EFFECT OF NALIDIXIC ACID ON BACTERIA POSSESSING MUTATIONS IN THE RECA AND LEXA GENES

N.T. Ratcliffe*, J.T. Smith, Microbiology Section, Department of Pharmaceutics, The School of Pharmacy, University of London, WC1N 1AX.

* Present address: ICI Pharmaceuticals, Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG.

If bacterial DNA suffers damage two of the repair pathways that act to alleviate such damage are SOS repair and recombination repair. RecA mutants are defective in both these pathways, while lexA mutants are deficient in SOS repair but remain proficient in recombination. It is not clear whether bacterial DNA repair systems are involved in the mode of action of drugs inhibiting bacterial DNA gyrase. Hays and Boehmer (1978) showed that coumermycin (an antagonist of the B subunit of gyrase) and oxolinic acid (an antagonist of the A subunit of gyrase) inhibited recombination in E.coli. However, Herrero et al (1981) reported that the synthesis of the recA protein, which is required for both SOS repair and recombination repair, did not increase when the B subunit of gyrase was inhibited by drugs or by thermal inactivation of gyrase in gyrB temperature-sensitive mutants.

In order to investigate how survival after nalidixic acid treatment is affected by mutations in DNA repair systems, E.coli strain AB1157 and lexA and recA mutants derived from it were investigated. The three strains were exposed to concentrations of nalidixic acid ranging between 0.15 µg/ml and 1500 µg/ml in nutrient broth for 3 hours at 37^0 C and then the survivors were estimated by viable counting.

The results showed that the most bactericidal concentration (Smith, 1984) of nalidixic acid for all three strains was the same at 300 µg/ml. All three strains also exhibited similar biphasic responses in that concentrations above and below the most bactericidal concentration were less effective. There was no significant difference between the sensitivity of strain AB1157 and its lexA derivative to nalidixic acid. However, at every concentration tested the recA mutant was more sensitive to nalidixic acid than either the parent strain (AB1157) or the lexA mutant.

The fact that the lexA mutant was no more sensitive to nalidixic acid than the parent strain shows that SOS repair does not contribute to nalidixic acid's lethality. It also suggests that the type of DNA damage caused by the drug is not repaired by the SOS pathway. On the other hand, the recA mutant was more susceptible to nalidixic acid than either the lexA mutant or the parent strain. As the recA mutant is deficient in recombination repair as well as in SOS repair these results suggest that recombination repair plays a role in repairing nalidixic acid-induced DNA damage but does not participate in nalidixic acid's lethality.

Hays, J.B., Boehmer, S. (1978) Proc. Natl. Acad. Sci. USA. 75: 4125
Herrero, E. et al (1981) Fems. Micro. Letts. 10: 369
Smith, J.T. (1984) Pharm.J. 233: 299