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Research Article

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Optimization of cooling rate in refrigeration system of freeze-drying for pharmaceuticals

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ABSTRACT

A quasi-steady state simulation was conducted on the cooling process of freeze-drying for pharmaceuticals. It is found that, unlike the system with a pure refrigerant, a peak value of the volumetric refrigerating capacity occurs as the cycle pressure level varies if composition and pressure ratio of mixture refrigerant are specified. After optimization of volumetric refrigerating capacity with constant and varying compositions, further analysis was carried out about the regular effects of mixture refrigerant on refrigerating capacity at varying temperatures, achieving design of mixture refrigerant which can satisfy the requirements of various cooling rates in refrigeration.

Keywords: refrigeration and cryogenic, cooling rate, optimization, mixture refrigerant

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INTRODUCTION

Freeze-drying is considered nowadays as the best one of the techniques which can avoid degeneration and activity loss of pharmaceuticals in drying at low temperatures. So it is widely applied in treatment of dried pharmaceuticals[1].

Because refrigeration system has the features of long performance and highly energy-consuming, energy consumed by refrigeration system accounting for 70% of that in the process of freeze-drying of pharmaceuticals, optimization of energy-consuming in it can remarkably save the running costs. Cooling rate is an important index used to describe refrigeration, and cooling rate has crucial effects on the quality of pharmaceuticals[2].

Here, optimization of cooling rate in refrigeration system is studied through a quasi-steady state simulation of steady circulation values in cooling process, as well as analysis of volumetric refrigerating capacity at varying temperatures to explain the effects of mixture refrigerant on the cooling process. The research emphasis lies in how to improve the cooling rates required by refrigeration techniques via changing the proportion of the mixture refrigerant. The thermophysical properties of the mixture refrigerant are illustrated by using sub-function calculations in the database of REFPROP710[3].

EXPERIMENTAL SECTION

Optimization of cooling rate in refrigeration system

Assumed conditions

In order to simplify the calculations, following assumptions are made [4]:

Utilization of environmental mixture refrigerant. Component: 600（i-C_4H_{10}), R23(CHF_3), R14(CF_4)

High temperature heat source is 30°C and low temperature heat source is respectively: 20°C, 10°C, 0°C,-10°C, -30°C, -40°C, - 50°C, -60°C.

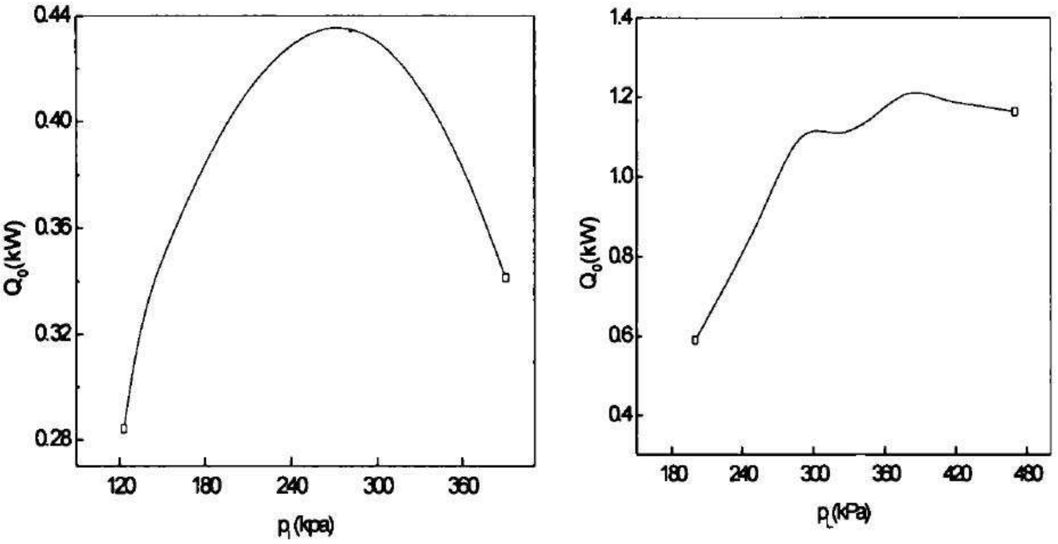
Lateral pressure of high pressure in circulation can be neglected, which includes 5*kpa*, from the evaporator; 2.5*kpa* from the regenerators. The pressure ratio is 6, and the pressure limitation is $p_H \le 2000kpa$和$p_L \ge 100kpa$.

The temperature margins between the condenser and higher heat source, between the evaporator and lower heat source, between the cool and the heat fluids in cross flow regenerator are 2℃.

This is an isentropic process. The total efficiency of the condenser is $\eta_{el} = 0.4$. The suction temperature is an ambient one.

No heat leakage exists in the throttle process; the refrigerator operates steady, conditional points unvarying with time going by.

Optimization of volumetric refrigerating capacity with constant compositions



$(a) t_L = -60$ ℃ $(b) t_L = 0$ ℃

Fig.1 effects of circulation pressure of mixture refrigerant on Q_0

When mixture refrigerant a (mole fractions of R14, R23 and R600a is respectively z_1=0.1,z_2=0.3,z_3=0.6) is used to make calculations, 2 figures are obtained about variation trend of Q_0 (volumetric refrigerating capacity) with circulation pressure variation at 2 typical temperatures.

The Figure 1 shows there is a peak value coming as the pressure increases, the peak value in Figure 1(a) coming inside the set pressure limit and the peak value in Figure 1(b) coming beyond it. (Up to approximate 2340 kpa)[5]. So firstly, this article attempts to make optimization of volumetric refrigerating capacity, which functions as nominal refrigerating capacity. On one occasion the peak value comes between the pressure limitations, pick it as refrigerating capacity; on the other occasion the peak value comes beyond the pressure limits, pick up the value at top limit of pressure.

Optimization of cooling rate with varying compositions

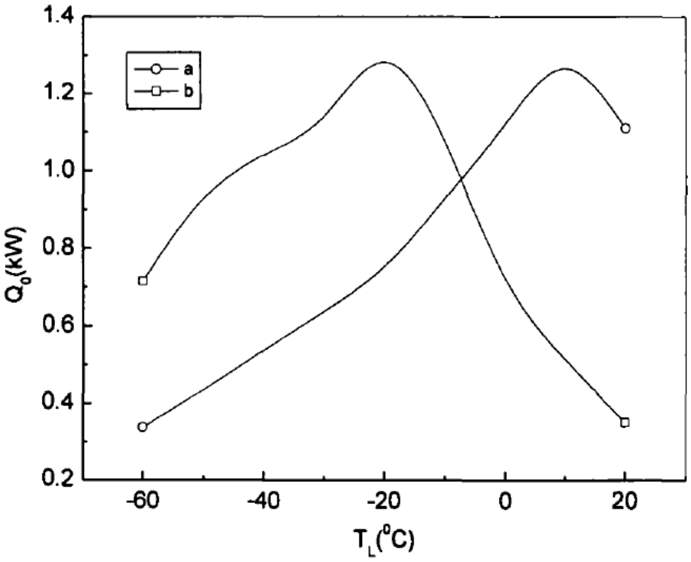


Fig.2 curve of nominal refrigerating capacity variation of mixture refrigerant a and b

Figure 2 provides curve of nominal refrigerating capacity variation of mixture refrigerant a and b (z_1=0.1, z2=0.5, z3=0.4) when the temperature of heat source varies from -60℃ to 20℃.

As Figure 2 shows the peak values appear in the both circulation of mixture refrigerant a and b, but at different temperatures. Because bigger is the proportion of low boiling components in mixture refrigerant, the peak value comes at relatively high temperature, 10°C. On the contrary, bigger is the proportion of high boiling components in mixed refrigerant b, the peak value comes at relatively low temperature, -20°C. At the mid-temperature, for example, at -10°C, 2 curves meet across, which represent the same refrigerating capacity. At relatively high temperatures, mixed refrigerant, a, can produce more refrigerating capacity. At relatively low temperatures, mixed refrigerant, b, can produce more refrigerating capacity. So, the components of the mixture refrigerant have remarkable effects on refrigerating capacity in the separate temperature ranges[6].

RESULTS AND DISCUSSION

To exactly describe the effects of nominal refrigerating capacity at the varying temperatures on cooling process, it is required to take into consideration the thermal capacity of the cooled objects. Suppose one temperature point as T , infinitesimal of temperature variation as d_T , the time taken is d_τ , it comes to resulting from energy balance:

$$Q_0 d_\tau = C d_T \qquad (1)$$

In Equation (1), Q_0 stands for refrigerating capacity at the specific temperature, C for thermal capacity of the cooled object at the temperature.

Cooling rates and total time-consumption in cooling can be derived from Equation (1):

$$\frac{d_T}{d_\tau} = \frac{Q_0}{C} \qquad (2)$$

$$\tau = \int_{T_L}^{T_H} \frac{C}{Q_0} d_T \text{或} \tau = \sum_{i=1}^{n} \frac{C_i}{Q_{0i}} \Delta T_i \qquad (3)$$

Q_{0i} and C_i stands for the refrigerating capacity and the thermal capacity of the cooled objects at specific temperature point i.

Equation (2) and (3) display the cooling rates and cooling time consumption from T_H to T_L. It is feasible to optimize the components in the mixture refrigerant to satisfy the requirements of cooling rates in different cooling techniques.

For example, the volume of the freeze-dried object is too much less, the ratio of thermal capacity of the freeze-dried object between shelf evaporator turns out too less as well. So, thermal capacity of the freeze-dried object approximately equals to that of shelf evaporator. And shelf evaporator is made from red brass[7], its thermal capacity can be considered as a constant. When $\Delta T_i = \Delta T_0$, Equation（3）can be simplified as:

$$\tau = C\Delta T_0 \sum_{i=1}^{n} \frac{1}{Q_{0i}} \tag{4}$$

As can be learned from Equation (4), $\frac{1}{Q_{0i}}$ is the time consumed in temperature reduction in thermal capacity unit freeze-dried object at the temperature, it can be called simply as unit time of temperature reduction. Less is unit time of temperature reduction, easier it is for the heat from shelf evaporator to go through the temperature. $\sum_{i=1}^{n} \frac{1}{Q_{0i}}$ is the total time taken in temperature reduction unit object of thermal capacity of the freeze-dried object at every temperature t, which can be called total time for temperature reduction unit object. Total time for temperature reduction unit object is the sum of each temperature reduction unit object at every temperature, displaying the total time taken in the complete cooling process. The contribution of refrigerating capacity on total shortened time for temperature reduction is displayed by time for temperature reduction unit object. Consequently, $\frac{1}{Q_{0i}}$ can explain more directly and precisely the contribution of refrigerating capacity at every temperature on total time for temperature reduction than Q_{0i} .

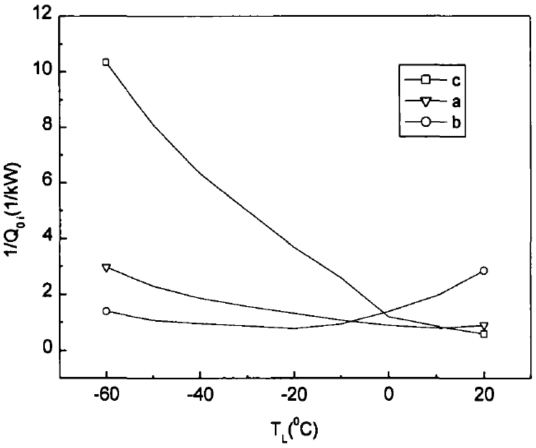


Fig.3 mixture refrigerant variation trend of $\frac{1}{Q_{0i}}$ with temperature changing

As Fig.3 indicates, when z_1=0.1, with z_2 and z_3 different, variation trend of $\frac{1}{Q_{0i}}$ with temperature changing. It is learned that the volley values appear in the time for temperature reduction per unit with the temperature going down in the circulation of the mixed refrigerant a and b, but at different temperatures and crossing at -10°C.The time for temperature reduction per unit in the circulation of mixed refrigerant c (z1=0.1, z2=0.1, z3=0.8) is monotone increasing, with no volley or peak value coming out. The time for temperature reduction per unit of the mixture refrigerant a and b bears less variations. The time for temperature reduction per unit of the mixed refrigerant c bears great variations, with the maximum coming at -60°C and the minimum coming at 20°C. This is because of high proportion of high-boiling components, leading to greatest refrigerating capacity at relatively higher temperature and to sharp decrease in refrigerating capacity at relatively lower temperature. Thus, the freeze-dried object can go through the minimum of temperature reduction at high temperature and the maximum at low temperature . We can learn that the various refrigerants can offer different control ranges for cooling rates, bringing various choices required by different techniques. If the minimum of time for temperature reduction is taken as the goal of optimization of the mixture refrigerant, the time for temperature reduction per unit $\sum_{i=1}^{n}\frac{1}{Q_{0i}}$ can serve as a measurement derived from Equation(4).

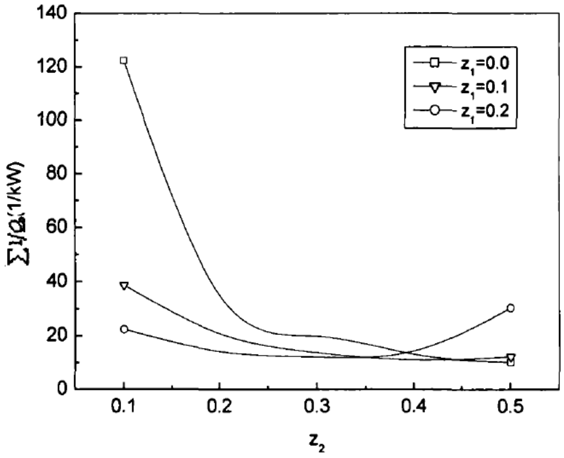


Fig.4 effects of various refrigerants on $\sum_{i=1}^{n}\frac{1}{Q_{0i}}$

As Fig4 offers a curve for the total time for drop in temperature per unit when $\Delta T_0 = 10$ ℃, $n = 9$, and z_1 ranges from 0.0 to 0.2 and z_2 from 0.1～0.5. It can be learned that the minimums of the total time for temperature drop per unit, which seem proximate, come respectively at the points where z_2=0.5,z_2=0.4,z_2=0.3. This suggests that the mixture refrigerant with different z_1 can all realize the minimum values of the total time for temperature drop per unit. However, z_2 decreases correspondingly in the refrigerants related to the minimum values of total time for temperature drop per unit[7,8].

When two-component mixed refrigerant with proper density is utilized, the total time for temperature drop can come the minimum. In the curve with z_1=0, when z_2 becomes too small, the total time for temperature drop increases greatly. This is because of too slow cooling rates with too small refrigerating capacity in the lower temperature range. In the curve with z_1=0.2, the total time for temperature drop is very great when z_2=0.5. Similarly, there are too slow cooling rates with too small refrigerating capacity in the lower temperature range because too low is the density of the component with higher boiling point in the refrigerants, although the refrigerant can produce more cooling capacity in the lower temperature range. When z_2 comes smaller, the refrigerating capacity increases in the high temperature range, binging rapidly decreasing in time for temperature drop per unit. The decrease of z_2 has little effect on time for temperature drop, although the time for temperature drop increases less at z_2=0.1. The features of time variation with z_1=0.1 for temperature drop lie between the curves of $z_{1=}$0.0 and z_1=0.2[9,12].

CONCLUSION

This article makes the numerical simulation of cooling process of the freeze-drying device with refrigeration system as cooling source, taking the refrigerants composed of R14, R23 and R600a as the samples. And, it makes further analysis of the effects of the components in the refrigerants on the refrigerating capacity at every temperature in the cooing process. When the components and the pressure ratio are given, there are peak values appearing in the refrigerating capacity with the variation of pressure, which is different from that in the pure refrigerant. Therefore, more can be learned about regularity of refrigerating capacity changing with the varying proportion of the refrigerants, which can improve the cooling rate control required by the techniques in practice through optimization of the refrigerating capacity respectively from the given and varying proportion of the components in the refrigerants.

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