38.2 LIPID-BASED VESICLES (LIPOSOMES)

38.2.1 Conventional Lipid-Based Vesicles

Lipid-based vesicles i.e., liposomes are colloidal spherical particles typically consisting of phospholipids, cholesterol, and other possible ingredients. These lipid molecules tend to self-aggregate, forming one or more concentric bimolecular layers enclosing an equal number of aqueous compartments. Thus, liposomes can be unilamellar or multilamellar. Liposomes containing only phospholipids and cholesterol are usually termed *conventional liposomes*. Further, liposomes can encapsulate hydrophilic drugs within the aqueous regions and lipophilic molecules within the lipid bilayers. They were discovered in the 1960s by Bangham and represent, among a variety of nanocarriers, the first ones studied for skin delivery of drugs (Siler-Marinkovic, 2016). The first approved and clinically available liposomal dermatic, Pevaryl Lipogel, containing 1% econazole, was marketed by Cilag AG, in Switzerland in 1988. This liposomal gel formulation revealed a quicker onset of drug action and shorter treatment duration due to increased drug levels in the stratum corneum (Kriftner, 1992). Conventional liposomes have been used since the 1980s as drug carrier systems for topical/dermal delivery, as they indeed have the potential to enhance drug penetration into/through the skin (Belhaj et al., 2017; Betz et al., 2005; El Maghraby et al., 2000; Joseph et al., 2018; Mostafa et al., 2018), improve therapeutic effectiveness (Jeong et al., 2017; Manca et al., 2016; Mura et al., 2007; Oh et al., 2011) and decrease side effects (Seth et al., 2004). Liposomes have also been used to deliver drugs to hair follicles, i.e., to the pilosebaceous unit, which is the desired target site in treating acne vulgaris. Adapalene encapsulated in liposomes showed enhanced drug delivery into the skin and hair follicles (Ingebrigtsen et al., 2017; Kumar and Banga, 2016), as well as retinoids (Latter et al., 2019). The application of argan oil–enriched liposomes containing allantoin seemed to provide a softening and relaxing effect on the skin, thus facilitating the drug penetration into and through the skin (Manca et al., 2016). Further, liposomes are used in cosmetology, noncoated as well as polysaccharide-coated (Ionosomes), and both types have shown to significantly improve penetration of hydrophilic-active molecules (caffeine, hexapeptide) into the skin (Belhaj et al., 2017). An interesting approach is the preparation of lipase-sensitive liposomes by coating of lipase-sensitive moieties onto conventional erythromycin liposomes for achieving an enhanced antimicrobial effect in treating acne vulgaris (Jeong et al., 2017). A further approach is the encapsulation of azithromycin into different liposomes, including conventional liposomes, to locally treat skin infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) strains. All liposomes delivered azithromycin into the skin more efficiently than the control and were shown to be biocompatible with keratinocytes and fibroblasts (Rukavina et al., 2018). Liposomes encapsulating active compounds have been used with high therapeutic effectiveness in wound healing and skin regeneration (Wang et al., 2017, 2019). Moreover, liposomes with co-incorporated quercetin and resveratrol led to a remarkable amelioration of the tissue damage in skin lesions, with a significant reduction of edema and leukocyte infiltration (Caddeo et al., 2016), which caused further investigation of resveratrol liposomes for the treatment of skin disorders such as chloasma, acne vulgaris, and skin aging, as well as wound and facial redness (Soleymani et al., 2019). Liposomes and other nanocarriers have been formulated to enhance the bioavailability and stability, as well as the therapeutic efficacy, of different polyphenols used for prevention and treatment of melanoma (Heenatigala Palliyage et al., 2019). Conventional liposomes are the most commonly and extensively studied vesicle carrier systems for the skin/dermal delivery of drugs.

38.2.2 Novel Deformable Lipid-Based Vesicles

As conventional liposomes are used for dermal drug delivery, i.e., they are not successful in achieving transdermal drug delivery, there was a need to develop a new generation of lipid-based vesicles. Different approaches were used to obtain these vesicles. At the end, vesicles were obtained that contain besides phospholipids in their membranes, i.e., bilayers, small amounts of edge activators,