of drug permeability using human and pig skin has demonstrated a good correlation, particularly for lipophilic substances, while skin from rodents generally exhibited higher permeation rates (Dick and Scott, 1992). In addition, pig skin exhibits less donor variability than human skin (Barbero and Frasch, 2009). Most of the literature reports on the use of pig ears in *ex vivo* permeation studies do not specify the age of the animal. It is important that ears have not been scalded or flamed after animal sacrificing because such a pretreatment completely destroys the integrity of the epidermis. The central region of the outer side of the porcine ear has been recommended because of the similarity with human skin layers (Meyer et al., 2006).

Various drug formulations, including creams, ointments, lotions, (micro)emulsions, microparticles, and colloidal drug delivery systems (nanosystems), have been assessed using *ex vivo* pig skin models (Flaten et al., 2015). It would extend beyond the scope of this chapter to enlist all literature reporting on the use of *ex vivo* pig skin to optimize different formulations; therefore, only some are mentioned here. For example, Scognamiglio et al. (2013) evaluated the penetration potential of deformable liposomes and ethosomes containing resveratrol using freshly excised pig ear. The deformable liposomes decreased the amount of resveratrol accumulated in the dermis as compared to ethosomes. Full-thickness porcine ear skin has been used for optimization of the nanostructured lipid carriers containing minoxidil or finasteride (Gomes et al., 2014) or polyamide nanocapsules containing sunscreen filters (Hanno et al., 2012). Senyigit et al. (2010) performed permeation studies using full-thickness porcine ear skin to determine the epidermal accumulation of clobetasol from lecithin/chitosan nanoparticles. The skin deposition of quercetin from W/O microemulsion and its percutaneous delivery was determined using the full-thickness porcine ear skin (Vicentini et al., 2008).

The W/O vehicle was found to be the superior to other vehicles (O/W and amphiphilic bases) when assessed on dermatomed porcine abdominal skin (0.7 mm thick) (Nagelreiter et al., 2013). Dermatomed dorsal porcine skin was also used in the optimization of microemulsion composition for transdermal delivery of testosterone (Hathout et al., 2010).

Newborn pig skin has attracted considerable attention as a model for dermal formulations (Cilurzo et al., 2007). However, the diversity in the thickness of newborn pig skin regarding the age of the animal from only 1 day old (~1.2 kg) (Manconi et al., 2011b; Mura et al., 2009) to 40 days old (~20 kg) needs to be considered (Wang et al., 2014).

48.6.2 Other *Ex Vivo* Animal Skin Models: Rodents, Snake, and Bovine Udder

Primate, mouse, rat, guinea pig, rabbit, bovine (udder), and snake models have also been proposed as *ex vivo* animal models. However, the primate research is almost inaccessible, and often too expensive, so rodent skin is often used as a replacement for pig skin. The use of rodent skin requires ethical permission, since it is obtained from a living animal and is not a by-product like pig skin. In addition, the hairless species are also available: nude mice, hairless rats, and hairless guinea pigs in which the absence of hair coat mimics the human skin better than hairy skin. The rodent exhibits an extremely high density of hair follicles, leading to an obligatory hair removal prior to formulation administration (Godin and Touitou, 2007). The guinea pig skin is therefore considered a more appropriate rodent surrogate for human skin studies (Barbero and Frasch, 2009).

The effect of the size of self-assembled nanoparticles on the effectiveness of transdermal delivery of minoxidil was assessed using several *ex vivo* rodent models (Shim et al., 2004). When using hairy guinea pig skin, the permeation of the drug in 40-nm-sized nanoparticles was 1.5-fold higher in the epidermis than that of 130-nm-sized nanoparticles. This influence of the nanoparticle size was not observed in hairless guinea pigs, thus showing that the follicular route is the main penetration pathway for the minoxidil-loaded nanoparticles, whereas the permeation was promoted with decreasing the size of the nanoparticles. The full-thickness abdominal rat