

the solvent/water exposure. There was an initial delay of 30 to 60 minutes in solvent absorption from the water-soluble dose, which was not seen with the higher dose that exceeded solubility. The lowest dose, 0.01%, was near analytical limitation. These data are then analyzed for human body rate distribution using a PBPK model and appropriate absorption and excretion rates produced (1).

13.2 PHARMACODYNAMIC DOSE RESPONSE

Pharmacodynamics is a biologic response to the presence of a chemical. The chemical needs to be bioavailable for the response to happen, and a dose response within the limits of the biological response can be measured. This can happen with in vivo human skin, and an example is blood flow changes measured by laser Doppler velocimetry (LDV). Minoxidil is a direct-acting peripheral vasodilator originally developed for hypertension, but is now available to promote hair growth. In a double-blind study, balding volunteers were dosed with 0%, 1%, 3%, and 5% minoxidil solutions once each day on two consecutive days and blood flow was measured by LDV (Figure 13.2).

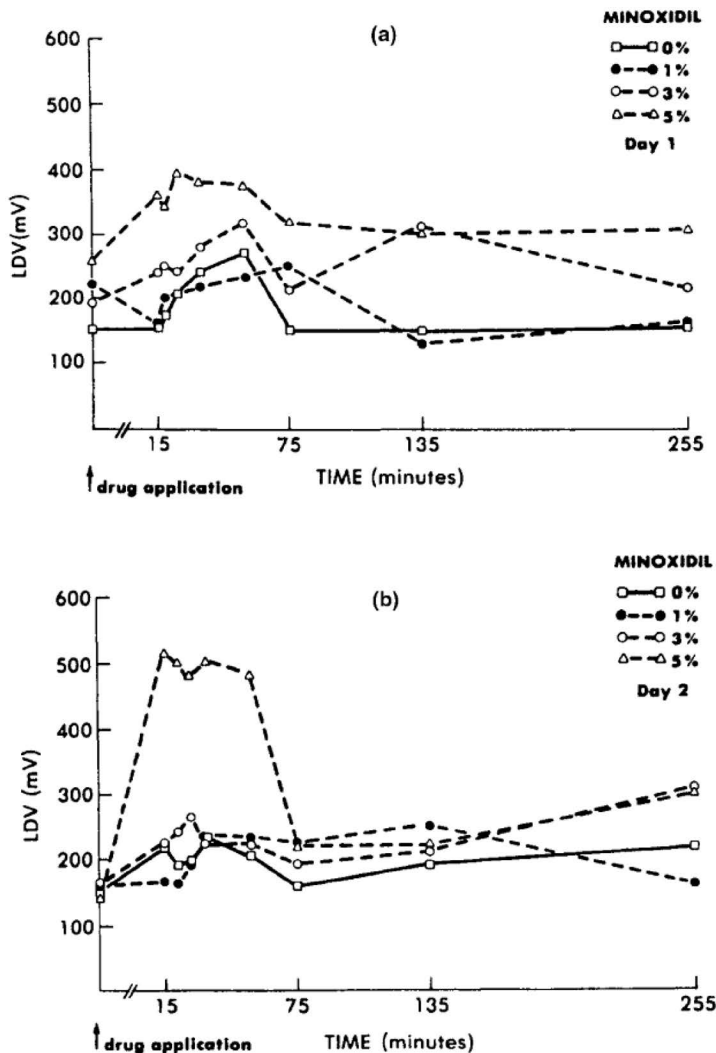


FIGURE 13.2 Pharmacodynamic laser Doppler velocimetry dose response of minoxidil stimulating skin blood flow in the balding scalp of male volunteers. (a) Day 1 and (b) Day 2.