Functioning of freeze drying equipment

1. 0 Introduction

This report is on the usage and functioning of freeze drying equipment. In this first chapter the principle of the sublimation process and applications of freeze drying equipement will be given.

1. 1 Freeze dryers

Freeze dryers are part of the group of solid-solid separating operations, this particular case of solid-solid separating operation makes use of the sublimation process. This kind of equipmentis used to separate a solid from another solid. Examples of other solid-solid separation methods include sorting-, screening-, hydrocyclones-, classifiers-, jigs-, tables-, centrifuges-, dense media-, flotation-, magnetic- and electrostatic separation[1].

1. 2 Applications of freeze drying

1. 2. 1 Pharmaceutical and biotechnology

Pharmaceutical companies often use freeze-drying to increase the shelf life of products, such as vaccines and other injectables. By removing the water from the material and sealing the material in a vial, the material can be easily stored, shipped, and later reconstituted to its original form for injection.

1. 2. 2 Food industry

Freeze-drying is used to preserve food and make it very lightweight. The process has been popularized in the forms offreeze-dried ice cream, an example ofastronautfood. It is also popular and convenient forhikersbecause the reduced weight allows them to carry more food and reconstitute it with available water. Instant coffeeis sometimes freeze-dried, despite high costs of freeze-dryers. The coffee is often dried by vaporization in a hot air flow, or by projection on hot metallic plates. Freeze-dried fruit is used in some breakfast cereal. Culinary herbs are also freeze-dried, although air-dried herbs are far more common and less expensive. However, the freeze-drying process is used more commonly in the pharmaceutical industry.

1. 2. 3 Technological industry

Inchemical synthesis, products are often lyophilized to make them more stable, or easier todissolveinwaterfor subsequent use. In bioseparations, freeze-drying can be used also as a late-stage purification procedure, because it can effectively remove solvents. Furthermore, it is capable of concentrating substances with low molecular weights that are too small to be removed by afiltrationmembrane.

Freeze-drying is a relatively expensive process. The equipment is about three times as expensive as the equipment used for other separation processes, and the high energy demands lead to high energy costs. Furthermore, freeze-drying also has a long process time, because the addition of too much heat to the material can cause melting or structural deformations. Therefore, freeze-drying is often reserved for materials that are heat-sensitive, such asproteins, enzymes, microorganisms, andblood plasma. The lowoperating temperatureof the process leads to minimal damage of these heat-sensitive products.

1. 2. 4 Other uses

Organizations such as the Document Conservation Laboratory at the United States National Archives and Records Administration (NARA) have done studies on freeze-drying as a recovery method of water-damaged books and documents. While recovery is possible, restoration quality depends on the material of the documents. If a document is made of a variety of materials, which have different absorption properties, expansion will occur at a non-uniform rate, which could lead to deformations. Water can also cause mold to grow or make inks bleed. In these cases, freeze-drying may not be an effective restoration method. Inbacteriologyfreeze-drying is used to conserve specialstrain.

In high-altitude environments, the low temperatures and pressures can sometimes producenatural mummiesby a process of freeze-drying. Advancedceramicsprocesses sometimes use freeze-drying to create a formable powder from a sprayedslurrymist. Freeze-drying creates softer particles with a more homogeneous chemical composition than traditional hotspray drying, but it is also more expensive.

Recently, sometaxidermistshave begun using freeze-drying to preserve animals, such aspets.

Freeze drying is also used for floral preservation. Weddingbouquetpreservation has become very popular with brides who want to preserve their wedding day flowers.

1. 3 Freeze drying equipment

There are essentially three categories of freeze-dryers: rotary evaporators, manifold freeze-dryers, and tray freeze-dryers.

1. 3. 1 Rotary evaporators

Rotary freeze-dryers are usually used with liquid products, such as pharmaceutical solutions andtissue extracts. Unloading trays of freeze-dried material from a small cabinet-type freeze-dryer

1. 3. 2 Manifold freeze dryers

Manifold freeze-dryers are usually used when drying a large amount of small containers and the product will be used in a short period of time. A manifold dryer will dry the product to less than 5wt% moisture content. Without heat, only primary drying (removal of the unbound water) can be achieved. A heater must be added for secondary drying, which will remove the bound water and will produce a lower moisture content.

1. 3. 3 Tray freeze dryers

Tray freeze-dryers are more sophisticated and are used to dry a variety of materials. A tray freeze-dryer is used to produce the driest product for long-term storage. A tray freeze-dryer allows the product to be frozen in place and performs both primary (unbound water removal) and secondary (bound water removal) freeze-drying, thus producing the driest possible end-product. Tray freeze-dryers can dry products in bulk or in vials. When drying in vials, the freeze-dryer is supplied with a stoppering mechanism that allows a stopper to be pressed into place, sealing the vial before it is exposed to the atmosphere. This is used for long-term storage, such as vaccines. Improved freeze drying techniques are being developed to extend the range of products that can be freeze dried, to improve the quality of the product, and to produce the product faster with less labor. Ever since the 1930s, industrial freeze drying is depended on a single type of equipment: the tray

freeze dryer. In 2005 a quicker and less-labor intensive freeze drying method is developed for bulk materials. This freeze drying process can produce free flowing powder from one single vessel. Known as [Active Freeze Drying]AFDtechnology. The new proces uses continuous motion to improve mass transfer and hence cutting processing time, while also eliminating the need to transfer to and from drying trays and downstream size reduction devices.

1. 4 Sublimation process

In this report the sublimation separation process will be used as solid-solid separation and further analyzed (in particular ice – ascorbic acid separation with use of sublimation). The sublimation process makes use of the physical properties of the component to be separated. The principle of sublimation is based on the fact that under certain circumstances the regular order of phases (solid -> liquid -> vapour) can be adjusted. Figure 4 displays the circumstances under which the phases of water exist.

Chapter 2

General Working principle

2. 0 Introduction

Freeze-drying (also known as lyophilization or cryodesiccation) is adehydrationprocess typically used topreservea perishable material or make the material more convenient for transport. Freeze-drying works byfreezingthe material and then reducing the surroundingpressureand adding enough heat to allow the frozen water in the material tosublimedirectly from the solid phase to the gas phase (see figure 2).

2. 1 The freeze-drying process

There are three stages in the complete drying process: freezing, primary drying, and secondary drying.

2. 1. 1 Freezing

In a lab, this is often done by placing the material in a freeze-drying flask and rotating the flask in a bath, called a shell freezer, which is cooled by mechanical refrigeration, dry iceandmethanol, orliquid nitrogen. On a larger-scale, freezing is usually done using a freeze-drying machine. In this step, it is important to cool the material below itstriple point, the lowest temperature at which the solid and liquid phases of the material can coexist. This ensures that sublimation rather than melting will occur in the following steps. Larger crystals are easier to freeze-dry. To produce larger crystals, the product should be frozen slowly or can be cycled up and down in temperature. This cycling process is calledannealing. However, in the case of food, or objects with formerly-living cells, large ice crystals will break the cell walls (discovered byClarence Birdseye), resulting in cell destruction, and, in the case of rehydrated foods, a poor texture. In this case, freezing is done rapidly, in order to lower the material to below itseutectic pointquickly, thus avoiding the formation of ice crystals. Usually, the freezing temperatures are between −50 °C and −80 °C. The freezing phase is the most critical in the whole freeze-drying process, because the product can be spoiled if badly done. Amorphousmaterials do not have a eutectic point, but do have a critical point, below which the product must be maintained to prevent melt-back or collapse during primary and secondary drying. Large objects take a few months to freeze-dry.

2. 1. 2 Primary drying

During the primary drying phase, the pressure is lowered (to the range of a fewmillibars), and enough heat is supplied to the material for the water tosublimate. The amount of heat necessary can be calculated using the sublimating molecules'latent heat of sublimation. In this initial drying phase, about 95wt% of the water in the material is sublimated. This phase may be slow (can be several days in the industry), because, if too much heat is added, the material's structure could be altered. In this phase, pressure is controlled through the application ofpartial vacuum. The vacuum speeds sublimation, making it useful as a deliberate drying process. Furthermore, a cold condenser chamber and/or condenser plates provide a surface(s) for the water vapour to re-solidify on. This condenser plays no role in keeping the material frozen; rather, it prevents water vapor from reaching the vacuum pump, which could degrade the pump's performance. Condenser temperatures are typically below −50°C (−60 °F). It is important to note that, in this range of pressure, the heat is brought mainly by conduction or radiation; the convection effect is considered to be inefficient.

2. 1. 2 Secondary drying

The secondary drying phase aims to remove unfrozen water molecules, since the ice was removed in the primary drying phase. This part of the freeze-drying process is governed by the material's adsorptionisotherms. In this phase, the temperature is raised higher than in the primary drying phase, and can even be above 0 °C, to break any physico-chemical interactions that have formed between the water molecules and the frozen material. Usually the pressure is also lowered in this stage to encourage desorption (typically in the range of microbars, or fractions of apascal). However, there are products that benefit from increased pressure as well. After the freeze-drying process is complete, the vacuum is usually broken with an inert gas, such as nitrogen, before the material is sealed. At the end of the operation, the final residual water content in the product is extremely low, from 0, 5wt% to 4wt %.

2. 1. 3 Semi-continuous and non-stop

The stirred freeze dryer (figure 5) is extremely suitable as a research tool for applications in aboratory-environment. This new technique can also be used for larger scale applications in the industrial field. For semi-continuous or even non-stop operation the filter is put next to the dryer. During the drying process already sufficiently dried particles end up in the filter. The advantage is twofold. In the first place, it is possible to get all dried material out of the filter for further processing, whilst the stirred freeze drying process continues. Secondly, material, already sufficiently dried, is not unnecessarily exposed to further movements and, consequently, risk of damage.

The CONRAD™ plant is fully automatic and requires minimal staff for the continuous operation. Every movement and process parameter is carefully controlled, monitored and tagged through the most modern PLC/PC system. The CONRAD™ plant consist of four main sections:

The cabinet, which is a long cylindrical chamber desgined to operate under vacuum. At the front-end – inside the cabinet – there is an elevator forstacking the trays with the frozen product. Each tray is entering the cabinet through an uniquely designed airlock system that allows the trays to enterwithout breakingthe vacuum, which would otherwise have a negative impact on the sublimationprocess. When the elevator has made a full stack, the entire stack is pushed forward into the first drying zone, where the temperature on the heating plates is adjusted to the actual product type, composition and water content. More stacks are filled and they are pushed in turn through the various and subsequent drying zones in the cabinet. The conditions in each zone is adjusted to provide the optimal drying characteristics. When the trays on the stack arrives at the dryer exit, an elevator will unload the trays and discharge them again through an airlock. The dried product is emptied from the trays and conveyed to the packing room.

In order to apply energy to the freeze drying process a number of heating plates made of anodized aluminum are placed inside the cabinet. Hot water is circulated through the system to secure an efficient heat transfer by radiation to the product to be freeze dried. The water temperature can be regulated during the freeze drying process to achieve the optimal evaporation laps and avoid overheating of the products. By correct loading into the cabinet the product trays are placed between the heating plates for optimal heat transfer. Direct contact between the product trays and heating plates must be avoided as heat damage of the product will be the result.

To condense the sublimated water vapor, the cabinet is equipped with a number of vapor condensers for Continuous De-Icing (CDI). When one of the vapor condensers has to be de-iced (typically after one hour operations the section is sealed off while the other takes over the condensation function. To melt the accumulated ice, water vapor (vacuum steam) at 25˚ C is led into the room. The water vapor will now condense on the cold icy surface of the condenser and thus melt the ice. In order to restore the de-iced condenser to operating conditions any remaining vapor in the condenser chamber must be condensed by cooling it down until operating temperature and vacuum is reached. A direct switch over when the next de-icing cycle is needed can now be done without loss of operating vacuum.

Via an external combined elevator and convey system the empty trays are conveyred back to the coldstore for refilling with frozen product.

The CONRAD™ benefits:

- Continuous production
- Economical operation
- 98% or more efficiency
- Low maintenance costs

Type CONRAD™	200	300	400	500	2×500
Extracts with 25wt% dry matter					
Capacity input kg/h	313	469	625	781	1,563
Capacity output	81	12	161	20	40

kg/h		1		1	3
Output kg/24h	1, 93 3	2, 90 0	3, 86 7	4, 83 3	9, 66 7

The internal vapor condenser with built-in de-icing system, is the unique feature of all Atlas freeze dryers. The benefits: it saves space, it is more reliable, it does not cause the loss of product and it uses less power compared with traditional external systems.

Space saving

The special vapor condensers are optimized and built into the side of the drying chamber.

More reliable

The condenser system does not rely on large external vacuum valves with pressure drops that are difficult to secure. Using the internal system, de-icing is performed under vacuum avoiding the need to seal the chamber against large pressure differentials.

Low product loss

Nor product abrasion and low vapor velocities within the dryer guarantee as little as 0. 1 wt% loss during the process.

Low power consumption.

De-icing under vacuum rather than at atmospheric pressure, eliminates the need to re-establish vaccum. This, combined with optimal vapor flow conditions, reduces power consumption by up to 40 wt% compared with ordinary freeze drying technology.

2. 2 Properties of freeze dried products

If a freeze-dried substance is sealed to prevent the reabsorption of moisture, the substance may be stored atroom temperaturewithout refrigeration, and be protected against spoilage for many years. Preservation is possible because the greatly reduced water content inhibits the action ofmicroorganismsandenzymesthat would normallyspoilor degrade the substance.

Freeze-drying also causes less damage to the substance than otherdehydrationmethods using higher temperatures. Freeze-drying does not usually cause shrinkage or toughening of the material being dried. In addition, flavours, smells and nutritional content generally remain unchanged, making the process popular for preserving food. However, water is not the only chemical capable ofsublimation, and the loss of other volatile compounds such as acetic acid (vinegar) and alcohols can yield undesirable results. Freeze-dried products can be rehydrated (reconstituted) much more quickly and easily because the process leaves microscopic pores. The pores are created by the ice crystals that sublimate, leaving gaps or pores in their place. This is especially important when it comes to pharmaceutical uses. Freeze-drying can also be used to increase the shelf life of somepharmaceuticalsfor many years.

2. 3 Basic components freeze dry process

Illustrates a simplified freeze-dry system whose basic components, usually placed in series as in the diagram, a chamber, a condenser, and a vacuum pump. The chamber can be of any cylindrical size as long as it can withstand an exterior pressure of 1. 033 kilograms per square centimeter (14. 7 pounds per square inch). It must be vacuum tight, refrigerated, and have an opening that provides easy accessibility. The important feature of a refrigerated condenser is that it should be located in the direct path of moving water vapor molecules where they can be trapped. When contact with the condenser surface is made, the water vapors give up their heat energy, turn to ice crystals, and are removed from the system and prevented from traveling to the vacuum pump. Condensers are primarily of two types, internal or remote. The choice depends on the application desired. In the remote type the condenser is housed in a vacuum chamber which is separate from the chamber that houses the frozen objects. This is shown in Figure 6 (the chamber next to A). This type of condenser can be isolated by a valve that will permit defrosting. Smaller freeze-dryers can be defrosted with warm water or natural air. Some mid-size freeze-dryers have internal condensers designed to form an ice " plug" that can be pulled out after using hot gas to that it loose. Apart from the technical design features required of a vacuum system, the pump should have the capacity to reduce the chamber pressure to levels below 4mm Hg. At pressures above this level the ice DO longer sublimes to water vapor but turns to liquid. A look at Figure 1 will bear this observation out. There are two refrigeration compressors in the simplified freeze-dry system shown in One serves the frozen object; it should have the capacity of producing controlled temperatures that go below -5 °C

(23 °F). The other serves the refrigerated condenser and should have the capacity to produce temperatures of -40 °C (-40 °F) or less. Keep in mind that the force that drives the water vapor from an ice surface is the difference in vapor pressure produced by the difference in the temperature between the frozen object and the condenser. As already pointed out, heat energy is required for the sublimation process. Where it appears that conducted or radiated heat will not suffice for the quantity of materials to be freeze-dried, heating devices can be installed. In certain types of proprietary vacuum chambers warming devices are incorporated with the design.

2. 3. 1 Freeze drying chamber

A condensation chamber for freeze drying apparatus is designed such that moisture containing air evacuated from a drying chamber passes substantially uniformly over the cooled interior surfaces of the condensation chamber thereby maximizing the available surface for moisture condensation and freezing. This desirable result is achieved by a tube which is connected to a vacuum pump and positioned through an end wall of the condensation chamber along the central axis of the chamber. One open end of the tube is positioned adjacent one end wall of the chamber and openings are provided through the wall of the tube adjacent the other end wall so that moisture containing air entering the chamber intermediate of the openings in the tube travel in both directions along the cooled interior surfaces of the chamber toward both openings in the tube.

2. 3. 2 Refrigerated condensor

The condensor is a pipe coil system or in smaller versions of freeze dryers, a cold trap, fitted in a vacuum tight container, which is connected to the drying chamber. In the smaller versions (laboratory) the condensor is cooled by means of a carbon dioxide or liquid nitrogen and in larger plants by refrigeration units. Because of the importance of the refrigeration system, a freeze dryer must be equipped with a condenser designed and constructed with the ability to:

- ondense all vapors from the product.
- Provide a vapor route of minimum distance to avoid hindering vapor flow.
- Permit easy defrosting after the run.
- Prevent vapors from contaminating the oil in the vacuum pump.
- Provide a simple cleaning operation.
- Provide the necessary BTU output under load to condense vapor at a maximum rate without disturbing the product's selected primary sublimation temperature.
- Insure the necessary low temperature (saturated suction) during the secondary drying to deliver the lower vacuum levels needed for this phase.
- Provide a high degree of reliability.

2. 3. 3 Refrigeration unit

During the freeze drying process, the water contained in the material passes three stages. The product should be cooled, frozen and then subjected to the sublimation stage. During this stage, heat must be applied to the material to compensate for the sublimation cold developed. This performance is regulated by the refrigeration unit. A failure in the refrigeration system leads to a chain reaction:

- A rise in condenser temperature.
- A rise in chamber pressure.
- A rise in product temperature.
- An irreversible eutectic melting and the boiling of liquid fractions.
- Product failure.

2. 3. 4 Vacuum pump

Freeze dryer or lyophilizer applications have long been debilitating to rotary vane vacuum pumps. The high concentrations of corrosive vapors that are pulled into the pump quickly condense and combine with the pump oil to form a thick molasses type substance that kills most traditional rotary vane pumps. In order to keep these pumps operational, the end user must change the oil and clean the oil chamber on a very regular basis. The continuous maintenance and disposal of the hazardous waste oil is both expensive and inconvenient. Even with regular maintenance, many rotary vane pumps still don’t live up to the end user’s expectations.

The new Cole-Parmer Rotary Vacuum Pump addresses the problems associated with difficult freeze dryer applications. These pumps combine the low base pressure and high pumping speeds of a rotary vane pump with the high chemical resistance of a PTFE diaphragm pump. The diaphragm pump holds a vacuum on the head space of the rotary vane pump. As the corrosive vapors are brought into the rotary vane pump, the diaphragm pump pulls them on through before they can condense in the oil. A pair of condensers on the outlet of the pump act to catch much of the solvents that have been evaporated, resulting in cleaner, longer lasting oil in the rotary vane pump.

This combination pump has proven to be quite effective in corrosive freeze dryer applications. ARUP Laboratories in Salt Lake City, Utah has been using the 72226-70 Cole-Parmer Rotary Vacuum Pump on one of their existing freeze dryer units for the past several months. This particular freeze dryer is in use nearly 24 hours a day, 7 days a week as they continuously process patient samples. As a result of the high usage, ARUP's Bioengineering Department had to change the oil in their previous pump on a monthly basis; a four-to five-hour flushing and cleaning process that resulted in costly downtime for the freeze dryer. They have now been operating the new pump for over six months without needing a single oil change. Expectations for oil maintenance on the Cole-Parmer Combination Vacuum Pump in this application is once per year, greatly reducing the maintenance costs associated with the freeze dryer.

If we assume some very reasonable values for maintenance costs, we can calculate the savings ARUP has realized through the addition of the Cole-Parmer Combination Vacuum Pump versus the standard rotary vane pump they previously used.

Maintenance Costs

Standard Rotary Vane Pump:	Cole-Parmer Pump (72226-70):
Bioengineering Labor: $100 / Hour	Bioengineering Labor:

	$100 / Hour
Labor and Downtime: 4 Hours	Labor and Downtime: 4 Hours
Downtime Cost to Production: $150/Hour	Downtime Cost to Production: $150/Hour
Cost of Replacement Oil: $15	Cost of Replacement Oil: $15
Cost of Oil Disposal: $10	Cost of Oil Disposal: $10
Annual Number of Oil Changes: 12	Annual Number of Oil Changes: 1
(($100 x 4) + ($150 x 4) + $15 + $10) x 12 = $12, 300 / yr	(($100 x 4) + ($150 x 4) + $15 + $10) x 1 = $1, 025 / yr

With a purchase price of $5, 031, the Cole-Parmer Rotary Vacuum Pump (72226-70) has a payoff of less than 6 months through the reduction in maintenance costs. The increased life of the oil also results in a longer lasting pump, which allows Cole-Parmer to safely offer a two year-warranty with the Cole-Parmer 72226-60, -65, -70, -75, -85 vacuum pumps.

Chapter 3

The process in practice

3. 1 Introduction

A process is restricted in general by a number of requirements related to the feed, product and other issues. The latter are discussed under QESH; quality safety and health.

3. 2 Feed requirements

The key variable in the feed requirements is the content dry substance in the feed, this determines the drying duration and energy consumption. The solubility of ascorbic acid in water is 1gr/3ml ≈ 1gr/3 gr water