Mechanism that enhances the action of rifampicin on multi-resistant mycobacteria tuberculosis when it is administered in combination with an iodine-containing anti-infection drug

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A new iodine-containing anti-infection drug (AID) has been created possessing a broad spectrum of antimicrobial and antiviral effects at the Scientific Center for Anti-infectious Drugs (Republic Kazakhstan). Unlike other iodine-containing drugs, AID is used for oral administration. AID promotes an increase in the permeability of the cell membrane and bacterial wall and has membraneolytic capacity. *In vivo* and *in vitro* experiments AID was found to possess an anti-tuberculosis effect. In clinical isolates of mycobacteria isolated in clinical trials from patients suffering from multidrug-resistant pulmonary tuberculosis, *in vitro* as well as *in vivo* sensitivity of *Mycobacterium tuberculosis* to rifampicin, isoniazid, streptomycin, ethambutol was found restored and enhanced where AID acted together with antibiotics. The active center of AID is a complex of magnesium ion with lithium halide, molecular iodine and triiodide. Therefore, it can form a complex with rifampicin (Fig.1). When interacting with mycobacterium DNA, the nucleotides displace the peptides and form a complex with the molecular iodine and the lithium halide. In paper, the crystal structure core of DNA-dependent RNA polymerase (RNAP) complex with rifampicin was determined; it is shown that rifampicin inhibits the β-loop of RNAP at a distance of about 12.1 Å from the active center of RNAP. Distinguished are amino acid residues of RNAP, which form hydrogen bonds with rifampicin. In paper, it is shown that the resistance to rifampicin is caused by mutations in the DNA of *Mycobacterium tuberculosis* that lead to the replacement of amino acid residues in the RNAP β-loop region that interacts with rifampicin and, as a consequence, to the weakening of binding energy of amino acid residues with rifampicin. Using the molecular modeling method, we have shown that an increase in the action of rifampicin and the restoration of Mycobacterium tuberculosis's sensitivity to it when administered together with AID are due to the following two reasons: (1) the AID active center binds both the bacterial DNA and the active center of RNAP, (2) when amino acid residues of RNAP are inhibited by the rifampicin complex with the AID active center, the inhibitory energy is enhanced.

Biography

Gulnara A Yuldasheva received her Ph.D from Central Asian Department of National Academy of Sciences. She is now a Leading Research in Scientific Center for Anti-Infective Drug, Kazakhstan, Almaty. She is membership American Chemical Society She works to use quantum-chemical methods. She has an interest in a mechanism the inhibition of DNA HIV replication, mechanisms of anti-cancer action of complex iodine with lithium halogenides and bioorganic ligands and influence on mechanisms biochemical reaction. of iodine complex compounds. Her current research is focused to find of new compounds having anti-infection and anticancer activity.

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