfu/g	982 cfu/g
8b.	Total number of fungi	Not more than 100 cfu/g	96 cfu/g	95 cfu/g	97 cfu/g
8c.	Escherichia coli	Must be absent in 1 g	Complies	Complies	Complies

CONCLUSION

The process validation has a major role in pharmaceutical industry for achieving & maintaining the efficacy, safety and quality of finished product. Each validation program follows validation master plan in industry. The process validation team i.e. quality assurance, production, quality control and engineering should identify the important parameters of the process and product to ensure that the product meats its predetermined quality standards, manufacturing and regulatory requirements.

Concurrent Process validation studies were executed for the three successive batches of amylmetacresol and 2, 4-dichloro benzyl alcohol lozenges. The methodology consisted three basic parts process parameters monitoring, the routine in-process and final product release testing & additional validation sampling and testing. Process validation studies of developed amylmetacresol and 2, 4-dichloro benzyl alcohol lozenges has been performed effectively.

- During this research work, three successive batches of A,B& C were chosen.
- The method used for the analytical testing in this process validation was taken from the official compendia.
- For the determination of the best parameters test were performed to calculate average weight, content of citric acid, content of Amylmetacresol and 2,4 dichlorobenzyl alcohol, average weight of 20 lozenges, diameter, thickness average.

- The observed average weight for final samples of Batch A, B and C were recorded as 2452.41, 2454.31 and 2464.61 mg.
- Process validation studies results for of amylmetacresol and 2, 4-dichloro benzyl alcohol lozenges were within the limits.

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