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Process Validation of Albendazole Tablet

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Abstract

Validation is the study of demonstrating and documenting at a manufacturing process operates efficiently. The pharmaceutical process validation refers that it should cover all the critical parameters in a manufacturing process for a pharmaceutical dosage form, from designing a process to final validation of that the formulation in the large scale production. Process validation acts as a tool for the pharmaceutical manufacturing companies to ensure the manufacturing process including instruments and facilities are in a state of control and also to provide evidence that the final product meets the quality, purity and integrity as specified. The major objective of the study is to demonstrate that the critical operations involved in the manufacturing of Albendazole 400 mg tablets are capable of consistently producing batch which meet the limit of acceptance criteria.

Keywords- bituminous mix, dense bituminous mix, Marshal Mix design, polymers, softening point, specific gravity.

I. INTRODUCTION

Validation is the study of demonstrating and documenting at a manufacturing process operates efficiently. The pharmaceutical process validation refers that it should cover all the critical parameters in a manufacturing process for a pharmaceutical dosage form, from designing a process to final validation of that the formulation in the large scale production. Accordingly it is obvious that compliance with the finished product specification itself maynot be sufficient to assure that the processes are valid and the Vendor has full control over the process. *[1]*

However, Validation is an essential part of Quality Assurance Program and is fundamental toan efficient production operation. *[2]*

In the Federal Register FDA issued a notice on May 11, 1987 (52 FR 17638), the availability of guidelines entitling Guidelines on General Principles of Process Validation (the 1987 guidance). *[3].*

Utilizing the plastic waste in the asphalt pavement application is a right approach and it will help to dispose the waste by eco-friendly way.

- **Reason for performing process validation:**

The principle goal for validation is to assure, completely, that all the manufacturing processes, procedures and machinery being used should ensure safety, quality and strength ofthat formulation. Validation is very eminent, if there are any prominent changes to the premises, the facilities, the process or the equipment which may interferes with the quality of that product, directly or indirectly, partially or fully, should be validated. *[6]*

A process should also be validated to meet regulatory requirements. The Regulatory bodies, such as the FDA, shall need process validation. The US-FDA Quality System Regulation requires manufacturers to perform validation when the process is not completely verified byan appropriate inspection or test. *[7]*

A properly and completely validated, controlled process results in little scrap or reprocessing, leads an increased output. Consistent compliance to specifications also results in fewer complaints and recalls. Whenever needed, the validation document contains the data toassist any improvements in a process or in the design of the next generation of the process. *[8]*

- **Importance of process validation**

1. Compliance to Regulatory bodies
2. Assurance in quality
3. Optimization in the process
4. Reduced cost of production
5. Reduction in Batch failures, enhancement in efficiency and productivity
6. Lowering down time
7. Reduced rejections
8. Increased output
9. Minimum complaints about process–related failures.

- **Mechanism of action of ALBENDAZOLE**

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by diminishing its energy production, ultimately leading to immobilization and death of the parasite. It works by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. As cytoplasmic microtubules are critical in promoting glucose uptake in larval and adult stages of the susceptible parasites, the glycogen stores of the parasites are depleted. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. As a vermicide, albendazole causes degenerative alterations in the intestinal cells of the

worm by binding to the colchicine-sensitive site of β-tubulin, thus inhibiting its polymerization or assembly into microtubules (it binds much better to the βtubulin of parasites than that of mammals)

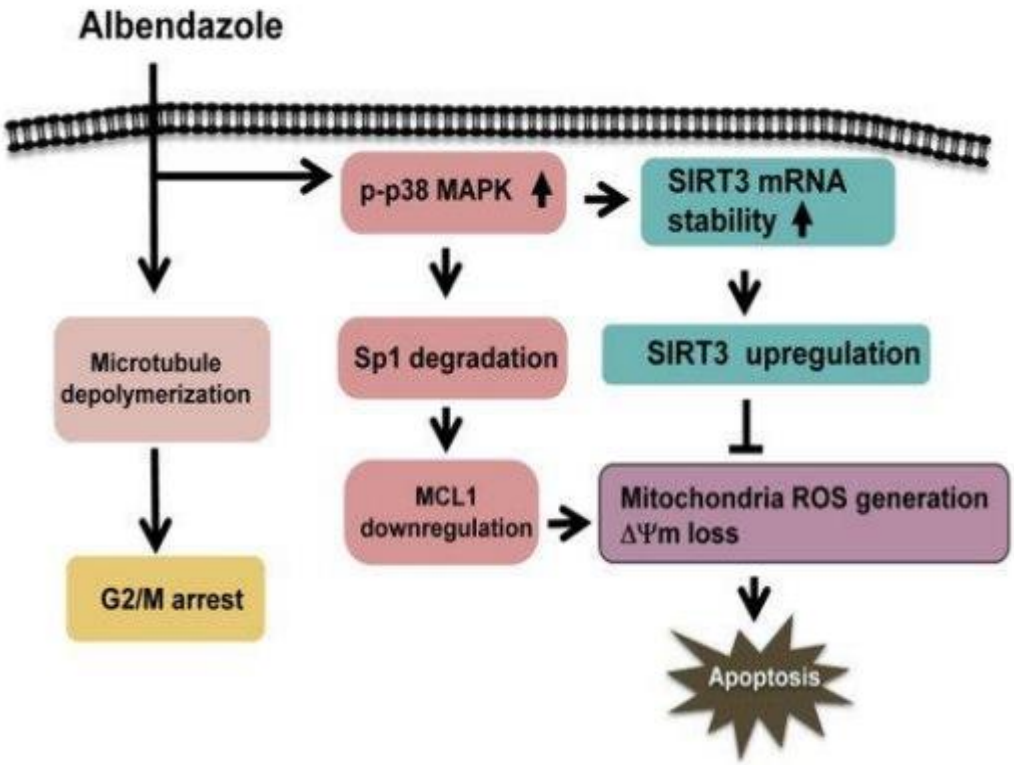

Fig. 1. Mechanism of action of ALBENDAZOLE

- **Batches studied for process validation**

MANUFACTURERS:

Vendor A- Recent Vendor (Need to validate)

Vendor B- Existing Vendor (Validated)

PROCESS VALIDATION BATHCES

PVA01- First batch of Albendazole Tablets

PVA02- Second batch of Albendazole Tablets

PVA03- Third batch of Albendazole Tablets

PVB01- First batch of Albendazole Tablets

PVB02- Second batch of Albendazole Tablets

PVB03- Third batch of Albendazole Tablets

II. MATERIAL USED

To establish scientific evidence that the manufacturing process will consistently produce Albendazole tablets, meeting its predetermined acceptance criteria and consistently deliverquality product.

Lable claim Each Uncoated tablet contains:

Albendazole USP 400mg

Chemical name: Methyl N-(6-propylsulfanyl-1H-benzimidazol-2-yl) carbamate

Formula : C12H15N3O4S

Molecular weight : 265.33 g/mol

Description: Albendazole is a white to yellowish powder. It is freely soluble in anhydrous formic acid and very slightly soluble in ether and in methylene chloride.

Melting point : 208 to 210 °C (406 to 410 °F)

Solubility: Albendazole is a white to off-white powder. It is soluble in dimethylsulfoxide, strong acids, and strong bases. It is slightly soluble in methanol, chloroform, ethyl acetate, and acetonitrile. Albendazole is practically insoluble in water.

Category : Antihelmintics

Albendazole is used to treat neurocysticercosis, an infection of the nervous system caused by pork tapeworms. This medicine is also used to treat cystic hydatid disease of the liver, lung, and peritoneum, an infection caused by dog tapeworms.

III. METHODOLOGY

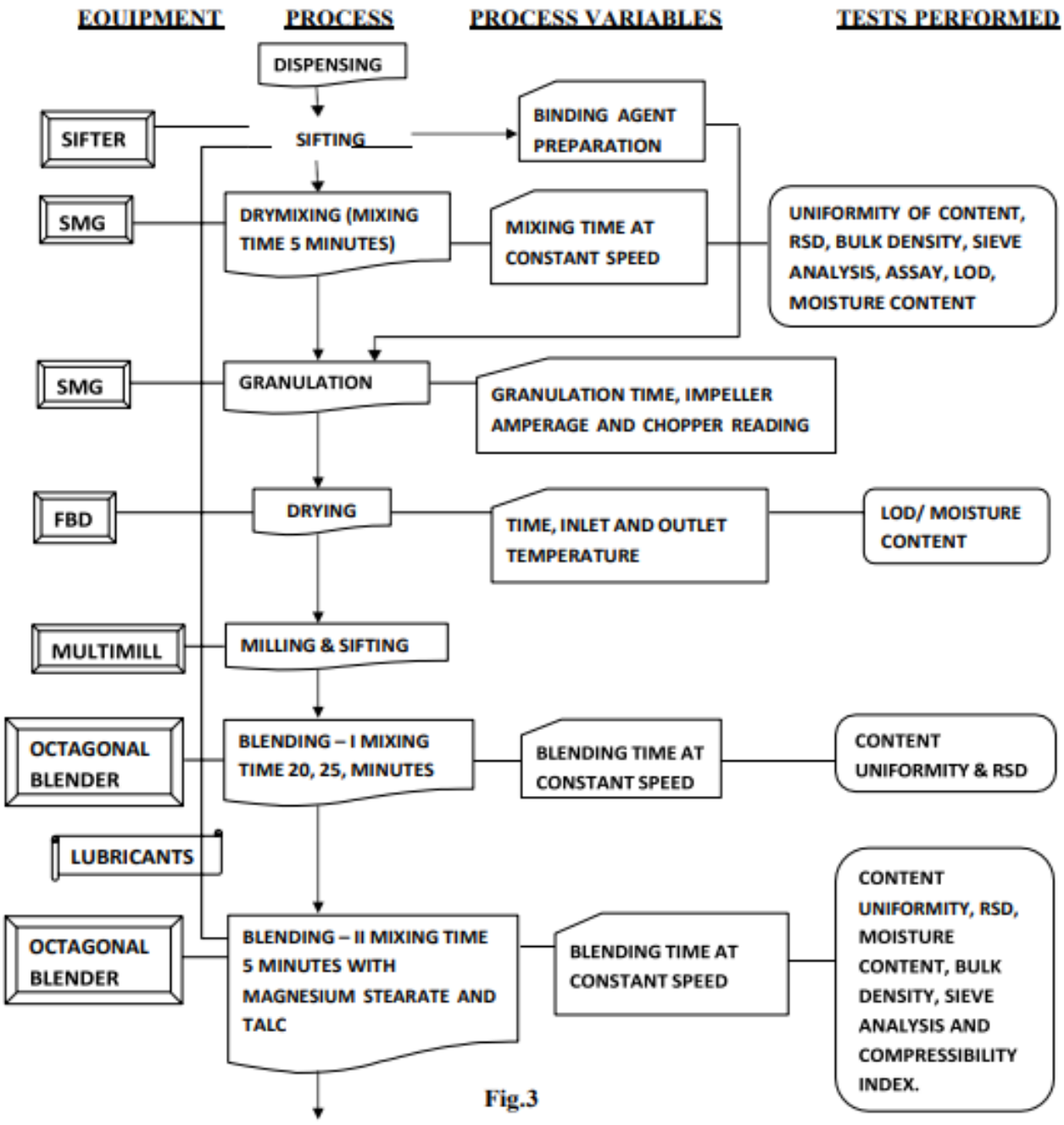

Fig.2 Flow chart for process validation

Table 1 Batch details of vendors

Manufacturer	Recent API Vendor (Need to validate)	Existing API Vendor (Validated)
1 st Batch	PVA01	PVB01
2 nd Batch	PVA02	PVB02
3 rd Batch	PVA03	PVB03

IV. RESULTS

- **Drying.**

  Parameters

  Critical process parameter : Drying time and Drying
  Temperature Measured response : LOD (loss on drying)
  Acceptance criteria : < 1.0 %w/w
  Batches taken for study : PVA01, PVA02 and PVA03.

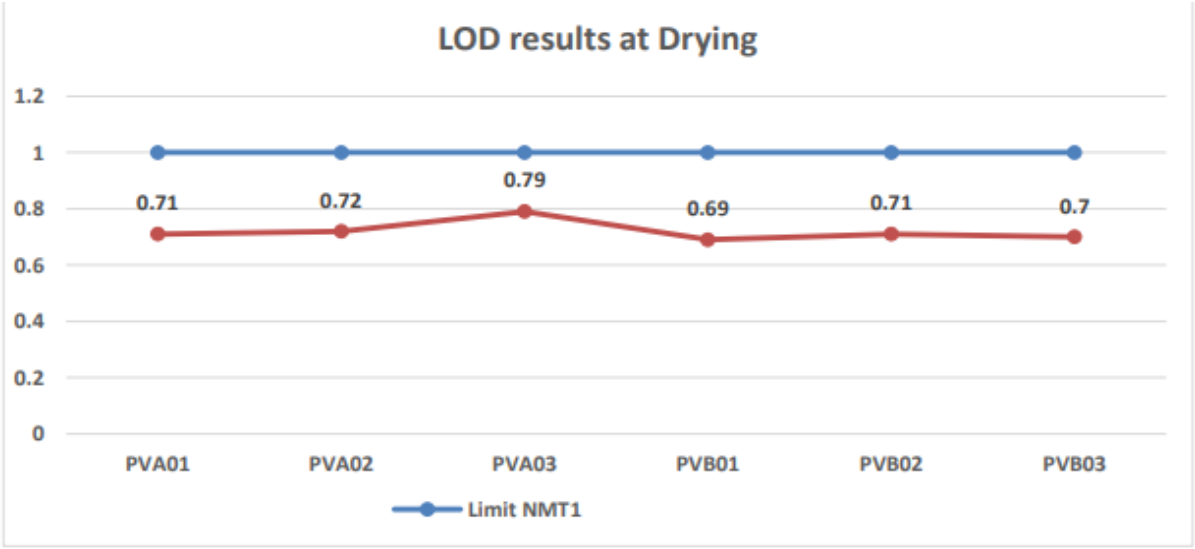

Fig.3 Inlet, Outlet, Product Temperatures and LOD Result

- **Blending**

  Blender RPM : 12 RPM
  Time interval : 25 minutes
  Critical process parameter : Blending time
  Measured response : Blend Uniformity and RSD
  Acceptance criteria : 90.0 -110.0 %(RSD NMT 5.0%)
  Batches taken for study : PVA01, PVA02, PVA03

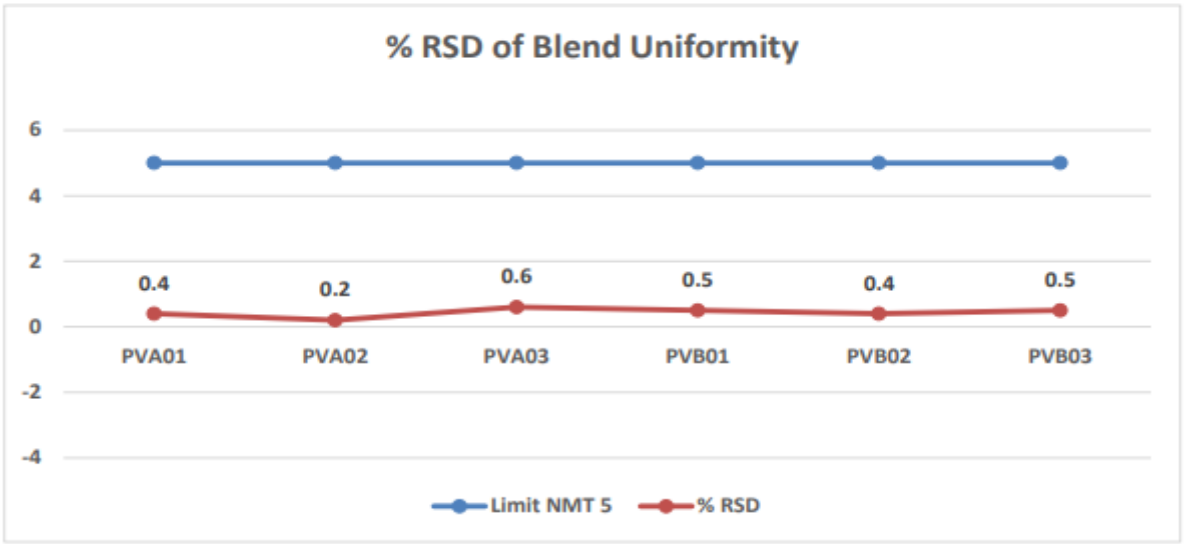

Fig.4 Blend Uniformity of Albendazole and RSD values after blending

V. CONCLUSION

All the raw materials used in the manufacturing of Albendazole 400 mg Tablets, were tested as per the given specifications and the results were within the limits. Hence the validation of raw materials was concluded. The equipment used in the manufacturing of the Albendazole 400 mg Tablets were checked for their Installation, Operation and Performance Qualification and concluded. The dry mixing time of 5 minutes is concluded as validated mixing time at fastspeed. The desired granular mass was obtained between impeller amperage 5 - 12 amps. Resultant granules after drying and milling have desired flow properties. All the three batches resulted in granules with desired flow and compaction, which is evident from data of compression tablets. Results of all three batches (PVA01, PVA02, and PVA03) with Vendor A are found comparable with existing validated batches (PVB01, PVB02, and PVB03) with Vendor B. Hence the granules stage of Albendazole 400 tablet is concluded as validated at impeller amperage of 5 – 12 amps. 5. According to observations during drying for all three batches, it was concluded that only air drying the granular material after granulation is required till the LOD is NMT 1.0%. 6. The blending time of 25 minutes is concluded as validated blending time at slow speed of blender for Albendazole 400 blending, when the process is performed in 450 liters capacity Octagonal blender for a batch size of 153.600 kg..

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