WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 3, Issue 8, 925-931. Review Article ISSN 2277 – 7105

PILOT SCALEUP TECHNIQUES FOR SOLID DOSAGE FORM - AN OVERVIEW FOR TABLETS

P. Ramasubramaniyan, C. Shibin raj, P. Nagarajan, D.Sherly, L. Subramanian, P. Solairaj

Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi - 626130.

Article Received on
09 August 2014,

Revised on 06 August 2014,
Accepted on 29 Sept 2014

*Correspondence for Author
Dr. P. Ramasubramaniyan
Sankaralingam
Bhuvaneswari College
of Pharmacy, Sivakasi

ABSTRACT

Pilot scale up techniques for solid dosage form will provide guid line for the manufacture of large scale process and this will play a pivotal role in large scale manufacturing. The parameters such as granulation feed rate, compression parameters, temperature and rate of drying will have a critical role in development of any solid dosage form.

KEYWORDS: Pilot plant technique, solid dosage form, tablets, compression.

INTRODUCTION [1]

Pilot plant technique is defined as a part of the pharmaceutical industry where a lab scale process is transformed into a viable product by the Development of liable practical procedure for manufacture of dosage forms. The Scale-up is the art of designing of prototype using the data obtained from the pilot plant model.

The Objective of Scale up Technique [2]

- To develop and formulate physically and chemically stable therapeutic dosage forms by optimizing various parameters.
- To create a guidelines for production and process control.
- Raw materials handling and its specifications requirements
- To identify the critical steps involved in the process.
- To develop a master manufacturing formula.
- Pilot plant studies may be developed to establish the identical examination of the formula to withstand batch scale.
- Infrastructure the related to scale up efforts in the pilot plant:

- Production and process controls are evaluated, validated and finalized.
- Any Process modification can be allowed
- To Evaluate and validate the developed product.
- To update the processing equipment.
- Physical and mechanical Compatibility of the equipment with the formulation.
- Time and cost factor.
- Need for current market strategies.
- To overcome the difficulties in small scale and create large scale production.

Rationale for Pilot Plant Studies

- A pilot plant allows investigation of a product and process on an intermediate scale before large amounts are committed to full-scale production
- It is usually not possible to predict the effects of a many-fold increase in scale
- It is not possible to design a large complex food processing plant from laboratory data alone with any degree of success.

Significance of Pilot Plant [3]

- Standardization of formulae.
- Review of range of relevant processing equipments.
- Optimization and control of production rate.
- Information on infrastructure of equipments during the scale up batches physical space required.
- Identification of critical features to maintain quality of a product.
- Appropriate records and reports to support GMP.

Scale Up Process [4]

Scale-up is defined as the process of increasing the batch size. Scale-up of a process can also be viewed as a procedure for applying the same process to different output volumes. Batch size enlargement does not always translate into a size increase of the processing volume. In mixing applications, scale-up is indeed concerned with increasing the linear dimensions from the laboratory to the plant size. On the other hand, processes exist (e.g., tableting) for which "scale-up" simply means enlarging the output by increasing the speed. In moving from R&D to production scale, it is sometimes essential to have an intermediate batch scale. This scale also makes possible the production of enough product for clinical testing and samples for

marketing. However, inserting an intermediate step between R&D and production scales does not in itself guarantee a smooth transition

Pilot Plant Design for Tablets: [1, 2, 5, 6, 7]

- The primary responsibility of the pilot plant staff is to ensure that the newly formulated tablets developed by product development personnel will prove to be efficiently, economically, and consistently reproducible on a production scale.
- The design and construction of the pharmaceutical pilot plant for tablet development should incorporate features necessary to facilitate maintenance and cleanliness.
- If possible, it should be located on the ground floor to expedite the delivery and shipment of supplies.
- Each stage considered carefully from experimental lab batch size to intermediate and large scale production.
- Same process, same equipment but different performance when amount of material increased significantly.
- May involve a major process change that utilizes techniques and equipment that were either unavailable or unsuitable on a lab scale.

Stages of Production of Tablets

- Material handling
- Dry blending
- Granulation
- Drying
- Reduction of particle size
- Blending
- Direct compression
- Slugging (dry granulation)

Material Handling System

In the laboratory, materials are simply scooped or poured by hand, but in intermediate- or large-scale operations, handling of this materials often become necessary. If a system is used to transfer materials for more than one product steps must be taken to prevent cross contamination. Any material handling system must deliver the accurate amount of the ingredient to the formulation. The More sophisticated methods of handling materials are

vacuum loading systems, metering pumps, screw feed system. The types of the system selected depend on the nature of the materials, e.g., density and static change.

Dry Blending

Inadequate blending at this stage could result in discrete portion of the batch being either high or low in potency. Steps should be taken to ensure that all the ingredients are free from lumps and agglomerates. For these reasons, screening and/or milling of the ingredients usually makes the process more reliable and reproducible. There are various equipment used in blending process they are V- blender, double cone blender, Ribbon blender, Slant cone blender Bin blender, Orbiting screw blenders vertical and horizontal high intensity mixers. The blending will be optimized by following parameters.

1. Time of blending.
2. Blender loading.
3. Size of blender

Granulation

Sigma blade mixer, Heavy-duty planetary mixer. More recently, the use of multifunctional "processors" that are capable of performing all functions required to prepare a finished granulation, such as dry blending, wet granulation, drying, sizing and lubrication in a continuous process in a single equipment.

Drying

The most common conventional method of drying a granulation continues to be the circulating hot air oven, which is heated by either steam or electricity. The important factor is to consider as part of scale-up of an oven drying operation are airflow, air temperature, and the depth of the granulation on the trays. If the granulation bed is too deep or too dense, the drying process will be inefficient, and if soluble dyes are involved, migration of the dye to the surface of the granules. Drying times at specified temperatures and airflow rates must be established for each product, and for each particular oven load. Fluidized bed dryers are an attractive alternative to the circulating hot air ovens. The important factor considered as part of scale up fluidized bed dryer are optimum loads, rate of airflow, inlet air temperature and humidity.

Reduction of Particle Size

First step in this process is to determine the particle size distribution of granulation using a series of "stacked" sieves of decreasing mesh openings. Particle size reduction of the dried granulation of production size batches can be carried out by passing all the material through an oscillating granulator, a hammer mill, a mechanical sieving device, or in some cases, a screening device. As part of the scale-up of a milling or sieving operation, the lubricants and glidants, in the laboratory are usually added directly to the final blend. This is done because some of these additives, especially magnesium stearate, tend to agglomerate when added in large quantities to the granulation in a blender.

Blending

Type of blending equipment often differs from that using in laboratory scale. In any blending operation, both segregation and mixing occur simultaneously are a function of particle size, shape, hardness, and density, and of the dynamics of the mixing action. Particle abrasion is more likely to occur when high-shear mixers with spiral screws or blades are used. When a low dose active ingredient is to be blended it may be sandwiched between two portions of directly compressible excipients to avoid loss to the surface of the blender.

Slugging (Dry Granulation)

This is done on a tablet press designed for slugging, which operates at pressures of about 15 tons, compared with a normal tablet press, which operates at pressure of 4 tons or less. Slugs range in diameter from 1 inch, for the more easily slugged material, to ¾ inch in diameter for materials that are more difficult to compress and require more pressure per unit area to yield satisfactory compacts. If an excessive amount of fine powder is generated during the milling operation the material must be screened & fines recycled through the slugging operation.

Dry Compaction

Granulation by dry compaction can also be achieved by passing powders between two rollers that compact the material at pressure of up to 10 tons per linear inch. Materials of very low density require roller compaction to achieve a bulk density sufficient to allow encapsulation or compression. One of the best examples of this process is the densification of aluminum hydroxide. Pilot plant personnel should determine whether the final drug blend or the active ingredient could be more efficiently processed in this manner than by conventional processing in order to produce a granulation with the required tabletting or encapsulation properties**.**

Compression

The ultimate test of a tablet formulation and granulation process is whether the granulation can be compressed on a high-speed tablet press. When evaluating the compression characteristics of a particular formulation, prolonged trial runs at press speeds equal to that to be used in normal production should be tried, only then are potential problems such as sticking to the punch surface, tablet hardness, capping, and weight variation detected. High-speed tablet compression depends on the ability of the press to interact with granulation. The following parameters are optimized during pilot plant techniques of Granulation feed rate, Delivery system should not change the particle size distribution., System should not cause segregation of coarse and fine particles, nor it should induce static charges. The die feed system must be able to fill the die cavities adequately in the short period of time that the die is passing under the feed frame. The smaller the tablet, the more difficult it is to get a uniform fill a high press speeds. For high-speed machines, induced die feed systems is necessary. These are available with a variety of feed paddles and with variable speed capabilities. So that optimum feed for every granulation can be obtained. Compression of the granulation usually occurs as a single event as the heads of the punches pass over the lower and under the upper pressure rollers. This cause the punches to the penetrate the die to a preset depth, compacting the granulation to the thickness of the gap set between the punches. During compression, the granulation is compacted to form tablet, bonds within compressible material must be formed which results in sticking. High level of lubricant or over blending can result in a soft tablet, decrease in wet ability of the powder and an extension of the dissolution time. Binding to die walls can also be overcome by designing the die to be 0.001 to 0.005 inch wider at the upper portion than at the center in order to relieve pressure during ejection. The machine used are high speed rotary machine, multi rotary machine, double rotary machine, upper punch and lower punch machine ,and single rotary machined.

CONCLUSION

From the above finding it was concluded that the Pilot scale up techniques is one of the important tool for the optimization of large scale production. The parameters such as Granulation feed rate, compression and presence of lubricant and blending will play a important, role the development of pilot scale up techniques to large scale production solid dosage form.

ACKNOWLEDGEMENT

Our sincere thanks to our Correspondent, Management, Principal, Teaching and Non Teaching members and Dear Friends of Sankaralingam Bhuvaneswary College of Pharmacy Sivakasi.

REFERENCE

1. Leon Lachman, Herbert A Lieberman, Joseph L Kanig: The Theory and Practice of Industrial Pharmacy: Section IV: Chapter 23: Pilot Plant Scale-Up Techniques: 3rd edition, published by Varghese Publishing house, 2009; 681-710.
2. James Swarbrick, James C Boylan: Encyclopedia of Pharmaceutical Technology: Pilot Plant Design, Volume 12 New York, 2001; 171-186.
3. Leon Lachman, Herbert A. Lieberman, Joseph B. Schwartz: Pharmaceutical dosage forms: Tablets. Volume 3. second edition. 303-365.
4. Johnner P. Sitompul, Hyung Woo Lee1, Yook Chan Kim & Matthew W. Chang A: Scaling-up Synthesis from Laboratory Scale to Pilot Scale and to near Commercial Scale for Paste-Glue Production J. of Eng. and Tech. Sci. 2013; 45(1): 9-24.
5. Joseph W. Zawistowski, A.I.A. and Joseph D. Rago, P.E. Pilot Plant Scale-Up Facilities: Establishing the Basis for a Design, 24 J. of pharm. eng. july/august. 1994; 24-32.
6. Kamya Chaudhary, A.C.Rana, Rajni Bala, Nimrata Seth, review: scale up process of tablet production: a prospective discussion, Int. J. of Pharm. and Bio. Sci. 2012; 2(3): 223-239.
7. Lippincott Williams and Wilkins, Remington, "the science and practice of pharmacy", 21st edition, 2008; 900-901.