CFD modelling of condensers for freeze-drying processes

MIRIAM PETITTI*, ANTONELLO A BARRESI
and DANIELE L MARCHISIO

Dipartimento di Scienza Applicata e Tecnologia, Istituto di Ing. Chimica,
Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129 Torino, Italia
e-mail: miriam.petitti@polito.it

MS received 22 December 2011; revised 30 July 2012; accepted 3 March 2013

Abstract. The aim of the present research is the development of a computational tool for investigating condensation processes and equipment with particular attention to freeze-dryers. These condensers in fact are usually operated at very low pressures, making it difficult to experimentally acquire quantitative knowledge of all the variables involved. Mathematical modelling and CFD (Computational Fluid Dynamics) simulations are used here to achieve a better comprehension of the flow dynamics and of the process of ice condensation and deposition in the condenser, in order to evaluate condenser efficiency and gain deeper insights of the process to be used for the improvement of its design. Both a complete laboratory-scale freeze-drying apparatus and an industrial-scale condenser have been investigated in this work, modelling the process of water vapour deposition. Different operating conditions have been considered and the influence exerted by the inert gas as well as other parameters has been investigated.

Keywords. Freeze-drying; condenser; CFD simulation; mathematical modelling; water vapour flow; ice deposition.

1. Introduction

Freeze-drying (also known as lyophilisation) is the most complex and expensive form of drying, in fact Liu *et al* (2008) have evaluated that the cost of the energy required to remove 1 kg of water by freeze-drying is at least a factor of 2 higher than that necessary for conventional drying operations, like hot-air tray drying or fluid-bed drying (Ratti 2001; Franks & Auffrett 2007); it is used for the stabilization and storage of delicate, heat-sensitive materials like biologicals (vaccines, blood fractions. . .), pharmaceuticals and diagnostics, whose activity and therapeutical properties would be damaged by traditional drying methods. It is also used for the storage of

---

*For correspondence

some specialist food products (i.e., instant coffee) that easily rehydrate because of the porous structure left after the ice has sublimed. Last but not least this process allows to keep volatile molecules that are responsible for the flavours and odours of food.

Freeze-drying is a slow (generally batch) process where the solvent is removed from the frozen product through sublimation at very low pressures. The product is usually contained in vials (especially in the case of pharmaceutical products) or in trays placed on the shelves of the freeze-drying chamber, where it undergoes freezing and then solvent sublimation under vacuum conditions. During the drying phases, the shelves are warmed up very slowly, the frozen solvent contained in the product (generally water) sublimates, with a sublimation rate dependent on shelf temperature and chamber pressure (Nail 1980; Pisano *et al* 2011), while the chamber is continuously evacuated through a cold condenser, often (but not always) connected with the chamber by a duct. Here, solvent vapour deposits (or desublimates) on the cooling surfaces forming ice layers, whereas the inert gas is pumped off by a vacuum pump. The condenser must be very efficient, because of the crucial role played in keeping the pressure in the chamber at the desired value, where a delicate balance exists between heat and mass transfer that if disturbed may lead to adverse effects on the product, eventually up to causing its collapse.

The factors that influence the condenser efficiency are condenser geometry, fluid dynamics of sublimated vapour, chamber design, duct size, location and type of closing valve used, and the dynamics of ice deposition (Rey & May 1999), but little work has been done to investigate in detail the influence of the condenser geometry on its efficiency (Kobayashi 1984). Most of the aspects mentioned above are investigated in this work in order to get a deeper understanding of the problem.

The goal of the present research is to investigate the effect of flow dynamics and of ice deposition on the efficiency of condensers used in freeze-drying equipment. This is done here via mathematical modelling and CFD (Computational Fluid Dynamics) simulation, in order to gain useful insights to be used for improving condenser design, leading thus to higher efficiencies.

CFD modelling represents a useful tool for these investigations since it is much cheaper than experiments and can give an accurate quantitative description of all the variables involved in the process. On the contrary, some of these quantities are in certain cases difficult to measure in experimental studies.

The drawback is that some simplifying assumptions must be done in order to give a mathematical description of the complex processes investigated, like ice deposition, and some stability problems may rise in numerical simulations.

Empirical guidelines for a freeze-dryer condenser design can be found in literature as in the work by Jennings (2002) and Oetjen & Haseley (2004), but not many modelling works have been carried out so far on this subject; in fact most of the modelling papers are about the description of the drying process within the vial (Pikal 1985; Millman *et al* 1985; Zhai *et al* 2005; Hottot *et al* 2006; Velardi & Barresi 2008) or investigated by means of CFD the drying chamber (Rasetto *et al* 2008; Barresi *et al* 2010; Rasetto *et al* 2010).

One of the most significant works found so far focuses on the use of different approaches to describe the gas flow in the duct connecting the freeze-drying chamber to the condenser (Alexeenko *et al* 2009). In particular, in this work CFD results are compared with the results obtained from Direct Simulation Monte Carlo (DSMC) and show that under extreme operating conditions the continuum approach (used by CFD) can be no longer valid.

In another work (Ganguly *et al* 2010) the attention was instead focused on the simulation of ice deposition in a laboratory scale condenser by means of DSMC, comparing the efficiencies of two different geometries, but without investigating the role played by the inert gas.

The parameter that determines the choice of the most suitable model to describe the gas flow is the Knudsen number, a dimensionless number defined as the ratio of the molecular mean free path to the physical representative length scale L , that characterises the non-continuum effects in a gas flow:

$$Kn = \frac{\lambda}{L}, \quad (1)$$

when Kn assumes very high values (larger than 1) the flow is in the molecular regime.

Under this regime collisions between molecules are not very frequent and the molecule velocity distribution is not Maxwellian; the Boltzmann equation has to be solved.

When Kn is very small the flow is in the continuum regime. The Boltzmann equation can be replaced by the equations for some of the moments of the velocity distribution (mean density, gas velocity and energy). When $Kn < 10^{-4}$ generally the Euler equations are used, whereas when $Kn < 10^{-3}$ the Navier–Stokes equations are solved. These are the equations generally implemented in standard CFD codes. The transport properties appearing in these equations (e.g., gas viscosity and thermal conductivity) are calculated with the standard kinetic theory (often resorting to simple molecular potentials).

It is generally accepted that the range of applicability of the continuum approach can be extended into the rarefied regime ($10^{-3} < Kn < 10^{-1}$) if special boundary conditions, that take into account the possibility of having a velocity slip or a temperature jump at the walls, are adopted. This is called the slip regime (Maxwell 1878). For the transition regime ($10^{-1} < Kn < 1$) no reliable model exists.

In the present work, two equipments are examined: a laboratory-scale freeze-dryer and an industrial-scale condenser; under the operating conditions investigated the Knudsen number falls in the slip regime, where the CFD modelling of the flow is acceptable with the use of these proper boundary conditions with possible velocity slip or temperature jump at the surfaces.

The presence of the inert gas is here taken into account both in the industrial condenser and in the laboratory scale LyoBeta, where the gas flow is modelled in the whole equipment (chamber, duct and condenser).

As concerns the deposition model, many uncertainties exist for the estimation of the kinetics of the phenomena involved. The assumption that the deposition process can be modelled as a first-order process seems however reasonable; a parametric study on the kinetic constant was also carried out. Knowledge of the ice deposition rate allows to locally evaluate (through temporal integration) the quantity of ice deposited in a certain time interval.

2. Modelling approach

In the present research the solvent that undergoes sublimation is water. All the simulations are performed considering a binary mixture of water vapour and nitrogen and have been carried out with the commercial CFD code Fluent (ANSYS) and in certain cases additional sub-models have been implemented via User Defined Functions (UDF). Nitrogen, an inert gas very much used in freeze-dryers, is introduced for pressure-control needs, but incondensable gases may also enter the system due to leakage from the outside of the chamber. It is then accumulated in the condenser where only water undergoes deposition and is pumped off by a vacuum pump.

In addition to the usual balance equations of mass, momentum and energy, additional equations must be thus considered to model the transport of these two species.

The local mass fraction of a generic species i , Y_i , is predicted through the solution of the following convection-diffusion equation:

$$\frac{\partial (\rho Y_i)}{\partial t} + \nabla \cdot (\rho \mathbf{U} Y_i) + \nabla \cdot \mathbf{J}_i = 0, \quad (2)$$

where ρ is the gas density, $\mathbf{U}$ is the gas velocity and $\mathbf{J}_i$ is the diffusive flux of component i .

The process of water vapour deposition on the condenser refrigerated walls cannot be neglected even in preliminary investigations of the general hydrodynamics, since it is not possible to set other outlet conditions that lead to reasonable pressure distributions.

Water deposition is modelled as finite-rate process due to possible limitations related to molecular phenomena and water transport resistance caused by the presence of the inert gas. Since many uncertainties exist for the estimation of the water sticking coefficients the process has been modelled as mass transfer-controlled, and a parametric study was carried out on the kinetic constant k .

A first-order kinetics has been assumed, with kinetic constant k :

$$R_{s,w} = k \rho Y_w, \quad (3)$$

where $R_{s,w}$ represents the water deposition process rate, k is the kinetic constant, ρ is the gas density and Y_w is the water mass fraction in the gas mixture (evaluated near the surface where deposition occurs). The value of k seems reasonable in the range 100 ms^{-1} – 1000 ms^{-1} , however from the sensitivity analysis carried out the influence of that parameter did not result so significantly and thus the results presented refer to the most reasonable values for the cases investigated.

The process of ice deposition has been then represented in the CFD model similarly to a first-order wall-surface reaction taking place only on the condenser refrigerated walls, where the reagent is represented by the water vapour and the product of the reaction is the deposited ice. The effect of the surface mass transfer has been included in the continuity equation and the refrigerated walls have been modelled as constant temperature surfaces at 223 K. This is reasonable if the cooling system is properly sized and is able to remove all the heat generated by ice deposition.

In all the simulations, due to the low pressure values considered, the transport properties of the species are modelled with the kinetic theory of gases.

The boundary conditions for velocity and temperature are taken from the original work of Maxwell (1878). According to Maxwell's model the components of the gas velocity at the wall are related to the wall velocity components by the following expressions. The relation between the parallel components is given by Equation (4), while the relation between the normal components is given by Equation (5):

$$U_{g,p} - U_{w,p} = \lambda \left(\frac{2 - \alpha_v}{\alpha_v} \right) \frac{\partial U_p}{\partial n} \approx \left(\frac{2 - \alpha_v}{\alpha_v} \right) \frac{\lambda}{\delta} (U_{c,p} - U_{g,p}) \quad (4)$$

$$U_{g,n} = (\mathbf{U} \cdot \mathbf{n}) = U_{w,n}. \quad (5)$$

In Equation (4) $U_{w,p}$ represents the component parallel to the wall of the wall velocity, $U_{g,p}$ is the component parallel to the wall of the velocity of the gas near the wall, $U_{c,p}$ is the component parallel to the wall of the velocity of the gas in the centre of the computational cell close to the

wall, $\partial U_p / \partial n$ is the derivative of the component parallel to the wall of the gas velocity along the direction normal to the wall and evaluated near the wall, α_v is the momentum accommodation coefficient of the gas mixture (whose value is calculated as the mass-fraction weighted average of those of the gas species present in the system), while δ represents the distance from the cell centre to the wall.

In Equation (5) instead $U_{w,n}$ represents the component normal to the wall of the wall velocity and $U_{g,n}$ is the component normal to the wall of the velocity of the gas near the wall.

Equation (4) gives the expression for the slip velocity at the wall, present only in direction parallel to the wall, whereas Equation (5) reports that the same values are assumed by the components normal to the wall of the velocities of the gas and of the wall respectively, thus expressing that no slip is present in the normal direction. Therefore, the slip between the gas and the wall exists only in the direction parallel to the wall, whereas in the normal direction the gas assumes the same velocity of the wall.

Another effect that is observed in the slip regime is the temperature jump at the wall, that according to Maxwell's model (Maxwell 1878) reads as follows

$$T_g - T_w = 2\lambda \left(\frac{2 - \alpha_T}{\alpha_T} \right) \frac{\partial T}{\partial n} \approx 2 \left(\frac{2 - \alpha_T}{\alpha_T} \right) \frac{\lambda}{\delta} (T_c - T_g), \quad (6)$$

where T_w represents the temperature of the wall, T_g is the temperature of the gas near the wall, T_c the temperature of the gas in the centre of the computational cell close to the wall, $\partial T / \partial n$ is the derivative of the gas temperature along the direction normal to the wall and evaluated near the wall, α_T is the thermal accommodation coefficient of the gas mixture (similar to the momentum accommodation coefficient, evaluated as the mass-fraction weighted average of the values relative to the single gas species present in the system), while δ represents the distance from the cell centre to the wall.

3. Geometries investigated and main simulation settings

Initially a laboratory scale equipment was investigated, LyoBeta25 by Telstar (Terrassa, Spain), where the volume occupied by the fluid (chamber, duct and condenser) is about 212 litres, represented by a computational mesh of 623,671 cells (most of them are hexahedral cells, except for the regions characterised by complex geometrical features, like those around the valve).

Then, after testing the fluid-dynamic model on the small scale apparatus the investigation has been carried out on an industrial scale condenser, resulting in a mesh with 3,287,544 cells.

The computational grids used were built with the grid generator GAMBIT by making reference to the standard guidelines. Grid-independence checks were performed in preliminary stages of the work and a systematic description relative to the chamber can be found in the PhD thesis by Rasetto (2009).

The laboratory-scale freeze dryer (LyoBeta^{TM}) is made up of a drying chamber with four shelves (total sublimating surface about 0.67 m²), of a duct connecting the chamber to the condenser and of a cylindrical condenser, refrigerated on the lateral surface. A butterfly valve is present in the duct and is modelled in open position. Even if the interest of the work is focused on what happens in the condenser, the whole equipment (i.e., chamber, duct, condenser) is modelled here, in order to give an accurate representation of the gas flow entering the duct and the condenser since the gas flow in the duct has a significant impact on the global fluid dynamics of the apparatus in such a simple geometry.

The equations are solved by resorting to finite-volume discretisation and with, single phase and steady state simulations, performed with the commercial CFD code ANSYS Fluent 6.12. The Semi-Implicit Method for Pressure-Linked Equations (SIMPLE) algorithm has been used to solve the pressure–velocity coupling, and high order numerical schemes (second-order upwind) have been adopted. In all the simulations the two chemical species (water vapour and nitrogen) enter the chamber (representing sublimation and inert gas inflow) through uniform sources placed on the upper side of four slabs. This boundary condition mimics the layers of vials on the four shelves, characterised by a thickness of 43 mm (corresponding to that of the vials partially stoppered, and considering a sublimating surface for each shelf equal to 0.168 m^2).

Two different inlet values for the inert gas mass fraction are considered (1%, 5%), taking into account possible leakage phenomena and/or controlled bleeding for pressure control. The fact that this is not represented in details, but as a distributed source, does not affect the validity of the conclusions concerning the condenser.

Different sublimation rates are considered ($0.1 \text{ kg m}^{-2} \text{ h}^{-1}$, $0.4 \text{ kg m}^{-2} \text{ h}^{-1}$, $1 \text{ kg m}^{-2} \text{ h}^{-1}$), these values representing the average sublimation rate per unit surface of the shelf corresponding to typical values observed during primary-drying. The interface product temperature is set equal to 239 K, the shelf temperature is 258 K, the walls of chamber, duct, valve and the condenser front and back walls are represented as adiabatic surfaces (zero heat flux), while the temperature of the refrigerated condenser walls is set equal to 223 K. Radiation is neglected and the pressure of 4 Pa is imposed at the condenser exit.

The industrial condenser investigated is made up of a vertical cylinder, 950 mm in diameter, where the refrigerating elements are constituted by winding pipes arranged in two spirals: one large and short, the other narrower and taller, both surrounded by a screen, and with a mushroom valve in front of the condenser entrance in open position. A lateral pipe is then present, representing the incondensable gases exhaust. Not all the internals have been reproduced in the geometry considered for the CFD simulations, but only the most significant ones: the spirals, the screen and the mushroom valve.

4. Results

4.1 Laboratory scale equipment (LyoBeta)

4.1a Effect of water sublimation rate: The influence of sublimation rate ($0.1 \text{ kg m}^{-2} \text{ h}^{-1}$, $0.4 \text{ kg m}^{-2} \text{ h}^{-1}$, $1 \text{ kg m}^{-2} \text{ h}^{-1}$) has been investigated at 5% of inlet inert gas and with a kinetic constant of 144 s^{-1} for the deposition rate; higher pressure values are observed both in the chamber and in the condenser with the increase of the entering mass flux as expected. A mean pressure of about 6 Pa is predicted in the chamber and of about 4.8 Pa in the condenser for a shelf sublimation rate of $0.1 \text{ kg m}^{-2} \text{ h}^{-1}$; these average pressures become 12 Pa and 7.5 Pa when the sublimation rate is $0.4 \text{ kg m}^{-2} \text{ h}^{-1}$; and 24 Pa and 14 Pa for a sublimation rate of $1 \text{ kg m}^{-2} \text{ h}^{-1}$.

The contour plots of the pressure and of water vapour mass fraction are reported in figure 1 for the sublimation rate of $0.4 \text{ kg m}^{-2} \text{ h}^{-1}$ on selected surfaces. If the pressure control system is not considered, the pressures predicted by the CFD simulations represent the minimum pressures that can be maintained in the system for the operating conditions investigated; however it is more interesting to observe the pressure drops from the chamber to the condenser and at the condenser exit.

Figure 1. Contours of the absolute pressure (Pa) (upper graphs) and of the water mass fraction (-) (lower graphs) predicted for the mass sublimation rate of $0.4 \text{ kg m}^{-2} \text{ h}^{-1}$ (with a kinetic constant taken equal to 144 m s^{-1} and with an inert mass fraction of 5%) in the whole apparatus (a, c) and in the condenser (b, d).

The condenser behaviour has in fact a significant influence on the pressure in the chamber. A wrong dimensioning of the exhaust gas pipe or low condensing efficiencies may in fact lead to a higher resistance and to higher pressure drop at the condenser exit, causing a significant increase of the pressure in the chamber with possible adverse effects on the product quality.

In the condenser, except for the region close to the exit where the pressure drop is concentrated (the white pipe in the middle of the condenser, shown in figure 1, represents the pipe for the exhaust of the incondensable gases), the pressure results rather uniform (see figure 1b). This is due to the presence of the inert gas, that becomes the main component moving along the condenser as the water vapour is transformed into ice on the refrigerated surfaces (figure 1d). When the sublimation rate increases a higher pressure drop is observed between chamber and condenser, leading to higher fluid velocities, but without reaching the sonic conditions for the cases investigated.

In figure 2 it is possible to compare the water vapour distribution over the condenser sections obtained with two different sublimation rates: at the lowest sublimation rate ($0.1 \text{ kg m}^{-2} \text{ h}^{-1}$) the water vapour contours result rather symmetric over all the reported sections of the condenser, but when the sublimation rate is higher ($1 \text{ kg m}^{-2} \text{ h}^{-1}$) this symmetry for the water vapour distribution is lost.

In fact, at higher sublimation rates, due to higher velocities, the water vapour molecules entering the condenser are able to reach and collide with the refrigerated wall opposite to the duct. According to our predictions high deposition rates may be expected in that region, but our model does not take into account possible ablation effects. Another region interested by water deposition, according to the CFD predictions, is that around the duct, at the condenser entrance (figure 3).

Figure 2. Contours of the water mass fraction (-) predicted in the condenser for the mass sublimation rates $0.1 \text{ kg m}^{-2} \text{ h}^{-1}$ (a) and $1 \text{ kg m}^{-2} \text{ h}^{-1}$ (b) (with a kinetic constant taken equal to 144 m s^{-1} and with an inert mass fraction of 5%).

4.1b Effect of the kinetic constant: A rough sensitivity analysis is carried out considering two different values ($k = 144 \text{ m s}^{-1}$ and 769 m s^{-1}) for the kinetic constant used in the model of water deposition. The water sublimation rate considered is equal to $1.0 \text{ kg m}^{-2} \text{ h}^{-1}$ and the inert gas represents the 5% of the overall entering mass flow.

Results show that the increase of the kinetic constant from 144 m s^{-1} to 769 m s^{-1} does not affect significantly the performance of the condenser and similar pressure distributions are obtained, not reported here for the sake of brevity. In fact, although as expected the ice deposition rate in the regions near the condenser entrance increases as the kinetic constant is increased (see

Figure 3. Contours of the surface deposition rate of ice ($\text{kg m}^{-2} \text{s}^{-1}$) predicted for the mass sublimation rates $0.1 \text{ kg m}^{-2} \text{h}^{-1}$ (a), $0.4 \text{ kg m}^{-2} \text{h}^{-1}$ (b), and $1 \text{ kg m}^{-2} \text{h}^{-1}$ (c, d) with $k = 144 \text{ m s}^{-1}$ (a, b, c) and $k = 769 \text{ m s}^{-1}$ (d). In all these cases the inlet inert mass fraction is equal to 5%.

figures 3 c, d), there is no relevant effect on the global fluid dynamics in both the chamber and the condenser.

4.1c Effect of the inlet mass fraction of inert gas: In order to investigate the role of the inert fraction on the performance of the condenser, two simulations, differing only in the inert (nitrogen) inlet mass fraction have been carried out. Values in the range 1–5% may be considered reasonable using controlled bleeding, while a much lower value (0.1%) corresponds to the case of normal leakage in the apparatus.

In the first case an inlet inert mass fraction of 5% is considered (total inlet mass flux $1.0526 \text{ kg m}^{-2} \text{h}^{-1}$), whereas in the second case the value used for the inert mass fraction in inlet is 1% (total inlet mass flux $1.010 \text{ kg m}^{-2} \text{h}^{-1}$); in both cases a water sublimation rate of $1 \text{ kg m}^{-2} \text{h}^{-1}$ is considered. The value assumed for the kinetic constant in these simulations is 144 m s^{-1} .

The decrease of the inert mass flow entering the chamber causes a significant reduction of the absolute pressure, especially in the condenser, where it falls to approximately 5 Pa as clearly visible in figure 4. In both cases anyway the pressure distribution in the condenser is rather uniform due to the presence of the inert gas that compensates the effect of water vapour disappearance (figure 4).

When the inert gas inlet mass fraction is varied, the chamber pressure remains quite high, at about 20–24 Pa, but a large change of the fluid dynamics in the duct is observed, as shown by the contour of the Mach number reported in figure 5. That causes some differences in the distribution

Figure 4. Contours of the absolute pressure, water mass fraction and ice deposition rate in the condenser (from top to bottom) for the case with 5% inert (left) and 1% inert (right). The sublimation rate considered is equal to $1 \text{ kg m}^{-2} \text{ h}^{-1}$ and the kinetic constant is 144 m s^{-1} .

of the water vapour at the condenser entrance, influencing the ice deposition rate in that region, as shown in the last two contour plots in figure 4.

These results clearly show that it is the inert flow that determines the pressure distribution in the apparatus and that the value in the chamber is determined by the pressure drop, as the outlet pressure value is fixed; this confirms the importance of the conditions for the pumping off of the inert gas at the exit. It must be noted that as a consequence of the much lower pressure in the condenser, the velocity of the vapour in the duct strongly increases: the pressure drop therefore increases significantly, but because of the much lower pressure at the exit, a lower pressure at the inlet will eventually result.

For all the cases examined so far the condenser efficiency, defined as the fraction of the entering water vapour molecules that deposits on its surface, has been evaluated, and a summary is reported in table 1.

Relatively high values are obtained for all cases ($>94\%$) confirming that the apparatus is safely designed, even if in case of small scale laboratory equipment low cost and simple design

Figure 5. Contours of the Mach number predicted for the two values of inert mass fraction: 5% (a) and 1% (b). The sublimation rate considered is equal to $1 \text{ kg m}^{-2} \text{ h}^{-1}$ and the kinetic constant is 144 m s^{-1} .

Table 1. LyoBeta condenser efficiency for the investigated operating conditions.

Water sublimation rate, $\text{kg m}^{-2} \text{ h}^{-1}$	Inlet inert %	Dep. rate constant k , m/s	Condenser efficiency, %
0.1	5	144	95.20
0.4	5	144	94.99
1	5	144	94.84
1	5	769	94.86
1	1	144	99.08

are kept in higher consideration. The main aim of the work anyway is to highlight the influence of the operating conditions on efficiency.

The highest condenser efficiency is obtained with the inert mass fraction at the inlet equal to 1%: for this case higher velocity values are predicted for water vapour molecules in the duct and higher deposition rates are observed near the condenser entrance. A slight increase of the condenser efficiency is then observed considering lower values for the sublimation flow rate, probably due to a greater uniformity of ice deposition.

4.1d Ice formation in the condenser and experimental evidence: It is hard to get quantitative validation of the previous simulations, but a few tests have been carried out to compare qualitative behaviours predicted with the experimental ones.

Figure 6 shows the distribution of ice over the cooling surface of the laboratory scale condenser (LyoBeta). Such results have been obtained during a typical freeze-drying cycle carried out at low temperature and low sublimation rate; only one shelf was loaded. During the sublimation step, the average water flux, calculated over the four shelves (for a total area of 0.672 m^2) was equal to $0.01 \text{ kg m}^{-2} \text{ h}^{-1}$. The product temperature at the moving interface was almost constant during the drying and equal to 233 K, while the temperature of the refrigerated condenser wall was 203 K.

It can be evidenced that water deposition was more significant near the condenser inlet, and in particular just around the duct entrance, and this is in good agreement with results predicted by the CFD analysis at lower flow rate (figure 3a); moreover, no ice accumulation was observed in the region opposite the duct: in fact, the last behaviour is typical only at very high flow rate (figures 3b, c, d). The highest sublimation rates have not been yet obtained in the apparatus in process runs, but a confirmation of the fact that in the runs at higher sublimation rate the jet reaches the opposite wall is supplied by the observation that in the predicted point of contact no ice is formed, which is in turn abundant around: this can be explained with an ablation effect, not included in the model, as discussed before.

Figure 6. Photography of the distribution of ice over the cooling surface of the LyoBeta condenser obtained with an experimental process run with a sublimation rate of $0.01 \text{ kg m}^{-2} \text{ h}^{-1}$.

Figure 7. Front view of the geometry of the industrial condenser built for CFD calculations.

4.2 Industrial scale apparatus

The first case considered has an inlet mass flow rate of $7.89 \cdot 10^{-4} \text{ kg s}^{-1}$ with an inert mass fraction of 1%, while the kinetic constant k for water deposition is taken equal to 720 m s^{-1} . A sketch of the condenser is reported in figure 7.

Under these operating conditions the overall condenser pressure is around 13.5 Pa. Figure 8a shows the contour of the absolute pressure in the vertical section of the condenser, showing that the main pressure drop occurs in correspondence of the mushroom valve, which is in front of the condenser entrance in open position.

Figure 8b instead shows the contour of water vapour mass fraction: high values are observed near the condenser entrance, but then they immediately decrease as a consequence of water vapour deposition on the refrigerated coils, where the value drops to zero. A large part of the ice deposition occurs in the regions above and below the entrance of the water vapour, not far from the mushroom valve, as shown in figure 9a. Here the hypothesis of perfectly clean coil surfaces is employed, but it is evident that, after some hours of operation, the regions initially involved in the water vapour removal will be covered by a thick layer of ice, reducing their ability to exchange heat (and mass), and thus, after this initial period, other regions of the coils will come in contact with fresh water vapour and transform it into ice.

Under these operating conditions the overall condenser efficiency is evaluated to be about 96%, since the amount of water bypassing the condenser and exiting without having been condensed is about 4%.

CFD predictions of the water vapour flow field and deposition patterns provide very useful information for understanding if the water vapour is well-distributed in the equipment investigated and if the cooling surfaces are used efficiently or, on the contrary, if there are stagnant fluid zones and regions of the refrigerating elements underused.

Figure 9b, for example, reports the streak-lines of the water vapour molecules in the condenser, thus showing which regions in the condenser are easily reached by the water molecules and

Figure 8. Contours of the absolute pressure (Pa) (upper graph) and of water vapour mass fraction (-) (lower graph) on the vertical section of the industrial condenser predicted for the case investigated.

which instead are less interested by the vapour flow, such as for example the region between the refrigerating elements.

Through the analysis of the previous results it is possible to presume that higher values for the condenser efficiency could be obtained by a better positioning of the two cooling coils. In fact the annular region confined between the two coils does not contribute much to the total water vapour deposition, since it appears to be stagnant.

Thus, CFD may be used to compare the efficiencies given by different geometries and provide useful information for improving the project of the equipment. From the simulations performed

Figure 9. Contour of ice deposition rate ($\text{kg m}^{-2} \text{s}^{-1}$) (upper graph), and particle streak-lines (coloured according to the water mass fraction, -) (lower graph), predicted in the industrial condenser for the case investigated.

on these two equipment it is possible. For example, to compare the effect exerted by the type of valve used.

In fact, different water vapour distributions are observed at the condenser entrance in the laboratory scale apparatus, where there is a butterfly valve in open position that does not affect significantly the flow field, giving a small pressure drop in the pipe, and in the industrial equipment where a mushroom valve is used and the vapour entering the condenser is obliged to change its direction, bumping against the valve disk, as shown in figure 10, resulting in a significant pressure drop. In the laboratory scale condenser the velocity vectors are not deviated by the valve; the vapour enters the condenser following the direction given by the duct, reaches the opposite wall where, the part which is not condensed, is reflected in both directions, moving towards the front and the back of the condenser respectively, giving rise to a sort of rotating flow (figure 10a). In the industrial condenser, instead of the vapour flow changes suddenly its direction after bumping against the mushroom valve, reaching thus the refrigerating elements not directly in perpendicular direction, but mainly flowing parallel to their surfaces. Rotating flows are then observed on both sides of the valve (see figure 10b).

Figure 10. Detail of the velocity vector contour plot near the entrance in the laboratory scale condenser (a) and in the industrial scale condenser (b).

The different water vapour distributions obtained lead to differences in the contact zones of the vapour with the cooling elements and thus in deposition rate patterns. In fact, in the industrial condenser the water vapour does not collide directly against the cooling surfaces, as in the laboratory scale condenser, but is deviated creating recirculation.

(a)

(b)

Figure 11. Detail of the velocity vector contour plot near the mushroom valve for the case with the valve at 215 mm from the entrance and the mass flow density equal to $1.4 \text{ g cm}^{-2} \text{ h}^{-1}$ (upper graph) and to $14 \text{ g cm}^{-2} \text{ h}^{-1}$ (lower graph).

Figure 12. Profile of the axial velocity before the tube bundle for the case with the valve at 215 mm from the entrance and with different mass sublimation flows.

Due to the significant influence exerted by water vapour inlet features on the ice deposition patterns, observed in these preliminary studies, further investigations have been carried out comparing two alternative positions for vapour inlet with regard to the refrigerating elements present in the condenser. In the first case, the vapour is introduced parallel to the refrigerating elements, while in the latter it enters perpendicular to the refrigerating elements.

For this purpose, the vertical condenser has been compared with another industrial condenser, that also employs a mushroom valve, but characterised by an horizontal arrangement, with the valve positioned in front of the cooling elements (with the disk perpendicular to refrigerating surfaces), rather than located laterally (with the disk parallel to the cooling surfaces) as it happens in the vertical condenser.

A schematic representation of this second condenser (horizontal condenser) is given in figure 11, where it is possible to see the profile of the mushroom valve and the initial part of the refrigerating elements arranged in a sort of equidistant arcs.

For this horizontal condenser it has not been estimated the overall efficiency, but it has been simulated only the vapour distribution in the inlet region, because here the attention was focused on how the vapour distribution changed as a consequence of a different inlet strategy.

Figure 11 shows the velocity vectors predicted by CFD simulation in the horizontal condenser, showing different flow patterns compared to those obtained in the vertical condenser. The results are reported here for two different values of the mass flow density: at the lowest mass flow density considered, $1.4 \text{ g cm}^{-2} \text{ h}^{-1}$, vapour recirculation zones are observed near the valve only for the distance of 215 mm (figure 11a), whereas in all the other cases the vapour flow pattern is well represented by the one reported in figure 11b.

Figure 12 reports the axial velocity profile before the tube bundle for different values of sublimation rates; it is here clearly visible the effect exerted by the mushroom valve on the axial velocity profiles.

5. Conclusions

A mathematical model has been developed to describe the fluid-dynamics and the process of ice deposition in freeze-dryer condensers, in order to get some useful information to improve condenser efficiency. Water vapour deposition as ice was modelled as a finite-rate first-order process.

It is hard to get quantitative validation of these simulations thus qualitative comparisons with experimental behaviours have been carried out for the laboratory-scale condenser (LyoBeta), resulting in good agreement.

Different operating conditions have been investigated for the laboratory scale equipment (LyoBeta): different values for the sublimation rate, the inlet inert mass fraction, the kinetic constant for the ice deposition process. For all the cases examined a relatively high condenser efficiency was achieved and the influence of the operating conditions on efficiency has been investigated.

The highest condenser efficiency was obtained with the lowest inert mass fraction in inlet (1%). In this case higher velocity values were predicted for water vapour molecules in the duct and higher deposition rates were obtained near the condenser entrance.

A slight increase of the condenser efficiency was then observed reducing the sublimation flow rate (the efficiency increased from 94.84% to 95.20% passing from a sublimation rate of $1 \text{ kg m}^{-2} \text{ h}^{-1}$ to a sublimation rate of $0.1 \text{ kg m}^{-2} \text{ h}^{-1}$) probably due to the a greater uniformity of ice deposition.

This model, preliminary tested on the laboratory scale equipment, was then applied to industrial apparatuses, showing how geometrical differences may affect the vapour distribution, and consequently influence the water deposition rate patterns. By means of CFD investigations it is thus possible to achieve a better insight of how some geometrical features of the equipment may affect the vapour distribution and consequently the condenser efficiency, achieving useful information for a possible improvement of its design.

Acknowledgments

Telstar s.p.a. (Terrassa, Spain) has financed this research and is gratefully acknowledged. The authors would also thank Dr. Miguel Galan (from Telstar) for his valuable discussions.

Nomenclature

$\mathbf{J}_i$	diffusive flux of the generic chemical species i , $\text{kg m}^{-2} \text{ s}^{-1}$
k	kinetic constant of water deposition process, m s^{-1}
Kn	Knudsen number,-
L	characteristic length scale of the system, m
$\mathbf{n}$	normal versor to wall surface
$R_{s,w}$	rate of water deposition process, $\text{kg m}^{-2} \text{ s}^{-1}$
t	time, s
T	temperature of the gas, K
T_c	temperature of the gas in the centre of the computational cell close to the wall, K
T_g	temperature of the gas near the wall, K
T_w	temperature of the wall, K
$\mathbf{U}$	gas velocity vector, ms^{-1}
$U_{c,p}$	component parallel to the wall of the velocity of the gas in the centre of the computational cell close to the wall, ms^{-1}
$U_{g,n}$	component normal to the wall of the velocity of the gas near the wall, ms^{-1}
$U_{g,p}$	component parallel to the wall of the velocity of the gas near the wall, ms^{-1}
U_p	component parallel to the wall of the gas velocity, ms^{-1}
$U_{w,n}$	component normal to the wall of the wall velocity, ms^{-1}

- $U_{w,p}$ component parallel to the wall of the wall velocity, ms^{-1}
 v_z axial velocity component, ms^{-1}
 Y_i mass fraction of the generic chemical species i , -
 Y_w water mass fraction, -

Greek Symbols

- α_T thermal accomodation coefficient of the gas mixture, -
 α_v momentum accomodation coefficient of the gas mixture, -
 δ distance of the cell centre from the wall, m
 λ mean free path of the gas molecules, m
 ρ fluid density, kg m^{-3}

References

- Alexeenko A, Ganguly A and Nail S L 2009 Computational analysis of fluid dynamics in pharmaceutical freeze-drying. *J. Pharm. Sci.* 98(9): 3483–3494
- Barresi A A, Fissore D and Marchisio D 2010 *Process analytical technology in industrial freeze-drying*, in: Freeze-drying/lyophilization of pharmaceuticals and biological products, 3 rd rev. Edition (L Rey and J C May, eds.), Chap. 20. New York: Informa Healthcare, pp. 463–496
- Franks F and Auffrett T 2007 *Freeze-drying of pharmaceuticals and biopharmaceuticals*. Cambridge: RSC
- Ganguly A, Venkattraman A and Alexeenko A 2010 3D DSMC simulations of vapor/ice dynamics in a freeze-dryer condenser, AIP Conf. Proc., Vol. 1333, 27th International Symposium on Rarefied Gas Dynamics, Pacific Grove, CA: 254–259
- Hottot A, Peczalski R, Vessot S and Andrieu J 2006 Freeze-drying of pharmaceutical proteins in vials: modeling of freezing and sublimation steps. *Drying Technol.* 24: 561–570
- Jennings T A 2002 *Lyophilization: introduction and basic principles*. New York: Interpharm, CRC
- Kobayashi M 1984 Development of a new refrigeration system and optimum geometry of the vapor condenser for pharmaceutical freeze dryers. *Proc. 4th Int. Drying Symp.*, Kyoto, Japan: 464–471
- Liu Y G, Zhao Y and Feng X 2008 Exergy analysis for a freeze-drying process. *Appl. Thermal Eng.* 28: 675–690
- Maxwell J C 1878 On stresses in rarefied gases arising from inequalities of temperature. *Proc. Roy. Soc. Lond.* 27: 304–308
- Millman M J, Liapis A I and Marchello J M 1985 An analysis of the lyophilisation process using a sorption sublimation model and various operational policies. *AIChE J.* 31(10): 1594–1604
- Nail S L 1980 The effect of chamber pressure on heat transfer in the freeze drying of parenteral solutions. *J. Parenteral Drug Assoc.* 34(5): 358–368
- Oetjen G and Haseley P 2004 *Freeze-drying*. Weinheim, Germany: Wiley-VCH
- Pikal M J 1985 Use of laboratory data in freeze-drying process design: heat and mass transfer coefficients and the computer simulation of freeze-drying. *J. Parenter. Sci. Technol.* 39: 115–139
- Pisano R, Fissore D and Barresi A A 2011 *Heat transfer in freeze-drying apparatus*, in: Developments in Heat Transfer M A dos Santos Bernardes, (ed), Chap. 6. InTech, Rijeka (Croatia), pp. 92–114. Open access book, available at <http://www.intechopen.com/books/show/title/developments-in-heat-transfer>
- Rasetto V 2009 *Use of mathematical models in the freeze-drying field: process understanding and optimal equipment design*. PhD Diss, Politecnico di Torino, Italy, 2009
- Rasetto V, Marchisio D L, Fissore D and Barresi A A 2008 *Model-based monitoring of a non-uniform batch in a freeze-drying process*, *Computer-Aided Chem. Eng.*, Vol. 25, paper FP_00210, 6 pp. Amsterdam: Elsevier, CD Edition

- Rasetto V, Marchisio D L, Fissore D and Barresi A A 2010 On the use of a dual-scale model to improve understanding of a pharmaceutical freeze-drying process. *J. Pharm. Sci.* 99(10): 4337–4350
- Ratti C 2001 Hot air and freeze-drying of high-value foods: A Review. *J. Food Eng.* 49: 311–319
- Rey L and May J C 1999 *Freeze-drying/lyophilization of pharmaceutical and biological products*. New York: Marcel Dekker, Inc
- Velardi S and Barresi A A 2008 Development of simplified models for the freeze-drying process and investigation of the optimal operating conditions. *Chem. Eng. Res. Des.* 86: 9–22
- Zhai S, Su H, Taylor R and Slater K H 2005 Pure ice sublimation within vials in a laboratory lyophiliser; comparison of theory with experiments. *Chem. Eng. Sci.* 60: 1167–1176