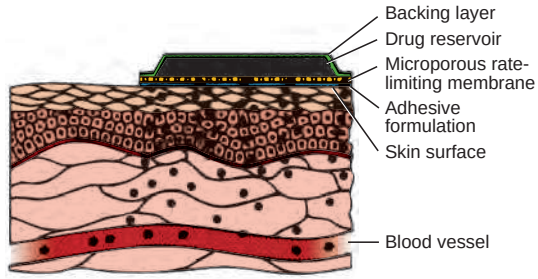

FIGURE 11.4 Four-layer therapeutic transdermal system showing the continuous and controlled amount of medication released from the system, permeating the skin, and entering the systemic circulation.

individual dosage units cut and assembled between the backing and frontal layers. Most TDDSs are designed to contain an excess of drug and thus have drug-releasing capacity beyond the time frame recommended for replacement. This ensures continuous drug availability and absorption as used TDDSs are replaced on schedule with fresh ones.

Membrane-controlled transdermal systems are designed to contain a drug reservoir, or pouch, usually in liquid or gel form; a rate-controlling membrane; and backing, adhesive, and protecting layers (Fig. 11.5). Transderm-Nitro (Summit) and Transderm Scop (Baxter) are examples of this technology. Membrane-controlled systems have the advantage over monolithic systems in that as long as the drug solution in the reservoir remains saturated, the release rate of drug through the controlling membrane remains constant (21,22). In membrane systems, a small quantity of drug is frequently placed in the adhesive layer to initiate prompt drug absorption and pharmacotherapeutic effects on skin placement. Membrane-controlled systems may be prepared by preconstructing the delivery unit, filling the drug reservoir, and sealing or by lamination, a continuous process of construction, dosing, and sealing (Figs. 11.8 to 11.10).

In summary, either the drug delivery device or the skin may serve as the rate-controlling mechanism. If the drug is delivered to the stratum corneum at a rate less than the absorption capacity, the *device* is the controlling factor; if the drug is delivered to the skin area to saturation, the *skin* is the controlling factor. Thus, the rate of drug transport in all TDDSs, monolithic and membrane, is controlled by either artificial or natural (skin) membranes.

TDDSs may be constructed of a number of layers, including (*a*) an occlusive backing membrane to protect the system from environmental entry and from loss of drug from the system or moisture from the skin; (*b*) a drug reservoir or matrix system to store and release the drug at the skin site; (*c*) a release liner, which is removed before application and enables drug release; and (*d*) an adhesive layer to maintain contact with the skin after application. Two types of adhesive layers, the peripheral adhesive and the face adhesive,

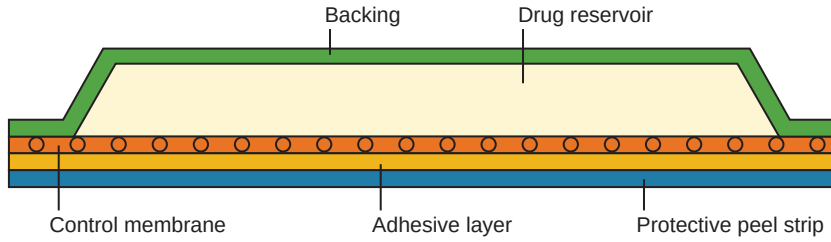

FIGURE 11.5 The Transderm-Nitro Transdermal Therapeutic System (Summit). The patch delivers nitroglycerin through the skin directly into the blood stream for 24 hours. Transderm-Nitro is used to treat and prevent angina. The system consists of a water-resistant backing layer, a reservoir of nitroglycerin, followed by a semipermeable membrane to control precisely and predictably the release of medicine, and an adhesive layer to hold the system onto the skin. The adhesive layer also contains an initial priming dose of nitroglycerin to ensure prompt release and absorption of the medication. (Courtesy of Summit Pharmaceuticals, Novartis.)