Synopsis of Original Research Paper

Evaluation of molecular state of cosmetic nanoparticles dispersed in water by suspended-state NMR spectroscopy

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We investigated the formation and stabilization mechanisms of drug/poloxamer 407 (P407) nanosuspensions by suspended-state NMR spectroscopy. Indomethacin (IMC) and piroxicam (PXC) used as models of poorly water-soluble drugs are nonsteroidal anti-inflammatory drugs. For IMC, the three different polymorphs of γ-form, α-form and amorphous form were used to evaluate the effect of initial crystal form of drug. P407, a tri-block copolymer composed of polyethylene glycol $(PEG)_{101}$-polypropyleneoxide $(PPO)_{56}$-PEG_{101}, was used as a stabilizer. Mean volume diameter in every suspension prepared with wet-milling was 240-270 nm with unimodal size distribution. Cryogenic transmission electron microscopy images of nanoparticles obtained using γ-form IMC indicated a rhombic-plate shape. In contrast, needle-like nanoparticles were observed in the nanosuspensions of α-form and amorphous IMC. The nanoparticle obtained with PXC showed an irregular shape. Suspended-state cross polarization ^{13}C NMR measurements directly detected the molecular states of drug in nanosuspensions. IMC existed in its initial crystal form when γ-form and α-form IMC were used; amorphous IMC transformed into crystalline α-form IMC. The PXC in the nanoparticle existed as the mixture of amorphous and crystalline states. Suspended-state ^{13}C pulse saturation transfer NMR measurements revealed the molecular state of P407 in the nanosuspensions. P407 could only adsorb to the surface of the IMC nanoparticles because IMC existed as crystals in the GM suspension. Conversely, the larger numbers of P407 were involved in the PXC nanoparticles where some of PXC existed as amorphous state. The difference between the nanoparticle structures in the IMC and PXC systems could be a consequence of the interaction strength of each drug with P407. The peaks of the PPO chains of P407 in the spectra of GM suspensions were split at lower and higher magnetic fields. The equilibrium of P407 between micelle and nanoparticle was slower than the NMR time scale, which could stabilize the dispersion of the nanoparticles in water.