

large amounts of the nylon membrane can be sterilized by various methods that will not change its chemical structure, and no further treatment is necessary for optimal attachment and growth of primary keratinocytes.

The studies described in this chapter also demonstrated that the epidermal culture formed from isolated rat keratinocytes behaved similarly to other *in vitro* systems in its initial reaction to topically applied BCES. DNA was the main target of this agent in this system, the morphological and biochemical structures of which mimic the *in situ* epidermis. More directed studies may elucidate what happens to the alkylated DNA molecule upon exposure to this agent and how this initial molecular event is related to subsequent cellular destruction leading to vesication. This approach can also be used to verify earlier observations in whole skin that the first cells destroyed after BCES exposure are basal and lower spinous cells, and that this leads to blister formation.

Studies of the untoward actions of drugs on the skin after topical application are necessary before these chemicals can be released for human use. Investigation of percutaneous absorption are frequently performed *in vitro* using membranes of animal or human cadaver skin that bear little similarity to the living human epidermis and suffer enormous variability. As a result, they may show little resemblance to the clinical performance of a given applied drug (31). Therefore, what is needed is an *in vitro* model that possesses barrier characteristics similar to those of the intact living epidermis and that offers highly reproducible characteristics. The epidermal culture developed in this laboratory resembles the *in situ* human epidermis both morphologically and biochemically. With further refinement this system may become a valuable tool in investigations of percutaneous characteristics pertaining to human health. Studies have been initiated to evaluate the effectiveness of this *in vitro* system in measuring transepidermal water loss (TEWL).

## REFERENCES

1. J. H. Draize, G. Woodard, and H. O. Calvery, *Pharmacol. Exp. Ther.*, 82:377, 1944.
2. C. S. Weil and R. A. Scala, *Toxicol. Appl. Pharmacol.*, 19: 276, 1971.
3. G. A. Nixon, C. A. Tyson, and W. C. Wertz, *Toxicol. Appl. Pharmacol.*, 31:481, 1975.
4. K. J. Falahee, C. S. Rose, H. E. Seifried, and D. Sawhney, in *Product Safety Testing* (A. M. Goldberg, ed.). Mary Ann Liebert, New York, p. 137, 1983.