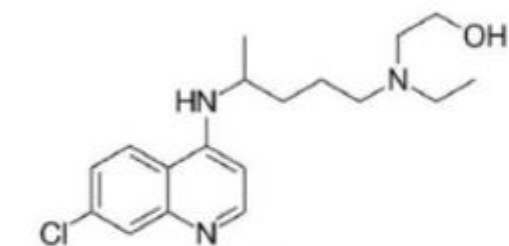
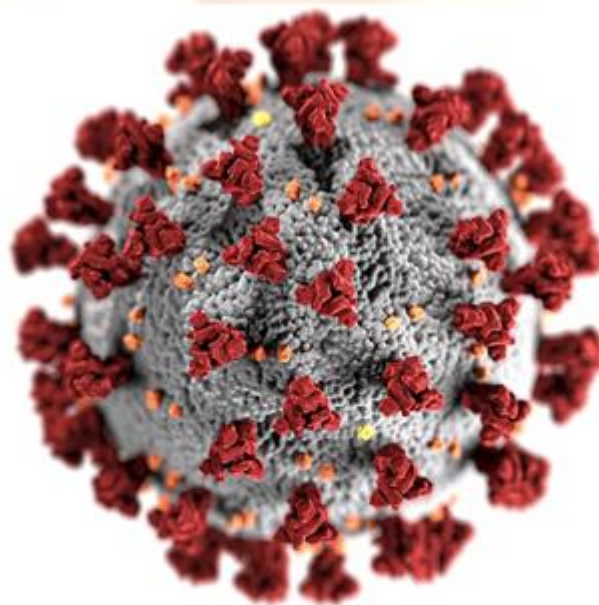
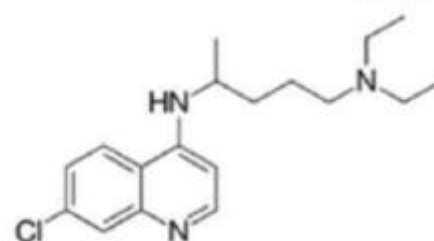


# Informativos sobre o uso da cloroquina no enfrentamento da COVID-19

ISSN 2675-4045



HIDROXICLOROQUINA



CLOROQUINA

VOLUME I  
INFORMATIVO Nº 02  
MATERIAL SUPLEMENTAR

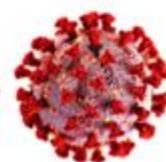
**MECANISMO DE AÇÃO E  
FARMACOCINÉTICA**

MAIO/2020

CiPharma - Ciência em Ação

**CLOROQUINA**

No enfrentamento da COVID-19



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## **MATERIAL SUPLEMENTAR**

Com o intuito de oferecer ao leitor um formato conjunto para apresentação dos dados farmacocinéticos da cloroquina e da hidroxicloroquina, na Tabela 1 estão compilados os principais parâmetros farmacocinéticos destes fármacos administrados sob a forma de seus sais.

Tabela 1. Principais propriedades farmacocinéticas da cloroquina e da hidroxicloroquina administradas sob a forma de seus sais.

Parâmetros	Cloroquina		Hidroxicloroquina	
	(via de administração) <sup>SAL</sup>	Dose (mg) <sup>[Referência]</sup>	(via de administração) <sup>SULFATO</sup>	Dose (mg) <sup>[Referência]</sup>
excreção urinária sem alteração	47±5,3 % (intravenosa, IV) <sup>DICLORIDRATO</sup>	300; base <sup>[1]</sup>	16–21 %	.. <sup>[10]</sup>
	42±7,7 % (oral, solução) <sup>DIFOSFATO</sup>		~ 10 %	200; sal <sup>[11]</sup>
	46±8,0 % (oral, comprimido) <sup>DIFOSFATO</sup>		27 %	155; base <sup>[11]</sup>
Volume aparente de distribuição	421±171 L/kg	600; base <sup>[2]</sup>	Sangue: 5522 L (IV infusão) Plasma: 44257 L (IV infusão)	.. <sup>[12]</sup>
	3410±720 L (R) (oral) <sup>DIFOSFATO</sup>	150; base <sup>[3]</sup>		.. <sup>[12]</sup>
	4830±1490 L (S) (oral) <sup>DIFOSFATO</sup>	241,8; sal <sup>[3]</sup>	2851±2147 L (oral)	400; sal <sup>[13]</sup>
	250±116 L/kg (oral) <sup>SULFATO</sup>	300 <sup>1x/SEMANA(n=3)</sup> , 900 <sup>[4]</sup>		310; base <sup>[13]</sup>
	302±102 L/kg (oral) <sup>SULFATO</sup>	200 <sup>2x/SEMANA(n=3)</sup> , 1200 <sup>[4]</sup>		
	283±112 L/kg (oral) <sup>SULFATO</sup>	50 <sup>7x/SEMANA(n=3)</sup> , 1050 <sup>[4]</sup>		
Clearance	204±86 L/kg (intravenosa) <sup>DICLORIDRATO</sup>	300; base <sup>[1]</sup>	12,0±6,8 L/h (oral)	400; sal <sup>[13]</sup>
	136±38 mL/min; 8,16±2,28 L/h (R) (oral) <sup>DIFOSFATO</sup>	150; base <sup>[3]</sup>		310; base <sup>[13]</sup>
	237±71 mL/min; 14,22±4,26 L/h (S) (oral) <sup>DIFOSFATO</sup>	241,8; sal <sup>[3]</sup>		
	plasmático total: 722±166 mL/min (IV) <sup>DICLORIDRATO</sup>	300; base <sup>[1]</sup>		
	renal: 412±139 mL/min (IV) <sup>DICLORIDRATO</sup>			
	454±49 mL/min (oral, solução) <sup>DIFOSFATO</sup>			
	430±141 mL/min (oral, comprimido) <sup>DIFOSFATO</sup>			
	corporal total: 0,748±0,227 L/h/kg (oral) <sup>SULFATO</sup>	600; base <sup>[2]</sup>	Renal: 19,9 mL/min (sangue); 211 mL/min (plasma) Total: 96 mL/min (sangue); 667 mL/min (plasma) (IV infusão)	155; base <sup>[12]</sup>
	0,441±0,143 L/h/kg (oral) <sup>SULFATO</sup>	300 <sup>1x/SEMANA(n=3)</sup> , 900 <sup>[4]</sup>		
	0,579±0,117 L/h/kg (oral) <sup>SULFATO</sup>	200 <sup>2x/SEMANA(n=3)</sup> , 1200 <sup>[4]</sup>		
0,571±0,114 L/h/kg (oral) <sup>SULFATO</sup>	50 <sup>7x/SEMANA(n=3)</sup> , 1050 <sup>[4]</sup>			
plasmático 8,61±1,031 mL/min/kg (oral)	600; base <sup>[5]</sup>			
sanguíneo total: 2,95±0,349 mL/min/kg (oral)				
Biodisponibilidade oral	78 (52-102) % (oral, solução) <sup>DIFOSFATO</sup>	300; base <sup>[1]</sup>	67±12 % (oral)	155; base <sup>[14]</sup>
	89 (67-114) % (oral, comprimido) <sup>DIFOSFATO</sup>		74±13 % (oral)	200; sal <sup>[14]</sup>
ASC	19,3±3,9 µg/mL.h (R) (oral) <sup>DIFOSFATO</sup>	150; base <sup>[3]</sup>	75,4±46,9 nmol.h/mL (ASC <sub>0-t</sub> ) (oral)	400; sal <sup>[13]</sup>
	11,3±3,0 µg/mL.h (S) (oral) <sup>DIFOSFATO</sup>	241,8; sal <sup>[3]</sup>	102,3±60,8 nmol.h/mL (ASC <sub>0-∞</sub> ) (oral)	310; base <sup>[13]</sup>
	7511 ± 2437 ng/mL.h (IV) <sup>DICLORIDRATO</sup>	300; base <sup>[1]</sup>	1679±385 ng.h/mL (ASC <sub>0-60d</sub> ) (oral, comprimido)	200; sal <sup>[16]</sup>
	4990±879 ng/mL.h (oral, solução) <sup>DIFOSFATO</sup>		1819±417 ng.h/mL (ASC <sub>0-∞</sub> ) (oral, comprimido)	
	6111±1315 ng/mL.h (oral, comprimido) <sup>DIFOSFATO</sup>			
		24751 µg/L.h (oral) <sup>SULFATO</sup>	300 <sup>1x/SEMANA(n=3)</sup> , 900 <sup>[4]</sup>	14706 ng.h/mL (ASC <sub>last</sub> ) hidroxicloroquina
	13977 µg/L.h (oral) <sup>SULFATO</sup>	200 <sup>2x/SEMANA(n=3)</sup> , 1200 <sup>[4]</sup>	8047 ng.h/mL (R)	155; base <sup>[17]</sup>

	13257 µg/L.h (oral) <sup>SULFATO</sup>	50 <sup>7x/SEMANA(n=3)</sup> ,1050 <sup>[4]</sup>	3835 ng.h/mL (S)	
	plasmática 23,66±3,824 µg/mL.h (oral)	600; base <sup>[5]</sup>		
	sanguínea total 66,43±7,309 µg/mL.h (oral)			
	122 (103–182) µg/mL.h (ASC <sub>0-28d</sub> ) (oral) <sup>DIFOSFATO</sup>	600 <sup>t0</sup> ,300 <sup>6,24,48h</sup> ,1500 <sup>[6]</sup>		
	837±248 ng/mL (IV) <sup>DICLORIDRATO</sup>		1,22±0,40 nmol/mL (oral)	400; sal <sup>[13]</sup>
	73±12 ng/mL (oral, solução) <sup>DIFOSFATO</sup>	300; base <sup>[1]</sup>	34,3±9,5 ng/mL (oral, comprimido)	310; base <sup>[13]</sup>
	76±14 ng/mL (oral, comprimido) <sup>DIFOSFATO</sup>		sangue 129,6 ng/mL (oral)	200; sal <sup>[16]</sup>
			plasma 50,3 ng/mL (oral)	200; sal <sup>[11]</sup>
				155; base <sup>[11]</sup>
C <sub>max</sub>	228,5±57 µg/L (oral) <sup>SULFATO</sup>	600; base <sup>[2]</sup>	166,0 ng/mL hidroxiclороquina	200; sal <sup>[17]</sup>
			103,1 ng/mL (R); 70,3 ng/mL (S)	155; base <sup>[17]</sup>
			plasma 46 (34–79) ng/mL (oral)	155; base <sup>[15]</sup>
			sangue 244(188–427) ng/mL (oral)	200; sal <sup>[15]</sup>
	838 (656–1587) ng/mL (oral) <sup>DIFOSFATO</sup>	600 <sup>t0</sup> ,300 <sup>6,24,48h</sup> ,1500 <sup>[6]</sup>	Sangue 1918 (1161–2436) ng/mL (IV) <sup>i</sup>	155 <sup>i</sup> ; base ou
			3312 (2290–4211) ng/mL (IV) <sup>ii</sup>	310 <sup>ii</sup> ; base <sup>[12]</sup>
			Plasma 793 (427–1080) ng/mL (IV) <sup>i</sup>	
			1747 (1378–2440) ng/mL (IV) <sup>ii</sup>	
	3,3±1,9 h (oral, solução) <sup>DIFOSFATO</sup>	300; base <sup>[1]</sup>	2,4 (2,1–3,7) h (oral)	400; sal <sup>[13]</sup>
	3,6±2,0 h (oral, comprimido) <sup>DIFOSFATO</sup>		3,65±1,14 h (oral, comprimido)	310; base <sup>[13]</sup>
			sangue 3,26 h (oral)	200; sal <sup>[16]</sup>
			plasma 3,74 h (oral)	200; sal <sup>[11]</sup>
				155; base <sup>[11]</sup>
T <sub>max</sub>	3,16±2,5 h (oral) <sup>SULFATO</sup>	600; base <sup>[2]</sup>	3,88±1,39 h hidroxiclороquina	200; sal <sup>[17]</sup>
			4,11±1,17 h (R); 3,15±1,39 h (S)	155; base <sup>[17]</sup>
				155; base <sup>[15]</sup>
			3,2 (2–4,5) h (oral)	200; sal <sup>[15]</sup>
	282 h (IV) <sup>DICLORIDRATO</sup>		172,3±39,0 h (oral)	400; sal <sup>[13]</sup>
	207 h (oral, solução) <sup>DIFOSFATO</sup>	300; base <sup>[1]</sup>		310; base <sup>[13]</sup>
	278 h (oral, comprimido) <sup>DIFOSFATO</sup>		272±76 h (0-60d) (oral, comprimido)	200; sal <sup>[16]</sup>
	plasmático 47,3±7,03 h (oral)	600; base <sup>[5]</sup>	sangue 537 h / 22,4 dias (oral)	200; sal <sup>[11]</sup>
	sanguíneo total 38,6±4,91 h (oral)		plasma 2963 h / 123,5 dias (oral)	155; base <sup>[11]</sup>
T <sub>1/2</sub>	432±122 h (oral) <sup>SULFATO</sup>	600; base <sup>[2]</sup>	676,0±161,0 h hidroxiclороquina	200; sal <sup>[17]</sup>
	386±108 h (oral) <sup>SULFATO</sup>	300 <sup>1x/SEMANA(n=3)</sup> , 900 <sup>[4]</sup>	691,8±480,8 h (R); 419,6±171,2 h (S)	155; base <sup>[17]</sup>
	374±144 h (oral) <sup>SULFATO</sup>	200 <sup>2x/SEMANA(n=3)</sup> ,1200 <sup>[4]</sup>	Plasma 32±9 dias (oral), 26±10 dias (IV)	155; base <sup>[15]</sup>
	479±323 h (oral) <sup>SULFATO</sup>	50 <sup>7x/SEMANA(n=3)</sup> ,1050 <sup>[4]</sup>	Sangue 50±16 dias (oral), 44±12 dias (IV)	200; sal <sup>[15]</sup>
	150 (103–266) h (oral) <sup>DIFOSFATO</sup>	600 <sup>t0</sup> ,300 <sup>6,24,48h</sup> ,1500 <sup>[6]</sup>	Sangue 44±12 dias (IV) <sup>i</sup> , 43±22 dias (IV) <sup>ii</sup>	155 <sup>i</sup> ; base <sup>[12]</sup> ou
			Plasma 26±10 dias (IV) <sup>i</sup> , 53±22 dias (IV) <sup>ii</sup>	310 <sup>ii</sup> ; base <sup>[12]</sup>
	57,8±3,0 % (oral) <sup>DIFOSFATO</sup>	150; base <sup>[3]</sup>	~ 50 %	_ <sup>[13]</sup>

Ligação às proteínas plasmáticas	42,7±2,1 % (R) (oral) <sup>DIFOSFATO</sup>	241,8; sal <sup>[3]</sup>	hidroxicloroquina	_[18]
	66,6±3,3 % (S) (oral) <sup>DIFOSFATO</sup>			
Metabólito ativo principal	58,8±1,8 % (Mistura racêmica)	_[7]	Desetilhidroxicloroquina	_[11]
	66,6±1,9 % (S); 48,5±2,4 % (R)			
	Monodesetilcloroquina	_[8]		
Metabolismo	De-etilcloroquina	_[3]	-	-
	Desetilcloroquina	_[9]		
Eliminação	Hepático 30–50 % dose administrada	_[9]	40–50 % excreção renal	_[10]
	Excreção renal (principal)	_[8]		

[1] Gustafsson et al., 1983; [2] De Vries et al., 1994; [3] Augustijns; Verbeke, 1993; [4] Wetsteyn et al., 1995; [5] Tulpule; Krishnaswamy, 1983; [6] Na-Bangchang et al., 1994; [7] Ofori-Adjei et al., 1986; [8] Krishna; White, 1996; [9] Ducharme; Farinotti, 1996; [10] Furst, 1996; [11] FDA, 2019; [12] Tett et al., 1988; [13] Lim et al., 2009; [14] Tett et al., 1992; [15] Tett et al., 1989; [16] Fan et al., 2015; [17] Midha et al., 1996; [18] McLachlan et al., 1993.

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