(membrane) integrity, OECD Guidance Document 28 (2004) recommends measuring transepidermal water loss (TEWL), electrical resistance, or the use of tritiated water as a permeation marker. Although TEWL measurements have the advantage in that no solutions have to be added to perform the barrier integrity test, Netzlaff et al. (2006a) have proven that TEWL measurement cannot detect small changes in the SC that could still influence drug diffusion. Therefore, calculation of the permeability coefficient is still a more precise method. The experiments could be done so that the donor chamber is left opened (nonocclusive conditions) or covered (occlusive conditions) to permit or escape drying or hydration of the skin surface (Schaefer et al., 2008). The composition of the receptor medium, which is continuously stirred during the experiment, should be chosen to mimic *in vivo* conditions; however, it should also ensure sufficient solubility of the drug. The experiments are usually performed at 32 ± 1°C. The addition of the solubility-increasing compounds to the receptor fluid (ethanol or PEG) may alter the barrier function of the skin due to a possible back-diffusion to the skin, particularly if ethanol is used at a higher concentration (40%). To reduce this risk, PEG-20-oleyl ether (6%) and bovine or porcine serum albumin are recommended, since they do not destabilize the integrity of the skin (Moser et al., 2001). It is important to consider that possible enzymatic degradation and microbiological contamination of the biological material might occur. Therefore, addition of preservatives such as sodium azide or ethanol could be beneficial, as long they do not have an effect on the barrier properties of skin by changing the lag time and duration of the experiment (Henning et al., 2009).

To quantify the skin penetration and deposition, the skin extraction measurements (Rastogi and Singh, 2001), horizontal stripping and sectioning (de Jalón et al., 2001), quantitative autoradiography, and spectroscopic methods (Pirot et al., 1997) can be employed. The tape stripping method has been widely used in both *in vivo* (Dick et al., 1997) and *in vitro (ex vivo*) evaluations of topical formulations on human (Cambon et al., 2001; Wagner et al., 2001) and animal (Raber et al., 2014) skin. A velocity should be kept constant throughout the procedure. A slowing down or stopping of the procedure could lead to an increase in the SC amount adhered on the tape strip, whereas an increase in speed could result in a reduced amount of corneocytes. The detached tape strips contain both the amount of corneocytes and the corresponding amount of the penetrated formulation, which can be determined by conventional analytical procedures. It has been proven that different types of formulations can strongly affect the amount of SC removed with every tape strip. For example, after application of an ethanolic solution, the adhesion of the horny layer to the tape strips is increased, while after application of an oily formulation, the adhesion to the tape is decreased. Therefore, for the comparison of the drug penetration from various drug formulations, it is crucial that the amount of formulation detected on the single tape strip is directly related to the standardized real position in the horny layer (Lademann et al., 2009).

48.6.1 Porcine Skin

Domestic pig skin is recognized as the most appropriate animal model due to the numerous anatomical, histological, and physiological similarities with human skin such as the epidermal thickness, dermal-epidermal thickness ratio, resemblance in hair follicle, and blood vessel density in the skin, as well as the content of SC glycosphingolipids, ceramides, dermal collagen, and elastin (Dick and Scott, 1992; Godin and Touitou, 2007). Although pig ear skin exhibits hair follicles larger than those of humans, the porcine ear skin represents a more suitable *in vitro* model for analysis of the penetration and storage of topically applied substances in the hair follicles than excised human skin, mainly due to the fact that the human skin contracts after removal. Namely, restretching of the skin to its original size mainly stretches the interfollicular fibers, while the fibers around the hair follicles remain contracted. In contrast to excised human skin, pig ear tissue does not contract when the cartilage is not removed (Lademann et al., 2010). Pig skin is readily obtained as a waste product from animals slaughtered for food. The comparison