ANTIMALARIAL ACTIVITY OF *BRUCEA JAVANICA* FRUITS

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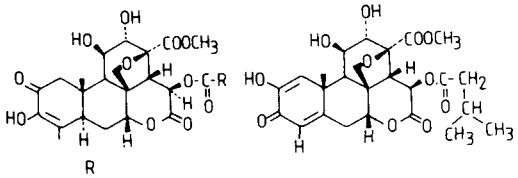
The incidence of chloroquine-resistant *Plasmodium falciparum* strains (Wernsdorfer and Kousnetov, 1980) has prompted the search for novel antimalarial drugs. *Brucea javanica* L. (Merr.) Simaroubaceae is one of the plants which is used in the traditional medicine of Asia and Africa for the treatment of malaria and an earlier study (Guru *et al*, 1983) revealed that one of the constituent quassinoids, bruceantin, is active against *P. falciparum in vitro*. Certain additional quassinoids from closely related species also possess *in vitro* antimalarial activities (Trager and Polonsky, 1981). In the present study fractions from *B. javanica* fruit and 6 quassinoids isolated from the plant have been assessed for *in vitro* antimalarial activity. Powdered *B. javanica* fruits, obtained from Thailand, were extracted sequentially with petroleum ether, methanol and water. The methanol extract was further partitioned between chloroform, butanol and water. The extracts were monitored for activity against *P. falciparum* (chloroquine-resistant strain K1) cultured *in vitro* (Desjardins *et al*, 1979). Activity was detected in the chloroform, butanol and aqueous extracts, each of which possessed IC_{50} values of ca 500 ng ml^{-1}. Subsequent purification by column chromatography of the chloroform extract showed that highest antimalarial activity was concentrated in quassinoid-containing fractions which were further purified by TLC and HPLC to yield bruceines A(1), B(2) and C(3), bruceantin (4), bruceantinol (5) and dehydrobruceine A(6) (identified by ^1H NMR and MS characteristics). The isolated quassinoids were active, having IC_{50} values below 50 ng ml^{-1} (Table 1). The results indicate the important contribution of the C-15 ester substituent to *in vitro* antimalarial activity: bruceantin (4) is approximately 10 times more active than bruceines A(1) and B(2). Also noteworthy is that bruceine A is over 4 times more active than its ring A dehydro derivative. Of considerable interest are the *in vitro* antimalarial activities of the butanol and aqueous extracts from the fruit. These extracts were found by TLC and HPLC to be devoid of typical quassinoids, but on acid hydrolysis bruceines A and C were extracted into chloroform and the remaining aqueous phase proved to be inactive. The results indicate that the antimalarial activity of *B. javanica* fruit is due to its quassinoid content and these compounds warrant further investigation for *in vivo* antimalarial activity and toxicity.



R

1. = $CH_2CH(CH_3)_2$
2. = CH_3
3. = $CH=C(CH_3)C(OH)(CH_3)_2$
4. = $CH=C(CH_3)CH(CH_3)_2$
5. = $CH=C(CH_3)C(OAc)(CH_3)_2$

6.

Table 1: *In vitro* antimalarial activities against *P. falciparum* (K1) of quassinoids obtained from *B. javanica* fruits.

Quassinoid	IC_{50}* ($ng\ ml^{-1}$)	95% confidence interval
bruceine A (1)	10.5	7.2 - 14.3
bruceine B (2)	10.8	8.4 - 13.8
bruceine C (3)	5.1	3.7 - 7.1
bruceantin (4)	0.8	0.4 - 1.6
bruceantinol (5)	2.1	1.3 - 3.4
dehydrobruceine A (6)	46.3	43.1 - 49.7

*based upon 2 fold dilutions in duplicate

Guru P.Y. *et al* (1983) Ann. Trop. Med. Parasit. 77: 433-435
Desjardins R.E. *et al* (1979) Antimicrob. Ag. Chemother. 16: 710-718
Trager W. and Polonsky J. (1981) Am. J. Trop. Med. Hyg. 30: 531-537
Wernsdorfer W.H. and Kousnetov R.L. (1980) Bull WHO 58: 341