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Effectiveness of the Combination of *Cryptolepis sanguinolenta* and *Clausena anisata* in Uncomplicated Malaria

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Abstract

Drug resistance is the single most important factor that continues to drive the search for new antimalarials. In this study, a Ghanaian herbal antimalarial product labelled *Nibima plus* was evaluated for its effectiveness in the treatment of malaria. The propriety product is prepared from a combination of *Cryptolepis sanguinolenta* and *Clausena anisata*. A total of twenty-two (22) subjects diagnosed with uncomplicated malaria were recruited and followed up for seven (7) days. Mean baseline temperature and parasitaemia for participants was 38.24 (±0.43) ºC and 5310 (±3488)/µl respectively. Treatment with the product resulted in a total parasite clearance for 21 (95.45 %) of subjects with marked improvement in the patient symptoms and haematological parameters by day 7. The results of the study indicate the product may be effective as an antimalarial agent.

Keywords: *Clausena anisata*, Clinical study, *Cryptolepis sanguinolenta*, Herbal medicine, Malaria

Contents

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1. Introduction

The effective control of malaria requires an integrated approach. This fact is seen in the list of previous and current interventions which have included both pharmacological and numerous infection prevention strategies; primarily involving the control of the vector (Murray *et al.*, 2012; Shetty, 2012). The infection prevention strategies of malaria has included the spraying of homes with insecticides such as DDT, use of insect repellents and very recently, the widespread use of insecticide treated bednets. Numerous pharmacological treatments are also currently available (GNDP, 2010). The role herbal medicines play in the economics of malaria cannot be ignored (Willcox and Bodeker, 2004). The current conventional treatment of choice: the artemisinin-based products, have

their roots from medicinal plants and so are the other existing treatments such as quinine used in complicated and cerebral malaria (Biamonte *et al.,* 2013).

Considering the burden of malaria, which the World Health Organisation (WHO) estimates as having 154–289 million diagnosed cases in 2010, with over a million associated deaths, there have suggestions for countries and communities to adapt practical and applicable solutions that would suit their circumstance (WHO, 2010). One challenge with malaria chemotherapy will always be the development of drug resistance in previously responding populations (Bloland, 2001). The WHO therefore strongly advocates for combinational therapy instead of monotherapy in malaria chemotherapy (Biamonte *et al.*, 2013). Although there is very little or no information on drug resistance when it comes to herbals, the calls for combinational therapy and multiple treatment options can apply to herbal medicines as well.

Cryptolepis sanguinolenta (Lindl.) Schltr (fam: Periplocaceae) is a plant well known in the West African region for it antimalarial properties (Wright *et al.*, 1996; Cimanga *et al.*, 1997). The Centre for Plant Medicine Research (CPMR) Mampong-Akwapim, has an existing product sold under the trade name *Nibima*, made from an aqueous extract of the plant. The desire to reduce treatment failures and provide other drug options for prescribers led to the investigation of *Nibima plus*, another *C. sanguinolenta*-based product. Aside *C. sanguinolenta*, the product also contains *Clausena anisata* (Wilde.) (fam: Rutaceae) stem bark prepared according to a proprietary formula. *Clausena anisata* has also been previously documented for its antiplasmodial activity (Okokon *et al.*, 2012). In this report, the efficacy of this product, *Nibima plus* was assessed for seven (7) days in patients diagnosed with uncomplicated malaria.

2. Experimental

Ethical Clearance and Patient Handling

The trial was performed in accordance with the declaration of Helsinki and good clinical practice. The trial documents and all related procedures were reviewed and approved by the institution's committee for human research. Patient consent was sought prior to the start of study-related procedures.

Study Plans

Patients reporting to the clinic of the CPMR diagnosed with uncomplicated malaria were recruited for the study after a confirmation from our reference laboratory. Trial protocol and related procedures were explained to the patient and when consent was obtained, participants were assigned to the herbal treatment of *Nibima plus.* Participants were then asked to report for a follow up 7 days after the initiation of treatment. Clinical examinations and laboratory investigations were repeated on the follow up day.

Selection Criteria

Participants recruited into the study included male and female patients between the ages of 10 to 50 years diagnosed with uncomplicated malaria. Participants were excluded from the study if they had received any orthodox antimalarial in the last 30 days. Exclusion criteria also included pregnant women and individuals with any life threatening disease including complicated malaria.

Investigational Product

The test drug, a Ghanaian herbal antimalarial product labelled *Nibima plus*, is prepared according to a proprietary recipe. The product comprises an aqueous decoction of *Cryptolepis sanguinolenta* and *Clausena anisata* and is dispensed in 330 mls bottles.

Treatment Dosage

Participants were instructed to administer the treatment at the standard dosage of 30 mls three times a day. However, in cases where subjects reported with severe symptoms and/or parasitaemia of ≥5000/µl dosage was varied between 60 mls-100 mls three times a day.

Clinical and Laboratory Evaluations

Subjects were assessed clinically by their vital signs and a complete systematic examination at the start and during follow up period. Laboratory investigations involved a full blood count (FBC) and a thin and thick blood film for parasite count. Active monitoring of adverse reactions was also done using the WHO standard questionnaire (WHO, 2004).

3. Results

Patient and Disease Characteristics

A total number of 30 participants diagnosed with uncomplicated malaria were recruited for the study with 8 (36.36%) participants being lost on follow up. In all, 22 participants completed the study and comprised 12 (54.54%) females and 10 (46.46%) males with a mean age of 43.73 (± 14.83) years. Subjects reported with some or all of the classical signs and symptoms of malaria: a body temperature of >37.5 ºC, chills, joint aches, generalised malaise, headaches and vomiting (Table 1.0).

Average temperature at the start of treatment was 38.24 (± 0.43) ºC with mean parasitaemia of 5310 (± 3488)/µl. Eight (36.36%) participants recorded a parasite count of ≥1000/µl, 11 (50%) participants had parasitaemia between 340/µl-960/µl and 3 (13.63%) participants had a count of <100/µl. *Plasmodium falciparum* was identified as the causative organism for all the infections.

Table 1.0: Presenting Signs and Symptoms of Particpants at Baseline and End of Study

Clinical Signs and Symptoms	Baseline	Day 7
Fever and Chills (%)	12 (54.54)	-
Joint aches (%)	22 (100)	2 (9.09)
Easy fatiguability and malaise (%)	22 (100)	-
Headaches (%)	20 (90.90)	4 (18.18)
Vomiting (%)	5 (22.72)	

Product Efficacy

Parasite clearance was achieved for 21 (95.45 %) of the population treated. One participant who reported with a parasitaemia of 640/µl had a delay in the clearance of parasites. After the 7-day treatment period, the subject had a count of 480/µl although the reporting symptoms of feverishness, malaise and vomiting had resolved. Clearance of parasites was achieved by day 14 after an increase in the dosage to 60 mls three times a day. Haematological parameters analysed is presented as Table 2.0. White blood cell count (WBC) which was within the reference range prior to the start of treatment declined marginally but remained within the acceptable limit. Parameter such as haemoglobin (HB) and haematocrit (HCT) increased when compared to baseline values, with platelets declining post-treatment. The reported differences in the haematological parameters were not significant. Generally, the improvements in the haematological parameters and parasite levels also reflected on participants physical well being as there was marked improvement in the symptoms reported by the end of the study (Table 1.0). During the study, an antipyretic effect of the treatment was also observed in a subject who reported with a temperature of 40.0ºC but after receiving a starting dose of 100 mls of the treatment recorded a temperature decline to 37.8ºC after an hour.

Table 2.0: *Haematological Data of Participants during the Study*

Haematological Parameter	Baseline	Day 7
White Blood Cell Count (10^3/mm^3)	5.80 (2.43)	4.79 (1.20)
Haemoglobin (g/dl)	11.14 (2.30)	11.56 (2.21)
Haematocrit (%)	43.14 (8.16)	43.15 (8.22)
Platelets (10^3/mm^3)	178.8 (59.85)	161.1 (33.26)
Temperature (ºC)	38.24 (0.43)	37.58 (0.09)

Treatment dosage was also increased for four (4) subjects who reported with acute symptoms and parasite count >5000µl including the participant who had persistent parasitaemia after 7 days of treatment. These participants recorded complete clearance of parasites on follow up.

4. Discussion

The results of this study indicate the potential for the use of this product as an antimalarial agent. The percentage cure (95.45%) attained for subjects is a confirmation of this potential, although a larger controlled study may be required to validate this evidence. Poor recovery from malaria has been indicated in some antimalarials. This is represented as a slow improvement in indices such as white blood cells, haemoglobin and haematocrit levels in infected individuals (Menendez *et al.*, 2000). The significant symptom-resolution seen in the participants at the end of the study could be attributed to the improvement of haematological indices. The antipyretic activity reported during the treatment period has been previously documented for the individual plant components of the product (Iwu, 1993; Okokon *et al.*, 2012). This property of the product was very essential as clearance of fever during periods of acute infections is important for any potential antimalarial product. Other previously run clinical studies have also reported on the antipyretic and antiplasmodial activity of *Cryptolepis sanguinolenta* as a monotherapy (Bugyei *et al*., 2010).The combination of *Cryptolepis sanguinolenta* with *Clausena anisata* with the intent of improving efficacy and reduce treatment failure is not a new pharmacological strategy as most of the conventional antimalarials are now used in combination (Biamonte *et al.*, 2013). However, some extensive studies should be undertaken to demonstrate and evaluate this benefit.

5. Conclusion

The Ghanaian herbal product *Nibima plus* based on the symptoms resolution, parasite and fever clearance may be useful as an alternative antimalarial product.

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7. References

1. MA Biamonte, J Wanner, KG Le Roch. Recent advances in malaria drug discovery. Bioorganic & Medicinal Chemistry Letters, **2013**, 23: 2829–2843.
2. PB Bloland. Drug resistance in malaria. WHO/CDS/CSR/DRS/**2001**, 4:12-15
3. KA Bugyei, GL Boye, ME Addy. Clinical Efficacy of a Tea-bag formulation of *Cryptolepis sanguinolenta* in the treatment of acute uncomplicated falciparum malaria. Ghana Medical Journal, **2010**, 44 (1): 3-9.
4. K Cimanga, T De Bruyne, L Pieters, AJ Vlietinck, CA Turger. *In vitro* and *in vivo* antiplasmodial activity of cryptolepine and related alkaloids from *Cryptolepis sanguinolenta*. J Nat Prod, **1997**, 60: 688-691.
5. GNDP. Standard Treatment Guidelines. Accra, Ghana, Ministry of Health. **2010**: 179.
6. MM Iwu. Handbook of African Medicinal Plants. 1st Edition, CRC Press, Boca Raton, Florida USA, **1993,** 786-789.
7. C Menendez, AF Fleming, PL Alonso. Malaria-related anaemia. Parasitol Today, **2000**, 16: 469-476.
8. CJ Murray, LC Rosenfeld, SS Lim, KG Andrews, KJ Foreman, D Haring, N Fullman, M Naghavi, R Lozano, AD Lopez. Global malaria mortality between 1980 and 2010: a systematic analysis. Lancet, **2012**, 379, 413.
9. JE Okokon, EO Etebong, JA Udobang, GE Essien. Antiplasmodial and analgesic activities of *Clausena anisata.* Asian Pacific Journal of Tropical Medicine, **2012**, 5: 214-219.
10. P Shetty. The Numbers Game. Nature, **2012**, 484, S14-S15.
11. WHO. Guidelines for the clinical study of Traditional Medicines in the WHO African Region Brazzaville, WHO Regional Office for Africa, **2004**, 57-66.
12. WHO. Guidelines for the treatment of malaria. 2nd Edition, WHO, Geneva, **2010,** 1-194.
13. ML Willcox, G Bodeker. Traditional herbal medicines for malaria. BMJ, **2004**, 329: 13.
14. CW Wright, JD Phillipson, SO Awe, GC Kirby, DC Warhurst. Quertin-Leclerq J, Angenot L. Antimalarial activity of cryptolepine and some other anhydronium bases. Phytother Res, **1996**, 10: 361-363.