Engesland and co-workers (2013) revealed that the barrier function of the PVPA model could be modified in a controlled manner. Therefore, the PVPA models for compromised skin were developed providing reproducible and consistent results. Importantly, the distinction could be made between the barriers mimicking compromised and healthy skin. The skin–PVPA models thus also have the potential to provide permeation predictions when investigating drugs or cosmeceuticals intended for various compromised skin conditions (Engesland et al., 2016).

48.4.4 *Stratum corneum* (SC) Substitute

Bouwstra and colleagues developed the SC substitute (SCS) consisting of a porous material covered with the synthetic SC lipids that closely mimics the SC lipid organization and SC barrier function (de Jager et al., 2006). The steady-state flux of the moderately hydrophobic to moderately lipophilic model compounds through the SCS and human SC has been shown to be similar (de Jager et al., 2006; Groen et al., 2008). The SCS thus may function as a standardized and reliable percutaneous penetration model. Another major advantage of the SCS is that the composition of the synthetic SC lipid mixtures can be easily modified. This allows studying the relationship between the lipid composition, lipid organization, and barrier function in one single model.

All this information was used to unravel the effect of lipid composition and additives such as penetration enhancers and moisturizers on changes in lipid organization and permeation. The SCS has thus been extensively used to study the effect of changes in the lipid composition both in respect to the lipid organization and on its barrier function (Groen et al., 2011; Mojumdar et al., 2014; Uche et al., 2019; Uchiyama et al., 2016).

The function of the different changes in lipid composition in diseased skin has also been studied, and modification to the original SCS been made to mimic lipid organization and composition in dry and diseased skin, with an emphasis on atopic dermatitis (Basse et al., 2013).

48.4.5 Others

Ochalek et al. (2012a) proposed SC lipid model membranes designed to study the impact of ceramide species and lipid composition on the drug diffusion and penetration. The effect of chain length of ceramides on the permeability of drugs and water through the barriers was studied to elucidate the reason for altered barrier properties in patients with atopic eczema or psoriasis (Pullmannová et al., 2017) and the influence of cholesterol depletion and separation of the model membrane accessed (Sochorová et al., 2019). These membranes have also been used to investigate the impact of transdermal penetration enhancers on the permeation of the model drugs. The enhancer exhibited a pronounced effect on the barrier properties of SC lipid model membranes, and the effect depended on the type of ceramides present in the barrier (Čuříková et al., 2017; Ochalek, et al., 2012b).

The Strat-M is synthetic barrier model that is composed of multiple layers of polyether sulfone, creating a morphology similar to human skin, including a very tight surface layer. Its porous structure could be impregnated with a proprietary blend of the lipids, thus adding skinlike properties to the barrier (Karadzovska et al., 2013; Zsikó et al., 2019). The flux of a model drug in the presence of different penetration enhancers through StratM barriers containing lipids in ratios similar to what is found in the SC correlated well with the results obtained in human cadaver skin (Haq et al., 2018). Further, the StratM was combined with lanoline to provide lipidic components similar to the lipidic matrix in the skin. By comparing the permeability obtained from the lanoline-covered barrier with the pig skin model, it was demonstrated that similar absorption was estimated for the model substances in those two models (Carrer et al., 2018).

Recently, an artificial SC model based on self-assembled organogelators, prepared from stearic acid, tristearin, or sorbitan tristearate, and gelled in squalene, have been proposed as a potential artificial *in vitro* skin model for assessment of permeation (Maretti et al., 2019).