The in vitro activities of 11 antifungal drugs against 68 Scopulariopsis and Microascus strains were investigated. Amphotericin B, 5-fluorocytosine, flucanazole, itraconazole, ketoconazole, miconazole, posaconazole, voriconazole, and ciclopirox showed no or poor antifungal effect. The best activities were exhibited by terbinafine and caspofungin, where the MIC and MEC (minimal effective concentration) ranges were 0.0313 to 16 μg/ml and 0.125 to 16 μg/ml, respectively. The MIC and MEC modes were both 1 μg/ml for terbinafine and caspofungin; the MIC90 and MEC90 were 1 μg/ml for both drugs, whereas the MIC90 and MEC90 were 4 μg/ml and 16 μg/ml, respectively.

The genera Scopulariopsis and Microascus include opportunistic fungal pathogens of humans. Taxonomically, they belong to the family Microascaceae within the class Sordariomycetes (Ascomycota). Scopulariopsis species are best known as the causative agents of onychomycoses, i.e., less common skin, subcutaneous, and deep tissue infections. They have been implicated in, for example, keratitis (1), sinusitis (2), bronchitis (3), endocarditis (4), meningitis (5), pulmonary infection (6), and disseminated mycoses (7). Infections due to Microascus species are locally invasive, involving organs such as the lungs (8), brain (9), and endocardium (10), or disseminated (11). The prognosis in invasive infections is poor, and many of the reported cases have ended in death. Therapeutic difficulties have been associated with patients’ underlying disease, lack of clear guidelines for treatment, and resistance of the fungi to antimycotics (12–22). Data on the in vitro antifungal susceptibility of Scopulariopsis and Microascus are scant and relate almost exclusively to multidrug-resistant phenotype (12–22). To the best of our knowledge, there have been only three published studies reporting on drug susceptibility results also for other than in the previous studies performed on Scopulariopsis brevicaulis species. The purpose of this study was to evaluate the in vitro activities of 11 antifungal drugs against various Scopulariopsis and Microascus species, including rare species, which were not tested before.

A total of 68 fungal strains were evaluated: 23 Microascus and 45 Scopulariopsis strains, representing 10 and 16 species, respectively. All strains were purchased from the Centraalbureau voor Schimmelcultures (CBS) culture collection (Utrecht, The Netherlands). The list of strains tested is presented in Table S1 in the supplemental material. Fungal inocula were prepared from 14-day-old cultures in Czapek yeast agar using the method described previously (20). The following antifungal drugs were used in the study: 5-fluorocytosine (5FC), amphotericin B (AMB), caspofungin (CFG), ciclopirox (CPX), flucanazole (FLC), itraconazole (ITC), ketoconazole (KTC), miconazole (MCZ), posaconazole (POS), terbinafine (TRB), and voriconazole (VRC). The MIC and MEC modes were both 1 μg/ml for terbinafine and caspofungin; the MIC90 and MEC90 were 1 μg/ml for both drugs, whereas the MIC90 and MEC90 were 4 μg/ml and 16 μg/ml, respectively.

The in vitro activities of 11 antifungal drugs against 68 Scopulariopsis and Microascus strains were investigated. Amphotericin B, 5-fluorocytosine, flucanazole, itraconazole, ketoconazole, miconazole, posaconazole, voriconazole, and ciclopirox showed no or poor antifungal effect. The best activities were exhibited by terbinafine and caspofungin, where the MIC and MEC (minimal effective concentration) ranges were 0.0313 to 16 μg/ml and 0.125 to 16 μg/ml, respectively. The MIC and MEC modes were both 1 μg/ml for terbinafine and caspofungin; the MIC90 and MEC90 were 1 μg/ml for both drugs, whereas the MIC90 and MEC90 were 4 μg/ml and 16 μg/ml, respectively.

The in vitro activities of 11 antifungal drugs against 68 Scopulariopsis and Microascus strains were investigated. Amphotericin B, 5-fluorocytosine, flucanazole, itraconazole, ketoconazole, miconazole, posaconazole, voriconazole, and ciclopirox showed no or poor antifungal effect. The best activities were exhibited by terbinafine and caspofungin, where the MIC and MEC (minimal effective concentration) ranges were 0.0313 to 16 μg/ml and 0.125 to 16 μg/ml, respectively. The MIC and MEC modes were both 1 μg/ml for terbinafine and caspofungin; the MIC90 and MEC90 were 1 μg/ml for both drugs, whereas the MIC90 and MEC90 were 4 μg/ml and 16 μg/ml, respectively.
with other Scopulariopsis and Microascus species (12–22). In our study, CPX had no activity, even against S. brevicaulis, for which good or moderate antifungal effect was previously demonstrated (19, 20, 24–26).

KTC had greater activity than other azoles (MIC range, 0.125 to 16 µg/ml; MEC mode, 8 µg/ml; MIC$_{50}$, 4 µg/ml; MIC$_{90}$, 16 µg/ml). The lowest MICs were recorded for S. acremonium and S. parva strains. Aguilera et al. (13) showed that different Scopulariopsis species reach MICs for KTC in the range of 1 to $\leq$16 µg/ml. Low KTC MICs were demonstrated for single S. acremonium, S. brevicaulis, S. chartarum, S. koningii (MICs, 1 µg/ml), and S. candida (MIC, 2 µg/ml) strains (13).

The highest antifungal activities were seen for TRB and CFG, whose MIC and MEC ranges, MIC/MEC modes, and MIC$_{50}$/MEC$_{50}$ and MIC$_{90}$/MEC$_{90}$ values amounted to 0.0313 to $\geq$16, 1, and 4 µg/ml and 0.125 to 16, 1, and 16 µg/ml, respectively. Species most sensitive to TRB were S. brumptii, S. chartarum, S. coprophila, and S. parva. The lowest CFG MECs were observed for S. acremonium, S. flavo, and S. parva. The TRB MIC values obtained were consistent with available data; the MICs for S. brevicaulis ranged from 0.01 to $\geq$16 µg/ml (14, 16, 20), whereas in the study by Sandoval-Denis et al. (12), who included other Scopulariopsis and Microascus species, the MIC for TRB ranged from 0.5 to 4 µg/ml. Studies on the efficacy of CFG against Scopulariopsis and Microascus are scarce and therefore quite ambiguous. Cuenca-Estrella et al. (16), when testing S. brevicaulis, established CFG MIC values in the range of 4 to $\geq$16 µg/ml. Similar results were obtained by Sandoval-Denis et al. (12) for S. brevicaulis and other Scopulariopsis and Microascus species (MEC range, 1 to 16 µg/ml). However, Odero et al. (21) demonstrated no CFG activity (MEC, $\geq$8 µg/ml) upon testing S. acremonium, S. brevicaulis, S. brumptii, S. candida, S. flavo, S. fusca, and S. koningii.

In conclusion, our results indicate a high level of drug resistance among Scopulariopsis and Microascus species. Only TRB and CFG showed some in vitro efficacy against these fungi and thus may be successfully used for the treatment of their infections. CPX and azoles are by far the most ineffective agents, and AMB has limited activity. Some potency has been observed for amorolfine and other echinocandins (12, 25–27). However, the data are limited, and further studies are required to decisively determine the utility of these drugs against Scopulariopsis and Microascus fungi.

**ACKNOWLEDGMENTS**

This study was supported by the Ministry of Science and Higher Education (IP20130323672). Some CBS strains were financed by a National Science Centre grant (N N401 548140) and by Jagiellonian University Medical College.

### Table 1: MIC/MEC individual values and MIC/MEC ranges obtained for Microascus and Scopulariopsis species groups

<table>
<thead>
<tr>
<th>Species name (no. of strains tested)</th>
<th>MIC/MEC parameter</th>
<th>AMB</th>
<th>CPX</th>
<th>TRB</th>
<th>5FC</th>
<th>FLC</th>
<th>ITC</th>
<th>KTC</th>
<th>MCZ</th>
<th>POS</th>
<th>VRC</th>
<th>CFG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microascus albonigrescens (2)</td>
<td>Individual values</td>
<td>8$^b$</td>
<td>&gt;16</td>
<td>0.5</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>0.5$^e$</td>
<td>1, &gt;16</td>
<td>&gt;16</td>
<td>8, &gt;16</td>
<td>0.5, 8</td>
</tr>
<tr>
<td>M. caviariformis (1)</td>
<td>Individual values</td>
<td>1</td>
<td>&gt;16</td>
<td>2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>0.5</td>
<td>4</td>
<td>&gt;16</td>
<td>16</td>
<td>0.25</td>
</tr>
<tr>
<td>Microascus cinereus (3)</td>
<td>Range</td>
<td>&gt;16</td>
<td>16–16</td>
<td>1–2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>16$^b$</td>
<td>4–&gt;16</td>
<td>&gt;16</td>
<td>16–16</td>
<td>1–8</td>
</tr>
<tr>
<td>M. cirrus (3)</td>
<td>Range</td>
<td>16–16</td>
<td>8–16</td>
<td>1$^b$</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>0.5–8</td>
<td>2–&gt;16</td>
<td>&gt;16$^b$</td>
<td>2–16</td>
<td>&gt;1$^b$</td>
</tr>
<tr>
<td>M. longirostris (3)</td>
<td>Range</td>
<td>2–16</td>
<td>4–16</td>
<td>8–16$^b$</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>0.5–2</td>
<td>&gt;16–16</td>
<td>&gt;8–16</td>
<td>0.5–1</td>
<td></td>
</tr>
<tr>
<td>M. magnoni (4)</td>
<td>Range</td>
<td>16–16$^b$</td>
<td>&gt;16</td>
<td>0.25–4</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>1–8$^b$</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>16–16</td>
<td>0.5–16</td>
<td></td>
</tr>
<tr>
<td>M. nidicola (1)</td>
<td>Individual values</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>8</td>
<td>0.5</td>
<td>ND$^a$</td>
<td>&gt;16</td>
<td>4</td>
<td>ND</td>
</tr>
<tr>
<td>M. pyramids (1)</td>
<td>Individual values</td>
<td>ND</td>
<td>&gt;16</td>
<td>8</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>ND</td>
<td>&gt;16</td>
<td>16</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>M. senegalensis (2)</td>
<td>Individual values</td>
<td>16, &gt;16</td>
<td>&gt;16</td>
<td>1–16</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>1.4</td>
<td>&gt;16–16</td>
<td>&gt;0.5, &gt;16</td>
<td>8, &gt;16</td>
<td>8</td>
</tr>
<tr>
<td>M. trigonosporus (3)</td>
<td>Range</td>
<td>2–16$^b$</td>
<td>16–16</td>
<td>1–2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>4–16$^b$</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>0.5–2</td>
</tr>
<tr>
<td>Scopulariopsis (3)</td>
<td>Range</td>
<td>4–16</td>
<td>8–16</td>
<td>1–2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;16</td>
<td>0.25–0.5</td>
<td>4–16</td>
<td>1–16</td>
<td>2–8</td>
<td>0.125–0.25</td>
</tr>
</tbody>
</table>

$^a$ AMB, amphotericin B; CPX, ciclopirox; TRB, terbinafine; 5FC, 5-fluorocytosine; FLC, fluconazole; ITC, itraconazole; KTC, ketoconazole; MCZ, miconazole; POS, posaconazole; VRC, voriconazole; CFG, minimal effective concentration; CFG, caspofungin.

$^b$ The results were not obtained for some strains because of poor or no fungal growth in the wells (i.e., with and/or without antifungal drug).

$^c$ ND, not determined.
We declare no conflicts of interest. We alone are responsible for the content and writing of the paper.

REFERENCES


