

Evaluation of Experimental Antimalarial Drugs in Rhesus  
Monkeys Infected with *Plasmodium cynomolgi*  
(Blood Schizonticidal Tests)

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**OBJECTIVE :** To evaluate blood schizonticidal activity of selected experimental drugs against *P. cynomolgi* malaria in rhesus monkeys. These studies are coordinated by the Division of Medicinal Chemistry, Walter Reed Army Institute of Research, and the results are used to aid in the selection of more effective antimalarial drugs for human use.

**BACKGROUND :** This is a continuation of studies initiated in 1971. A chronological report of methodology and results are available in SEATO Medical Research Laboratory Annual Reports for 1971 through 1976.

**METHODS :** Experimental drugs were evaluated in rhesus monkeys (*Macaca mulatta*) utilizing various dosage levels (mg/kg). Only those monkeys found to be free of malarial parasites on prestudy examination were utilized, a total of 187 rhesus. Each animal was infected by intravenous inoculation of  $5 \times 10^8$  parasitized erythrocytes obtained from donor monkeys infected with *P. cynomolgi* strain B. Post-inoculation day 4, test drugs were administered orally (by gastric intubation) for seven days. The monkeys were bled to determine their level of parasitemia daily for the first fifteen days following inoculation and every other day for the remainder of the study. Suppression of parasitemia was indicative of blood schizonticidal activity. Post-treatment, day 20, splenectomy was performed on monkeys in which there was no evidence of parasitemia. Monkeys positive for malaria parasites were terminated. Splenectomized monkeys continuously negative for malaria parasites through post-treatment day 50 were considered cured.

Table 1. Summary of Blood Schizonticidal Tests in Rhesus Monkeys

Type of Compound	WRAIR Drug Number	Minimum Curative Dose (mg/kg/day)
4 - Aminoquinoline	219774	1.0
	225449	1.0
8 - Aminoquinoline	225448	1.0
	228710	1.0
	231030	1.0
	231033	1.0
	231530	1.0
2, 4 - Diaminoquinazoline	148799	3.16
	199361	3.16
	206891	*NC (31.6)
	222448	0.1
	223143	0.316
	225329	1.0
	226337	1.0
Quinoline methanols	226253	10.0
	226663	3.16
	228974	31.6
	229561	31.6
Phenanthrenemethanol	181613	*NC (31.6)
Miscellaneous	49808	*NC (31.6) (Administered I.M.)

\* Not Curative. The compound had suppressive activity but did not cure at the maximum dose tested. The maximum tested dose is indicated in parentheses.