TITLE: EXPRESSION OF *ompF* AND *recA* GENES IN *Escherichia coli* AFTER EXPOSURE TO ANTIMICROBIAL AGENTS AND MOLECULAR DOCKING FOR INHIBITORS OF SOS RESPONSE

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ABSTRACT:

Some antimicrobial agents (AA), such as ciprofloxacin (CIP), can lead to genetic changes in *Escherichia coli* by inducing the SOS response. In sub-inhibitory concentrations (sub-MIC) of CIP, the expression of genes related to bacterial stress is modulated, increasing the mutagenesis and benefiting the appearance of drug resistance. Therefore, the aim of this study was to evaluate the impact of sub-MIC of AA can cause in wildtype strains of *E. coli* encoding plasmid-mediated quinolone resistance (*qnrB* and *S* genes). Three *E. coli* were exposed to sub-MICs of CIP and nitrofurantoin (NIT) and the expression of *ompF* and *recA* genes was determined by Real-time PCR. Also, the effect of the sub-MIC exposure was evaluated in solid medium using disk-diffusion (DD) assays. Furthermore, a mode of interaction between RecA inhibitors and RecA protein that has a major role in SOS Response was proposed. In the proposed trials, bacterial growth was slower in the strains at sub-MICs of CIP and NIT. Differences of inhibition zone diameters obtained by DD were statistically significant. Positive average differences (AD) were obtained for JF-234 strain exposed to CIP when tested ertapenem, imipenem, cefoxitin and tigeciclin disks, and to NIT when tested cefoxitin and tigeciclin disks. Negative AD was obtained for U-79 strain in sub-MIC of CIP and NIT. U-414 strain showed positive AD in sub-MIC of NIT when tested amoxicilin/clavulanic acid, ertapenem and levofloxacin disks. By RT-PCR, an 1,2-4,7-fold increases in *recA* expression were noted in all *E. coli* studied. However, the level of *ompF* expression varied: an 1,16 and 1,41-fold increases in *ompF* expression was observed in JF-234 and U-414 by exposure to sub-MIC of NIT and CIP, respectively and a 0,72-fold decrease in *ompF* in JF-234 exposed to CIP and a 0,54 and 0,406-fold decreases to U-79 exposed to CIP and NIT, respectively. Based on these results, 2 protocols that can be used for the molecular docking studies with the RecA inhibitors compounds were obtained. These protocols showed an overlap frequency between theorical poses and the original pose about 76 and 75%. These results showed that sub-CIM of CIP and NIT affect directly the bacterial growth, the resistance phenotypes and the expression of genes related to resistance phenotypes and bacterial persistence. In addition, these findings suggest a strategy to inhibit SOS response controlled by RecA in *E. coli* that could be useful for the development of new AA.

KEYWORDS: *Escherichia coli, qnr* gene*,* SOS Response, RecA Inhibitors, Molecular Docking.

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