Pol. J. Food Nutr. Sci., 2011, Vol. 61, No. 3, pp. 165-171
http://journal.pan.olsztyn.pl

Review Article
Section: Food Technology

DOI: 10.2478/v10222-011-0017-5

Freeze-Drying – Application in Food Processing and Biotechnology – A Review

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Key words: freeze-drying, food industry, pharmaceutical products

Freeze-drying is a method of removing water by sublimation of ice crystals from frozen material. Suitable parameters of process application allow us to obtain best quality products compared to products dried with traditional methods. Very good physical and chemical properties of food and biotechnological products make this method the best for drying exclusive products. On the domestic market there is a large selection of different types of freeze-dried products, and there is still increasing interest of consumers in these products. A high cost of the freeze-drying still limits the wide-scale application in the food industry. Equipment innovation and pretreatment of raw material can reduce the time and energy needed for this process.

INTRODUCTON

It is common knowledge that processing may partially or totally affect the quality of a food product. Various changes may occur in physical, chemical and/or biological characteristics of foodstuffs during processing, storage and distribution. The criterion of quality is becoming of increasing importance to consumers' choice. Thus, industrial products and ingredients are expected to offer various convenient properties (taste, health promotion, safety, *etc.*) that correspond to those of fresh products. At the same time, new market demands are emerging that could concern freeze-dried products, for example dehydrated fruits to be added to corn, flakes, cereal bars, ice cream, or pastry making.

GENERAL CHARACTERISTICS

Air-drying is an ancient process used to preserve foods in which the material to be dried is exposed to a continuously flowing hot stream of air where moisture evaporates. The phenomenon underlying this process is a complex problem involving simultaneous mass and energy transport in a hygroscopic, shrinking system. Air-drying offers dehydrated products with their shelf life being extended by a year, but the quality of a conventionally-dried product is usually drastically reduced compared to that of the original foodstuff [Ratti, 2001]. These changes involve physical alterations, chemical reactions and biochemical effects. Physical alterations include shrinkage, increased or decreased porosity, and decreased ability to bind water and damage to microscopic structure [Chirife & Buera, 1995; Stapelfeldt *et al*., 1997; Witrowa-Rajchert & Lewicki, 2006].

Freeze-drying (lyophilization) is a drying process in which the solvent (usually water) and/or the suspension medium is crystallized at a low temperature and thereafter sublimated from the solid state directly into the vapor phase [Liu *et al*., 2008]. Freeze-drying has become one of the most important processes for the preservation of heat-sensitive biological material [George & Datta, 2002; Dincer, 2003; Liu *et al*., 2008]. Today, the field of its applications ranges from relatively simple preservable food, over complex biotechnological or pharmaceutical products, to proliferating bacteria and fungi [Tsinontides *et al*., 2004]. In addition to food products (coffee, tea, crispy fruits and vegetables, ingredients for ready-to-eat foods and some aromatic herbs) [Pan *et al*., 2008; Chan *et al*., 2009], it is suitable for other goods, including: flowers, microorganisms, pharmaceuticals, medical devices, and cosmetics, specially chemicals and pigments, enzymes and ceramic powders [Liu *et al*., 2008]. Although today a great variety of foods, pharmaceuticals, *etc.* are produced by lyophilization, a successful application for long-term preservation of a living system, like *e.g.* cells, is still one of the greatest challenges for scientists in this field [Ciurzyńska & Lenart, 2009].

Freeze-drying has become a standard processing technique in the bio-industry sector, where it enables stable products of high quality to be manufactured. Yet until quite recently, no monograph has been published that would analyse various aspects, scientific, engineering, economic, and regulatory ones, which make effective freeze-drying such a complex operation [Franks, 2000].

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EVALUATION PROCESS

The popularity of freeze-drying is based on some well-known advantages compared to competitive processes: sample stability at a room temperature, the easy reconstitution by the addition of water, the defined porous product structure, the reduction in weight, and the possibility of easy sterile handling. Since these advantages often result in the saving of time or money, the demands to develop or improve freeze-drying processes for more complex systems are continuously increasing. With increasing complexity of the biological material (structure, activity, and metabolism), the prospects for a successful preservation by freeze-drying are decreasing [Rindler *et al*., 1999].

Compared to conventional food preservation technologies (conventional drying and others), the key benefits of freeze-drying include the following: retention of morphological, biochemical, and immunological properties, high viability/activity levels, lower temperature, and shear conditions compared with other drying methods, high recovery of volatiles, retention of structure, surface area, and stoichiometric ratios, high yield, long shelf life, and reduced weight for storage, shipping, and handling [Dincer, 2003]. The product from freeze-drying should also be much crisper than that from hot air drying [Pan *et al*., 2008].

Despite unmatched advantages, freeze-drying has always been considered the most expensive operation for manufacturing a dehydrated product owing to high energy consumption and high costs of both operation and maintenance. The analysis of energy requirements for the conventional drying methods and freeze-drying have shown that the basic energy required to remove 1 kg of water is almost double for freeze-drying than for the conventional drying [Flink, 1977]. In addition, compared with air-drying, the cost of freeze-drying, is 4–8 times higher [Ratti, 2001]. Minimizing energy losses in freeze-drying is of outmost significance, for a great energy input is needed in the process to achieve low temperatures and low pressures, as well as heating to meet the requirement of drying [Dincer, 2002]. Ratti [2001] illustrated that, among the freeze-drying operations, sublimation accounts for about 45% of the total energy consumption in a freeze-drying cycle, while the energy consumption of freezing is about 4% of the total.

Conditions for low energy consumption and high productivity were investigated by many scientists. In Table 1 there are presented examples of optimal conditions of freeze-drying.

ENERGY

Quite few studies have been conducted so far that have addressed energy utilization of the freeze-drying process, with this being predominantly dependent on the operational strategies and the inherent drying dynamics for the material of interest [Liu *et al*., 2008]. The freeze-drying process usually falls into three stages: freezing, the primary drying stage and the secondary drying stage. Within the three stages, the process comprises five primary operations: freezing, sublimation, desorption, vacuum pumping and vapor condensation [Liu *et al*., 2008].

In brief, a typical lyophilization process might proceed as follows. The sample would be contained in a vial, which is placed on a cooled, temperature-controlled shelf within the lyophiliser. The shelf temperature is reduced and the sample is frozen to a uniform, set temperature. At this point the pressure in the lyophiliser would be reduced to a set pressure to initiate primary drying. During the primary drying water vapour is progressively removed from the frozen mass by sublimation whilst the shelf temperature is controlled at a constant, low temperature (through a variety of different control strategies) [Franks, 1998]. At the end of the primary drying, the shelf temperature would be raised so that water physisorbed to the semi-dried mass can be removed [Zhai *et al*., 2003].

REALIZATION OF PROCESS

Different pretreatment methods applied before freeze-drying and modification of the freeze-drying process have been investigated by many authors. Rindler *et al*. [1999] were able to show a significant dependence of the recovery rate on the shelf temperature. They have explained that if the shelf temperature is too high, it is more likely that the sample temperature exceeds the critical damaging temperature leading to glass transition, diversification, recrystallization, or collapse. If the sample temperature is too low, the driving force for water transport is not high enough for a sufficient intracellular dehydration. This also affects cell recovery, since the intracellular glassy state, which is a prerequisite for a safe cell preservation, becomes unstable when the samples are re-warmed to a room temperature [Rindler *et al*., 1999] (Figure 1).

The limiting stage of the traditional freeze-drying process under vacuum is the transfer of heat to the product due to the decrease in thermal conductivity coupled with lowering the pressure of the freeze-drying chamber. But the main drawback of atmospheric freeze-drying is the time increase due to the decrease of the freeze-drying rate. This is due to the decrease in water vapour diffusivity with an increasing pressure in the chamber [Di Matteo *et al*., 2003].

Di Matteo *et al.* [2003] investigated atmospheric freeze-drying in fluidized bed of absorbent material. They have

TABLE 1. Optimal conditions for freeze-drying process.

Authors	Product	Pressure (Pa)	Temperature (°C)	Sample thickness (mm)
Yunfei & Chengzhi [1996]	bovine colostrums	54.5	–	10
Hammani & Rene [1997]	strawberry	30	50	–
Hammani *et al.* [1999]	apple slices	50	55	–
Ciurzyńska & Lenart [2009]	strawberry	63	30	whole fruit

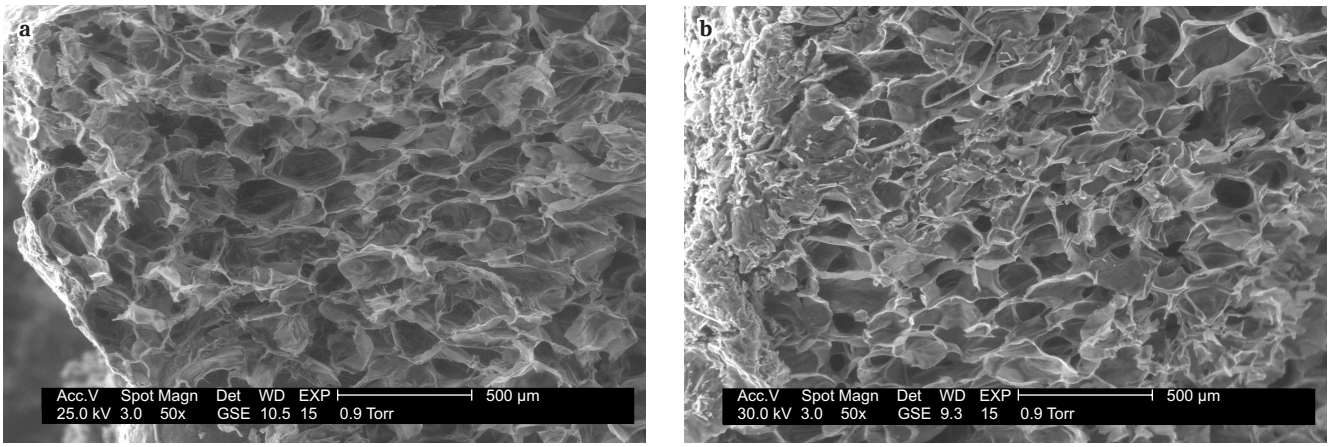

FIGURE 1. Microstructure of freeze-dried strawberries. Process temperature: a – 30°C, b – 70°C. Zoom 50x. Scanning microscope FEI.

shown that this is an interesting alternative to the traditional freeze-drying process. This technique, compared to operation under vacuum, enables a considerable reduction in plant and energy cost. Moreover, carrying out the operation in the presence of a gaseous environment improves external heat and mass transfer coefficients, which are further enhanced by the utilization of fluidization as the contact technique between adsorbent and products.

APPLICATION

Freeze-drying (lyophilization), was developed to preserve bioactive molecules (DNA, enzymes, and proteins), pharmaceuticals products (antibiotics) and other delicate, solvent--impregnated materials [Kusakabe & Kamiguchi, 2004]. Freeze-drying is becoming an increasingly popular method for the long-term preservation of various biological materials. Although today a great variety of foods, pharmaceuticals, *etc.* are produced by lyophilization, a successful application for long-term preservation of living systems, like cells, is still one of the greatest challenges for scientists in this field [Rindler *et al*., 1998].

Continuous innovation and process optimization have increasingly led to more and more new applications of this process on an industrial scale [Rey & May, 2001]. Freeze-drying appears, therefore, as a promising technique for dehydration of thermal-sensitive materials, such as fruits [Marques *et al*., 2007]. Processing conditions have an influence on the quality criteria used to evaluate freeze-dried fruits, and on freeze--drying time. In fact, two criteria (rehydration and texture) are closely linked with the ultimate use of the freeze-dried product and cannot be considered as absolute criteria. Dehydrated fruits are intended primary to be added to products such as corn flakes, cereal bars, ice cream, pastry sauces, *etc*. [Hammami & Rene, 1997]. Also Krokida *et al*. [1998] have shown that physical properties of freeze-dried materials depend on temperature during freeze-drying. For all materials, collapse occurs above the glass transition temperature and the phenomenon becomes more intense as the temperature increases, controlling the bulk density and porosity of the dried materials.

The freezing step explains the instantaneous rehydration capacity of the product, and the texture loss due to the cell wall damage. However, freezing rate has no significant effect on the quality of freeze-dried strawberry, nor on the freeze-drying time [Hammami & Rene, 1997]. While, Gawałek [2005] has shown that slower freezing of apples before the lyophilization process results in an increase in the rate and amount of absorbed water, as well as in greater dry matter losses in the rehydration process. Also the density of the freeze-dried apples obtained decreased slightly along with an increase in freezing time, *i.e.* a slower freezing rate in a decrease in drying shrinkage.

Freeze-drying including precrystallization and rapid freezing, allows the functional properties of egg yolk, without ingredients, to be preserved. Since full contact rapid freezing makes it possible without liquid nitrogen, freeze-dried egg yolk can be produced even at marketable costs [Jaekel *et al*., 2008].

Investigations conducted by Marques *et al.* [2007] have shown that in the freeze-drying of acerola, fast pre-freezing of the material contributes to the preservation of the original porous structure of the product and results in a powder material being little susceptible to degradation reactions. From the techniques tested by these authors, cryogenic freezing using N_2 has been found the most recommended technique for freezing the samples. Freeze-dried acerola fruits were characterized by minimum shrinkage. In addition, their rehydration capacity was high, because the samples did not suffer cellular rupture. With their values thus preserved, the freeze-dried acerola can be considered a good source of vitamin C [Marques *et al*., 2007].

High rehydration capacity restricts the application of freeze-dried strawberry in liquid carriers because the texture of such dried strawberries may collapse. Therefore, a suitable coating needs to be developed to slow the rehydration rate of freeze-dried strawberries in order to maintain their taste over a long period of time. It was shown that a whey protein coating solution could be used to reduce the rehydration rate of freeze-dried strawberry pieces because of its physicochemical properties [Huang *et al*., 2009].

For osmotically-dehydrated freeze-dried strawberries a decrease of rehydration (Figure 2) and sorption capacity in relation to freeze-dried fruit not subjected to osmotic dehydration was noticed [Ciurzyńska & Lenart, 2010].

Freeze-dried fruit after previous osmotic pre-treatment were characterised by lower water contents after 120 min

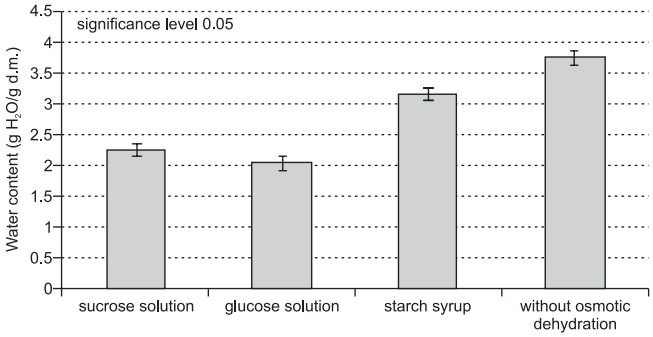

FIGURE 2. Water content of rehydrated freeze-dried strawberries preliminary osmotically dehydrated.

of rehydration than fruit not subjected to osmotic dehydration. It was also noted that osmotic dehydration in starch syrup caused a significant difference in rehydration in relation to the analogical process conducted in sucrose and glucose solution [Ciurzyńska & Lenart, 2010].

The rehydration and sorption properties were related to structural changes in freeze-dried strawberries during osmotic dehydration and freeze-drying (Figure 3) [Ciurzyńska & Lenart, 2010].

According to Girard & Omolosho, [1983; cited after Babic *et al*., 2009] the freeze-dried meat products, which have been adequately packed, can be stored for unlimited periods retaining the majority of their physical, chemical, biological and sensorial properties as in the fresh state. Set against this, Bird [1965] claims that a major defect of freeze-dehydrated meats is the typical deterioration of texture. The aim of a research by Babic *et al*. [2009] was to study the effect of freeze-drying process factors on the quality of broiler chicken breast meat, one of the most commonly consumed and perishable meats. From the results obtained, it has been demonstrated that it is possible to achieve good quality and long shelf-life in freeze-dried chicken, but it is necessary to adjust the different parameters for each thickness.

MODIFICATION

To modify the properties of freeze-dried food products a combination of infrared (IR) and freeze-drying can be applied. This method was studied for drying sweet potato. It has been shown that the application of far-infrared radiation in freeze-drying could reduce drying time [Lin *et al*., 2005]. The IR drying has been reported to offer a higher drying rate and better colour retention in the products than other drying methods [Nowak & Lewicki, 2004], and to be applicable as a pre-dehydration method before freeze-drying [Pan *et al*., 2008]. Infrared freeze-drying could effectively reduce the freeze-drying time and overall drying time, as well as improve the crispness of strawberry slices [Shih *et al*., 2008]. In turn, banana chips freeze-dried with infrared had much crisper texture and golden colour appearance compared to the regular freeze-dried products. The infrared pre-dehydration did not reduce the required drying time during the subsequent freeze-drying process. It additionally resulted in greater shrinkage of the finished product compared to the regular freeze-dried products [Pan *et al*., 2008].

Freeze-drying can be used in the field of radioactivity metrology. The availability of small-scale freeze driers on the market allowed De Sanoit *et al*. [2004] to use the freeze--drying method as a potential routine method for quantitative source preparation. In order to compare the freeze-drying with the conventional drying method, a study was undertaken at the BNM-Laboratoire National Henri Becquerel in France and the results obtained with ^{65}Zn sources have been presented. With the use of a commercial apparatus, quantitative freeze-dried sources were successfully prepared with an improvement of the crystallization homogeneity in comparison to the conventional method. Also, better detection efficiencies to the electron emission of ^{65}Zn were achieved that confirm the results obtained in the past [De Sanoit *et al*., 2004].

In Branger *et al*. [2008] experiments, contrary to the study by De Sanoit *et al*. [2004], no pre-cooling step was applied at atmospheric pressure, allowing a significant decrease in the time to freeze the sources (roughly less than 1 min), depending on the deposited drop mass and the drop spreading. The cooling and subsequent freezing of the radioactive deposit were due to self-evaporation under reduced pressure. The chamber pressure was lowered to 1 Pa during the sublimation phase to obtain a complete solidification of the unfrozen mixture. The additional experiments have shown that

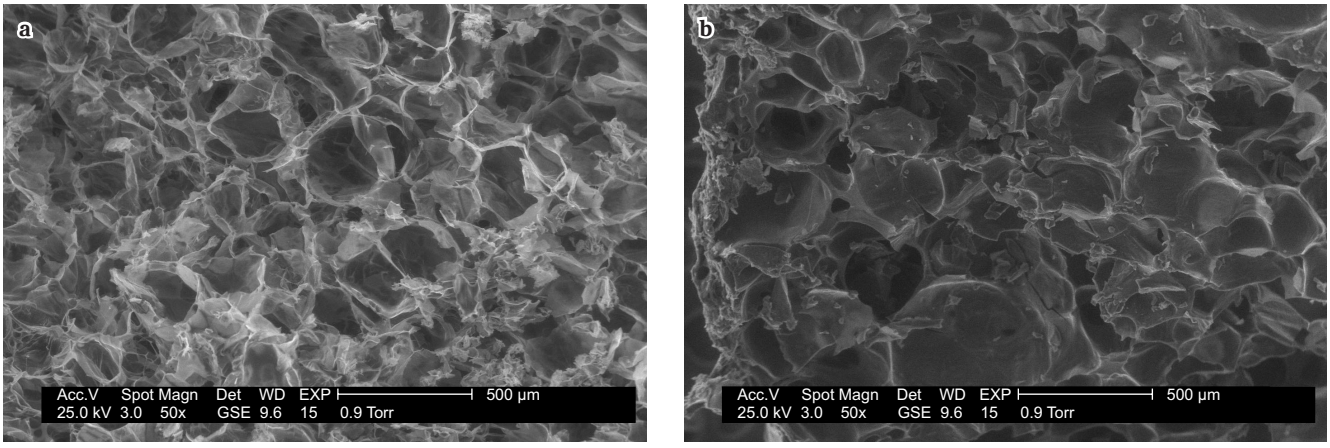

FIGURE 3. Microstructure of freeze-dried strawberries. Osmotic pre-treatment: a – without, b – in sucrose solution. Zoom 50x. Scanning microscope FEI.

the duration of the sublimation phase may be significantly reduced (to under 20 min) when operating is done at a higher pressure (around 30 Pa). Finally, nitrogen gas was introduced inside the chamber to prevent source rehydration while the atmospheric pressure and the ambient temperature were recovered [Branger *et al*., 2008].

Osmotic dehydration is an important technology that enables both the removal of water from the product and the modification of its functional properties by the impregnation of desired solutes. The process is often applied as a pretreatment process for fruits and vegetables, which reduces the physical, chemical and biological changes during drying at a high temperature [Long-yuan Li, 2006; Lewicki & Lenart, 2007]. The osmotic treatment has been used mainly as pretreatment to some conventional processes such as freezing, air drying, but also to vacuum and freeze drying, in order to improve the final quality, reduce energy costs or even to develop new products [Sereno *et al.*, 2001], and can also minimize colour losses [Nsonzi & Ramaswamy, 1998; Ciurzyńska & Lenart, 2009].

Some studies showed that the addition of tertiary butyl alcohol (TBA) can considerably enhance the rate of ice sublimation, resulting in short drying cycles of sucrose solutions [Oesterle *et al*., 1998]. Therefore, it is desirable to freeze-dry liposomes using TBA/water co-solvent systems if for economy concerns. Based on above data, it is possible to produce dehydrated HSPC (hydrogenated soybean phosphatidylcholine) liposomes by means of freeze-drying of HSPC liposomes with TBA/water co-solvent system. The addition of a small amount of TBA not only has no obvious influences on the HSPC vesicle size and the retention of trapped calcein, but may also result in short freeze-drying cycles. Moreover, freeze-drying of HSPC liposomes from TBA/water co-solvent systems can provide sterile powder for specialized applications. In conjunction with a modified alcohol injection method, this technology may be used to produce dehydrated HSPC liposomes on a large scale [Cui *et al*., 2006]. Vast majority of published works describe the freeze-drying and ultrasonication that belong to the most frequently employed treatments. These techniques were used in shaping up the final properties of montmorillonite materials modified by inorganic or organic intercalation [Lee *et al*., 2004; Pacuła *et al*., 2006]. The freeze-drying and ultrasound pretreatments have been shown to greatly affect the appearance of the PXRD (powdered montmorillonite) patterns of randomly oriented montmorillonite samples. Both treatments lead to the disruption of larger clay agglomerates into finer, more prone to mutual self orientation particles, but sonication – even mild, constitutes a more efficient means of clay disintegration and induces greater textural ordering [Pacuła *et al*., 2006].

TECHNOLOGICAL APPLICATION

Freeze-drying is a widely used process for dehydration and improving the stability of various pharmaceutical products, including: viruses, vaccines, proteins, peptides, or colloidal carriers: liposomes, nanoparticles, nanoemulsions [Abdelwahed *et al*., 2006]. Recent progress in biotechnology has enabled obtaining sufficient quantities of biological trace components and further stimulation of the application of the lyophilization technique in pharmaceutical manufacturing. Biomaterials are liable to be damaged by various factors, even during the freeze-drying process, resulting in biological inactivation [Pikal, 1991]. Nowadays, in the pharmaceutical field, there is a great number of substances which need to be stored in a dry state due to their instability in the presence of water, for example, antibiotics, vaccines, peptides and proteins [Rey & May, 2001].

Lyophilization is commonly used in the pharmaceutical and biotechnology industries to improve the stability of formulations. The active pharmaceutical ingredient and accompanying excipients are first solubilized in a solvent (usually water), mass of the solution is rendered sterile by filtering it through 0.2 μm or equivalent sterilizing grade filters. The sterilized solution is filled into vials, then loaded into a lyophilizer where the solution is frozen, and subsequently heated at a very low pressure to sublime the solvent and remove it from the formulation. Once the water is removed, the product vials are sealed under vacuum or an inert gas space (*i.e.* N_2, Ar). The resulting highly porous cake has a low moisture content and can be stored over extended periods of time at the designated storage conditions until its intended use [Tsinontides *et al*., 2004].

Freeze-drying of nanoparticles is a very complex process that requires a major investigation of the formulation and the process conditions. Many parameters of the formulation may determine the success of freeze-drying, particularly the composition of nanoparticles (type of polymer, type and concentration of surfactant, type and concentration of cryo and lyoprotectants, interaction between cryoprotectants and nanoparticles, surface modification of nanoparticles). Furthermore, the applied conditions of freeze-drying can impact the stabilization of nanoparticles during and after freeze-drying, especially the rate of freezing with or without annealing, the pressure and shelf temperature, and the duration of each stage of the process. Many methods are available for assessing the final freeze-dried product to ensure the conservation of nanoparticles properties and the required qualities of freeze-dried cake [Abdelwahed *et al*., 2006].

The freeze-drying method, which allows the long-term storage of intact RNA in the freeze-dried tissues, is available for the isolation of intact RNA from prostate tissues and will help elucidate the pathogenesis of CaP (carcinoma of the prostate). All the procedures adopted in the study by Tsuka *et al*. [1997] will be applicable to the isolation of intact RNA from other tissues and long-term storage of the freeze-dried tissues accompanied by no degradation of RNA. Also human erythrocytes, as a model for very simple living cells, appear to be a well-known example for the intensive research on the freeze-drying problem. While some authors claim they are able to freeze-dry erythrocytes, most critics are not convinced of those successes [Franks, 1996].

Freeze-drying is often used to improve storage stability of therapeutic proteins. In order to obtain a product with optimal storage stability it is important to understand the mechanisms by which solutes protect the protein against freeze-drying-induced stresses and also against damage induced during subsequent storage. The best protection was

noted with trehalose and sucrose, which formed a glass during lyophilization and which had the capacity to hydrogen bond in place of water with the protein in the dried solid [Kreilgaard *et al*., 1998].

Freeze-drying is also commonly used for culture conservation and for the production of concentrated starter cultures. During freeze-drying the cells experience extreme environmental conditions, such as low temperature and low water activity, which decrease their viability. In addition, cell viability after freeze-drying as affected by culture pH was also studied by Palmfeldt & Hahn-Hägerdal [2000].

A freeze-drying technique was also successfully employed to halt the setting reaction for two dental stones so that scanning electron microscopy could be used to visually evaluate the various stages during the transformation of calcium sulfate hemihydrates into calcium sulfate dihydrate [Winkler *et al*., 1995].

It seems to be feasible that the addition of saccharide affected the crystallization behavior of medicinals during the freeze-drying process to vary the stability of the medicinals. Oguchi *et al*. [1995] reported previously the effect of saccharide addition on the crystallinity and stability of freeze-dried preparations, and demonstrated that the amorphization of the drugs was proportional to the amount of saccharide added [Oguchi *et al*., 1995].

The cryoprotective effect of four carbohydrates (glucose, fructose, mannose and maltose) on para-dodecanoyl-calixarene based SLNs (solid lipid nanoparticles) has been investigated by PCS (photon correlation spectroscopy) and these four carbohydrates have been shown to act as good cryoprotectants, allowing reconstitution of the suspensions after the freeze-drying process [Shahgaldian *et al*., 2003].

CONCLUSIONS

With hundreds of variants actually used in drying of particulate solids, pastes, continuous sheets, slurries or solutions, it provides the greatest diversity among food engineering units operations. These changes alter the physical properties such as colour and structure. They can also develop undesirable biochemical reactions, such as deterioration of aroma compounds or degradation of nutrients. All these physical and biochemical changes certainly diminish product's quality and reduce process' efficiency. Freeze-drying is a specific drying method which allows obtaining dried materials with features typical of raw material.

Freeze-drying is used for the reliable preservation of a wide variety of heat-sensitive products and demands the highest standards of reliability and control. In addition to food products, it is suitable for other goods, including: flowers, cultured microorganisms, bulk pharmaceuticals, medical devices, and cosmetics, specially chemicals, pigments and enzymes. The most important in this process are time, temperature and pressure. If they are well defined they may indeed affect the quality of the final product. Unfortunately, high porosity of dried materials has a negative effect on storage stability. Thus, freeze-dried materials need to be stored in a hermetic package.

The freeze-drying process is still expensive, which restricts its application on wide range in the food industry. New technical solutions are applied to modify the freeze-drying process and make it time- and cost-effective, *e.g.* if we replace traditional heating source by microwaves radiation or we use a spray nozzle in dryer chamber. Another solution to limit process time is to use pre-treatment as blanching, dehydration by infrared radiation or osmotic dehydration.

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Received April 2010. Revision received June and accepted August 2010.