

# CHARACTERIZATION OF HEAT TRANSFER THROUGH GAS AND ITS IMPACT ON VIAL HEAT TRANSFER DURING PRIMARY AND SECONDARY DRYINGS

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The importance of heat transfer during the secondary drying stage cannot be overstated as it greatly influences the temperature profile of the material, which has a direct impact on the removal of bound water. Historically, it has been assumed that the heat transfer coefficient ( $K_v$ ) during secondary drying is the same as during primary drying and that most of the heat goes towards drying the material. However, recent studies have challenged these assumptions and have suggested that  $K_v$  should be a function of the moisture content in the chamber, implying that it should be different in primary and secondary drying [1].

Our recent work [2,3] was the first to experimentally test these claims through the lyophilization of various excipients under different operating conditions in primary and secondary drying using laboratory-scale freeze dryers. To estimate the impact of gas conduction on the overall vial heat transfer, we calculated the theoretical heat transfer coefficient of gas conduction ( $K_g$ ) based on scanned images of the vial bottom as shown in **Figure 1**.

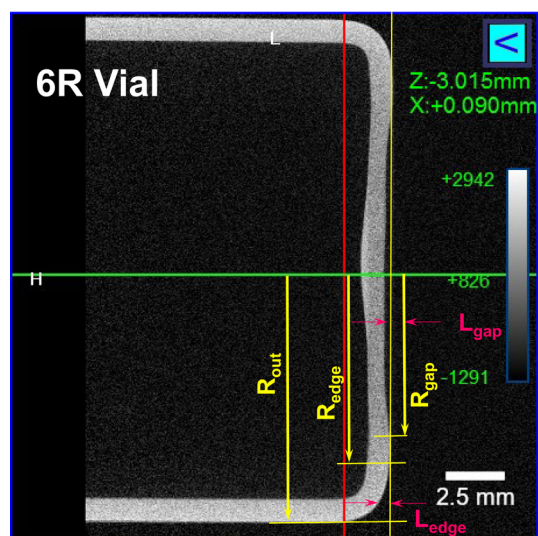
Our findings showed that the heat transfer coefficient during primary drying increases significantly with increasing chamber pressure, regardless of vial type. This trend is likely

due to the high thermal conductivity of water vapor, which depends heavily on pressure. During secondary drying, the vial heat transfer coefficient ( $K_{v, sec}$ ) showed a weak dependence on chamber pressure and was found to be 20-60% of  $K_v$  in primary drying, depending on the chamber pressure [3]. Theoretical calculations of  $K_g$  support these experimental observations, showing a monotonic increase in  $K_g$  with increasing chamber pressure during both primary and secondary drying as shown in **Figure 2**. However,  $K_g$  during secondary drying was noticeably different from that during primary drying due to the lower thermal conductivity, resulting in a smaller magnitude change in  $K_g$  with chamber pressure compared to water vapor.

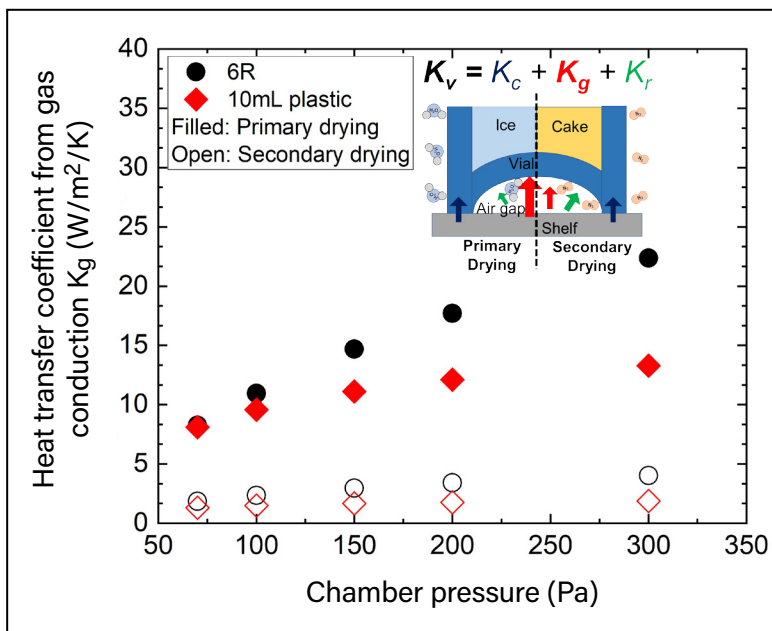
Based on these findings and ongoing measurements of moisture content, a simple-to-use calculator for secondary drying is under development. Further investigation will establish a molecular understanding of desorption kinetics in lyophilization.

## References:

- [1] Sahni, E.K & Pikal, M. (2017). J. Pharm. Sci., 106(3) 779-791.
- [2] Yoon, K. & Narsimhan, V. (2022). J. Pharm. Sci., 111(2), 368-381.
- [3] Yoon, K. & Narsimhan, V. (2023) Int. J. Pharm., 635, 122746.



**Figure 1:** Schematics of scanned geometric parameters for a vial bottom. Image captured with Purdue Imaging Facility instrument.



**Figure 2:** Theoretical heat transfer through gas conduction of 6R and 10ml SiO<sub>2</sub> vial during primary and secondary drying stages at the different chamber pressure ( $70 \text{ mTorr} < P_{ch} < 300 \text{ mTorr}$ ).