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Ciclopirox: a broad spectrum antifungal with antibacterial and anti-inflammatory properties

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Original Article

# Evaluation of *in vitro* activity of ciclopirox olamine, butenafine HCl and econazole nitrate against dermatophytes, yeasts and bacteria

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## Abstract

**Background** In many instances, a cutaneous fungal infection may exist concomitantly with bacterial involvement. In this study we compared the *in vitro* activity of three antifungal agents against the dermatophytes, yeasts and bacteria recovered most commonly from cutaneous mycoses and bacterial infections.

**Methods** Using a microdilution method adapted from the National Committee for Clinical Laboratory Standards (NCCLS), we determined the minimum inhibitory concentrations (MICs) of ciclopirox olamine, econazole nitrate and butenafine HCl against a panel of dermatophyte fungi and yeasts ($n = 39$) and bacterial isolates ($n = 45$).

**Results** All three antifungals demonstrated comparable activity against the dermatophytes tested, with a MIC range of 0.03–0.25 μg/ml for ciclopirox, < 0.001–0.25 μg/ml for econazole and 0.03–0.25 μg/ml for butenafine. For yeasts, ciclopirox showed activity against all isolates, with an MIC range of 0.001–0.25 μg/ml, whereas econazole had a broader range of 0.125–> 0.5 μg/ml. Butenafine displayed limited activity against the yeast *Candida albicans* and no activity against *Malassezia furfur*. For the antibacterial activity studies, ciclopirox demonstrated activity against all isolates tested with a range of 0.06–2 μg/ml, while econazole showed activity against Gram-positive bacteria only, with a MIC range of 0.004–0.25 μg/ml. Butenafine HCl had a limited activity against bacterial isolates tested, showing activity against β-hemolytic *Streptococcus* Group A and *Corynebacterium* only. Neither econazole nitrate nor butenafine HCl demonstrated activity against any of the Gram-negative strains evaluated in this study.

**Conclusions** The data suggest that ciclopirox olamine has the broadest *in vitro* activity, in comparison to econazole and butenafine HCl, against bacteria, yeasts and bacteria. These findings may have implications in the use of these antimycotics in the treatment of mixed cutaneous infections where bacteria or yeasts are present in addition to dermatophytes.

## Introduction

Superficial fungal infections are among the world's most common diseases. Dermatophytes are a unique group of fungi that infect keratinous tissue, with the skin, hair and nails being the most common sites. Certain yeasts, such as *Candida albicans*, also have the capability of infecting the skin and causing superficial fungal infections. Gram-positive and Gram-negative bacteria are commonly found as secondary infections at the site of fungal infections, with all organisms potentially contributing to the pathogenesis of many skin diseases. Secondary bacterial infection superimposed on a fungal infection, a noted sequela in interdigital tinea pedis, is known as dermatophytosis complex[1]. Dermatophytosis complex is characterized by increases in the density of the resident bacterial population including aerobic diphtheroid bacteria, Gram-positive cocci and Gram-negative bacteria, particularly *Brevibacterium epidermidis*, *Corynebacterium minutissimum*, *Pseudomonas* species, *Staphylococcus aureus* and *Micrococcus sedentarius*. The primary event in these infections may be damage to the stratum corneum by dermatophytes. This is followed by an overgrowth of the resident bacterial population[2].

The main classes of antifungals employed for the topical treatment of superficial fungal infections are polyenes, imidazoles and allylamine drugs[3]. These agents differ in their mechanism of action. The polyenes act by binding irreversibly to ergosterol, an essential component of fungal cell membranes.



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The interaction of the polyene with fungal membrane sterol results in production of aqueous pores; thus, altered permeability and leakage of vital cytoplasmic components[4]. Polyenes are not active against dermatophytes and their clinical use is limited to the treatment of infections caused by *Candida* species[4]. Because of their inactivity against dermatophytes, they were not included for testing in this study.

The imidazoles, discovered in the late 1960s, are relatively broad-spectrum antifungals that are primarily fungistatic, and act by inhibiting ergosterol synthesis, causing defects in the fungal cell membrane. Specifically, azole antifungals interfere with the ability of the cytochrome P-450 enzyme lanosterol 14-demethylase to catalyze the conversion of lanosterol to ergosterol[5].

Allylamines suppress the biosynthesis of ergosterol at an earlier stage of the metabolic pathway than the azoles, independent of the P-450 enzymes, by inhibiting the activity of squalene epoxidase. The resulting ergosterol deficiency is accompanied by an accumulation of squalene in the fungal cell resulting in the disruption of fungal cell membranes. Allylamines are primarily fungicidal against dermatophytes and fungistatic against *C. albicans* at therapeutic drug concentrations[6].

In addition to these broad classes of antifungals, ciclopirox, a hydroxypyridone, is also marketed worldwide for the treatment of superficial fungal infections. It differs from other antifungal agents in its chemical structure and its mechanism of action. Unlike most antifungal agents, ciclopirox olamine does not affect sterol biosynthesis. The mode of action of this drug is very complex, targeting a variety of metabolic processes in the fungal cell. Ciclopirox has a high affinity for trivalent metal cations such as $Fe^{3+}$. The trapping of this essential enzymatic cofactor has an inhibitory effect on enzymes such as cytochromes, which are involved in mitochondrial electron transport processes[7]. Additionally, the activity of catalase and peroxidase, which are responsible for the intracellular degradation of toxic peroxides, is strongly inhibited by the presence of this drug. Ciclopirox also affects the cytoplasmic membrane where it appears to impair active transport mechanisms resulting in reduced uptake of nutrients into the internal pool[7]. In growing cells, this intracellular depletion of essential amino acids and nucleotides secondarily contributes to the reduced synthesis of proteins or nucleic acids.

The imidazoles, allylamines and ciclopirox are reported to possess antibacterial activity as well as antifungal activity and, in light of the occurrence of secondary bacterial infections, are often prescribed for skin infections that may have a bacterial component.

The objective of this *in vitro* study was to compare three antifungals commonly used to treat superficial fungal infections: ciclopirox (a substituted pyridone), econazole nitrate (an azole derivative) and butenafine HCl (an allylamine). The antifungal agents were tested against selected fungi and yeast isolates most commonly implicated in tinea infections as well as bacterial isolates typically found as secondary infections to primary fungal infections. Our data show that of the three antifungals tested, ciclopirox olamine had the broadest antimicrobial activity against both the fungi and bacteria tested.

## Materials and methods

### Antifungals

The three antifungal agents tested in this study were ciclopirox olamine, econazole nitrate and butenafine hydrochloride (HCl). Ciclopirox and econazole were purchased from Sigma-Aldrich Chemical Company (St. Louis, MO). Butenafine HCl was isolated from Mentax 1.0% Cream (containing 10 mg butenafine HCl), (DPT Laboratories, San Antonio, TX).

### Organisms

The antifungal susceptibility of the following organisms was determined: dermatophytes (five strains each): *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Trichophyton rubrum*, *Microsporum canis*, *Microsporum gypseum*, and *Epidermophyton floccosum*; yeasts (five strains each): *Candida albicans*, and *Malassezia furfur*; Gram-positive bacteria (five strains each): *Staphylococcus aureus*, β-Hemolytic *Streptococcus* Group A, *Micrococcus* species, *Brevibacterium* species, and *Corynebacterium* species; Gram-negative bacteria (five strains each): *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Escherichia coli*, and *Klebsiella pneumoniae*. All organisms tested were from the culture collection available at the Center for Medical Mycology, University Hospital of Cleveland.

### Susceptibility testing of dermatophytes and yeasts

Preparation of antifungal agents: All antifungal agents were standardized according to their weights and units of activity as determined by the assays of each batch lot. Ciclopirox olamine and econazole nitrate were dissolved in distilled water. RPMI-1640 media, without sodium bicarbonate and supplemented with L-glutamine, was added to achieve a final stock solution containing 1280 μg/ml of antifungal agent. Butenafine was dissolved in ethanol and the final stock concentration was adjusted to the same concentration with RPMI-1640 media. Ten serial two-fold dilutions of each antifungal were prepared. For ciclopirox and econazole, the concentration range was 0.001–0.5 μg/ml while the concentration range for butenafine was 0.06–32 μg/ml.

#### *Preparation of dermatophytes and yeasts*

Dermatophytes and *C. albicans* were grown on potato dextrose agar (Difco Laboratories, Detroit, MI) at 35 °C for 24–48 h. Five colonies ≥ 1 mm in diameter were selected from each culture and placed in 5 ml of 0.85% sterile saline. The suspensions were vortexed and then counted using a hemacytometer. *M. furfur* was grown at 35 °C for 10 days on Sabouraud dextrose broth (Difco) containing 10 μl Tween 80. This cell suspension was counted

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using a hemacytometer and adjusted to a final working concentration of 2–5 × 10$^3$ cells per ml in RPMI 1640 medium.

### *Microtiter plate preparation*

The method used to determine the antifungal susceptibilities of dermatophytes was developed at Center for Medical Mycology at University Hospital of Cleveland[8]. This method is an adaptation of the NCCLS document M27-A[9] having a microdilution format that uses RPMI-1640 as the medium and 2–5 × 10$^3$ conidia per ml as an inoculum. Using a multichannel pipette, 100 μl of 2X antifungal concentrations were dispensed into columns 2–11 of sterile disposable 96-well (U-shaped) microtiter plates. Column 2 contained the highest concentration and column 11 the lowest concentration of drug. Columns 1 and 12 (controls) received 100 μl of diluent (RPMI-1640 media). Using a multichannel pipette, 100 μl of working dermatophyte or yeast suspension prepared above were dispensed into each well of columns 2–12. Column 12 served as the growth control while column 1 remained uninoculated and served as the sterility control. The plates were covered and incubated at 35 °C for 4–5 days for the dermatophytes, 24–48 h for *C. albicans* and 5 days for *M. furfur*. Following the incubation period, the MICs were read visually. MIC (μg/ml) end point was defined as the minimum concentration causing 80% inhibition compared to the growth control (see Tables 1 and 2).

## Susceptibility testing of bacteria

### *Preparation of antifungal agents*

Same as described above.

### *Preparation of bacteria*

At least three to five well-isolated colonies of the same morphological type were selected from an overnight culture. The top of each colony was transferred, using a wire loop, to a test tube containing 4–5 ml of a Mueller Hinton broth medium (Difco). The broth was incubated at 35 °C for 2 h. This actively growing broth culture was then adjusted with sterile saline to obtain turbidity optically comparable to the 0.5 McFarland standard.

### *Microtiter plate preparation*

The microsdilution format used for measuring antibacterial suscepstibility of bacteria is the method developed by the NCCLS

**Table 1** Minimum inhibitory concentrations (MIC, μg/ml) of ciclopirox olamine, econazole nitrate and butenafine HCl against 30 isolates representing different dermatophyte species

| Organism Name | Isolate # | Ciclopirox olamine | Econazole nitrate | Butenafine HCl |
|---|---|---|---|---|
| *Trichophyton mentagrophytes* | M1 | 0.125 | < 0.001 | 0.25 |
| | M2 | 0.125 | < 0.001 | 0.125 |
| | M3 | 0.06 | < 0.001 | 0.125 |
| | M4 | 0.125 | < 0.001 | 0.25 |
| | M5 | 0.125 | < 0.001 | 0.06 |
| *Trichophyton tonsurans* | 32 | 0.06 | < 0.001 | 0.25 |
| | 33 | 0.03 | < 0.001 | 0.125 |
| | 34 | 0.06 | 0.008 | 0.25 |
| | 35 | 0.03 | < 0.001 | 0.125 |
| | 170 | 0.06 | < 0.001 | 0.125 |
| *Trichophyton rubrum* | 18 | 0.125 | 0.25 | 0.03 |
| | 20 | 0.125 | 0.25 | 0.06 |
| | M17 | 0.125 | 0.125 | 0.03 |
| | M18 | 0.125 | 0.25 | 0.03 |
| | 28188 | 0.125 | < 0.001 | 0.125 |
| *Microsporum canis* | M25 | 0.06 | < 0.001 | 0.25 |
| | M26 | 0.03 | < 0.001 | 1 |
| | M27 | 0.06 | < 0.001 | 1 |
| | M28 | 0.004 | < 0.001 | 1 |
| | M29 | 0.06 | < 0.001 | 0.5 |
| *Microsporum gypseum* | 797 | 0.125 | < 0.001 | 0.25 |
| | 418 | 0.125 | < 0.001 | 0.25 |
| | M9 | 0.125 | < 0.001 | 0.06 |
| | 604 | 0.25 | < 0.001 | 0.25 |
| | 213 | 0.06 | < 0.001 | 0.06 |
| *Epidermophyton floccosum* | 404 | 0.03 | < 0.001 | 0.25 |
| | 389 | 0.03 | < 0.001 | 0.25 |
| | 406 | 0.03 | < 0.001 | 0.25 |
| | 61 | 0.03 | < 0.001 | 0.125 |
| | 373 | | No growth obtained | |

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**Table 2** Minimum inhibitory concentrations (MIC, μg/ml) of ciclopirox olamine, econazole nitrate and butenafine HCl against 10 isolates of two species of yeasts

| Organism Name | Isolate # | Ciclopirox olamine | Econazole nitrate | Butenafine HCl |
|---|---|---|---|---|
| *Candida albicans* | 799 | 0.06 | > 0.5 | > 32 |
| | 798 | 0.06 | 0.25 | 16 |
| | 405 | 0.25 | > 0.5 | > 32 |
| | 648 | 0.25 | 0.25 | 16 |
| | 593 | 0.06 | > 0.5 | 16 |
| *Malassezia furfur* | 5099 | 0.008 | > 0.5 | > 32 |
| | 5100 | 0.001 | 0.125 | > 32 |
| | 2117 | 0.008 | > 0.5 | > 32 |
| | 3850 | 0.008 | 0.125 | > 32 |
| | 2121 | 0.125 | 0.25 | > 32 |

**Table 3** Minimum inhibitory concentrations (MIC, μg/ml) of ciclopirox olamine, econazole nitrate and butenafine HCl against 25 isolates representing different Gram-positive bacteria species

| Organism Name | Isolate # | Ciclopirox olamine | Econazole nitrate | Butenafine HCl |
|---|---|---|---|---|
| *Staphylococcus aureus* | 730 | 0.5 | 0.03 | > 128 |
| | 731 | 0.5 | 0.03 | > 128 |
| | 732 | 0.5 | 0.03 | > 128 |
| | 733 | 0.5 | 0.03 | > 128 |
| | 734 | 0.5 | 0.03 | > 128 |
| β-Hemolytic *Strep.* Group A | 735 | 0.125 | 0.03 | 16 |
| | 736 | 0.06 | 0.03 | 8 |
| | 737 | 0.06 | 0.25 | 4 |
| | 738 | 0.125 | 0.25 | 4 |
| | 739 | 0.125 | 0.25 | 4 |
| *Micrococcus luteus* | 783 | 2 | 0.004 | > 32 |
| | 784 | 0.25 | 0.004 | > 32 |
| *Micrococcus sedentarius* | 495 | 0.25 | 0.002 | > 32 |
| | 496 | 0.25 | 0.015 | > 32 |
| | 497 | 0.25 | 0.008 | > 32 |
| *Brevibacterium linens* | 776 | 0.25 | 0.008 | > 32 |
| *Brevibacterium acetylicium* | 777 | 0.125 | 0.015 | > 32 |
| *Brevibacterium linens* | 778 | 0.25 | 0.008 | > 32 |
| *Brevibacterium helvolum* | 779 | < 0.060 | 0.004 | > 32 |
| *Brevibacterium linens* | 780 | 0.25 | 0.008 | > 32 |
| *Corynebacterium* species | 781 | 0.25 | 0.008 | < 0.001 |
| | 782 | 0.25 | 0.004 | > 32 |
| *Corynebacterium minutissimum* | 492 | 0.25 | 0.015 | < 0.001 |
| | 494 | 0.25 | 0.015 | < 0.001 |
| | 495 | 0.25 | 0.008 | < 0.001 |

document M7-A5[10]. Briefly, drugs were added to sterile disposable 96-well microtiter plates as described above. Within 15 min of preparation, the bacterial inoculum suspensions, containing approximately $5 \times 10^5$ colony forming units (CFU)/ml, were dispensed into the wells as described above. The plates were covered and incubated. *S. aureus* isolates, β-Hemolytic *Streptococcus* Group A isolates and the Gram-negative bacteria were incubated at 35 °C for 24 h. All other bacterial isolates were incubated at 30 °C for 48 h. Following the incubation period, the MICs were read visually. MIC (μg/ml) end point was defined as the minimum concentration causing 80% inhibition compared to the growth control (see Tables 3 and 4).

## Results

The data show that all three antifungals tested demonstrated activity against the dermatophytes (Table 1). Ciclopirox olamine showed MIC ranging from 0.03 to 0.25 μg/ml; econazole nitrate's range was < 0.001–0.25 μg/ml while butenafine HCl had a range of 0.03–1.0 μg/ml. A comparison of the MIC activity against the tested dermatophytes is shown in Fig. 1. For yeasts, ciclopirox showed activity against *C. albicans* and *M. furfur* isolates (Table 2), with an MIC range of 0.001–0.25 μg/ml, whereas econazole had a broader range of 0.125 to > 0.5 μg/ml and butenafine showed limited activity against


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**Table 4** Minimum inhibitory concentrations (MIC, μg/ml) of ciclopirox olamine, econazole nitrate and butenafine HCl against 20 isolates representing different Gram-negative bacteria species

| Organism Name | Isolate # | Ciclopirox olamine | Econazole nitrate | Butenafine HCl |
|---|---|---|---|---|
| *Pseudomonas aeruginosa* | 720 | 1 | > 128 | > 128 |
| | 721 | 0.5 | > 128 | > 128 |
| | 722 | 2 | > 128 | > 128 |
| | 723 | 2 | > 128 | > 128 |
| | 724 | 2 | > 128 | > 128 |
| *Proteus mirabilis* | 723 | 0.5 | > 128 | > 128 |
| | 724 | 0.5 | > 128 | > 128 |
| | 725 | 0.5 | > 128 | > 128 |
| | 726 | 0.5 | > 128 | > 128 |
| | 727 | 0.5 | > 128 | > 128 |
| *Escherichia coli* | 744 | 0.5 | > 128 | > 128 |
| | 745 | 0.5 | > 128 | > 128 |
| | 746 | 0.5 | > 128 | > 128 |
| | 747 | 0.5 | > 128 | > 128 |
| | 748 | 0.5 | > 128 | > 128 |
| *Klebsiella pneumoniae* | 740 | 0.5 | > 128 | > 128 |
| | 741 | 0.5 | > 128 | > 128 |
| | 742 | 0.5 | > 128 | > 128 |
| | 743 | 0.5 | > 128 | > 128 |
| | 749 | 0.5 | > 128 | > 128 |

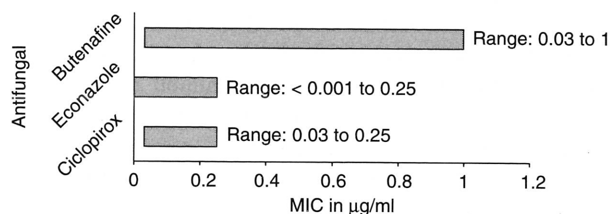


**Figure 1** Minimum inhibitory concentrations for dermatophytes.

*C. albicans* and no activity against *M. furfur* (Table 2). A comparison of these activities is depicted in Fig. 2.

For the bacterial MIC studies, ciclopirox olamine demonstrated activity against all isolates with a range of 0.06–2 μg/ml. Econazole showed activity against Gram-positive bacteria, with a MIC range of 0.004–0.25 μg/mL. Butenafine HCl showed activity against β-hemolytic *Streptococcus* Group A and *Corynebacterium* but failed to inhibit *S. aureus* (MIC > 128 μg/ml). Neither econazole nor butenafine had activity against any of the Gram-negative strains tested. Table 3 shows MIC determinations for Gram-positive bacteria while Table 4 shows the results for the Gram-negative bacteria.

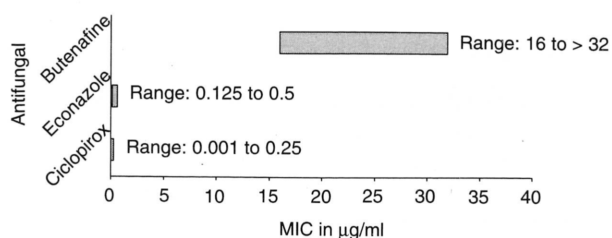


**Figure 2** Minimum inhibitory concentrations for yeasts.

## Discussion

This study reports that ciclopirox olamine had MIC activity in a range of 0.004–0.125 μg/ml for the dermatophytes tested and a range of 0.06–0.25 μg/ml for the yeast isolates tested. The MIC data reported in this current study may include MIC values that are lower than previously reported in the literature. In a review of the antimicrobial activity of ciclopirox olamine reported by Jue *et al.*[11] *in vitro* studies report an MIC range of 0.5–3.9 μg/ml for dermatophytes and a range of 0.9–3.9 μg/ml for various *Candida* species. The Jue study utilized a macrodilution method for testing antimicrobial susceptibility and the results are considerably higher than those observed in the current study[11]. Comparisons of MIC data obtained from the original agar macrodilution method vs. the more recent broth microdilution test reported in this study may not be valid since there are reported differences between the two methods.

In a study reported by Niewerth *et al.*[12] 50 dermatophyte strains obtained from clinical specimens were examined for their susceptibility to five systemic or topical antifungal agents using both an agar macrodilution and a broth microdilution method. A comparison of the MIC clearly showed differences between the two test methods applied. For all five

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antifungal agents tested, MIC data were 3–7-fold lower in the microdilution test system. The lower MIC ranges reported in this study confirm Niewerth's observation of lower MIC values with microdilution testing methods. These differences have to be taken into account when comparing MIC data in the literature. Physicians frequently rely on comparative MIC data to aid in the selection of an appropriate antifungal agent to treat tinea infections. This study, comparing MIC data performed with the same test method, in the same laboratory under the same test conditions may be a more appropriate comparison for comparing the antimicrobial activity of various agents.

The current study, using a microdilution method, reports a MIC maximum of 2 µg/ml for ciclopirox olamine for Gram-negative and Gram-positive bacteria while the Jue study reports an MIC range of 0.25 to > 125 µg/ml for these same organisms. Comparisons between the two studies are difficult since the variables involved in determining the MIC results are not the same. However, there is accordance with Niewerth's report that microdilution testing methods will generate lower MIC values.

The current study also shows butenafine HCl having an MIC range against dermatophytes of 0.03–0.25 µg/ml with limited activity against *C. albicans* and no activity against *M. furfur*. An overview by Brennan and Leyden in 1997[13] reported MIC values from several different published studies and is complimented by the results obtained in the current study. This overview reported a MIC range for butenafine HCl of 0.12–0.24 µg/ml for dermatophytes and a considerably higher range of 64–128 µg/ml for *C. albicans*.

Limbert and Ulbricht[14] investigated the activity of ciclopirox olamine and other antifungals against two Gram-negative bacteria: *Proteus mirabilis* and *Pseudomonas aeruginosa*, confirming the current study results by showing that ciclopirox is far more effective than econazole nitrate at killing Gram-negative bacteria. Although the method used was not the microdilution method reported in this current study, ciclopirox was clearly more active against the two Gram-negative organisms with MIC values of 0.02–0.5 g/l, compared to econazole nitrate's MIC value reported as > 1.00 g/l.

In an article by Pierard *et al.*[15] the reported antifungal activity of both ciclopirox olamine and econazole nitrate against dermatophytes and yeasts was comparable to that of the current work. However, the testing method was a combination method of culturing pathogenic dermatophytes and yeasts on human stratum corneum. Topical antifungals were applied *in vivo* and the stratum corneum was removed by cyanoacrylate skin surface strippings. After inoculation of the test organisms, the extent of fungal growth was measured, and the level of inhibition was determined by comparing the growth to a control. Even though MIC levels were not reported, the activity of ciclopirox olamine and econazole against the tested organisms was similar to the activity reported in this study.

If accurate identification of the pathogenic organism is made in a tinea infection, and the only pathogenic organism present is a dermatophyte, use of any of the three antifungal agents reported here will likely prove efficacious. If a yeast causes the infection however, there may be an advantage to prescribing ciclopirox because of its lower MIC and activity against all yeasts tested. Although *in vitro* tests may not accurately predict the outcome of an *in vivo* infection, they may provide some information about the ability of an antifungal agent to inhibit or eradicate a pathogenic organism.

If the tinea infection has a superimposed bacterial component, something that may occur with moderate to severe cases of tinea pedis, also termed dermatophytosis complex, identification of the bacteria would provide clinically relevant information for selection of an antifungal agent that would treat both the dermatophyte and bacteria. The clinical spectrum of tinea pedis represents a continuum from mild scaling to a painful, macerated inflammatory process associated with pruritus and a foul smell, due to dense colonization by resident bacteria, including Gram-negative organisms[16]. Symptomatic tinea pedis is therefore likely to be caused by a mixed fungal and bacterial infection. Whenever the interspaces become macerated, bacteria grow rapidly and reach densities of millions per interspace. In a study by Talwar *et al.*[17] Gram-positive organisms were isolated regularly and in increasing numbers commensurate with the severity of the disease. Gram-negative bacteria were also common in increasing numbers and with increasing frequency as the severity of the disease progressed[17]. Indeed, the most severe form of tinea pedis occurs when there is an overgrowth of *Pseudomonas* species that produces an extremely painful, erosive, purulent interspace that can be incapacitating[16]. Treatments that simultaneously inhibit bacteria and fungi would be the most efficacious since they attack all aspects of the disorder. Since a Gram-negative bacterial infection, superimposed on tinea pedis is a common clinical presentation, ciclopirox would be the antifungal of choice since econazole and butenafine demonstrated no activity against the Gram-negative organisms, as indicated from the results of the MIC tests reported here. If a physician does not perform a culture to ascertain the pathogenic organism, then use of ciclopirox would be the most prudent selection since the activity against all test organisms predicts a more favorable outcome for the patient.

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