Interaction of epicatechin gallate, a green tea polyphenol, with phospholipid membranes as revealed by solid-state NMR spectroscopy

Yoshinori Uekusa[2], Miya Kamihira-Ishijima[2], Osamu Sugimoto[2], Takeshi Ishii[2], Shigenori Kumazawa[2], Ken-ichi Tanji[2], Akira Naito[3], and Tsutomu Nakayama[1,2]

[1]Global COE Program, [2]Department of Food and Nutritional Sciences, Graduate School of Nutritional and Environmental Sciences, University of Shizuoka, [3]Graduate School of Engineering, Yokohama National University

Epicatechin gallate (ECg), a galloyl-type green tea catechin, has various physiological effects. It has been speculated that ECg interacts with the biological phospholipid membranes to exert their activities. Our previous NOESY study using solution NMR spectroscopy demonstrated that ECg interacts with the surface of phospholipid bilayers. However, the dynamic behavior of ECg in the phospholipid bilayers, especially the mobility and molecular arrangement of the galloyl moiety, has not been clarified. In this study, we synthesized [^{13}C]-ECg, in which the carbonyl carbon of the galloyl moiety was labeled with the isotope, and analyzed it in the presence of the phospholipids by solid-state NMR spectroscopy. Solid-state ^{31}P NMR analysis indicated that ECg changes the gel-to-liquid-crystalline phase transition temperature of DMPC bilayers as well as the dynamics and mobility of the phospholipids. In the solid-state ^{13}C NMR analysis under static conditions, the [^{13}C]-ECg carbonyl carbon signal exhibited an axially symmetric powder pattern. This indicates that the ECg molecules rotate about an axis tilting at a constant angle to the bilayer normal. The accurate intermolecular–interatomic distance between the labeled carbonyl carbon of [^{13}C]-ECg and the phosphorus of the phospholipid was determined to be 5.3 ± 0.1 Å by ^{13}C–^{31}P rotational echo double resonance (REDOR) measurements. On the basis of the solid-state and the previous solution NMR analyses, the galloyl moiety contributes to hydrophobicity, and consequently to high affinity of galloyl-catechins for the phospholipid membranes, as well as to stabilization of catechin molecules in the bilayers by cation–π interaction between π electron of the galloyl ring and the quaternary amine of the choline in phospholipid head-group. We conclude that the existence of galloyl moiety effectively enhances the ECg–phospholipid membranes interaction, leading to high biological affinities.