Abstract

Background: We studied antituberculosis spectra of the newly synthesized OPC-67683 (OPC; 6-[2,4-dimethoxyphenyl]-3H-1,4-oxazin-3-one) and PA-824 (2-[(2R)-3-[(2R)-3-fluorophenyl]propanoyl]-2-imidazolidinone), comparing with the existing first-line drugs to using Mycobacterium tuberculosis isolates with various resistance potential. OPC and PA-824 were synthesized and tested for their antituberculosis activities from piezoelectric polyanion.

Methods: MICs of OPC and PA were evaluated by the agar dilution method, comparing with clarithromycin (RMP), terizidone (TM), amikacin (AMK), ciprofloxacin (CPFX) and imipenem (IPM). A total of 31 clinical isolates of M. tuberculosis and 16 isolates of various NTM were tested. Drug-susceptible Mycobacterium (DS-TB; n=21), Drug-Resistant Mycobacterium (MDR-TB; n=10), M. tuberculosis (n=14), M. avium (n=14), M. intracellulare (n=12), M. chelonae (n=12), M. abscessus (n=12), M. fortuitum (n=12), M. kansasii (n=14), M. avium (n=14), M. intracellulare (n=12), M. chelonae (n=12), M. abscessus (n=12), and M. fortuitum (n=12) were tested for the 3 species of slowly-growing non-tuberculous mycobacteria (NTM) are summarized in Table 2, respectively.

Results: The results for the 3 species of slowly-growing non-tuberculous mycobacteria (NTM) are summarized in Table 2, respectively. Neither of the tested candidates OPC-67683 and PA-824 demonstrated any activities against NTM species except M. abscessus. Against all isolated isolates, OPC-67683 showed the level of in vitro activity (MIC90: 0.25 µg/ml) which was the lowest level comparing with those of RMP (3.125 µg/ml), IPM (0.0015 µg/ml), RMP (0.78 µg/ml), and IPM (0.0015 µg/ml). In contrast, PA-824 showed the lowest activity against all isolated (MIC90: 100 µg/ml) that were comparable to that of SM (100 µg/ml).

Conclusions: OPC-67683 and PA-824 demonstrated potent activity of OPC-67683 with the First-Line Anti-TB drugs against M. tuberculosis and M. intracellulare, M. chelonae, M. abscessus, and M. fortuitum. M. tuberculosis and M. intracellulare were almost similar to those of MIC 90s against DS-TB candidates having none of cross-resistance with the current anti-TB drugs.

Introduction

Drug susceptibility testing of Mycobacterium tuberculosis (MTB) is essential for determining proper anti-TB chemotherapy, and this test is performed by the proportion method, the radiometric method, and/or the agar dilution method. The agar dilution method is one of the most commonly performed methods, and this method is usually performed by broth microdilution or agar dilution methods. The standard methods of the agar dilution method were established by the Clinical and Laboratory Standards Institute (CLSI) in 2012. OPC-67683 and PA-824 were synthesized and tested for their antituberculosis activities from piezoelectric polyanion.

Materials and Methods

Drug-susceptible Mycobacterium (DS-TB; n=21), Drug-Resistant Mycobacterium (MDR-TB; n=10), M. tuberculosis (n=14), M. avium (n=14), M. intracellulare (n=12), M. chelonae (n=12), M. abscessus (n=12), and M. fortuitum (n=12) were tested. Drug-susceptible Mycobacterium (DS-TB; n=21), Drug-Resistant Mycobacterium (MDR-TB; n=10), M. tuberculosis (n=14), M. avium (n=14), M. intracellulare (n=12), M. chelonae (n=12), M. abscessus (n=12), and M. fortuitum (n=12) were tested for the 3 species of slowly-growing non-tuberculous mycobacteria (NTM) are summarized in Table 2, respectively.

Methods: MICs of OPC and PA were evaluated by the agar dilution method, comparing with clarithromycin (RMP), terizidone (TM), amikacin (AMK), ciprofloxacin (CPFX) and imipenem (IPM). A total of 31 clinical isolates of M. tuberculosis and 16 isolates of various NTM were tested. Drug-susceptible Mycobacterium (DS-TB; n=21), Drug-Resistant Mycobacterium (MDR-TB; n=10), M. tuberculosis (n=14), M. avium (n=14), M. intracellulare (n=12), M. chelonae (n=12), M. abscessus (n=12), and M. fortuitum (n=12) were tested for the 3 species of slowly-growing non-tuberculous mycobacteria (NTM) are summarized in Table 2, respectively.

Results: The results for the 3 species of slowly-growing non-tuberculous mycobacteria (NTM) are summarized in Table 2, respectively. Neither of the tested candidates OPC-67683 and PA-824 demonstrated any activities against NTM species except M. abscessus. Against all isolated isolates, OPC-67683 showed the level of in vitro activity (MIC90: 0.25 µg/ml) which was the lowest level comparing with those of RMP (3.125 µg/ml), IPM (0.0015 µg/ml), RMP (0.78 µg/ml), and IPM (0.0015 µg/ml). In contrast, PA-824 showed the lowest activity against all isolated (MIC90: 100 µg/ml) that were comparable to that of SM (100 µg/ml).

Conclusions: OPC-67683 and PA-824 demonstrated potent activity of OPC-67683 with the First-Line Anti-TB drugs against M. tuberculosis and M. intracellulare, M. chelonae, M. abscessus, and M. fortuitum. M. tuberculosis and M. intracellulare were almost similar to those of MIC 90s against DS-TB candidates having none of cross-resistance with the current anti-TB drugs.