water contents (< 1 % water content) [193], which is the condition normally used for the preparation of dried nonviral lipid/DNA formulations [102, 178, 179, 185]. Our preliminary attempt on the effect of low (Initial %, *w/w*: ~ 0.41 ± 0.06) and moderate (Initial %, *w/w*: ~ 1.13 ± 0.15) RM on the stability of dried plasmid DNA-based formulations containing trehalose and chelator (DTPA) are shown in Fig. 4a, b. Our findings show that very dry DNA (< 0.5 %, *w/w*) was less prone to oxidative damage than moderate moisture-containing (1.51 %, *w/w*) formulations within 8 weeks under storage conditions of forced degradation (e.g., 40 °C; see Figs. 4a, b). Furthermore, DNA recovery (SC content, ROS levels) as well as biological (transfection, data not shown) was not affected by higher levels of moisture when formulations were stored at room temperature (Fig. 4c, d). Although DNA purity (≥ 90 % SC) for up to 6 months at 25 °C/60 % RH has been documented in lyophilized cGMP-DNA preparations with relatively high RM (2.41 %), these increases in time (from initial 0.7 %) were due to rubber stoppers [194] that exceeded water-content specifications [112]. Although these results are not ample to provide definitive conclusions regarding the role of water in preserving DNA during storage, our data clearly show that DNA degradation (higher levels of ROS and loss in SC content) was exacerbated in formulations with higher levels of RM at temperatures approaching the glass transition temperature (Fig. 4a–d). The fact that ROS are still active in the dried cake [115, 178, 183, 185] and considering that water [191] and traces of transition metal contaminants are a potential source of ROS together with the role of molecular oxygen in the propagation step of the oxidative damage in DNA samples [111, 191, 195, 196], we suggest that levels of RM need to be optimized (and maximize T_g) in combination with the aforementioned strategies to minimize formation of ROS (molecular oxygen displacement, including chelators and/or antioxidants, using metal-free materials as possible) during prolonged storage in order to prevent free radical-mediated damage to DNA-based pharmaceuticals.

Lipids

Liposomes are bilayer vesicles that are composed of cationic, anionic, and/or neutral lipids. Liposomes are often used as delivery vehicles; currently 12 liposomal products are being marketed which deliver small molecule therapeutics [197]. The commercially available products, which employ lipid-based delivery vehicles, are typically composed of saturated, hydrogenated, or singly unsaturated lipids. These lipids are primarily used due to their greater chemical stability. Although this chapter examines the chemical stability of lipids with a focus on pharmaceutically relevant work, other studies have investigated the stability of lipids in relation to food and beverage products [198–204].

The main degradation pathways that are of concern for liposomal formulations are peroxidation and hydrolysis. Peroxidation, which is a complex free radical-mediated process, consists of three distinct steps: initiation, propagation, and termination [205, 206]. Peroxidation initiation involves the abstraction of a hydrogen atom from the fatty acid tail of a lipid resulting in the formation of lipid radicals. The ease with which the hydrogen can be abstracted is related to the number of unsaturated sites