viscous flow) to the average diameter of the pore created by the sublimation process (74). Many of the cosolvents selected for freeze-drying increase sublimation rate because they have higher vapor pressures than water and hence an expected larger driving force for sublimation because the latter depends on this vapor pressure difference (75).

The potential acceleration of the freeze-drying rates of aqueous solutions of lactose and sucrose with 5% and 10% aqueous solutions of *tert*-butanol has been studied (76). It was found that both lactose and sucrose solutions could be successfully freeze-dried in the presence of *tert*-butanol at considerably higher shelf temperatures than corresponding aqueous solutions of either lactose or sucrose. The drying rates were significantly increased when using the *tert*-butanol as a cosolvent. The drying times were decreased by approximately 50% when drying sucrose in the presence of *tert*-butanol. The collapse temperature for the frozen solutions appeared to increase when *tert*-butanol was present. The *tert*-butanol readily froze and remained frozen during the primary drying phase. The *tert*-butanol sublimed during primary drying and created a porous structure that facilitated the mass transfer of water vapor due to decreased cake resistance. The resulting dried cakes exhibited significantly increased surface areas. Freeze-drying of a similar amorphous carbohydrate such as a lactose base formulation from a *tert*-butanol/water cosolvent (e.g., CAVERJECT Sterile Powder) also produces a very porous cake structure, as illustrated by the SEM shown in Figure 3. Alternatively, it was demonstrated that using other organic cosolvents at a 5% level (e.g., methanol, ethanol, isopropanol, acetone, *n*-butanol, or dioxane) that do not freeze under operating conditions for conventional commercial freeze-dryers produced unacceptable freeze-dried cakes of either lactose or sucrose due to boiling of solvent and cake collapse.

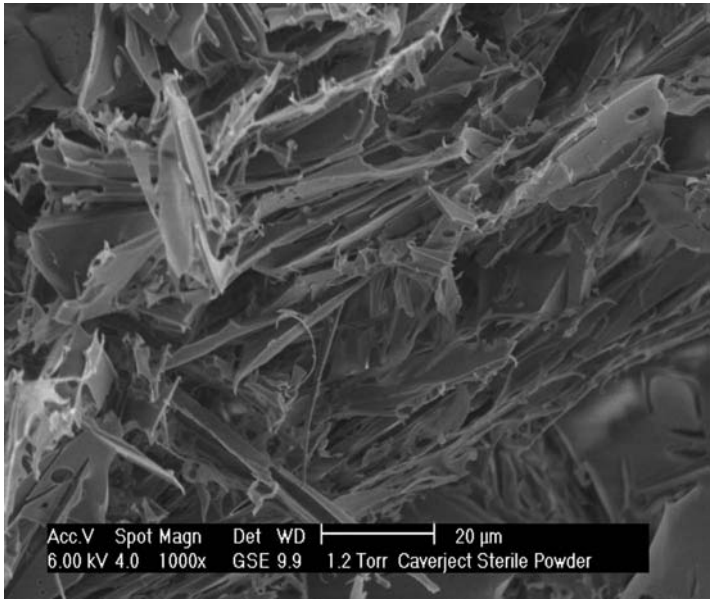

FIGURE 3 SEM picture of CAVERJECT Sterile Powder that has been lyophilized from a 20% vol/vol *tert*-butanol/water solution. *Abbreviation*: SEM, scanning electron microscopy.