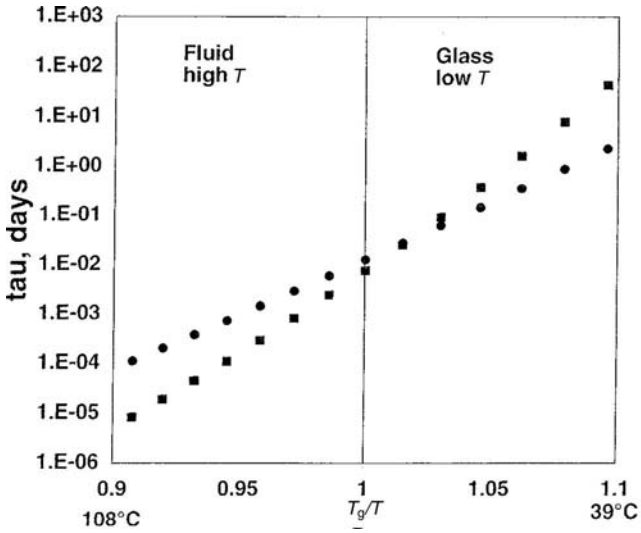

FIGURE 7 Comparison of structural relaxation times for fragile and strong glasses with glass transition temperatures of 70°C. The data were calculated using input data characteristic of sucrose except for the strength parameter, *D*. Key: circles = strong glass ($D = 23$), squares = fragile glass ($D = 7$).

glass). Above the glass transition temperature in the fluid state, the strong glass has the longer relaxation time, but in the glassy state the fragile glass has a longer relaxation time. Thus, assuming that pharmaceutical stability is correlated with structural relaxation, a protein formulation above T_g would be more stable in the strong glass, but below T_g the fragile glass would provide better stability. For the strong glass, temperature dependence is nearly Arrhenius both above and below T_g. For the fragile glass, significant deviations from linearity in the plot indicate non-Arrhenius temperature dependence both above and below T_g, although the non-Arrhenius behavior is more pronounced above T_g. To the extent that the thermal history of the glass will impact the value of γ_c, thermal history will impact the value of relaxation time. Thus, one might speculate that thermal history may well impact pharmaceutical stability in a glassy formulation. Evidence for such an effect is limited, but several studies do suggest greater chemical stability for samples annealed below T_g (51,52).

Structural relaxation times determined from enthalpy relaxation studies with sucrose and trehalose (39,53) are given in Figure 8. The structural relaxation times observed are qualitatively similar to those estimated for the fragile glass example in Figure 7. While there is considerable scatter in the data, it seems clear that the temperature dependence for sucrose is nonlinear and therefore non-Arrhenius. Insufficient data are available for trehalose to judge linearity. The trehalose structural relaxation times are lower than those for sucrose at the same T_g/T, indicating different fragility and/or a different value of γ_c.