

**TABLE 11.7**  
**Site Variation in Transdermal Delivery**

Transdermal Drug	Body Site	Reason
Nitroglycerin Scopolamine	Chest Postauricular	Psychological: the patch is placed over the heart Scientific: behind the ear was found to be the best absorbing area
Estradiol Testosterone	Trunk Scrotum	Convenience: easy to place, and out of view Scientific: highest skin absorbing area
Testosterone	Trunk	Scientific/convenience: removal from trunk skin is easier than scrotal skin

The barrier properties of skin relative to oral mucosa have been a benefit for longer-term transdermal delivery. Nitroglycerine buccal tablets are effective for about 20 minutes due to rapid buccal absorption. In contrast, transdermal nitroglycerin is prescribed for 24 hours of continuous-dose delivery. The transdermal nitroglycerin patch is placed on the chest more for psychological reasons than that related to scientific regional variation skin absorption. Some transdermal systems take advantage of regional variation skin absorption, and some do not (Table 11.7).

Shriner and Maibach (10) studied skin contact irritation and showed that areas of significant response were neck > perioral > forehead. The volar forearm was the least sensitive of eight areas tested. This is in contrast to the commonly held belief that the forearm is one of the best locations to test for immediate contact irritation.

### 11.3 REGIONAL VARIATION IN ANIMALS

Percutaneous absorption data obtained in man are most relevant for human exposure. However, many estimates for humans are made from animal models. Therefore, regional variation in animals may affect prediction for humans. Also, if regional variation exists in an animal, that variation should be relative to humans.

Bronaugh (11) reported the effect of body site (back vs. abdomen) on male rat skin permeability. Abdominal rat skin was more permeable to water, urea, and cortisone. Skin thickness (stratum corneum, whole epidermis, and whole skin) is less in the abdomen than in the back. With the hairless mouse, Behl et al. (12) showed dorsal skin to be more permeable than abdominal skin (reverse that of the male rat) (Table 11.8). Hairless mouse abdominal skin is thicker than dorsal skin (also reverse that of the male rat) (Table 11.8).

**TABLE 11.8**  
**Effect of Body Site on Rat Skin Permeability**

Compound	Permeability Constant (cm/hr × 10 <sup>4</sup> )
<i>Water</i>	
Back	4.9 ± 0.4
Abdomen	13.1 ± 2.1
<i>Urea</i>	
Back	1.6 ± 0.5
Abdomen	18.8 ± 5.5
<i>Cortisone</i>	
Back	1.7 ± 0.4
Abdomen	12.2 ± 0.6