ACTIVITY OF NITRO-COMPOUNDS AGAINST STRAINS OF *ESCHERICHIA COLI* DEFICIENT IN DNA REPAIR

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Nitrofurans and nitroimidazoles are heterocyclic nitro-compounds, which have a wide range of therapeutic uses (Hamilton-Miller & Brumfitt, 1976). There is disagreement whether these two classes of drugs have the same mechanism of action against bacteria. Edward, Dye & Carne (1973) showed that Clostridia reduced nitrofurazone and nitroimidazoles by different routes. However, the antibacterial activity of both nitroimidazoles and nitrofurans against *Bacteroides fragilis* correlated with the electron affinity of the drugs (Reynolds, 1979) suggesting that they possessed similar mechanisms of action. Nitrofurans cause single strand breaks in the DNA of *E.coli* (McCalla, Reuvers & Kaiser, 1979) and they are more active against DNA repair deficient mutants (Jenkins & Bennett, 1976). The mechanism of action of nitroimidazoles against *E.coli* has been studied rarely but the primary target of L8580 (a 2-nitroimidazole) in *E.coli* is known to be DNA (Goldstein et al., 1977). In Clostridia, DNA is the target site of action for nitroimidazoles, although with nitrofurazone, RNA synthesis is also affected (Plant & Edwards,1976).

In this report the antibacterial activity of metronidazole (a 5-nitroimidazole) misonidazole & L8580 (both 2-nitroimidazoles), & nitrofurazone (a nitrofuran) were compared against strains of *E.coli* deficient in DNA repair and also against nitrofurazone-resistant mutants.

The minimum inhibitory concentrations for the parent strain were metronidazole 1028 µg/ml, misonidazole, 128 µg/ml, L8580 1 µg/ml, and nitrofurazone 2 µg/ml. Strains which possessed *recA* or *recA* & *uvrA* mutations were 8 to more than 16 times more sensitive to these drugs than the parent strain. *Rec B*, *recC*, *uvrA* and *lop*, *lig2* mutants also exhibited increased sensitivity but only 2-4 fold, whil the *polA* mutation was without effect. The nitrofurazone-resistant mutants were at least 8 times more resistant than their parent strains to all four drugs.

These findings where the repair-deficient and nitrofuran-resistant mutants have similarly altered responses to all four drugs suggest that their mechanisms of action are similar. It can also be concluded that, as the DNA repair-deficient mutants are more sensitive to all four drugs, the primary target site is DNA. These conclusions contrast with those of Edwards, Dye & Carne (1973) and Edwards (1979) who postulated that nitroimidazoles are inactive against aerobic bacteria because the organisms cannot reduce the nitro-groups of these drugs.

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