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A REVIEW: STUDIES IN PROSPECTIVE PROCESS VALIDATION OF MULTI COMPONENT ANTI-RETRO VIRAL TABLET DOSAGE FORMULATION

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ABSTRACT

Tablet may be defined as the solid unit dosage form of medicament with or without suitable diluents and prepared either by molding or by compression.Tableted drug delivery system can range from relatively simple immediate-release formulation to complex extended or modified release dosage forms. The most important role of a drug delivery system is to get the drug "delivered" to the site of action in sufficient amount and at the appropriate rate; however, it must also meet a number of other essential criteria. Granulation is a part of pharmaceutical process that attempts to improve the flow of powdered materials by forming sphere like or regularly shaped aggregates called granules. Wet granulation form granules by binding the powder together, with an adhesive instead of compaction. Tablets require a certain amount of strength or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping.The principle objective of dosage form design is to achieve a predictable therapeutic response to a drug included in a formulation which is capable of large scale manufacture with reproducible product quality, numerous features are required, like chemical and physical stability, suitable preservation against microbial contamination if appropriate, uniformity of dose of drug, acceptability to users including prescriber and patient, as well as suitable packing, labelling and validation.

KEY WORDS: Tablet, Compression, Drug delivery, Wet granulation, Stability.

1. INTRODUCTION:

Tablet may be defined as the solid unit dosage form of medicament with or without suitable diluents and prepared either by molding or by compression. A tablet is a combination of ingredients that is compressed into a solid mass. Despite the long and continuing history of the development of new technologies for administration of drugs, the tablet form remains the most commonly used dosage form.[1]

1.1 Types and Classes of Tablet:

Tableted drug delivery system can range from relatively simple immediate-release formulation to complex extended or modified release dosage forms. The most important role of a drug delivery system is to get the drug "delivered" to the site of action in sufficient amount and at the appropriate rate; however, it must also meet a number of other essential criteria. These include physical and chemical stability, ability to be ecnomically mass produced in a manner that assures the proper amount of drug in each and every dosage unit and in each batch produced, and as far as possible, patient acceptability (for example, reasonable size, shape, taste, colour etc.

1.2 Properties of an Ideal Tablet:

The objective of formulation and fabrication of tabletis to deliver the correct amount of drug in proper form at over proper time.

- Tablet should be elegant having its own identity and free from defects such as cracks, chips contamination, discolouration etc.
- It should have chemical and physical stability to maintain in physical integrity over time.
- It should be capable to prevent any alteration in the chemical and physical properties of medicinal agents.
- It should be capable of withstanding the rigors of mechanical shocks encountered in its production, packaging, shipping and dispensing.

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- An ideal tablet should be able to release the medicament in body in predictable and reproducible manner.

1.3 Tablet Granulation:

Material intended for compression into a tablet must posse's two characteristics

a. Fluidity
b. Compressibility

1.3.1 Method of granulation:

A) Direct Compression

There are a few crystalline substances that can be compressed directly. In addition, compression of single substances may produce tablets that do not disintegrate.

B) Compression Granulation

Compression granulation involves the compaction of the components of a tablet formulation by means of a tablet press or specially designed machinery, followed by milling and screeninig, prior to final compression into a tablet.

C) Wet-Granulation

Wet granulation form granules by binding the powder together, with an adhesive instead of compaction. Liquid plays a key role in the granulation process, liquid bridges are developed between particles and tensile strength of these bonds increases as the amount of the liquid added is increased.

1.4 Evaluation of the Tablets:

To design tablets and later monitor tablet production quality, quantitative evaluations and assesmentsof a tablet chemical, physical, and bioavailability properties must be made.

A) General Appearance:

- Size
- Shape
- Colour
- Presence or absence of an odour
- Surface texture
- Legibility of any identifying markings

B) Hardness, Thickness and Friability:

Tablets require a certain amount of strength or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging and shipping. Hardness is sometimes termed as Tablet Crushing Strength. Several devices used to test tablet hardness are given below

- Monsanto tester
- Strong-cobb tester
- Pfizer tester
- Erweka tester
- Schleuniger tester

Hardness and thickness are oppostie to each other i.e if thickness is less, moreharder tablets are formed and vice-versa. With constant die fill the hardness value increases and thickness decreases as additional compression force is applied, and with constant compressive force (i.e fixed distance between upper and lower punches) hardness increases and thickness decreases with increasing die fill. Tablet thickness at constant compressive force varies with particle size distribution and tablet weight.

C) Weight variation and Content uniformity

Table 1: Weight Variation Tolerances for Uncoated Tablets (USP)

Average Weight Of Tablets (mg)	Maximum Percentage Difference Allowed
130 or less	10
130 – 324	7.5
More than 324	5

The use of weight cannot be used as a potency indicator, except when the active ingredient is 90 – 95% of the total tablet weight. In tablets with smaller dosages, a good weight variation dose not ensures good content uniformity, but a large weight variation precludes good content uniformity. For evaluating content uniformity total 30 tablets are taken, and 10 of them are assayed individually 9 of 10 tablets must contain NLT 85% or NMT 115%, the 10^{th} tablet may not contain NLT 75% or NMT 125% of the label content, if these condition are not met, the tablets remaining from the 30 must be assayed individually and none may fall of 85 to 115% range.

D) Disintegration and Dissolution:

For tablets, the first important step toward solution is breakdown of the tablet into smaller particles or granules, a process known as disintegration. The USP device to test disintegration uses 6 glass tubes that are 3 inches long, open at the top and held against a 10 mesh screen at the bottom end of the basket rack assembly. To test for disintegration time, one tablet is placed in each tube, and the basket rack is positioned in a 1-L beaker of water at $37^0C \pm 2^0C$. A standard motor-driven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6 cm at a frequency of 28 to 32 cycles per minute.

2. VALIDATION:

The principle objective of dosage form design is to achieve a predictable therapeutic response to a drug included in a formulation which is capable of large scale manufacture with reproducible product quality, numerous features are required, like chemical and physical stability, suitable preservation against microbial contamination if appropriate, uniformity of dose of drug, acceptability to users including prescriber and patient, as well as suitable packing, labelling and validation.

The U.S. Food and Drug Administration (FDA) has proposed guidelines which define process validation as: 'Process validation is establishing documented evidence which provides a high degree of assurance that a specific process (such as the manufacture of pharmaceutical dosage forms) will consistently produce a product meeting its predetermined specifications and quality characteristics

2.1 Four types of process validation:

- **Prospective Validation**

Prospective process validation is carried out during the development stage by means of risk analysis of the production process which is broken down into individual steps. Prospective validation makes validation an integral part of a carefully planned, logical process developmental program. In prospective process validation, an experimental plan called the validation protocol is executed (following completion of the qualification trials) before the process is put into commercial use.[5,6]

- **Concurrent Validation**

Concurrent Validation means establishing documented evidence that a process does what it is supposed to do based on data generated during actual implementation of the process.This is normaly performed by conducting in-process testing and/or monitoring of critical operation during the manufacture of each production batch. The first three production-scale batches must be monitored as comprehensively as possible.

- **Retrospective Validation**

Retrospective Validation means establishing documented evidence a process does what it is supposed to do based on review and analysis of historical data. Historical data may be utilized to provide necessary documentary evidence that the processes are validated. For a product to be considered for retrospective validation, it must have a stable process; that is, one in which the method of manufacture has remained essentially unchanged for a period of time.

- **Re-Validation**

Re-validation is usually performed to the confirmation of initial validation for a Periodic review. Re-validation provides the evidence that changes in a process and /or the process environment that are introduced do not adversely affect process characteristics and product quality.

2.2 Phases of validation:

The USFDA guidance describes process validation activities in three phases.

Phase 1–Qualification Phase /Process Designthe commercial manufacturing process is defined during this stage based on knowledge gained through development and scale-up activities. It covers all activities relating to product research and development, formulation, pilot batch studies, scale-up studies, transfer of technology to commercial scale batches, establishing stability conditions, storage and handling of in-process and finished dosage forms, Equipment Qualification, master production documents, Process Capability.

Phase 2–Process Validation Phase/ Process Qualification it is designed to verify that all established limits of the Critical Process Parameters are valid and that satisfactory products can be produced even under the "worst case" conditions.

Phase 3–Validation Maintenance Phase/Continued Process Verification ongoing assurance is gained during routine production that the process remains in a state of control. This require frequent review of all process related documents, including validation audit reports to assure that there have been no changes, deviations, failures, modifications to the production process, and that all SOPs have been followed, including Change Control procedures.

2.3 Need of prospective process validation:

- It would not be feasible to use the equipments without knowing whether it will produce the product we wanted or not.
- The pharmaceutical industry uses expensive materials, sophisticated facilities &equipments and highly qualified personnel.
- The efficient use of these resources is necessary for the continued success of the industry. The cost of product failures, rejects, reworkand recalls complaints are the significant parts of the total production cost.

- Detailed study and control of the manufacturing process-validation is necessary if failures are to be reduced and productivity is to be improved.

2.4 Benefits of prospective process validation:

Adequate validation is beneficial to the manufacturer in many ways:

- It deepens the understanding of processes and decreases the risk of problems and thus assures the quality of the product
- The smooth runnig of the process
- It decreases the risk of defect costs
- It decreases the risk of regulatory noncompliance
- A fully validated process may require less in-process controls and end product testing.

2.5 Approaches to process validation:

There are two basic approaches to the validation of process itself (apart from the qualification of equipment use in the production, the calibration of control and measurement instruments, the evaluation of environmental factors, etc). The experimental approach and the approach based on the analysis of the historical data. The experimental approach, which is applicable to both, prospective and concurrent validation may involve

- Extensive product testing
- Simulation process trials
- Challenge / Worst case trials and
- Control of process parameters (mostly physical)

2.6 Validation report:

A written report should be available after the completion of the validation, if found acceptable, it should be approved and authorized (signed and dated). The report should include at least the following

- Title and objective of the study
- Reference to the protocol
- Details of the material
- Equipment
- Programs and cycle used
- Details of the procedure and test methods
- Result compared with the acceptance criteria
- Recommendation on the limit and criteria to be applied on future basis.

3. CONCLUSION:

The cGMP regulations states that “there shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess”. This regulation requires manufacturers to design a process, including operations and controls, which results in a product meeting these attributes. According to the cGMP control procedures shall be established to monitor output and to validate performance of the manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

4. REFERENCES:

1. Lachman L, Lieberman HA, Kanig JL. The theory and practice of industrial Pharmacy. 3rd ed. Bombay: Varghese publishing house; 1990. p. 293-373.
2. Aulton ME. The science of dosage form design. 2nd ed. Elsevier: Churchill livingstone; 2006.p. 1-2.
3. Patel VB, Rathwa MR, Patel K. Studies in prospective process validation of cimetidine tablet dosage form. Int J Res Pharm BiomSci 2011;2(4):1823-1836.
4. Seager H. Drug Delivery Products and Zydis Fast Dissolving Dosage form. J Pharm Pharma. 1998; 50: 375-82.
5. Leblane DA. Establishing scientifically justified acceptance criteria for cleaning validation of finished drug product. Pharm Tech 1998;23:134–148.
6. Nash RA. Process validation of a 17 year retrospective study of solid dosage forms. Drug DevInd Pharm 1996; 22:25-34.
7. Porter SC, Verseput RP, Cunningham CR. Process optimization using design of experiments. Int J Pharm Tech Res 1980;4 (3):66–72.