nail plate, the chemical penetrated further down to the nail supporting bed (cotton pad) samples. These two pieces of data give important information related to the drug's nail absorption/penetration capacities and deep concentrations.

With this *in vitro* nail penetration model, the drug can be measured in the dorsal/intermediate layers, the ventral/intermediate layers, and cotton pad/nail supporting bed samples to determine the distances and levels of the drug penetration. Table 61.4 provides weight normalized concentrations (μg eq./g) of eight antifungal agents: ciclopirox (18), econazole (19), efinaconazole, ketoconazole (15), luliconazole, ME1111 (20,21), tavaborole (16), and terbinafine (22) in the deep nail plate, ventral/intermediate layer and cotton pad, and nail supporting bed samples. These values determined not only the transungual delivery rate and kinetics but also antifungal efficacies with corresponding minimum inhibitory concentration (MIC) values. Antifungal efficacy is calculated by the ratio of an antifungal agent concentration in the deep nail sample (μg/g) to MIC. The MIC is an important laboratory index to determine antifungal potency. The value of an antifungal agent is defined as the lowest antifungal concentration at which no growth is visible in the wells when detected visually (80% to 100% inhibition). The MIC_{90} values, the minimum concentration of eight antifungal agents that inhibited 90% of *T. rubrum* isolates (MIC90), are shown in Table 61.4. The antifungal efficacy of these agents' concentration in the deep nail layer or the nail bed could be a few orders of magnitude greater than the MIC deemed necessary to inhibit the growth of the causative dermatophyte species. However, one has to keep in mind that keratin affinity of each agent should be concluded with related MIC value to assess antifungal efficacy.

Keratin affinity is an important physicochemical property affecting the efficiency of antifungal agents' permeability into and through the nail plate following topical or systemic administration (28). If a high-keratin-affinity drug is administered topically, the drug may cumulate in the nail surface- dorsal layer and has insufficient amount to release and diffusion to the deep part: the ventral layer and the bed. In addition, the drug needs to be an unbound form to exert

TABLE 61.4
Analysis of Efficacy Coefficient of Eight Antifungal Agents

	Determination of Antifungal Efficacy				
Chemicals	**MIC_{90} *T. rubrum***	**Deep Nail Plate (ventral/intermediate center)**		**Cotton Pad (nail supporting bed)**	
	pH = 7.0	**Concentration**	**Efficacy**	**Concentration**	**Efficacy**
	μg/mL	**μg/g**		**μg/g**	
Ciclopirox (8%)[18]	0.25[23]	310 ± 80	1240 ± 320	52 ± 10	206 ± 41
Econazole (5%)[19]	8[24]	8890 ± 3098	1111 ± 387	294 ± 46	37 ± 6
Efinaconazole (10%)*	0.008[23, 27]	67.7 ± 55.6	8459 ± 6950	1.54 ± 0.83	193 ± 104
Ketoconazole (2%)[15]	0.5[25]	810 ± 390	1620 ± 780	180 ± 90	360 ± 180
Luliconazole (1%)*	0.0002[26]	3.49E ± 1.58E ($\times 10^5$)	1.75E ± 0.79E ($\times 10^9$)	1922 ± 309	9.61E ± 1.55E (10^6)
ME1111 (10%)[20,21]	0.25[20]	2884 ± 924	11536 ± 3696	121 ± 27	484 ± 108
Tavaborole (10%)[16]	81[6]	6000 ± 748	750 ± 94	726 ± 176	91 ± 22
Terbinafine (1%)[22]	0.125[24, 27]	487 ± 132	3896± 1056	27 ± 1.2	216 ± 10

Note: Each number represents mean ± S.D. of five to six samples.

*Unpublished data.

The MIC is an important laboratory index to determine of antifungal potency. The value of an antifungal agent is defined as the lowest antifungal concentration at which no growth is visible in the wells when detected visually (80%–100% inhibition). The MIC_{90} values is the minimum concentration of eight antifungal agents that inhibited 90% of *T. rubrum*.

Antifungal efficacy is calculated by the ratio of an antifungal agent concentration in the deep nail sample (μg/g) to MIC isolates (MIC_{90}).