MECHANISM OF QUINOLONE ACTION AND RESISTANCE. NEW 3-ALKYLQUINOLONYL CARBOXYLIC ACIDS AS POTENTIAL ANTIMICROBIAL AGENTS

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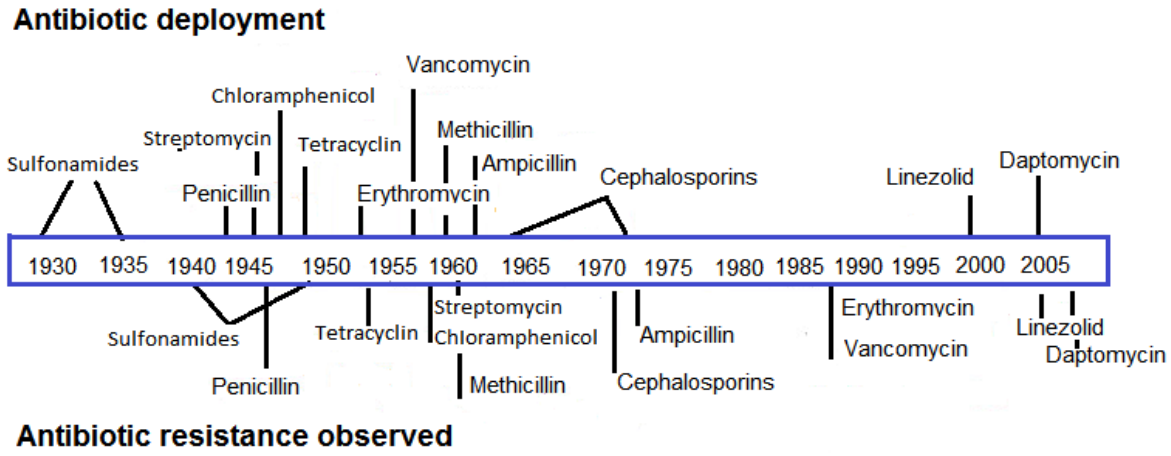
The discovery of antibiotics was one of the most significant events in the history of medicine which had led to significantly increasing of the humans' life expectancy. However, from the first application of penicillin in practical medicine, humanity was faced with the serious problem as emerging antimicrobial resistance (AMR). In consequence, after the first time employment of any new antibiotics were identified cases of clinically significant resistance to this drugs, which was always developed by microorganisms in a relatively short period of time.



Quinolones are one of the most commonly prescribed classes of antibacterials in the world and are used to treat a variety of bacterial infections in humans. Because of the wide use (and overuse) of these drugs, the number of quinolone-resistant bacterial strains has been growing steadily since the 1990s. The general mechanism of action employed by the fluoroquinolone class is inhibition of type II topoisomerases DNA gyrase or topoisomerase IV (topoIV).Taking into account the latest data of the key role of magnesium in the cation complex forming quinolone-topoisomerase-DNA we carried out molecular modeling (force field MMFF94) for 3-(2-methyl-4-oxo-1,4-dihydroquinoline-3-yl)propanoic acid with cation $Mg2^{+}$. The possibility of forming a strong complex between them has been showed.

The results of the antimicrobial activity screening have shown that two compounds - 1,3-diethoxy-2-[(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl)methyl]-1,3-dioxopropan-2-ylcarbamic acid and 3-(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl) propanoic acid have moderate broad-spectrum activity.