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In Vitro Activity of the Active Metabolite of Prulifloxacin (AF 3013) Compared with Six Other Fluoroquinolones

Since the synthesis and introduction of ciprofloxacin [1], the first broad-spectrum fluoroquinolone, into clinical practice, many molecules have been synthesised, with some attaining important positions in the therapeutic armory, thanks to their spectrum of activity and good patient tolerance. Ciprofloxacin, ofloxacin and levofloxacin all have a broad spectrum of activity, including efficacy against gram-negative and gram-positive bacteria [1, 2]. New derivatives, such as trovafloxacin [3], moxifloxacin [4] and grepafloxacin [5], have subsequently been developed, and they possess even greater activity against gram-positive bacteria and anaerobes.

Prulifloxacin, 6-fluoro-1-methyl-7-(4-[5-methyl-2-oxo-1, 3-dioxolen-4-yl] methyl-1-piperazinyl)-4-oxo-4H-(1, 3) thiaceto (3, 2-α) quinoline-3-carboxylic acid, is a prodrug that, following oral administration, is rapidly absorbed and hydrolysed to AF 3013, presenting an in vitro activity similar to that of ciprofloxacin [6, 7, 8, 9]. It has a half-life of 7–10 h, penetrates tissues well, and reaches bactericidal concentrations in biological liquids. This quinolone has a broad spectrum of activity covering enterobacteria and pseudomonas, as well as enteropathogenic bacteria, including *Campylobacter jejuni*, and respiratory pathogens, such as *Haemophilus influenzae*, *Moraxella catarrhalis*, beta-haemolytic streptococci and methicillin-sensitive *Staphylococcus aureus*. The present study was conducted to evaluate the in vitro activity of the active metabolite of prulifloxacin, AF 3013, and to compare it with that of six other fluoroquinolones (nalidixic acid, ciprofloxacin, moxifloxacin, trovafloxacin, levofloxacin and grepafloxacin).

A total of 537 bacterial strains were included in the study, all of which were isolated from different pathological specimens at the Microbiology Laboratory of the Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, in 1999. All strains were clinically significant. The mi-croorganisms and the number of strains studied are listed in Table 1. The control strains used were *Streptococcus pneumoniae* ATCC 49619, *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Haemophilus influenzae* ATCC 49247, *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853.

The antibiotics studied were in powder form and of a known potency. They were obtained from their respective manufacturing laboratories as follows: AF 3013, the active metabolite of prulifloxacin (ACRAF, Italy), nalidixic acid (Prodes, Spain), ciprofloxacin and moxifloxacin (Bayer, Spain), trovafloxacin (Pfizer, Spain), levofloxacin (Aventis, Spain) and grepafloxacin (Miquel, Spain). Minimal inhibitory concentrations (MICs) were determined using a standard agar dilution method following the guidelines of the National Committee for Clinical Laboratory Standards [10].

The MICs of AF 3013 for the 172 strains of nalidixic acid-susceptible enterobacteria studied were comparable and slightly below those of ciprofloxacin for the majority of species (Table 1). While the new fluoroquinolones conserve the spectrum of activity against enterobacteria, none of those studied, barring prulifloxacin, surpass the activity of ciprofloxacin against these pathogens, and all of them are less active than ciprofloxacin against *Pseudomonas aeruginosa*.

Resistance to first-generation quinolones, such as nalidixic acid, follows a mutation in the subunit A of the DNA gyrase, but these strains remain susceptible to ciprofloxacin and the other fluoroquinolones, despite the slightly increased MICs of these agents. Indeed, the MIC values against the nalidixic acid-resistant strains studied were greater than those against the susceptible strains. The MIC90 scores of ciprofloxacin and AF 3013 against *Escherichia coli* increased from ≤0.015 for the nalidixic acid-susceptible strains to 1 µg/ml for the resistant ones, while those of moxifloxacin and grepafloxacin increased from 0.12 to 2 µg/ml and those of trovafloxacin and levofloxacin increased from 0.06 to 1 and 2 µg/ml, respectively.

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Table 1 Comparative in vitro activity of AF 3013 and six other quinolones against 537 bacterial isolates

Microorganism	Antimicrobial agent	MIC (μg/ml)											
		MIC$_{50}$	MIC$_{90}$	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
E. coli Nal^S (n=11)	AF 3013	≤0.015	≤0.015	10	1								
	nalidixic acid	4	4								5	5	1
	ciprofloxacin	≤0.015	≤0.015	11									
	moxifloxacin	0.06	0.12		1	8	1		1				
	trovafloxacin	0.03	0.06	1	7	3							
	grepafloxacin	0.03	0.12		7	2	1	1					
	levofloxacin	0.03	0.06		6	3	2						
E. coli Nal^R (n=15)	AF 3013	0.12	1				10	2	1	2			
	nalidixic acid	>32	>32										15[a]
	ciprofloxacin	0.25	1					10	2	3			
	moxifloxacin	1	2						1	11	2	1	
	trovafloxacin	0.5	1					4	6	4	1		
	grepafloxacin	2	2						2	5	7		1
	levofloxacin	1	2						2	11	2		
E. coli enterohaemorrhagic (n=10)	AF 3013	≤0.015	≤0.015	9					1				
	nalidixic acid	2	2							2	7		1[a]
	ciprofloxacin	0.03	0.03	1	8						1		
	moxifloxacin	0.06	0.06			9					1		
	trovafloxacin	0.06	0.06		2	7						1	
	grepafloxacin	0.06	0.06		1	8						1	
	levofloxacin	0.5	0.5						9	1			
E. coli enterotoxigenic (n=12)	AF 3013	≤0.015	≤0.015	11							1		
	nalidixic acid	2	2							1	9	2	
	ciprofloxacin	0.03	0.03	12									
	moxifloxacin	0.06	0.12		2	6	3	1					
	trovafloxacin	0.06	0.06	9	1	1	1						
	grepafloxacin	0.06	0.06	2	6	1	2	1					
	levofloxacin	0.5	0.5					2	7	3			
K. pneumoniae Nal^S (n=9)	AF 3013	0.03	0.12	2	4	2	1						
	nalidixic acid	4	8								4	1	4
	ciprofloxacin	0.03	0.25	1	5	2		1					
	moxifloxacin	0.12	1			2	3	2	1	1			
	trovafloxacin	0.12	0.5		1	2	3	2	1				
	grepafloxacin	0.12	0.5		2	2	2	2	1				
	levofloxacin	0.06	1			5	1	2		1			
K. pneumoniae Nal^R (n=14)	AF 3013	0.25	0.25			1	5	7	1				
	nalidixic acid	32	>32										14/7[a]
	ciprofloxacin	0.25	1				1	9	2	2			
	moxifloxacin	1	2					1	2	6	4	1	
	trovafloxacin	0.5	2					2	9	1	2		
	grepafloxacin	1	2						2	9	2	1	
	levofloxacin	1	1					1	5	7	1		
K. oxytoca (n=10)	AF 3013	≤0.015	0.03	8	2								
	nalidixic acid	2	8								6	1	3
	ciprofloxacin	≤0.015	0.03	6	4								
	moxifloxacin	0.12	0.25				8	2					
	trovafloxacin	0.12	0.12			1	9						
	grepafloxacin	0.12	0.12			2	8						
	levofloxacin	0.06	0.06			9	1						
P. mirabilis Nal^S (n=10)	AF 3013	≤0.015	≤0.015	10									
	nalidixic acid	4	8									7	3
	ciprofloxacin	0.03	0.03	4	6								
	moxifloxacin	0.25	0.5					6	3	1			
	trovafloxacin	0.25	0.5					8	2				
	grepafloxacin	0.25	0.5					7	2	1			
	levofloxacin	0.06	0.12			8	1	1					
P. mirabilis Nal^R (n=12)	AF 3013	1	>4				1			2	5	1	3
	nalidixic acid	>32	>32										12[a]
	ciprofloxacin	>4	>4							1		1	10
	moxifloxacin	>4	>4								1		11
	trovafloxacin	>4	>4								1		11
	grepafloxacin	>4	>4									1	11
	levofloxacin	4	>4							1	4	4	3

Table 1 (continued)

Microorganism	Antimicrobial agent	MIC (µg/ml)											
		MIC50	MIC90	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
E. aerogenes (n=11)	AF 3013	≤0.015	0.03	8	2						1		
	nalidixic acid	4	4								3	7	1[a]
	ciprofloxacin	0.03	0.03	5	5						1		
	moxifloxacin	0.12	0.5			4	3	2	1		1		
	trovafloxacin	0.12	0.12		2	2	6				1		
	grepafloxacin	0.12	0.25		1	3	5	1			1		
	levofloxacin	0.06	0.12		2	6	2				1		
E. cloacae (n=14)	AF 3013	≤0.015	0.12	9	2		3						
	nalidixic acid	4	>32								3	7	4/3[a]
	ciprofloxacin	≤0.015	0.12	9	2	1	1		1				
	moxifloxacin	0.12	0.5	1		2	4	5	1		1		
	trovafloxacin	0.06	0.5	1	5	·1	5		1	1			
	grepafloxacin	0.12	0.5	1	1	3	5	2	1	1			
	levofloxacin	0.06	0.5		5	4	3		1	1			
S. marcescens (n=11)	AF 3013	0.12	0.5	2	1	1	4	1	1	1			
	nalidixic acid	2	8							2	7		2/1[a]
	ciprofloxacin	0.12	0.5	2	1		5	1	1	1			
	moxifloxacin	0.5	4			1	2		4	1	1	2	
	trovafloxacin	0.5	4				3		3	3		2	
	grepafloxacin	1	4				3		2	3		3	
	levofloxacin	0.25	2		2	1	2	3	1		2		
C. freundii (n=12)	AF 3013	≤0.015	0.25	7		2	1	1		1			
	nalidixic acid	4	16									6	6/1[a]
	ciprofloxacin	0.03	0.5	5	3	1	1		1		1		
	moxifloxacin	0.5	4				4	1	3	2		2	
	trovafloxacin	0.12	4			1	6		1	2		2	
	grepafloxacin	0.25	4			3	2	1	1	3		2	
	levofloxacin	0.12	1		1	4	1	4		1	1		
C. koseri (n=11)	AF 3013	≤0.015	≤0.015	10							1		
	nalidixic acid	4	4								1	9	1[a]
	ciprofloxacin	≤0.015	0.12	9			1				1		
	moxifloxacin	0.06	0.12			7	3					1	
	trovafloxacin	0.03	0.12	5	2		3						1
	grepafloxacin	0.06	0.12		5	1	4						1
	levofloxacin	0.03	0.06		6	4						1	
P. vulgaris (n=10)	AF 3013	≤0.015	≤0.015	10							1		
	nalidixic acid	4	4								3	7	
	ciprofloxacin	0.03	0.03	2	8								
	moxifloxacin	0.25	0.5					7	3				
	trovafloxacin	0.12	0.5				5	3	2				
	grepafloxacin	0.25	0.5				2	6	2				
	levofloxacin	0.06	0.06			10							
M. morganii (n=11)	AF 3013	≤0.015	0.03	9	1	1							
	nalidixic acid	2	4							2	7	1	1[a]
	ciprofloxacin	≤0.015	0.03	8	2	1							
	moxifloxacin	0.12	0.5			1	6	1	3				
	trovafloxacin	0.12	0.5				8	1	1	1			
	grepafloxacin	0.12	0.25				6	4	1				
	levofloxacin	0.03	0.12			6	2	2	1				
P. rettgeri (n=6)	AF 3013	0.03	1	1	2	1				2			
	nalidixic acid	4	>32									4	2/1[a]
	ciprofloxacin	0.03	1	3		1			1	1			
	moxifloxacin	0.5	2					2	2	1	1		
	trovafloxacin	0.25	2					3	1	1	1		
	grepafloxacin	0.25	2					3	1	1	1		
	levofloxacin	0.12	2				1	2	1	1	1		
P. stuartii (n=10)	AF 3013	2	>4			2	1	1			1	3	2
	nalidixic acid	>32	>32								1	1	8/6[a]
	ciprofloxacin	1	>4			3			1	1		3	2
	moxifloxacin	2	>4					2	1	1	1	1	4
	trovafloxacin	2	>4					1	2	1	1	1	4
	grepafloxacin	1	>4					1	2	2			5
	levofloxacin	1	>4				2	1	1	1		1	4

Table 1 (continued)

Microorganism	Antimicrobial agent	MIC (μg/ml)											
		MIC50	MIC90	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
S. enterica (*n*=11)	AF 3013	≤0.015	0.03	8	2		1						
	nalidixic acid	4	4							2	1	7	1[a]
	ciprofloxacin	≤0.015	0.03	8	2			1					
	moxifloxacin	0.12	0.12	2		2	6			1			
	trovafloxacin	0.12	0.12	2	2	1	5			1			
	grepafloxacin	0.12	0.12	2		3	5			1			
	levofloxacin	0.06	0.06	1	2	7			1				
S. sonnei (*n*=10)	AF 3013	≤0.015	≤0.015	10									
	nalidixic acid	2	2							4	6		
	ciprofloxacin	≤0.015	≤0.015	10									
	moxifloxacin	0.03	0.03		9	1							
	trovafloxacin	≤0.015	≤0.015	10									
	grepafloxacin	0.03	0.03	3	7								
	levofloxacin	0.03	0.03	3	7								
S. flexneri (*n*=10)	AF 3013	≤0.015	≤0.015	10									
	nalidixic acid	≤1	2							6	4		
	ciprofloxacin	≤0.015	≤0.015	10									
	moxifloxacin	0.03	0.03		9	1							
	trovafloxacin	≤0.015	≤0.015	10									
	grepafloxacin	≤0.015	0.03	6	4								
	levofloxacin	0.03	0.03	4	6								
P. aeruginosa Cip^S (*n*=75)	AF 3013	0.25	1	1	7	6	9	22	16	14			
	nalidixic acid	>32	>32									3	72[a]
	ciprofloxacin	0.5	1				6	31	24	14			
	moxifloxacin	4	>4						3	12	21	24	15
	trovafloxacin	1	2					6	24	25	19	1	
	grepafloxacin	1	4					2	11	29	23	8	2
	levofloxacin	1	2					5	24	21	21	4	
P. aeruginosa Cip^R (*n*=30)	AF 3013	>4	>4							3	5	3	19
	nalidixic acid	>32	>32									1	29[a]
	ciprofloxacin	>4	>4								7	2	21
	moxifloxacin	>4	>4							2	2	1	25
	trovafloxacin	>4	>4								1		29
	grepafloxacin	>4	>4									1	29
	levofloxacin	>4	>4									5	25
H. influenzae (*n*=20)	AF 3013	≤0.015	≤0.015	20									
	nalidixic acid	≤1	2							15	5		
	ciprofloxacin	≤0.015	0.03	12	6	2							
	moxifloxacin	≤0.015	0.03	15	5								
	trovafloxacin	0.03	0.06	9	8	3							
	grepafloxacin	0.03	0.03	7	13								
	levofloxacin	0.06	0.06			20							
M. catarrhalis (*n*=8)	AF 3013	0.03	0.06	1	3	4							
	nalidixic acid	4	4								2	6	
	ciprofloxacin	0.12	0.12				8						
	moxifloxacin	0.12	0.12				8						
	trovafloxacin	0.03	0.06		6	2							
	grepafloxacin	0.06	0.06			8							
	levofloxacin	0.12	0.12				8						
L. pneumophila (*n*=14)	AF 3013	1	1							14			
	nalidixic acid	2	2								14		
	ciprofloxacin	0.25	0.5					7	7				
	moxifloxacin	1	1							14			
	trovafloxacin	0.12	0.12				14						
	grepafloxacin	0.5	0.5						14				
	levofloxacin	0.25	0.25					14					
C. jejuni (*n*=10)	AF 3013	0.25	0.5					3	5	1			1
	nalidixic acid	4	8								3	3	4/1[a]
	ciprofloxacin	0.5	1					3	5	1			1
	moxifloxacin	0.25	0.5				3	3	3				1
	trovafloxacin	0.06	0.12		1	6	2						1
	grepafloxacin	0.25	0.5				1	6	2				1
	levofloxacin	0.25	1				3	2	3	1			1

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Table 1 (continued)

MIC (µg/ml) — values in the concentration columns (≤0.015 … >4) are numbers of isolates.

Microorganism	Antimicrobial agent	MIC50	MIC90	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
S. pneumoniae Pc[S] (n=20)	AF 3013	≤0.015	0.03						3	13	1	3	
	nalidixic acid	>32	>32										20[a]
	ciprofloxacin	1	2						5	12	3		
	moxifloxacin	0.06	0.12	2	5	8	4	1					
	trovafloxacin	0.12	0.25	4	3	6	3	3	1				
	grepafloxacin	0.25	0.25				2	9	7	2			
	levofloxacin	1	2						4	12	4		
S. pneumoniae Pc[I] (n=21)	AF 3013	1	1					1	3	11	5		1
	nalidixic acid	>32	>32										21[a]
	ciprofloxacin	2	4						1	6	11	3	
	moxifloxacin	0.06	0.12		1	9	9	2					
	trovafloxacin	0.12	0.25	1		1	10	8	1				
	grepafloxacin	0.25	0.5				5	12	4				
	levofloxacin	1	2						10	11			
S. pneumoniae Pc[R] (n=17)	AF 3013	2	4				1	1		4	9	2	
	nalidixic acid	>32	>32										17[a]
	ciprofloxacin	1	2						4	6	5	2	
	moxifloxacin	0.06	0.12		3	6	8						
	trovafloxacin	0.12	0.25		3	1	8	5					
	grepafloxacin	0.25	0.5				4	9	4				
	levofloxacin	1	2						2	8	7		
S. pyogenes (n=17)	AF 3013	0.25	0.25				1	15	1				
	nalidixic acid	>32	>32										17[a]
	ciprofloxacin	0.5	1					1	13	3			
	moxifloxacin	0.25	0.25				1	16					
	trovafloxacin	0.12	0.12			2	14	1					
	grepafloxacin	0.5	1					3	11	3			
	levofloxacin	1	1						3	14			
S. agalactiae (n=16)	AF 3013	0.25	1					8	2	6			
	nalidixic acid	>32	>32										16[a]
	ciprofloxacin	1	1						6	9	1		
	moxifloxacin	0.25	0.25					16					
	trovafloxacin	0.12	0.25				10	6					
	grepafloxacin	0.5	0.5					7	9				
	levofloxacin	1	1							15	1		
S. aureus (n=10)	AF 3013	0.5	0.5					2	7		1		
	nalidixic acid	>32	>32										10[a]
	ciprofloxacin	0.5	0.5						9	1			
	moxifloxacin	0.06	0.06			9	1						
	trovafloxacin	0.03	0.03	1	8	1							
	grepafloxacin	0.06	0.12			5	4	1					
	levofloxacin	0.25	0.25				3	6	1				
S. aureus methicillin[R] (n=10)	AF 3013	>4	>4										10
	nalidixic acid	>32	>32										10[a]
	ciprofloxacin	>4	>4										10
	moxifloxacin	2	4								7	3	
	trovafloxacin	2	4							2	6	2	
	grepafloxacin	>4	>4										10
	levofloxacin	>4	>4										10
E. faecium (n=11)	AF 3013	2	2							3	7	1	
	nalidixic acid	>32	>32										11[a]
	ciprofloxacin	2	2							3	7	1	
	moxifloxacin	1	1						4	6	1		
	trovafloxacin	1	1					2	3	6			
	grepafloxacin	4	>4							2	1	4	4
	levofloxacin	1	1						2	9			
E. faecium Vm[R] (n=7)	AF 3013	4	>4									5	2
	nalidixic acid	>32	>32										7[a]
	ciprofloxacin	4	>4									4	3
	moxifloxacin	5	>4								3	2	2
	trovafloxacin	2	>4								4	1	2
	grepafloxacin	>4	>4									2	5
	levofloxacin	4	>4								1	4	2

Table 1 (continued)

Microorganism	Antimicrobial agent	MIC (μg/ml)											
		MIC50	MIC90	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4
E. faecalis (n=11)	AF 3013	2	4						2	1	6	2	
	nalidixic acid	>32	>32										11[a]
	ciprofloxacin	1	1						2	8	1		
	moxifloxacin	0.25	0.25				4	6		1			
	trovafloxacin	0.25	0.5				1	8	1		1		
	grepafloxacin	0.5	0.5					1	9				1
	levofloxacin	1	2						1	8	2		
E. faecalis VmR (n=10)	AF 3013	4	>4										10
	nalidixic acid	>32	>32										10[a]
	ciprofloxacin	>4	>4										10
	moxifloxacin	>4	>4										10
	trovafloxacin	>4	>4									2	8
	grepafloxacin	>4	>4										10
	levofloxacin	>4	>4										10

[a] MIC>32 μg/ml
Nal, nalidixic acid; Vm, vancomycin; Cip, ciprofloxacin; Pc, penicillin; S, susceptible; R, resistant; I, intermediate

Against *Klebsiella pneumoniae*, the MIC values of the different compounds were also higher for the strains resistant to nalidixic acid. In the case of AF 3013, the MIC increased from 0.12 to 0.25 μg/ml. On the other hand, all the nalidixic acid-resistant *Proteus mirabilis* strains studied were resistant to all the quinolones, with MIC90 values equal to or higher than 8 μg/ml. The 75 ciprofloxacin-susceptible strains of *Pseudomonas aeruginosa* were susceptible to AF 3013, which, along with ciprofloxacin, was the most active fluoroquinolone (MIC90, 1 μg/ml); however, the 30 ciprofloxacin-resistant strains presented cross-resistance to all the other fluoroquinolones.

The enteropathogenic enterobacteria studied were very susceptible to all the fluoroquinolones, with AF 3013 and ciprofloxacin, showing the greatest activity (MIC90 ≤0.015 μg/ml for the enteropathogenic *Escherichia coli* and shigellae and 0.03 μg/ml for the salmonellae). Only one nalidixic acid-resistant strain presented cross-resistance to the other fluoroquinolones evaluated.

The fluoroquinolones were active against the other gram-negative bacteria tested. *Haemophilus influenzae* was susceptible to all the fluoroquinolones evaluated, with AF 3013 presenting the lowest MIC, inhibiting all strains at concentrations below 0.015 μg/ml. Against *Moraxella catarrhalis* the MIC90 of AF 3013, trovafloxacin and grepafloxacin was 0.06 μg/ml, which was below that of the other quinolones evaluated, *Legionella pneumophila*, however, was inhibited with 1 μg/ml of AF 3013, a concentration that was slightly higher than that of the other fluoroquinolones.

The in vitro activity of AF 3013 and the other fluoroquinolones was evaluated against 58 strains of *Streptococcus pneumoniae*, using penicillin and ampicillin as reference antibiotics. The MIC50 of AF 3013 was 1 μg/ml against the penicillin-susceptible strains and 2 μg/ml for those presenting moderate and high resis-

tance; the MIC90 was 4 μg/ml for the penicillin-sensitive and -intermediate strains and 2 μg/ml for the highly resistant strains. The fluoroquinolone presenting the greatest activity of those evaluated was moxifloxacin, which had MIC50 and MIC90 values of 0.06 and 0.12 μg/ml, respectively, for all strains, regardless of their susceptibility to penicillin. This was followed by trovafloxacin, with an MIC90 of 0.25 μg/ml, and grepafloxacin, with an MIC90 of 0.25 μg/ml for the penicillin-susceptible strains and 0.5 μg/ml for the -resistant strains.

Generally speaking, AF 3013 exerted an activity against gram-positive bacteria that was similar to that of ciprofloxacin and levofloxacin but lower than that of grepafloxacin, moxifloxacin and trovafloxacin. Against enterococci, the MICs were higher than those for the other gram-positive organisms evaluated, with AF 3013 exhibiting extreme concentrations of 0.5–4 and 1–4 μg/ml for *Enterococcus faecalis* and *Enterococcus faecium*, respectively.

The chemical modifications made to the fluoroquinolones to attain activity against gram-positive cocci and anaerobic bacteria usually entail a certain degree of toxicity, preventing their use in clinical practice, as well as a reduction in activity against gram-negative bacteria. Prulifloxacin, a prodrug of the thiaceto-quinoline derivative AF 3013, belongs to the group of fluoroquinolones with major activity against gram-negative bacteria, including enterobacteria, *Pseudomonas* spp. and respiratory pathogens, such as *Haemophilus influenzae* and *Moraxella catarrhalis*. AF 3013 has demonstrated potent antibacterial activity, but its oral absorption was found to be poor in a previous study [6]. To improve oral absorption, the prodrug prulifloxacin has been synthesised, with hydrolysis to AF 3013 probably occurring in blood [6]. In that study, the mean plasma concentrations of active metabolite AF 3013 peaked between 0.5 and 1 h, and the maxi-
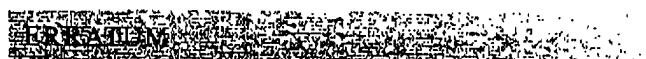
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mum concentrations were 0.68, 1.09 and 1 µg/ml at doses of 100, 200 and 400 mg, respectively. The Cmax, area under the concentration-time curve, and urinary excretion rates are not altered by food intake [9].

Since the in vitro activity of AF 3103 is similar to ciprofloxacin, or slightly better with regard to some gram-negative strains, clinical studies to evaluate its in vivo efficacy would be useful.

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In Vitro Activity of the Active Metabolite of Prulifloxacin (AF 3013) Compared with Six Other Fluoroquinolones

Eur J Clin Microbiol Infect Dis (2002) 21:328–334

In Table 1, page 332, some of the MIC values were incorrect. The corrected values are as follows.

Microorganism	Antimicrobial agent	MIC (µg/ml)	
		MIC50	MIC90
S. pneumoniae Pc^S (*n*=20)	AF 3013	1	4
S. pneumoniae Pc^I (*n*=21)	AF 3013	2	4
S. pneumoniae Pc^R (*n*=17)	AF 3013	2	2
E. faecium Vm^R (*n*=7)	moxifloxacin	4	>4

Pc, penicillin; Vm, vancomycin; ^{S}, susceptible; ^{R}, resistant; ^{I}, intermediate

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