Table 3 Effect of Picroliv on certain biochemical parameters of serum in alcohol-fed rats.

Serum parameters	Control	Alcohol	Alcohol + Picroliv
Enzymes			
Alcohol dehydrogenase[a] (ADH)	1.12 ± 0.10	1.72 ± 0.16 (53)	1.39 ± 0.12 (56)
γ-Glutamyl transpeptidase[b] (γ-GT)	31.51 ± 2.72	87.14 ± 4.88 (177)	58.91 ± 2.75 (51)
Alkaline Phosphatase[c] (ALP)	17.47 ± 1.44	42.13 ± 2.41 (141)	28.71 ± 2.53 (55)
Glutamate oxaloacetate transaminase[d] (GOT)	100.77 ± 7.18	148.75 ± 5.56 (48)	127.11 ± 4.74 (45)
Glutamate pyruvate transaminase[d] (GPT)	50.19 ± 3.08	71.06 ± 8.22 (42)	53.82 ± 3.63 (83)
Chemical Constituents			
Bilirubin[e]	0.474 ± 0.028	0.822 ± 0.090 (73)	0.601 ± 0.056 (64)
Triglycerides[f]	76.46 ± 6.16	123.77 ± 4.85 (62)	98.67 ± 12.26 (53)
Total proteins[f]	7.68 ± 0.19	6.92 ± 0.16 (10)	7.48 ± 0.16 (74)
Albumin[f]	3.22 ± 0.18	2.44 ± 0.11 (24)	2.89 ± 0.15 (58)

Units: [a] μmoles/min/dl; [b] μg/min/dl; [c] μmoles of *p*-nitrophenol released/min/dl; [d] μmoles of pyruvate formed/min/l; [e] mg/dl; [f] g/dl.
Values are mean ± SD from 6 animals. Alcohol group was compared with control while alcohol + Picroliv group was compared with alcohol group. All differences are significant. ($^*P < 0.01$).
Figures in parentheses indicate % change (alcohol) or % protection (alcohol + Picroliv).

Acknowledgements

The authors are grateful to Dr. D. K. Kulshreshtha, Scientist, Medicinal Chemistry Division, CDRI, Lucknow for kindly preparing Picroliv. Technical assistance by Suresh Yadav and secretarial assistance by Mrs. Uma Shukla is acknowledged.

References

1 Lieber, C. S. (1984) Hepatology 6, 1243–1260.
2 Ansari, R. A., Aswal, B. S., Chander, R., Dhawan, B. N., Garg, N. K., Kapoor, N. K., Kulshreshtha, D. K., Mehdi, H., Mehrotra, B. N., Patnaik, G. K., Sharma, S. K. (1988) Ind. J. Med. Res. 87, 401–404.
3 Dwivedi, Y., Rastogi, R., Chander, R., Sharma, S. K., Kapoor, N. K., Garg, N. K., Dhawan, B. N. (1990) Ind. J. Med. Res. 92, 195–200.
4 Dwivedi, Y., Rastogi, R., Garg, N. K., Dhawan, B. N. (1991) Phytother. Res. 5, 115–119.
5 Dwivedi, Y., Rastogi, R., Garg, N. K., Dhawan, B. N. (1991) Med. Sci. Res. 91, 711–713.
6 Dwivedi, Y., Rastogi, R., Garg, N. K., Dhawan, B. N. (1992) Pharmacol. Toxicol. 71, 383–387.
7 Dwivedi, Y., Rastogi, R., Mehrotra, R., Garg, N. K., Dhawan, B. N. (1993) Pharmacol. Res. 27, 189–199.
8 Saksena, S., Rastogi, R., Garg, N. K., Dhawan, B. N. (1994) Drug Dev. Res. 33, 46–50.
9 Rastogi, R., Saksena, S., Garg, N. K., Dhawan, B. N. (1995) Phytother. Res. 9, 364–367.
10 Chander, R., Singh, C., Kapoor, N. K. (1988) Biochem. (Life Sci. Adv). 7, 25–27.
11 Agarwal, D. P., Goedde, H. W. (1990) in: Alcohol metabolism, alcohol intolerance and alcoholism: biochemical and pharmacogenetic approaches, (Agarwal, D. P., Goedde, H. W., eds.), pp. 126–144, Springer Verlag, Berlin.

The Effect of Some 2-Substituted Quinolines Isolated from *Galipea longiflora* on *Plasmodium vinckei petteri* Infected Mice

J. C. Gantier[1], A. Fournet[2,5], M. H. Munos[3], and R. Hocquemiller[4]

[1] Laboratoire de Biologie et Contrôle des Organismes Parasites, Faculté de Pharmacie, Université Paris-Sud, Rue J. B. Clément, F-92296 Cedex Châtenay-Malabry, France
[2] Institut Français de Recherche Scientifique pour le Développement en Coopération (ORSTOM), CC 97, Asuncion, Paraguay
[3] Laboratoire de Chimie organique, associé au CNRS, Faculté de Pharmacie, rue J. B. Clément, F-92296 Châtenay-Malabry Cedex, France
[4] Laboratoire de Pharmacognosie, Laboratoire associé au CNRS, Faculté de Pharmacie, Rue J. B. Clément, F-92296 Cedex Châtenay-Malabry, France
[5] Address for correspondence

Received: September 20, 1995; Revision accepted: November 18, 1995

Planta Medica 62 (1996) 285–286

Abstract: We have evaluated the *in vivo* antiplasmodial activity of six 2-substituted quinolines and a total alkaloidal extract of *Galipea longiflora*. BALB/c mice infected with *Plasmodium vinckei petteri* were treated orally at single dose of 50 mg/kg with quinolines or extract. Contrary to the previous results obtained with the *Leishmania* murine infection, 2-*n*-pentylquinoline showed activity against *P. vinckei petteri*. This result seems to confirm the antimalarial efficacy of infused stem bark of *G. longiflora*.

We have reported the efficacy of the quinoline alkaloids isolated from a Bolivian plant, *Galipea longiflora* Kr. (Rutaceae) for the experimental treatment of the cutaneous New World leishmaniasis (1), and recently in the experimental treatment of the visceral leishmaniasis on *Leishmania donovani*-infected mice treated by subcutaneous or oral route (2). Infused stem bark of *G. longiflora* is used in traditional medicine to treat cutaneous leishmaniasis and recurrent typical fevers such as malaria in the tropical region of Bolivia. The active compounds of this plant have been identified as 2-substituted quinolines (3) and recently we have synthesized in our laboratory the most active compounds, the 2-substituted three carbon chain quinolines and phenylethyl chain quinolines (4).

The aim of the present investigation was to determine if the 2-subsituted quinoline alkaloids had *in vivo* plasmodial activity like the 2-substituted 8-aminoquinolines (primaquine) or

quinine and its analogs. The suppressive activity was assessed against *Plasmodium vinckei petteri* 279 BY in mice (5). We have evaluated the plasmodial activity of the total alkaloidal extract of stem bark of *G. longiflora* and several 2-substituted quinolines (see Fig. 1), 2-*n*-propylquinoline (**1**), 2-(*E*)-prop-1'-enylquinoline or chimanine B (**2**), 2-(1',2'-*trans*-propyl) quinoline or chimanine D (**3**), 2-*n*-pentylquinoline (**4**), 4-methoxy-2-phenylquinoline (**5**), and 2-(3,4-methylenedioxyphenyl)quinoline (**6**). The drugs were orally given at a single dose of 0.31 mmol/kg or approximately 50 mg/kg and the reference drug, chloroquine at 0.031 mmol/kg or 5.8 mg/kg. The drugs were administered to the mice (n = 5) 72 h after infection with 1.5×10^7 *P. vinckei petteri* infected erythrocytes. A control group received distilled water only. We assessed the number of surviving mice each day for 14 days.

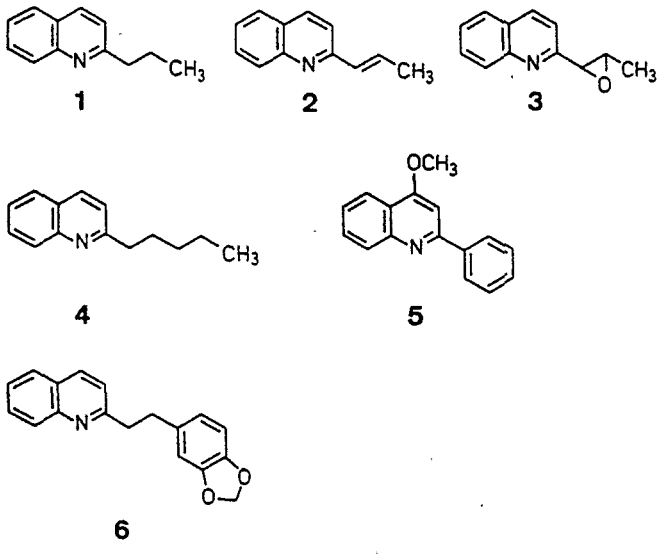

Fig. 1 Structures of 2-substituted quinolines.

After 14 days post-infection, 2-*n*-pentylquinoline (**4**) was found to be as effective as chloroquine with 100% survival (see Table 1). The animals treated with other quinolines or with the extracts of *G. longiflora* did not present the same level of survival. Results were as follows: 2-*n*-propylquinoline (**1**) (60%), 4-methoxy-2-phenylquinoline (**5**) (60%), 2-(3,4-methylenedioxyphenyl)quinoline (**6**) (40%), chimanine B (**2**) (40%), chimanine D (**3**) (60%), the total extract of stem bark (40%) and control group (0%), respectively. Contrary to the results obtained in the experimental murine infections with *Leishmania* species, 2-*n*-pentylquinoline (**4**) (1) which did not present any activity against this protozoa, showed effectivity in *Plasmodium vinckei petteri* infected mice. This selectivity of 2-*n*-pentylquinoline (**4**) against *Plasmodium* may be explained by its different mode of action in the parasite and the host. We do not understand the mechanisms by which the 2-substituted quinolines act against parasites such as *Leishmania* or *Plasmodium*. Wright and Philipson (6) indicated that drugs could act selectivity either on the synthetic pathways unique to the parasite where these are present or on salvage pathways utilized by the parasite to assimilate substrates from the host which cannot be made *de novo*. *Plasmodium* make their own pyrimidines but are unable to synthesize purines in common with *Leishmania*. This relative selectivity of 2-*n*-pentylquinoline may be due to one or more differences between the biochemistry of host and parasite.

It seems from these results that the traditional use of infused stem bark of *Galipea longiflora* is justified as a treatment for malaria.

References

[1] Fournet, A., Gantier, J. C., Gautheret, A., Leysalles, L., Munos, M. H., Mayrargues, J., Moskowitz, H., Cavé, A., Hocquemiller, R. (1994) J. Antimicrob. Chemother. 33, 537–544.

[2] Fournet, A., Angelo Barrios, A., Muñoz, V., Hocquemiller, R., Bruneton, J. (1993) Antimicrob. Agents Chemother. 37, 859–863.

[3] Fournet, A., Hocquemiller, R., Roblot, F., Cavé, A., Richommel, P., Bruneton, J. (1993) J. Nat. Prod. 56, 1547–1552.

[4] Munos, M. H., Mayrargue, J., Fournet, A., Gantier, J. C., Hocquemiller, R., Moskowitz, H. (1994) Chem. Pharm. Bull. Tokyo 42, 1914–1916.

[5] Peters, W. (1970) Chemotherapy and Drug Resistance in Malaria, Academic Press, London, New York, pp. 164–171.

[6] Wright, C. W., Phillipson, J. D. (1990) Phytother. Res. 4, 127–139.

Table 1 Survival of mice treated with 2-substituted quinolines, totsl extract of *Galipea longiflora*, and chloroquine.

Drug	Dose (mMol/kg)	Quantal survival by days[a]						% Surviving mice
		J_6	J_8	J_9	J_{10}	J_{11}	J_{14}	
2-*n*-propylquinoline (1)	0.31	5/5	3/5	3/5	3/5	3/5	3/5	60[b]
chimanine B (2)	0.31	5/5	4/5	3/5	3/5	3/5	2/5	40
chimanine D (3)	0.31	5/5	4/5	4/5	4/5	3/5	3/5	60[b]
2-*n*-pentylquinoline (4)	0.31	5/5	5/5	5/5	5/5	5/5	5/5	100[c]
4-methoxy-2-phenylquinoline (5)	0.31	5/5	4/5	3/5	3/5	3/5	3/5	60[b]
2-(3,4-methylenedioxy-phenylethyl)quinoline (6)	0.31	5/5	4/5	3/5	2/5	2/5	2/5	40
Total extract of stem bark of *Galipea longiflora*	50 mg/kg	5/5	3/5	2/5	2/5	2/5	2/5	40
Chloroquine	0.031	5/5	5/5	5/5	5/5	5/5	5/5	100[c]
None		7/7	5/7	4/7	4/7	0/7	0/7	0

[a] The numerators represent the number of surviving mice each day relative to the total number in each group.

[b] $P < 0.01$ by Student's t test as compared to the untreated group.

[c] $P < 0.05$ by Student's t test as compared to the untreated group.