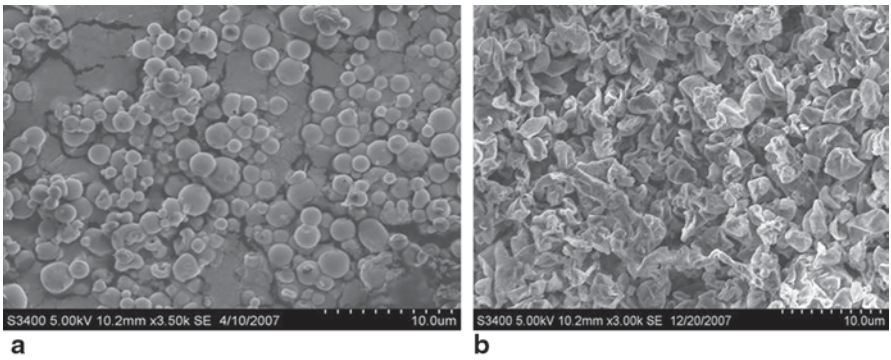

Fig. 3 Representative scanning electron microscope images of spray-dried particles. **a** PLGA/propranolol/trehalose particles sprayed at an inlet temperature of 55 °C, outlet temperature of 38–40 °C, airflow rate of 800 L/h, and pump rate of 3 %, and **b** blank PLGA particles sprayed at an inlet temperature of 55 °C, outlet temperature of 41–43 °C, airflow rate of 600 L/h, and pump rate of 6 %. PLGA poly(lactic-co-glycolic acid)

Alternative Spray-Drying Methods

Conventional spray-drying removes a solvent from a feed stream using heated gas leaving a dry particulate product, but spray-drying has evolved to include other drying processes which are applicable to the pharmaceutical industry. A solvent is not the only component of a feed stream which can be removed; heat can also be removed. Removing heat from the feed stream of a melted material by spraying into a stream of cooled gas is called spray-congealing or spray-cooling and also results in a solidified product [14–16]. Generally, disk and two-fluid atomizers are utilized for spray-cooling/-congealing, but the liquid feed, atomizer, and spray gas must be maintained at the melt temperature of the feed stream, requiring auxiliary equipment to maintain the feed material at the melt temperature. In the drying chamber, a stream of cooled gas is delivered to remove heat from the sample, and a traditional cyclone collector is used. This process is used in the pharmaceutical industry to form solid lipid composites and other hot-melt materials. Spray-cooling has limited use in the biopharmaceutical field to date because the constituents of the feed stream must be stable at the melt temperature of the matrix compound. For those peptides and proteins that are thermally stable, this technique has found some application [17–19]. Another option for spray-cooling biopharmaceuticals is to use a low melting point lipid as was done with milk thistle (*Silybum marianum*) to increase its oral bioavailability [20].

Another alternative spray-drying methodology, which is particularly popular in the preparation of biopharmaceuticals, is spray-freeze-drying [21–23]. Spray-freeze-drying is similar to traditional spray-drying in that the feed stream, which includes a solute dissolved in water, is sprayed with one of the standard atomizers