EDITORIAL COMMENTARY

THE CLINICAL EFFICACY OF *CRYPTOLEPIS SANGUINOLENTA* IN THE TREATMENT OF MALARIA

The roots of cryptolepis, also known as nibima, kadze, gangamau, Ghanaian quinine and yellow-dye root (*Cryptolepis sanguinolenta*) have been used in Ghanaian traditional medicine for treatment of malaria for many generations. A Ghanaian drug company developed an herbal tea formulation trademarked as Phyto-Laria based on this plant, and the clinical evaluation of its potential as a herbal drug treatment for malaria was conducted, with the results published in this issue of the journal by Bugyei, et al (page 3). The active antiplasmodial components found in the root are known to be the indoquinoline alkaloids, which independently have been to have shown to have both *in vitro* and *in vivo* activity against *Plasmodium falciparum*,including chloroquine-resistant strains.[1-5] A previously published open label anti-malarial clinical study on the water extract of this plant containing the Cryptolepis alkaloids taken orally indicated efficacy comparable to chloroquine.[6] Therefore, the authors expected that the tea bag formulation, which contains significant amounts of the Cryptolepis alkaloids, would also be clinically efficacious.

An herbal tea bag preparation, free of preservatives (including chloroform found on other herbal preparations), based on 2.5 grams of dried ground roots of *C. sanguinolenta*, was studied in forty four patients with clinical features of uncomplicated malaria. Potential patients who had taken chloroquine or sulfadoxine/pyremethamine within the previous two and four weeks, respectively, where excluded from this study. In three open label out-patient settings in Ghana, the patients were dosed three times daily for five days under the WHO extended seven day test, and followed for 28 days post-treatment. More than half of the patients were cleared of *P. falciparum* parasitaemia within 72 h, with mean clearance of 82.3 h. The mean fever clearance time was 25.2 h compared to 48 h typical for chloroquine treatment, which is consistent with the previously reported antipyretic activity of *C. sanguinoleta*. Besides fever, the other symptoms of chills, vomiting and nausea were cleared totally in 72 h. The majority of biochemical parameters were not significantly modified following treatment, although ALP (alkaline phosphatase) and uric acid levels where elevated during the treatment period, with uric acid levels returning to normal by day 28. In comparison, halofantrine has also been reported to produce elevated levels of ALP during treatment.[7] Overall, Phyto-Laria appears to be quite safe when taken orally, which is consistent with numerous animal toxicity testing data (mice, rats and rabbits) reported previously).[8]

It should be noted that there were two cases of late recrudescence on days 21 and 28, which may be attributed to reinfection, due to the out-patient trial design. However, as no genetic testing was included as part of the study design, this remains a hypothesis. Any further testing of Cryptolepis should include this a part of the trial design if an out-patient clinical setting is used.

Overall, the antimalarial cure rate in this patient population was 93.5%, and suggests that Phyto-Laria could be used as a safe effective treatment of acute uncomplicated malaria, and may also be useful in treatment of patients infected with chloroquine-resistant strains of *P. falciparum* as well.

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Conflict of Interest: *Phytica, Inc. has an extract of Cryptolepis sanguinolenta under clinical development for malaria treatment.*

REFERENCES

1. Wright CW, Phillipson JD, Awe SO, Kirby GC, Warhurst DC, Quertin-Leclerq J, Angenot L. Antimalarial activity of cryptolepine and some other anhydronium bases. *Phytother Res* 1996; 10:361-363
2. Cimanga K, De Bruyne T, Pieters L, Vlietinck AJ, Turger C.A. In vitro and in vivo antiplasmodial activity of cryptolepine and related alkaloids from Cryptolepis sanguinolenta. *J Nat Prod* 1997; 60:688-691
3. Grellier P, Ramiaramanana L, Milleriox V, Deharo E, Shrevel J, Frappier F. Antimalarial activity of cryptolepine and isocryptolepine, alkaloids isolated from *Cryptolepis sanguinolenta*. *Phytother Res* 1996; 10: 317-321

4. Kirby GC, Paine A, Warhurst DC, Noamesi BK, Phillipson JD. In vitro and in vivo antimalarial activity of cryptolepine, a plant-derived indoloquinoline. *Phytother Res* 1995; 9: 359-363
5. Noamesi BK, Paine A, Kirby GC, Warhurst DC, Phillipson JD. In vitro antimalarial activity of cryptolepine, an indoquinoline. *Trans Roy Soc Trop Med Hyg* 1991; 85:315
6. Boye GL. Studies on antimalarial action of Cryptolepis sanguinolenta extract. *Proceedings of the International Symposium on East-West Medicine*. 1989. October 10-11; p 243 – 251. Seoul, Korea.
7. Ofori-Adjei D, Parr SNL. Halofantrine for falciparum malaria in Ghana. *J Pharm Med* 1992; 2:229-240
8. Addy, M., Cryptolepis: An African Traditional Medicine that Provides Hope for Malaria Victims *HerbalGram*. 2003;60:54-59,67

TREATMENT OF FALCIPARUM MALARIA WITH A TEA-BAG FORMULATION OF *CRYPTOLEPIS SANGUINOLENTA* ROOT

The use of plant medicine is widespread in the Ghanaian population to meet health care needs. The challenges pose by malaria, the biggest killer disease in Ghana, to many people who do not have access to orthodox drugs makes plant medicine a popular option for them in treating the disease. However, dosage, effectiveness and safety issues associated with plant medicine demand highest research.

A clinical study reported in this issue of the Ghana Medical Journal by K. Bugyei *et al.*, (page 3) has come as a big relief for the development of plant medicine in malaria treatment and control efforts. The outcome of the clinical studies on safety and efficacy of a product formulated from *Cryptolepis sanguinolenta* root in the form of powder conveniently packaged as a tea-bag, provide evidence of safe and effective treatment of acute uncomplicated *falciparum* malaria in Ghanaian subjects. Notably, the subjects with fever did not require antipyretic. The results of the study bring hope to several millions of people who are affected by the killer malaria disease mainly in tropical countries worldwide. The severest form of the disease, *falciparum* malaria, is widespread in sub-Sahara Africa including Ghana.

The World Health Organisation (WHO) acknowledges the important role plant medicine, with proven effectiveness and safety, could play in the formal health system and is encouraging research into plant medicine discovery to treat malaria. This has become imperative in view of strains of *falciparum* parasite resistant to chloroquine and according to WHO 2009 report the emergence of malaria parasites resistant to artemisinin in Asia.

It is assuring that *Cryptolepis sanguinolenta* used in this formulation can clear chloroquine resistant strains of *falciparum* parasitaemia. This will make malaria treatment affordable and accessible in Ghana. It also establishes scientific basis for the claim of efficacy of *Cryptolepis sanguinolenta* against malaria at the prescribed dosage. The post treatment rise in serum alkaline phosphatase in the study subjects provides basis for further observation on repeated use of this formulation of *Cryptolepis sanguinolenta* in addition to resolution of issues on genotoxicity in mammalian cell lines and anxiety in mice. Caution must, however, be exercised in extrapolating *in vitro* and laboratory animal findings to humans.

The present result is indeed welcome news since it advances the vision to incorporate plant medicine into the health care delivery system in Ghana, and now for treating *falciparum* malaria, the biggest killer disease in the country.

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