Tunable Diode Laser Adsorption Spectroscopy

TDLAS can be used to continuously measure trace concentrations of selected gases for various applications, and has recently matured into the lyophilization field as a process-monitoring tool. The TDLAS control unit provides two coupled outputs from the same laser, which are connected to two fiber optic collimators mounted on the duct connecting the drying chamber and the condenser. The diode laser light is transmitted through the gas mixture containing water vapor, and the beam's wavelength is adjusted to water vapor absorption lines to accurately measure the absorption [5]. The concentration of water vapor was measured based on the Beer–Lambert's law, and the gas flow velocity can be obtained from the Doppler-shifted water vapor absorption spectrum.

TDLAS was used to measure sublimation rate during the lyophilization process on both a laboratory and a pilot scale freeze dryer [5]. The time integrated sublimation rate obtained from TDLAS was compared to a gravimetric determination of the total weight of water removed based on the mass difference before and after the sublimation. The ratio of ''gravimetric/TDLAS'' measurements of water sublimed was 1.02 ± 0.06, suggesting that this in-line tool can be used for accurate measurements of total amount of water removed. In addition, the application of TDLAS for endpoint detection has been studied for 5% mannitol runs in both laboratory and pilot scale freeze dryers. As shown in Fig. 4, the sublimation rate was about 0.5 g/s during the early primary drying stage, and then gradually decreased to almost zero at the end of primary drying. During secondary drying, a bump in the baseline mass flux was observed with a maximum value of 1.0×10^{-2} g/s, and then dropped to zero at the end of secondary drying. Therefore, the TDLAS can also be used to detect the endpoints of primary and secondary drying for the product run.

TDLAS can be used for a rapid determination of vial heat transfer coefficient based on the sublimation rate profiles. Traditionally, several cycles are needed to be performed at different pressures in order to obtain the pressure-dependent vial heat transfer parameters. Since the sublimation rates can be frequently measured by TDLAS, the pressure effect can be incorporated into one cycle by using step-changes in chamber pressure, which makes it much more efficient to measure vial heat transfer parameters. Kuu et al. showed that both the contact parameter K_{cs} and the separation distance ℓ_v can be rapidly determined using the sublimation rate continuously measured by TDLAS within a short cycle. The determined K_{cs} and ℓ_v values closely fit both the sublimation rate and product temperature profiles, suggesting the validity of the approach employed [11]. Note that the TDLAS measured sublimation rate is the average of all vials in the whole batch, and thus the measured vial heat transfer coefficient using TDLAS is also the average value.

In order to evaluate the drying heterogeneity of vials, position-dependent vial heat transfer coefficients (K_v) were studied using TDLAS during sublimation tests with pure water [29]. The K_v data obtained from TDLAS were found to be comparable with K_v data obtained by the traditional gravimetric procedure. Edge vials were found to run at higher temperatures, which results in that K_v of edge vials was