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Exploring the Antimalarial Efficacy of *Globimetula oreophila* Leaf Fractions in *Plasmodium berghei*-infected Mice: *In Vivo* Approach

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Therapeutic Potential of Fractions of *Globimetula oreophila* (Oliv. ex Hook.f.) Leaf Extract Growing on *Azadirachta indica* Against *Plasmodium berghei*-infected Mice: *In Vivo* Approach

Graphical Abstract

G. Oreophila leaves

Pulverized into powder

Extraction

Crude Ethanol Extract

Partitioning

Hexane | Chloroform | Ethyl acetate | Butanol

In vivo antimalarial study

Data acquisition

Abstract: Introduction: The development of parasite resistance to first-line antimalarial medicines, especially the ACTs, has made the research and development of novel antimalarial medications vital. *Globimetula oreophila*, a plant used in traditional medicine to treat malaria, is an example of a natural product that may provide new antimalarial drugs with fewer side effects, less drug resistance with greater efficacy than synthetic drugs. This study aims to evaluate the antiplasmodial properties of *G. oreophila's* fractions. Method: The leaves of the plant were air-dried and reduced in size using a pestle and mortar. The pulverized plant was macerated in 70% ethanol and fractionated with solvent in increasing polarity of n-hexane, chloroform, ethyl acetate, and n-butanol to produce the various fractions. The antiplasmodial activity of the n-hexane, chloroform, ethyl acetate, and n-butanol fractions of *Globimetula oreophila* leaf extract was assessed using an in vivo method in *Plasmodium berghei*-infected mice via prophylactic, suppressive, and curative test. Results: In mice, the fractions' median fatal dose (LD_{50}) was calculated to be more than 5000 mg/kg. At doses of 125, 250, and 500 mg/kg, the fractions significantly ($p<0.001$) reduced the parasitemia level. Conclusion: The fractions of the *G. oreophila* showed significant in vivo antiplasmodial activity which upholds the earlier in vivo findings for the crude extract as well as its folkloric use. Further study should be carried out to isolate active secondary metabolites responsible for this observed antimalarial activity in all the four fractions being investigated.

Keywords: antiplasmodial property; *Globimetula oreophila*; natural product; resistance

INTRODUCTION

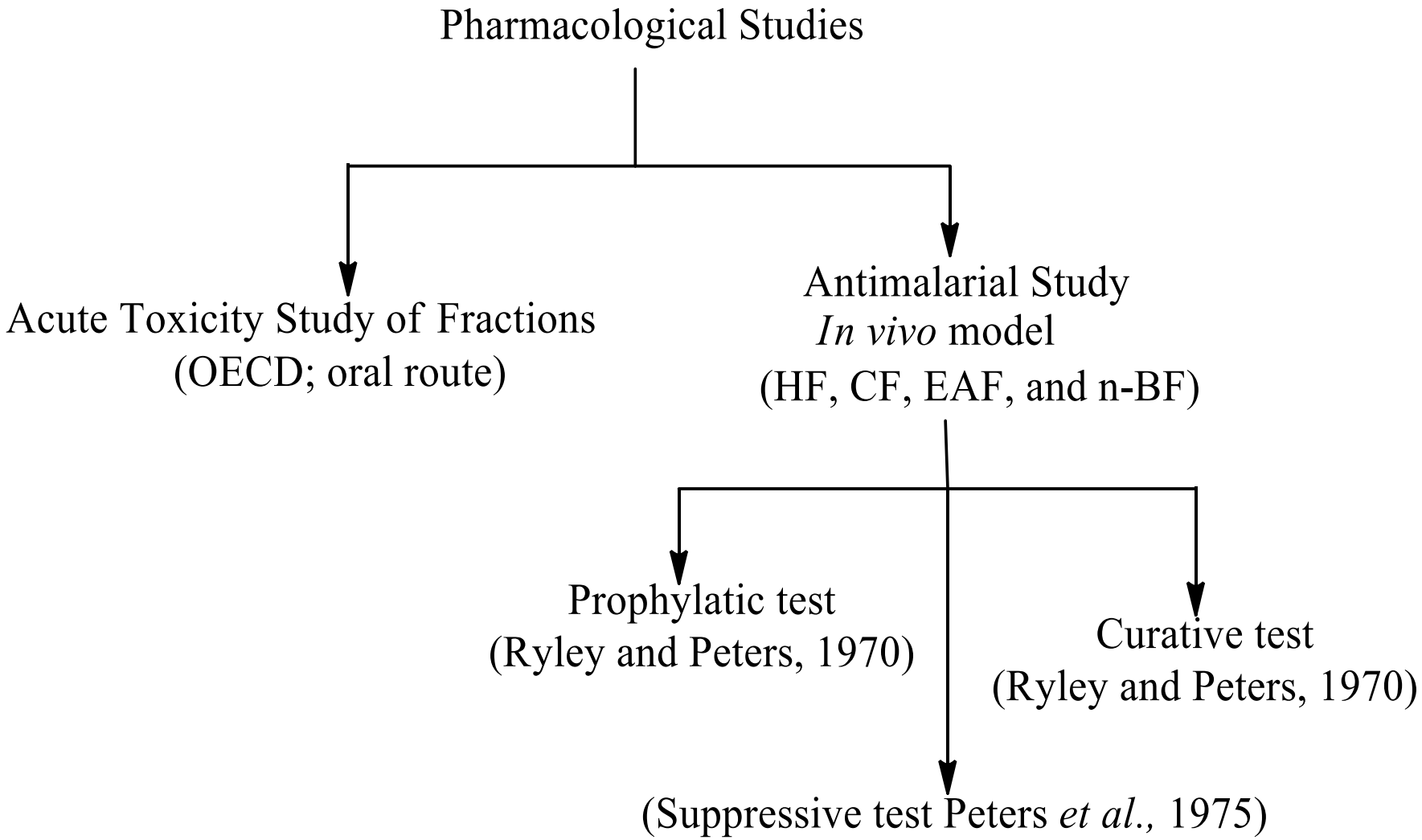
- *Globimetula oreophila* is a hemiparasitic plant commonly called mistletoe, found growing on several dicotyledonous trees thus using them as a host for its root-like structure called haustoria.
- Ethnobotanical information indicates that *G. oreophila* is used in northern Nigeria in the management of diarrhea, stomachache, headache, and malaria and the crude extract of the plant was previously reported to have antimalarial activity (Dauda *et al.*, 2016).
- *G. oreophila* was found to a beneficial source of secondary such as flavonoids, terpenoids, alkaloids, phenols, and steroids where found to be present on the crude and fraction of this plant (Dauda *et al.*, 2017; 2023). *G. oreophila* was also found to good source of essential trace metals in appropriate with the permissible limit by FAO/WHO (Dauda *et al.*, 2022).

AIM

- To evaluate the antimalarial activity of the partitioned fractions of *G. oreophila* leaves in mice.

OBJECTIVES

- To establish the oral median lethal dose (LD_{50}) using Organization for Economic Cooperation and Development (OECD) guidelines 2008,
- To determine the antiplasmodial activity of the partitioned fractions using prophylactic, suppressive, and curative *in vivo* methods in mice.



HF: Hexane Fraction; CF: Chloroform Fraction; EAF: Ethyl acetate Farction, n-BF: n-Butanol Fraction

Results

Table 1: Prophylactic effect of fractions of *Globimetula oreophila* in repository infection in mice

Groups	Treatment (mg/kg)	Average Parasitemia ± SEM	% Suppression Effect
Distilled water	10 mL/kg	25.20 ± 0.86	-
n-HFGO	125	17.04 ± 0.50 *	32.38
	250	15.88 ± 0.26 *	36.98
	500	14.52 ± 0.53 *	42.38
CFGO	125	13.48 ± 0.46 *	46.51
	250	12.84 ± 0.71 *	49.05
	500	13.12 ± 0.70 *	47.94
EFGO	125	15.08 ± 0.90 *	40.16
	250	15.32 ± 0.81 *	39.21
	500	8.22 ± 0.55 *	67.38
n-BFGO	125	18.15 ± 0.24 *	27.98
	250	17.34 ± 0.94 *	31.19
	500	15.88 ± 0.47 *	36.98
Pyr	1.2	6.00 ± 0.86 *	76.19

Values are presented as Mean ± SEM; Data analyzed by one-way ANOVA followed by Dunnett's *post-hoc* test; n=6, $p<0.001$*, n-HFGO: Hexane fraction of *G. oreophila*, CFGO: Chloroform fraction of *G. oreophila*, EFGO: Ethyl acetate fraction of *G. oreophila*, n-BFGO: n-Butanol fraction of *G. oreophila*

Table 2: Suppressive Effect of Fractions of *Globimetula oreophila* in Early Malarial Infection in Mice

Group	Treatment (mg/kg)	Average Parasitemia ± SEM	% Suppression Effect
Distilled water	10 mL/kg	26.40 ± 0.60	-
n-HFGO	125	16.4 ± 0.46*	37.89
	250	11.4 ± 0.71*	56.82
	500	10.72 ± 0.55*	59.39
CFGO	125	16.12 ± 0.31*	38.94
	250	14.12 ± 0.19*	46.52
	500	11.60 ± 0.54*	56.06
EFGO	125	15.12 ± 0.83*	42.73
	250	12.88 ± 0.58*	51.21
	500	10.52 ± 0.78*	60.15
n-BFGO	125	16.42 ± 0.30*	37.80
	250	11.74 ± 0.51*	55.53
	500	14.76 ± 0.85*	44.09
CQ	5	6.72 ± 0.69*	74.55

Values are presented as Mean ± SEM; Data analyzed by one-way ANOVA followed by Dunnett's post-hoc test; n=6, $p<0.001$*, n-HFGO: Hexane fraction of *G. oreophila*, CFGO: Chloroform fraction of *G. oreophila*, EFGO: Ethyl acetate fraction of *G. oreophila*, n-BFGO: n-Butanol fraction of *G. oreophila*, CQ: Chloroquine.

Table 3: Curative effect of fractions of *Globimetula oreophila* in established infection in mice

Groups	Treatment (mg/kg)	Average Parasitemia ± SEM	% Suppression Effect
Distilled water	10 mL/kg	28.80 ± 1.93	-
n-HFGO	125	16.80 ± 0.76*	41.67
	250	12.68 ± 0.66*	55.97
	500	12.72 ± 0.94*	55.83
CFGO	125	16.38 ± 0.56*	43.13
	250	17.12 ± 0.67*	40.56
	500	11.08 ± 0.89*	61.53
EFGO	125	16.0 ± 0.11*	44.44
	250	10.80 ± 0.62*	62.50
	500	9.80 ± 0.49*	65.97
n-BFGO	125	16.48 ± 0.42*	42.78
	250	15.72± 0.16*	45.42
	500	11.60± 0.60*	59.72
CQ	5	4.78 ± 0.41*	83.40

Values are presented as Mean ± SEM; Data analyzed by one-way ANOVA followed by Dunnett's post-hoc test; n=6, $p<0.001$*, n-HFGO: Hexane fraction of *G. oreophila*, CFGO: Chloroform fraction of *G. oreophila*, EFGO: Ethyl acetate fraction of *G. oreophila*, n-BFGO: n-Butanol fraction of *G. oreophila*, CQ: Chloroquine.

Conclusion

- The median oral dose (LD_{50}) of the different factions of *G. oreophila* leaf in mice was estimated to be greater than 5000 mg/kg suggesting that they were orally safe and non-toxic at the tested doses.
- The fractions of the leaf extract of *G. oreophila* possess antiplasmodial activity, thus supporting the earlier *in vivo* findings of the crude extract of the plant as well as its traditional use of the plant in the management of malaria.