for a selection of model drugs in accordance with the available literature. A positive correlation was also established between the membrane retention of the compounds and SC/water partition coefficients. This model has been further exploited in combination with *in silico* methods in a combined approach to predict the skin penetration and distribution of model substances (Ottaviani et al., 2007). The model has been proposed as a suitable model for differentiating highly permeable compounds, since the model seemed to be able to distinguish between the compounds trapped in the barrier and compounds not retained in the barrier. The capacity of the detection of a substance retained in the barrier mimicking the SC could be useful to assess the effects of the formulations (Ottaviani et al., 2006). Further, the model has been used in the initial lead compound selection of synthesized steroids and standard corticosteroids (Dobričić et al., 2014; Markovic et al., 2012), as well as in studying the effect of the vehicles on the permeation of drugs (Karadzovska and Riviere, 2013). Karadzovska et al. (2013) tested a selection of drugs in different vehicles. The permeability data obtained from the PAMPA model were compared with the data from the porcine skin diffusion experiments. The non-lipid-containing PAMPA model performed better than a lipid-containing skin–PAMPA model and other synthetic membranes, namely the Strat-M membrane (further described in the section on lipid-based models). However, both the PAMPA and Strat-MTM showed potential in predicting absorption, as well as discriminating between the different vehicles (Karadzovska et al., 2013).

48.4.2.2 Silicone Model Membranes

The poly(dimethylsiloxane) (PDMS) or silicone membranes have been used for decades for screening of the effects of different vehicles and assessing their impact on the overall mechanisms of drug transport across the human skin (Oliveira et al., 2011). In 1970 Nakano and Patel used silicone membranes to study the release of salicylic acid from five ointment bases. The *in vitro* release pattern from various bases was found to be in an agreement with the *in vivo* data reported in the literature, enabling identification of the most promising ointment bases (Nakano and Patel, 1970). Several studies determining the effect of various additives on the skin penetration of a drug have been performed utilizing this model. Dias et al. (2007) conducted a study on a wide selection of vehicles (mineral oil, isopropyl myristate, oleic acid, decanol, octanol, butanol, ethanol, propylene glycol, glycerin, and water, as well as their mixtures) on the permeation of caffeine, salicylic acid, and benzoic acid. For example, the effect of both hydrophilic and lipophilic vehicles (water, ethanol, propylene glycol, mineral oil, Miglyol 812) on the penetration of ibuprofen has been studied (Watkinson et al., 2009a,b, 2011). The studies focused on the molecular mechanism of interactions between different vehicles (ethanol, isopropyl myristate, dimethyl isosorbide, PEG 200 and PEG 400 and Transcutol P) with the model membranes through the thermodynamics, and kinetic analyses of the uptake, membrane partitioning, and transport studies of a model compound have also been conducted (Oliveira et al., 2010, 2011, 2012a,b).

Although these membranes could be used to predict the skin permeability of the lipophilic compounds, it has been suggested that they could not be used for the hydrophilic compounds (Miki et al., 2015). This was revealed in a study by Uchida et al. (2016) examining the efficacy of a silicone membrane as a substitute for human skin to determine the skin permeation parameters of the drugs differing in lipophilicity and molecular weight. Thus for the hydrophilic compounds, such as antipyrine and caffeine, calculated partition parameter (KL) values were almost 100-fold lower for the silicone membrane than for the human and hairless rat skin, while permeability coefficient (P) values for the silicone membrane were similar to those in human and hairless rat skin. Conversely, for the lipophilic drug (n-butyl paraben and flurbiprofen), KL values for the silicone membrane were similar to or tenfold higher than those achieved in human and hairless rat skins, while P values for the silicone membrane were almost 100-fold higher than those in human and hairless rat skins. Interestingly, the permeation parameters of the drugs with Mw between 151 (methyl p-aminobenzoate) and 234 (lidocaine) and log Ko/w values from 1.10 (aminopyrine) to 2.81 (propyl paraben) for the silicone membrane and human or hairless rat skin showed a significant correlation, meaning that the silicone membranes can be applied to assess the permeability of these model compounds. Nevertheless, for the other drugs, based on their lipophilicity, underestimation or overestimation