applied in the treatment of skin diseases, an amount of 20% to 30% of SAAs appears to be the threshold of acceptance in dermal use.

36.2.2 Cosurfactants

Mostly MEs contain co-SAAs to sufficiently lower the oil–water interfacial tension and to fluidize the interfacial film [6]. They are amphiphilic molecules accumulating at the interfacial layer, with the SAA thereby affecting the interfacial structure, disrupting the liquid crystalline phases, promoting drug solubility, and expanding the one-phase region in the phase diagram [6, 24]. They also modify the chemical composition and relative polarities of the phases by partitioning themselves between lipophilic and hydrophilic phases [6]. Different alcohols (such as ethanol, butanol, propylene glycol, pentylene glycol [1,2-pentandiol], and glycerol) [12, 25, 26], polyethylene glycols (PEGs) (such as PEG 400) [1], and nonionic SAAs (such as diethylene glycol monoethyl ether [Transcutol P]) [14, 27] have been used as co-SAAs in the formulation of MEs. Unlike the medium-chain alcohols, which are potentially toxic/irritating to the skin, alkanediols and alkanetriols are nontoxic co-SAAs but, due to their extreme hydrophilic nature, they are used at high amounts to produce MEs. Generally, however, nonalcohol co-SAAs are promoted for the formulation of MEs [6, 28, 29]. As a result of the low toxicity and irritancy and biodegradability of the nonionic SAAs, the interest in using them both as a SAA and as a co-SAA is increasing [30]. On the other hand, some twin-tailed SAAs such as AOT are capable of forming MEs by themselves and they don't need the addition of co-SAAs [1].

36.2.3 Oil Phases

Several lipophilic compounds such as fatty acids (e.g. oleic acid) [14], fatty acid esters (e.g. isopropyl myristate [IPM], isopropyl palmitate, ethyl oleate, and decyl oleate) [22, 30, 31], alcohols, medium-chain triglycerides (e.g. Miglyol 812) [10, 32], terpenes (e.g. menthol and limonene) [15], and vegetable oils (e.g. jojoba oil) [33] have been used in the formulation of MEs. A lipophilic component is mostly selected based on its drug solubilization capacity and penetration-enhancing properties [22]. The ability of the oil to produce a broader ME region is also important, though fulfilling both requirements (high drug loading capacity and producing a broader ME region) by a single oil component is difficult. Sometimes a mixture of lipophilic components is used to meet these requirements [6]. It has been shown that, compared to high molecular volume, oils with low molecular volume such as fatty acid esters and medium-chain triglycerides improve the solubilization efficiency of SAAs possibly by penetrating the interfacial monolayer and providing optimal film curvature [30]. As a result they are easily microemulsified and give a wider homogeneity, unlike oils with long hydrocarbon chains such as soybean oil [6].

36.2.4 Penetration Modifiers and Solubilizers

MEs often contain cosolvents to increase the solubility of the drug and to stabilize the dispersed phase [24]. Besides, chemical penetration enhancers such as oleic acid (also used as a lipophilic phase) [12, 34], N-methyl-pyrrolidone [35], terpenes [36], dimethyl sulfoxide (DMSO) [37], and propylene glycol may be incorporated in the ME formulations. Nevertheless, the necessity of these ingredients is still contentious because of the superior penetration properties of the vehicle ME itself. Solubilizers such as β-cyclodextrin have also been used in MEs.

36.3 CHARACTERIZATION

Combinations of various complementary techniques have been used to fully characterize MEs. The physicochemical characterization of MEs include phase stability and phase behavior, microstructure, dimension (size and distribution), shape (or conformation), surface features (specific area, charge and distribution), local molecular arrangements, interactions, and dynamics. Among these