correlated with presence of beta-lactamase activity, it is thought to be associated with the penetration of the drug through the outer membrane (4). The mechanism of ciprofloxacin resistance of these strains has not yet been studied.

In conclusion, ciprofloxacin showed very high activity against *Haemophilus influenzae* and *Branhamella catarrhalis* with MIC values well below 1 mg/l for all strains tested. The activity against anaerobic bacteria of the *Bacteroides fragilis* group was less impressive; MIC values were often higher than achievable serum levels after a 500 mg oral dose (5). The clinical usefulness of ciprofloxacin therefore remains to be evaluated.

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## In Vitro Activity of Ciprofloxacin Against *Brucella melitensis*

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Ciprofloxacin (Bay o 9867), a new antibacterial agent structurally related to nalidixic acid, has a broad antimicrobial spectrum against both gram-positive and

Service of Microbiology and Unit of Experimental Bacteriology, La Fe Hospital, Valencia 10, Spain. gram-negative bacteria (1). We evaluated its in vitro activity against *Brucella* spp. in comparison to that of three other quinoline derivatives and gyrase inhibitors, norfloxacin, pipemidic acid and nalidixic acid (2-3), using 68 clinical isolates of *Brucella melitensis*.

Susceptibility tests were performed by the agar dilution technique using chocolate agar plates inoculated with the organism and incubated for 48 h at 37  $^{\circ}$ C in an atmosphere enriched with CO<sub>2</sub>.

Table 1: Comparative in vitro activity of four quinoline derivatives against 68 isolates of *Brucella melitensis*.

Agent	MIC range	Concentration (mg/l) required to inhibit the following per- centages of isolates		
		50	75	90
Ciprofloxacin	.5 –1	.5	1	1
Norfloxacin	.25-16	2	4	8
Pipemidic acid	64	64	64	64
Nalidixic acid	64	64	64	64

The results are summarized in Table 1. Brucella melitensis was resistant to nalidixic and pipemidic acids. Whereas ciprofloxacin inhibited 100 % of the isolates at concentrations  $\leq 1 \text{ mg/l}$ , the MICs of norfloxacin ranged from 0.25 to 16 mg/l, with a MIC 90 of 8 mg/l. Although ciprofloxacin has superior in vitro activity against Brucella spp., further clinical and pharmacological studies are necessary to determine its role in the treatment of brucellosis.

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