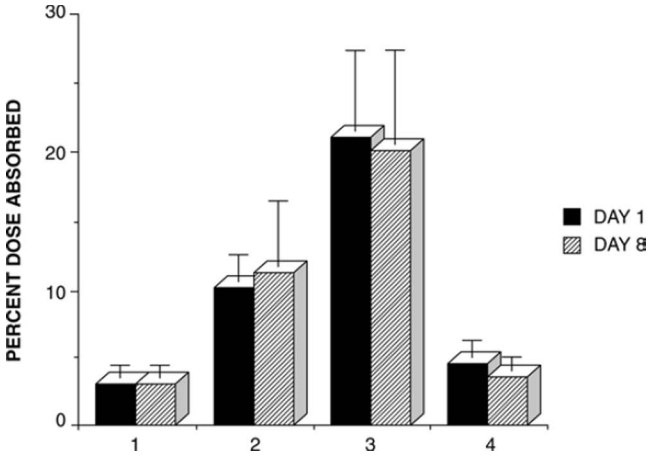

FIGURE 16.2 Skin absorption single (day 1) and multiple (day 8) dose in humans.

the absorption from days 15 to 21 skin application was 2.72 ± 1.21%. Statistical analysis showed a significant difference for day 1 dosing versus day 8 dosing ($p < 0.001$) and for day 1 dosing versus day 15 dosing ($p < 0.008$). No difference was observed in percutaneous absorption for day 8 versus day 15 dosing (Figure 16.3). The daily excretion patterns show that peak excretion occurred at 24 or 48 hours following topical application. The results show that an increase occurs in the absorption of Azone with long-term multiple application, but that this enhanced self-absorption occurs early in use, and a steady-state absorption amount is established after the initial enhancement (4).

16.1.2 Triple Daily Dose Application: Hydrocortisone

16.1.2.1 Study Design

The study was specifically designed to compare a single low dose (13.33 μg/cm^2) to a single larger dose (40.0 μg/cm^2; three times the amount) and to three multiple-application therapy (13.33 μg/cm^2 × 3 = 40.0 μg/cm^2) treatments. Student two-tailed, paired *t*-tests were employed to

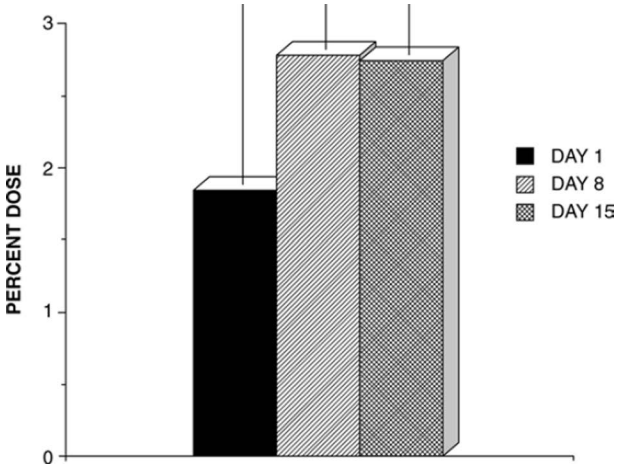

FIGURE 16.3 Azone multiple dosing in human volunteers.