ester between the choline group and the glycerol backbone, and accordingly have greater resistance to hydrolysis and enzymatic degradation. However, these synthetic lipids may present a toxicity associated with the inability to metabolize ether linkages.

Structure and Properties of Lipid Bilayer

Mechanism of Formation of Lipid Bilayers

Phospholipids, by virtue of their hydrophobic acyl hydrocarbon chains and the hydrophilic polar headgroup are amphipathic molecules, with a hydrophilic–lipophilic balance (HLB) number generally around 4–6. As such, molecules of PC are not soluble in water in the accepted sense, and in aqueous media, they align themselves closely into planar bilayer sheets to minimize the unfavorable interactions between the bulk aqueous phase and the long hydrocarbon fatty acid chains. Such interactions are completely eliminated when the sheets fold on themselves to form closed sealed vesicles. Their geometry dictates that phospholipids form lamellar bilayers, owing to the double tails, in contrast to most other surfactants, whose geometry (single tails) leads to micelles. Under certain conditions, an alternate form, the inverse hexagonal phase (H_{II}), can exist, wherein water is entrapped as cylinders surrounded by the polar headgroups of the lipid while the tail groups fill the interstitial regions of the hexagonal lattice. This can be prominent at high lipid/water ratios (>20% lipid), particularly for PE with unsaturated fatty acyl chains (due to its small headgroup). The kinetics of the lamellar (L_α) to H_{II} phase transition has been studied by time resolved X-ray diffraction techniques (Tate et al., 1992). The H_{II} and other phases could be transient intermediates on hydration of phospholipids.

Temperature Effect and Phase Transitions

At different temperatures, phospholipid bilayer membranes can exist in different phases and states of fluidity. This aspect of the order/disorder properties of membranes can be complex. For example, fully hydrated distearoyl phosphatidyl choline (DSPC) undergoes as many as three transitions. Two transitions, a pretransition at 51°C (ΔH = 1.3 kcal/mol) and the main transition at 55°C (ΔH = 10.8 kcal/mol), are well known. An additional non-reversible subtransition around 30°C can also be observed upon prolonged refrigerated storage (Mattai et al., 1987). The pretransition involves a *rippling* or undulation of the lipid bilayer (Cevc, 1991). The main phase transition is the most relevant and general phenomenon, and reflects the passage of the membrane from a tightly ordered *gel* or *solid* phase, to a fluid phase. The fluid phase retains some order and is hence termed a liquid crystalline phase, but the freedom of movement of individual molecules (in terms of translational movement and acyl chain conformational changes) is higher than in the gel phase. As the temperature increases, the fatty acid chains tend to adopt conformations other than the all-trans straight chain configuration, such as the gauche conformation state. This has the effect of expanding the area occupied by the chains, reducing the overall length of the hydrocarbon chains, and decreasing the bilayer thickness on transition from a gel to a liquid crystalline phase. For single-component systems, especially for saturated diacyl phospholipids of chain length C_{12}–C_{20}, the transition occurs over a narrow temperature range above room temperature, with the melting temperature (T_m) increasing with increasing chain length. A theoretical expression of the dependence of T_m on chain length has been devised by Marsh (1991), wherein the incremental effects of methylene groups on changes in transition entropy and enthalpy are accounted for. Detailed analysis of the transition region reveals strong density fluctuations, and it has been suggested from computer simulations that transient domains form on a nanoscale, that is, domains of fluid lipid form within the gel phase, or domains of gel-phase lipid form within the fluid phase, just before or after the crystallization temperature (T_c), respectively (Mouritsen and Jorgensen, 1993). An increase in volume is associated with the gel to liquid crystalline phase, with ΔV = 15.2, 22.5, 30.0, and 27.4 mL/mol for dimyristoyl phosphatidyl ethanolamine (DMPE), dipalmitoyl phosphatidyl ethanolamine (DPPE), distearoyl