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Effect of Salts on Solubility, Absorption and Stability of Food Ingredients Evaluated by Noninvasive Analytical Methods

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Summary

Organic salts offer advantages over the corresponding free acid or base in terms of solubility and dissolution. However, the potential disadvantages including hygroscopic and deliquescent properties, result in poor stability of the salt formulations. Recently, multiple-quantum magic-angle-spinning (MQMAS) method has been reported as a new solid-state NMR technique in order to observe the molecular states of half-integer quadrupolar nuclei directly. In the present study, we have conducted ^{23}Na (I=3/2)-MQMAS NMR experiment on four different hydrates of sodium naproxen (SN): anhydrous (ASN), monohydrated (MSN), dihydrated (DSN), and tetrahydrated (TSN) forms. Conventional ^{23}Na-MAS NMR spectrum of ASN showed broad peaks because of the nuclear quadrupole coupling of ^{23}Na. On the other hand, two well-separated peaks were observed on the two-dimensional ^{23}Na-MQMAS NMR spectrum of ASN. The isotropic chemical shift (δ_{CS}) and the quadrupolar parameter (P_Q) of the peaks derived from projection onto the chemical shift (CS) and quadrupolar induced shift (QIS) axes respectively, were different each other. From the results of X-ray crystallographic analysis, there are two different types of sodium nuclei in a crystal lattice of ASN. They were well reflected on the two peaks in MQMAS NMR spectrum. ^{23}Na-MQMAS NMR measurements were carried out on the other hydrates. Two peaks were observed in DSN spectrum, while MSN and TSN showed one peak in each spectrum. The values of δ_{CS} and P_Q were different among the four hydrates. Furthermore, the molecular states of sodium nuclei in the 1.0% MSN formulation, which were not observed by powder X-ray diffraction and ^{13}C solid state NMR measurements, were accurately evaluated by ^{23}Na-MQMAS NMR technique. In conclusion, four different hydrates of sodium naproxen were clearly distinguished by ^{23}Na-MQMAS NMR measurement. MQMAS NMR spectroscopy would be a useful method for evaluating molecular states of organic salts containing quadrupolar nuclei in the formulation as well as the product, especially at the low dose.