

Letters to the Editor

Activity of Ofloxacin and Pefloxacin against *Mycobacterium leprae* in Mice

The fluorinated quinolones are potent antibacterial compounds active against both gram-negative and gram-positive bacteria (1, 3-5, 11-13). Some are also active against mycobacteria in general (3, 9, 10, 13) and *Mycobacterium tuberculosis* in particular (1; unpublished observations).

In view of the limited number of drugs active against *Mycobacterium leprae*, it was of interest to test some of these drugs against *M. leprae* in the mouse footpad model (7). *M. leprae* L6382 and L90, isolated in our laboratory in 1963 (6) and 1980, respectively, from previously untreated patients infected in Rwanda and Mali and continuously passaged in the mouse footpad were used.

Ofloxacin was a gift from Hoechst, Brussels, Belgium, and pefloxacin was a gift from Rhone-Poulenc, Brussels, Belgium.

The anti-*M. leprae* activity of the drugs was determined by the proportional bactericidal test (2). Groups of five mice were inoculated in the left hind footpad with 10^4 , 10^3 , 10^2 , and 10^1 acid-fast bacilli. One group of mice served as untreated controls; the others were given the drugs by stomach gavage in 0.5-ml quantities at the dosages and intervals indicated in Tables 1 and 2. Treatment lasted from day 35 until day 154.

At 1 year after infection, the mice were killed, and the acid-fast bacilli were counted in individual footpads. Statistical calculations were performed as described by Shepard (7). The results are shown in Tables 1 and 2.

Ofloxacin was bactericidal against *M. leprae* when administered five times a week at dosages of 150, 100, and even 50 mg/kg (body weight). Pefloxacin showed no activity when administered at 100 mg/kg 5 days a week or at 150 mg/kg at lower frequencies. However, the drug showed activity at 300

TABLE 2. Proportional bactericidal test with pefloxacin against *M. leprae* L6382

Treatment group and dose (mg/kg [body wt])	Freq. ^a	No. of mice ^b with the following no. of organisms inoculated per footpad:				Significance (P) ^c
		10 ⁴	10 ³	10 ²	10 ¹	
Controls		5	5	4	4	
Pefloxacin (300)	3/7 (54)	5	4	4	0	0.01
	2/7 (36)	5	5	5	4	0.56
	1/7 (18)	5	3	5	5	1
	1/14 (9)	5	5	5	1	0.24
	1/21 (6)	5	4	4	2	0.7
1/28 (3)	5	5	5	2	1	

^{a-c} See footnotes to Table 1.

mg/kg three times a week (Table 2). The activity vanished when frequency of administration was more spaced.

On the basis of these results, studies with ofloxacin should be undertaken in humans (8) to determine its usefulness in the treatment of human leprosy.

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TABLE 1. Proportional bactericidal test with ofloxacin and pefloxacin against *M. leprae* L90

Treatment group and dose (mg/kg [body wt])	Freq. ^a	No. of mice ^b with the following no. of organisms inoculated per footpad:				Significance (P) ^c
		10 ⁴	10 ³	10 ²	10 ¹	
Controls		5	4	2	1	
Ofloxacin						
150	5/7 (90)	0	0	0	0	0
100	5/7 (90)	0	0	0	0	0
50	5/7 (90)	2	1	0	0	0.02
Pefloxacin						
100	5/7 (90)	5	4	3	0	1
150	3/7 (54)	5	4	— ^d	—	0.47
150	2/7 (36)	5	4	—	—	0.47
150	1/7 (18)	5	5	—	—	0.80
150	1/14 (9)	5	4	—	—	0.47
150	1/21 (6)	—	5	—	—	0.80
150	1/28 (3)	5	4	0	0	0.34

^a Freq., Frequency of administration per 7, 14, 21, and 28 days. The number of drug administrations is shown in parentheses.

^b Number of mice revealing multiplication at 1 year after inoculation. Five mice were inoculated.

^c P values for comparison of each titration with controls.

^d —, Not examined.

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In Vitro Activity of Antiprotozoal Drugs against *Giardia intestinalis* of Human Origin

Newly developed culture techniques enable the determination of the in vitro susceptibility to antiprotozoal agents of *Giardia intestinalis* strains that infect humans (1, 3). Earlier work reported on the activity of metronidazole, tinidazole,

The results are shown in Table 1. The cat isolate showed decreased susceptibility to metronidazole, but also to paromomycin and chloroquine. It is interesting to note also that of *Giardia* strains of human origin isolated in Poland,

TABLE 1. In vitro activity of six antiprotozoal agents against nine *G. intestinalis* isolates

Strain	MIC ($\mu\text{g/ml}$)					
	Metronidazole	Tinidazole	Paromomycin	Chloroquine	Furazolidone	Pyrimethamine
HP34	<0.5	<0.5	50.0	10.0	<0.5	100.0
HP63	0.5	<0.5	100.0	100.0	5.0	100.0
HP89	<0.5	<0.5	50.0	100.0	<0.5	100.0
HP100	1.0	<0.5	50.0	100.0	1.0	100.0
HP102	<0.5	<0.5	50.0	100.0	1.0	100.0
HP103	<0.5	<0.5	<1.0	100.0	0.5	100.0
HP104	1.0	<0.5	>100.0	10.0	<0.5	100.0
HP105	<0.5	<0.5	50.0	100.0	<0.5	100.0
CAT1	2.5	<0.5	>100.0	>100.0	1.0	100.0

furazolidone, paromomycin, pyrimethamine, and chloroquine on 25 *G. intestinalis* strains isolated from Belgian patients (2). It showed tinidazole to be the most active drug in vitro. Metronidazole was as active against almost all the isolates, but the susceptibility of the strains to paromomycin, pyrimethamine, and chloroquine was quite variable. Because all the strains had been isolated in one hospital and strain characterization of *G. intestinalis* is a controversial issue, we tested another population of clinical *G. intestinalis* isolates.

In this study, eight *Giardia* strains of human origin recovered in Poland (4) and one strain isolated from a cat (5) were tested for in vitro susceptibility to the same antiprotozoal agents. The same macrodilution method in semisolid medium was used for all the strains (2). Briefly, glass tubes were filled with 6 ml of modified TPS-1 medium (2, 3), and variable amounts of antibiotic stock solutions were added to obtain final test concentrations of 0.5, 1.0, 2.5, and 10.0 μg of tinidazole, metronidazole, furazolidone per ml and 1.0, 10.0, 50.0, and 100.0 μg of pyrimethamine, paromomycin, and chloroquine per ml. Trophozoites were inoculated at a final concentration of 50,000/ml. The medium was then semisolidified with 0.16% agar. The tubes were incubated at 37°C for 2 to 7 days. The MIC of a drug was determined as the lowest concentration at which no visible growth was detected before or until day 7 of the experiment.

some strains were less susceptible to metronidazole than to tinidazole and one simultaneously showed a high paromomycin MIC. Another striking feature was the uniform distribution of high pyrimethamine MICs for this new population of strains and, to a lesser degree, chloroquine MICs, which is very different from results with the Belgian isolates tested earlier. These results indicate that the superiority of the in vitro activity against *G. intestinalis* of nitroimidazole compounds over that of the other tested antiprotozoal drugs is probably not the result of strain repetition in the earlier tested population.

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