the standard vehicle ointment. The colloidal carrier systems significantly enhanced the penetration profile of tacrolimus ($p < 0.01$). High amounts of drug loaded in the MEs penetrated the target site in a short period of time.

36.4.7 Other Drugs

Several antiacne drugs including antimicrobial agents like basil oil [114], tea tree oil [115], retinoic acid [25], and azelaic acid [116, 117], as well as some antibiotics, have been incorporated into MEs. Bhatia et al. developed an ME formulation for the transfollicular delivery of adapalene, a synthetic analog of retinol used for the treatment of acne [76]. Confocal laser scanning microscopy images suggested the transfollicular permeation of the ME. The microstructure was also shown to affect drug penetration into hair follicles (bicontinuous ME enhanced the drug penetration compared to o/w ME). The proposed transfollicular pathway of MEs might be advantageous for acne treatment.

Dermal delivery of antioxidants plays a role in prophylaxis and treatment of ultraviolet-induced damage of the skin such as photoaging and photocarcinogenesis, which are related to increased levels of free radicals. An effective skin protection by ascorbyl palmitate, incorporated into an ME, has been demonstrated [117], but also α-tocopherol is in use [119].

8-Methoxsalen (8-MOP), a photoactive furocoumarin, has been widely used for the treatment of hyperproliferative skin diseases such as psoriasis. The cutaneous accumulation and *in vitro* penetration on newborn pig skin of 8-MOP–loaded MEs containing varying amounts of SAA, IPM, and water were investigated [120]. All MEs exhibited an increase in both parameters compared to a saturated IPM solution and a clinically used aqueous solution. Since 8-MOP is effective in psoriasis therapy, retaining of the drug in the skin is required and can be realized by varying the composition of the MEs.

ME-based transdermal delivery has also been investigated for the administration of a number of other classes of drugs, including beta-blockers, antihypertensives, antiparkinsonian agents, antivirals, and others. Kemken et al. studied the pharmacodynamic effects of several beta-blockers incorporated into water-free ME preformulations [121]. The vehicles were saturated with the drugs and, after application under occlusion, water uptake from the skin leads to *in situ* formation of water containing MEs, decreasing the solubility of the lipophilic drugs (therefore supersaturated). The observed high pharmacodynamic effects were assumed to be due to rising thermodynamic activity as the driving force for enhanced dermal drug uptake. Trotta et al. studied the *in vitro* skin permeation of felodipine loaded in o/w MEs [122]. Keeping the amount of the other phases nearly constant, it was shown that drug flux depends on the composition of the lipophilic phase. The ME system with the highest drug solubility could favor permeability, probably due to the droplets of the internal phase acting as an effective drug reservoir.

In vitro (using hairless mouse skin) as well as clinical studies have shown the use of MEs for the transdermal delivery of apomorphine in the treatment of Parkinson disease [26, 123]. In the former study, lipophilic apomorphine–octanoate ion pairs were formed to improve drug permeability [26]. The *in vivo* steady-state plasma concentration was estimated from the *in vitro* steady-state flux, suggesting the future *in vivo* application. The *in vivo* studies on Parkinson disease patients also demonstrated the clinical efficacy and long action of ME-mediated transdermal delivery of apomorphine [123].

ME has been investigated as a possible carrier for transdermal delivery of theophylline using oleic acid and Cremophor RH40/Labrasol (1:2) as the oil phase and SAA/co-SAA, respectively [124]. The *in vivo* pharmacokinetic study using rabbits indicated that $AUC_{0\rightarrow\infty}$ of transdermal administration was 1.65-fold higher than that of oral solution administration. In another study, the potential application of ME containing oleic acid, Cremorphor EL, and ethanol was investigated for the dermal delivery of penciclovir [125]. The optimized ME formulation significantly increased the permeation of penciclovir through excised mouse skins compared to the commercial cream.