



FIGURE 1 Free induction decay of proton in freeze-dried γ -globulin formulation containing dextran at 10°C (A) and 60°C (B) at 60% RH. *Abbreviation:* RH, relative humidity.

proton in freeze-dried formulation containing γ -globulin as a model protein drug and dextran (molecular weight of 10 kDa) as a polymer excipient, measured by a low-frequency NMR using “solid echo” in the detection stage (26). The FID shows two relaxation processes at 10°C and 60% relative humidity (RH) (Fig. 1A); a slower decay described by the Lorentzian equation (equation 1) and a faster decay described by a Gaussian-type equation (the Abragam equation, equation 2 with a constant c of 0.12). This slower decay is attributed to protons with higher mobility, that is, water protons, and the faster decay is attributed to protons with lower mobility, that is, protons of γ -globulin and dextran. The contribution of protein protons to the FID is not significant because the content of protein was 50 times less than that of dextran. Therefore, the Abragam decay can be considered to be due to dextran protons. The observed FID is describable by an equation representing the sum of the Abragam and Lorentzian equations (equation 3). The T_2 of water protons can be calculated from the FID signals at the latter stage. Subsequently, the T_2 of dextran proton with lower mobility can be calculated from the FID signals at the former stage by inserting the calculated T_2 of water proton into equation (3).

$$F(t) = A \exp\left(-\frac{t}{T_{2(\text{hm})}}\right) \quad (1)$$

$$F(t) = A \exp\left(-\frac{t^2}{2T_{2(\text{lm})}^2}\right) \frac{\sin(ct)}{ct} \quad (2)$$

$$F(t) = (1 - P_{\text{hm}}) \exp\left(-\frac{t^2}{2T_{2(\text{lm})}^2}\right) \frac{\sin(ct)}{ct} + P_{\text{hm}} \exp\left(-\frac{t}{T_{2(\text{hm})}}\right) \quad (3)$$

where $T_{2(\text{hm})}$ and $T_{2(\text{lm})}$ are the spin-spin relaxation times of protons with higher mobility and lower mobility, respectively. P_{hm} is the proportion of protons with higher mobility.