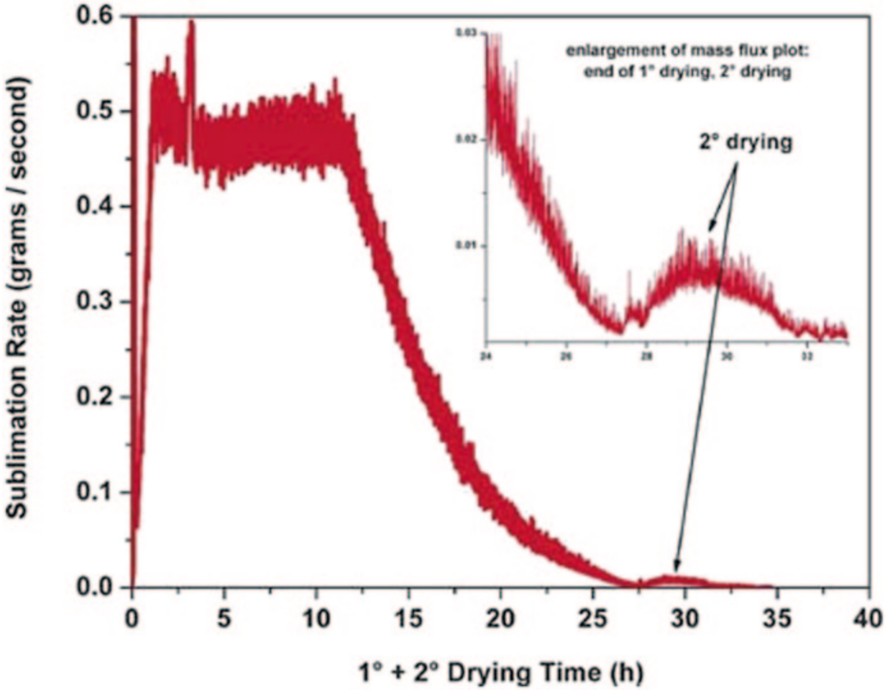

Fig. 4 Mass flow temporal profile over time for a 5 % mannitol formulation in a pilot scale freeze dryer (Adapted with permission from [5])

about 20–30 % higher than that of center vials. The combination of TDLAS mass flow rate measurements and the heat and mass transfer model based on a weighted K_v were employed for nonintrusive, real-time product temperature determinations. It was demonstrated that product temperatures calculated from TDLAS mass flow data were in excellent agreement with thermocouple data in the center vials during product runs with 5, 7.5, or 10 % (w/w) sucrose, mannitol, and glycine, respect tively. TDLAS product temperatures for all freeze-drying runs were within 1–2 °C of "center vial" steady-state thermocouple data [29].

TDLAS has also been applied to the measurement of dry layer mass transfer resistance. By combining the TDLAS and the pore diffusion model, the effective pore radius of the dry layer can be estimated from the sublimation rate and product temperature profiles measured during primary drying. This method does not require solution of the complex heat and mass transfer equations, and has been demonstrated with product runs with 5 % mannitol, sucrose, lactose, 3 % mannitol plus 2 % sucrose, etc. [12].

In addition to the process monitoring, effort has been made to achieve automatic product temperature control to reduce the primary drying time. Kuu et al. developed computer programs to determine the optimal shelf temperature and chamber pressure while ensuring the product temperature profile is below the target temperature