



Finite elements model of heat transfer predicts the edge vial effect in different freeze-drying configurations

Bernadette Scutella, Stéphanie Passot, Erwan Bourlés, Fernanda Fonseca, Artemio Plana-Fattori, Denis Flick, Ioan-Cristian Trelea

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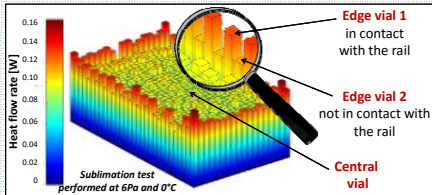
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What is the “edge vial effect”?



What is the “edge vial effect”?

During freeze-drying process, products in vials located at the periphery of the shelf are warmer and have an higher sublimation rate of about 15% compared to vials in the centre [1]. This phenomenon results from the combined effects of radiation from external sources (walls, rail) and conduction due to direct contact of the vial with the rail.

Which are the consequences?

The “edge vial effect” results in different thermal histories among the vials and thus in a non-homogeneous final quality of the product.

Why this study and which strategy?

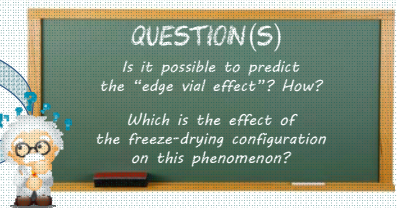
The “edge vial effect” causes...

Heterogeneity within product batch

Issues in process control

Problematic scale-up

Mathematical model of heat transfer in freeze-drying in 3D using COMSOL MULTIPHYSICS



Mathematical model of heat transfer in freeze-drying

Main hypotheses

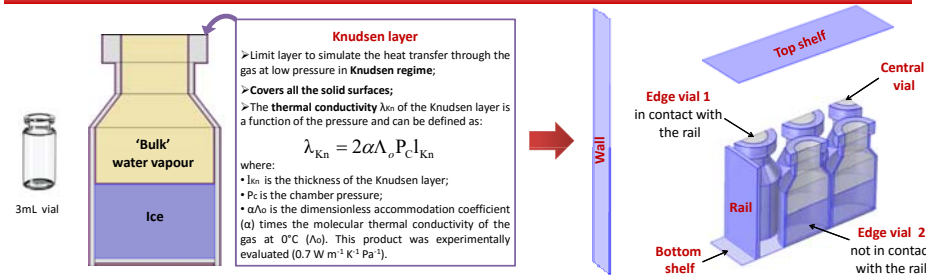
- Pseudo-stationary state: all the heat received from the vial is used for ice sublimation;
- Constant ice thickness in the vials and flat ice-vapour interface;
- Pure water vapour in the drying chamber;
- Heat transfer by convection is negligible.

Relevant parameters

Parameter	Symbol	Value
‘Bulk’ vapour conductivity	λ_w	0.025 [W m ⁻¹ K ⁻¹]
Knudsen layer conductivity	λ_{Kn}	$2 \cdot 10^{-3} P_c$ [W m ⁻¹ K ⁻¹]
Depth of vial bottom curvature	l_w	0.1 [mm]
Knudsen layer thickness	l_{Kn}	0.1 [mm]

From the vial...

...to the system



Heat transfer in solid and gaseous bodies

$$\vec{q}_c = -\lambda_i \nabla T$$

• \vec{q}_c : heat flux by conduction in the solid or gas [W m⁻²];
 • λ_i : thermal conductivity of the body material [W m⁻¹ K⁻¹];
 • ∇T : gradient of temperature [K].

Heat transfer by contact conduction

$$q_{cc} = K_{cc,i} (T_1 - T_2)$$

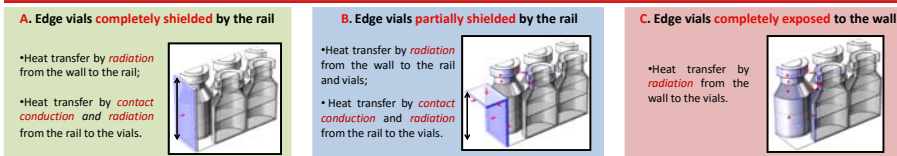
• q_{cc} : heat flux by contact conduction [W m⁻²];
 • $K_{cc,i}$: heat transfer coefficient of contact conduction [W m⁻² K⁻¹];
 • $T_{1,2}$: temperatures of the bodies [K].

Heat transfer by radiation

$$q_r = F_{1 \rightarrow 2} \sigma (T_1^4 - T_2^4)$$

• q_r : heat flux by radiation [W m⁻²];
 • $F_{1 \rightarrow 2}$: visualization factor [-];
 • $T_{1,2}$: temperatures of the bodies [K];
 • σ : Stefan-Boltzmann constant [W m⁻² K⁻⁴].

“Edge vial effect” in different freeze-drying configurations



Experimental procedure

Gravimetric method

- Fill the vials with 1.8ml of purified water...
 - ...weight them to evaluate the initial mass (m_i)...
 - ...freeze-dry them until 30% of ice is sublimated...
 - ...re-weight them to evaluate the final mass (m_f)...
- Mass flow rate
 $\dot{m} = \frac{m_i - m_f}{\text{sublimation time}}$
 \dot{m} : mass flow rate [g s⁻¹].

Sublimation test

- Freezing step: 2h at -50°C;
- Ramp: 1°C/min;
- Sublimation:
 - 9Pa and -25°C for configuration A and C (MillRock freeze-dryer);
 - 6Pa and -40°C and 0°C for configuration B (Aqua-Finn GT6 freeze-dryer).

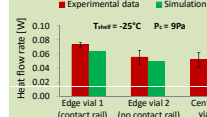
Heat flow rate

$$\dot{Q} = \Delta H \dot{m}$$

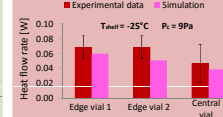
• \dot{Q} : heat flow rate [J s⁻¹];
 • ΔH : latent heat of sublimation [J kg⁻¹].

Model validation

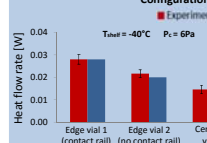
Configuration A – vials fully shielded



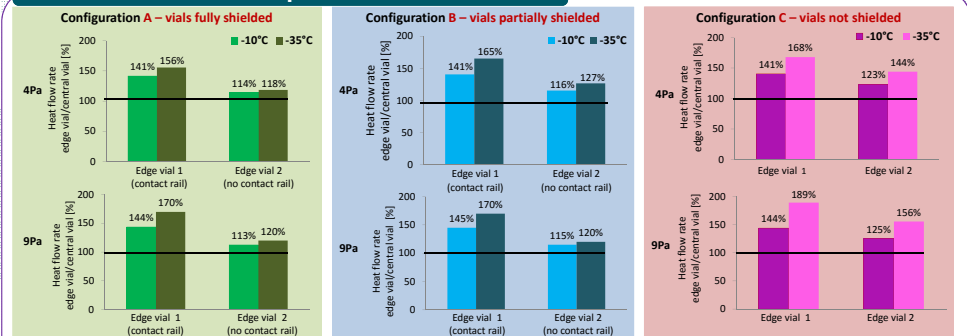
Configuration C – vials not shielded



Configuration B – vials partially shielded



Virtual experiments



Impact of the operating parameters

- The heat flux difference between central and edge vials...
- ... is higher if the shelf temperature is lower (in a range of -10 to -25°C);
- ... is higher if the chamber pressure is higher (in a range of 4 to 9Pa).

Impact of the edge configuration

- Configurations A and B are equivalent (±5%) except at low shelf temperature (-35°C) and pressure (4Pa);
- The best edge configuration appears to be the configuration A, in all the possible combination of operating parameters.

Conclusions and perspective

- ✓ The developed model predicts the heat flow rate in edge and central vials in different freeze-drying configurations;
- ✓ The edge effect is less important if the edge vials are shielded by the rail but not in contact with it;

- ✓ The edge effect is more important at low shelf temperature and high chamber pressure (for a range of -10 to -35°C and 4 to 9Pa);
- ✓ Next step will involve the use of the model as smart tool to predict the “edge vial effect” in freeze-dryers at commercial scale.