INDUSTRIAL PROCESS VALIDATION OF COATED TABLET: A REVIEW

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ABSTRACT
The validation is a fundamental segment that supports to a commitment of company towards quality assurance. It also assures that product meets its predetermined quality specification and quality characteristics. Validation is the art of designing and practicing the designed steps alongside with the documentation. Validation and quality assurance will go hand in hand, ensuring the through quality for the products. Validation of individual step of manufacturing is called as process validation. Different dosage form has different validation protocol. Here this validation article concentrates on process validation of tablet dosage form protocol preparation and regulatory basis of the pharmaceutical industry.

Keywords: Validation, Quality assurance, Protocol.

INTRODUCTION
The prime objective of any pharmaceutical plant is to manufacture products of requisite attribute and quality consistently, at the lowest possible cost. Although validation studies have been conducted in the pharmaceutical industry for a long time, there is an ever increasing interest in validation owing to their industry’s greater emphasis in recent years on quality assurance program and is fundamental than efficient production operation. Validation is a concept that has evolved in United States in 1978. Validation is a team effort where it involves people from various disciplines of the plant.¹

A tablet is a pharmaceutical dosage form. It comprises a mixture of active substances and excipients, usually in powder form, pressed or compacted into a solid. Tablets Dosage form is one of a most preferred dosage form all over the world. Almost all drug molecules can be formulated in a tablet and process of manufacturing of tablets is very simple, and is very flexible.

TABLET COATING: Coating is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form in order to confer specific benefits over uncoated variety. Coating may be applied to a wide range of oral solid dosage form, such as particles, powders, granules, crystals, pellets and tablets.² ³
TYPES OF VALIDATION

a) Analytical validation

Validation is the product quality attributes through testing to demonstrate reliability is being maintained throughout the product life cycle and that the precision, accuracy, strength, purity and specification has not been compromised.

b) Equipment Validation:

Studies which establish with confidence that the process equipment and ancillary systems are capable of consistently operating within established limits and tolerances. The studies must include equipment specifications, installation qualification (IQ), and operational qualification (OQ) of all major equipment to be used in the manufacture of commercial scale batches. Equipment qualification should simulate actual production conditions, including "worst case"/stressed conditions.

c) Process Validation:

Establishing documented evidence with a high degree of assurance, that a specific process will consistently produce a product meeting its predetermined specifications and quality characteristics. Process validation may take the form of prospective, concurrent or retrospective validation and process qualification or re-validation.

d) Cleaning validation

The documented act of demonstrating that cleaning procedures for the equipment used in fabricating/packaging will reduce to an acceptable level all residues (products/cleaning agents) and to demonstrate that routine cleaning and storage of equipment does not allow microbial proliferation.

PROCESS VALIDATION PROTOCOL

It is a written process which includes all the steps which take place for the manufacturing of the tablet process. It includes manufacturing process, process flow, ingredients, packaging equipments and acceptance criteria. The Protocol provides us an idea that what to accomplished. The process validation provide us an idea that how the process will done. if any change will be done it will be done by the validation team.

PROCESS OF MANUFACTURING SOLID DOSAGE FORM

The manufacture of oral solid dosage forms such as tablet is a complex multi stage process under which the starting materials change their physical characteristics a number
of times before the final dosage form is produced. Tablets have been made by a granulation, a process that imparts two primary requisites to formulate compatibility and fluidity. Both wet granulation and dry granulation (slugging and roll compaction) are used. Regardless of whether tablets are made by direct compression or granulation, the first step is milling, mixing is the same and subsequent step is differing.

Numerous unit processes are involved in making, tablets, including, particle size reduction and sizing, blending, granulation, drying, compaction, and coating. Various factor associated with these process can seriously affect content uniformity, bioavailability or stability.

CRITICAL PROCESS PARAMETERS

a) Dispensing (weighing and measuring)

Dispensing is the first step in any pharmaceutical manufacturing process. Dispensing is one of the most critical step in the pharmaceutical manufacturing as during this step, the weight of each ingredient in the mixture is determined according to dose.

b) Milling/Blending

It is process in which drugs are uniformly mixed together. In manufacturing of compressed tablets, the mixing or blending of several solid pharmaceutical ingredients is easier and more uniform if the ingredients are about the same size. This provides a greater uniformity of dose. A fine particle size is essential in case of lubricant mixing with granules for its proper function.

c) Granulation

Particle size reduction and blending, the formulation may be granulated, which provides homogeneity of drug distribution in blend. This process also is very important and needs experience to attain proper quality of granule before tableting, quality of granule determines the smooth and trouble free process of tablets manufacturing.

d) Wet Granulation

In the Wet Granulation process a liquid ‘binder’ is used to lightly agglomerate the powder mixture. The binder is some kind of wet material used to bind the mixture of ingredients together into a homogeneous mass. When the wet binding material (WBM) is used care is taken to not add too much, or you are left with a mess of hard granules.
bunched together. If not enough wet binding material is used, the granules are a gloppy mushy mess. The wet binding material can be water-based or solvent-based

e) Dry Granulation

In dry granulation process the powder mixture is compressed without the use of heat and solvent. It is the least desirable of all methods of granulation. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain a granules. Two methods are used for dry granulation. The more widely used method is slugging, where the powder is recompressed and the resulting tablet or slug are milled to yield the granules.

f) Drying

Drying is a most important step in the formulation and development of pharmaceutical product. It is important to keep the residual moisture low enough to prevent product deterioration and ensure free flowing properties. The commonly used dryers include Fluidized – bed dryer, Vacuum tray dryer, Microwave dryer, Spray dryer, Freeze dryer, Turbo - tray dryer, Pan dryer, etc.

f) Direct Compression

This method is used when a group of ingredients can be blended and placed in a tablet press to make a tablet without any of the ingredients having to be changed. This is not very common because many tablets have active pharmaceutical ingredients which will not allow for direct compression due to their concentration or the excipients used in formulation are not conducive to direct compression.

COATING\textsuperscript{11,12}

1. SUGAR COATING:

• It involves successive application of sucrose based coating formulations to tablet core, in suitable coating equipment.
• Water evaporates from the syrup leaving a thick sugar layer around each tablet.
• Sugar coats are often shiny and highly colored.

STEPS IN SUGAR COATING:

• Seal coating
• Sub coating
• Syrup coating/Smoothing
• Color coating
• Polishing

1. Sealing (Waterproofing)

This involved the application of one or more coats of a water proofing substance in the form of alcoholic spray, such as pharmaceutical Shellac (traditionally) or synthetic polymers, such as CAP. Sugar-coatings are aqueous formulations which allow water to penetrate directly into the tablet core and thus potentially affecting product stability and possibly causing premature tablet disintegration.

2. Subcoating

Large quantities of sugar-coatings are usually applied to the tablet core , typically increasing the tablet weight by 50-100%

3. Smoothing / syrup coating

• To cover and fill in the imperfections in tablet surface caused by subcoating.
• To impart desired color
• The first syrup coat contains some suspended powders and are called “grossing syrups”.
• Dilute colorants can be added to provide tinted base that facilitates uniform coating in later steps.
• Syrup solutions containing the dye are applied until final size and color are achieved.

4. Finishing

• Final syrup coating step
• Few clear coats of syrup may be applied.

5. Polishing

• Desired luster is obtained in this final step
• Clean standard coating pan, canvas-lined coating pans
• Application of powdered wax or warm solution of waxes in suitable volatile solvent

2) Film coating

Film coating and sugar coating shares the same equipments and process parameters. Two methods,
1) **Pan-Pour method:**

- Same as that of pan-pour sugar coating
- Method is relatively slow and relies heavily on skill and technique of operator
- Aqueous based film coating is not suitable due to localized over-wetting.

2) **Pan-Spray method:**

Use of automated spraying system

Modern approach to coating tablets, capsules, or pellets by surrounding them with a thin layer of polymeric material. Polymer, Solvent, Plasticizer, Colourant.

The solution is sprayed onto a rotating tablet bed followed by drying, which facilitates the removal of the solvent leaving behind the deposition of thin film of coating mate

**Advantages**

Produce tablets in a single step process in relatively short period of time. Process enables functional coatings to be incorporated into the dosage form.

**Disadvantages**

There are environmental and safety implications of using organic solvents as well as their financial expense.

3) **Enteric coat**

The technique involved in enteric coating is protection of the tablet core from disintegration in the acidic environment of the stomach by employing pH sensitive polymer, which swell or solubilise in response to an increase in pH to release the drug.

An ideal enteric coating materials should have the following properties:

- permeable to intestinal fluid
- Compatibility with coating solution and drug
- Formation of continuous film
- Nontoxic
- Cheap and ease of application
- Ability to be readily printed
- Resistance to gastric fluids

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**FINISHED PRODUCT TEST DONE IN THE INDUSTRY**\(^{14,15}\)

1. **Appearance:** The tablet should be examined for various problems as tablet mottling, picking, bridging and filling, color variation, cracking.

2. **Assay:** This test will determine whether or not the product contains the labeled amount of the drug.

3. **Content uniformity:** Samples are taken from the batch profile (beginning, middle and end) and analyzed to ensure that the dosage form comply with in standards (15% of the labeled amount). It will indicate the whether the batch will have segregation during flow of granulation.

4. **Tablet hardness:** A critical parameter for dosage form handling and performance.

5. **Tablet friability:** Friability is an important characteristic on the tablets ability to withstand chipping, cracking, dusting during the packaging operations and shipping.

6. **Dissolution:** Dissolution is important to ensure proper drug release characteristics (in vitro availability) and batch to batch uniformity.

**CONCLUSION**
Tablet dosage form should be integral part of the industry. The total program should begin with the API so that uniform from batch to batch. The scientific information which is obtained during the preformulation stage can form the basis for the validation. Validation principle will thus ensure that pharmaceutical products will be able to be developed and produced with the quality and reproducibility required from regulatory agency.

**REFERENCE**

1. FDA guidelines on General Principles of Process Validation (May 1987).

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