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Investigation for antimicrobial resistance-modulating activity of diethyl malate and 1-methyl malate against beta-lactamase class A from Bacillus licheniformis by molecular dynamics, *in vitro* and *in vivo* studies

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Resistance to antibiotics in bacteria, is one of the major problems of mankind. Each year, a large number of patients due to infection, lose their lives. One of the main mechanisms of antibiotic resistance is beta-lactamase secretion. This enzyme hydrolyzes the amide bond of a lactam ring in beta-lactam antibiotics. Bacillus licheniformis is a mesophilic gram-positive bacterium, which has a high potential to produce beta-lactamase class A. In this study, the inhibitory effects of some malate analogous were studied by in vitro and *in vivo* studies. In addition, the effects of inhibitor binding on beta-lactamase were studied using MD simulations. Our results showed that diethyl malate and 1-methyl malate can decrease the MIC value of benzyl penicillin by sixteen and eight-fold, respectively. Data derived from in vitro studies revealed that decrease in MIC values is correlated with beta-lactamase inhibition. Molecular docking studies predicted the binding mode of inhibitors with the beta-lactamase active site. The structural analysis from MD simulations exhibits that binding of citrate and diethyl malate causes earlier equilibrium of beta-lactamase. After binding, the fluctuation of Ser 70 is also decreased. Based on our data, diethyl malate can be used to design the potent inhibitor against betalactamase class A.

Biography

Fatemeh Abdi is a PhD candidate at North branch, Islamic Azad Univeity of Tehran. She has more than 6 intranational papers and patents. Her expertise is in drug design and discovery, analytical biochemistry and physical biochemistry.

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