Table 2. Antimalarial activities of other membrane-active peptides

Name of peptide or class	Source of original peptide(s)	IC_{50}, erythrocytic *P. falciparum*[a]	Activity in animal models	References
Gramicidin D	*Bacillus brevis*	0.035–1.3 ng/ml	ED_{50} 0.75 mg/kg (single dose s.c. 24 h post-infection, *P. yoelii,* mice); 1.4 mg/kg daily, 2 mg/kg twice daily (i.p., 4-day suppressive test, *Plasmodium vinckei petteri,* mice)	(49, 51, 96)
Gramicidin A	"	17–270 pM		(47, 97)
Gramicidin A'[b]	"	0.8–4.4 nM		(46)
NFG[c], other modified gramicidins	"	0.0026–18 μM	1.2–7.5 mg/kg partially effective i.p. or i.v. (4 doses, various schedules, *P. berghei,* mice)	(46-48, 52)
Valinomycin	*Streptomyces fulvissimus*	1.3–5.9 nM		(51, 96, 97)
Alamethicin	*Trichoderma viride*	2 μg/ml		(96)
Gramicidin S	*Bacillus brevis*	0.58 – 1.3 μM		(45, 96)
Tyrocidines	"	0.58–460 nM		(45)
Tyrothricin[d]	"		≥2 mg/kg effective i.v. (multiple doses, *P. gallinaceum,* chickens)	(53)
Colistin	*Bacillus colistinus*	120 μg/ml		(51)
Polymyxin B	*Bacillus polymyxa*	170 μg/ml		(51)
Antiamoebin I	*Emericellopsis poonensis*	4.7–6.2 μM		(50)
Efrapeptins	*Tolypocladium niveum*	1.2–1.4 μM		(50)
Zervamicins	*Emericellopsis salmosynnemata*	450–480 nM		(50)

Blanks indicate not determined.

s.c., subcutaneous; i.p., intraperitoneal; i.v., intravenous.

[a] See note a, Table **1**.

[b] A mixture of gramicidins A, B and C at a ratio of 20:1:4 (46).

[c] Tryptophan-*N*-formylated gramicidin.

[d] A mixture of gramicidin and tyrocidine (53).

Table 3. Antimalarial activities of hydrophobic peptides

Name of peptide or class	Source of original peptide(s)	IC_{50}, erythrocytic stages[a]	Activity in mouse malaria	References
Cyclosporin (Cs) A	*Tolypocladium inflatum*	0.2–3.75 μM; 1.4 μM (*P. vivax*)	≥25 mg/kg/day (4 days) effective in most studies when first administered at start of or after infection; lower doses (3–10 mg/kg) partially or fully effective	(57, 58, 61-63, 69, 70, 98-102)
Other cyclosporins	"	0.032–3.2 μM	10 mg/kg CsC or CsD (days 5 & 6 post-infection) effective	(62, 69, 101)
Cyclolinopeptides	*Linum usitatissimum*	0.8–>16 μg/ml		(103)
Cycloaspeptides	*Penicillium algidum*	3.5–4.7 μg/ml		(104)
Hirsutellic acid	*Hirsutella* sp. BCC 1528	8.0 μM		(105)

Blanks indicate not determined.

[a] See note a, Table **1**.

Table 4. Antimalarial activities and host toxicities (if known) of miscellaneous peptides

Name of peptide or class	Original source	IC_{50} on erythrocytic stages[a]	Host cytotoxicity[b]	Refer-ences
Beauvericins	*Paecilomyces tenuipes*	1.3–12 μg/ml	2.5–>20 μg/ml (KB, BC-1, Vero)	(106, 107)
Enniatins	*Verticillium hemipterigenum*	0.20–1.9 μg/ml	1.4–>50 μg/ml (KB, BC-1, Vero)	(108)
Hirsutellide A	*Hirsutella kobayasii* BCC 1660	2.8 μg/ml	>50 μg/ml (Vero)	(109)
Munumbicins	*Streptomyces* NRRL 3052	4.5–175 ng/ml	No haemolysis up to 80 μg/ml	(110)
Jasplakinolide	*Jaspis*	74 nM		(82)
Dolastatin 10	*Dolabella auricularia*	100 pM	7.7–500 pM	(84)
Dolastatin 15	"	200 nM		(84)
Auristatins	"	0.34–240 nM	0.0029–800 nM	(84)
Hirsutatin B	*Hirsutella nivea* BCC 2594	5.8 μg/ml	>50 μg/ml (Vero)	(111)
Isariins, isaridin A	*Isaria*	87–230 μM		(112)
Venturamides	*Oscillatoria* sp.	5.2–8.2 μM	13.1–86 μM (Vero, MCF-7)	(113)
Aerucyclamides	*Microcystis aeruginosa* PCC 7806	0.7–6.3 μM	106–>168 μM (L6)	(113a)
Paecilodepsipeptide A	*Paecilomyces cinnamomeus*	4.9 μM	5.9–>67 μM (KB, BC, Vero)	(114)
Dragomabin, drago-namide, carmabin A	*Lyngbya majuscula*	4.3–7.7 μM	9.8–180 μM (Vero)	(115)
Mollamide B	*Didemnum molle*	2.0–2.1 μg/ml	>100 μM (various)	(116)
Cyclic β-amino acid-containing dipeptides	(synthetic)	3.5–22 μM		(86)
'Ultra-short' peptides	(synthetic)	2.6–>200 μM (*P. berghei*)		(117)
Gallinamide A	*Schizothrix* sp.	8.4 μM	10.4 μM (Vero)	(118)

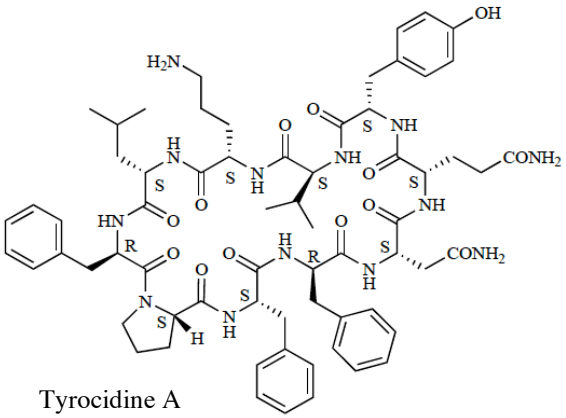
Blanks indicate not determined.

[a] See note a, Table **1**.

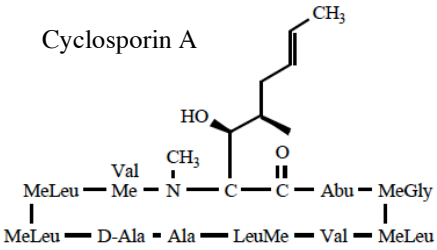
[b] See note c, Table **1**.

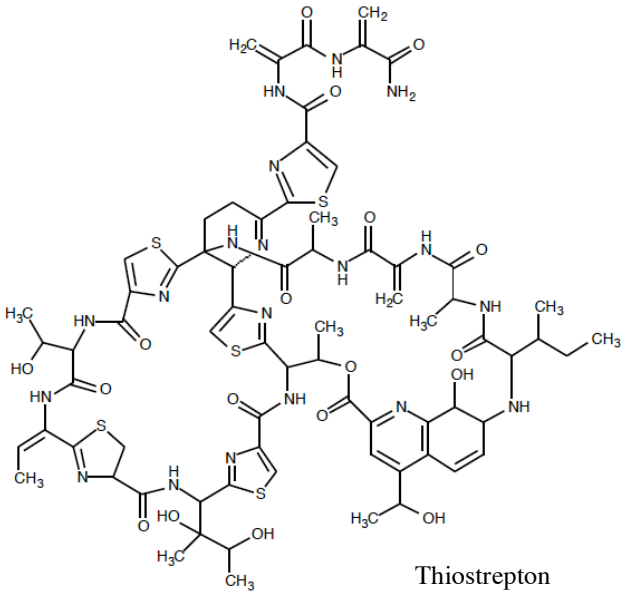
Cecropin A1 (*Hyalophora*)	**K**W**K**LF**KK**IE**K**VGQNI**R**DGII**K**AGPAVAVVGQATQIA**K**
Defensin A (*Phormia*)	ATCDLLSGTGIN<u>H</u>SACAA<u>H</u>CLL**R**GN**R**GGYCNG**K**GVCVC**R**N
Dermaseptin-S3	ALW**K**NML**K**GIG**K**LAG**K**AALGAV**KK**LVGAES
Dermaseptin-S4	ALWMTLL**KK**VL**K**AAA**K**AALNAVLVGANA
Psalmopeotoxin I	ACGIL<u>H</u>DNCVYVPAQNPCC**R**GLQC**R**YG**K**CLVQV
Psalmopeotoxin II	**R**CLPAG**K**TCV**R**GPM**R**VPCCGSCSQN**K**CT
NK-2	**K**IL**R**GVC**KK**IM**R**TFL**RR**IS**K**DILTG**KK**
Gramicidin A	VGA*L*A*V*V*VWLWLWLW*

Fig. (1). Amino acid sequences of some antimalarial peptides discussed in the text. Positively charged residues are in **bold**, histidines are <u>underlined</u>, and D-amino acids are in *italics*. Some of the peptides have modifications at one or both termini: see original references or the Antimicrobial Peptide Database for details.

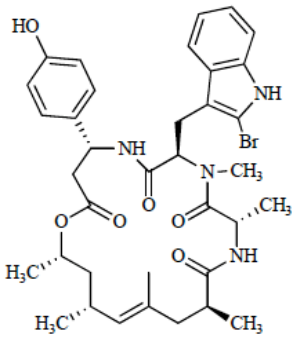


Tyrocidine A

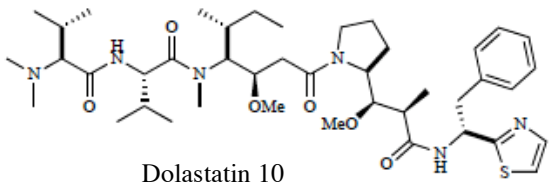




Thiostrepton



Jasplakinolide



Dolastatin 10

Fig. (2). Structures of some antimalarial peptides discussed in the text. Abu, L-α-aminobutyrate.

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