ANTIBACTERIAL ACTIVITY AND ELECTRON AFFINITY OF NITRO-HETEROCYCLIC COMPOUNDS

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The most common anaerobes causing hospital infections are the Gram-negative anaerobic bacilli, particularly Bacteroides fragilis. These organisms are resistant to most broad-spectrum antibiotics, including aminoglycosides, penicillins and cephalosporins. Resistance to tetracyclines is also widespread. In this country, metronidazole, a nitroimidazole, is widely used to treat infections caused by anaerobic bacteria. In the United States, however, the use of this drug has been questioned because of genotoxicity in bacteria and animals (Medical Letter, 1975).

In order to search for new drugs to replace metronidazole, the in vitro activity against Gram-negative anaerobic bacilli of some compounds containing a primary nitro group was compared. The drugs tested are shown in the table and their minimum inhibitory concentrations (MIC) assessed by an agar dilution method against B.fragilis. (Reynolds et al, 1975, 1976.)

DRUG	TYPE OF COMPOUND	MIC (µg/ml)	E_7^1 (mV)
metronidazole	5-nitroimidazole	0.34	-486
tinidazole	"	0.28	-464
nimorazole	"	1.05	-457
MABN	"	0.097	
ornidazole	"	0.66	-467
dimetridazole	"	0.74	
misonidazole	2-nitroimidazole	1.36	-389
Ro-07-1051	"	4.00	
nitrofurantoin	nitrofuran	7.65	-264
nitrofurazone	"	2.51	-257
SQ 18,506	"	1.69	
nifuratel	"	0.30	
furazolidone	"	0.24	
nitrovin	"	≤0.023	
pyrrolnitrin	nitrobenzene	90.5	
niridazole	nitrothiazole	≤0.0059	

The values of the electron affinity (E_7^1) of the nitro group of seven of the compounds are known. The E_7^1 values correlate with the degree of radiosensitization obtained against anoxic tumor cells. (Wardman, 1977.)

When the MIC (as nanomoles/ml) was plotted against the corresponding values for E_7^1 obtained from the literature, linear regression analysis gave a correlation coefficient of 0.896, which is significant ($0.01 > P > 0.001$). Obviously further work is needed to substantiate these observations with the hope that a compound may be obtained with reduced or absent genotoxicity but still retaining the other desirable properties of metronidazole.

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