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An Analysis of the Lyophilization Process Using a Sorption-Sublimation Model and Various Operational Policies

The freeze-drying process is studied under various operational policies through the use of a sorption-sublimation model. The operational policy that provides the shortest drying times keeps the pressure at its lowest value. The upper and lower heating plates are independently controlled so that the material constraints are encountered and held throughout the free water removal phase.

Under certain conditions, and for the case of samples of small thickness, the sorbed water profiles may have segments whose bound water concentrations are higher than those at the start of the free water removal phase. It is shown that the criterion used in terminating the freeze-drying process is of extreme importance, since it may lead to an undesirable sorbed water profile which may deteriorate the quality of the dried product.

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SCOPE

Certain biological materials, pharmaceuticals, biochemical products, and foodstuffs which may not be heated even to moderate temperatures in ordinary drying, are freeze-dried. Recent developments in biotechnology and biochemical engineering (Hill and Hirtenstein, 1983) have established the importance of lyophilization—freeze-drying—in biochemical processing.

As a rule, freeze-drying produces the highest quality product obtainable by any drying method (Goldblith et al., 1975; Mellor, 1978). Prominent factors are the structural rigidity of the product, which facilitates rapid and almost complete rehydration at a later time, little loss of flavor and aroma, and minimization of degradative reactions which normally occur in ordinary drying processes, such as nonenzymatic browning, protein denaturation, and enzymatic reactions.

However, freeze-drying is an expensive form of drying because of the slow drying rates and the use of vacuum. Thus, it is essential to develop operational policies which would reduce the drying times by improving the drying rates.

The interactions in the variables of the freeze-drying process

are complex, and an experimental approach of examining the various operational policies is tedious, expensive, and time-consuming. But the experiment will finally confirm or disprove the validity of operational policies suggested by theoretical work, and which are supposed to improve or minimize the drying times. A mathematical model which can predict known freeze-drying experimental results accurately, can be used in the analysis of the freeze-drying process and in the examination of various operational policies which may maximize the drying rates.

This work develops a sorption-sublimation model which is used to study operational policies that may significantly reduce the drying times. This model is also used to examine the effects on the bound water profiles of the criteria employed to end the terminal drying phase. Skim milk was used as a model material.

The development of bound water profiles incorporates an important factor for optimization policies for quality retention in freeze-drying.

CONCLUSIONS AND SIGNIFICANCE

A sorption-sublimation model is presented and used to simulate the freeze-drying process under various operational policies. It is found that the operational strategy which produces

the shortest free water removal phase is also the policy that provides the shortest overall drying time. This policy keeps the chamber pressure at its lowest value. Heat is supplied to the upper sample surface by radiation and to the lower surface by conduction, and the heating plates are operated at different temperatures such that the scorch and melting constraints are encountered and both held throughout the free water removal

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phase. The results show that at least 80% of the heat used during the free water removal phase is transferred through the frozen region of the sample.

It is found that during the free water removal phase a certain amount of the initial sorbed water is desorbed. The amounts of desorbed water in this drying phase are larger when thick samples are freeze-dried and significantly smaller for thin samples. In fact, under certain operating conditions and when small sample thicknesses are considered, the profiles of bound water at the beginning of the terminal drying phase may have segments in which the concentration of sorbed water is higher than the concentration of bound water at the beginning of the free water removal phase. The operational policy leading to such profiles of bound water is shown to produce much higher overall

drying times than any of the other policies studied.

It is also shown that the type of criterion used in terminating the freeze-drying process is of extreme importance, especially for samples of large thicknesses, since it may lead to an undesirable sorbed water profile which may deteriorate the quality of the dried product.

This study, by developing bound water profiles, incorporates an important factor for operational policies for quality retention in freeze-drying. The temperature and sorbed water data predicted by the sorption-sublimation model during drying, can be combined with kinetic data on product deterioration (Aguilera and Flink, 1974; Mellor, 1978) to determine operational policies which may minimize not only the drying time but also the deteriorative changes.

INTRODUCTION

Freeze-drying plays an important part in the manufacture of many substances which would otherwise suffer bacterial degradation in the presence of relatively small amounts of moisture. Some common manufacturing examples are the freeze-drying of blood plasma, bones, cartilage, and vaccines; the production of antibiotics, hormones, alkaloids, and other biologicals; and the processing of vegetables, meats, and liquids such as coffee, soup, and milk.

Although freeze-drying at present finds its largest application in food and drug dehydration, other interesting applications have been suggested and explored, including dehydration of radioactive wastes (Cerre and Mestre, 1964), stabilization of free radicals, sublimation of nonaqueous solvents to allow operation in different media at different temperatures (Rey, 1964; King, 1971; Mellor, 1978), and preparation of porous catalysts (Rey, 1964).

The particular desirable qualities conferred by the freeze-drying process are:

- Drying takes place at a relatively low temperature, so that thermal degradation is prevented.
- Volatile materials other than water are largely retained, so that flavor qualities are preserved (Flink and Karel, 1972; Chirife and Karel, 1973; Goldblith et al., 1975; Omatete and King, 1978; Etzel and King, 1980).
- The final product, once packaged, is not subject to bacterial degradation at ambient temperature.
- Structural rigidity is afforded by the frozen substance when sublimation occurs and this prevents collapse of the remaining porous structure after drying.
- The product is of low density and is easily rehydrated, retaining much of its original structural form.

As a rule, freeze-drying produces the highest-quality dried product obtainable by any drying method (Mellor, 1978; Hill and Hirtenstein, 1983). However, freeze-drying is an expensive form of dehydration because of the slow drying rate, low condenser temperature, and the use of vacuum. Thus the major disadvantage of freeze-drying relates to energy costs and the lengthy drying times encountered.

Energy usage constitutes a major cost factor and is composed of energy of sublimation, desorption, and energy to support the vacuum and refrigerate a condensing plate. The lengthy drying times are caused by resistances to heat and mass transfer and other factors which have been investigated extensively, both experimentally and theoretically, (Saravacos and Stinchfield, 1965; Bralsford, 1967; Sandall et al., 1967; King et al., 1968; Hatcher et al., 1971; King, 1971; Cox and Dyer, 1972; Gentzler and Schmidt, 1972; Meo, 1972; Flink and Aguilera, 1974; Greenfield, 1974;

Goldblith et al., 1975; Ma and Peltre, 1975a,b; MacKenzie, 1977a,b; Kerkhof and Thijssen, 1977; Sheng and Peck, 1977; To and Flink, 1978; Liapis and Litchfield, 1979a; Litchfield and Liapis, 1979, 1982; Liapis, 1980a,b; Litchfield et al., 1981a,b; Liapis and Marchello, 1982, 1983a,b). A reduction in the drying time can result in reduced energy and labor costs.

The work in this paper presents a sorption-sublimation mathematical model for the freeze-drying process which accounts for the removal of free and bound water. This model can provide the profiles of sorbed or bound water during the freeze-drying process, and this information is of paramount importance in deciding when the drying operation should terminate. The criterion for terminating the drying process should be that the water concentration at any point in the dried product, does not exceed a critical concentration, since values above the critical value may initiate degradative reactions (Mellor, 1978). The sorption-sublimation model is used to investigate the performance of a freeze-dryer whose heat-supplying plates may be heated by controlled means. Batch freeze-dryers are examined, but the results should have general qualitative applicability to other designs currently in use or contemplated.

CONTROL VARIABLES AND PROCESS CONSTRAINTS

In the freeze-drying process, the drying rates are initially very fast because there is little resistance either to heat transport from the heating plates to the material, or to mass flux from the material to the condenser. However, as the drying proceeds, a dried, highly resistive layer builds up as the interface separating the dried and frozen regions of the material moves toward the lower surface of the sample, Figure 1. This dried layer is highly insulating to heat

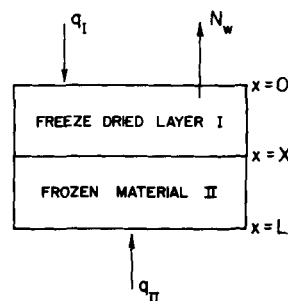


Figure 1. Schematic of a sample during freeze-drying.

TABLE 1. HEAT TRANSFER MECHANISMS AND PLATE CONDITIONS

Case	Heat Transfer Mechanisms	Plate Conditions
A	Radiation only to both upper and bottom surfaces	Upper and lower plates at the same temperature, $T_{UP} = T_{LP}$, with a maximum permissible value of 30°C
B	Radiation to upper dried surface; conduction through a film layer at $x = L$	Upper and lower plates at the same temperature, $T_{UP} = T_{LP}$; plate temperatures are controlled subject to the constraints that $T_I \leq T_s$ for $0 \leq x < X$, and $T_{II} \leq T_m$ for $X \leq x \leq L$
C	Same as in case B	Upper and lower plates operate at different temperatures; the plate temperatures are controlled subject to the constraints that $T_I \leq T_s$ for $0 \leq x < X$, and $T_{II} \leq T_m$ for $X \leq x \leq L$
D	No radiation to upper dried surface, otherwise as case B	Lower plate temperature, T_{LP} controlled subject to the constraint that $T_{II} \leq T_m$ for $X \leq x \leq L$

flux, but is usually less resistive at low pressures to mass transfer. Both resistances, however, are functions of pressure, and it is possible to raise the chamber pressure so that heat transfer is enhanced, but at the expense of an increased resistance to mass transport. Thus, in the freeze-dryer, pressure is a major control variable.

Another important variable is the plate temperature, which affects the rate of heat transmission to the surfaces and the energy reaching the interface between the dried and frozen layers. The condenser temperature is normally kept as low as possible (Mellor, 1978; Millman et al., 1984; Millman, 1984) to promote rapid drying, and therefore it is not usually considered for the purpose of drying time control.

The control variables must always be at settings that maintain the characteristic high product quality. The conditions for quality control are not to have a surface temperature higher than the scorch temperature of the dried layer ($T_O > T_s$) or an interface temperature which exceeds the melting temperature of the interface ($T_X > T_m$). Previous work (Liapis and Litchfield, 1979a; Litchfield and Liapis, 1982; Liapis and Marchello, 1983a) with a sublimation model that accounts only for the removal of free water and for the heat being supplied through the dried layer only, has shown that considerable reductions in drying time can be obtained by choosing a slightly elevated pressure and simultaneously maintaining the dried surface temperature at its constraint. The optimum pressure, in fact, also maintains the ice interface at its constraint, so that the driving force for mass transfer is maximized. The studies of Litchfield et al. (1981a,b) and Liapis and Marchello (1983a) with the use of a sublimation model have shown that cycling the chamber pressure, as proposed by Greenfield (1974) and Mellor (1978), would provide no advantage when compared to near optimal constant pressure operation.

In the present study, the chamber pressure is kept constant during a drying run, and the effects of the heat transfer mechanisms and plate conditions of Table 1 on the drying time are examined. In all cases the water vapor enters the drying chamber through the upper surface of the sample. The plate conditions of case A are usually encountered in the freeze-drying of pharmaceutical and biological products (Mellor, 1978).

Freeze-dehydration by microwave energy is not considered here; a comprehensive research program at Nestle (Bouldoires and LeViet, 1980) has shown that the problems encountered when microwave energy is used substantially outweigh the advantages of microwave freeze-drying. Microwave freeze-drying is at present only a potential development (Liapis, 1985).

THE SORPTION-SUBLIMATION MODEL

A number of freeze-drying models have been published (Lusk et al., 1964; Clark and King, 1971; King, 1971; Cox and Dyer, 1972; Massey and Sunderland, 1972; Meo, 1972; Greenfield, 1974; Mellor, 1978; Liapis and Litchfield, 1979a) and used to describe the drying rates and times during the removal of the free water. The free water may account for 70–90% of the moisture, and the remaining water is due to mechanisms of (i) physical adsorption, (ii) chemical absorption, and (iii) water of crystallization. In addition, moisture may be physically trapped within pockets in the material, from which it can leave only via small channels offering a high resistance to mass transfer.

In most systems (Goldblith et al., 1975; Mellor, 1978), the remaining 10–30% of the water in the sample is physically adsorbed, and is termed sorbed or bound water. Although the bound water constitutes a rather small portion of the total, its effect is significant as it frequently takes as long to remove as the free water (Meo, 1972; Mellor, 1978; Litchfield and Liapis, 1979). It has been found by comparison with experimental data (Liapis and Litchfield, 1979b; Liapis, 1980b) that the "sublimation" model of Liapis and Litchfield (1979a) describes the removal of the free water more accurately than the commonly used "uniformly retreating ice front" model (King, 1971).

The one-dimensional system considered in the sorption-sublimation model is shown in Figure 1. A heat source such as a heating plate or an infrared heat lamp is positioned above a slab of material of thickness L and provides the heat flux q_I . The base of the slab ($x = L$) may receive heat by radiation only, or through a thin film layer between its surface and the heat source (i.e., a heating plate) that provides the heat flux q_{II} . The slab has a frozen region and a porous dried region. The boundary between the dried and frozen regions is termed the sublimation interface. Sublimation occurs as a result of heat being conducted to this interface through the dried and frozen layers. The resulting water vapor flows through the porous dried layer, diffuses through the vacuum chamber and finally collects upon the condenser plate. The following assumptions are made in the development of the mathematical model:

1. Only one-dimensional heat and mass flows, normal to the interface and surfaces, are considered.
2. Sublimation occurs at an interface parallel to, and at a distance X from, the surface of the sample.
3. The thickness of the interface is taken to be infinitesimal (Harper and El Sahrighi, 1964; Goldblith et al., 1975; Mellor, 1978).
4. A binary mixture of water vapor and inert gas flows through the dried layer.
5. At the interface, the concentration of water vapor is in equilibrium with the ice.
6. In the porous region, the solid matrix and the enclosed gas are in thermal equilibrium.
7. The frozen region is considered to be homogeneous, of uniform thermal conductivity, density, and specific heat, and to contain an insignificant proportion of dissolved gases.
8. For the situation of freeze-drying material in a phial, which is typical of the process used in the production of drugs (Cise, 1982), the thickness of the phial is considered to be infinitesimal when it is compared to the thickness of the sample, and the phial offers insignificant resistance to the transfer of heat (Goldblith et al., 1975; Mellor, 1978; Liapis and Marchello, 1983b).

Energy and material balances can now be made in the dried (I) and frozen (II) layers:

$$\frac{\partial T_I}{\partial t} = \alpha_{Ie} \frac{\partial^2 T_I}{\partial x^2} - \frac{N_t C_{pg}}{\rho_{Ie} C_{ple}} \frac{\partial T_I}{\partial x} + \frac{\Delta H_v \rho_I}{\rho_{Ie} C_{ple}} \frac{\partial C}{\partial t} \quad 0 \leq x \leq X \quad (1)$$

$$\frac{\partial T_{II}}{\partial t} = \alpha_{II} \frac{\partial^2 T_{II}}{\partial x^2} \quad X \leq x \leq L. \quad (2)$$

In the dried layer, effective parameters are considered which include the physical properties of both the gas and solid, which have been considered to be independent of space. The initial and boundary conditions are:

$$T_I = T_{II} = T_X = T^0(x) \text{ at } t = 0, 0 \leq x \leq L \quad (3)$$

$$q_I = -k_{Ie} \frac{\partial T_I}{\partial x} \text{ at } x = 0, t > 0 \quad (4)$$

and,

$$q_I = \sigma F (T_{UP}^4 - T_{I,0}^4) \quad (5)$$

for radiation heat transfer to the upper dried surface,

$$k_{II} \frac{\partial T_{II}}{\partial x} - k_{Ie} \frac{\partial T_I}{\partial x} + V(\rho_{II} C_{pII} T_{II} - \rho_I C_{pI} T_I) + N_t C_{pg} T_X \\ = -\Delta H_s N_t \text{ at } x = X, 0 < t \leq t_{X=L} \quad (6)$$

$$T_I = T_X = T_{II} \text{ at } x = X, t > 0 \quad (7)$$

$$q_{II} = k_{II} \frac{\partial T_{II}}{\partial x} \text{ at } x = L, t > 0. \quad (8)$$

For radiation only,

$$q_{II} = \sigma F (T_{LP}^4 - T_{II,L}^4) \quad (9)$$

For a thin film between the frozen material and lower plate,

$$q_{II} = k_f (T_{LP} - T_{II,L}). \quad (10)$$

The value of the film thermal conductivity, k_f , can be estimated from Carslaw and Jaeger (1976), and suitably adjusted to account for the lowered pressure in the freeze-drying process.

The continuity equations for the dried layer are:

$$\frac{1}{R} \frac{\partial}{\partial t} \left(\frac{P_w}{T_I} \right) = - \frac{1}{M_w \epsilon} \frac{\partial N_w}{\partial x} - \frac{\rho_I}{M_w \epsilon} \frac{\partial C}{\partial t} \quad (11)$$

$$\frac{1}{R} \frac{\partial}{\partial t} \left(\frac{P_{in}}{T_I} \right) = - \frac{1}{M_{in} \epsilon} \frac{\partial N_{in}}{\partial x} \quad (12)$$

$$\frac{\partial C}{\partial t} = K_g (C^* - C). \quad (13)$$

C^* is the weight fraction of sorbed water in the solid which would be in local equilibrium with the partial pressure of water vapor. The study presented in this work uses skim milk as the model material, and the functional form of C^* used in the calculations is given in the studies of Gentzler and Schmidt (1972) and Aguilera and Flink (1974).

The dusty gas model equations (Greenfield, 1974; Liapis and Litchfield, 1979a; Mason and Malinauskas, 1983) are used to develop the following expressions for the fluxes N_w and N_{in} :

$$N_w = - \frac{M_w}{RT_I} \left(k_1 \frac{\partial P_w}{\partial x} + k_2 P_w \left(\frac{\partial P_w}{\partial x} + \frac{\partial P_{in}}{\partial x} \right) \right) \quad (14)$$

$$N_{in} = - \frac{M_{in}}{RT_I} \left(k_3 \frac{\partial P_{in}}{\partial x} + k_4 P_{in} \left(\frac{\partial P_w}{\partial x} + \frac{\partial P_{in}}{\partial x} \right) \right) \quad (15)$$

The contribution of thermal mass diffusion to the mass fluxes, is insignificant by comparison to the contributions of the mass transfer mechanisms (Mellor, 1978) included in Eqs. 14 and 15. This has led us to exclude the mechanism of thermal mass diffusion from the expressions of the sorption-sublimation model.

TABLE 2. PARAMETER VALUES

Parameter	Value
C_2	0.428
C_{pg} , kJ/kg·K	1.6747
C_{pl} , kJ/kg·K	2.595
C_{pII} , kJ/kg·K	1.9678
C^* , kg Water/kg solid	$\exp[2.3\{1.36 - 0.036(T - T^0)\}]/100$
$D_{w,in}^0$, kg·m/s ³	$8.729 \times 10^{-7}(T_O + T_X)^{2.334}$
k_f , kW/m ² ·K	0.03
k_{Ie} , kW/m ² ·K	$0.68(12.98 \times 10^{-8}P + 39.806 \times 10^{-6})$
k_{II} , kW/m ² ·K	0.0021
K_g , s ⁻¹	11.08×10^{-5}
K_w , m ² /s	$1.429 \times 10^{-4}(T_O + T_X)^{0.5}$
P_{wO} , Nt/m ²	5.2668
P_{wX} , Nt/m ²	$133.32 \left[\exp \left(23.9936 - \frac{2.19\Delta H_s}{T_X} \right) \right]$
T^0 , K	241.8
T_m , K	263.15
T_s , K	303.15
ΔH_s , kJ/kg	2,791.2
ΔH_v , kJ/kg	2,791.2
ρ_I , kg/m ³	145.13
ρ_{II} , kg/m ³	1,058.0

Equations 14 and 15 can be substituted into the continuity Eqs. 11 and 12, and the resulting expressions are integrated using the following boundary and initial conditions:

$$P_w = P_{wO}, P_{in} = P_O - P_w \text{ at } x = 0 \quad (16)$$

$$P_w = P_w^O, P_{in} = P_{in}^O \text{ at } t = 0, 0 \leq x \leq X \quad (17)$$

$$P_w = f(T_X), \frac{\partial P_{in}}{\partial x} = 0 \text{ at } x = X, 0 < t \leq t_{X=L} \quad (18)$$

$$C = C^O \text{ at } t \leq 0, 0 < x < X. \quad (19)$$

The variable P_{wO} is the chamber water vapor pressure, usually determined by the condenser design and assumed constant within the chamber. The mathematical model is completely specified by a material balance at the interface which defines its velocity as:

$$V = \frac{dX}{dt} = - \frac{N_w}{\rho_{II} - \rho_I}. \quad (20)$$

Equations 1-13 and 14-20 represent the sorption-sublimation model which involves a moving boundary (the position of the sublimation interface). External transport resistances can easily be incorporated into this model by including the expressions developed by Liapis and Litchfield (1979a). However, in a well-designed freeze-dryer, the external mass and heat transfer resistances are not significant (King, 1971; Mellor, 1978). The sorption-sublimation model has been shown by comparison with experimental data (Litchfield and Liapis, 1979; Liapis and Marchello, 1982, 1983a) to predict the drying rates and times quite accurately.

The sorption-sublimation model equations were solved for different sets of operating conditions using the numerical method developed by Liapis and Litchfield (1979b), and Millman (1984). This method immobilizes the moving boundary and transforms the problem of the freeze-drying process into a problem of fixed extent. Millman (1984) presents in a comprehensive manner the numerical approach employed in solving the equations of the sorption-sublimation model, and also gives examples of the computer programs used to obtain the numerical solutions.

Certain simplifications can be made in the expressions given in Eqs. 2, 14, and 15, and are discussed by King (1971), Meo (1972), Liapis and Litchfield (1979a), Litchfield and Liapis (1979), and Millman (1984).

TABLE 3. DRYING TIMES WITH OPERATING POLICIES FOR FOUR CASES (TABLE 1) AND CONDENSER TEMP. OF 225 K

Chamber Pressure mm Hg	Sample Size mm	Sublimation Model Free Water Removal Phase min	Free Water Removal Phase min	Sorption-Sublimation Model	
				Total Drying Time	
				Criterion 1 Final Avg. Water Wt. Fraction $0.05 \frac{\text{kg Water}}{\text{kg Solid min}}$	Criterion 2 Final Max. Water Wt. Fraction at Any Point in Material $0.05 \frac{\text{kg Water}}{\text{kg Solid min}}$
<i>Case A</i>					
0.1	3.0	211.51	221.92	447.68	462.59
	4.0	292.62	307.41	508.14	542.96
	5.0	378.09	399.23	576.23	632.37
	6.0	466.88	494.48	649.94	727.36
	9.0	758.97	802.57	901.62	1,035.45
	12.0	1,070.87	1,139.10	1,198.57	1,372.03
	15.0	1,405.43	1,498.47	1,528.65	1,731.46
1.0	3.0	212.76	225.08	444.40	458.42
	4.0	295.14	309.97	503.45	542.96
	5.0	380.70	401.76	570.89	634.67
	6.0	470.09	495.40	641.23	729.25
	9.0	763.47	800.32	888.47	1,033.11
	12.0	1,073.72	1,133.21	1,179.35	1,366.05
	15.0	1,407.03	1,489.34	1,503.69	1,722.21
2.0	3.0	223.83	226.34	438.48	469.68
	4.0	309.04	311.18	497.21	544.22
	5.0	397.01	401.78	562.91	634.70
	6.0	490.09	496.36	634.16	729.21
	9.0	790.54	800.99	880.33	1,033.77
	12.0	1,118.66	1,133.01	1,169.08	1,365.99
	15.0	1,470.37	1,488.46	1,489.61	1,721.26
<i>Case B</i>					
0.1	3.0	18.87	19.37	240.53	251.20
	4.0	29.78	30.40	246.38	262.23
	5.0	42.60	43.26	252.03	275.09
	6.0	57.54	58.13	259.56	289.96
	9.0	124.47	125.90	297.06	357.73
	12.0	223.79	226.27	358.63	458.10
	15.0	352.25	355.94	448.58	587.77
1.0	3.0	17.15	17.55	239.71	249.38
	4.0	30.84	31.54	246.52	263.36
	5.0	48.96	49.81	255.62	281.64
	6.0	71.25	72.40	267.33	304.23
	9.0	163.23	165.30	319.95	397.12
	12.0	293.28	296.55	405.63	528.37
	15.0	460.73	466.07	532.59	697.89
2.0	3.0	21.92	22.36	242.07	254.18
	4.0	39.68	40.28	250.85	272.10
	5.0	62.68	63.52	262.70	295.34
	6.0	90.93	92.03	277.88	323.85
	9.0	207.51	209.59	347.62	441.41
	12.0	371.27	375.20	463.11	607.02
	15.0	582.33	588.77	634.69	820.59
<i>Case C</i>					
0.1	3.0	13.42	13.47	238.01	245.29
	4.0	23.87	24.30	243.15	256.12
	5.0	37.30	37.90	249.67	269.72
	6.0	53.75	54.07	257.51	286.89
	9.0	120.98	121.62	292.25	353.44
	12.0	215.10	216.88	347.07	448.70
	15.0	336.03	338.38	425.26	570.20
1.0	3.0	16.73	16.96	239.32	248.78
	4.0	29.78	30.05	245.06	261.87
	5.0	46.58	46.87	252.72	278.69
	6.0	67.08	67.43	262.39	299.25
	9.0	150.98	151.84	305.39	383.66

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TABLE 3. DRYING TIMES WITH OPERATING POLICIES FOR FOUR CASES (TABLE 1) AND CONDENSER TEMP. OF 225 K (cont'd)

Chamber Pressure mm Hg	Sample Size mm	Sublimation Model Free Water Removal Phase min	Free Water Removal Phase min	Sorption-Sublimation Model	
				Total Drying Time	
				Criterion 1	Criterion 2
				Final Avg. Water Wt. Fraction $0.05 \left(\frac{\text{kg Water}}{\text{kg Solid}} \right) / \text{min}$	Final Max. Water Wt. Fraction at Any Point in Material $0.05 \left(\frac{\text{kg Water}}{\text{kg Solid}} \right) / \text{min}$
2.0	12.0	268.28	270.23	374.26	502.05
	15.0	419.20	422.57	478.46	654.39
	3.0	20.28	20.50	240.47	252.32
	4.0	36.05	36.34	247.32	267.16
	5.0	56.37	56.69	256.38	288.51
	6.0	81.20	81.62	267.89	313.44
	9.0	182.68	183.85	319.88	415.67
	12.0	324.75	327.24	405.65	559.06
Case D 0.1	15.0	507.37	511.59	535.29	742.41
	3.0	14.80	15.16	241.17	246.98
	4.0	26.40	27.08	248.96	258.90
	5.0	41.30	41.85	257.77	273.67
	6.0	59.52	60.15	269.33	291.97
	9.0	134.08	134.96	319.73	366.78
	12.0	238.52	241.59	398.00	473.41
	15.0	372.72	377.37	516.37	605.80
1.0	3.0	19.45	19.98	243.43	251.80
	4.0	34.65	35.26	252.28	267.08
	5.0	54.18	56.09	265.73	287.91
	6.0	78.08	80.27	280.46	312.09
	9.0	175.87	178.97	345.19	410.79
	12.0	312.65	317.37	447.11	549.19
	15.0	488.65	495.42	592.48	727.24
	2.0	3.0	24.45	25.13	245.91
4.0		43.52	44.26	256.61	276.08
5.0		68.07	68.97	270.97	300.79
6.0		98.07	99.12	289.11	330.94
9.0		220.83	222.99	371.12	454.81
12.0		392.73	396.58	502.72	628.40
15.0		613.78	619.65	691.73	851.47

RESULTS AND DISCUSSION

Skim milk was chosen as a model material in this study; the values of the parameters used in the sorption-sublimation model are given in Table 2. Four cases of operating strategies are examined; their heat transfer mechanisms and plate conditions are shown in Table 1. In Table 3, the drying times predicted by the sublimation model (Liapis and Litchfield, 1979a) and the sorption-sublimation model are presented for various chamber pressures and sample thicknesses. The sublimation model does not account for bound water, and therefore the drying times predicted by this model are only for the removal of free water. The free water removal phase starts at $t = 0$ and terminates at a time such that $X = L$. Then the terminal drying phase for the removal of sorbed water only starts; it ends when a certain desired water weight-fraction criterion in the dried product, determined by product quality considerations (Aguilera and Fling, 1974; Mellor, 1978), is satisfied. In Table 3, the drying times for two different water weight-fraction criteria are given. One criterion requires that the average water weight-fraction in the dried product be 0.05 kg water/kg solid. The second criterion requires that the water weight-fraction at any point in the dried product not exceed 0.05 kg water/kg solid. The

drying times for both criteria shown in Table 3 represent the sums of the times of the free water removal and terminal drying phases. It should be noted that in the terminal drying phase, the only active material constraint is the requirement that the temperature at any point in the dried layer does not exceed the scorch temperature. Therefore, at the beginning of the terminal drying phase for cases B, C, and D, the heat input at the sample surfaces is increased until the scorch temperature constraint is met, if that constraint has not been encountered during the free water removal phase.

The results in Table 3 show clearly that case C provides the best strategy of operation since its drying times are shorter than those of any other case of Table 1. During the removal of free water in case C, the plates are operating at different temperatures such that the surface and melting constraints are encountered and both held throughout the free water removal phase. The benefits of this operational policy have also been suggested from optimal control theory in the studies by Liapis and Litchfield (1979a) and Litchfield and Liapis (1982), in which the sublimation model was used and heat was supplied through the top surface of the sample only ($q_I \neq 0, q_{II} = 0$). It is also of importance that for case C the times for the free water removal phase obtained from the sorption-sublimation model, are larger than the times from the sublimation

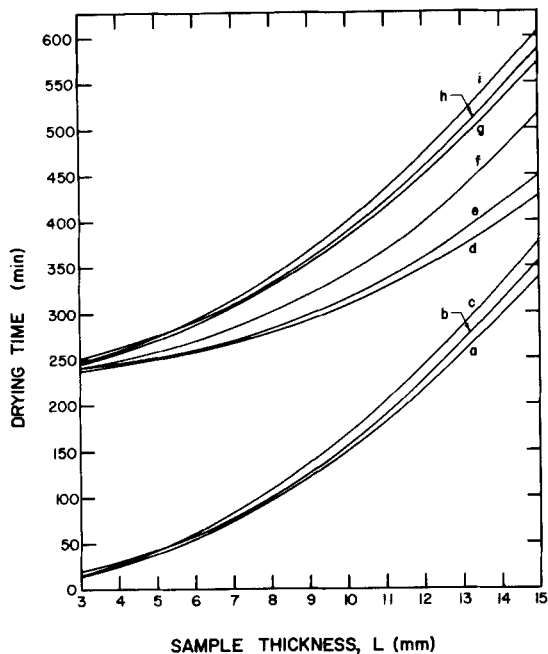


Figure 2. Effect of sample size on drying time; chamber pressure 0.1 mm Hg, condenser temp. 225 K.

Operating Conditions (Table 1)	Curves: Drying Times		
	Free Water Rem. Phase	Total Time Criterion I	Total Time Criterion II
Case C	a	d	g
Case B	b	e	h
Case D	c	f	i

model by less than 1%. This is not the case for the other three operational policies, where the times obtained from the sorption-sublimation model can be, as in case A, up to 7% larger than those obtained from the sublimation model. These results indicate that for case C both models would provide almost identical average speeds for the moving sublimation interface during the free water removal phase. But the temperatures in the dried layer predicted by the sorption-sublimation model are lower than those obtained by the sublimation model, since a certain amount of the energy accumulated in the dried region is used to desorb bound water. In cases A, B, and D, and especially for samples of small thickness, the longer times predicted by the sorption-sublimation model for the free water removal phase are due to desorption of bound water and to lower heat fluxes through the dried and frozen regions of the sample. The heat fluxes are lower for case A because the plate temperatures and the thermal conductivity of the dried layer have low values, thus none of the material constraints are encountered. For case B, the heat fluxes are lower than those of case C because the plate temperatures are not independently set, but they are substantially higher than those of case A since the thermal conductivity of the ice layer is over two orders of magnitude higher than that of the dried layer. In case B, the scorch temperature constraint was encountered for sample thicknesses of 6 mm or less. Otherwise, only the melting constraint is met during the free water removal phase. In case D, heat is supplied only through the lower surface of the sample and the scorch temperature constraint is never encountered, while the melting constraint is held throughout the free water removal phase.

The policies of case C during the free water removal phase always give the largest time-averaged heat and mass fluxes through the layers of the sample, and this occurs when both material con-

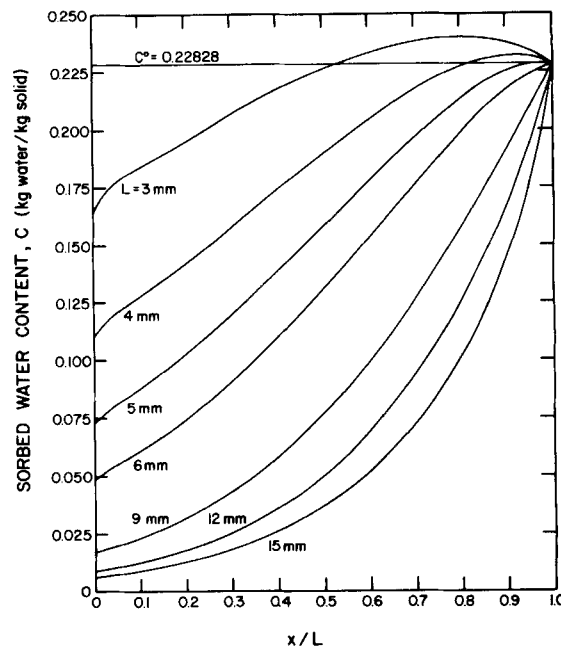


Figure 3. Sorbed water profiles at end of free water removal phase. Operating conditions, case A; chamber pressure 0.1 mm Hg; condenser temp. 225 K.

straints are active for most of the time of this drying phase.

It is also evident that purely radiative heat transfer, case A, requires the longest drying times. The duration of its terminal drying phase is about 1–16% larger than the duration of its free water removal phase when large sample thicknesses are considered, and approximately 93–108% larger for samples of 3 mm. For cases B, C, and D, the trend with respect to sample size is similar to that of case A: for large samples the times of the terminal drying phase are about 5–68% larger than those of the free water removal phase, and about 11–18 times longer for samples of 3 mm. For the small sample thicknesses of cases B, C, and D, the speed of the moving sublimation interface is much higher than that of the larger samples whose thick dried layers provide higher heat and mass transfer resistances during the free water removal phase. This allows for more bound water to desorb in the large samples than in the small samples, and then the terminal drying phase of the small samples requires substantially longer times than those of their free water removal phase. The data in Table 3 strongly indicate that, in general, the best policy of operation is the one that produces the shortest free water removal drying times since the free water accounts for 70–90% of the total amount of water at the beginning of the freeze-drying process; also, a certain amount of bound water will be desorbed during the free water removal phase as it is shown in Figures 3–6 as well as by the difference in the times predicted by the sublimation and the sorption-sublimation models for the removal of free water. In Figure 2, the drying times for the removal of free water and the times for free water removal plus terminal drying phase times are plotted vs. sample thickness for cases B, C, and D, at a chamber pressure of 0.1 mm Hg. It is clearly observed that for small thicknesses, 3–6 mm, the difference between the total drying times obtained by the two criteria on the final required water weight fraction is not significantly large, but it becomes substantial when thick samples are considered. Large samples give smaller differences between the drying time for the free water removal and the total drying time for the system required to satisfy the first criterion about the final water weight-fraction, than the time differences obtained by smaller samples. Also, the differences

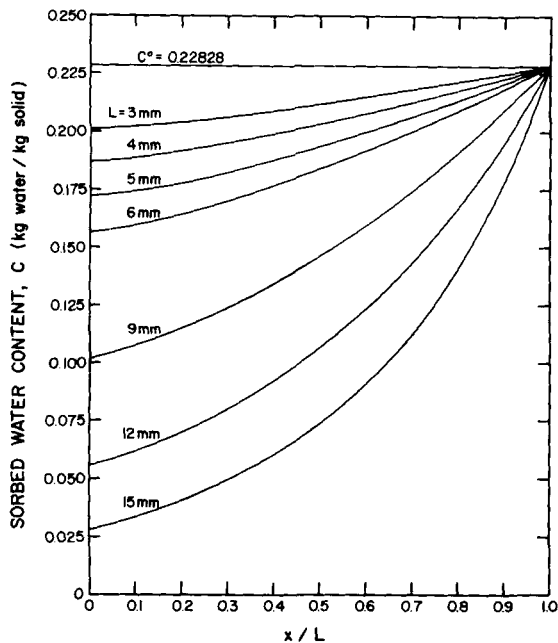


Figure 4. Sorbed water profiles at end of free water removal phase. Operating conditions, case B; chamber pressure 0.1 mm Hg; condenser temp. 225 K.

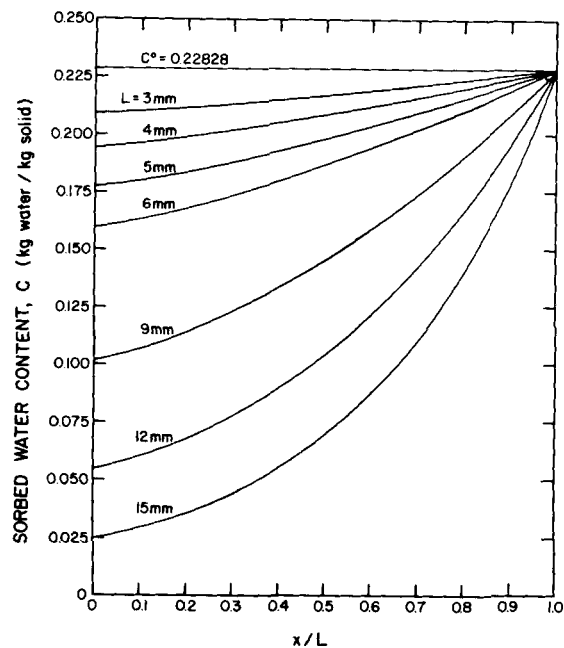


Figure 5. Sorbed water profiles at end of free water removal phase. Operating conditions, case C; chamber pressure 0.1 mm Hg; condenser temp. 225 K.

in drying times obtained by the policies of cases B, C, and D become larger as the sample thickness increases. It is of interest to note that the difference in times for cases B, C, and D, between the free water removal phase and the total drying time for the system required to satisfy the second criterion about the final water weight-fraction, is constant at about 230 min. This is due to the isotherm used to calculate the equilibrium bound water concentration C^* and to the fact that the scorch point is held at $x = L$ throughout the terminal drying phase.

The results in Table 3 show that for cases C and D higher chamber pressures substantially increase the drying times of the free water removal phase. This implies that while the increased pressure improves the thermal conductivity in the dried layer, the water vapor flux is decreased significantly and this outweighs any benefit due to the improved heat transfer in the dried layer. The same phenomenon is observed for case B, except for the smallest sample thickness at a chamber pressure of 1.0 mm Hg. For the smallest sample thickness, the scorch constraint is reached very fast and the heat inputs q_I and q_{II} are reduced. The reduction in q_{II} is more significant since most of the heat reaching the interface is conducted through the frozen region. Thus, an increase in chamber pressure improves the thermal conductivity in the dried layer significantly enough to outweigh any reduction to mass transfer and to delay the time before the scorch constraint is encountered, and this implies a delay in the reduction of the heat inputs q_I and q_{II} , with a corresponding higher sublimation rate that reduces the drying time of the free water removal phase. In case A, an increase in chamber pressure may slightly reduce the drying times of the free water removal phase for large sample thicknesses where the resistance to heat transfer may be significant because of the thick dried layers as well as the fact that the plates are kept at a low temperature. The increase in pressure, for case A, improves the thermal conductivity of the dried layer without significantly reducing the water vapor flux in this porous region.

A comparison of the drying times for the free water removal phase of cases C and D shows that at least 80% of the heat used in this drying phase is transferred through the frozen region. This results from the fact that the thermal conductivity of the ice region

is over two orders of magnitude higher than that of the dried layer. This finding suggests that case A may be of use only for materials and freeze-drying systems for which cases B, C, and D are not applicable. Also, case D provides shorter drying times than case B for small sample thicknesses, 3–6 mm (Figure 2 and Table 3). This occurs because the heat input q_{II} in case D is larger than that of case B. For large samples, case B is preferable since the scorch constraint is not encountered and q_I is not reduced, while its q_{II} is comparable to the q_{II} of case D. Results similar to those presented in Table 3 but for different condenser temperatures are found in the work of Millman (1984).

In Figures 3–6, the profiles of sorbed water at the end of the free water removal phase are shown for cases A, B, C, and D, and for a chamber pressure of 0.1 mm Hg. The sorbed water profile at $t = 0$ is flat and the value of C at any point in the sample is equal to $C^0 = 0.22828$ (Millman, 1984). Since neither adsorption nor desorption are considered to take place in the frozen region, the concentration of sorbed water at the moving sublimation interface is taken to be equal to C^0 . This condition is clearly illustrated in Figures 3–6, where at the end of the free water removal phase, $X = L$, all the profiles at $x = L$ start with the bound water concentration C^0 .

The sorbed water profiles for case A, Figure 3, exhibit a very interesting behavior for the samples of small thickness, 3–4 mm. In case A, heat is supplied to the sample with the mode of radiation heat transfer from heating plates which are constrained to a maximum temperature of 30°C. Therefore, the heat flux into the material is initially small, about 0.3 kW/m², while the rate of sublimation of the ice at the interface is relatively high. Due to the large heat of sublimation, 2,791.2 kJ/kg ice, the temperature of the moving sublimation interface drops drastically, by as much as 20 K from its initial value of 241.8 K. This drop in temperature has been experimentally observed by Meo (1972) and Mellor (1978); a detailed explanation of this phenomenon as well as theoretical results on the interface temperature variation with time is given by Millman (1984). As the drying proceeds, the temperatures in the dried layer close to the moving interface can be below the initial temperature, T^0 , for a certain time, and some of the water vapor

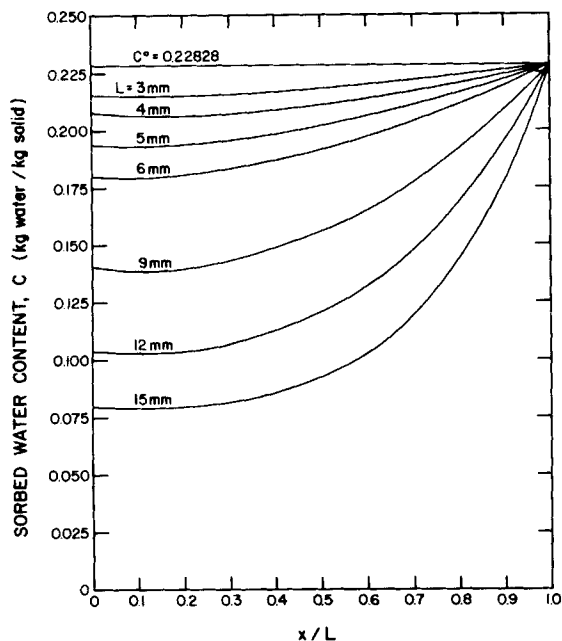


Figure 6. Sorbed water profiles at the end of the free water removal phase. Operating conditions of case D; chamber pressure of 0.1 mm Hg; condenser temperature of 225 K.

produced by the sublimation of ice is adsorbed onto the solid matrix instead of diffusing through the porous dried layer and out through the upper surface into the drying chamber. Of course, the temperature drop at $x = X$ results in a higher temperature driving force that in turn provides higher heat fluxes through the dried layer with corresponding temperature elevations at various points in the dried layer, and certain desorption of bound water. It is of interest that the segments of the profiles of sorbed water having concentrations above C^o , attain a maximum value. This is due to the fact that while the points very close to the moving interface may be cooler than the points higher up in the dried layer, these points have been at temperatures lower than T^o for longer times than the points next to the sublimation front, and have adsorbed larger amounts of water vapor. As the temperature at these points of the dried layer increases toward T^o less water vapor is adsorbed, and when their temperature values exceed T^o desorption occurs, as is clearly shown for the points closer to the upper sample surface. For the larger samples, the interface temperature also drops below T^o at the beginning of the free water removal phase, but their thick dried layers provide higher resistances to heat and mass transfer than the dried layers of the smaller samples and thus the speeds of their sublimation fronts are lower (longer drying times) and have higher temperatures in their dried layers. These higher temperatures are responsible for the desorption of any water vapor adsorbed at the beginning of the free water removal phase as well as for the desorption of a certain amount of the bound water that was in the solid matrix at $t = 0$. This effect of the thickness of the dried layer is responsible for the fact that the 4 mm sample has a smaller segment with $C > C^o$ than the 3 mm sample, as well as a larger segment with $C < C^o$; in this latter segment of the profile, the bound water concentration of the 4 mm sample is significantly lower than that of the 3 mm sample.

The profiles of sorbed water for cases B, C, and D (Figures 4–6) have values of C always lower than C^o . For these systems, the interface temperature can initially experience an insignificant drop in magnitude below T^o , and very quickly adjusts itself above T^o . Since the heat fluxes for these cases are higher than those in case

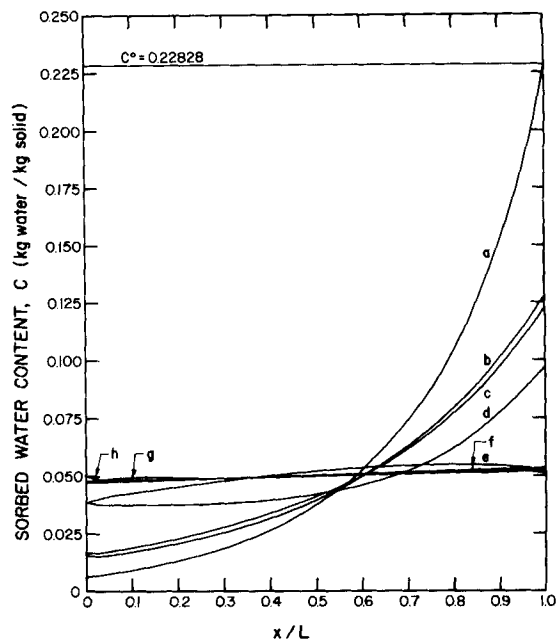


Figure 7. Sorbed water profiles at end of terminal drying phase when criterion I is used. Chamber pressure 0.1 mm Hg; condenser temp. 225 K.

Case	Curves	
	L = 15 mm	L = 3 mm
A	a	e
B	b	f
C	c	g
D	d	h

A, any amount of water vapor that may have been initially adsorbed is all desorbed, as well as a certain amount of the bound water that was in the solid matrix at $t = 0$. Cases B and C desorb more of the bound water during the free water removal phase than that desorbed by case D during the same phase. This difference occurs because the temperatures in the dried region for cases B and C are higher than those in case D where heat is supplied through the lower surface only. These differences are more noticeable at larger sample thicknesses and near the upper surface, $x = 0$. In case D, the value of C is higher at $x = 0$ than the values of C at points very close to the upper surface; this is due to the fact that these points are at higher temperatures than the surface. The points close to $X = L$ are at higher temperatures than the points toward the surface, but these latter points have been desorbing bound water for longer periods of time.

The results in Figures 3–6 show that at the end of the free water removal phase, the average sorbed water concentration gradients of the larger samples are significantly higher than those of the smaller samples, and substantially larger amounts of the bound water at $t = 0$ have been desorbed. An explanation for the observations by Bralsford (1967), Brajnikov et al., (1969), and Mellor (1978) of a soft broadening zone between the ice zone and the dried layer is obtainable from Figures 3–6, since various levels of moisture build up continuously against the sublimation front. The sorbed water profiles at the end of the free water removal phase may have important implications on the chamber pressure and heat input policies during the terminal drying phase. It would be desirable that these policies maximize the desorption rate of bound water as well as the heat and mass transfer rates in the porous dried layer. These rates will definitely depend on the initial sorbed water profile

of the terminal drying phase that was established by the drying history of the free water removal phase. Millman (1984) gives graphs depicting the temperature profiles of the systems in Figures 3–6, and provides a detailed analysis and discussion of the effect of pressure during the two stages of the freeze-drying process; he also discusses how the application of a programmed pressure cycle may improve the operating characteristics, especially during the terminal drying phase.

In Figure 7, the sorbed water profiles for sample thicknesses of 3 mm and 15 mm at the end of the terminal drying phase are shown for cases A, B, C, and D. The results satisfy the criterion that requires that the average water weight-fraction in the dried product be 0.05 kg water/kg solid. It is apparent that the drying history has a significant influence on the final sorbed water profiles, especially on the profiles for the 15 mm sample. It is clear that case D provides a more uniform sorbed water profile than cases B and C, while case A gives the least uniform profile. These results indicate that for this criterion of process termination, case D may provide a final product for large samples that may be less susceptible to degradative reactions and quality changes during storage. Of course, if the second criterion in Table 3 is used, and if the maximum concentration of water at any point in the dried layer allowed at the end of the terminal drying phase is below a certain value above which degradative reactions start, then the operational policy that provides the shortest overall drying time would also provide a sorbed water profile that would not be susceptible to drastic quality changes. Therefore it is suggested that the second criterion of process termination is more useful since it provides a better quality product, and through that a more proper comparison of the overall drying times obtained from different operation policies can be made. The profiles for the 3 mm sample thickness are similar to one another and fairly uniform. The profiles for the other sample thicknesses not shown in Figure 7 fall between those shown (Millman, 1984).

For freeze-drying, many examples of temperature profiles are available from the literature. Contrary to this is the limited number of sorbed water profiles available (Goldblith et al., 1975; Mellor, 1978; Flink and Modelina, 1982; Sagara and Hosokawa, 1982). Since destruction rates of various important nutrients (Aguilera and Flink, 1974; Mellor, 1978) as well as activation energies are a function of temperature and sorbed water content, knowledge of temperature and bound water profiles in the sample during freeze-drying is extremely important for predicting the extent of quality deterioration for particular process conditions.

The present work, by developing bound water profiles, incorporates an important factor for optimization policies for quality retention in freeze-drying. The temperature and sorbed water data predicted by the sorption-sublimation model during drying can be combined with kinetic data on product deterioration to determine operational policies which may minimize not only the drying time but also the deteriorative changes. More results like those shown in Figures 3–7 and for different chamber pressures and condenser temperatures are reported by Millman (1984).

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NOTATION

C	= weight fraction of bound water in dried layer
C_p	= heat capacity
C_{01}	= constant dependent only upon structure of porous medium and giving relative D'Arcy flow permeability
C_1	= constant dependent only upon structure of porous

	medium and giving relative Knudsen flow permeability
C_2	= constant dependent only upon structure of porous medium and giving the ratio of bulk diffusivity within the porous medium to the free gas bulk diffusivity, dimensionless
$D_{w,in}$	= free gas mutual diffusivity in a binary mixture of water vapor and inert gas
$D_{w,in}^o$	= $D_{w,in}P$
$f(T_X)$	= water vapor pressure-temperature functional form = $133.32 \exp(23.9936 - 2.19\Delta H_s/T_X)$, N/m ²
k	= thermal conductivity
k_1	= bulk diffusivity constant = $C_2 D_{w,in} K_w / (C_2 D_{w,in} + K_{mx} P)$
k_2, k_4	= self diffusivity constant = $K_w K_{in} / (C_2 D_{w,in} + K_{mx} P) + (C_{01} / \mu_{mx})$
k_3	= bulk diffusivity constant = $C_2 D_{w,in} K_{in} / (C_2 D_{w,in} + K_{mx} P)$
K_g	= internal mass transfer coefficient
K_w	= Knudsen diffusivity, $K_w = C_1 (RT/M_w)^{0.5}$
K_{in}	= Knudsen diffusivity, $K_{in} = C_1 (RT/M_{in})^{0.5}$
K_{mx}	= mean Knudsen diffusivity for binary gas mixture, ($K_{mx} = y_w K_{in} + y_{in} K_w$)
L	= sample thickness
M	= molecular weight
N_t	= total flux ($N_t = N_w + N_{in}$)
N_w	= water vapor flux
N_{in}	= inert gas flux
P	= total pressure in dried layer
P_T	= total pressure in drying chamber
P_O	= drying chamber pressure at surface of dried layer
P_w	= partial pressure of water vapor
P_{in}	= partial pressure of inert gas
q	= energy flux
R	= universal gas constant
T^O	= sample temperature at $t = 0$
T	= temperature
t	= time
V	= velocity of interface
X	= position of frozen interface
x	= space coordinate
y_w	= mole fraction of water vapor
y_{in}	= mole fraction of inert gas

Greek Letters

α	= thermal diffusivity
ϵ	= voidage fraction
ΔH_s	= enthalpy of sublimation of frozen water
ΔH_v	= enthalpy of vaporization of sorbed water
μ	= viscosity
ρ	= density
σ	= Stefan-Boltzmann constant

Superscripts

o	= initial value at time zero
*	= equilibrium value

Subscripts

e	= effective value
f	= film
g	= gas
in	= inert
L	= value at $x = L$
LP	= lower plate
m	= melting
mx	= mixture

s	= scorch
w	= water vapor
X	= interfacial value
UP	= upper plate
O	= surface value
I	= dried region
II	= frozen region

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