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Abstract

Nitrosyl [2Fe-2S] Ferredoxin Mimetics as New Nitric Oxide Donating Antibacterial Agents †

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Nitric oxide (NO) therapy is the newest approach to the treatment of socially important diseases all over the world. Nitric oxide (NO) is a multi-functional molecule able to interact with many cellular targets. Both direct and indirect NO effects (through the formation of reactive nitrogen species) have been shown in many investigations. Considerable experimental material has been accumulated, which demonstrates that NO participates both in the development of pathologic processes, and in their correction by chemotherapeutic methods [1]. In addition to many studies aimed at the search for compounds-traps for the excess NO, interest is growing in the search for new classes of compounds that generate NO, which could be the base for a new generation of medications easily delivering NO to biologic targets. Fundamentals for the creation of a new class of NO donors have been developed based on a detailed study of the chemical nature of Fe–S and Fe–N bonds of nitrosyl ferredoxin active sites. Nitrosyl binuclear iron complexes with pharmacologically active sulfur-containing ligands $[Fe_2(SR)_2(NO)_4]$ were isolated in the crystalline state. Heterocyclic functional thiols having a high coordination activity were used for the isolation of these complexes. Basic research of the structures and properties of these compounds in the solid phase and in the solutions was performed [2].

The functions of nitrogen oxide (NO) in the regulation of the reversible processes of Fe–S cluster assembly in proteins and the formation of *E. coli* biofilms have been investigated for the first time. Cationic [2Fe–2S] tetranitrosyl complex with cysteamine at physiological concentrations suppressed the formation of mature biofilms, and the activity of these compounds was comparable to that of antibiotic ciprofloxacine as a positive control. The study of the antibacterial activity of a series of neutral [2Fe–2S] tetranitrosyl iron complexes with nitro- and amino-thiophenolyls was carried out also by the serial dilutions method by determining the minimum concentration suppressing the growth of the microorganisms in culture. Double consecutive dilutions of the concentrations of the test compounds in a suspension of Gram-negative bacteria *E. coli* (strain BB) at a concentration of 106 cfu/mL were used. Evaluation of antibacterial activity was carried out 24 h after the application of the test compounds. The greatest antibacterial activity was shown by compounds with 4-nitro-thiophenolyl and 3-hydroxythiophenolyl at a concentration of 250 μM and 125 μM, respectively. This, apparently, is due to the more effective NO-donating activity of these complexes.

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