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In Vivo Efficacy of a New Fluoroquinolone, Sparfloxacin, against Penicillin-Susceptible and -Resistant and Multiresistant Strains of *Streptococcus pneumoniae* in a Mouse Model of Pneumonia

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The increasing emergence of penicillin-resistant and multiresistant strains of *Streptococcus pneumoniae* may pose a problem in coming years. We therefore compared sparfloxacin, a new fluoroquinolone with improved potency against streptococci, with amoxicillin, the "gold standard" in this setting, and another fluoroquinolone, ciprofloxacin, in a mouse pneumonia model. Their efficacies against penicillin-susceptible (serotype 3), macrolide-resistant (serotype 1), penicillin-resistant (serotype 23), and multiresistant (serotype 6) *S. pneumoniae* strains were evaluated. Immunocompetent Swiss mice (serotypes 1 and 3) and leukopenic mice (serotypes 6 and 23) were infected by peroral tracheal delivery of 10^4 to 10^6 CFU. Subcutaneous injections of antibiotics were initiated at 6, 18, 48, or 72 h after infection (six injections at 12-h intervals). In the immunocompetent mice, 100% survival was obtained with sparfloxacin (50 mg/kg) and amoxicillin (5 mg/kg) against both penicillin-susceptible and macrolide-resistant strains; ciprofloxacin gave significantly lower survival rates. Two to four injections of sparfloxacin completely cleared bacteria from lungs and blood; the most rapid eradication was achieved with amoxicillin. Sparfloxacin also fully protected leukopenic mice against penicillin-resistant strains. The dose of amoxicillin (50 mg/kg) required to protect mice and eradicate penicillin-resistant and multiresistant strains was 10 times higher than that effective against penicillin-susceptible strains. The microbiological and pharmacokinetic properties of sparfloxacin (e.g., the time during which concentrations exceed the MIC of the test pathogen) accounted for its efficacy against susceptible and resistant strains of *S. pneumoniae* in this model.

Sparfloxacin (AT-4140) is a new quinolone with a broad spectrum of activity against both gram-positive and gram-negative bacteria (10, 11). Its potency against gram-negative organisms is similar to that of ciprofloxacin and greater than that of ofloxacin, enoxacin, or norfloxacin. Against gram-positive organisms, sparfloxacin is more potent than the other quinolones (15). Given orally (p.o.) sparfloxacin is highly effective against systemic infections due to *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, and *Pseudomonas aeruginosa* in mice and is more potent than the other quinolones (15). The pharmacokinetics of sparfloxacin result in good absorption following oral administration, good tissue penetration, and a long half-life in plasma and tissues (14).

Streptococcus pneumoniae remains the leading cause of community-acquired pneumonia (12). In addition, there is an increasing emergence of respiratory tract pathogens resistant to the most widely used drugs, i.e., penicillin G and macrolides (3, 9). We therefore compared the efficacy of sparfloxacin with that of another fluoroquinolone, ciprofloxacin, in acute and subacute mouse models of *S. pneumoniae* pneumonia induced by penicillin-susceptible (P^S), penicillin-resistant (P^R), macrolide-resistant (M^R), and multiresistant *S. pneumoniae* strains. Animal survival, bacterial clearance from lungs, and pharmacokinetic data in both noninfected and infected mice were used to evaluate the feasibility of reducing the sparfloxacin treatment period.

(Part of this work was presented at the 30th Interscience Conference on Antimicrobial Agents and Chemotherapy [2].)

MATERIALS AND METHODS

Animals. Female C57Black/6 mice (body weight, 18 to 20 g) and Swiss mice (20 to 22 g) were obtained from Iffa-Credo Laboratories, L'Arbresle, France.

Challenge organisms. Pneumococcal pneumonia was induced in healthy immunocompetent mice with a virulent P^S serotype 3 strain (P 4241) and a virulent M^R serotype 1 strain (P 6254) originally isolated from blood culture and provided by the Centre de Référence du Pneumocoque (P. Geslin, Créteil, France). We failed to find any virulent P^R strains, which accords with the report by Briles et al. (5) that most clinical strains (serotypes 6, 14, 19, and 23) are avirulent in mice. Pneumonia was thus induced in leukopenic mice with a P^R serotype 23 strain (54 B; isolated from a patient with sinusitis), a P^R (intermediate resistance [P^I]) and M^R (P^IM^R) serotype 23 strain (170 B; also isolated from a patient with sinusitis), and a P^RM^R serotype 6 strain (Div 27; isolated from the cerebrospinal fluid of a patient with underlying sickle cell anemia and meningitis).

In vitro studies. MICs and MBCs were determined in Mueller-Hinton infusion broth (Diagnostic Pasteur, Marnes-la-Coquette, France) by means of the tube dilution method (16). Each tube contained twofold dilutions of antibiotic and a final bacterial density of 10^6 CFU/ml. After incubation of cells for 18 h at 37°C aerobically, the MIC was defined as the

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TABLE 1. Microbiological data for *S. pneumoniae* challenge strains

Study drug[a]	MIC/MBC (μg/ml)				
	P 4241 (P^S)	P 6254 (M^R)	54 B (P^R)	170 B (P^IM^R)	Div 27 (P^RM^R)
Amoxicillin	0.03/0.03[a]	0.03/0.03	1/2	0.5/1	0.5/1
Penicillin	<0.01/<0.01	<0.01/<0.01	2/2	0.5/1	2/2
Erythromycin	0.06/0.12	>32/>32	0.5/1	>32/>32	>32/>32
Sparfloxacin	0.25/0.5	0.25/0.5	0.25/0.5	0.25/0.5	0.25/0.25
Ciprofloxacin	1/2	1/2	1/2	1/2	1/2

[a] Inoculum was 10^6 CFU/ml.

lowest concentration of antibiotic at which no turbidity was visible to the naked eye. The MBC was determined by plating 0.01-ml aliquots from tubes with no visible growth onto Columbia agar supplemented with 5% sheep blood (Bio-Mérieux, Lyon, France). The plates were incubated overnight at 37°C in 10% CO_2–air, and the MBC was defined as the lowest concentration of antibiotic killing ≥99.9% of the original inoculum.

Leukocyte depletion in mice. We induced sustained leukopenia in Swiss mice by giving three daily intraperitoneal injections (150 mg/kg) of cyclophosphamide (Endoxan; Sarget Laboratories, Mérignac, France) starting 3 days before infection. Counts of circulating leukocytes in blood were reduced from about 7,000 to 1,000/mm^3, and mice became more susceptible to P^R and multiresistant strains.

Experimental pneumococcal pneumonia in mice. Pneumococcal pneumonia was induced in female mice as described in detail elsewhere (1). Briefly, animals were anesthetized by intraperitoneal injection of sodium pentobarbital and then infected with approximately 10^4 (M^R), 10^5 (P^S), or 10^6 (P^R, P^IM^R, and P^RM^R) logarithmic-phase CFU of *S. pneumoniae* by delivering 40 μl of an appropriate dilution through the mouth into the trachea. Immunocompetent and leukopenic Swiss mice developed acute pneumonia and died within 2 to 5 days, while C57BL/6 mice developed subacute pneumonia and died within 7 to 10 days. All the animals quickly became bacteremic. Since the bacterial population in the lung increased slowly in C57BL/6 mice, this model provides an opportunity to study antibiotic efficacy at various stages of the disease. The bacterial population exceeded 10^8 CFU per lung at the time of death.

Antibiotics. The study drugs included the fluoroquinolones ciprofloxacin (Ciflox; Bayer Laboratories, Wuppertal, Germany) and sparfloxacin (AT-4140; Rhône-Poulenc Rorer, Vitry sur Seine, France). Amoxicillin sodium salt was used as the reference antibiotic. Sparfloxacin free base was prepared by homogenizing the powder in a standard diluent containing carboxymethylcellulose (70 cP) at 2 g% in sodium chloride (0.09 g%). The other antibiotics were reconstituted according to instructions on package inserts and diluted in sterile water.

Pharmacokinetic studies. The pharmacokinetic profiles of sparfloxacin and ciprofloxacin were examined in parallel in healthy (control) and infected immunocompetent Swiss mice. Concentrations in lungs and sera were determined after single p.o. and subcutaneous (s.c.) doses of 50 mg of sparfloxacin and 100 mg of ciprofloxacin per kg of body weight. In infected mice, the antibiotic was given 18 h after challenge with strain P 4241. At 0.5, 1, 3, 6, 8, and 24 h following administration of drug, six animals per group were killed with CO_2 and exsanguinated by intracardiac puncture. Blood samples were centrifuged to isolate serum, pooled (n = 6) each time, and frozen at −80°C until assay. Lungs were harvested from exsanguinated mice, washed in sterile sodium chloride solution, and frozen. On the day of the assay, organs were weighed, pooled (n = 6), and homogenized in phosphate buffer (pH 6.8). Homogenates were centrifuged, and supernatants were used for the assay. Antibiotic activities were determined by means of the agar well diffusion method using *E. coli* as the bioassay organism and Antibiotic Medium 1 (Difco Laboratories, Detroit, Mich.) as the growth medium. Standard solutions of sparfloxacin and ciprofloxacin were made in phosphate buffer (pH 6.8) for serum and tissue determinations in order to evaluate the active fractions of the antibiotics. Results were expressed as micrograms per milliliter or per gram of lung tissue. The standard curve was linear from 0.125 to 32 μg/ml. The sensitivity of the assay was about 0.1 μg/ml of sample, and the coefficient of between- and within-day variations for replicates (n = 5) was ≤7.5%.

Pharmacokinetic analysis. Concentration-time data were fitted to one- or two-compartment open models according to

TABLE 2. Pharmacokinetic parameters of sparfloxacin and ciprofloxacin in Swiss mice following single s.c. injection[a]

Mice and treatment	Tissue	C_{max} (μg/ml or μg/g)	$t_{1/2\beta}$ (h)	Δt MIC[b] (h)	AUC_{0-24} (μg · h/ml or μg · h/g)
Noninfected control					
Sparfloxacin (50 mg/kg)	Serum	8.0	2.8	8	18
	Lung	18.5	2.9	24	38
Ciprofloxacin (100 mg/kg)	Serum	12.6	1.6	8	15
	Lung	58.0	1.2	8	50
Infected					
Sparfloxacin (50 mg/kg)	Serum	9.4	4.2	24	25
	Lung	27.0	5.7	24	64
Ciprofloxacin (100 mg/kg)	Serum	12.6	1.9	8	15
	Lung	62.0	1.1	8	47

[a] Values are for six pooled samples of serum and lung tissues taken at 0.5, 1, 3, 6, 8, and 24 h postdosing.
[b] Δt MIC, the time during which concentrations exceeded the MIC of the test pathogen (P 4241).

TABLE 3. Pharmacokinetic parameters of sparfloxacin and ciprofloxacin in Swiss mice following a single p.o. dose[a]

Mice and treatment	Tissue	C_{max} (μg/ml or μg/g)	$t_{1/2\beta}$ (h)	Δt MIC[b] (h)	AUC_{0-24} (μg · h/ml or μg · h/g)
Noninfected control					
Sparfloxacin (50 mg/kg)	Serum	2.8	2.1	8	4
	Lung	7.7	2.2	8	9
Ciprofloxacin (100 mg/kg)	Serum	2.3	2.6	8	2
	Lung	2.9	1.8	8	6
Infected					
Sparfloxacin (50 mg/kg)	Serum	4.9	1.9	8	11
	Lung	7.0	9.0	24	18
Ciprofloxacin (100 mg/kg)	Serum	1.9	2.2	8	3
	Lung	9.5	1.9	8	11

[a] Values are for six pooled samples of serum and lung tissues taken at 0.5, 1, 3, 6, 8, and 24 h postdosing.
[b] Δt MIC, the time during which concentrations exceeded the MIC of the test pathogen (P 4241).

the curves of plotted data, and parameters were estimated by standard methods (7). C_{max} is the maximal concentration observed; $t_{1/2\beta}$ is the terminal elimination half-life calculated by using linear least-square regression for the log linear terminal-elimination phase; Δt MIC is the time during which concentrations exceed the MIC of the test pathogen (P 4241); and AUC_{0-24} is the area under the curve calculated by using the trapezoidal rule. The oral bioavailability is evaluated by the ratio of serum AUCs for p.o. and s.c. routes.

Protection studies. Treatments were initiated at 6 or 18 h postinfection (p.i.) in Swiss mice (acute pneumonia) and were delayed from 24 to 72 h p.i. in C57BL/6 mice (subacute pneumonia). Detailed treatment schedules are presented in the figure legends with the results. Fifteen animals per treatment group were used, and the animals in each experiment were infected simultaneously. Experiments were repeated at least twice. The antibiotics were given s.c. (sparfloxacin, ciprofloxacin, amoxicillin) or p.o. (sparfloxacin) in 0.5 ml of diluent at 12-h intervals; controls received the same volume of isotonic saline. Cumulative survival rates were recorded daily.

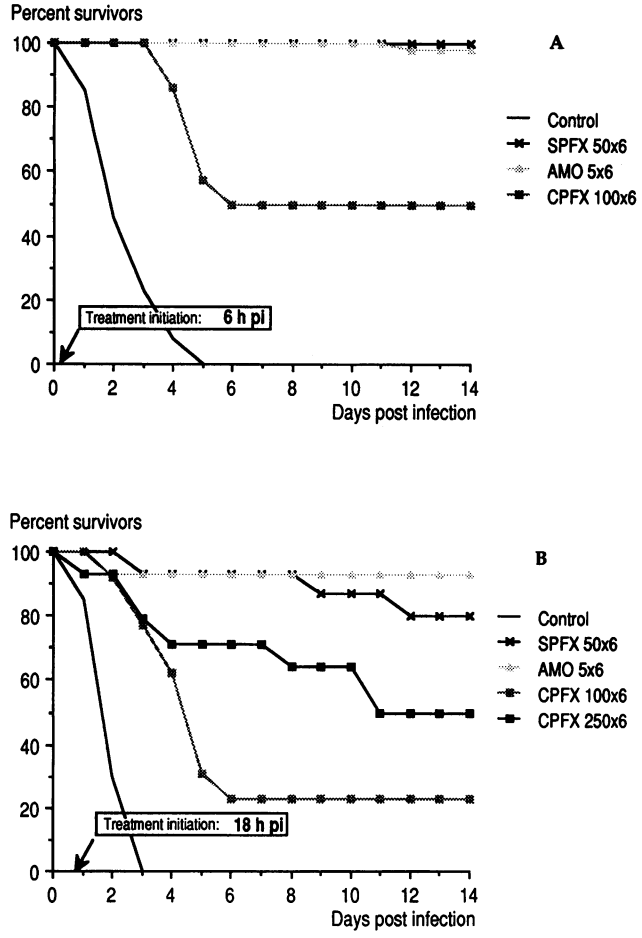

FIG. 1. Effects of treatment on survival rates in Swiss mice infected with a susceptible strain of *S. pneumoniae* (P 4241) (acute infection model). (A) Treatment was initiated at 6 h p.i. Mice received six oral administrations at 12-h intervals as follows: 50 mg of sparfloxacin (SPFX), 5 mg of amoxicillin (AMO), or 100 mg of ciprofloxacin (CPFX) per kg. (B) Treatment was initiated at 18 h p.i. with 50 mg of sparfloxacin, 5 mg of amoxicillin, and 100 or 250 mg of ciprofloxacin per kg.

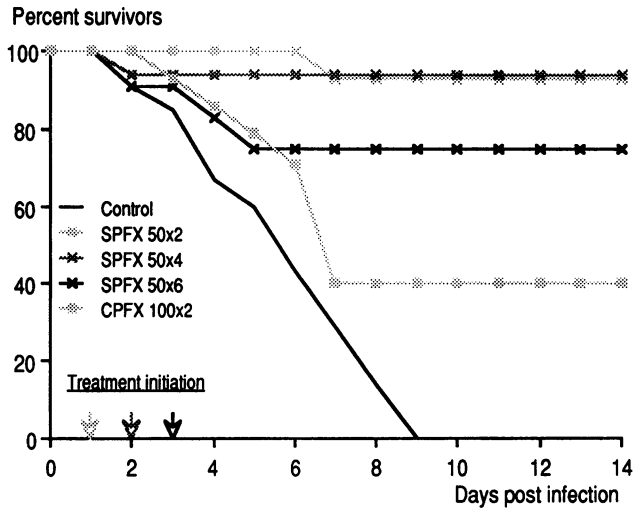

FIG. 2. Effects of treatment on survival rates in C57BL/6 mice infected with a susceptible strain of *S. pneumoniae* (P 4241) (subacute infection model). Mice received two s.c. injections of sparfloxacin (SPFX; 50 mg/kg) or ciprofloxacin (CPFX; 100 mg/kg) starting 24 h p.i.; sparfloxacin was also given in four or six injections starting at 48 and 72 h p.i., respectively.

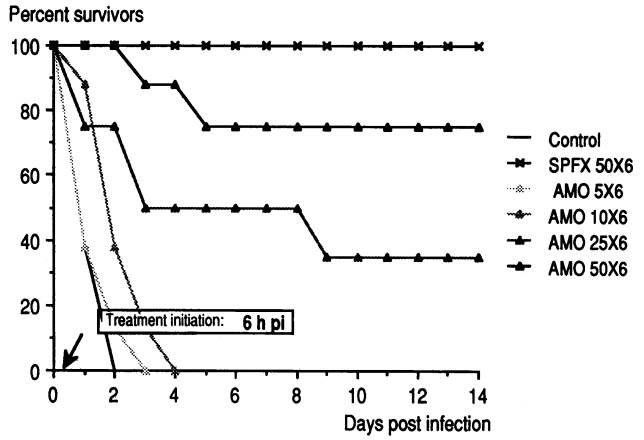

FIG. 3. Effects of treatment on survival rates in Swiss mice infected with a P^R strain of *S. pneumoniae* (54 B). Mice received six s.c. administrations of 50 mg of sparfloxacin (SPFX) or amoxicillin (AMO) per kg at 12-h intervals.

Clearance of bacteria from lungs and blood. The total recoverable CFU from whole-lung homogenates and intracardiac-blood samples were determined in both models. Antibiotics were given s.c. at 50 or 100 mg/kg per injection. In the acute model (Swiss mice), treatments were initiated at 18 h p.i.; five subgroups were studied: untreated mice and mice receiving one, two, four, or six injections at 12-h intervals. In the subacute model (C57BL/6 mice), treatments were initiated at 48 h p.i.; three subgroups were studied: untreated mice and mice receiving either one or two injections at a 12-h interval. Detailed schedules are given in the tables with the results.

Statistical analysis. Survival rates were analyzed by using Fisher's test. Bacterial counts were compared by using analysis of variance; the degree of significance was determined by using Snedecor's F test with the appropriate degree of freedom. When the *F* value was significant, each treatment group was compared with the control group and with each of the other treatment groups by using Student's *t* test. *P* values of 0.05 or less were considered significant.

RESULTS

In vitro activity data. Against the P^S strains (P 4241, P 6254), β-lactams showed lower MICs and MBCs, while sparfloxacin was four times as active as ciprofloxacin. Against the P^R strains (54 B[P^R]), P 170 [P^IM^R], and Div 27 [P^RM^R]), sparfloxacin was again the most active quinolone, and its MICs and MBCs were lower than those of penicillin and amoxicillin (Table 1).

Serum and lung pharmacokinetics. Concentrations in serum and lungs after a single s.c. or p.o. dose of sparfloxacin and ciprofloxacin are shown in Tables 2 and 3, respectively. In noninfected mice, concentration-time data could be fitted to a one-compartment open model in which the concentration of sparfloxacin (50 mg/kg) and its tissue penetration were lower than those of ciprofloxacin (100 mg/kg). However, the longer $t_{1/2\beta}$ of sparfloxacin resulted in AUCs in serum and tissue similar to those of ciprofloxacin. After oral administration, the bioavailability of sparfloxacin (22%) was greater than that of ciprofloxacin (13%).

In infected mice, the pharmacokinetic profiles of ciprofloxacin were not modified by infection, whatever the route of administration: C_{max}, AUC, and $t_{1/2\beta}$ were similar to those of noninfected mice. In contrast, the $t_{1/2\beta}$s of sparfloxacin in serum and lungs were much longer than those for noninfected animals, resulting in active concentrations against the test pathogen still detectable at 24 h compared with only 8 h with ciprofloxacin. Finally, the $t_{1/2\beta}$s of sparfloxacin in serum and lungs were three- to fivefold those of ciprofloxacin. When the drugs were administered p.o., the bioavailability of sparfloxacin (44%) remained better than that of ciprofloxacin (20%) in infected animals.

Therapeutic efficacy in experimental pneumonia. (i) Virulent strains in immunocompetent mice. In the acute model (Swiss mice), results with P^R strain P 4241 were as follows. When the treatments (six administrations) were initiated at 6 h p.i. (Fig. 1A), the survival rates with sparfloxacin (50 mg/kg p.o.) and amoxicillin (5 mg/kg s.c.) were 100% compared with about 50% with ciprofloxacin (100 mg/kg s.c.). When treatment was initiated at 18 h after infection (Fig. 1B), sparfloxacin at 50 mg/kg was significantly more effective (80% survival) than ciprofloxacin at 100 mg/kg (23%) and 250 mg/kg (50%).

Results with the M^R strain P 6254 were as follows. When treatments were initiated early, at 6 h p.i., sparfloxacin and ciprofloxacin similarly protected the animals. When treatments were delayed until 18 h after infection, sparfloxacin (50 mg/kg; six administrations) showed greater efficacy (80% survival) than ciprofloxacin at 100 mg/kg (40% survival).

In the subacute model (C57BL/6 mice), survival rates with sparfloxacin (50 mg/kg) were the same (94%) when treatment

TABLE 4. Clearance of *S. pneumoniae* from lungs and blood of Swiss mice infected with P4241 and treated with s.c. injections of antibiotic

Time (h) p.i.	Values after treatment with:							
	Nothing (control)		Amoxicillin (50 mg/kg)		Sparfloxacin (50 mg/kg)		Ciprofloxacin (100 mg/kg)	
	Lung[a]	Blood[b]	Lung	Blood	Lung	Blood	Lung	Blood
24 (6 h after 1 injection)	6.9 ± 0.7[c]	3/3	4.1 ± 1.3	3/3	3.6 ± 1.4	3/3	3.9 ± 1.1	3/3
42 (12 h after 2 injections)	6.6 ± 0.4[c]	3/3	2.7 ± 0.2[d]	3/3	<2.6[d]	3/3	4.4 ± 1.7	3/3
66 (12 h after 4 injections)	7.2 ± 0.3[c]	3/3	<2.6[d,e]	3/3	<2.6[d]	3/3	5.8 ± 1.0	3/3
90 (12 h after 6 injections)			<2.6[d]	0/3	<2.6[d]	0/3	5.7 ± 0.5	1/3

[a] Log_{10} CFU per milliliter of lung homogenate. Values are means ± standard deviations (n = 3).
[b] Number of animals with positive blood cultures/total number of animals.
[c] Greater than in all treatment groups ($P < 0.01$ to 0.001).
[d] Lower than values for ciprofloxacin ($P < 0.05$ to 0.001).
[e] The lower limit of detection was 2.6 log_{10} CFU/ml (4×10^2 CFU/ml).

was initiated at 24 h (two s.c. injections) or 48 h (four s.c. injections) and remained still high (75%) when started at 72 h p.i. (six s.c. injections). Ciprofloxacin (100 mg/kg) initiated at 24 h p.i. protected only 40% of the animals (Fig. 2).

(ii) Avirulent strains in leukopenic mice (Swiss mice). For P^R strain 54 B, sparfloxacin (50 mg/kg; six administrations s.c. initiated at 6 h p.i.) protected all the animals. Amoxicillin gave 70% protection at 50 mg/kg, a dosage 10 times higher than that effective against the P^S strain (Fig. 3).

For multiresistant strains 170 B and Div 27, sparfloxacin (50 mg/kg; six s.c. administrations initiated at 6 h p.i.) gave 100% protection. In contrast, ciprofloxacin at the same dosage (50 mg/kg) gave only 7% protection, but there was 92% survival at 100 mg/kg. Amoxicillin (50 mg/kg) gave 90% protection.

Bacterial clearance from lungs. In the acute model (Swiss mice), results with P^S strain P 4241 (Table 4) were as follows. Six hours after a single s.c. injection of sparfloxacin and amoxicillin (50 mg/kg) or of ciprofloxacin (100 mg/kg), bacterial counts in the lungs were significantly lower than in controls. Twelve hours after a second antibiotic injection, bacteria were undetectable in the lungs of sparfloxacin-treated animals, whereas counts in ciprofloxacin-treated animals were only 34% lower than in controls; sparfloxacin and amoxicillin were significantly more effective than ciprofloxacin. Bacteria were still detected in the lungs 12 h after six injections of ciprofloxacin. Blood from sparfloxacin-treated mice was sterile 12 h after six injections, whereas blood from controls was not. Some animals treated with ciprofloxacin were bacteremic 12 h after the last injection.

For M^R strain P 6254, four injections of sparfloxacin at 50 mg/kg each completely cleared bacteria from the lungs and blood, whereas five or six injections of ciprofloxacin at twice the dose (100 mg/kg) were necessary to clear the lungs.

In the subacute model (C57BL/6 mice), sparfloxacin completely cleared lungs and blood by 24 h after two injections.

DISCUSSION

Several studies have shown that sparfloxacin is at least as potent as ciprofloxacin against a wide spectrum of gram-positive and gram-negative bacteria and is more active against *S. pneumoniae* (6, 10, 14, 15). In contrast, results of few in vivo studies have been published. Nakamura et al. (15) found that oral sparfloxacin was highly effective against systemic infections with *S. pneumoniae* and generally more active than ciprofloxacin. Bouanchaud et al. (4) found that sparfloxacin was more active than ofloxacin against three clinical isolates (M^S and M^R strains) both in vitro and in mouse septicemia and pneumonia models on the basis of 50% effective doses. Our data support these results. Sparfloxacin at two- or fivefold-smaller doses than ciprofloxacin was more effective than this quinolone against a susceptible *S. pneumoniae* strain in the acute model of Swiss mice. Moreover, sparfloxacin remained effective late in the disease process when the lungs were severely inflamed and at a time when ciprofloxacin had lost all its activity, as shown in the subacute model. The efficacy of sparfloxacin in these models was similar to that previously reported for temafloxacin compared with ciprofloxacin and ofloxacin (1). These results were confirmed by using an M^R strain.

Against P^R and multiresistant strains, sparfloxacin was also highly effective. Increasing the dose of amoxicillin improved survival rates in animals infected with these P^R pneumococci, in agreement with data reported by Pallares (17), who found that pneumonia due to P^R pneumococci (0.1 < MIC <2 μg/ml) responded to intravenous high-dose penicillin therapy. Highly resistant *S. pneumoniae* strains (MIC, ≥ 8 μg/ml) might, however, require alternative antibiotic therapy, and a fluoroquinolone such as sparfloxacin could be effective.

The excellent activity of sparfloxacin in vivo is partly accounted for by the fact that its activity against gram-positive organisms in vitro is generally higher than that of the other quinolones, but its pharmacokinetic behavior also appears to be involved. In both uninfected and infected mice given a single s.c. or p.o. dose of 50 mg/kg, the concentrations of sparfloxacin exceeded the MIC and the MBC for *S. pneumoniae* for up to 24 h, whereas at twice the dose, ciprofloxacin levels exceeded the MIC for 8 h and the MBC for no more than 2 h. These results are well correlated with pharmacokinetic data. Regardless of the route of administration, half-lives in serum and lung and the AUC of sparfloxacin in lung exceeded those of ciprofloxacin in healthy controls. These results are in agreement with those reported by Nakamura et al. (14), who studied noninfected mice. Similar favorable pharmacokinetic behavior has also been found in healthy male volunteers (13): following oral administration of 200 to 800 mg, peak levels in plasma (0.70 to 1.97 μg/ml) occurred at 4 to 5 h postdose; the mean $t_{1/2\beta}$ for plasma ranged from 18 to 21 h, and AUCs for plasma ranged from 18 to 57 μg · h/ml. We also found that the superior pharmacokinetics of sparfloxacin relative to ciprofloxacin were maintained in infected animals, and the prolonged residence times of sparfloxacin in the infected host could be another major determinant of its efficacy. This specific behavior was also previously reported for temafloxacin compared with ciprofloxacin and ofloxacin (1) and explains the greater efficacy of these new quinolones compared with ofloxacin and ciprofloxacin.

In conclusion, sparfloxacin, a new quinolone, is highly effective in a murine model of pneumonia induced by M^S and M^R (P 6254) strains of *S. pneumoniae* as well as against multiresistant strains in immunocompromised animals. Clinical evaluation of this antibiotic as an alternative for patients with community-acquired pneumonia appears to be justified, as preliminary studies in humans suggest favorable pharmacokinetics. Indeed, Soejima et al. (18) found that sparfloxacin (300 mg once daily) was as effective as ofloxacin (200 mg three times daily) in the treatment of patients with bacterial pneumonia, and Hara et al. (8) have also reported that once-daily administration of sparfloxacin (300 mg) is as effective as ofloxacin (600 mg/day) for the treatment of chronic respiratory infections.

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