tosan to make carrier particles for an inhaled insulin formulation [104]. With mannitol as a stabilizer during spray-drying with a Büchi Mini Spray Dryer B-290, their processing conditions were as follows: 0.7 mm two-fluid nozzle, liquid feed rate of 2.5 mL/min, inlet temperature of 160 °C, resulting outlet temperature of 40 °C, and airflow rate of 400 L/h—resulting in approximately 73 % yield. The yields of these studies are typical of the yield values expected from optimal spray-drying of any biopharmaceutical. As discussed in sections "Basics of Spray Drying" and "Lyophilization Versus Spray Drying," this loss of product remains one of the drawbacks of any conventional spray-drying process.

Maltesen et al. (2008) examined several processing parameters including nozzle gas flow rate (7.3–17.5 L min), feed flow rate (1.8–5.25 mL/min), inlet air temperature (75–220 °C), and insulin concentration (5–60 mg/ml), using a Büchi B-290 Spray Dryer equipped with a two-fluid nozzle (7 mm) [31]. They found that the insulin concentration influenced the MMAD, mass median diameter (MMD), yield, tap density, droplet size, HMWP content, and morphology—all of these parameters were positively correlated with insulin concentration except HMWP content which decreased with increasing insulin content. The inlet drying air temperature mainly correlated with the outlet air temperature and the final moisture content; as inlet air temperature increased, outlet air temperature increased and moisture content decreased. The particle density was equally influenced by the insulin concentration and inlet air temperature. Maltesen et al. found that the least important processing parameters were the aspirator rate and feed flow rate, with no significant relationship to any of the parameters studied. As observed by Maltesen et al., particle size properties (such as the MMAD and MMD) are the most difficult powder characteristics to predict due to the numerous influential processing parameters. While insulin concentration had the greatest influence on the MMAD and MMD, at high insulin concentrations its influence on the MMAD plateaued, and drying conditions became the controller of particle aerodynamics. This study is a reminder that formulation choices, such as drug solubility, concentration, and excipient choices, should carry equal (and often more weight) than drying parameters with formulating spray-dried biopharmaceuticals.

Concluding Remarks

In recent years, spray-drying has become popular in the preparation of powdered biopharmaceuticals. The root of its popularity lies in the diversity of equipment, excipients, and process conditions available to fine-tune particle characteristics. The introduction of new spray nozzles, alternative spray-drying methods, and more efficient particle collection devices has broadened the range of biopharmaceuticals amenable to the spray-drying process. However, because of the diversity of the research, a more systematic approach of processing parameters is warranted, particularly for the selection of appropriate solvents and excipients. In contrast, freeze-drying offers the advantage of a longer, proven history of extending the storage life