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## New therapy from old drugs: Synergistic bactericidal activity of colistin combined with Sulfadiazine and fusidic acid against colistin-resistant bacteria including *mcr-1* strains

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**Background & Objective**: Recent emergence of colistin-resistance in Gram-negative bacteria, especially in clinical isolates is of growing concern. The limitation of current treatment options has led to a new interest of antibiotic combinations with old antibiotics to overcome clinical therapeutic impasses. Here, we investigate the potential synergistic activity of colistin combined with sulphonamide or fusidic acid against colistin-resistant Gram-negative bacteria.

**Material & Methods**: A collection of 57 clinical isolates (susceptible and resistant to colistin, including isolates harboring the new *mcr-1* gene), available in our laboratory, from different origin (Laos, Thailand and France) were analyzed in this study. In order to evaluate the efficacy of Colistin (CT) combination with Sulfadiazine (SUL), Sulfamethoxazole (SMX), Trimethoprime (TMP), Trimethoprime/Sulfamethoxazole (SXT) and fusidic acid (FA), several standard *in vitro* methods to study synergy were applied: E-test on pre-treated plate agar, cross wise E-test, checkerboard and time kill assay. The time kill assay was performed to evaluate the bactericidal activity of the synergistic combinations.

**Result**: With the multiple synergistic tested methods, all combinations showed synergistic bactericidal activity. The most effective combinations were Colistin-Sulfadiazine and Colistin-Fusidic acid. Both combinations showed synergistic effect against 89% and 80% of strains tested, respectively. These two combinations have also bactericidal activity, proved by time kill assay and no re-growth was observed after 24 hours. Synergy was observed independently to the mechanism of colistin resistance.

**Conclusion**: These *in vitro* results suggest that such combination would appear to be justifiable in patients with multidrug resistant bacterial infections which failed to be treated by monotherapy.

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