

EVALUATION OF THAI MEDICINAL PLANT PREPARATION FOR
in vitro ANTIMALARIAL ACTIVITY AGAINST
DRUG RESISTANT STRAINS OF
Plasmodium falciparum

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OBJECTIVE : To identify and chemically isolate components of Thai Medicinal Plants exhibiting *in vitro* inhibitory effects on *Plasmodium falciparum*.

BACKGROUND : With the increase of *P. falciparum* strains resistant to conventional antimalarials there is an urgent need to identify new compounds effective against these resistant forms of the parasite. Medicinal plants specified in traditional medicine for treatment of malaria are of special interest because they represent a natural resource of considerable economic and therapeutic potential.

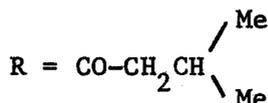
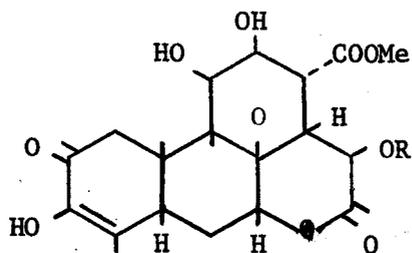
METHODS : Preliminary screening of antimalarial activity of crude plant extracts was made by morphological comparison of parasites exposed to appropriate concentrations of test preparations in a modified microcultivation system (1). Further confirmation of antimalarial activity of pure compounds isolated from screening preparations was made by a radioisotope micro-dilution technique (2). In this procedure, incorporation of (³H) hypoxanthine serves as an indicator of parasite growth. Inhibition of parasite uptake of radioisotope at various dilutions of the test compound provides a quantitative measure of antimalarial activity. An inhibitory dose-50 (ID 50) is computed as the concentration (ng/ml), of compound producing 50% inhibition of incorporation of (³H) hypoxanthine.

RESULTS : The following Thai medicinal plants were selected for this study:

- a) *Brucea javanica* (L.) Merr.
- b) *Harrisonia perforata* Merr.
- c) *Dolichandrone serrulata* Seem.
- d) *Homalomena aromatica* Schott
- e) *Fiscus racemosa* Linn.

Crude chloroform extract of *Brucea javanica* (L.) Merr. exhibited the most potent antimalarial activity. Upon succeeding intensive chemical analysis, four different compounds (A-D) were isolated. Two compounds (A) and (B) were obtained as pure crystals with 0.075% and 0.19% yields respectively.

In vitro assessment of these compounds confirmed the preliminary findings but showed a greater potency (compound (A) ID 50 = 9 ng/ml), (B) ID 50 = 10 ng/ml). Structure determination studies revealed that compound (A) was Bruceine A.



In vitro antimalarial activity of these compounds were comparable to that observed for mefloquine (ID 50 = 7 ng/ml). Work to recrystallize compound (C) and (D) is in progress.

REFERENCES :

1. Trager W, & Jensen J.B. Human Malaria Parasite in Continuous Culture. *Science* 1976; 193: 674-675.
2. Desjardins RE, Canfield CJ, Haynes JP, Chulay JD. Quantitative Assessment of Antimalarial Activity *In vitro* by a Semiautomated Microdilution Technique. *Antimicrob. Agents Chemother.* 1979, 16:710-718.