

SUPPLEMENTAL TABLE 1
In vitro effects of antimalarial drugs on microfilaria (all filarial species)*

Drug	Parasite	Concentration†	Results	Reference
Chloroquine	<i>Onchocerca volvulus</i>	Not specified	No effect	30
	<i>O. volvulus</i>	0.4–100 µg/mL, 7 h	TBI inversely related with concentration: 0.4–4 µg/mL: ≤ 7 h; 100 µg/mL: ≤ 15 min	31
	<i>Brugia patei</i>	10 µM	No effect on motility	37
Amodiaquine	<i>Breinlia booliati</i>	20 µM, 8 h	TBI = 3 h (all control mf motile at 8 h)	40
Amodiaquine congeners	<i>B. booliati</i>	20 µM, 8 h	TBI = 3–7 h (all control mf motile at 8 h)	40
Mefloquine	<i>B. patei</i>	2, 5, or 10 µM, 4 d	TBI inversely related with concentration: 2 µM: ≤ 3 d; 5 µM: ≤ 2 d; 10µM: ≤ 10 h)	37

*All studies included control parasites (not exposed to the drug). In all studies, the effect was assessed by follow-up of motility of microfilariae. h = hours; TBI = time before immobilization of all microfilaria; mf = microfilaria; min = minutes; d = days.
† Concentration (in µg/mL or in µM) and duration of follow-up.

SUPPLEMENTAL TABLE 2
In vitro effects of chloroquine on adult filariae (all species)*

Parasite	Concentration†	Assessment method‡	Results	Reference
<i>Onchocerca volvulus</i>	12–120 µg/mL	Motility	12 µg/mL: longevity reduced by 65%, 120 µg/mL: all worms dead within 1 h	31
<i>O. volvulus</i> ♀	10 µM, 72 h	Microscopic (MI at 0, 24, 48, and 72 h)	Marked paralyzing effect (>> <i>B. pahangi</i> , <i>D. immitis</i> , and <i>A. vitae</i>)	20
<i>O. volvulus</i> ♂	0.3, 0.5, 1.0, and 2.0 µg/mL, 48 h	Motility meter and MTT assay	Marked paralyzing effect and inhibition of formazan formation	35
<i>O. gutturosa</i> ♂	50 µM and then 1 in 4 dilutions, 7 d	Microscope (MS every 30 min for the first 4.5 h, then at 1, 2, 3, 4, and 7 d and IC ₅₀ on days 1, 2, 3, 4, and 7)	IC ₅₀ at 1, 3, and 4 d > 50 µM; IC ₅₀ at 2 d = 11.8 µM; IC ₅₀ at 7 d = 6.7 µM	32
<i>O. gutturosa</i> ♂	0.05 µM–20 mM, 72 h	Motility meter (MI at 0, 1, 3, 6, 12, 24, 48, and 72 h and IC ₅₀ at 24 h)	Marked paralyzing effect (> <i>B. pahangi</i> and <i>A. vitae</i>): IC ₅₀ at 24 h = 2.9 µM	33
<i>O. gutturosa</i> ♂	10 µM, 72 h	Motility meter (MI at 0, 24, 48, and 72 h)	Marked paralyzing effect (>> <i>B. pahangi</i> , <i>D. immitis</i> , and <i>A. vitae</i>)	20
<i>Brugia pahangi</i> ♀	0.05 µM–20 mM, 72 h	Motility meter (MI at 0, 1, 3, 6, 12, 24, 48, and 72 h and IC ₅₀ at 24 h)	Moderate paralyzing effect (< <i>O. gutturosa</i>): IC ₅₀ at 24 h = 25 µM	33
<i>B. pahangi</i> ♀	0.032, 0.1, 0.32, 1.0, 3.2, 10, or 32 µM, 72 h	Motility-meter (MI at 0, 24, 48, and 72 h and IC ₅₀ at 24 and 72 h) Lactate excretion (24, 48, and 72 h)	Moderate paralyzing effect (IC ₅₀ at 24 h > 32 µM; at 72 h = 2.3 µM), Reduced lactate excretion	20
<i>B. patei</i>	10 µM	Microscope and lactate excretion	No effect on motility and survival	37
<i>Dirofilaria immitis</i> ♀	10 µM, 72 h	Microscope (MI at 0, 24, 48, and 72 h)	No paralyzing effect	20
<i>Acanthocheilonema vitae</i> ♀	0.05 µM–20 mM, 72 h	Motility meter (MI at 0, 1, 3, 6, 12, 24, 48, and 72 h and IC ₅₀ at 24 h)	Low paralyzing effect: IC ₅₀ at 24 h = 74 µM	33
<i>A. vitae</i> ♀	10 µM, 72 h	Motility meter (MI at 0, 24, 48, and 72 h)	Sensitivity similar to that of <i>B. pahangi</i>	20

*All assays included control worms. h = hours; MI = motility index (percentage of the motility of time-matched control parasites); MTT assay = viability assessed by the rate of reduction of MTT tetrazolium salt to formazan; MS = motility score on a scale of 0 (completely immotile) to 10 (normal); min = minutes; IC₅₀ = concentration needed to reduce motility by 50%; d = days.
† Concentration (in µg/mL or in µM) and duration of follow-up.
‡ Methods used to measure motility and express data.

SUPPLEMENTAL TABLE 3
In vitro effects of 4-amino-quinolines (except chloroquine) on adult filariae (all species)*

Drug	Parasite	Concentration†	Assessment method‡	Results	Reference
Amodiaquine	<i>Brugia pahangi</i> ♀	0.032, 0.1, 0.32, 1.0, 3.2, 10, or 32 µM, 72 h	Motility meter (MI at 0, 24, 48, and 72 h and IC ₅₀ at 24 and 72 h), Lactate excretion (72 h)	Marked paralyzing effect (IC ₅₀ at 24 h = 15 µM; at 72 h = 0.2 µM), Marked reduction in lactate excretion	20
	<i>Breinlia booliati</i>	20 µM, 8 h	Motility (TBI)	TBI = 3 h (all controls motile at 8 h)	40
Amodiaquine congeners	<i>B. booliati</i>	20 µM, 8 h	Motility (TBI)	TBI = 3–7 h (all controls motile at 8 h)	40
Quinacrine	<i>B. pahangi</i> ♀	0.032, 0.1, 0.32, 1.0, 3.2, 10, or 32 µM, 72 h	Motility meter (MI at 0, 24, 48, and 72 h and IC ₅₀ at 24 and 72 h), Lactate excretion (72 h)	Moderate paralyzing effect (IC ₅₀ at 24 h = 2.4 µM; at 72 h = 1.9 µM), Reduced lactate excretion	20

*All assays included control worms. h = hours; MI = motility index (percentage of the motility of time-matched control parasites); IC₅₀ = concentration needed to reduce motility by 50%; TBI = time before immobilization of all parasites.
† Concentration (in µg/mL or in µM) and duration of follow-up.
‡ Methods used to measure motility and express data.

SUPPLEMENTAL TABLE 4
In vitro effects of quinine, mefloquine, and primaquine on adult filariae (all species)*

Drug	Parasite	Concentration†	Assessment method‡	Results	Reference
Quinine	<i>Brugia pahangi</i> ♀	0.032, 0.1, 0.32, 1.0, 3.2, 10, or 32 µM, 72 h	Motility meter (MI at 0, 24, 48 and 72 h and IC ₅₀ at 24 and 72 h), Lactate excretion (72 h)	Low paralyzing effect (IC ₅₀ at 24 h > 32 µM; at 72 h = 15 µM). No reduction in lactate excretion	20
Mefloquine	<i>Onchocerca gutturosa</i> ♂	3.13 µM, 7 d	Microscopic (MS every 30 min for the first 4.5 hours, then at 1, 2, 3, 4 and 7 d) and MTT assay	From 24 h, mean MS < 5 (vs. 9–10 for controls), Significant inhibition of formazan formation	49
	<i>B. malayi</i>	1, 2, 5, or 10 µM, 14 d medium with or without FCS and HS	Microscopic	No FCS plus HS: concentration-related paralyzing effect: TBI for 1, 2, 5 and 10 µM = ≤ 4 d, ≤ 3 d; ≤ 1 d and ≤ 10 h, respectively; With FCS plus HS: no paralyzing effect (for 2 weeks)	37
	<i>B. patei</i>	1, 2, 5, or 10 µM, 14 d	Microscopic, Lactate excretion (at 4, 9, 22 and 26 h)	No FCS plus HS: concentration-related paralyzing effect: TBI for 1, 2, 5 and 10 µM = ≤ 4 d, ≤ 3 d; ≤ 1 d and ≤ 10 h, respectively; Decrease in lactate excretion inversely related to concentration, With FCS plus HS: no paralyzing effect (for 2 weeks)	37
Primaquine	<i>B. pahangi</i> ♀	0.032, 0.1, 0.32, 1.0, 3.2, 10, or 32 µM, 72 h	Motility meter (MI at 0, 24, 48 and 72 h and IC ₅₀ at 24 and 72 h), Lactate excretion (24, 48, and 72 h)	Marked paralyzing effect (IC ₅₀ at 24 h = 13 µM; at 72 h = 0.19 µM), Marked reduction in lactate excretion	20

* All assays included control worms. h = hours; MI = motility index (percentage of the motility of control parasites); IC₅₀ = concentration needed to reduce motility by 50%; d = days; MS = motility score on a scale of 0 (completely immotile) to 10 (normal); min = minutes; FCS = 10% fetal calf serum; HS = 5% human serum; TBI = time before immobilization of all parasites.
† Concentration (in µg/mL or in µM) and duration of follow-up.
‡ Methods used to measure motility and express data.

SUPPLEMENTAL TABLE 5
In vivo effects of antimalarial drugs on microfilarial loads (all filarial species)*

Drug	Parasite	Host†	Dose‡	C§	Time points of follow-up¶	Results	Reference
Chloroquine	<i>Onchocerca volvulus</i>	Humans (39)	25 mg/kg over 3 d	No	Probably D1	Significant reduction (38%)	12
	<i>O. volvulus</i>	Humans (48)	2,500 mg over 3 d	Yes	D7, 14, 21, 28, 35	MFL = 0 on D7 then reincrease to initial levels on D28	13
	<i>O. volvulus</i>	Humans (46)	2,500 mg over 2–3 d, then 500 mg/week for 27 weeks	Yes	W4, 8, 16, 21, 28, 52	Decrease up to week 20 (50% reduction), then remained stable	13
	<i>Dirofilaria immitis</i>	Dogs (12)	6 mg/kg, 1 im dose	No	Min 30, 60, 90, 120	Marked rise within 30 min post-injection	38
Amodiaquine	<i>O. volvulus</i>	Humans (8)	1,800–3,000 mg over 3–10 d	No	D30, 180, 365, 730	No significant change	41
	<i>Wuchereria bancrofti</i>	Humans (9)	600–2,400 mg over 1–4 d	No	Repeated measures up to 7 mo. (no dates)	Little change except in patient treated with 2,400 mg: gradual decrease to 0 after 7 mo.	15
	<i>W. bancrofti</i>	Humans (14)	600 mg/d × 15 d	No	D1, D30, and monthly up to 11 mo.	No significant change	42
	<i>Litomosoides carinii</i>	<i>Meriones unguiculatus</i> (27)	25–100 mg/kg/d × 5 d	Yes	1, 4, 7, 8, 11, and 15 d after first dose	No clear change	43
	<i>L. carinii</i>	<i>Sigmodon hispidus</i> (5)	100 mg/kg/d × 5 d	Yes	1, 4, 7, 8, 11, and 15 d after first dose	No clear change	43
	<i>L. carinii</i>	<i>Mastomys natalensis</i> (15)	25–100 mg/kg/d × 5 d	Yes	3, 7, 14, 21, 42, 70, and 100 d after first dose	Decrease up to D100 (= in controls)	44
Amodiaquine congeners	<i>L. carinii</i>	<i>M. unguiculatus</i>	25–100 mg/kg/d × 5 d	Yes	Repeated measures up to 15 d after the first dose	No effect	47
	<i>L. carinii</i>	<i>M. natalensis</i>	100 mg/kg/d × 5 d, po or sc	Yes	Not specified	No effect	40
4-aminoquinoline derivatives	<i>Acanthocheilonema vitae</i>	<i>M. natalensis</i>	200 mg/kg/d × 5 days	Yes	Not specified	Reduction for 3 compounds	48
Quinacrine	<i>O. volvulus</i>	Humans (6)	200 mg/d × 5 or 7 d	No	D30, D120, D180, D365, D540, D730	No effect	46
Primaquine	<i>W. bancrofti</i>	Humans (5)	15 mg/d × 5 days	No	D1, D2, D3; then monthly up to 11 mo., and after 22 mo.	Reduction from 6 months; 0 or low counts after 12 mo	50

* d = days; MFL = microfilarial load; mo = months.

† Values in parentheses are numbers of treated hosts.

‡ Treatment given orally (po) except when specified. im = intramuscular; sc = subcutaneous.

§ C = controlled trial (Yes) vs. non-controlled trial (No)

¶ Pretreatment MFL measured in all studies. Min = minutes; D = days; W = weeks.

SUPPLEMENTAL TABLE 6
In vivo effects of antimalarial drugs on adult filariae (all species)*

Drug	Parasite	Host†	Dose‡	C§	Assessment¶	Results	References
Chloroquine	<i>Onchocerca volvulus</i>	Humans	2,500 mg over 3 d	Yes	Histologic, D210	No visible change	13
	<i>O. volvulus</i>	Humans	2,500 mg over 2 d, then 500 mg weekly for 27 weeks	Yes	Histologic, D210	No visible change	13
Amodiaquine	<i>O. volvulus</i>	Humans (52)	15–50 mg, IN	Yes	Histologic, D180	Macrofilaricide (100%)	14
	<i>O. volvulus</i>	Humans (3)	1,800–3,000 mg over 3–10 d	No	Histologic or EIW, D120–180	No visible change	41
	<i>Litomosoides carinii</i>	<i>Meriones unguiculatus</i> (27)	25–100 mg/kg/d × 5 d	Yes	No. of live and dead worms at necropsy (15 d after first dose)	Macrofilaricide, dose effect	43
	<i>L. carinii</i>	<i>Sigmodon hispidus</i> (5)	100 mg/kg/d × 5 d	Yes	No. of live and dead worms at necropsy (15 d after first dose)	Low macrofilaricidal effect	43
	<i>L. carinii</i>	<i>Mastomys natalensis</i> (15)	25–100 mg/kg/d × 5 d	Yes	No. of live and dead worms at necropsy (D95)	Less worms in treated animals; dead worms: 75% in treated, 0% in controls	44
Amodiaquine congeners	<i>L. carinii</i>	<i>M. natalensis</i>	100 mg/kg/d × 5 d	Yes	Necropsy and MCD	MCD > 100 mg/kg × 5	45
	<i>L. carinii</i>	<i>M. unguiculatus</i>	25–100 mg/kg/d × 5 d	Yes	No. of live and dead worms at necropsy (15 d after first dose)	10 compounds with macrofilaricidal activity	47
	<i>L. carinii</i>	<i>M. natalensis</i>	100 mg/kg/d × 5 d, po or sc	Yes	Necropsy (date not specified)	No macrofilaricidal effect	40
4-aminoquinoline derivatives	<i>Acanthocheilonema vitae</i>	<i>M. natalensis</i>	200 mg/kg/d × 5 days	Yes	Not specified	Reduction in adult load, or in females fecundity for some compounds	48

* d = days.

† Values in parentheses are number of treated hosts.

‡ Treatment given orally (po) except when specified. IN = infiltration of nodule; sc = subcutaneous.

§ C = controlled trial (Yes) vs. non-controlled trial (No).

¶ Histologic = examination of worms in sections of nodules; EIW = examination of isolated *O. volvulus* (after collagenase digestion of nodules); MCD = minimum curative dose = dose killing more than 95% of the adult parasites; D = date (days after last dose, except when specified) of collection of nodules (for *O. volvulus*) or of necropsy (for other species).