Hindawi
BioMed Research International
Volume 2017, Article ID 1584658, 13 pages
https://doi.org/10.1155/2017/1584658

*Research Article*

# Drug Susceptibility of 33 Reference Strains of Slowly Growing Mycobacteria to 19 Antimicrobial Agents

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Received 23 December 2016; Revised 24 March 2017; Accepted 6 April 2017; Published 20 April 2017

Academic Editor: Frederick D. Quinn



*Objectives*. Slowly growing mycobacteria (SGM) are prevalent worldwide and cause an extensive spectrum of diseases. *Methods*. In this study, the antimicrobial susceptibility of 33 reference strains of SGM to 19 antimicrobial agents was tested using a modified microdilution method. *Results*. Cefmetazole (32/33) and azithromycin (32/33) exhibited the highest antimicrobial activity, and dapsone (9/33) exhibited the lowest activity against the tested strains. Cefoxitin (30/33), cefoperazone (28/33), and cefepime (28/33) were effective against a high proportion of strains, and macrolides were also highly effective as well as offering the benefit of convenient oral administration to patients. Linezolid (27/33), meropenem (26/33), sulfamethoxazole (26/33), and tigecycline (25/33) showed the highest activity; clofazimine (20/33) and doxycycline (18/33) showed intermediate activity; and rifapentine (13/33), rifabutin (13/33), and minocycline (11/33) showed low antimicrobial activity, closely followed by thioacetazone (10/33) and pasiniazid (10/33), against the tested organisms. According to their susceptibility profiles, the slowly growing species *Mycobacterium avium* and *Mycobacterium simiae* were the least susceptible to the tested drugs, whereas *Mycobacterium intracellulare*, *Mycobacterium asiaticum*, *Mycobacterium scrofulaceum*, *Mycobacterium szulgai*, *Mycobacterium branderi*, and *Mycobacterium holsaticum* were the most susceptible. *Conclusions*. In summary, cephalosporins and macrolides, particularly cefmetazole, azithromycin, clarithromycin, and roxithromycin, showed good antimicrobial activity against the reference strains of SGM.

## 1. Introduction

Slowly growing mycobacteria (SGM) species are ubiquitous organisms that are widely distributed in the environment [1], not only in tap water, soil, dust, and food products but also in domestic and wild animals [2]. SGM form colonies visible to the naked eye in more than 7 days on subculture media [3]. SGM comprise some common species, such as the *Mycobacterium avium* complex (*Mycobacterium avium*, *Mycobacterium intracellulare*, and *Mycobacterium chimaera*), *Mycobacterium kansasii*, *Mycobacterium haemophilum*, *Mycobacterium marinum*, and *Mycobacterium ulcerans*, in addition to some less common pathogens, such as *Mycobacterium scrofulaceum*, *Mycobacterium simiae*, *Mycobacterium malmoense* and *Mycobacterium xenopi*. *Mycobacterium xenopi* is largely distributed in Canada and northern Europe [4]. Slowly growing species were the first nontuberculous mycobacteria (NTM) to be recognized as causing chronic lung disease [4, 5], which may bring about diverse infections from minor sicknesses to serious widespread disorders [6].

At present, standard therapeutic strategies to treat SGM infections are lacking. In this study, 19 new antimicrobial agents were tested against 33 reference SGM pathogens using a modified broth microdilution method with the aim of identifying optimal schemes according to the Clinical Laboratory Standards Institute (CLSI) (USA) [7, 8] and World Health Organization (WHO) [9] guidelines.

## 2. Materials and Methods

*2.1. Reference Strains.* Thirty-three international reference SGM strains were purchased from Deutsche Sammlung von

Mikroorganismen und Zellkulturen (DSMZ) and the American Type Culture Collection (ATCC), including *Mycobacterium avium*, *Mycobacterium intracellulare*, *Mycobacterium shimoidei*, *Mycobacterium farcinogenes*, and *Mycobacterium simiae* (Table 1). These strains were cultured at the appropriate temperatures.

*2.2. Antimicrobial Agents.* Nineteen chemicals were purchased from Sigma-Aldrich Company: cefoxitin (FOX), cefoperazone (CFP), cefmetazole (CMZ), cefepime (FEP), rifapentine (RPT), rifabutin (RBT), azithromycin (AZM), clarithromycin (CLR), roxithromycin (ROX), thioacetazone (THI), doxycycline (DOX), minocycline (MIN), tigecycline (TIG), meropenem (MEM), clofazimine (CLO), sulfamethoxazole (SMZ), pasiniazid (PASI), linezolid (LNZ), and dapsone (DAP). All of the antituberculous agents were freshly prepared.

*2.3. Drug Susceptibility Test.* SGM strains were incubated using Difco Middlebrook 7H10 Agar (BD company) with 5% oleic acid-albumin-dextrose-catalase (OADC) [8]. The drug sensitivity tests were performed using a cation-adjusted Mueller-Hinton (CAMH) broth microdilution method, with the addition of 5% OADC, according to the CLSI standard operating procedure [8]. All of the experiments were performed in 96-well microplates and repeated. The minimum inhibitory concentration (MIC) for each antibiotic for each strain was the mean of two experiments. Firstly, the bacterial suspensions were prepared as follows: bacterial inocula were adjusted with normal saline to a density of a 0.5 McFarland standard with an inoculum density of approximately $1 \times 10^7$ colony forming units (CFU)/mL; then 50 $\mu$L of the bacterial suspension was mixed with 10 mL of CAMH and 5% OADC broth for a 1 : 200 dilution. Secondly, 100 $\mu$L of CAMH and 5% OADC medium were added to each well of a 96-well microplate, with the exception of the first well of every row to which 180 $\mu$L of medium and a 20 $\mu$L drug dilution were added. The solution in the first well was successively diluted into subsequent wells, up to the 11th well. The 12th well in every row was used as a blank control. Finally, 100 $\mu$L of the bacterial dilution was added to all of the wells. The ultimate volume in each well was 200 $\mu$L. All of the 96-well microplates were sealed in a plastic bag and incubated at 37°C. The concentrations of sulfamethoxazole, dapsone, cefoxitin, cefmetazole, cefoperazone, cefepime, thioacetazone, pasiniazid, minocycline, doxycycline, tigecycline, and meropenem were 0.25–256 $\mu$g/mL; the concentrations of clarithromycin, azithromycin, roxithromycin, clofazimine, rifapentine, and rifabutin were 0.03–32 $\mu$g/mL; and the concentration of linezolid was 0.06–64 $\mu$g/mL. Two negative controls were applied: a no drug control (CAMH + OADC + bacteria) and a no bacteria control (barely CAMH and OADC) [10]. The MIC breakpoints of the drugs exhibiting susceptibility, moderate susceptibility, and resistance were assigned according to the CLSI [7, 8] and WHO [9] guidelines (Table 2).

## 3. Results

The antimicrobial susceptibility profiles of the 33 SGM reference species to 19 antibacterial agents are presented in Table 1. Cephalosporins including cefoxitin (30/33, 90.91%), cefoperazone (28/33, 84.85%), cefmetazole (32/33, 96.97%), and cefepime (28/33, 84.85%) exhibited high activity against the tested strains. Macrolide antibiotics including azithromycin (32/33, 96.97%), clarithromycin (30/33, 90.91%), and roxithromycin (31/33, 93.94%) were also effective against the SGM strains. Linezolid (27/33, 81.82%), meropenem (26/33, 78.79%), and sulfamethoxazole (26/33, 78.79%) showed similar levels of activity against the tested strains, and clofazimine (20/33, 60.61%) inhibited most of the SGM strains. The tetracyclines, doxycycline (18/33, 54.55%), minocycline (11/33, 33.33%), and tigecycline (25/33, 75.76%), exhibited different levels of activity against the SGM standard species, whereas rifapentine (13/33, 39.39%) and rifabutin (13/33, 39.39%) showed weak antimicrobial activity against the SGM, as did thioacetazone (10/33, 30.30%), pasiniazid (10/33, 30.30%), and dapsone (9/33, 27.27%).

The drug susceptibility profiles of the tested organisms revealed that *Mycobacterium avium* and *Mycobacterium simiae* were the least susceptible to the tested drugs, whereas *Mycobacterium intracellulare*, *Mycobacterium asiaticum*, *Mycobacterium scrofulaceum*, *Mycobacterium szulgai*, *Mycobacterium branderi*, and *Mycobacterium holsaticum* were the most susceptible (Table 3 and Figure 1). Among the *Mycobacterium avium* complex, *Mycobacterium avium* was the most resistant to the tested drugs, whereas *Mycobacterium intracellulare* was the most susceptible (Figure 2). Azithromycin was identified as the most effective antimicrobial agent against SGM species among the drugs tested, and dapsone was the least effective.

## 4. Discussion

In this study, 19 antimicrobial susceptibility tests were performed against 33 SGM organisms by a Microplate Alamar Blue Assay. The current first-line drugs for the treatment of nontuberculous mycobacteria are capreomycin, clarithromycin, and rifampin. And the current second-line drugs for the treatment of nontuberculous mycobacteria are moxifloxacin, linezolid, amikacin, ciprofloxacin, ethambutol, isoniazid, rifabutin, streptomycin, and trimethoprim-sulfamethoxazole [7]. Our findings indicated that cephalosporins and macrolides, particularly cefmetazole, azithromycin, clarithromycin, and roxithromycin, showed effective antimicrobial activity against the tested strains.

In recent studies [4, 11–15], cefoxitin and meropenem have been reported to show some activity against *Mycobacterium abscessus*, *Mycobacterium chelonae*, and *Mycobacterium fortuitum*, whereas *Mycobacterium kansasii* has been shown to be susceptible to clarithromycin and linezolid. Macrolides were active against isolates of *Mycobacterium avium* [12, 16, 17], and tigecycline has been demonstrated to exhibit high level antimicrobial activity against RGM in vitro [18]. In other studies, *Mycobacterium kansasii* was reported to

Table 1: The MIC ($\mu$g/mL) of 19 antimicrobial agents against 33 reference slowly growing mycobacteria.

(a)

| Sp. (international code) | FOX | CFP | CMZ | FEP | RPT | RBT | AZM | CLR | ROX | THI |
|---|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium avium* (DSM44133) | >256 | 128 | >256 | >256 | 4 | **0.25** | **4** | **0.5** | **1** | >256 |
| *Mycobacterium intracellulare* (ATCC13950) | **0.5** | **8** | **1** | **4** | **<0.03** | **<0.03** | **<0.03** | **0.13** | **<0.03** | **<0.25** |
| *Mycobacterium shimoidei* (ATCC27962) | **8** | **16** | **4** | >256 | 2 | **0.06** | **0.13** | **<0.03** | **0.06** | >256 |
| *Mycobacterium farcinogenes* (ATCC35753) | **4** | **16** | **2** | **<0.25** | **<0.03** | **<0.03** | **0.13** | **<0.03** | **<0.03** | **2** |
| *Mycobacterium simiae* (ATCC25275) | >256 | 256 | 256 | 128 | 16 | 4 | **16** | **1** | **4** | 256 |
| *Mycobacterium asiaticum* (ATCC25276) | **2** | **<0.25** | **<0.25** | **1** | 4 | **<0.03** | **0.5** | **<0.03** | **0.13** | **1** |
| *Mycobacterium scrofulaceum* (ATCC19981) | **64** | **64** | **32** | **32** | **<0.03** | **<0.03** | **2** | **0.06** | **0.13** | **<0.25** |
| *Mycobacterium szulgai* (ATCC35799) | **4** | **2** | **2** | **1** | **<0.03** | **<0.03** | **0.13** | **<0.03** | **<0.03** | 256 |
| *Mycobacterium africanum* (ATCC35711) | **64** | **64** | **8** | 256 | 16 | 32 | 32 | 32 | 32 | >256 |
| *Mycobacterium alvei* (DSM44176) | **16** | **64** | **0.5** | **<0.25** | 1 | **0.13** | **0.06** | **0.06** | **<0.03** | 256 |
| *Mycobacterium branderi* (ATCC51788) | **4** | **16** | **1** | **16** | 32 | **0.25** | **0.25** | **<0.03** | **<0.03** | >256 |
| *Mycobacterium celatum* (ATCC44243) | 128 | 128 | **64** | **64** | 32 | **0.5** | **1** | **0.06** | **0.25** | 128 |
| *Mycobacterium chimaera* (DSM44623) | **64** | **32** | **16** | **64** | 16 | 16 | **8** | **0.5** | **0.5** | 64 |
| *Mycobacterium cosmeticum* (DSM44829) | **64** | >256 | **8** | 256 | >32 | 32 | **2** | **0.25** | **1** | >256 |

(a) Continued.

| Sp. (international code) | FOX | CFP | CMZ | FEP | RPT | RBT | AZM | CLR | ROX | THI |
|---|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium duvalii* (ATCC43910) | **<0.25** | **16** | **1** | **0.5** | **0.06** | **<0.03** | **0.5** | **0.06** | **0.13** | 8 |
| *Mycobacterium elephantis* (DSM44368) | **8** | 256 | **2** | **4** | 8 | 2 | **8** | **1** | **4** | 32 |
| *Mycobacterium hassiacum* (DSM44199) | 128 | >256 | **16** | 256 | 32 | **0.5** | **<0.03** | **<0.03** | **<0.03** | >256 |
| *Mycobacterium hiberniae* (DSM44241) | **1** | **2** | **<0.25** | **16** | **0.25** | **<0.03** | **2** | **0.06** | **0.13** | 64 |
| *Mycobacterium holsaticum* (DSM44478) | **1** | **32** | **<0.25** | **0.5** | 4 | 1 | **<0.03** | **<0.03** | **<0.03** | 256 |
| *Mycobacterium houstonense* (DSM44676) | **32** | **32** | **64** | **32** | 64 | >32 | 32 | **8** | **2** | 64 |
| *Mycobacterium kubicae* (DSM44627) | **64** | **16** | **0.5** | **16** | 64 | >32 | **2** | **<0.25** | **16** | 256 |
| *Mycobacterium lentiflavum* (DSM44418) | **2** | **4** | **4** | **0.13** | **0.5** | >32 | **8** | **2** | 32 | >256 |
| *Mycobacterium mageritense* (DSM44476) | **8** | **1** | **0.5** | **8** | 32 | >32 | **8** | **4** | ***16*** | 64 |
| *Mycobacterium nonchromogenicum* (DSM44164) | **2** | **<0.25** | **4** | **<0.25** | 1 | >32 | **8** | **2** | **<0.03** | **2** |
| *Mycobacterium palustre* (DSM44572) | **<0.25** | **<0.25** | **0.5** | **<0.25** | **0.06** | >32 | **<0.03** | **0.5** | **0.06** | **4** |
| *Mycobacterium parascrofulaceum* (DSM44648) | **<0.25** | **<0.25** | **4** | **0.25** | **0.06** | 8 | **1** | **16** | **<0.03** | 64 |
| *Mycobacterium senuense* (DSM44999) | **0.5** | **<0.25** | **2** | **<0.25** | **<0.03** | 32 | **1** | **<0.25** | **0.06** | **2** |
| *Mycobacterium seoulense* (DSM44998) | **<0.25** | **<0.25** | **4** | **<0.25** | **0.5** | >32 | **2** | 32 | **<0.03** | 128 |
| *Mycobacterium thermoresistibile* (DSM44167) | **8** | **0.25** | **4** | **2** | 2 | >32 | **2** | **1** | **1** | **2** |

(a) Continued.

| Sp. (international code) | FOX | CFP | CMZ | FEP | RPT | RBT | AZM | CLR | ROX | THI |
|---|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium triplex* (DSM44626) | **0.25** | **0.5** | **<0.25** | **1** | 4 | >32 | **1** | **<0.25** | **0.13** | **0.5** |
| *Mycobacterium vanbaalenii* (DSM7251) | **8** | **0.25** | **0.5** | **1** | **0.06** | >32 | **<0.25** | 64 | **1** | 256 |
| *Mycobacterium murale* (DSM44340) | **0.5** | **<0.25** | **0.25** | **0.25** | **0.25** | >32 | **<0.25** | **8** | **<0.03** | **2** |
| *Mycobacterium gordonae* (ATCC14470) | **4** | **0.5** | **16** | **0.5** | 1 | >32 | **8** | **8** | **16** | 128 |

(b)

| Sp. (international code) | DOX | MIN | TIG | MEM | CLO | SMZ | PASI | LNZ | DAP |
|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium avium* (DSM44133) | >256 | 64 | 32 | >256 | 16 | **32** | 32 | 32 | >256 |
| *Mycobacterium intracellulare* (ATCC13950) | **<0.25** | **<0.25** | **0.5** | **0.5** | **0.13** | **<0.25** | **<0.25** | **<0.06** | **<0.25** |
| *Mycobacterium shimoidei* (ATCC27962) | 256 | 64 | **1** | >256 | **0.13** | **4** | **0.5** | **0.5** | 64 |
| *Mycobacterium farcinogenes* (ATCC35753) | **0.25** | 8 | **<0.03** | **<0.25** | **<0.03** | **1** | 16 | **0.25** | 4 |
| *Mycobacterium simiae* (ATCC25275) | >256 | 16 | 16 | >256 | **<0.03** | **16** | 16 | 32 | 16 |
| *Mycobacterium asiaticum* (ATCC25276) | **<0.25** | **0.5** | **<0.03** | **<0.25** | **<0.03** | **<0.25** | 2 | **0.13** | **<0.25** |
| *Mycobacterium scrofulaceum* (ATCC19981) | **0.25** | **2** | **0.5** | 32 | **<0.03** | **16** | **1** | **1** | **2** |
| *Mycobacterium szulgai* (ATCC35799) | **<0.25** | **<0.25** | **0.13** | **0.5** | **<0.03** | **<0.25** | **1** | **0.13** | **<0.25** |
| *Mycobacterium africanum* (ATCC35711) | **4** | 8 | **0.25** | **4** | 32 | 256 | >256 | **16** | 4 |
| *Mycobacterium alvei* (DSM44176) | **<0.25** | 32 | **<0.03** | **<0.25** | **0.5** | **4** | 8 | **16** | 64 |
| *Mycobacterium branderi* (ATCC51788) | **<0.25** | **0.5** | **0.06** | **0.5** | **<0.03** | **0.5** | **1** | **<0.06** | **<0.25** |

(b) Continued.

| Sp. (international code) | DOX | MIN | TIG | MEM | CLO | SMZ | PASI | LNZ | DAP |
|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium celatum* (ATCC44243) | **2** | **0.5** | **4** | 64 | **<0.03** | **2** | **0.5** | **16** | **<0.25** |
| *Mycobacterium chimaera* (DSM44623) | 8 | 32 | **4** | 32 | **0.5** | 64 | >256 | **16** | 64 |
| *Mycobacterium cosmeticum* (DSM44829) | **2** | 128 | **1** | **8** | 32 | 256 | >256 | 32 | 256 |
| *Mycobacterium duvalii* (ATCC43910) | **<0.25** | 16 | **<0.03** | **2** | 1 | **4** | **0.5** | **0.25** | 8 |
| *Mycobacterium elephantis* (DSM44368) | **<0.25** | **0.5** | **<0.03** | **8** | **0.13** | **<0.25** | **0.5** | **0.5** | **0.5** |
| *Mycobacterium hassiacum* (DSM44199) | **<0.25** | 8 | **<0.03** | 256 | **0.13** | **8** | 8 | **4** | 16 |
| *Mycobacterium hiberniae* (DSM44241) | **1** | 8 | **0.13** | **4** | **<0.03** | **1** | 8 | **1** | 4 |
| *Mycobacterium holsaticum* (DSM44478) | **<0.25** | **1** | **0.25** | **16** | **0.13** | **<0.25** | **1** | **0.5** | **0.5** |
| *Mycobacterium houstonense* (DSM44676) | 64 | 64 | 16 | **16** | 32 | 256 | 64 | 32 | 256 |
| *Mycobacterium kubicae* (DSM44627) | >256 | 16 | **2** | **2** | 32 | >256 | 16 | 32 | >256 |
| *Mycobacterium lentiflavum* (DSM44418) | >256 | 128 | **4** | **4** | 4 | 128 | 128 | **4** | 128 |
| *Mycobacterium mageritense* (DSM44476) | >256 | 128 | 8 | **8** | 32 | **8** | 128 | 32 | 8 |
| *Mycobacterium nonchromogenicum* (DSM44164) | 128 | 128 | 16 | **16** | 2 | **4** | 128 | **2** | 4 |
| *Mycobacterium palustre* (DSM44572) | **2** | 32 | **0.06** | **<0.25** | **0.25** | **8** | 32 | **0.25** | 8 |
| *Mycobacterium parascrofulaceum*(DSM44648) | 64 | 32 | **0.03** | **<0.25** | 2 | **32** | 32 | **2** | 32 |
| *Mycobacterium senuense* (DSM44999) | **1** | **4** | **1** | **1** | **0.5** | **4** | 4 | **0.5** | 4 |
| *Mycobacterium seoulense* (DSM44998) | **2** | 128 | 8 | **8** | 4 | **8** | 128 | **4** | 8 |

(b) Continued.

| Sp. (international code) | DOX | MIN | TIG | MEM | CLO | SMZ | PASI | LNZ | DAP |
|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium thermoresistibile* (DSM44167) | 256 | 256 | ***2*** | **2** | 1 | **8** | 256 | **1** | 8 |
| *Mycobacterium triplex* (DSM44626) | 256 | **0.5** | **0.06** | <**0.25** | **0.13** | **0.5** | **0.5** | **0.13** | **0.5** |
| *Mycobacterium vanbaalenii* (DSM7251) | 8 | **4** | 8 | **8** | 2 | **4** | 4 | **2** | 4 |
| *Mycobacterium murale* (DSM44340) | 256 | 16 | **0.06** | <**0.25** | **0.5** | **8** | 16 | **0.5** | 8 |
| *Mycobacterium gordonae* (ATCC14470) | >256 | 16 | 16 | **16** | **0.5** | 256 | 16 | **0.5** | 256 |

*Note 1*. FOX: cefoxitin; CFP: cefoperazone; CMZ: cefmetazole; FEP: cefepime; RPT: rifapentine; RBT: rifabutin; AZM: azithromycin; CLR: clarithromycin; ROX: roxithromycin; THI: thioacetazone; DOX: doxycycline; MIN: minocycline; TIG: tigecycline; MEM: meropenem; CLO: clofazimine; SMZ: sulfamethoxazole; PASI: pasiniazid; LNZ: linezolid; DAP: dapsone.
*Note 2*. Bold numbers indicate drug susceptibility. Numbers in bold and cursive indicate intermediate drug susceptibility.

TABLE 2: The MIC ($\mu$g/mL) breakpoints of 19 antibacterial agents.

| | Susceptibility | Intermediate susceptibility | Resistance |
|---|---|---|---|
| Cefoxitin | ≤16 | 32–64 | ≥128 |
| Cefoperazone | ≤16 | 32–64 | ≥128 |
| Cefmetazole | ≤16 | 32–64 | ≥128 |
| Cefepime | ≤16 | 32–64 | ≥128 |
| Rifapentine | — | — | >1 |
| Rifabutin | — | — | >2 |
| Azithromycin | ≤8 | 16 | ≥32 |
| Clarithromycin | ≤8 | 16 | ≥32 |
| Roxithromycin | ≤8 | 16 | ≥32 |
| Thioacetazone | — | — | ≥8 |
| Doxycycline | ≤1 | 2–4 | ≥8 |
| Meropenem | ≤4 | 8–16 | ≥32 |
| Clofazimine | — | — | ≥1 |
| Sulfamethoxazole | ≤38 | — | ≥76 |
| Pasiniazid | — | — | ≥2 |
| Minocycline | ≤1 | 2–4 | ≥8 |
| Linezolid | ≤8 | 16 | ≥32 |
| Dapsone | — | — | ≥4 |
| Tigecycline | ≤1 | 2–4 | ≥8 |

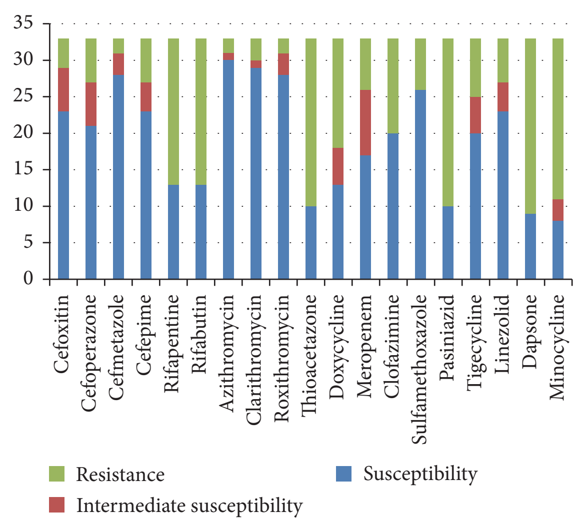


FIGURE 1: The sensitivity profiles of 33 reference slowly growing mycobacteria to 19 antimicrobial agents.

be the most susceptible NTM species in vitro [19], and *Mycobacterium simiae* was found to be resistant to clarithromycin, doxycycline, and sulfamethoxazole [20, 21]. However, few studies have tested the activity of cefoperazone, cefmetazole, and cefepime against SGM. In our study, cephalosporins were found to be effective antimicrobial agents and cefmetazole in particular was identified as a good candidate for the treatment of SGM infections. In previous research [15, 22], clarithromycin has been widely used as an antimicrobial agent to SGM, whereas azithromycin and roxithromycin have rarely been tested. Among the tetracyclines, tigecycline was found to be the most effective against SGM. Previous studies have reported that *Mycobacterium kansasii* was 100% resistant to doxycycline, and *Mycobacterium simiae* isolates were 100% resistant to clarithromycin, doxycycline, and sulfamethoxazole.

*Mycobacterium avium* and *Mycobacterium intracellulare* are important members of the SGM. Macrolides and sulfamethoxazole are recognized as useful drugs against *Mycobacterium avium* and *Mycobacterium intracellulare*, but rifapentine is ineffective against *Mycobacterium avium*. *Mycobacterium chimaera*, a recently described species distinct from

Table 3: Susceptibility of 33 international standard slowly growing mycobacterial strains to 19 antibacterial agents.

| Sp. (international code) | FOX | CFP | CMZ | FEP | RPT | RBT | AZM | CLR | ROX | THI | DOX | MIN | TIG | MEM | CLO | SMZ | PASI | LNZ | DAP | Susceptibility rate (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium avium* (DSM44133) | − | − | − | − | − | + | + | + | + | − | − | − | − | − | − | + | − | − | − | 26.32 |
| *Mycobacterium intracellulare* (ATCC13950) | + | + | + | + | + | + | + | + | + | + | + | + | − | + | + | + | + | + | + | 94.74 |
| *Mycobacterium shimoidei* (ATCC27962) | + | + | + | − | − | + | + | + | + | − | − | − | + | − | + | + | + | + | − | 63.16 |
| *Mycobacterium farcinogenes* (ATCC35753) | + | + | + | + | + | + | + | + | + | + | + | − | + | + | + | + | − | + | − | 84.21 |
| *Mycobacterium simiae* (ATCC25275) | − | − | − | − | − | − | + | + | + | − | − | − | − | − | + | + | − | − | − | 26.32 |
| *Mycobacterium asiaticum* (ATCC25276) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | − | + | + | 94.74 |
| *Mycobacterium scrofulaceum* (ATCC19981) | + | + | + | + | + | + | + | + | + | + | + | + | + | − | + | + | + | + | + | 94.74 |
| *Mycobacterium szulgai* (ATCC35799) | + | + | + | + | + | + | + | + | + | − | + | + | + | + | + | + | + | + | + | 94.74 |
| *Mycobacterium africanum* (ATCC35711) | + | + | + | − | + | + | + | − | − | − | + | − | + | + | − | − | − | + | − | 52.63 |
| *Mycobacterium alvei* (DSM44176) | + | + | + | + | + | + | + | + | + | − | + | − | + | + | + | + | − | + | − | 78.95 |
| *Mycobacterium branderi* (ATCC51788) | + | + | + | + | + | + | + | + | + | − | + | + | + | + | + | + | + | + | + | 94.74 |
| *Mycobacterium celatum* (ATCC44243) | − | − | + | + | + | + | + | + | + | − | + | + | + | − | + | + | + | + | + | 78.95 |
| *Mycobacterium chimaera* (DSM44623) | + | + | + | + | + | + | + | + | + | − | − | − | + | − | + | − | − | + | − | 63.16 |

Table 3: Continued.

| Sp. (international code) | FOX | CFP | CMZ | FEP | RPT | RBT | AZM | CLR | ROX | THI | DOX | MIN | TIG | MEM | CLO | SMZ | PASI | LNZ | DAP | Susceptibility rate (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium cosmeticum* (DSM44829) | + | − | + | − | + | + | + | + | + | − | + | − | + | + | − | − | − | − | − | 52.63 |
| *Mycobacterium duvalii* (ATCC43910) | + | + | + | + | + | + | + | + | + | − | + | − | + | + | − | + | + | + | − | 78.95 |
| *Mycobacterium elephantis* (DSM44368) | + | − | + | + | + | + | + | + | + | − | + | + | + | + | + | + | + | + | + | 89.47 |
| *Mycobacterium hassiacum* (DSM44199) | − | − | + | − | + | + | + | + | + | − | + | − | + | − | + | + | − | + | − | 57.89 |
| *Mycobacterium hiberniae* (DSM44241) | + | + | + | + | + | + | + | + | + | − | + | − | + | + | + | + | − | + | − | 78.95 |
| *Mycobacterium holsaticum* (DSM44478) | + | + | + | + | + | + | + | + | + | − | + | + | + | + | + | + | + | + | + | 94.74 |
| *Mycobacterium houstonense* (DSM44676) | + | + | + | + | + | − | + | + | + | − | − | − | − | + | − | − | − | − | − | 47.37 |
| *Mycobacterium kubicae* (DSM44627) | + | + | + | + | + | − | + | + | + | − | − | − | + | + | − | − | − | − | − | 52.63 |
| *Mycobacterium lentiflavum* (DSM44418) | + | + | + | + | + | − | + | + | − | − | − | − | + | + | − | − | − | + | − | 52.63 |
| *Mycobacterium mageritense* (DSM44476) | + | + | + | + | + | − | + | + | + | − | − | − | − | + | − | + | − | − | − | 52.63 |
| *Mycobacterium nonchromogenicum* (DSM44164) | + | + | + | + | + | + | + | + | + | + | − | − | − | + | − | + | − | + | − | 68.42 |
| *Mycobacterium palustre* (DSM44572) | + | + | + | + | + | + | + | + | + | + | + | − | + | + | + | + | − | + | − | 84.21 |
| *Mycobacterium parascrofulaceum* (DSM44648) | + | + | + | + | + | + | + | + | + | − | − | − | + | + | − | + | − | + | − | 68.42 |

Table 3: Continued.

| Sp. (international code) | FOX | CFP | CMZ | FEP | RPT | RBT | AZM | CLR | ROX | THI | DOX | MIN | TIG | MEM | CLO | SMZ | PASI | LNZ | DAP | Susceptibility rate (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Mycobacterium senuense* (DSM44999) | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | + | − | + | − | 89.47 |
| *Mycobacterium seoulense* (DSM44998) | + | + | + | + | + | − | + | − | + | − | + | − | − | + | − | + | − | + | − | 57.89 |
| *Mycobacterium thermoresistibile* (DSM44167) | + | + | + | + | + | − | + | + | + | + | − | − | + | + | − | + | − | + | − | 68.42 |
| *Mycobacterium triplex* (DSM44626) | + | + | + | + | + | − | + | + | + | + | − | + | + | + | + | + | + | + | + | 89.47 |
| *Mycobacterium vanbaalenii* (DSM7251) | + | + | + | + | + | + | + | − | + | − | − | + | − | + | − | + | − | + | − | 63.16 |
| *Mycobacterium murale* (DSM44340) | + | + | + | + | + | − | + | + | + | + | − | − | + | + | + | + | − | + | − | 73.68 |
| *Mycobacterium gordonae (*ATCC14470*)* | + | + | + | + | + | − | + | + | + | − | − | − | − | + | + | − | − | + | − | 57.89 |

*Note*. “+” indicates sensitivity; “−” indicates resistance.

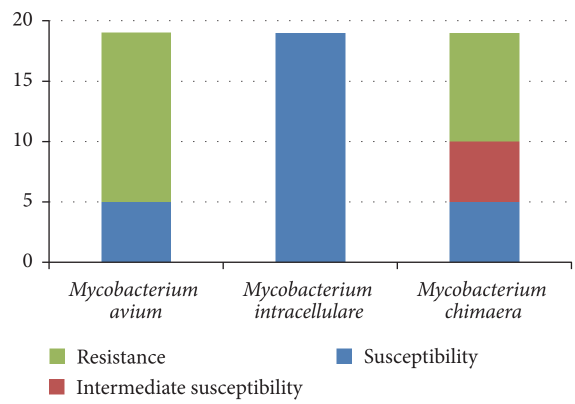


Figure 2: The sensitivity profiles of the *Mycobacterium avium* complex to 19 antimicrobial agents.

*Mycobacterium intracellulare*, is regarded as less virulent than *Mycobacterium intracellulare* [23, 24], but neither rifapentine nor rifabutin was effective against *Mycobacterium chimaera*.

*Mycobacterium simiae* was highly resistant to the tested drugs. It was first isolated from monkeys in 1965 and is now most frequently isolated from human respiratory specimens [25, 26], predominantly being reported in the southwest of the United States and Middle Eastern countries, including Israel and Iran [27].

## 5. Conclusions

Our findings present the drug susceptibility profiles of representative SGM species to a range of antimicrobial agents and provide insight into potentially effective therapeutic strategies. In the future, susceptibility testing of clinical isolates may help to tailor therapeutic strategies to individual patients. Combination therapy should also be explored as a means to increase the efficacy of drug treatment against SGM pathogens. Furthermore, the synergistic activity of some drugs will be analyzed, and drug susceptibility in vivo response must be performed in our recent research.

## Conflicts of Interest

The authors have declared that no conflicts of interest exist.

## Acknowledgments

This paper is financially supported by the Project of the National Key Program of Mega Infectious Diseases (no. 2013ZX10004-101), the Key Project of the State Key Laboratory for Infectious Disease Prevention and Control (no. 2014SKLID104), Science and Technology of Shanxi Province for Youth Science Foundation (no. 2016021161), a Science and Technology Innovation Team support project (no. CX201412) from Changzhi Medical College, and innovation project of university students in Shanxi Province (no. 2016303). The authors thank the staffs of National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention.

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