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Recent Advances in Lyophilization Technology.

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ABSTRACT

Lyophilization is a process which extracts the Water from foods and other products so that the foods or products remain stable and are easier to store at room temperature (ambient temperature). It includes the recent advances in instrumentation and lyophilization process. A traditional lyophilizer consists of a vacuum chamber that contains product shelves capable of cooling and heating containers and their contents. A modern lyophilizer consist of Separated drying chamber and ice condenser to reduce cross contamination. Lyophilization process includes freezing, vacuum, heat and condensation process. Lyophilization maintains food/biochemical and chemical reagent quality. Lyophilization greatly reduces weight, and this makes the products easier to transport. Pharmaceutical companies often use freeze-drying to increase the shelf life of the products, such as vaccines and other injectables.

Keywords: Lyophilization, traditional lyophilizer, modern lyophilizer

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INTRODUCTION

Lyophilization is carried out using a simple principle of physics called sublimation. Sublimation is the transition of a substance from the solid to the vapour state, without first passing through an intermediate liquid phase. To extract water from foods, the process of lyophilization consists of:

- Freezing the food so that the water in the food becomes ice.
- Under a vaccum , sublimating the ice into water vapour.
- Drawing off the water vapour.
- Once the ice is sublimated, the foods are freeze-dried and can be removed from the machine.

Lyophilization is a process which extracts the Water from foods and other products so that the foods or products remain stable and are easier to store at room temperature (ambient temperature). A Method of drying food or blood plasma or pharmaceuticals or tissue without destroying their physical structure and creation of stable preparation.

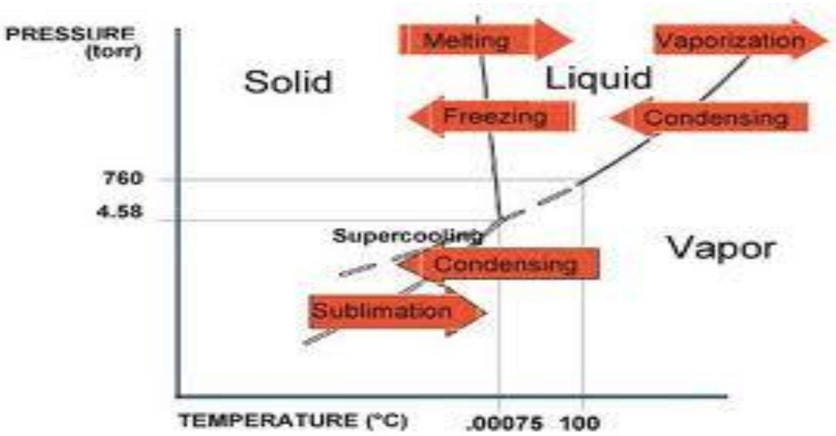
Traditional Lyophilization Technology

Traditional lyophilization is a complex process that requires a careful balancing of product, equipment, and processing techniques. For nearly 30 years, lyophilization has been used to stabilize many types of chemical components. In their liquid form, many such biochemicals and chemical reagents are unstable, biologically and chemically active, temperature sensitive, and chemically reactive with one another. Because of these characteristics, the chemicals may have a very short shelf life, may need to be refrigerated, or may degrade unless stabilized. Heat- and moisture-sensitive compounds retain their viability. Thus, lyophilization ensures maximum retention of biological and chemical purity. Lyophilization gives unstable chemical solutions a long shelf life when they are stored at room temperature [1-7].

Processing

The fundamental process steps are:

- Freezing: The product is frozen. This provides a necessary condition for low temperature drying.
- Vacuum: After freezing, the product is placed under vacuum. This enables the frozen solvent in the product to vaporize without passing through the liquid phase, a process known as sublimation.
- Heat: Heat is applied to the frozen product to accelerate sublimation.
- Condensation: Low-temperature condenser plates remove the vaporized solvent from the vacuum chamber by converting it back to a solid. This completes the separation process.



Lyophilization Process

Instrumentation

The lyophilization equipment

- The environmental conditions necessary for the lyophilization process, sub ambient temperatures and sub atmospheric pressures, are achieved by the lyophilization equipment.
- The following gives a general description of the essential components and their function in a lyophilizer.
- A lyophilizer consists of a vacuum chamber that contains product shelves capable of cooling and heating containers and their contents.
- A vacuum pump, a refrigeration unit, and associated controls are connected to the vaccum chamber.
- Chemicals are generally placed in containers such as glass vials that are placed on the shelves within the vaccum chamber.
- Cooling elements within the shelves freeze the product. Once the product is frozen, the vaccum pump evacuates the chamber and the product is heated.
- Heat is transferred by thermal conduction from the shelf, through the vial, and ultimately into the product.

Recent advances in lyophilization equipments

Equipments used in large scale production

- Freeze dryer scitek
- Sterile steam production freeze dryer Mill rock

Equipments used in small scale production

- Benchtop Pro freeze dryer
- Freezemobile Freeze Dryer
- Vaccum concentrators

Equipments used in large scale production

Freeze dryer scitek

- It offer cGMP vacuum freeze drying equipment for the reliable lyophilization of a wide range of pharmaceutical and biotech products.

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Sterile steam production freeze dryer Mill rock

- **Temperature Range**-60C to +65C (+80C option.)
- **Shelf Heat Transfer** Hollow Fluid Fill.
- **Shelf Area**8 sq ft to 10 sq ft.
- **Shelf Assembly** Bulk or Hydraulic Stoppering.
- **Condenser Temperatue** -75 C.
- **Chamber Configuration** Cylindrical or Rectangular.
- **Condenser Style** Coil or Plate.
- **Defrost** Steam.
- **Vacuum Pump** Leybold Rotary Vane or Dry Pumps.
- **Vacuum Control** Capacitance Manometer with Solenoid/Needle Valve.

Equipment used in small scale production

Bench top Pro freeze dryer

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Key features

- Compact, bench-top design
- Available in 3, 8 and 9 liter configurations
- Direct chamber, flask and/or rack drying capabilities
- PLC-based Omnitronics™ controller
- Choice of refrigeration system to meet various process requirements
- Optional manifolds, racks and accessories available

Advantages

- Benchtop freeze dryers with temperature-controllable shelves similar to those on larger systems.
- The precise freeze drying control is ideal for processing valuable or sensitive biological materials or developing safe, repeatable processes.
- It is ideal for pilot or R&D laboratories that need a more advanced level of process control but lack the space for free-standing research systems.

Freezemobile Freeze Dryer

Freeze mobile freeze dryers are designed with flexibility and convenience in mind.

- A broad selection of multiple users to configure the same system for a wide range of different applications.
- With an optional shell freezing bath and a wide range of single and multi-tier horizontal "T" type manifolds the Freezemobile can dry multiple flasks simultaneously.

Vaccum concentrators

- Concentration can be a tedious laboratory procedure, so the miVac features several innovations designed to speed up concentration times.
- The miVac Speed Trap is radically different from traditional cold traps.
- The cold condenser coils are suspended directly in the vapour path, enabling the condensed solvent to run off into the jug without freezing and causing a decline in the condensing power of the coils.

Modern lyophilizers incorporate refinements

- Separated drying chamber and ice condenser to reduce cross contamination.
- Provision of an isolation valve between chamber and ice condenser to allow for end point determination and simultaneous loading and defrosting.
- Construction of the chamber and ice condenser as pressure valves to allow for steam sterilization at 121° C or higher.
- Cooling and heating of the product support shelves by a circulating intermediate heat exchange fluid to give even and accurate temperature.
- Additional instruments to control, monitor, and record process variables.
- Movable product-support shelves to close the slotted bungs used in vials and to facilitate cleaning and loading.
- Automatic control system with safety interlocks and alarms, duplicated vaccum pumps, refrigeration system.

Recent advances and further challenges in lyophilisation

- Lyophilization beyond drying of pharmaceutical proteins.
- Pharmaceutical applications of lyophilisates in the solid state.
- Novel formulation aspects.
- Importance of the freezing step in lyophilization.
- Lyophilization above Tg. (glass transition temp. of the maximal freeze concentrate)
- Stabilization by thermal treatment/ high secondary drying temperatures.
- Individual factors contributing to protein stability during Lyophilization.

Advantages

- Minimum damage and loss of activity in delicate heat-liable materials.
- Speed and completeness of rehydration.
- Possibility of accurate, clean dosing into final product containers.
- Porous , friable structure.

Disadvantages

- High capital cost of equipment.
- High energy costs.
- Long process time(typically 24hr.drying cycle).

Uses

- Use of lyophilization for the pre-treatment of samples and standards prior to their storage and/or pre concentration is presented.
- It is often used to prepare dry pharmaceutical formulations to achieve commercially viable shelf lives.

Application

- Lyophilization maintains food/biochemical and chemical reagent quality.
- Lyophilization greatly reduces weight, and this makes the products easier to transport.
- Pharmaceutical and biotechnology

Pharmaceutical companies often use freeze-drying to increase the shelf life of the products, such as vaccines and other injectables.

- **Food industry**

Freeze-drying is used to preserve food, the resulting product being very lightweight.

- **Technological industry**

In chemical synthesis, products are often freeze-dried to make them more stable, or easier to dissolve in water for subsequent use. Lyophilization technique for bone tissue engineering.

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