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A number of mathematical models have been used to describe percutaneous absorption kinetics. In general, most of these models have used either diffusion or compartmental-based equations. The object of any mathematical model is to (1) be able to represent the processes associated with absorption accurately, (2) be able to describe/summarize experimental data with parametric equations or moments, and (3) predict kinetics under varying conditions. However, in describing the processes involved, some developed models often suffer from being too complex to be practically useful. In this chapter, we have attempted to approach the issue of mathematical modeling in percutaneous absorption from four perspectives. These are to (1) describe simple practical models, (2) provide an overview of the more complex models, (3) summarize some of the more important/useful models used to date, and (4) examine some practical applications of the models. This chapter revises an earlier one [1] incorporating some of the more recent findings.

The range of processes involved in percutaneous absorption and considered in developing the mathematical models in this chapter are shown in [Figure 2.1](#). We initially address in vitro skin diffusion models and consider (1) constant donor concentration and receptor conditions, (2) the corresponding flux, donor, skin, and receptor amount–time profiles for solutions, and (3) amount and flux–time profiles when the donor phase is removed. More complex issues such as finite volume donor phase, finite volume receptor phase, the presence of an efflux rate constant at the membrane–receptor interface, and two-layer diffusion are then considered. We then look at specific models and issues concerned with (1) release from topical products; (2) use of compartmental models as alternatives to diffusion models; (3) concentration-dependent absorption; (4) modeling of skin metabolism; (5) role of solute–skin–vehicle interactions; (6) effects of vehicle loss; (7) shunt transport; and (8) in vivo diffusion, compartmental, physiological, and deconvolution models. We conclude by examining topics such as (1) deep tissue penetration, (2) pharmacodynamics, (3) iontophoresis, (4) sonophoresis, and (5) pitfalls in modeling.

Each model is described in diagrammatic and equation form. Given that the analytical solution to most models is in the form of infinite series, often involving solutions to transcendental equations,