



## **Clinical Evaluation of Efficacy of a Herbal Formulation Used in the Treatment of Malaria**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **ABSTRACT**

Malaria is a public health problem and continues to be a major cause of morbidity and mortality in most tropical and subtropical countries. A rapid spread of malarial disease globally due to treatment failure has led to an urgent need for new effective antimalarials which medicinal plants have contributed to in medicine.

The objective of this research is to determine the effectiveness of *Mist Amen Fevermix* which is a decoction of the stem bark of *Morinda lucida* and *Parinari robusta* in the treatment of uncomplicated malaria in humans, at the Tafo Government Hospital, Kumasi.

Clinically established malaria in male and female patients aged, 15-60 years were treated with *Mist Amen Fevermix*, at the specified dose of 45 mls (0.45 g) three times daily for six days.

A total of 50 patients were diagnosed with malaria disease. At the randomization visit, a detailed medical history was obtained and the patients underwent laboratory investigation was done at entry and after completing the study.

All the 50 patients completed the study and there was a statistically significant difference between the mean levels of malaria parasite load recorded 28 indicating a significant effectiveness of *Mist*

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*Amen Fevermix* used by the patients. Parasitaemia clearance was 82.35% within the first three days in clients who responded positively to treatment. Results of the study suggest that *Mist Amen Fevermix* is an effective herbal antimalarial agent when used as specified by the manufacturer.

**Keywords:** *Malaria; effectiveness; herbal; integrated; antimalarial; parasitaemia.*

## 1. INTRODUCTION

Malaria is a mosquito-borne disease caused by infection with unicellular parasites belonging to the genus *Plasmodium*. These parasites are transmitted through the bite of infected female *Anopheles* mosquitoes. The main symptoms of uncomplicated malaria are fever, chills and headache and if left untreated could lead to severe consequences including death.

Malaria is one of three globally important infectious diseases, including tuberculosis (TB) and HIV/AIDS which cause substantial morbidity, mortality, negative socioeconomic impact, and human suffering [1]. The World Health Organization (WHO) estimates 3.3 billion people are at risk of infection worldwide, resulting in about 500 million clinical cases and around one million deaths per year. Malaria is currently endemic in tropical and sub-tropical regions of the world including: Africa, Asia, Latin America, the Middle East and some parts of Europe. However, majority of the malaria related deaths occur in sub-Saharan Africa where it is the leading cause of mortality for children under the age of five years and pregnant women [2]. Therefore, immediate diagnosis and appropriate treatment of the disease is deemed urgent in the fight against malaria.

Malaria is hyper-endemic in Ghana and remains a major public health problem, requiring focused interventions including immediate and effective case management and has also been a major cause of poverty and low productivity accounting for about 32.5 percent of all out-Patient Department (OPD) attendances and 48.8 percent of under five years admissions in the country [3]. It also resulted in 36.9 percent of hospital admissions in 2009 for all ages with more than 80 percent among children alone in Ghana [3].

According to an estimate by the WHO, at least 80 percent of the populations in most developing countries of the world rely on traditional medicine for their primary health care needs. Considering this fact and also that, modern healthcare system alone could not meet the health needs of the global community, the WHO launched the policy,

'Health for All by 2000' (Alma-Ata Declaration of 1978) urging its member states to promote and integrate traditional medicine into their national health care systems [4]. The important contribution traditional knowledge and practices have made to orthodox medicine can be attested to by the fact that more than 40 percent of commonly prescribed medicines throughout the world find their origin directly or indirectly from plants or animals [4].

It is known that about 70 percent of Ghanaians depend on herbal medicinal products for their primary health care needs. This is due to the fact that, the herbal products are mostly cheap, easily available and thought to be very effective and safe as compared to orthodox medicines. Many of such products have been used in Ghana for the treatment of malaria. One of such products is *Mist Amen Fevermix*, produced by Amen Scientific Herbal Hospital, which is on the recommended essential herbal medicines list of the Ministry of Health and used throughout the pilot Herbal Medicine Unit in Ghana.

*Mist Amen Fevermix* is an herbal decoction prepared from: *Morinda lucida* Benth. (Family: Rubiaceae) and *Parinari robusta* Oliv., synonym of *Maranthes robusta* (Oliv.) Prance ex F. White (Family Chrysobalanaceae) [5].

*Morinda lucida* is a tropical West Africa rainforest tree also called Brimstone tree [6]. It is an evergreen shrub or small to medium-sized tree up to 18-25 m high [7]. The leaves are used to prepare infusions which are used not only for the treatment of malaria but also as a general febrifuge and analgesic. All parts of the plant are used as laxative. A weak decoction of the stem bark is administered for the treatment of severe jaundice often characterized by haemoglobinuria and haematuria [8].

*Parinari robusta* is a small to medium-sized deciduous tree with characteristic habitats of swamp-forest. It occurs in drier types of semi-evergreen rainforest. It grows up to 13 m high and low-branching in coastal areas, or to 35 m or more inland with a cylindrical bole up to 1.70 m girth [9,10]. The plant occurs in West Africa, from

Côte d'Ivoire to Nigeria [11]. Bark decoction and pounded leaves are applied as anodyne. Pregnant women take a decoction of the bark as a tonic [12,13].

Although *Mist Amen Fevermix* has been successfully used in the treatment of uncomplicated malaria, there is no available empirical clinical data to support this claim.

### 1.1 Aim(S)

The goal of the study is to validate the claims for the use of *Mist Amen Fevermix* as a safe and effective herbal product in the treatment of uncomplicated malaria in humans.

### 1.2 Objectives of the Study

The primary objective of the study was to assess data from open clinical trial on *Mist Amen Fevermix*, an herbal anti-malarial product.

Specific objectives of the study were to determine the effectiveness of *Mist Amen Fevermix* in the treatment of uncomplicated malaria in humans.

### 1.3 Study Site

The study was conducted at the Herbal Medicine Unit of the Tafo Government Hospital, Kumasi, between the months of May 2014 to November 2014, after Ethics Committee approval.

## 2. MATERIALS AND METHODS

### 2.1 Study Design

The study design was based on an open, prospective, non-comparative clinical trial in 50 participants with clinically established malaria, and confirmed by laboratory investigations. Study commenced after Ethics Committee approval.

### 2.2 Treatment and Duration of Study

A decoction of *Mist Amen Fevermix* is dispensed as 45 mls (0.45 g) three times daily after meals for a period of 6 days.

## 3. PATIENTS SELECTION CRITERIA AND MONITORING FOR MALARIA

### 3.1 Inclusion Criteria

Patients were recruited and managed as out-patients in a normal clinical setting. The selection criterion included the following;

- Gender: male and females
- Age between 15 and 60 years
- Health status: Absence of anaemia
  - Absence of severe malnutrition
  - Absence of general signs of severe and complicated malaria
  - Presence of axillary temperature ~37.5 and < 39.5°C at visit
- Ability to come for the stipulated follow-up visits
- Easy access to the health facility
- Informed consent of parent/guardian

### 3.2 Exclusion Criteria

- Patients on concurrent treatment with orthodox antimalarial medicines, or other related antimalarials.
- Any disease condition which might compromise the renal, hepatic or any other body system
- Intake of any medication within 14 days before start of the study
- Presence of clinically significant abnormal laboratory results during screening
- Pregnant women
- Use of any recreational drugs or a history of drug addiction
- Any chronic /non-communicable disease condition

### 3.3 Monitoring for Malaria

Patients were reviewed and monitored on days; 3, 7, 14 and 28. Remission of signs and symptoms or otherwise were noted. Blood films were taken to check for malarial parasites on the review dates as above.

### 3.4 Recruitment of Participants

During out-patient departmental (OPD) herbal medicine clinic days, an announcement is made using the Public Address (PA) system of the Hospital to inform patients about the Herbal Medicine Unit and invite clients who want to use the services of the unit. Interested patients were examined and those determined clinically to have malaria were made to undergo laboratory tests to confirm the presence of malaria parasites or otherwise. *Mist Amen Fevermix* was then dispensed according to standard dosing for six days. Patients were to report for review purposes on day three, seven, fourteen and twenty-eight.

During the review period, the history was retaken. An assessment was made to establish if there was compliance with their medication, and any side effect was noted. Blood film examination for malaria parasites was done on the 3<sup>rd</sup>, 7<sup>th</sup>, 14<sup>th</sup> and 28<sup>th</sup> day visits.

The study was conducted at the Herbal Medicine Unit of the Tafo Government Hospital, Kumasi, between the months of May 2014 to November 2014, after Ethics Committee approval.

Data on the effectiveness of *Mist Amen Fevermix* was statistically analyzed using IBM Statistical Package for the Social Sciences (SPSS), version 19. Exploratory statistics were computed to measure the frequency distribution, central tendencies and dispersions of the data. These were presented in tables and bar charts. To this, a hypothesis was postulated. The null hypothesis was that the mean amount of element after every visit was in the range of the control. The alternate hypothesis being that there is an increase or decrease in the amount of elements measured at every visit.

A paired sample t-test of the mean amount of elements over the three various visits was performed to test the difference between the first visit and the second visit and then that of the second and the third. To this, a hypothesis was

postulated. The null hypothesis was that the mean amount of elements at various visits was no different from each other. The alternate hypothesis being that the amounts of elements tested over the visits are not equal.

#### 4. RESULTS

The total number of patients was 50. There were 20 males and 30 females. Age and sex distribution are presented in Fig 1.

##### 4.1 Signs and Symptoms of Malaria Presented by Participants

The participants presented with underlying signs and symptoms due to malaria as shown in Fig. 2.

##### 4.2 Levels of Improvement in Signs and Symptoms after Administering *Mist Amen Fevermix*

General improvement in signs and symptoms presented in Fig. 2 found 28 patients (82.35%) showing complete improvement, Slight improvement 2 patients representing (5.88%) and No improvement 4 patients representing (11.77%). This data clearly specifies that *Mist Amen Fevermix* treatment exerted a beneficial effect. This result is presented in Fig. 3.

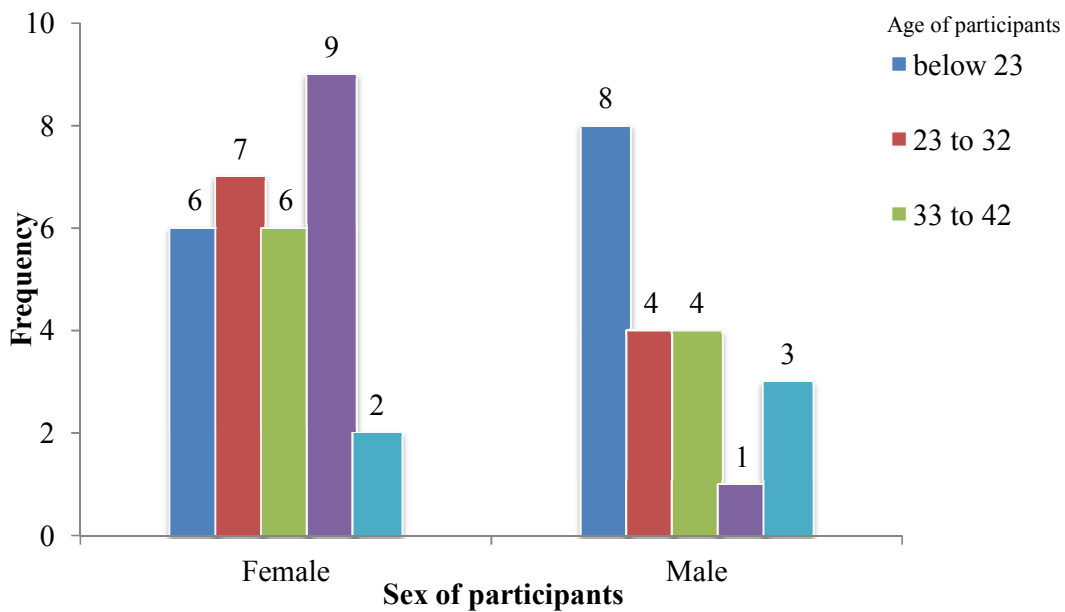


Fig. 1. Age-sex distribution

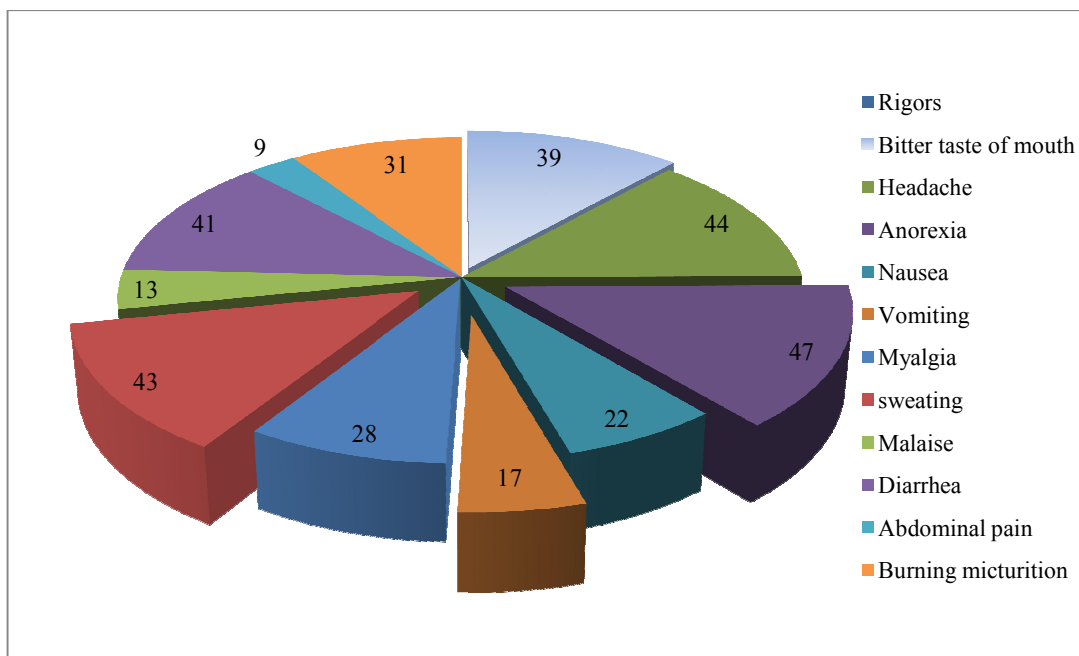


Fig. 2. Signs and symptoms of malaria presented by patients

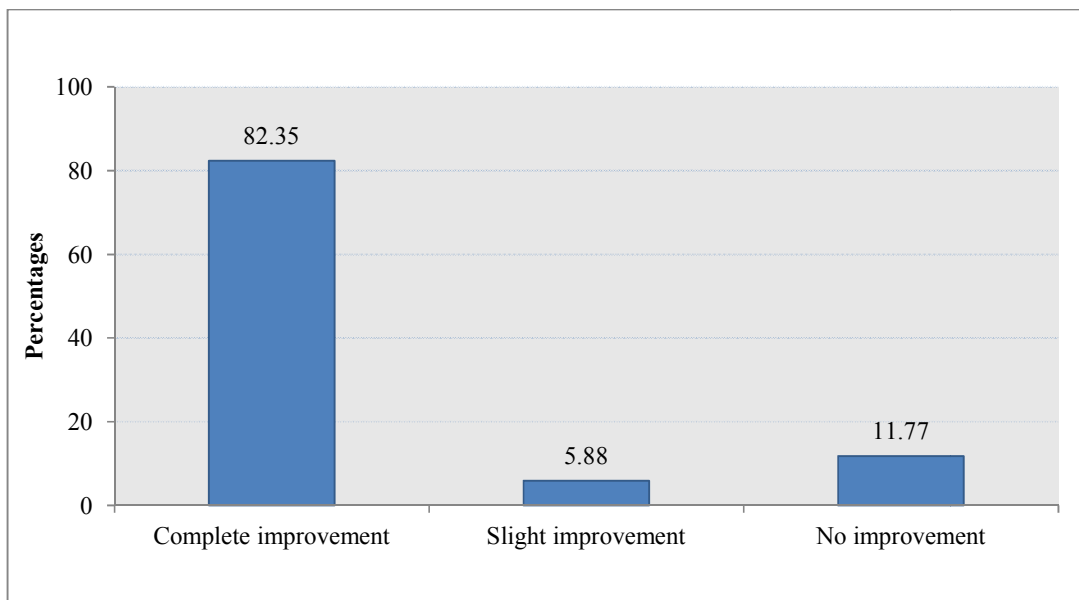
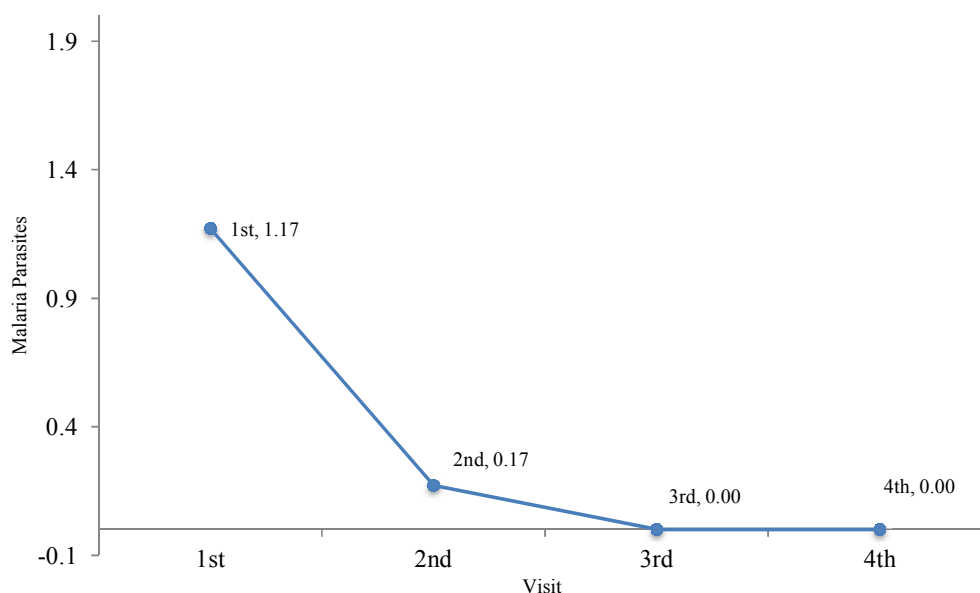


Fig. 3. Improvement in signs and symptoms after treatment

#### 4.3 Effectiveness of Mist Amen Fevermix

A paired-sample t-test was performed to test the difference between the results of test for parasite load at first visit against the second visits, the second against third visits and third against fourth visits. The null hypothesis for the pairing of first visit and second visit test is that, the mean

levels of malaria parasite load are equal. The alternate hypothesis states that the first visits' level of malaria parasite load is not the same as the second visit. Similarly, the null hypothesis for the pairing of the second visit and third visit pairing states that there are equal level of malaria parasite loads and the alternate states there is a difference. Finally, the null hypothesis for the



**Fig. 4. Mean levels of malaria parasites on review**

pairing of the third and fourth visit states that there is equal level of malaria at the both visit while the alternates state otherwise. The results are as shown in Fig. 4.

The test indicates a statistically significant difference between the mean levels of malaria parasite load recorded at the first visit and those recorded at the second visit,  $t(34) = 12.20$ ,  $p = .000$ . Similarly, there was statistically significant difference between the malaria parasite load recorded on the second visit and that of the third visit,  $t(24) = 2.50$ ,  $p = .022$ . This shows a significant effectiveness of *Mist Amen Fevermix* used by the patients. The third and final pairing test was not possible as a result of the incalculability of the value of  $t$  and its correlations.

## 5. DISCUSSION

This study sought to validate the claim for the clinical effectiveness of *Mist Amen Fevermix* in the management of uncomplicated malaria in human.

This study was undertaken as a prospective one with open-ended questionnaire in which an attempt was made to explore malaria patients with *Mist Amen Fevermix* a bi-herbal antimalarial product so as to assess the effectiveness. The

diagnosis of malaria was established by using microscopic examination of blood, utilizing blood films on the day of visit. Different parameters, that is, age, sex, duration of signs and symptoms, and other clinical sign and symptoms base line was studied and compared during the 3<sup>rd</sup>, 7<sup>th</sup>, 14<sup>th</sup> and 28<sup>th</sup> visits at base line and end of the dispensing of *Mist Amen Fevermix*.

The clearance of the malaria parasite may be due to the presence of *Morinda lucida* which is known to possess an anti malarial property (Mshana et al. 2000).

## 6. CONCLUSION

*Mist Amen Fevermix* appears to be an effective herbal treatment for the management of uncomplicated malaria in human. Its ability to clear the *Plasmodium* parasites makes it a potential useful antimalarial agent.

## CONSENT

Informed written consent of parent/guardian was preserved by the authors.

## ETHICAL APPROVAL

The study was conducted at the Herbal Medicine Unit of the Tafo Government Hospital, Kumasi after Ethics Committee approval.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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