جامعة الجزيرة الخاصة
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Introduction to industrial pharmacy

Elements of the manufacturing process

- Formula listing ingredients and their percentages
- Procedure to manufacture the formula
- Equipment to be used during manufacturing
- Personnel: people who run equipment and follow the procedure.

Extemporaneous dispensing vs. Mass Production

- Extemporaneous compounding is a small scale production of dosage forms prepared in community or hospital pharmacy.

Vs.

- Mass production of pharmaceutical dosage forms is based on large (commercial) scale performed in industrial pharmaceutical companies.

Challenges of mass production

1. Production requires large-scale equipment.
2. Production requires personnel with good knowledge of operation, maintenance, and calibration of the equipment.
3. The dosage form must have long-term stability, because it may remain for long time on shelf and not prepared for the patients on order (as in extemporaneous compounding).
4. Mass production is for many patients, which means that an error would have devastating effect on public health. Accordingly, the manufacturing process must be performed under strict quality control system that ensures that the manufacturing process leads to safe, effective and stable dosage forms.

Product development

1. Preformulation.
2. Optimization.
3. Scale up.
4. Process validation.

1. Preformulation

- Definition:

  Preformulation is an investigation of physical and chemical properties of drug substance alone and when combined with excipients.

- The objective of preformulation is:

  to generate information useful in the development of a dosage form that is stable, bioavailable and can be mass produced.

2. Optimization

- Optimization consists in the precise determination of the best formula, manufacturing process parameter and analytical methods.
- In general, optimization is required for:
  - Formula (e.g. excipient levels)
  - Process (i.e. manufacturing process parameters)
  - Analytical method to test the formula

3. Scale up

- Definition: gradual increase of the size of the batch of a pharmaceutical dosage forms.
- As the batch size is increased, more problems are usually encountered during the manufacturing process. Such problems must be solved during the scale-up phase.
- Scale up process is usually performed in three stages:
  - Laboratory batch (1X – e.g. 3-5 kg of solid or semisolid, 3-5 L of liquids)
  - Laboratory pilot batch (e.g. 10X - 30-50 kg for solids and semisolids, 30-50 L for liquids)
  - Pilot production (e.g. 100 X - 300-500 kg for solids and semisolids, 300-500 L for liquids)

4. Process validation

- The objective of PV is to check for the stability and reproducibility of a process.
- After a pilot production was reached and showed good characteristics during the scale up, validation is done by manufacturing several batches (minimum 3) at different times.
- The manufactured batches should show low variability with respect to certain parameters (such as in the case of tablets: disintegration, dissolution and tablet hardness).

Departments of a pharmaceutical company

- Research and Development (R&D) department.
- Production department.
- Quality Control department (QC).
- Quality Assurance department (QA).

R&D department

R&D department is usually based on two sections:

1. Product development section.

- It is responsible for the preformulation, optimization, scale up and stability studies.
- It usually has small scale laboratory and pilot plant for the scale up. The pilot plant uses the same equipment used for manufacturing in the production department but on a smaller scale.

2. Analytical method development section.

- It is responsible for the development of analytical testing procedures (e.g. analytical method development for drug assay).
- It carries out the work in analytical laboratories.

Production department

- This department is responsible for running the manufacturing processes on a large scale according to the formulation and procedure developed by the R&D department.

- It has manufacturing rooms for milling, mixing, granulation, tableting etc. with large scale equipment to perform these tasks.

QC department

- Responsible for sampling and testing the semi-finished and finished product.
- It has analytical labs with instruments (e.g. UVs and HPLCs) to run various tests.
- Test procedures developed by the R&D department (analytical method development section) are followed by the QC.

QA department

- Responsible for making sure that the Good Manufacturing Practices (GMPs) are actually being applied.
- How does QA check that GMPs are followed?
  - ✓ By inspecting the practices followed during manufacturing.

GMPs are guidelines that are translated into procedures that will ensure the product's quality during its manufacturing.

GMPs cover all elements of manufacturing process: personnel, raw material, equipment, documentation.