Cystic fibrosis is a congenital genetic abnormality commonly encountered in the U.S. As a result of this disease patients suffer from recurrent bouts of pneumonia often caused by methicillin-resistant Staphylococcus aureus (MRSA). The recurrent nature of these infections leads to multi-drug resistance and sometimes sepsis, with combination therapy often being the only therapeutic option (1, 3). There is a lack of new experimental agents active against resistant Gram-negative and Gram-positive strains in general, and CF strains in particular (4). Recently, a survival analysis on 19,833 patients with CF in a multicenter study showed that colonization with MRSA is associated with shortened survival, with a risk of death 1.27 times higher than controls (5). Currently, linezolid (or thienamycin, which is used to treat linezolid-resistant MRSA but has relatively low frequencies of resistance (7)).

Fusidic acid is an antibiotic used in the treatment of staphylococcal infections (3, 6). Although it was introduced more than 4 decades ago, fusidic acid remains useful as an antibiotic, because it is not cross-resistant with other antibiotics used to treat staphylococci and has relatively low frequencies of resistance (7).

This study tested activity of CEM-102 (sodium fusidate, a new formulation of fusidic acid) against MRSA strains isolated from cystic fibrosis patients at Hershey Medical Center alone and in combination with amikacin and tobramycin.

Cystosporium is a congeneric fungal pathogen commonly encountered in the U.S. As a result of this disease patients suffer from recurrent bouts of pneumonia often caused by methicillin-resistant Staphylococcus aureus (MRSA). The recurrent nature of these infections leads to multi-drug resistance and sometimes sepsis, with combination therapy often being the only therapeutic option (1, 3). There is a lack of new experimental agents active against resistant Gram-negative and Gram-positive strains in general, and CF strains in particular (4). Recently, a survival analysis on 19,833 patients with CF in a multicenter study showed that colonization with MRSA is associated with shortened survival, with a risk of death 1.27 times higher than controls (5). Currently, linezolid (or thienamycin, which is used to treat linezolid-resistant MRSA but has relatively low frequencies of resistance (7)).

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### Activity of CEM-102 (sodium fusidate) against 40 MRSA from Cystic Fibrosis Patients

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### Materials and Methods

#### Background

Infections caused by MRSA occur oftentimes in CF patients and there is a lack of new agents to treat them. Sodium fusidate has been successfully used in Europe to describe the long-term effectiveness of CEM-102. This is a study using MIC to test activity of CEM-102, vancomycin, teicoplanin, linezolid, fusidic acid, and amikacin against a range of recent CF MRSA strains and 2 tested CEM-102 in combination with tobramycin or amikacin by time-kill against two CF MRSA strains. Methods: Forty MRSA strains were isolated from patients at Hershey Medical Center, Hershey, PA. The variable number of tandem repeats (VNTR, formerly MLVA) method was done on all strains to ensure only one strain per patient. CEM-102 MIC determination was done using conventional, or in-house, prepared plates (TRIEK, MRC, Cleveland, OH). Vancomycin MICs were read after 24 h. Sulfonamide concentration of CEM-102 was combined with subinhibitory concentrations of each antimicrobial to look for synergistic or antagonistic time-kill results. MICs (µg/mL) are listed in the Table.

#### Results

Each individual strain tested proved to be an individual clone. S. aureus MICs (µg/mL) are listed in Table 1. CEM-102 was very potent with MICs between 0.125 and 0.5 against all strains tested. Vancomycin and teicoplanin were also active at MICs 0.25-1 µg/mL, linezolid at MICs 1-4 µg/mL, quinupristin/dalfopristin at MICs 0.25-1 µg/mL, and linezolid at 0.5-1 µg/mL against clindamycin.

#### Discussion

After initial time-kills with drugs alone had been done, CEM-102 was tested in combination with amikacin and tobramycin. Combinations were tested 1-2 dilutions below the MIC (1/2 x MIC) against two strains of MRSA. The kill kinetics of each drug were tested alone by incubating an initial inoculum of 5 x 10^5 to 5 x 10^6 cfu/mL with drug concentrations at the MIC, three dilutions above and three dilutions below the MIC (1/2, 1/4 and 1/8 x MIC). Validity counts were performed after 0, 3, 6, 12 and 24 h incubations at 37°C in a shaking water bath by plating onto Tripticase soy-5% sheep blood agar plates (12).

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### References


