

Supplementary Table S1: An overview of mean/median Cmax values of various disease-modifying antirheumatic drugs (DMARDs) described in the literature.

DMARDs	Mean/median Cmax ($\mu\text{g/mL}$)	Study conc. ($\mu\text{g/mL}$)	Subjects	Dose	References
Aurothiomalate/Auranofin	1.38	1.4	Healthy volunteers	Population kinetics for 21 mg daily over 14 days First intramuscular injection of 50mg sodium aurothiomalate	[1]
	4		Patients with rheumatoid arthritis		[2]
Azathioprine	0.048	0.05	Healthy volunteers	Single dose of 100 mg p.o.	[3]
Chloroquine	0.494	0.5	intermittent presumptive malaria treatment in pregnant and nonpregnant women	Three doses of 750mg chloroquine base each	[4]
D-Penicillamine	1.22	2.0	Patients with rheumatic arthritis	Single dose of 250mg p.o.	[5]
Hydroxychloroquine	0.034	0.05	Healthy volunteers	Single dose of 200mg p.o.	[6]
Leflunomide	2.0	2.0	Healthy volunteers	Single oral dose of 20mg Leflunomide	[7]
Methotrexate	0.323	0.3	patients with psoriasis, psoriatic arthritis or rheumatoid arthritis on a stable dose of methotrexate	10 mg p.o. once weekly	[8]
	0.607			20 mg p.o. once weekly	[8]
	0.229		Healthy volunteers	Single dose of 10mg p.o.	[*]
Sulfasalazine	6.0	6.0	Healthy volunteers	Single dose of 1000 mg p.o.	[*]
Sulfapyridine	11.48		Healthy volunteers	Single dose of 2000mg (4x500mg) p.o.	[9]
Tofacitinib	0.038	0.05	Healthy volunteers	Multiple dose phase with 11 mg extended release tofacitinib once daily	[10]
ANTIBIOTICS					
Cefuroxime	100	100	Healthy volunteers	Single dose of 1500 mg i.v.	[*]
	~100		Healthy volunteers		[11]
Benzylpenicillin	240	240	n.a.	Single dose of 5 mio IE i.v.	[*]

*DMARDs, disease-modifying antirheumatic drugs; Cmax, maximum serum concentration; Study.conc., Drug concentrations used as 1x Cmax for antimicrobial activity testing in this study

References:

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*Summary of product characteristics

Supplementary Table S2. Minimum inhibitory concentrations (MICs) presented as multiple times of the peak serum concentration (Cmax) of all disease-modifying anti rheumatic drugs (DMARDs) which demonstrated antimicrobial activity in the diffusion disk screening assay against respective bacterial species.

Bacteria	ATM ¹	AZA	DPM	CQ	HCQ	LEF	MTX ¹	SSZ ¹	TOF
Anaerobic bacteria									
<i>Actinomyces</i> spp.									
<i>A. naeslundii</i> DSMZ 43013	>70xCmax							>100xCmax	
<i>A. israelii</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>A. israelii</i>	17.5xCmax	-	-	-	-	-		>100xCmax	-
<i>A. oris</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>A. oris</i>	>70xCmax	-	-	-	-	-		50xCmax	-
<i>A. oris</i>	35xCmax	-	-	-	-	-		>100xCmax	-
<i>Capnocytophaga</i> spp.									
<i>C. sputigena</i> DSMZ 7273	8.8xCmax							100xCmax	
<i>C. gingivalis</i>	4.4xCmax	-	-	-	-	-		100xCmax	-
<i>C. granulosa</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>C. granulosa</i>	8.8xCmax	-	-	-	-	-		>100xCmax	-
<i>C. granulosa</i>	4.4xCmax	-	-	-	-	-		>100xCmax	-
<i>C. ochracea</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>Eikenella</i> spp.									
<i>E. corrodens</i> DSMZ 8340	4.4xCmax							>100xCmax	
<i>E. corrodens</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>E. corrodens</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>E. corrodens</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>E. corrodens</i>	>70xCmax	-	-	-	-	-		>100xCmax	-
<i>E. corrodens</i>	17.5xCmax	-	-	-	-	-		50xCmax	-
<i>Fusobacterium</i> spp.									
<i>F. nucleatum</i> DSMZ 15643	70xCmax						>100xCmax	50xCmax	
<i>F. nucleatum</i>	17.5xCmax	-	-	-	-	-	100xCmax	25xCmax	-
<i>F. nucleatum</i>	8.8xCmax	-	-	-	-	-	>100xCmax	50xCmax	-
<i>F. nucleatum</i>	17.5xCmax	-	-	-	-	-	100xCmax	25xCmax	-
<i>F. nucleatum</i>	8.8xCmax	-	-	-	-	-	50xCmax	50xCmax	-
<i>F. nucleatum</i>	4.4xCmax	-	-	-	-	-	12.5xCmax	50xCmax	-
<i>Parvimonas</i> spp.									
<i>P. micra</i> DSMZ 20468	17.5xCmax								
<i>P. micra</i>	35xCmax	-	-	-	-	-			
<i>P. micra</i>	>70xCmax	-	-	-	-	-			
<i>P. micra</i>	>70xCmax	-	-	-	-	-			
<i>P. micra</i>	>70xCmax	-	-	-	-	-			
<i>P. micra</i>	35xCmax	-	-	-	-	-			
<i>Prevotella</i> spp.									
<i>P. intermedia</i> DSMZ 20706	>70xCmax								
<i>P. intermedia</i>	>70xCmax	-	-	-	-	-			
<i>P. intermedia</i>	>70xCmax	-	-	-	-	-			
<i>P. intermedia</i>	>70xCmax	-	-	-	-	-			
<i>P. intermedia</i>	>70xCmax	-	-	-	-	-			
<i>P. intermedia</i>	>70xCmax	-	-	-	-	-			
<i>Porphyromonas</i> spp.									
<i>P. gingivalis</i> DSMZ 20709	8.8xCmax							25xCmax	
<i>P. gingivalis</i>	17.5xCmax	-	-	-	-	-		100xCmax	-
<i>P. gingivalis</i>	35xCmax	-	-	-	-	-		>100xCmax	-
<i>P. gingivalis</i>	17.5xCmax	-	-	-	-	-		100xCmax	-
<i>P. gingivalis</i>	4.4xCmax	-	-	-	-	-		50xCmax	-
<i>P. gingivalis</i>	8.8xCmax	-	-	-	-	-		50xCmax	-
Streptococci									
<i>Streptococcus</i> spp.									

*Anginosus group**S. anginosus*

>70xCmax	-	-	-	-	-	1.56xCmax	-	-
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*Mitis group**S. parasanguinis*

>70xCmax	-	-	-	-	-	1.56xCmax	-	-
>70xCmax	-	-	-	-	-	12.5xCmax	-	-

S. sanguinis

>70xCmax	-	-	-	-	-	1.56xCmax	-	-
>70xCmax	-	-	-	-	-	3.13xCmax	-	-

S. sanguinis

>70xCmax	-	-	-	-	-	3.13xCmax	-	-
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*Salivarius group**S. salivarius* ATCC 7073

>70xCmax	-	-	-	-	-	12.5xCmax	-	-
>70xCmax	-	-	-	-	-	50xCmax	-	-

S. salivarius

>70xCmax	-	-	-	-	-	50xCmax	-	-
>70xCmax	-	-	-	-	-	50xCmax	-	-

S. vestibularis

>70xCmax	-	-	-	-	-	50xCmax	-	-
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Aerobic bacteria*Escherichia coli**E. coli* ATCC 25922

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

E. coli

>70xCmax	-	-	-	-	-	-	-	-
35xCmax	-	-	-	-	-	-	-	-

E. coli

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

E. coli

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

*Proteus mirabilis**P. mirabilis* ATCC 14273

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

P. mirabilis

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

P. mirabilis

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

P. mirabilis

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

*Staphylococcus aureus**S. aureus* ATCC 29213

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

S. aureus

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

S. aureus

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

S. aureus

>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

S. aureus

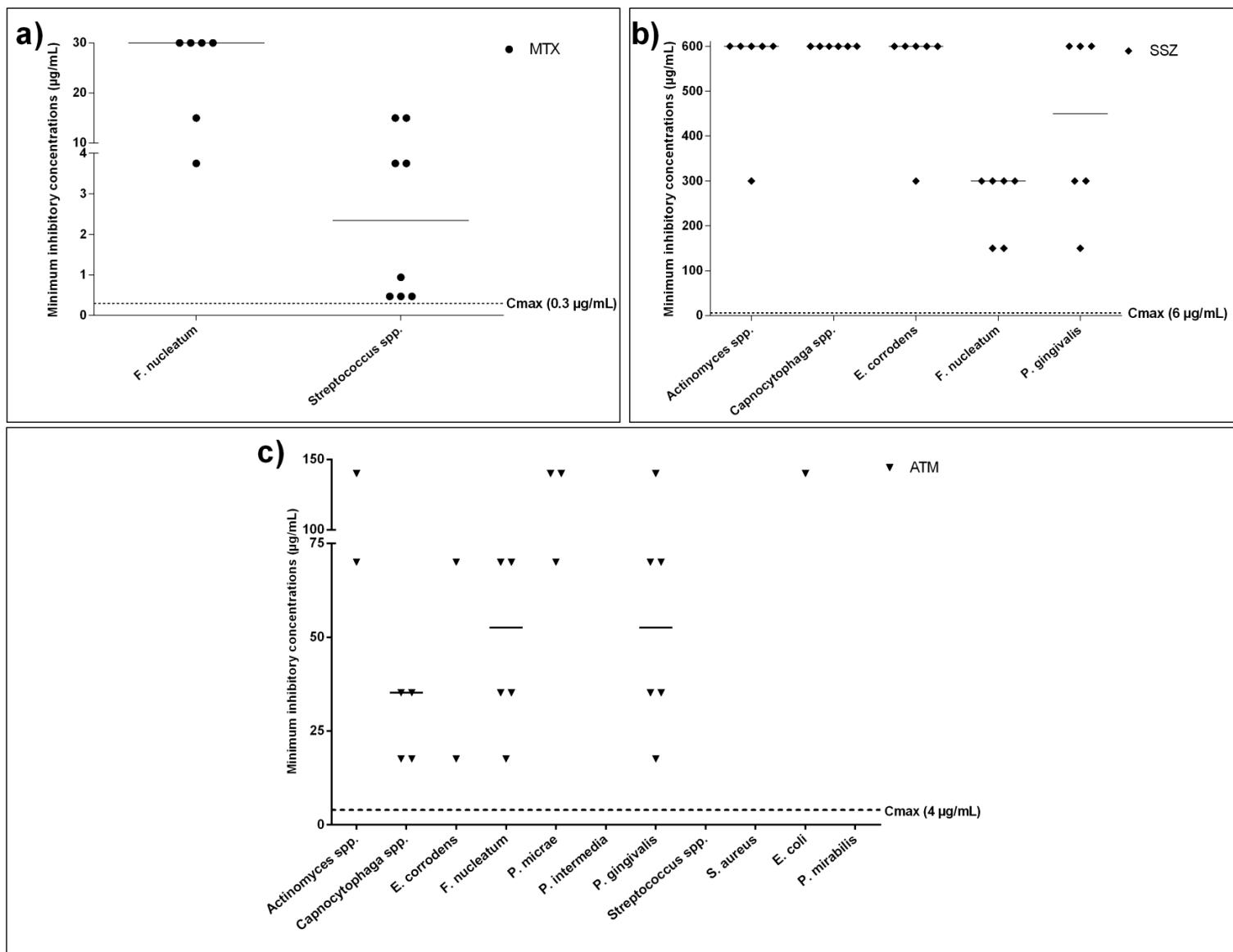
>70xCmax	-	-	-	-	-	-	-	-
>70xCmax	-	-	-	-	-	-	-	-

*ATM, Aurothiomalate; AZA, Azathioprine; CQ, Chloroquine; HCQ, Hydroxychloroquine; DPM, D-Penicillamine; LEF, Leflunomide; MTX, Methotrexate; SSZ, Sulfasalazine; TOF, Tofacitinib; DSMZ, German Collection of Microorganisms and Cell cultures GmbH; *A. israelii*, *Actinomyces israelii*; *A. naeslundii*, *Actinomyces naeslundii*; *A. oris*, *Actinomyces oris*; *C. gingivalis*, *Capnocytophaga gingivalis*; *C. granulosa*, *Capnocytophaga granulosa*; *C. ochracea*, *Capnocytophaga ochracea*; *E. corrodens*, *Eikenella corrodens*; *F. nucleatum*, *Fusobacterium nucleatum*; *P. micra*, *Parvimonas micra*; *P. intermedia*, *Prevotella intermedia*; *P. gingivalis*, *Porphyromonas gingivalis*; *S. anginosus*, *Streptococcus anginosus*; *S. parasanguinis*, *Streptococcus parasanguinis*; *S. sanguinis*, *Streptococcus sanguinis*; ATCC, American Type Culture Collection; *S. salivarius*, *Streptococcus salivarius*; *S. vestibularis*, *Streptococcus vestibularis*; *E. coli*, *Escherichia coli*; *P. mirabilis*, *Proteus mirabilis*; *S. aureus*, *Staphylococcus aureus*; Cmax, maximum serum concentration; n.a., not applicable because no antimicrobial activity was observed in the agar diffusion screening assay

¹ The concentrations used to calculate the minimum inhibitory concentrations as multiple times of the peak serum levels were as follows:

ATM 4µg/mL, MTX 0.3µg/mL, SSZ 6µg/mL.

Supplementary Figure S1. Antimicrobial activity of a) methotrexate (MTX), b) sulfasalazine (SSZ) and c) aurothiomalate (ATM) for rheumatoid arthritis associated pathogens. Minimum inhibitory concentrations are presented as median (min; max) $\mu\text{g}/\text{mL}$. The dashed lines indicate the drug-specific maximum serum concentrations (Cmax).



* *F. nucleatum*, *Fusobacterium nucleatum*, *E. corrodens*, *Eikenella corrodens*; *P. gingivalis*, *Porphyromonas gingivalis*; *P. micra*, *Parvimonas micra*, *S. aureus*, *Staphylococcus aureus*; *E. coli*, *Escherichia coli*; *P. mirabilis*, *Proteus mirabilis*