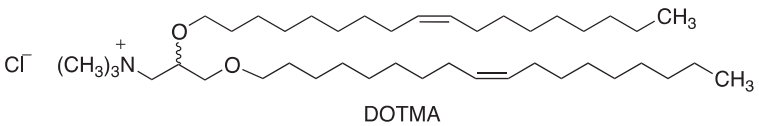
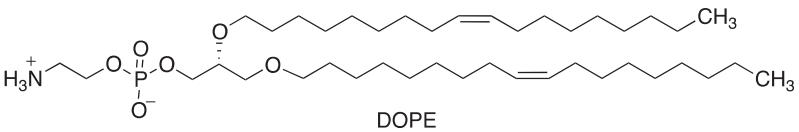
wall breast cancers. Similarly, Lipoplatin® (liposomal cisplatin) is a PEGylated formulation used for treatment of epithelial malignancies such as lung, head and neck, ovarian, bladder, and testicular cancer.

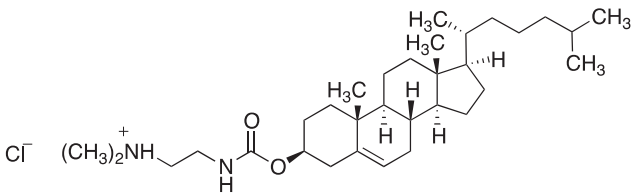
Cationic liposomes have been studied as non-viral vectors in gene therapy and are formed by positively charged amphiphilic molecules whose positive charges interact electrostatically with negative charges in DNA phosphate groups, forming complexes that are capable of entering the cells. Some of the positively charged amphiphilic molecules (cationic lipids) used to this purpose are DOTMA, DOPE and DC-Chol.



DOTMA



DOPE



DC-Chol

The inherent target selectivity of "stealth" liposomes, based on the preferential accumulation and leaking into the tumor vascular bed, can be dramatically enhanced by their chemical coupling to tumor-specific Abs, antibody fragments, or other targeting moieties—essentially any molecule that selectively recognizes and binds to target antigens or receptors overexpressed or selectively expressed on cancer cells. Vascular-targeted liposomes are based on the fact that endothelial cells in the angiogenic vessels within solid tumors express several proteins that are absent or barely detectable in established blood vessels. Preclinical studies have been conducted on numerous liposome-based agents actively targeted to tumor neovasculature. The targets for these formulations have included membrane type 1 matrix metalloproteinase, endoglin (CD105), vascular cell adhesion molecule-1 (CD106), epithelial cell adhesion molecule (CD326), $\alpha v\beta 3$ integrin (CD51/CD61), and aminopeptidase N (CD13). CD13 has become widely recognized as a rational target for therapeutic development,[100] and several NGR-conjugated agents are now in preclinical and clinical development. One example of this approach is the NGR–peptide-targeted liposomal doxorubicin (TVT-DOX), in which the linear peptide containing the asparagine–glycine–arginine motif (NGR) specifically binds to CD13-expressing cells (Figure 13.44).[101]

Antibody-targeted immunoliposomes bear the corresponding antibody covalently coupled either to the reactive phospholipids in the membrane or to the PEG hydroxy groups (Figure 13.45). Alternatively, they may be hydrophobically anchored into the liposomal membrane after being modified