at 60 °C. This experiment was designed to evaluate the effect of utilizing different lyoprotectants (i.e., sugars) on the storage stability of DLPC (18:3) samples. It was hypothesized that the rate of degradation for the DLPC–sugar samples would correlate with the glass transition temperature of the sugars, and that the samples lyophilized in trehalose (113 °C), sucrose (72 °C), and sorbitol (−3 °C) would exhibit slow, intermediate, and fast degradation rates, respectively [183, 244]. In contrast, the rate of degradation for DLPC formulated with trehalose, sucrose, and sorbitol was 0.069 day^{-1}, 0.024, and 0.021 day^{-1} which is not consistent with a predominant role of glass transition temperature on lipid degradation. One possible explanation for this surprising result involves the structure of the lyophilized cakes. At 60 °C, the DLPC–trehalose cakes maintained their structure with no visible change in the cake. Conversely, the DLPC–sucrose cakes collapsed over time and the DLPC–sorbitol cakes collapsed during the lyophilization process itself. It is possible that the porosity of the noncollapsed trehalose cakes allowed for the greater permeation of the headspace gases, which promoted DLPC degradation. It was also observed that the degradation of DLPC plateaued, that is, the rate of degradation slowed considerably for the DLPC–sugar samples. Perhaps the change in the rate of degradation reflects the rates of oxidation for the lipid on the surface versus the interior of the cake. The lipid on the surface of the lyophilized cake is more exposed to the headspace gases, (e.g., oxygen) in the lyophilization vial and would be expected to be more susceptible to peroxidation than the lipid embedded in the cake interior. Alternatively, the decomposition of preexisting lipid hydroperoxides could have been playing a role. Both iron (II) and iron (III) are known to catalyze the decomposition of hydroperoxides leading to the formation of alkoxyl and peroxyl lipid radicals which can further propagate the reactions leading to oxidative degradation [220]. Thus, the change in the rate of DLPC degradation could be the result of depletion of the preexisting hydroperoxides (i.e., the source of alkoxyl and peroxyl radicals). Further studies are being conducted to investigate these hypotheses.

Hydrolysis

The hydrolysis of lipids leads to the formation of lysophospholipids and fatty acids [245]. The carboxy esters which form the connection between the glycerol backbone and the fatty acid tails are most susceptible to hydrolytic degradation. Lysophospholipids can also be further hydrolyzed leading to the formation of glycerophospho compounds and fatty acids [245]. Hydrolysis can be acid or base catalyzed. Although several studies have examined the factors that affect the hydrolysis of lipids in aqueous formulations, it is difficult to compare the results due to the use of different liposomal systems and conditions. Temperature, pH, and the use of anionic/cationic lipids are the factors which have been shown to have the largest effect on the rate of hydrolysis [246].